DOI: 10.1002/ejoc.201402222

Synthesis of Chondroitin Sulfate Oligosaccharides Using *N*-(Tetrachlorophthaloyl)- and *N*-(Trifluoroacetyl)galactosamine Building Blocks

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Keywords: Carbohydrates / Oligosaccharides / Glycosylation / Glycosaminoglycans / Protecting groups

We have explored synthetic routes for the preparation of chondroitin sulfate (CS) oligosaccharides based on the use of *N*-tetrachlorophthaloyl- (*N*-TCP) and *N*-trifluoroacetyl-substituted (*N*-TFA) galactosamine building blocks. Using *N*-TCP units, we carried out the total synthesis of two CS disaccharides, demonstrating the compatibility of TCP protection with the final deprotection/sulfation steps. However, an attempted 2+2 coupling of *N*-TCP-containing disaccharides for the synthesis of CS tetrasaccharides failed. In contrast, a synthetic route using *N*-TFA galactosamine units efficiently led to biologically relevant CS-like oligosaccharides. The *N*-TFA groups could easily be removed at the end of the synthesis, and microwave irradiation greatly facilitated the sulfation reactions. The utility of this approach is illustrated with the total synthesis of two CS-like tetrasaccharides with different sulfate distribution patterns. Finally, we used a fluorescence polarization assay to estimate the relative abilities of the synthesized compounds to inhibit the interaction between FGF-2 and heparin.

Introduction

Chondroitin sulfate (CS) is a linear sulfated polysaccharide that belongs to the glycosaminoglycan family.[1] CS is made up of repeating of GlcA-β(1→3)-GalNAc-β(1→4) disaccharide units (GlcA = D-glucuronic acid, GalNAc = *N*-acetyl-D-galactosamine). This repeating unit can be sulfated at various positions, giving rise to CS polymer chains with different sulfation patterns and a high level of structural diversity. CS chains are classified into different types based on the distribution pattern of the sulfate groups, although a combination of different patterns is often found in CS samples. For instance, CS-A predominantly contains one sulfate at position 4 of the GalNAc unit, CS-C has a sulfate group at position 6 of the GalNAc, and CS-E has two sulfates at positions 4 and 6 of the GalNAc residue (Figure 1).

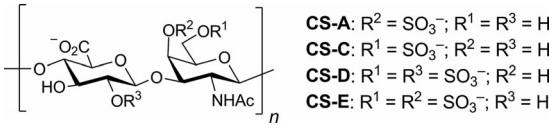

Figure 1. Some of the typical disaccharide units found in CS.

CS is involved in important biological processes such as central nervous system development[2] and malaria infection.[3] The participation of CS in these processes is due to the action of certain oligosaccharide sequences, with particular sulfate distributions, which interact with several protein receptors.[4] For example, CS-E binds to several heparin-binding growth factors and chemokines,[5,6] and so plays important roles in the central nervous system. Recent studies indicated that a CS-E tetrasaccharide interacts with midkine, a growth factor that participates in the development and repair of neural tissues.[7] This interaction requires a specific arrangement of sulfate groups, since other oligosaccharides with different sulfation patterns bind significantly more weakly (or not at all) to midkine. A different class of CS, CS-A, has an important role in pregnancy-associated malaria.[8] This subtype of CS binds to *Plasmodium falciparum* erythrocyte membrane protein 1 (PfEMP1), and this binding event is a critical step in the adhesion of *P. falciparum* infected red blood cells to the placenta.

Due to the heterogeneity of the polymer, structurally defined CS oligosaccharides are not easily obtained in significant amounts from natural sources. Therefore, well-defined synthetic oligosaccharides are required for the study of CS–protein interactions at the molecular level, the establishment of structure–activity relationships, and the evaluation of the biological activities and potential therapeutic applications of this type of compounds. Despite recent advances in the synthesis of CS oligosaccharides and their ana-

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Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201402222.

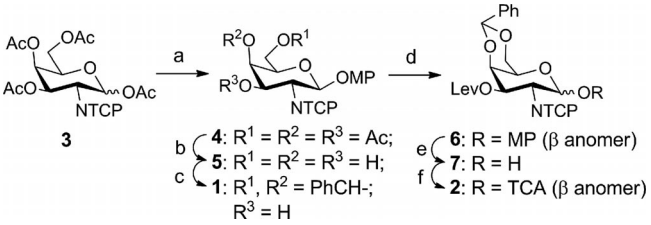
logues,[7,9–19] new approaches to the preparation of these molecules are still required. A well-designed protecting group strategy is required to obtain the right configurations for the glycosidic bonds and the correct positions for the sulfate groups. The choice of protection for the amino group[20] of the GalNAc units is an important point in this design. Most reported syntheses of CS oligomers have used *N*-(trichloroacetyl)galactosamine building blocks.[21] However, the use of this type of units presents some limitations. The formation of stable trichlorooxazoline by-products has been reported in glycosidation reactions of 2-deoxy-2-trichloroacetamido donors.[22–24] Additionally, the final transformation of the 2-trichloroacetamide to the desired 2-acetamido group can be problematic. The basic hydrolysis of multiple trichloroacetamide groups requires very long reaction times,[22] and the alternative reduction method [using tributylstannane/AIBN (azobisisobutyronitrile) or Zn/acetic acid] leads, in some cases, to significant amounts of mono- and dichloroacetamide intermediates.[25–27] For these reasons, we decided to explore the use of new galactosamine monomers that contain a *N*-tetrachlorophthaloyl (*N*-TCP)[28,29] or a *N*-trifluroacetyl (*N*-TFA)[30–32] protecting group for the synthesis of CS oligosaccharides.

We envisioned that the TCP group would be a good alternative for 2-amino protection because this group avoids the formation of stable oxazolines, while strongly favouring the formation of 1,2-*trans* glycosidic linkages.[20,33] Moreover, cleavage of the *N*-TCP moiety does not require the harsh reaction conditions needed for the removal of the analogous *N*-phthaloyl group.[34] On the other hand, we envisioned that the *N*-TFA group could facilitate the final deprotection steps, since it can be removed under milder conditions than the trichloroacetyl group. The *N*-TFA group also ensures high β selectivities in glycosidation reactions.[35,36] Below, we describe the results obtained with both types of building block. As a first goal, we considered the synthesis of CS tetrasaccharides, since it has been demonstrated that tetramers are long enough to interact with several proteins and show biological activity.[7,9,37,38]

Results and Discussion

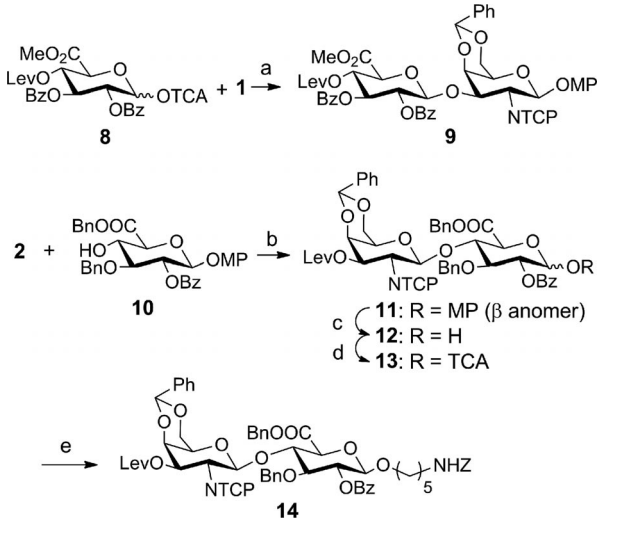
N-TCP Galactosamine Building Blocks for the Synthesis of CS Oligosaccharides

We prepared GalNAc monomers **1** and **2** (Scheme 1), which can be used as glycosyl acceptor and donor, respectively, in coupling reactions with glucuronic acid derivatives to give CS-like disaccharides. The 4,6-*O*-benzylidene acetal allows the regioselective sulfation of these positions at the end of the synthesis (see below). Tetraacetate **3**[39] was converted into 4-methoxyphenyl glycoside **4** by treatment with 4-methoxyphenol and $BF_3{\cdot}Et_2O$. De-*O*-acetylation of **4** is not trivial: the *N*-TCP group is base-sensitive, and the formation of methyl glycoside by-products has been observed during the acid-catalysed hydrolysis of a similar glucosamine derivative.[40] Therefore, de-*O*-acetylation was carried out under strictly controlled basic conditions to give, after benzylidenation, compound **1**. Donor **2** was prepared from **1** by levulination at position 3, followed by oxidative removal of the 4-methoxyphenyl group with cerium(IV) ammonium nitrate (CAN) and trichloroacetimidate activation.

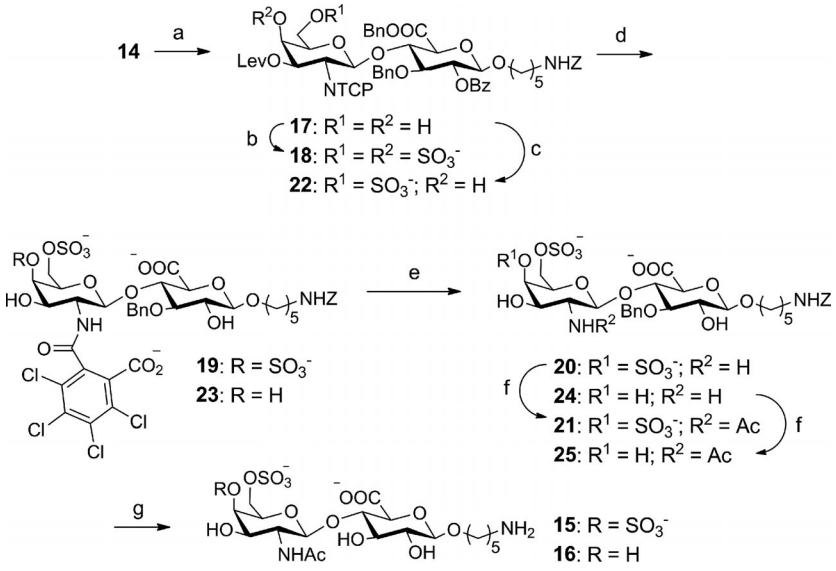


Scheme 1. *Reagents and conditions:* a) 4-methoxyphenol, $BF_3{\cdot}Et_2O$, CH_2Cl_2; b) NaOMe, MeOH, 0 °C; c) $PhCH(OMe)_2$, *p*TsOH, CH_3CN, 50% (3 steps, from **3**); d) Lev_2O, DMAP [4-(dimethylamino)pyridine], CH_2Cl_2, 92%; e) CAN, toluene/CH_3CN/H_2O, 0 °C, 84%; f) Cl_3CCN, DBU (1,8-diazabicycloundec-7-ene), CH_2Cl_2, 91%; MP = 4-methoxyphenyl, Lev = levulinoyl, TCA = trichloroacetimidoyl.

Next, we studied the utility of **1** and **2** in glycosylation reactions with glucuronic acid moieties to give fully protected CS disaccharide precursors (Scheme 2). Glucuronic acid trichloroacetimidate **8**[41,42] was coupled with acceptor **1** to give disaccharide **9** in good yield. We tested different reaction conditions, and the best results were obtained with $BF_3{\cdot}Et_2O$ as catalyst and toluene as solvent. On the other hand, donor **2** was coupled to acceptor **10**[43] to give disaccharide **11**, with the alternative monosaccharide sequence GalNAc-GlcA. To introduce an amine-terminated linker at the reducing end of the chain to allow further conjugation of the final molecules, **11** was transformed into trichloroacetimidate **13**. Glycosylation between **13** and 5-(benzyloxycarbonylamino)-1-pentanol gave the desired disaccharide (i.e., **14**) in good yield.



Scheme 2. *Reagents and conditions:* a) $BF_3{\cdot}Et_2O$, toluene, 54% + 27% recovered **1**; b) TMSOTf (trimethylsilyl trifluoromethanesulfonate), CH_2Cl_2, 58% + 16% recovered **10**; c) CAN, $CH_2Cl_2/CH_3CN/H_2O$, 84%; d) Cl_3CCN, K_2CO_3, CH_2Cl_2, 95%; e) 5-(benzyloxycarbonylamino)-1-pentanol, TMSOTf, CH_2Cl_2, 67%; Z = benzyloxycarbonyl.



Scheme 3. *Reagents and conditions:* a) TFA, CH_2Cl_2, 0 °C, 99% b) $SO_3{\cdot}Me_3N$ (10 equiv.), DMF, 100 °C, 40 min, MW, 83%; c) $SO_3{\cdot}Me_3N$ (2 equiv.), DMF, 50 °C, 30 min, MW, 84%; d) H_2O_2, LiOH, THF; NaOH, MeOH, 86% for **19**, 89% for **23**; e) $NH_2(CH_2)_2NH_2$, DMF, 100 °C, 90 min, MW; f) Ac_2O, Et_3N, MeOH, 75% for **21**, 88% for **25** (2 steps, from **19** and **23**, respectively); g) H_2, $Pd(OH)_2$, H_2O/MeOH, quantitative for **15**, quantitative for **16**.

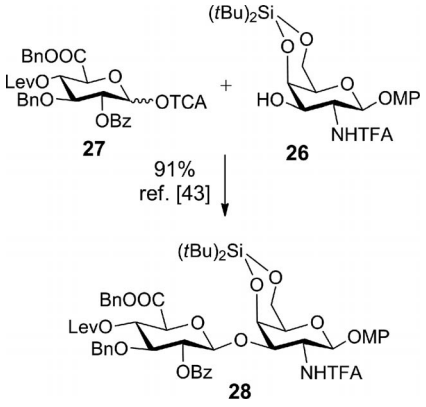
Having achieved the synthesis of these fully protected disaccharides, we then checked the compatibility of the *N*-TCP group with the deprotection and sulfation steps required for the synthesis of final deprotected CS oligomers. Thus, starting from **14**, we successfully prepared disaccharides **15** and **16**, which correspond to the sulfation patterns of CS-E and CS-C, respectively (Scheme 3). The benzylidene acetal of **14** was removed using TFA (trifluoroacetic acid), and the resulting diol was extensively sulfated to give **18**. Here, the reaction time was significantly decreased (40 min) using microwave heating (MW).[44] The next step was the basic hydrolysis of the ester groups, which occurred with concomitant partial hydrolysis of the *N*-TCP moiety to give **19**. The amide bond in **19** was cleaved by treatment with ethylenediamine in DMF. This reaction took only 90 min using microwave heating.[45,46] Finally, the amine group of **20** was selectively acetylated, and the resulting derivative **21** was hydrogenated to give CS-E disaccharide **15** in good yield. For the preparation of CS-C dimer **16**, diol **17** was heated at 50 °C under microwave irradiation in the presence of $SO_3{\cdot}NMe_3$ complex (2 equiv.). The mixture was stirred for 30 min, and 6-*O*-sulfated compound **22** was obtained in high yield. When we carried out the selective 6-OH sulfation with conventional heating in an oil bath, the reaction time was much longer, and the yield was lower, due to the recovery of some unsulfated starting material. Saponification, followed by amide bond cleavage, *N*-acetylation, and hydrogenolysis gave final disaccharide **16**.

Next, we attempted the synthesis of longer CS sequences by a 2+2 coupling of disaccharide units. For this purpose, disaccharide **9** was transformed into the corresponding glycosyl acceptor (by delevulination) and donor (by cleavage of the anomeric 4-methoxyphenyl group and trichloroacetimidate formation). Unfortunately, the 2+2 glycosylation failed, and the desired $(GlcA\text{-}GalNAc)_2$ tetrasaccharide could not be isolated. In an alternative approach, we tried to prepare a $(GalNAc\text{-}GlcA)_2$ tetrasaccharide from compound **11**. Compound **11** was similarly converted into the corresponding acceptor and donor disaccharides, but the 2+2 condensation of these units failed again. In all these glycosylation trials, most of the starting glycosyl acceptor was recovered from the reaction mixture.

Synthesis of CS Oligomers Using *N*-TFA-Protected Galactosamine Units

For the synthesis of biologically relevant CS tetrasaccharides, we turned our attention to *N*-TFA-protected GalNAc units. We have previously reported the preparation and use of this type of building blocks for the synthesis of a hybrid chondroitin/dermatan sulfate oligosaccharide,[43] containing both GlcA and L-iduronic acid (IdoA). Monosaccharide **26**, containing a 4,6-*O*-di-*tert*-butylsilylene group, acted as an excellent glycosyl acceptor in a coupling reaction with poorly reactive GlcA trichloroacetimidate **27** to generate key intermediate **28** (Scheme 4).[43]

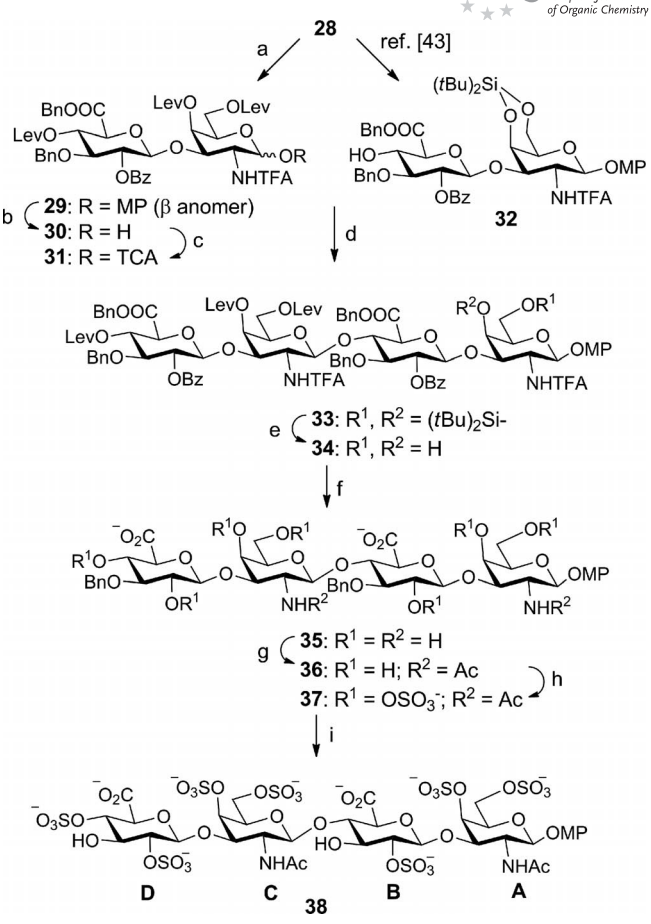
Here, we expand the utility of this *N*-TFA monomer to the preparation of a CS tetrasaccharide sequence, containing exclusively GlcA (Scheme 5). For this purpose, we planned a 2+2 condensation of appropriate disaccharide derivatives. First, **28** was transformed into a suitable donor containing acyl groups at positions 4 and 6 of the GalNAc moiety in order to selectively obtain the β(1→4) glycosidic bond. Thus, compound **28** was treated with $(HF)_n{\cdot}Py$ and then with levulinic anhydride and DMAP to give disaccharide **29**. Trichloroacetimidate **31** was obtained by cleavage of the anomeric 4-methoxyphenyl group followed by treatment with trichloroacetonitrile and DBU. Coupling between **31** and **32**[43] gave tetrasaccharide **33** in good yield. Importantly, **31** was prepared immediately before its use in



Scheme 4. Synthesis of key disaccharide **28** using *N*-TFA unit **26**.

the glycosidation reaction, since we observed partial decomposition of this trichloroacetimidate after extended storage, even at low temperature (–28 °C/4 °C range). Tetrasaccharide **33** has a versatile protecting group distribution that paves the way for the preparation of CS sequences with different sulfation motifs. We decided to prepare, for the first time, unnatural oversulfated compound **38**, since we have found that analogous IdoA-containing tetrasaccharides (Figure 3, see below) are able to interact with FGF-2 (basic fibroblast growth factor), a heparin-binding protein involved in angiogenesis. Thus, removal of the silylene group was followed by basic hydrolysis and selective *N*-acetylation to give **36**. Treatment with SO_3·NMe_3 complex at 100 °C using microwave irradiation[47] gave hepta-*O*-sulfated tetrasaccharide **37**. The introduction of the sulfate groups at the desired positions was confirmed by ^1H and ^{13}C NMR spectroscopic data, which showed typical downfield shifts for the sulfated positions (Tables 1 and 2). Finally, hydrogenolysis of **37** yielded the fully deprotected CS tetramer **38**. NMR spectroscopic analysis confirmed the structure of **38**. The ^1H and ^{13}C NMR spectroscopic data are in full agreement with those reported for similar CS derivatives.

As mentioned before, **38** is an oversulfated CS sequence with a sulfation pattern not found in nature. To demonstrate that *N*-TFA building blocks can be also used for the preparation of oligosaccharides with naturally occurring sulfation patterns, we synthesized, for the first time, tetrasaccharide **50** (Scheme 6). This compound contains sulfate groups at positions 4 and 6 of the GalNAc units, the sulfation pattern of biologically relevant CS-E. Moreover, **50** has a IdoA unit at the nonreducing end. It has been reported that the presence of IdoA (instead of GlcA) in CS chains, giving rise to hybrid chondroitin/dermatan sulfate



Scheme 5. Reagents and conditions: a) $(HF)_n$·Py, THF, 0 °C; Lev_2O, Py, DMAP, 83%; b) CAN, CH_2Cl_2/CH_3CN/H_2O, 81%; c) Cl_3CCN, DBU, CH_2Cl_2, 70%; d) TMSOTf, CH_2Cl_2, 0 °C, 71%; e) $(HF)_n$·Py, THF, 0 °C, 75%; f) LiOH, H_2O_2, THF; NaOH, MeOH; g) Ac_2O, MeOH, Et_3N, 90% (2 steps, from **34**); h) SO_3·Me_3N, DMF, 100 °C, MW, 2 h, 56%; i) H_2, $Pd(OH)_2$, H_2O/MeOH, 97%.

Table 2. ^{13}C NMR chemical shifts [ppm] for sulfated positions of compounds **37** and **38**, and the corresponding nonsulfated positions of **36**.

	C-4A	C-6A	C-2B	C-4C	C-6C	C-2D	C-4D
36[a]	67.6	61.1	72.7	67.6	61.1	73.0	–[c]
37[b]	76.9	69.3–68.6	80.0	76.9	69.3–68.6	80.0	77.2
38[b]	77.0	69.0–68.7	80.7	77.0	69.0–68.7	80.7	79.0

[a] Sodium salt, in [D_4]methanol. [b] Sodium salt, in D_2O. [c] Not determined.

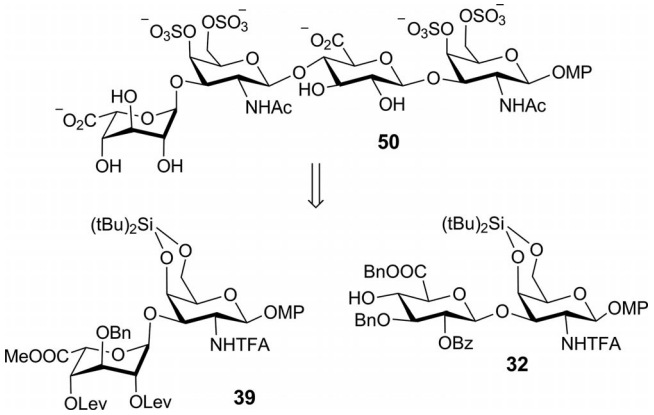
copolymers, has critical roles in the development of the central nervous system.[2,48] Oligosaccharide sequences containing GlcA/IdoA-GalNAc (4,6-OSO_3^-) interact with

Table 1. ^1H NMR Chemical shifts [ppm] for sulfated positions of compounds **37** and **38**, and the corresponding nonsulfated positions of **36**.

	4A-H	6A-H	2B-H	4C-H	6C-H	2D-H	4D-H
36[a]	4.19–4.12	3.86–3.56	3.46	4.19–4.12	3.86–3.56	3.41	3.72–3.56
37[b]	4.96	4.36–4.10	4.41	4.96	4.36–4.10	4.41	4.93–4.85
38[b]	4.95	4.36–4.21	4.28–4.21	4.93	4.36–4.21	4.28–4.21	4.51

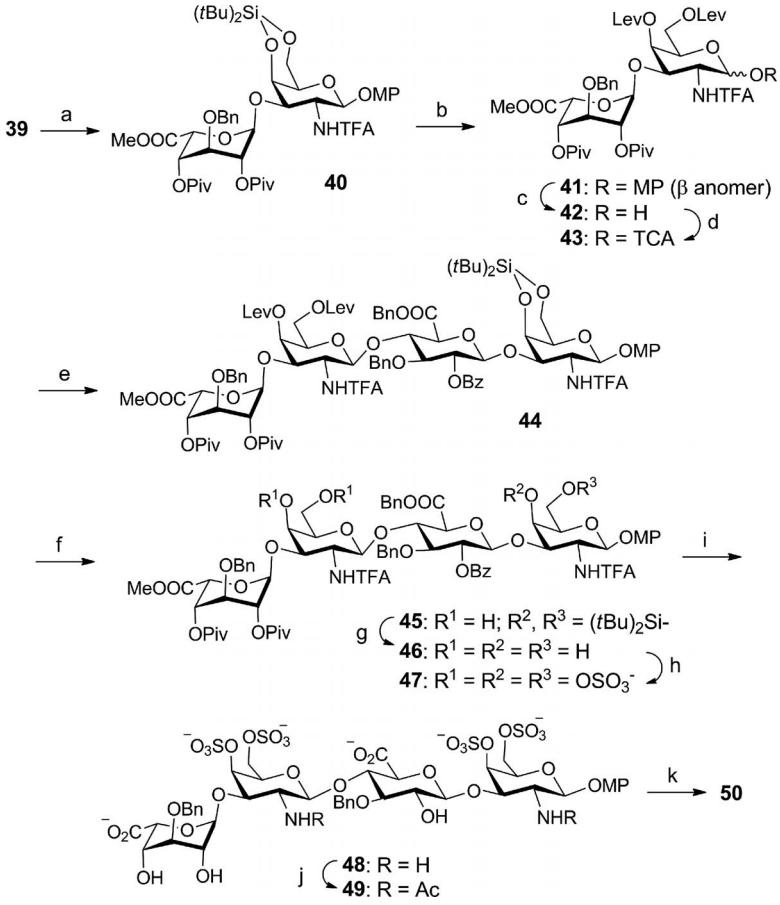
[a] Sodium salt, in [D_4]methanol. [b] Sodium salt, in D_2O.

L- and P-selectins and several chemokines and heparin-binding growth factors.[6,49] The chemical synthesis of these structures, containing both GlcA and IdoA, will contribute to determine the role of hybrid sequences in biological processes, including stem-cell proliferation, neurogenesis, and neural network formation.



Scheme 6. Building blocks required for the synthesis of tetrasaccharide **50**.

Tetrasaccharide **50** was obtained from disaccharides **39**[43] and **32** (Scheme 6). The protecting groups of **39** were rearranged to produce the CS-E sulfation pattern at the end of the synthesis. Delevulination followed by pivaloylation gave compound **40** (Scheme 7). The silylene group was then exchanged for two levulinoyl groups (→**41**). This allows selective deprotection and subsequent sulfation at positions 4 and 6 of the GalNAc moiety, and, at the same time, favours the correct stereochemistry for the glycosidic bond in the 2 + 2 condensation. The formation of trichloroacetimidate **43** was then achieved by oxidative removal of the anomeric 4-methoxyphenyl group with CAN followed by treatment with trichloroacetonitrile and DBU. Fully protected tetramer **44** was prepared by glycosylation of **43** and **32**. The protecting group distribution of **44** can lead, among other outcomes, to a CS-E sulfation pattern. Treatment with hydrazine monohydrate and then with $(HF)_n$·Py complex gave tetraol **46**. The released hydroxy groups were sulfated in 30 min, using microwave heating, to give **47**. The ^{1}H NMR spectrum of **47** showed the expected downfield shifts for 4-H GalNAc (δ = 4.14–3.93 ppm in **46**; δ = 4.85–4.80 ppm in **47**) and 6a,b-H GalNAc (δ = 3.83–3.48 ppm in **46**; δ = 4.52–4.25 in **47**). The ^{13}C NMR spectrum of **47** also



Scheme 7. Reagents and conditions: a) NH_2NH_2·H_2O, Py/AcOH, CH_2Cl_2; PivCl, DMAP, Py, 87%; b) $(HF)_n$·Py, THF, 0 °C; Lev_2O, Py, DMAP, 81%; c) CAN, CH_2Cl_2/CH_3CN/H_2O, 70%; d) Cl_3CCN, DBU, CH_2Cl_2, 78%; e) **32**, TMSOTf, CH_2Cl_2, 0 °C, 53%; f) NH_2NH_2·H_2O, Py/AcOH, CH_2Cl_2, 87%; g) $(HF)_n$·Py, THF, 0 °C, 97%; h) SO_3·Me_3N, DMF, 100 °C, MW, 30 min, quantitative; i) LiOH, H_2O_2, THF; NaOH, MeOH; j) Ac_2O, MeOH, Et_3N, 86% (2 steps, from **47**); k) H_2, $Pd(OH)_2$, H_2O/MeOH, quantitative.

showed the expected downfield shifts of the signals for C-4 GalNAc (δ = 68.6 ppm in **46**; δ = 75.4–75.1 ppm in **47**) and C-6 GalNAc (δ = 62.7–62.5 ppm in **46**; δ = 68.0–67.5 ppm in **47**). Hydrolysis of ester and amide functionalities followed by *N*-acetylation and hydrogenolysis gave tetrasaccharide **50** in high yield. The structure of this compound was confirmed by NMR spectroscopy (COSY, TOCSY, and HSQC experiments) and mass spectrometry. The ^{1}H and ^{13}C NMR chemical shifts are in good agreement with those published for similar oligosaccharides.

Fluorescence Polarization Competition Assay

FGF-2 is a heparin-binding protein[50,51] that also recognizes CS sequences.[5] We finally screened the interactions between FGF-2 and the synthetic water-soluble CS oligosaccharides (**15**, **16**, **38**, and **50**, and dibenzylated tetrasaccharide precursors **37** and **49**). For this purpose, we used a fluorescence polarization competition assay, previously developed in our group.[43] This assay measures the relative ability of the synthetic CS oligomers to inhibit the interaction between FGF-2 and a fluorescently labelled heparin probe. Briefly, the fluorescence polarization of samples containing fixed concentrations of protein and fluorescent probe were measured in the presence of the different CS oligosaccharides (Figure 2). The binding of a CS oligomer to FGF-2 displaces the fluorescent probe from its complex with the protein, resulting in a decrease of the polarization value. In this experiment we included two control samples (in white, Figure 2). The first one (on the left) contained only the fluorescent probe, and indicates the expected value for 100% inhibition. The second one (on the right) contained FGF-2 and fluorescent probe, without inhibitor, and indicates the expected value for 0% inhibition. As shown in Figure 2, at a 25 μM inhibitor concentration, disaccharides **15** and **16** and tetrasaccharides **49** and **50** showed only low inhibitory activity, while compounds **37** and **38** were able to inhibit 47 and 63%, respectively, of the interaction. However, the inhibitory activities of oversulfated compounds **37** and **38** were lower than those obtained with previously synthesized IdoA-containing tetrasaccharides **51** and **52** (Figure 3).[43] In summary, these data indicate that oversulfated, unnatural tetrasaccharides (i.e., **37**–**38** and **51**–**52**) show stronger inhibitory abilities that those tetrasaccharides with natural sulfation patterns (i.e., **49** and **50**). These results also suggest that the presence of an IdoA unit, instead of a GlcA, at the nonreducing end of oversulfated structures, as in compounds **51** and **52**, can increase the relative binding affinities of the synthetic unnatural CS oligosaccharides to FGF-2. The interaction between FGF-2 and heparin is crucial for tumor growth and angiogenesis. Therefore, the discovery of compounds that inhibit the FGF-2/heparin interaction is an area of great interest.[52,53] Although the tested compounds showed modest activities, this experiment gives some interesting data on structural features beneficial for the inhibition of heparin binding to FGF-2. Moreover, this assay illustrates the potential of our fluorescence polarization method for the fast comparison of relative inhibitory activities.

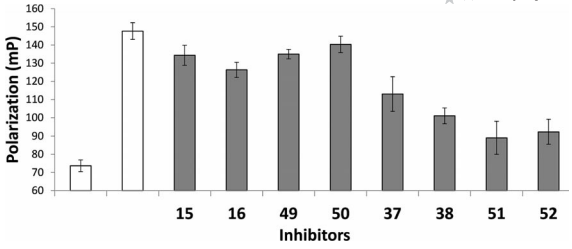


Figure 2. Competition assay to compare the relative inhibitory potencies of the synthetic CS-like oligosaccharides. The graphic presents (in grey) the polarization values obtained from wells containing inhibitor (25 μM), FGF-2 (73 nM), and fluorescent heparin-like probe (10 nM). The composition of the control wells (in white) is described in the main text. All the measurements are the average of three replicate wells, and the error bars show the standard deviations for these measurements.

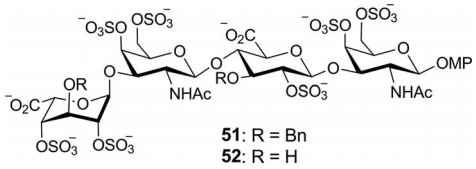


Figure 3. Structures of IdoA-containing tetrasaccharides **51** and **52**.

Conclusions

We have explored and compared the utility of two differently protected galactosamine units for the preparation of CS oligosaccharides. Although *N*-TCP protection was useful at the disaccharide level, we were not able to synthesize longer sequences with this type of unit. In contrast, we have showed that a strategy based on *N*-TFA building blocks can be used to synthesize biologically relevant CS oligosaccharides in good yield. The efficiency of this approach was exemplified by the synthesis of two new CS-like tetrasaccharides, with different sulfation patterns and uronic acid distributions. The *N*-TFA groups led to the stereoselective formation of 1,2-*trans* glycosidic bonds, and they could be easily removed at the end of the synthesis. Microwave irradiation facilitated the sulfation reactions. Finally, we compared the abilities of the synthetic CS oligosaccharides to inhibit heparin binding to FGF-2, and we obtained some interesting information about structural features that influence inhibitory activity.

Experimental Section

General Procedures: Thin-layer chromatography (TLC) analysis was carried out on silica gel 60 F_{254} precoated on aluminium plates (Merck), and the compounds were detected by staining with sulfuric acid/ethanol (1:9), with cerium(IV) sulfate (10 g)/phosphomolybdic acid (13 g)/sulfuric acid (60 mL) solution in water (1 L), or with anisaldehyde solution [anisaldehyde (25 mL) with sulfuric acid (25 mL), ethanol (450 mL), and acetic acid (1 mL)], followed by heating at >200 °C. Column chromatography was carried out on silica gel 60 (0.2–0.5 mm, 0.2–0.063 mm or 0.040–0.015 mm; Merck). Optical rotations were determined with a Perkin–Elmer 341 polarimeter. ^{1}H and ^{13}C NMR spectra were acquired on

Bruker DPX-300, Avance III-400, and DRX-500 spectrometers. Unit A refers to the reducing-end monosaccharide in the NMR spectroscopic data. Electrospray mass spectra (MS (ESI)) were recorded with an Esquire 6000 ESI-Ion Trap from Bruker Daltonics. High-resolution mass spectra (HRMS) were carried out by CITIUS (Universidad de Sevilla), CCiT (Universitat de Barcelona), and SIdI (Universidad Autónoma de Madrid). Microwave-based sulfation reactions were carried out using a Biotage Initiator Eight synthesizer in sealed reaction vessels.

4-Methoxyphenyl 4,6-*O*-Benzylidene-2-deoxy-2-tetrachlorophthalimido-β-D-galactopyranoside (1): $BF_3{\cdot}Et_2O$ (731 μL, 5.82 mmol) was added to a mixture of **3** (1.79 g, 2.91 mmol) and 4-methoxyphenol (723 mg, 5.82 mmol) in dry CH_2Cl_2 (8.0 mL) under an argon atmosphere at 0 °C. The temperature was gradually raised to room temperature over 2 h, and the mixture was stirred for 24 h. Then it was diluted with CH_2Cl_2 (40 mL), and washed with H_2O, saturated aqueous $NaHCO_3$, and H_2O. The organic phase was dried ($MgSO_4$) and concentrated to dryness. The residue was purified by column chromatography (hexane/EtOAc, 3:1) to give **4** (1.63 g). TLC (toluene/acetone, 3:2): R_f = 0.44. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.86 (m, 2 H, Ar), 6.75 (m, 2 H, Ar), 5.79 (d, $J_{1,2}$ = 8.5 Hz, 1 H, 1-H), 5.78 (dd, $J_{2,3}$ = 11.3, $J_{3,4}$ = 3.1 Hz, 1 H, 3-H), 5.53 (d, 1 H, 4-H), 4.79 (dd, 1 H, 2-H), 4.28–4.10 (m, 3 H, 5-H, 6a-H, 6b-H), 3.74 [s, 3 H, Me(OMP)], 2.23, 2.06, 1.91 (3 s, 9 H, OAc) ppm. MS (ESI): calcd. for $C_{27}H_{23}Cl_4NO_{11}Na$ [M + Na]$^+$ 700.0; found 700.1.

Compound **4** (1.63 g, 2.4 mmol) was dissolved in MeOH (186 mL), and NaOMe (1 M in MeOH; 3.2 mL) was added. The mixture was stirred at 0 °C for 10 min, and then AcOH (15.5 mL) was added. The mixture was stirred at room temperature for 10 min, and then it was coconcentrated twice with toluene. The residue was filtered through a silica column (toluene/acetone, 2:1) to give **5** (855 mg) and a mixture of partially deacetylated compounds (348 mg). The partially deprotected products were dissolved in MeOH (40 mL) and treated with additional NaOMe (1 M in MeOH; 0.68 mL) at 0 °C. After stirring for 7 min at 0 °C, AcOH (3.3 mL) was added, and the mixture was concentrated. The residue was purified by column chromatography to give additional **5** (197 mg). TLC (toluene/acetone, 2:1): R_f = 0.29. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.87 (m, 2 H, Ar), 6.74 (m, 2 H, Ar), 5.62 (d, $J_{1,2}$ = 8.4 Hz, 1 H, 1-H), 4.61 (br. t, 1 H, 2-H), 4.46 (dd, $J_{2,3}$ = 11.0, $J_{3,4}$ = 3.0 Hz, 1 H, 3-H), 4.03 (d, 1 H, 4-H), 3.84–3.75 (m, 3 H, 5-H, 6a-H, 6b-H), 3.69 [s, 3 H, Me(OMP)] ppm. MS (ESI): calcd. for $C_{21}H_{17}Cl_4NO_8Na$ [M + Na]$^+$ 574.0; found 574.1.

Compound **5** (1.052 g, 1.90 mmol) was dissolved in dry MeCN (19 mL). Benzaldehyde dimethyl acetal (0.43 mL, 2.85 mmol) and *p*TsOH (0.5 M solution in dry MeCN; 188 μL) were added, and the mixture was stirred for 45 min. Then it was diluted with EtOAc (200 mL), and washed with saturated aqueous $NaHCO_3$ and H_2O. The organic phase was dried ($MgSO_4$) and concentrated to dryness. The residue was purified by column chromatography (toluene/EtOAc, 8:1) to give **1** (930 mg, 50% over three steps from **3**). TLC (toluene/EtOAc, 8:1): R_f = 0.27. $[\alpha]_D^{20}$ = +11 (c = 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.55 (m, 2 H, Ar), 7.40 (m, 3 H, Ar), 6.91 (m, 2 H, Ar), 6.75 (m, 2 H, Ar), 5.75 (d, $J_{1,2}$ = 8.3 Hz, 1 H, 1-H), 5.61 (s, 1 H, Ph-CH), 4.69 (br. t, 1 H, 2-H), 4.51 (dd, $J_{2,3}$ = 10.9, $J_{3,4}$ = 3.1 Hz, 1 H, 3-H), 4.38 (d, $J_{6a,6b}$ = 12.4 Hz, 1 H, 6a-H), 4.33 (br. d, 1 H, 4-H), 4.13 (d, 1 H, 6b-H), 3.73 [s, 3 H, Me(OMP)], 3.70 (s, 1 H, 5-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.2, 163.6 (2 CO), 155.8, 150.6, 140.5, 140.4, 137.3, 130.1, 129.8 (Ar-C), 129.6, 128.5 (Ar-CH), 127.6, 127.3 (Ar-C), 126.6, 119.3, 114.5 (Ar-CH), 101.7 (Ph-CH), 97.6 (C-1), 74.9 (C-4), 69.2 (C-6), 67.8 (C-3), 67.0 (C-5), 55.7 [Me(OMP)], 55.4 (C-2) ppm. HRMS: calcd. for $C_{28}H_{21}Cl_4NO_8Na$ [M + Na]$^+$ 661.9919; found 661.9899.

4-Methoxyphenyl 4,6-*O*-Benzylidene-2-deoxy-3-*O*-levulinoyl-2-tetrachlorophthalimido-β-D-galactopyranoside (6): Lev_2O preparation: LevOH (2.0 mL, 19.1 mmol) was added to a solution of 1,3-dicyclohexylcarbodiimide (1.97 g, 9.54 mmol) in CH_2Cl_2 (16 mL) at 0 °C. The mixture was stirred for 5 min at room temperature, then it was cooled and filtered, and the urea precipitate was washed with additional CH_2Cl_2 (2.7 mL), to give a Lev_2O solution (0.51 M; 18.7 mL).

Lev_2O (0.51 M solution in CH_2Cl_2; 16.4 mL) was added at room temperature to a mixture of **1** (2.16 g, 3.37 mmol) and DMAP (61.1 mg, 0.51 mmol). The mixture was stirred for 1 h 30 min, then it was diluted with CH_2Cl_2, and washed with saturated aqueous $NaHCO_3$ and H_2O. The organic phase was dried ($MgSO_4$), filtered, and concentrated to dryness. The residue was purified by column chromatography (toluene/EtOAc, 9:1) to give **6** (2.29 g, 92%). TLC (toluene/EtOAc, 6:1): R_f = 0.31. $[\alpha]_D^{20}$ = +14 (c = 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.60–7.55 (m, 2 H, Ar), 7.42–7.38 (m, 3 H, Ar), 6.90 (m, 2 H, Ar), 6.74 (m, 2 H, Ar), 5.82 (d, $J_{1,2}$ = 8.5 Hz, 1 H, 1-H), 5.80 (dd, $J_{2,3}$ = 11.4, $J_{3,4}$ = 3.6 Hz, 1 H, 3-H), 5.58 (s, 1 H, Ph-CH), 5.00 (dd, 1 H, 2-H), 4.45 (br. d, 1 H, 4-H), 4.37 (dd, $J_{5,6a}$ = 1.4, $J_{6a,6b}$ = 12.5 Hz, 1 H, 6a-H), 4.12 (dd, $J_{5,6b}$ = 1.4 Hz, 1 H, 6b-H), 3.73 [s, 3 H, Me(OMP)], 3.72 (m, 1 H, 5-H), 2.76–2.39 [m, 4 H, CH_2(Lev)], 1.93 [s, 3 H, CH_3(Lev)] ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 206.4 [CO(Lev)], 172.0 [CO(Lev)], 164.0, 163.0 (2 CO), 155.8, 150.5, 140.3, 140.2, 137.6, 130.1, 129.9 (Ar-C), 129.3, 128.4 (Ar-CH), 127.7, 127.4 (Ar-C), 126.5, 119.3, 114.5 (Ar-CH), 101.1 (Ph-CH), 97.6 (C-1), 73.0 (C-4), 69.1 (C-6), 68.7 (C-3), 66.9 (C-5), 55.7 [Me(OMP)], 51.7 (C-2), 37.9 [CH_2(Lev)], 29.6 [CH_3(Lev)], 28.2 [CH_2(Lev)] ppm. HRMS: calcd. for $C_{33}H_{27}Cl_4NO_{10}Na$ [M + Na]$^+$ 760.0287; found 760.0278.

4,6-*O*-Benzylidene-2-deoxy-3-*O*-levulinoyl-2-tetrachlorophthalimido-α,β-D-galactopyranose (7): CAN (6.65 g, 11.9 mmol) was added at 0 °C to a solution of **6** (2.2 g, 3.0 mmol) in toluene/MeCN/H_2O (1:6:1; 104 mL). The mixture was stirred for 1 h at 0 °C, then it was diluted with EtOAc, and washed with H_2O, saturated aqueous $NaHCO_3$, and H_2O. The organic phase was dried ($MgSO_4$), filtered, and concentrated to dryness. The residue was purified by column chromatography (toluene/EtOAc, 4:1) to give **7** (1.60 g, 84%) as a mixture of α/β anomers (2:10). TLC (toluene/EtOAc, 4:1): R_f = 0.23 (for a mixture of α/β anomers). ^{1}H NMR (300 MHz, $CDCl_3$, data for β anomer): δ = 7.55–7.48 (m, 2 H, Ar), 7.39–7.33 (m, 3 H, Ar), 5.77 (dd, $J_{2,3}$ = 11.3, $J_{3,4}$ = 3.5 Hz, 1 H, 3-H), 5.54 (s, 1 H, Ph-CH), 5.47 (d, $J_{1,2}$ = 8.3 Hz, 1 H, 1-H), 4.67 (dd, 1 H, 2-H), 4.40 (br. d, 1 H, 4-H), 4.34 (dd, $J_{5,6a}$ = 1.4, $J_{6a,6b}$ = 12.6 Hz, 1 H, 6a-H), 4.08 (dd, $J_{5,6b}$ = 1.4 Hz, 1 H, 6b-H), 3.84 (br. s, 1 H, OH), 3.67 (m, 1 H, 5-H), 2.69–2.35 [m, 4 H, CH_2(Lev)], 1.91 [s, 3 H, CH_3(Lev)] ppm. ^{13}C NMR (75 MHz, $CDCl_3$, data for β anomer): δ = 206.5 [CO(Lev)], 171.9 [CO(Lev)], 163.8, 163.5 (2 CO), 140.1, 137.5, 129.9, 129.8 (Ar-C), 129.3, 128.3 (Ar-CH), 127.6, 127.5 (Ar-C), 126.3 (Ar-CH), 100.9 (Ph-CH), 92.8 (C-1), 72.9 (C-4), 69.2 (C-6), 68.5 (C-3), 66.9 (C-5), 53.5 (C-2), 37.9 [CH_2(Lev)], 29.6 [CH_3(Lev)], 28.2 [CH_2(Lev)] ppm. ^{1}H NMR (300 MHz, $CDCl_3$, data for α anomer): δ = 7.55–7.48 (m, 2 H, Ar), 7.39–7.33 (m, 3 H, Ar), 6.33 (dd, $J_{2,3}$ = 12.1, $J_{3,4}$ = 3.4 Hz, 1 H, 3-H), 5.57 (s, 1 H, Ph-CH), 5.50 (m, 1 H, 1-H), 5.04 (dd, $J_{1,2}$ = 3.1 Hz, 1 H, 2-H), 4.57 (br. d, 1 H, 4-H), 4.26 (br. d, $J_{6a,6b}$ = 12.2 Hz, 1 H, 6a-H), 4.14–4.07 (m, 2 H, 5-H, 6b-H), 4.00 (br. s, 1 H, OH), 2.69–2.35 [m, 4 H, CH_2(Lev)], 1.97 [s, 3 H, CH_3(Lev)] ppm. ^{13}C NMR (75 MHz, $CDCl_3$, significant data for α anomer): δ = 93.0 (C-1), 73.3 (C-4), 69.5 (C-6), 65.5 (C-3), 62.6 (C-5), 51.3 (C-2) ppm.

HRMS: calcd. for $C_{26}H_{21}Cl_4NO_9Na$ [M + Na]$^+$ 653.9868; found 653.9876.

***O*-(4,6-*O*-Benzylidene-2-deoxy-3-*O*-levulinoyl-2-tetrachlorophthalimido-β-D-galactopyranosyl) Trichloroacetimidate (2):** Trichloroacetonitrile (5.3 mL, 54 mmol) and catalytic DBU (0.11 M solution in dry CH_2Cl_2; 96 μL) were added to a solution of **7** (680 mg, 1.07 mmol) in dry CH_2Cl_2 (15 mL). The mixture was stirred for 7 h at room temperature, then it was concentrated to dryness. The residue was purified by flash chromatography (toluene/EtOAc, 5:1 + 1% Et_3N) to give **2** (763 mg, 91%). TLC (toluene/EtOAc, 3:1): R_f = 0.40. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.64 (s, 1 H, NH), 7.57 (m, 2 H, Ar), 7.41 (m, 3 H, Ar), 6.54 (d, $J_{1,2}$ = 8.9 Hz, 1 H, 1-H), 5.90 (dd, $J_{2,3}$ = 11.4, $J_{3,4}$ = 3.6 Hz, 1 H, 3-H), 5.59 (s, 1 H, PhCH), 5.05 (dd, 1 H, 2-H), 4.49 (d, 1 H, 4-H), 4.43 (d, $J_{6a,6b}$ = 12.4 Hz, 1 H, 6a-H), 4.14 (d, 1 H, 6b-H), 3.87 (br. s, 1 H, 5-H), 2.71–2.41 [m, 4 H, CH_2(Lev)], 1.93 [s, 3 H, CH_3(Lev)] ppm. MS (ESI): calcd. for $C_{28}H_{21}Cl_7N_2O_9Na$ [M + Na]$^+$ 796.9; found 797.0.

4-Methoxyphenyl 3-*O*-(Methyl 2,3-Di-*O*-benzoyl-4-*O*-levulinoyl-β-D-glucopyranosyluronate)-4,6-*O*-benzylidene-2-deoxy-2-tetrachlorophthalimido-β-D-galactopyranoside (9): BF_3·Et_2O (0.26 M solution in dry toluene; 326 μL) was added under an argon atmosphere at room temperature to a mixture of **1** (154 mg, 0.24 mmol) and **8** (475 mg, 0.72 mmol) containing freshly activated 4 Å molecular sieves in dry toluene (2.5 mL). The mixture was stirred for 45 min at room temperature, then it was neutralized with Et_3N, and concentrated to dryness. The residue was purified by column chromatography (toluene/acetone, 8:1) to give **9** (148 mg, 54%), and unreacted acceptor (41 mg, 27%). TLC (toluene/acetone, 3:1): R_f = 0.48. $[\alpha]_D^{20}$ = +18 (c = 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.76–7.09 (m, 15 H, Ar), 6.79 (m, 2 H, Ar), 6.68 (m, 2 H, Ar), 5.64 (t, $J_{2,3}$ = $J_{3,4}$ = 9.5 Hz, 1 H, 3B-H), 5.59 (s, 1 H, PhCH), 5.49 (d, $J_{1,2}$ = 8.3 Hz, 1 H, 1A-H), 5.41 (t, $J_{4,5}$ = 9.6 Hz, 1 H, 4B-H), 5.34 (dd, $J_{1,2}$ = 7.6 Hz, 1 H, 2B-H), 5.07 (d, 1 H, 1B-H), 4.99 (dd, $J_{2,3}$ = 11.3 Hz, 1 H, 2A-H), 4.82 (dd, $J_{3,4}$ = 3.2 Hz, 1 H, 3A-H), 4.63 (br. d, 1 H, 4A-H), 4.36 (br. d, $J_{6a,6b}$ = 12.2 Hz, 1 H, 6aA-H), 4.24 (d, 1 H, 5B-H), 4.13 (br. d, 1 H, 6bA-H), 3.72, 3.69 [2 s, 6 H, COOMe, Me(OMP)], 2.66–2.30 [m, 4 H, CH_2(Lev)], 2.03 [m, 3 H, CH_3(Lev)] ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.3, 167.0, 165.6, 164.4, 164.1, 162.0 [CO(Lev, *N*-TCP, COOMe, Bz], 155.6, 150.5, 140.3, 140.0, 137.7 (Ar-C), 133.5, 133.1, 129.9–125.4, 119.0, 114.4 (Ar-CH, Ar-C), 101.7 (C-1B), 100.9 (PhCH), 97.7 (C-1A), 76.2 (C-3A), 75.1 (C-4A), 72.3 (C-5B), 72.2 (C-3B), 71.9 (C-2B), 69.4 (C-4B), 69.0 (C-6A), 66.9 (C-5A), 55.5, 52.9 [COOMe, Me(OMP)], 52.0 (C-2A), 37.4 [CH_2(Lev)], 29.5 [CH_3(Lev)], 27.6 [CH_2(Lev)] ppm. HRMS: calcd. for $C_{54}H_{45}Cl_4NO_{18}Na$ [M + Na]$^+$ 1158.1288; found 1158.1327.

Benzyl [4-Methoxyphenyl 2-*O*-Benzoyl-3-*O*-benzyl-4-*O*-(4,6-*O*-benzylidene-2-deoxy-3-*O*-levulinoyl-2-tetrachlorophthalimido-β-D-galactopyranosyl)-β-D-glucopyranoside]uronate (11): Donor **2** (655 mg, 0.842 mmol) and acceptor **10** (274 mg, 0.468 mmol) were dissolved in dry CH_2Cl_2 (5 mL) in the presence of freshly activated 4 Å molecular sieves. The mixture was stirred for 10 min at room temperature, then TMSOTf (0.18 M solution in dry CH_2Cl_2; 229 μL) was added under an argon atmosphere. The mixture was stirred for 9 min, then it was neutralized with Et_3N and concentrated to dryness. The residue was purified by column chromatography (toluene/EtOAc, 9:1) to give **11** (325 mg, 58%), and unreacted **10** (45 mg, 16%). TLC (toluene/EtOAc, 4:1): R_f = 0.43. $[\alpha]_D^{20}$ = –9 (c = 1.0, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.94 (m, 2 H, Ar), 7.56 (m, 1 H, Ar), 7.48–7.15 (m, 17 H, Ar), 6.77 (m, 2 H, Ar), 6.64 (m, 2 H, Ar), 5.75 (dd, $J_{2,3}$ = 11.4, $J_{3,4}$ = 3.6 Hz, 1 H, 3B-H), 5.48 (s, 1 H, PhCH), 5.46 (dd, $J_{1,2}$ = 7.4, $J_{2,3}$ = 8.6 Hz, 1 H, 2A-H), 5.38 (d, $J_{1,2}$ = 8.4 Hz, 1 H, 1B-H), 5.20 [d, 1 H, CH_2(Bn)], 5.04 [d, 1 H, CH_2(Bn)], 4.99 [d, 1 H, CH_2(Bn)], 4.91 (d, 1 H, 1A-H), 4.81 [d, 1 H, CH_2(Bn)], 4.70 (dd, 1 H, 2B-H), 4.36 (t, $J_{3,4}$ = $J_{4,5}$ = 9.0 Hz, 1 H, 4A-H), 4.31 (d, 1 H, 4B-H), 4.17 (d, $J_{6a,6b}$ = 12.4 Hz, 1 H, 6aB-H), 3.95–3.89 (m, 2 H, 3A-H, 5A-H), 3.86 (d, 1 H, 6bB-H), 3.69 [s, 3 H, Me(OMP)], 3.19 (br. s, 1 H, 5B-H), 2.69–2.32 [m, 4 H, CH_2(Lev)], 1.92 [s, 3 H, CH_3(Lev)] ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 206.3 [CO(Lev)], 171.9, 167.3, 165.1, 164.2, 163.4 [CO(Lev, *N*-TCP, COOBn, Bz)], 155.8, 151.0, 140.0, 139.8, 138.3, 137.7, 135.1 (Ar-C), 133.3 (Ar-CH), 130.0, 129.8, 129.7, 129.5, 129.1, 128.7, 128.5, 128.2, 128.1, 127.9, 127.6, 127.3, 126.4 (Ar-C, Ar-CH), 119.1, 114.5 (Ar-CH), 101.1, 101.0 (PhCH, C-1A), 97.9 (C-1B), 80.2 (C-3A or C-5A), 77.8 (C-4A), 74.7 (C-3A or C-5A), 74.5 [CH_2(Bn)], 73.0 (C-2A), 72.7 (C-4B), 68.9 (C-6B), 68.3 (C-3B), 67.5 [CH_2(Bn)], 66.4 (C-5B), 55.7 [Me(OMP)], 52.0 (C-2B), 37.9 [CH_2(Lev)], 29.6 [CH_3(Lev)], 28.2 [CH_2(Lev)] ppm. HRMS: calcd. for $C_{60}H_{51}Cl_4NO_{17}Na$ [M + Na]$^+$ 1220.1809; found 1220.1812.

Benzyl [2-*O*-Benzoyl-3-*O*-benzyl-4-*O*-(4,6-*O*-benzylidene-2-deoxy-3-*O*-levulinoyl-2-tetrachlorophthalimido-β-D-galactopyranosyl)-α,β-D-glucopyranose]uronate (12): A solution of CAN (79 mg, 0.14 mmol) in H_2O (0.3 mL) was added to a solution of **11** (42 mg, 0.035 mmol) in CH_2Cl_2/MeCN (1:2; 2.7 mL). The mixture was vigorously stirred for 1 h at room temperature, then it was diluted with EtOAc, and washed with H_2O, saturated aqueous $NaHCO_3$, and H_2O. The organic phase was dried ($MgSO_4$), filtered, and concentrated to dryness. The residue was purified by column chromatography (CH_2Cl_2/MeOH, 80:1) to give **12** (40 mg, 84%) as a mixture of α/β anomers (2:1). TLC (CH_2Cl_2/MeOH, 80:1): R_f = 0.23, 0.27. ^{1}H NMR [300 MHz, $CDCl_3$, for major anomer (α)]: δ = 7.94 (m, 2 H, Ar), 7.58–7.07 (m, 18 H, Ar), 5.69 (dd, $J_{2,3}$ = 11.3, $J_{3,4}$ = 3.6 Hz, 1 H, 3B-H), 5.49–5.45 (m, 3 H, PhCH, 1B-H, 1A-H), 5.19 [d, 1 H, CH_2(Bn)], 5.11–5.00 [m, 3 H, CH_2(Bn), 2A-H], 4.85 [d, 1 H, CH_2(Bn)], 4.69 (m, 1 H, 2B-H), 4.39 (d, $J_{4,5}$ = 9.0 Hz, 1 H, 5A-H), 4.29–4.08 (m, 4 H, 4B-H, 3A-H, 4A-H, 6aB-H), 3.80 (d, $J_{6a,6b}$ = 12.0 Hz, 1 H, 6bB-H), 3.10 (s, 1 H, 5B-H), 2.68–2.37 [m, 4 H, CH_2(Lev)], 1.91 [s, 3 H, CH_3(Lev)] ppm. ^{13}C NMR [75 MHz, $CDCl_3$, for major anomer (α)]: δ = 206.3 [CO(Lev)], 171.9, 168.5, 165.9, 164.2, 163.5 [CO(Lev, *N*-TCP, COOBn, Bz)], 140.0, 139.8, 138.3, 137.7, 135.2 (Ar-C), 133.4 (Ar-CH), 130.0–126.5 (Ar-C, Ar-CH), 101.0 (PhCH), 98.0 (C-1B), 90.7 (C-1A), 77.8, 77.4 (C-3A, C-4A), 74.8 [CH_2(Bn)], 73.2 (C-2A), 72.8 (C-4B), 70.5 (C-5A), 68.9 (C-6B), 68.5 (C-3B), 67.5 [CH_2(Bn)], 66.4 (C-5B), 52.1 (C-2B), 37.9 [CH_2(Lev)], 29.6 [CH_3(Lev)], 28.2 [CH_2(Lev)] ppm. ^{1}H NMR [300 MHz, $CDCl_3$, for minor anomer (β)]: δ = 7.94 (m, 2 H, Ar), 7.58–7.07 (m, 18 H, Ar), 5.71 (dd, $J_{2,3}$ = 11.4, $J_{3,4}$ = 3.6 Hz, 1 H, 3B-H), 5.49–5.45 (m, 1 H, PhCH), 5.39 (d, $J_{1,2}$ = 8.4 Hz, 1 H, 1B-H), 5.21 [d, 1 H, CH_2(Bn)], 5.11–5.00 [m, 3 H, CH_2(Bn), 2A-H], 4.83 [d, 1 H, CH_2(Bn)], 4.72–4.66 (m, 2 H, 1A-H, 2B-H), 4.29–4.08 (m, 3 H, 4B-H, 4A-H, 6aB-H), 3.97–3.78 (m, 3 H, 3A-H, 5A-H, 6bB-H), 3.12 (s, 1 H, 5B-H), 2.68–2.37 [m, 4 H, CH_2(Lev)], 1.91 [s, 3 H, CH_3(Lev)] ppm. ^{13}C NMR [75 MHz, $CDCl_3$, selected data for minor anomer (β)]: δ = 101.0 (PhCH), 97.8 (C-1B), 96.3 (C-1A), 79.9 (C-3A), 77.8 (C-4A), 75.4 (C-2A), 74.8 [CH_2(Bn)], 74.7 (C-5A), 73.2 (C-4B), 68.9 (C-6B), 68.3 (C-3B), 67.7 [CH_2(Bn)], 66.4 (C-5B), 52.0 (C-2B), 37.9 [CH_2(Lev)], 29.6 [CH_3(Lev)], 28.2 [CH_2(Lev)] ppm. HRMS: calcd. for $C_{53}H_{45}Cl_4NO_{16}Na$ [M + Na]$^+$ 1114.1390; found 1114.1425.

***O*-[Benzyl 2-*O*-Benzoyl-3-*O*-benzyl-4-*O*-(4,6-*O*-benzylidene-2-deoxy-3-*O*-levulinoyl-2-tetrachlorophthalimido-β-D-galactopyranosyl)-α,β-D-glucopyranosyluronate] Trichloroacetimidate (13):** Trichloroacetonitrile (1.57 mL, 15.8 mmol) and K_2CO_3 (47 mg, 0.35 mmol) were added to **12** (345 mg, 315 μmol) in dry CH_2Cl_2 (8 mL) under an argon atmosphere. The mixture was stirred at room temperature

for 15 h, then it was filtered and concentrated in vacuo to give **13** (370 mg, 95%) as an α/β mixture (75:100). TLC (toluene/acetone, 8:1): R_f = 0.40. ^{1}H NMR [300 MHz, $CDCl_3$, for major anomer (β)]: δ = 8.53 (s, 1 H, NH), 7.91 (m, 2 H, Ar), 7.58–7.09 (m, 18 H, Ar), 6.00 (d, $J_{1,2}$ = 6.1 Hz, 1 H, 1A-H), 5.69 (dd, $J_{2,3}$ = 11.3, $J_{3,4}$ = 3.6 Hz, 1 H, 3B-H), 5.52–5.43 (m, 3 H, PhCH, 1B-H, 2A-H), 5.19–4.87 [m, 4 H, CH_2(Bn)], 4.70 (m, 1 H, 2B-H), 4.48 (dd, $J_{3,4}$ = 8.0, $J_{4,5}$ = 9.8 Hz, 1 H, 4A-H), 4.34–4.20 (m, 1 H, 4B-H), 4.16–4.08 (m, 2 H, 5A-H, 6aB-H), 4.00 (dd, $J_{2,3}$ = 6.5 Hz, 1 H, 3A-H), 3.84 (d, $J_{6a,6b}$ = 11.5 Hz, 1 H, 6bB-H), 3.13 (s, 1 H, 5B-H), 2.69–2.32 [m, 4 H, CH_2(Lev)], 1.92 [s, 3 H, CH_3(Lev)] ppm. ^{13}C NMR [75 MHz, $CDCl_3$, for major anomer (β)]: δ = 206.2 [CO(Lev)], 171.9, 167.4, 164.9, 164.2, 163.4 [CO(Lev, *N*-TCP, COOBn, Bz)], 160.8 (C=NH), 140.0, 139.8, 138.2, 137.7, 135.0 (Ar-C), 133.5 (Ar-CH), 129.9–126.4 (Ar-C, Ar-CH), 100.9 (PhCH), 98.2 (C-1B), 95.5 (C-1A), 90.5 (CCl_3), 80.5 (C-3A), 77.4 (C-4A), 74.4 (C-5A), 73.7 [CH_2(Bn)], 72.7 (C-4B), 71.4 (C-2A), 68.9 (C-6B), 68.5 (C-3B), 67.5 [CH_2(Bn)], 66.5 (C-5B), 52.0 (C-2B), 37.9 [CH_2(Lev)], 29.6 [CH_3(Lev)], 28.2 [CH_2(Lev)] ppm. ^{1}H NMR [300 MHz, $CDCl_3$, for minor anomer (α)]: δ = 8.50 (s, 1 H, NH), 7.91 (m, 2 H, Ar), 7.58–7.09 (m, 18 H, Ar), 6.56 (d, $J_{1,2}$ = 3.6 Hz, 1 H, 1A-H), 5.70 (dd, $J_{2,3}$ = 11.4, $J_{3,4}$ = 3.8 Hz, 1 H, 3B-H), 5.52–5.43 (m, 2 H, PhCH, 1B-H), 5.34 (dd, $J_{2,3}$ = 9.3 Hz, 1 H, 2A-H), 5.21–4.82 [m, 4 H, CH_2(Bn)], 4.70 (m, 1 H, 2B-H), 4.34–4.08 (m, 5 H, 3A-H, 4A-H, 5A-H, 4B-H, 6aB-H), 3.80 (d, $J_{6a,6b}$ = 11.6 Hz, 1 H, 6bB-H), 3.11 (s, 1 H, 5B-H), 2.69–2.32 [m, 4 H, CH_2(Lev)], 1.92 [s, 3 H, CH_3(Lev)] ppm. ^{13}C NMR [75 MHz, $CDCl_3$, selected data for minor anomer (α)]: δ = 160.4 (C=NH), 129.9–126.4 (Ar-C, Ar-CH), 100.9 (PhCH), 98.4 (C-1B), 93.4 (C-1A), 79.9, 77.9, 75.0 (C-3A, C-4A, C-5A), 73.5 [CH_2(Bn)], 72.7 (C-4B), 71.9 (C-2A), 68.9 (C-6B), 68.5 (C-3B), 67.6 [CH_2(Bn)], 66.4 (C-5B), 52.1 (C-2B) ppm. HRMS: calcd. for $C_{55}H_{45}Cl_7N_2O_{16}Na$ $[M + Na]^+$ 1257.0486; found 1257.0470.

Benzyl [*N*-Benzyloxycarbonyl-5-aminopentyl 2-*O*-Benzoyl-3-*O*-benzyl-4-*O*-(4,6-*O*-benzylidene-2-deoxy-3-*O*-levulinoyl-2-tetrachlorophthalimido-β-D-galactopyranosyl)-β-D-glucopyranoside] Uronate (14): Donor **13** (184 mg, 0.15 mmol) and benzyl *N*-(5-hydroxypentyl) carbamate (107 mg, 0.45 mmol) were dissolved in dry CH_2Cl_2 (1 mL) in the presence of freshly activated 4 Å molecular sieves. The mixture was stirred for 45 min at room temperature, then TMSOTf (0.092 M solution in dry CH_2Cl_2; 162 μL) was added under an argon atmosphere. The mixture was stirred for 15 min, then it was neutralized with Et_3N and concentrated to dryness. The residue was purified by column chromatography (toluene/acetone, 10:1) to give **14** (130 mg, 67%). TLC (toluene/EtOAc, 3:1): R_f = 0.44. $[\alpha]_D^{20}$ = –5 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.92 (m, 2 H, Ar), 7.53 (m, 1 H, Ar), 7.48–7.02 (m, 22 H, Ar), 5.71 (dd, $J_{2,3}$ = 11.5, $J_{3,4}$ = 3.5 Hz, 1 H, 3B-H), 5.46 (s, 1 H, PhCH), 5.36 (d, $J_{1,2}$ = 8.4 Hz, 1 H, 1B-H), 5.21 [m, 2 H, 2A-H, CH_2(Bn)], 5.05 [m, 3 H, CH_2(Z), CH_2(Bn)], 4.94 [d, 1 H, CH_2(Bn)], 4.79 [d, 1 H, CH_2(Bn)], 4.68 (dd, 1 H, 2B-H), 4.55 (br. t, 1 H, NH), 4.44 (d, $J_{1,2}$ = 7.5 Hz, 1 H, 1A-H), 4.26 (br. d, 1 H, 4B-H), 4.24 (t, $J_{3,4}$ = $J_{4,5}$ = 9.5 Hz, 1 H, 4A-H), 4.13 (d, $J_{6a,6b}$ = 12.1 Hz, 1 H, 6aB-H), 3.88–3.80 (m, 3 H, 3A-H, 5A-H, 6bB-H), 3.70, 3.30 (2 m, 2 H, CH_2-O), 3.10 (br. s, 1 H, 5B-H), 2.89 (m, 2 H, CH_2-N), 2.69–2.32 [m, 4 H, CH_2(Lev)], 1.92 [s, 3 H, CH_3(Lev)], 1.49–1.06 [m, 6 H, $(CH_2)_3$] ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 206.3 [CO(Lev)], 171.9, 167.7, 165.1, 164.2, 163.5 [CO(Lev, *N*-TCP, COOBn, Bz)], 156.4 [CO(Z)], 140.0, 139.8, 138.4, 137.7, 136.8 (Ar-C), 133.3 (Ar-CH), 129.9, 129.8, 129.4, 129.1, 128.7, 128.6, 128.5, 128.4, 128.2, 127.9, 127.4, 127.3, 126.4 (Ar-C, Ar-CH), 101.4 (C-1A), 100.9 (PhCH), 97.9 (C-1B), 80.4 (C-3A), 78.0 (C-4A), 74.7 (C-5A), 74.3 [CH_2(Bn)], 73.2 (C-2A), 72.7 (C-4B), 69.8 (CH_2-O), 68.9 (C-6B), 68.3 (C-3B), 67.5 [CH_2(Bn)], 66.6 [CH_2(Z)], 66.3 (C-5B), 52.1 (C-2B), 40.9 (CH_2-N), 37.9 [CH_2(Lev)], 29.6 (CH_2), 29.4 [CH_3(Lev)], 28.9 (CH_2), 28.1 [CH_2(Lev)], 23.1 (CH_2) ppm. HRMS: calcd. for $C_{66}H_{62}Cl_4N_2O_{18}Na$ $[M + Na]^+$ 1333.2649; found 1333.2604.

Benzyl [*N*-Benzyloxycarbonyl-5-aminopentyl 2-*O*-Benzoyl-3-*O*-benzyl-4-*O*-(2-deoxy-3-*O*-levulinoyl-2-tetrachlorophthalimido-β-D-galactopyranosyl)-β-D-glucopyranoside] Uronate (17): TFA (100 μL) was added to a solution of **14** (25 mg, 19 μmol) in CH_2Cl_2 (1 mL) at 0 °C. The solution was stirred for 2 h at 0 °C, then it was diluted with CH_2Cl_2, and washed with saturated $NaHCO_3$ aqueous solution and brine. The organic layer was dried ($MgSO_4$), filtered, and concentrated in vacuo. The residue was purified by column chromatography (toluene/acetone, 7:2) to give **17** (23 mg, 99%). TLC (toluene/acetone, 7:2): R_f = 0.14. $[\alpha]_D^{20}$ = –12 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.97 (m, 2 H, Ar), 7.55 (m, 1 H, Ar), 7.43–7.13 (m, 17 H, Ar), 5.59 (dd, $J_{2,3}$ = 11.3, $J_{3,4}$ = 3.1 Hz, 1 H, 3B-H), 5.28–5.13 [m, 4 H, 1B-H, 2A-H, CH_2(Bn)], 5.06 [m, 2 H, CH_2(Z)], 4.85 [d, 1 H, CH_2(Bn)], 4.66–4.55 [m, 3 H, CH_2(Bn), 2B-H, NH], 4.48 (d, $J_{1,2}$ = 7.4 Hz, 1 H, 1A-H), 4.25 (t, $J_{3,4}$ = $J_{4,5}$ = 9.3 Hz, 1 H, 4A-H), 4.13 (br. d, 1 H, 4B-H), 3.87 (d, 1 H, 5A-H), 3.82 (t, $J_{2,3}$ = 8.9 Hz, 1 H, 3A-H), 3.73 (m, 1 H, CH_2-O), 3.62 (m, 2 H, 6aB-H, 6bB-H), 3.34 (m, 2 H, CH_2-O, 5B-H), 2.91 (m, 2 H, CH_2-N), 2.66, 2.40 [2 m, 4 H, CH_2(Lev)], 2.03 [s, 3 H, CH_3(Lev)], 1.49–1.11 [m, 6 H, $(CH_2)_3$] ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 207.4 [CO(Lev)], 171.8, 167.6, 165.1, 164.1, 163.3 [CO(Lev, *N*-TCP, COOBn, Bz)], 156.4 [CO(Z)], 140.0, 139.8, 137.9, 136.8, 135.1 (Ar-C), 133.4 (Ar-CH), 129.8, 129.7, 129.6, 128.7, 128.6, 128.5, 128.3, 128.2, 128.0, 127.6, 127.3 (Ar-C, Ar-CH), 101.4 (C-1A), 97.0 (C-1B), 79.3 (C-3A), 76.9 (C-4A), 74.9 (C-5A), 73.7 (C-5B), 73.5 [CH_2(Bn)], 72.5 (C-2A), 70.1 (C-3B), 69.7 (CH_2-O), 67.4 [CH_2(Bn)], 67.2 (C-4B), 66.5 [CH_2(Z)], 62.7 (C-6B), 51.7 (C-2B), 40.8 (CH_2-N), 38.0 [CH_2(Lev)], 29.5 [CH_2, CH_3(Lev)], 28.8 (CH_2), 28.1 [CH_2(Lev)], 22.9 (CH_2) ppm. HRMS: calcd. for $C_{59}H_{58}Cl_4N_2O_{18}Na$ $[M + Na]^+$ 1245.2336; found 1245.2332.

Benzyl [*N*-Benzyloxycarbonyl-5-aminopentyl 2-*O*-Benzoyl-3-*O*-benzyl-4-*O*-(2-deoxy-3-*O*-levulinoyl-4,6-di-*O*-sulfo-2-tetrachlorophthalimido-β-D-galactopyranosyl)-β-D-glucopyranoside] Uronate (18): Compound **17** (13 mg, 11 μmol) and sulfur trioxide–trimethylamine complex (15 mg, 0.11 mmol) were dissolved in dry DMF (1.0 mL), and the mixture was heated at 100 °C for 40 min using microwave irradiation (28 W average power). The reaction vessel was cooled, and Et_3N (150 μL), MeOH (1 mL), and CH_2Cl_2 (1 mL) were added. The solution was loaded onto a Sephadex LH-20 chromatography column, which was eluted with CH_2Cl_2/MeOH (1:1) to give **18** as its triethylammonium salt (14 mg, 83%). TLC (CH_2Cl_2/MeOH, 9:2): R_f = 0.40. ^{1}H NMR (300 MHz, CD_3OD): δ = 7.98 (m, 2 H, Ar), 7.60 (m, 1 H, Ar), 7.50–7.05 (m, 17 H, Ar), 5.77 (dd, $J_{2,3}$ = 11.6, $J_{3,4}$ = 3.3 Hz, 1 H, 3B-H), 5.35 (d, $J_{1,2}$ = 8.3 Hz, 1 H, 1B-H), 5.29 [d, 1 H, CH_2(Bn)], 5.17 [d, 1 H, CH_2(Bn)], 5.06 (t, $J_{1,2}$ = 8.0, $J_{2,3}$ = 8.7 Hz, 1 H, 2A-H), 5.02 [m, 2 H, CH_2(Z)], 4.96 [d, 1 H, CH_2(Bn)], 4.86 (br. d, 1 H, 4B-H), 4.68 (d, 1 H, 1A-H), 4.56 [m, 2 H, CH_2(Bn), 2B-H], 4.45 (dd, $J_{5,6a}$ = 3.4, $J_{6a,6b}$ = 11.9 Hz, 1 H, 6aB-H), 4.22 (m, 2 H, 6bB-H, 4A-H), 4.11 (m, 2 H, 5A-H, 5B-H), 4.00 (t, $J_{3,4}$ = 9.2 Hz, 1 H, 3A-H), 3.69 (m, 1 H, CH_2-O), 3.42 (m, 1 H, CH_2-O), 3.19 (q, 12 H, Et_3NH^+), 2.82 [m, 3 H, CH_2-N, CH_2(Lev)], 2.60 [dt, 1 H, CH_2(Lev)], 2.39 [m, 2 H, CH_2(Lev)], 1.92 [s, 3 H, CH_3(Lev)], 1.44–1.08 [m, 24 H, $(CH_2)_3$, Et_3NH^+] ppm. ^{13}C NMR (75 MHz, CD_3OD, Significant data from HSQC experiment): δ = 102.2 (C-1A), 97.8 (C-1B), 79.8 (C-3A), 77.8 (C-4A), 74.9 (C-5A), 74.5 (C-5B), 74.2 [CH_2(Bn)], 73.7 (C-2A), 72.7 (C-4B), 70.6 (CH_2-O), 68.5 (C-3B), 68.4 (C-6B), 68.1 [CH_2(Bn)], 66.9 [CH_2(Z)], 52.9 (C-2B), 47.4 (Et_3NH^+), 41.3 (CH_2-N), 38.1 [CH_2(Lev)], 29.8 (CH_2), 29.6 (CH_2), 29.1 [CH_3(Lev)], 28.8

[CH_2(Lev)], 23.5 (CH_2), 8.7 (Et_3NH^+) ppm. MS (ESI): calcd. for $C_{59}H_{56}Cl_4N_2O_{24}S_2Na$ [M + Na]$^-$ 1403.1; found 1402.7. HRMS: calcd. for $C_{59}H_{56}Cl_4N_2O_{24}S_2$ [M]$^{2-}$ 690.0715; found 690.0709.

***N*-Benzyloxycarbonyl-5-aminopentyl 4-*O*-(2-Acetamido-2-deoxy-4,6-di-*O*-sulfo-β-D-galactopyranosyl)-3-*O*-benzyl-β-D-glucopyranosiduronic Acid (21):** H_2O_2 (30%; 0.52 mL) and an aqueous solution of LiOH (0.7 M; 0.32 mL) were added at –5 °C to a solution of **18** (21 mg, 13 μmol) in THF (1.4 mL). The mixture was stirred for 20 h at room temperature, then MeOH (1.4 mL) and NaOH (4 M aq.; 0.33 mL) were added. The mixture was stirred for 24 h at room temperature, then it was neutralized with Amberlite IR-120 (H^+) resin, filtered, and concentrated. The residue was dissolved in CH_2Cl_2/MeOH/Et_3N (1.0 mL/1.0 mL/0.1 mL) and purified by Sephadex LH-20 chromatography (CH_2Cl_2/MeOH, 1:1) to give compound **19** as its triethylammonium salt (16 mg, 86%). TLC (EtOAc/pyridine/H_2O/AcOH, 9:5:3:1): R_f = 0.27. ^{1}H NMR (300 MHz, CD_3OD): δ = 7.59–7.19 (m, 10 H, Ar), 5.06 [m, 3 H, CH_2(Z), CH_2(Bn)], 4.79 (br. d, 1 H, 4B-H), 4.72 [d, 1 H, CH_2(Bn)], 4.62 (d, $J_{1,2}$ = 8.3 Hz, 1 H, 1B-H), 4.45 (dd, $J_{5,6a}$ = 3.9, $J_{6a,6b}$ = 11.8 Hz, 1 H, 6aB-H), 4.41 (d, $J_{1,2}$ = 8.0 Hz, 1 H, 1A-H), 4.22 (m, 2 H, 2B-H, 6bB-H), 4.06 (br. t, 1 H, 4A-H), 3.96 (m, 1 H, 5B-H), 3.86 (m, 1 H, CH_2-O), 3.77 (dd, $J_{2,3}$ = 10.8, $J_{3,4}$ = 2.9 Hz, 1 H, 3B-H), 3.58 (m, 3 H, CH_2-O, 3A-H, 5A-H), 3.37 (t, $J_{2,3}$ = 8.0 Hz, 1 H, 2A-H), 3.19 (q, 24 H, Et_3NH^+), 3.11 (m, 2 H, CH_2-N), 1.66–1.38 [3 m, 6 H, $(CH_2)_3$], 1.29 (t, 36 H, Et_3NH^+) ppm. ^{13}C NMR (75 MHz, CD_3OD, Significant data from HSQC experiment): δ = 129.5, 128.9, 128.7, 128.3 (Ar-CH), 104.0 (C-1A), 100.8 (C-1B), 83.7 (C-3A), 78.9 (C-4A), 76.8 (C-4B), 75.4 [CH_2(Bn)], 74.5 (C-5B), 74.0 (C-2A), 72.8 (C-3B), 70.5 (CH_2-O), 68.6 (C-6B), 67.0 [CH_2(Z)], 55.3 (C-2B), 47.6 (Et_3NH^+), 41.3 (CH_2-N), 30.1, 30.0, 23.8 [$(CH_2)_3$], 8.9 (Et_3NH^+) ppm. MS (ESI): calcd. for $C_{40}H_{43}Cl_4N_2O_{22}S_2$ [M + 3H]$^-$ 1107.1; found 1106.7.

Ethylene diamine (76 μL, 1.1 mmol) was added to a solution of **19** (16 mg, 11 μmol) in dry DMF (1.3 mL) under an argon atmosphere, and the reaction mixture was subjected to microwave irradiation for 90 min at 100 °C. The reaction vessel was cooled under a stream of nitrogen, and the mixture was concentrated to dryness. The residue was purified by Sephadex LH-20 chromatography (CH_2Cl_2/MeOH, 1:1) to give **20**. TLC (EtOAc/pyridine/H_2O/AcOH, 9:5:3:1): R_f = 0.38. MS (ESI): calcd. for $C_{32}H_{42}N_2O_{19}S_2$ [M + H]$^{2-}$ 411.1; found 410.8.

Triethylamine (0.18 M solution in dry MeOH; 207 μL) and acetic anhydride (5 μL, 0.05 mmol) were added to a cooled solution of **20** (11 μmol) in dry MeOH (2.3 mL). The mixture was stirred for 2 h at 0 °C, then additional triethylamine (0.18 M solution in dry MeOH; 207 μL) and acetic anhydride (5 μL, 0.05 mmol) were added, and the reaction mixture was stirred for 1 h at room temperature. The mixture was purified by Sephadex LH-20 chromatography (CH_2Cl_2/MeOH, 1:1). The residue was converted into the sodium salt by elution from a column of Dowex 50WX4-Na^+ with MeOH/H_2O, 9:1 to give **21** (7.9 mg, 75% from **19**). TLC (EtOAc/pyridine/H_2O/AcOH, 9:5:3:1): R_f = 0.28. ^{1}H NMR (500 MHz, CD_3OD): δ = 7.54–7.19 (m, 10 H, Ar), 5.04 [m, 3 H, CH_2(Z), CH_2(Bn)], 4.78 (br. s, 1 H, 4B-H), 4.68 [m, 2 H, CH_2(Bn), 1B-H], 4.38 (dd, $J_{5,6a}$ = 5.0, $J_{6a,6b}$ = 11.3 Hz, 1 H, 6aB-H), 4.28 (d, $J_{1,2}$ = 7.3 Hz, 1 H, 1A-H), 4.16 (dd, $J_{5,6b}$ = 6.3 Hz, 1 H, 6bB-H), 4.05 (t, $J_{1,2}$ = $J_{2,3}$ = 9.5 Hz, 1 H, 2B-H), 3.99 (t, $J_{3,4}$ = $J_{4,5}$ = 9.1 Hz, 1 H, 4A-H), 3.96 (m, 1 H, 5B-H), 3.86 (m, 1 H, CH_2-O), 3.66 (m, 2 H, 5A-H, 3B-H), 3.52 (m, 1 H, CH_2-O), 3.44 (br. t, 1 H, 3A-H), 3.38 (br. t, 1 H, 2A-H), 3.11 (t, 2 H, CH_2-N), 2.04 (s, 3 H, NAc), 1.62, 1.51, 1.40 [3 m, 6 H, $(CH_2)_3$] ppm. ^{13}C NMR (125.5 MHz, CD_3OD, Significant data from HSQC experiment): δ = 104.1 (C-1A), 101.5 (C-1B), 83.8 (C-3A), 79.8 (C-4A), 78.0 (C-5A), 76.8 (C-4B), 75.6 [CH_2(Bn)], 74.0 (C-5B, C-2A), 73.5 (C-3B), 70.4 (CH_2-O), 67.8 (C-6B), 67.0 [CH_2(Z)], 54.4 (C-2B), 41.5 (CH_2-N), 30.4, 30.0, 23.8 [$(CH_2)_3$], 23.0 (NAc) ppm. MS (ESI): calcd. for $C_{34}H_{44}N_2O_{20}S_2$ [M + H]$^{2-}$ 432.1; found 431.8. HRMS: calcd. for $C_{34}H_{44}N_2O_{20}S_2$ [M + H]$^{2-}$ 432.0969; found 432.0956.

5-Aminopentyl 4-*O*-(2-Acetamido-2-deoxy-4,6-di-*O*-sulfo-β-D-galactopyranosyl)-β-D-glucopyranosiduronic Acid (15): A solution of **21** (7.9 mg, 8.5 μmol, as sodium salt) in H_2O/MeOH (2.7 mL/0.3 mL) was hydrogenated in the presence of $Pd(OH)_2$. After 24 h, the suspension was filtered through Celite, and the filtrate was concentrated. The residue was purified by Sephadex G-10 chromatography (H_2O/MeOH, 9:1) to give **15** as its sodium salt after lyophilization (6.0 mg, quantitative; 53% over six steps from **14**, 90% average yield per step). ^{1}H NMR (500 MHz, D_2O): δ = 4.72 (br. d, $J_{3,4}$ = 2.1 Hz, 1 H, 4B-H), 4.58 (d, $J_{1,2}$ = 7.6 Hz, 1 H, 1B-H), 4.47 (d, $J_{1,2}$ = 8.1 Hz, 1 H, 1A-H), 4.32 (dd, $J_{5,6a}$ = 3.3, $J_{6a,6b}$ = 11.3 Hz, 1 H, 6aB-H), 4.25 (dd, $J_{5,6b}$ = 8.7 Hz, 1 H, 6bB-H), 4.12 (dd, 1 H, 5B-H), 3.94–3.87 (m, 3 H, 2B-H, 3B-H, CH_2-O), 3.77 (m, 3 H, 4A-H, 5A-H, CH_2-O), 3.62 (t, $J_{2,3}$ = $J_{3,4}$ = 9.2 Hz, 1 H, 3A-H), 3.35 (t, 1 H, 2A-H), 3.00 (t, 2 H, CH_2-N), 2.05 (s, 3 H, NAc), 1.67, 1.46 [2 m, 6 H, $(CH_2)_3$] ppm. ^{13}C NMR (125.5 MHz, D_2O, Significant data from HSQC experiment): δ = 102.8 (C-1A), 102.2 (C-1B), 82.3 (C-4A), 77.2 (C-5A), 76.0 (C-4B), 74.9 (C-3A), 73.1 (C-2A), 72.9 (C-5B), 70.6 (CH_2-O), 70.5 (C-3B), 68.3 (C-6B), 53.0 (C-2B), 39.9 (CH_2-N), 28.6, 26.8 (CH_2, CH_2), 23.1 (NAc), 22.5 (CH_2) ppm. MS (ESI): calcd. for $C_{19}H_{33}N_2O_{18}S_2$ [M + 2H]$^-$ 641.1; found 640.8. HRMS: calcd. for $C_{19}H_{33}N_2O_{18}S_2$ [M + 2H]$^-$ 641.1188; found 641.1170.

Benzyl [*N*-Benzyloxycarbonyl-5-aminopentyl 2-*O*-Benzoyl-3-*O*-benzyl-4-*O*-(2-deoxy-3-*O*-levulinoyl-6-*O*-sulfo-2-tetrachlorophthalimido-β-D-galactopyranosyl)-β-D-glucopyranoside] Uronate (22): Compound **17** (27 mg, 22 μmol) and sulfur trioxide–trimethylamine complex (6.2 mg, 44 μmol) were dissolved in dry DMF (3.0 mL), and the mixture was heated at 50 °C for 30 min using microwave irradiation (15 W average power). The reaction vessel was cooled, and Et_3N (150 μL), MeOH (1 mL), and CH_2Cl_2 (1 mL) were added. The solution was purified by Sephadex LH-20 chromatography (CH_2Cl_2/MeOH, 1:1) and silica gel column chromatography (CH_2Cl_2/MeOH, 12:1 + 1% Et_3N) to give **22** as its triethylammonium salt (26 mg, 84%). TLC (CH_2Cl_2/MeOH, 10:1): R_f = 0.41. ^{1}H NMR (300 MHz, CD_3OD): δ = 7.97 (m, 2 H, Ar), 7.60 (m, 1 H, Ar), 7.47 (m, 2 H, Ar), 7.39–7.26 (m, 10 H, Ar), 7.13–7.03 (m, 5 H, Ar), 5.66 (dd, $J_{2,3}$ = 11.4, $J_{3,4}$ = 3.2 Hz, 1 H, 3B-H), 5.42 (d, $J_{1,2}$ = 8.5 Hz, 1 H, 1B-H), 5.30 [d, 1 H, CH_2(Bn)], 5.14 [d, 1 H, CH_2(Bn)], 5.08 (t, $J_{1,2}$ = 7.8, $J_{2,3}$ = 8.6 Hz, 1 H, 2A-H), 5.02 [m, 2 H, CH_2(Z)], 4.89 [d, 1 H, CH_2(Bn)], 4.68 (d, 1 H, 1A-H), 4.59 (dd, 1 H, 2B-H), 4.55 [d, 1 H, CH_2(Bn)], 4.23–4.08 (m, 5 H, 4A-H, 4B-H, 5A-H, 6aB-H, 6bB-H), 3.99 (t, 1 H, 3A-H), 3.81 (br. t, 1 H, 5B-H), 3.69 (m, 1 H, CH_2-O), 3.40 (m, 1 H, CH_2-O), 3.18 (q, 6 H, Et_3NH^+), 2.82 (m, 2 H, CH_2-N), 2.65 [m, 2 H, CH_2(Lev)], 2.38 [m, 2 H, CH_2(Lev)], 1.89 [s, 3 H, CH_3(Lev)], 1.44–1.10 [m, 15 H, $(CH_2)_3$, Et_3NH^+] ppm. ^{13}C NMR (75 MHz, CD_3OD, Significant data from HSQC experiment): δ = 134.4, 130.6, 129.4, 129.2, 129.0, 128.6, 128.5 (Ar-CH), 102.2 (C-1A), 97.9 (C-1B), 79.8 (C-3A), 77.7 (C-4A, C-5A), 75.3 (C-4B), 73.8 [C-5B, CH_2(Bn)], 73.7 (C-2A), 70.8 (C-3B), 70.6 (CH_2-O), 68.1 [CH_2(Bn)], 67.1 [CH_2(Z)], 66.2 (C-6B), 53.1 (C-2B), 47.7 (Et_3NH^+), 41.2 (CH_2-N), 38.2 [CH_2(Lev)], 30.3 (CH_2), 29.9 (CH_2), 29.1 [CH_3(Lev)], 28.7 [CH_2(Lev)], 23.8 (CH_2), 9.0 (Et_3NH^+) ppm. MS (ESI): calcd. for $C_{59}H_{57}Cl_4N_2O_{21}S$ [M]$^-$ 1301.2; found 1301.0. HRMS: calcd. for $C_{59}H_{57}Cl_4N_2O_{21}S$ [M]$^-$ 1301.1934; found 1301.2029.

***N*-Benzyloxycarbonyl-5-aminopentyl 4-*O*-(2-Acetamido-2-deoxy-6-*O*-sulfo-β-D-galactopyranosyl)-3-*O*-benzyl-β-D-glucopyranosiduronic Acid (25):** H_2O_2 (30%; 0.73 mL) and an aqueous solution of LiOH (0.7 M; 0.45 mL) were added at –5 °C to a solution of **22** (26 mg, 18 μmol) in THF (2.0 mL). The mixture was stirred for 20 h at room temperature, then MeOH (2.0 mL) and NaOH (4 M aq.; 0.46 mL) were added. The mixture was stirred for 24 h at room temperature, then the reaction mixture was neutralized with Amberlite IR-120 (H^+) resin, filtered, and concentrated. The residue was dissolved in CH_2Cl_2/MeOH/Et_3N (1.0 mL/1.0 mL/0.1 mL) and purified by Sephadex LH-20 chromatography (CH_2Cl_2/MeOH, 1:1) to give compound **23** as its triethylammonium salt (22 mg, 89%). TLC (EtOAc/pyridine/H_2O/AcOH, 9:5:3:1): R_f = 0.34. ^{1}H NMR (300 MHz, CD_3OD): δ = 7.54 (m, 2 H, Ar), 7.35–7.20 (m, 8 H, Ar), 5.06 [m, 2 H, CH_2(Z)], 5.04 [d, 1 H, CH_2(Bn)], 4.72 [d, 1 H, CH_2(Bn)], 4.68 (d, $J_{1,2}$ = 8.8 Hz, 1 H, 1B-H), 4.36 (d, $J_{1,2}$ = 7.6 Hz, 1 H, 1A-H), 4.29 (dd, $J_{5,6a}$ = 7.4, $J_{6a,6b}$ = 10.5 Hz, 1 H, 6aB-H), 4.23 (br. t, 1 H, 2B-H), 4.15 (dd, $J_{5,6b}$ = 5.8 Hz, 1 H, 6bB-H), 4.07 (t, $J_{3,4}$ = $J_{4,5}$ = 8.4 Hz, 1 H, 4A-H), 3.99–3.94 (m, 2 H, 4B-H, 5A-H), 3.85 (m, 1 H, CH_2-O), 3.76 (m, 1 H, 5B-H), 3.67 (m, 1 H, 3B-H), 3.54 (m, 2 H, CH_2-O, 3A-H), 3.38 (t, $J_{2,3}$ = 8.0 Hz, 1 H, 2A-H), 3.18 (q, 18 H, Et_3NH^+), 3.11 (m, 2 H, CH_2-N), 1.66–1.35 [3 m, 6 H, $(CH_2)_3$], 1.29 (t, 27 H, Et_3NH^+) ppm. ^{13}C NMR (75 MHz, CD_3OD, Significant data from HSQC experiment): δ = 129.4, 128.9, 128.4 (Ar-CH), 103.9 (C-1A), 100.7 (C-1B), 83.8 (C-3A), 78.7 (C-4A), 77.0 (C-5A), 75.4 [CH_2(Bn)], 74.6 (C-5B), 74.2 (C-2A), 74.0 (C-3B), 70.6 (CH_2-O), 68.5 (C-4B), 67.1 [CH_2(Z)], 66.7 (C-6B), 55.0 (C-2B), 47.4 (Et_3NH^+), 41.5 (CH_2-N), 30.3, 30.1, 23.8 [$(CH_2)_3$], 8.9 (Et_3NH^+) ppm. MS (ESI): calcd. for $C_{40}H_{42}Cl_4KN_2O_{19}S$ [M + H + K]$^-$ 1065.0; found 1065.0.

Ethylene diamine (111 μL, 1.65 mmol) was added to a solution of **23** (22 mg, 16 μmol) in dry DMF (1.0 mL) under an argon atmosphere, and the reaction mixture was subjected to microwave irradiation for 90 min at 100 °C. The reaction vessel was cooled, and the mixture was concentrated to dryness. The residue was purified by Sephadex LH-20 chromatography (CH_2Cl_2/MeOH, 1:1) to give **24**. TLC (EtOAc/pyridine/H_2O/AcOH, 12:5:3:1): R_f = 0.23. MS (ESI): calcd. for $C_{32}H_{43}N_2O_{16}S$ [M + H]$^-$ 743.2; found 743.2.

Triethylamine (0.36 M solution in dry MeOH; 150 μL) and acetic anhydride (7.8 μL, 83 μmol) were added to a cooled solution of **24** (16 μmol) in dry MeOH (1.5 mL). The mixture was stirred for 3 h at room temperature, then additional Et_3N (0.2 mL) was added, and the reaction mixture was purified by Sephadex LH-20 chromatography (CH_2Cl_2/MeOH, 1:1). The residue was converted into the sodium salt by elution from a column of Dowex 50WX4-Na^+ with MeOH/H_2O, 9:1 to give **25** (12 mg, 88% over two steps from **23**). TLC (EtOAc/pyridine/H_2O/AcOH, 12:5:3:1, two elutions): R_f = 0.41. ^{1}H NMR (400 MHz, CD_3OD): δ = 7.50–7.20 (m, 10 H, Ar), 5.06 [s, 2 H, CH_2(Z)], 5.02 [d, 1 H, CH_2(Bn)], 4.69 [d, 1 H, CH_2(Bn)], 4.62 (d, $J_{1,2}$ = 8.3 Hz, 1 H, 1B-H), 4.28 (d, $J_{1,2}$ = 6.9 Hz, 1 H, 1A-H), 4.25 (dd, $J_{5,6a}$ = 8.2, $J_{6a,6b}$ = 10.2 Hz, 1 H, 6aB-H), 4.10 (dd, $J_{5,6b}$ = 5.4 Hz, 1 H, 6bB-H), 4.03–3.93 (m, 2 H, 2B-H, 4A-H), 3.91 (br. s, 1 H, 4B-H), 3.86 (m, 1 H, CH_2-O), 3.74–3.65 (m, 2 H, 5B-H, 5A-H), 3.52 (m, 2 H, 3B-H, CH_2-O), 3.44 (t, $J_{2,3}$ = $J_{3,4}$ = 8.9 Hz, 1 H, 3A-H), 3.39 (t, 1 H, 2A-H), 3.11 (t, 2 H, CH_2-N), 2.06 (s, 3 H, NAc), 1.62, 1.51, 1.41 [3 m, 6 H, $(CH_2)_3$] ppm. ^{13}C NMR (100 MHz, CD_3OD, Significant data from HSQC experiment): δ = 128.9–128.1 (Ar-CH), 103.9 (C-1A), 101.2 (C-1B), 83.8 (C-3A), 79.7 (C-4A), 77.7 (C-5A), 75.2 [CH_2(Bn)], 74.5 (C-3B), 73.9 (C-2A), 73.8 (C-5B), 70.2 (CH_2-O), 68.2 (C-4B), 66.9 [CH_2(Z)], 66.2 (C-6B), 54.4 (C-2B), 41.3 (CH_2-N), 30.1, 29.8, 23.6 [$(CH_2)_3$], 22.6 (NAc) ppm. MS (ESI): calcd. for $C_{34}H_{45}N_2O_{17}S$ [M + H]$^-$ 785.2; found 785.1. HRMS: calcd. for $C_{34}H_{44}N_2O_{17}S$ [M]$^{2-}$ 392.1185; found 392.1180.

5-Aminopentyl 4-*O*-(2-Acetamido-2-deoxy-6-*O*-sulfo-β-D-galactopyranosyl)-β-D-glucopyranosiduronic Acid (16): A solution of **25** (10 mg, 12 μmol, as sodium salt) in H_2O/MeOH (3.6 mL/0.4 mL) was hydrogenated in the presence of $Pd(OH)_2$. After 24 h, the suspension was filtered through Celite, and the filtrate was concentrated. The residue was purified by Sephadex G-10 chromatography (H_2O/MeOH, 9:1) to give **16** as its sodium salt after lyophilization (7.4 mg, quantitative; 66% over five steps from **17**, 92% average yield per step). ^{1}H NMR (500 MHz, D_2O): δ = 4.53 (d, $J_{1,2}$ = 8.5 Hz, 1 H, 1B-H), 4.48 (d, $J_{1,2}$ = 8.1 Hz, 1 H, 1A-H), 4.25 (m, 2 H, 6aB-H, 6bB-H), 4.00 (m, 2 H, 4B-H, 5B-H), 3.92 (m, 2 H, 2B-H, CH_2-O), 3.74 (m, 4 H, 3B-H, 4A-H, 5A-H, CH_2-O), 3.63 (t, $J_{2,3}$ = $J_{3,4}$ = 8.7 Hz, 1 H, 3A-H), 3.36 (t, 1 H, 2A-H), 3.00 (t, 2 H, CH_2-N), 2.06 (s, 3 H, NAc), 1.68, 1.47 [2 m, 6 H, $(CH_2)_3$] ppm. ^{13}C NMR (125.5 MHz, D_2O, Significant data from HSQC experiment): δ = 102.7 (C-1A), 102.0 (C-1B), 81.6 (C-4A), 77.1 (C-5A), 74.6 (C-3A), 73.2 (C-5B), 73.1 (C-2A), 71.2 (C-3B), 70.6 (CH_2-O), 67.9 (C-4B), 67.6 (C-6B), 52.5 (C-2B), 39.8 (CH_2-N), 28.5, 26.9 (CH_2, CH_2), 23.0 (NAc), 22.4 (CH_2) ppm. MS (ESI): calcd. for $C_{19}H_{33}N_2O_{15}S$ [M + H]$^-$ 561.1613; found 561.0. HRMS: calcd. for $C_{19}H_{33}N_2O_{15}S$ [M + H]$^-$ 561.1619; found 561.1599.

4-Methoxyphenyl 3-*O*-(Benzyl 2-*O*-Benzoyl-3-*O*-benzyl-4-*O*-levulinoyl-β-D-glucopyranosyluronate)-2-deoxy-4,6-di-*O*-levulinoyl-2-trifluoroacetamido-β-D-galactopyranoside (29): An excess of $(HF)_n$·Py (5.5 mL) was added to a solution of **28** (1.23 g, 1.14 mmol) in dry THF (25 mL) at 0 °C under an argon atmosphere. After 24 h at 0 °C, the mixture was diluted with CH_2Cl_2 and washed with H_2O and saturated $NaHCO_3$ solution until neutral pH. The organic layer was dried ($MgSO_4$), filtered, and concentrated in vacuo to give the corresponding diol, which was used in the next step without further purification [TLC (toluene/EtOAc, 1:4): R_f = 0.46].

LevOH (2.32 mL, 22.8 mmol) was added to a solution of 1,3-dicyclohexylcarbodiimide (2.35 g, 11.4 mmol) in CH_2Cl_2 (20 mL) at 0 °C. The mixture was stirred for 5 min at room temperature, then the mixture was cooled, filtered, and concentrated to give levulinic anhydride quantitatively (Lev_2O, 11.4 mmol).

A solution of the diol (1.14 mmol) in dry pyridine (30 mL) was added to a flask containing Lev_2O (11.4 mmol) and DMAP (140 mg, 1.14 mmol) under an argon atmosphere. The mixture was stirred for 5 h at room temperature, then the reaction mixture was diluted with CH_2Cl_2 and washed with HCl (1 M aq.), saturated aqueous $NaHCO_3$, and H_2O. The organic layers were dried ($MgSO_4$), filtered, and concentrated in vacuo. The residue was purified by column chromatography (toluene/EtOAc, 2:1) to give **29** (950 mg, 83%). TLC (toluene/EtOAc, 2:1): R_f = 0.37. $[a]_D^{20}$ = +20 (c = 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.94 (m, 2 H, Ar), 7.59 (m, 1 H, Ar), 7.44 (m, 2 H, Ar), 7.39–7.30 (m, 5 H, Ar), 7.13–7.07 (m, 5 H, Ar), 6.89 (m, 2 H, Ar), 6.77 (m, 2 H, Ar), 6.69 (br. s, 1 H, N*H*), 5.47 (d, $J_{3,4}$ = 2.6 Hz, 1 H, 4A-H), 5.32 [pt (pseudotriplet), 1 H, 4B-H], 5.28 (pt, 1 H, 2B-H), 5.19–5.11 [m, 3 H, 1A-H and CH_2(Bn)], 4.79 (d, $J_{1,2}$ = 7.5 Hz, 1 H, 1B-H), 4.61–4.52 [m, 3 H, 3A-H and CH_2(Bn)], 4.15–4.09 (m, 2 H, 2 6A-H), 4.07 (d, $J_{4,5}$ = 9.6 Hz, 1 H, 5B-H), 3.89–3.80 (m, 3 H, 5A-H, 3B-H and 2A-H), 3.75 (s, 3 H, OCH_3), 2.80–2.20 [m, 12 H, 3 OC-O$(CH_2)_2$], 2.15 (s, 3 H, $COCH_3$), 2.14 (s, 3 H, $COCH_3$), 2.10 (s, 3 H, $COCH_3$) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 206.84 [CO(Lev)], 206.81 [CO(Lev)], 206.1 [CO(Lev)], 172.3 (CO), 171.5 (CO), 171.2 (CO), 166.9 (CO), 165.0 (CO), 157.6 (q, $J_{C,F}$ = 38.7 Hz, *C*OCF$_3$), 155.9 (Ar), 151.0 (Ar), 137.4–114.3 (Ar-C and Ar-CH), 115.5 (q, $J_{C,F}$ = 289.0 Hz, CO*C*F$_3$), 100.1 (C-1B), 98.9 (C-1A), 79.2

(C-3B), 74.2 [CH_2(Bn)], 73.2 (C-3A), 72.8 (C-5B), 72.6 (C-2B), 71.6 (C-5A), 70.8 (C-4B), 68.7 (C-4A), 67.9 [CH_2(Bn)], 62.3 (C-6A), 55.7 (OCH_3), 54.6 (C-2A), 38.2 [$OCO(CH_2)_2$], 38.0 [$OCO(CH_2)_2$], 37.7 [$OCO(CH_2)_2$], 29.9 ($COCH_3$), 29.8 (2 $COCH_3$), 28.0 [$OCO(CH_2)_2$], 27.9 [$OCO(CH_2)_2$], 27.8 [$OCO(CH_2)_2$] ppm. HRMS: calcd. for $C_{57}H_{60}F_3NNaO_{20}$ $[M + Na]^+$ 1158.3558; found 1158.3596.

3-*O*-(Benzyl 2-*O*-Benzoyl-3-*O*-benzyl-4-*O*-levulinoyl-β-D-glucopyranosyluronate)-2-deoxy-4,6-di-*O*-levulinoyl-2-trifluoroacetamido-α,β-D-galactopyranose (30): CAN (0.44 M solution in H_2O; 7.6 mL) was added to a solution of **29** (950 mg, 0.84 mmol) in CH_2Cl_2/MeCN (1:2; 22.8 mL), and the mixture was stirred vigorously for 1 h at room temperature. It was then diluted with EtOAc, and washed with H_2O, saturated aqueous $NaHCO_3$, and H_2O. The organic phase was dried ($MgSO_4$), filtered, and concentrated to dryness. The residue was purified by column chromatography (toluene/acetone, 3:1) to give **30** (695 mg, 81%) as a mixture of α/β anomers. TLC (toluene/acetone, 3:2): R_f = 0.44 and 0.31. ^{1}H NMR (500 MHz, $CDCl_3$, data for α anomer): δ = 7.94 (m, 2 H, Ar), 7.57 (m, 1 H, Ar), 7.44–7.32 (m, 7 H, Ar), 7.15–7.05 (m, 5 H, Ar), 6.69 (d, $J_{2,NH}$ = 8.7 Hz, 1 H, N*H*), 5.39 (d, $J_{3,4}$ = 2.3 Hz, 1 H, 4A-H), 5.31–5.25 (m, 3 H, 1A-H, 2B-H and 4B-H), 5.19–5.11 [2 d, J_{gem} = 11.9 Hz, 2 H, CH_2(Bn)], 4.81 (d, $J_{1,2}$ = 7.7 Hz, 1 H, 1B-H), 4.55 [2 d, J_{gem} = 11.6 Hz, 2 H, CH_2(Bn)], 4.40–4.32 (m, 2 H, 2A-H and 5A-H), 4.27–4.20 (m, 2 H, 6aA-H and 3A-H), 4.05 (d, $J_{4,5}$ = 9.7 Hz, 1 H, 5B-H), 3.94 (dd, $J_{5,6b}$ = 8.8, $J_{6a,6b}$ = 11.4 Hz, 1 H, 6bA-H), 3.82 (pt, 1 H, 3B-H), 2.84–2.21 [m, 12 H, 3 $OCO(CH_2)_2$], 2.16 (s, 3 H, $COCH_3$), 2.10 (s, 3 H, $COCH_3$), 2.09 (s, 3 H, $COCH_3$) ppm. ^{13}C NMR (125 MHz, $CDCl_3$, data for α anomer): δ = 208.8 [CO(Lev)], 206.9 [CO(Lev)], 206.0 [CO(Lev)], 172.2 (CO), 171.8 (CO), 171.2 (CO), 166.8 (CO), 165.0 (CO), 157.1 (q, *C*OCF_3), 137.3–127.8 (Ar-C and Ar-CH), 115.7 (q, CO*C*F_3), 99.6 (C-1B), 91.4 (C-1A), 79.3 (C-3B), 74.2 [CH_2(Bn)], 73.0 (C-5B), 72.2 (C-2B), 72.0 (C-3A), 71.0 (C-4B),68.9 (C-4A), 68.0 [CH_2(Bn)], 67.0 (C-5A), 63.0 (C-6A), 50.1 (C-2A), 38.5 [$OCO(CH_2)_2$], 38.1 [$OCO(CH_2)_2$], 37.7 [$OCO(CH_2)_2$], 30.0 ($COCH_3$), 29.9 ($COCH_3$), 29.8 ($COCH_3$), 28.3 [$OCO(CH_2)_2$], 28.0 [$OCO(CH_2)_2$], 27.7 [$OCO(CH_2)_2$] ppm. HRMS: calcd. for $C_{50}H_{54}NO_{19}NaF_3$ $[M + Na]^+$ 1052.3140; found 1052.3175.

***O*-[3-*O*-(Benzyl 2-*O*-Benzoyl-3-*O*-benzyl-4-*O*-levulinoyl-β-D-glucopyranosyluronate)-2-deoxy-4,6-di-*O*-levulinoyl-2-trifluoroacetamido-α,β-D-galactopyranosyl] Trichloroacetimidate (31):** Compound **30** (120 mg, 0.11 mmol) was dissolved in dry CH_2Cl_2 (3 mL), and Cl_3CCN (234 μL, 2.3 mmol) and DBU (0.066 M solution in CH_2Cl_2; 261 μL) were added. The mixture was stirred at room temperature for 5 h, then it was concentrated in vacuo. Flash chromatography on silica gel (toluene/acetone, 5:1 + 1% Et_3N) gave **31** (95 mg, 70%) as an α/β mixture. TLC (toluene/acetone, 3:2): R_f = 0.65 and 0.48. ^{1}H NMR (500 MHz, $CDCl_3$, data for α anomer): δ = 8.71 [s, 1 H, N*H*(TCA)], 7.96 (m, 2 H, Ar), 7.59 (m, 1 H, Ar), 7.44 (m, 2 H, Ar), 7.37 (m, 5 H, Ar), 7.13–7.05 (m, 5 H, Ar), 7.00 [br. d, $J_{NH,2}$ = 7.3 Hz, 1 H, N*H*(TFA)], 6.54 (d, $J_{1,2}$ = 3.4 Hz, 1 H, 1 H, 1A-H), 5.55 (br. d, 1 H, 4A-H), 5.35 (pt, 1 H, 2B-H), 5.23 (pt, 1 H, 4B-H), 5.18–5.06 [2 d, J_{gem} = 12.1 Hz, 2 H, CH_2(Bn)], 4.93 (d, $J_{1,2}$ = 7.9 Hz, 1 H, 1B-H), 4.62–4.51 [m, 3 H, 2A-H and CH_2(Bn)], 4.35 (dd, $J_{3,4}$ = 2.9, $J_{2,3}$ = 11.0 Hz, 1 H, 3A-H), 4.28 (m, 1 H, 5A-H), 4.12–4.04 (m, 3 H, 5B-H and 2 6A-H), 3.85 (pt, 1 H, 3B-H), 2.74–2.16 [m, 12 H, 3 $OCO(CH_2)_2$], 2.14 (s, 3 H, $COCH_3$), 2.10 (s, 3 H, $COCH_3$), 2.03 (s, 3 H, $COCH_3$) ppm.

4-Methoxyphenyl *O*-(Benzyl 2-*O*-Benzoyl-3-*O*-benzyl-4-*O*-levulinoyl-β-D-glucopyranosyluronate)-(1→3)-*O*-(2-deoxy-4,6-di-*O*-levulinoyl-2-trifluoroacetamido-β-D-galactopyranosyl)-(1→4)-*O*-(benzyl 2-*O*-Benzoyl-3-*O*-benzyl-β-D-glucopyranosyluronate)-(1→3)-2-deoxy-4,6-*O*-di-*tert*-butylsilylene-2-trifluoroacetamido-β-D-galactopyranoside (33): Donor **31** (143 mg, 0.12 mmol) and acceptor **32** (67 mg, 0.07 mmol) were coevaporated with toluene, concentrated in vacuo and dissolved in dry CH_2Cl_2 (3 mL) in the presence of freshly activated 4 Å molecular sieves. The mixture was stirred for 10 min at 0 °C, then TMSOTf (0.09 M solution in dry CH_2Cl_2; 264 μL) was added under an argon atmosphere. The mixture was stirred for 30 min at 0 °C, then it was neutralized with Et_3N, filtered, and concentrated to dryness. The residue was purified by column chromatography (toluene/acetone, 5:1) to give **33** (97 mg, 71%). TLC (toluene/EtOAc, 2:1): R_f = 0.34. $[\alpha]_D^{20}$ = +11 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.96 (m, 2 H, Ar), 7.91 (m, 2 H, Ar), 7.57 (m, 2 H, Ar), 7.46–7.29 (m, 14 H, Ar), 7.15–7.08 (m, 10 H, Ar), 6.90 (m, 2 H, Ar), 6.84 (d, $J_{2,NH}$ = 6.9 Hz, 1 H, N*H*), 6.78 (m, 2 H, Ar), 6.52 (d, $J_{2,NH}$ = 8.7 Hz, 1 H, N*H*), 5.37–5.33 (m, 2 H, 1A-H and 4D-H), 5.27–5.15 [m, 8 H, 1B-H, 2B-H, 4C-H, 2D-H and 2 CH_2(Bn)], 4.78 [d, J_{gem} = 11.1 Hz, 1 H, CH_2(Bn)], 4.73 (d, $J_{1,2}$ = 7.4 Hz, 1 H, 1D-H), 4.61–4.52 [m, 3 H, 4A-H and CH_2(Bn)], 4.46 [d, J_{gem} = 11.1 Hz, 1 H, CH_2(Bn)], 4.33 (dd, $J_{2,3}$ = 11.1, $J_{3,4}$ = 1.9 Hz, 1 H, 3A-H), 4.15–4.08 (m, 3 H, 1C-H, 5D-H and 6A-H), 4.05–4.02 (m, 2 H, 4B-H and 6A-H), 3.96–3.81 (m, 6 H, 2A-H, 2C-H, 2 6C-H 5B-H and 3D-H), 3.75 (s, 3 H, OCH_3), 3.69 (m, 1 H, 3C-H), 3.63 (m, 1 H, 3B-H), 3.34 (m, 2 H, 5A-H and 5C-H), 2.75–2.21 [m, 12 H, 3 $OCO(CH_2)_2$], 2.18 (s, 3 H, $COCH_3$), 2.11 (s, 3 H, $COCH_3$), 2.07 (s, 3 H, $COCH_3$), 1.04 [s, 9 H, $C(CH_3)_3$], 0.99 [s, 9 H, $C(CH_3)_3$] ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 207.1 [CO(Lev)], 206.6 [CO(Lev)], 206.0 [CO(Lev)], 172.2 (CO), 171.4 (CO), 171.2 (CO), 168.6–164.9 (4 CO), 157.6 (2 q, 2 *C*OCF_3), 156.0–114.5 (Ar-C and Ar-CH), 117.9 (2 q, 2 CO*C*F_3), 100.2 (C-1B), 99.8, 99.7 (C-1C and C-1D), 99.3 (C-1A), 80.1 (C-3B), 79.2 (C-3D), 77.8 (C-4B), 75.4 (C-3A), 75.1 [CH_2(Bn)], 74.3, 74.2, 74.1, 73.2, 73.0 [C-3C, C-5B, CH_2(Bn), C-4A, C-5D], 72.5, 72.4 [2 C: C-2B or C-4C or C-2D or CH_2(Bn)], 71.4, 71.1 (C-5A and C-5C), 70.9 (C-4D), 68.2, 68.1, 67.9 [3 C: CH_2(Bn) or C-2B or C-4C or C-2D], 67.0 (C-6A), 61.5 (C-6C), 55.7 (OCH_3), 54.0, 53.0 (C-2A and C-2C), 38.1 [$OCO(CH_2)_2$], 38.0 [$OCO(CH_2)_2$], 37.7 [$OCO(CH_2)_2$], 29.9 ($COCH_3$), 29.8 ($COCH_3$), 29.7 ($COCH_3$), 28.1 [$OCO(CH_2)_2$], 27.9 [$OCO(CH_2)_2$], 27.7 [$OCO(CH_2)_2$], 27.6, 27.5, 27.5 [$C(CH_3)_3$], 23.3, 20.8 [$C(CH_3)_3$] ppm. HRMS: calcd. for $C_{100}H_{110}N_2O_{32}F_6NaSi$ $[M + Na]^+$ 2015.6607; found 2015.6607.

4-Methoxyphenyl *O*-(3-*O*-Benzyl-2,4-di-*O*-sulfo-β-D-glucopyranosyluronic Acid)-(1→3)-*O*-(2-acetamido-2-deoxy-4,6-di-*O*-sulfo-β-D-galactopyranosyl)-(1→4)-*O*-(3-*O*-benzyl-2-*O*-sulfo-β-D-glucopyranosyluronic Acid)-(1→3)-2-acetamido-2-deoxy-4,6-di-*O*-sulfo-β-D-galactopyranoside (37): An excess of $(HF)_n$·Py (102 μL, 3.8 mmol) was added at 0 °C under an argon atmosphere to a solution of **33** (39 mg, 0.02 mmol) in dry THF (1.0 mL). After 24 h at 0 °C, the mixture was diluted with CH_2Cl_2, and then washed with H_2O and saturated $NaHCO_3$ solution until it reached neutral pH. The organic layer was dried ($MgSO_4$), filtered, and concentrated in vacuo. The residue was purified by column chromatography (toluene/EtOAc, 2:3) to give **34** (27 mg, 75%). TLC (toluene/EtOAc, 1:2): R_f = 0.36. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.96 (m, 2 H, Ar), 7.86 (m, 2 H, Ar), 7.56 (m, 2 H, Ar), 7.46–7.33 (m, 14 H, Ar), 7.13–7.06 (m, 10 H, Ar), 6.86 (m, 2 H, Ar), 6.74 (m, 2 H, Ar), 5.34–5.11 [m, 9 H, 4D-H, 2D-H, 1A-H, H2B, 4C-H and CH_2(Bn)], 4.75 [m, 3 H, 1B-H, 1D-H and CH_2(Bn)], 4.60–4.49 [m, 4 H, 1C-H and CH_2(Bn)], 4.38 (br. s, 1 H, 3A-H), 4.15 (br. s, 1 H, 4B-H), 4.08–3.97 (m, 4 H, 4A-H, 5D-H, 5B-H and 3C-H), 3.90 (m, 3 H, 2C-H and 2 6A-H or 6C-H), 3.82 (m, 3 H, 2A-H, 3D-H and 6A-H or 6C-H), 3.72 (m, 4 H, 3B-H and OCH_3), 3.56 (m, 3 H, 5A-H, 5C-H and 6A-H or 6C-H), 2.74–2.17 [m, 12 H, 3 $OCO(CH_2)_2$],

2.12 (s, 3 H, $COCH_3$), 2.10 (s, 3 H, $COCH_3$), 2.06 (s, 3 H, $COCH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, selected data from HSQC experiment): δ = 100.1 (C-1B), 99.7 (C-1D), 99.6 (C-1C), 98.7 (C-1A), 79.3 (C-3B), 79.1 (C-3D), 77.5 (C-3A), 77.3 (C-4B), 74.5 [CH_2(Bn)], 74.1 [CH_2(Bn)], 74.1 (C-5B or C-5D), 74.0 (C-5A or C-5C), 73.9 (C-3C), 72.7 (C-5B or C-5D), 72.4 (C-2B, C-4C), 71.0 (C-5A or C-5C), 70.7 (C-4D), 68.3 (C-4A), 68.0 [C-2D, 2 CH_2(Bn)], 62.6 (C-6A or C-6C), 61.7 (C-6A or C-6C), 55.7 ($CO\mathit{C}H_3$), 54.1 (C-2A), 53.2 (C-2C) ppm. HRMS: calcd. for $C_{92}H_{94}F_6N_2Na_2O_{32}$ $[M + 2Na]^{2+}$ 949.2739; found 949.2735.

H_2O_2 (30%; 0.26 mL) and a solution of LiOH (0.7 M; 0.16 mL) were added at –5 °C to a solution of **34** (12 mg, 6.5 μmol) in THF (1.0 mL). The mixture was stirred for 24 h at room temperature, then MeOH (1 mL) and a solution of NaOH (4 M; 0.33 mL) were added. The mixture was stirred for 3 d at room temperature, then it was neutralized with Amberlite IR-120 (H^+) resin, filtered, and concentrated to give **35**. MS (ESI): calcd. for $C_{45}H_{56}N_2NaO_{22}$ $[M + Na]^-$ 999.3; found 999.4.

Et_3N (12 μL, 85 μmol) and Ac_2O (12 μL, 129 μmol) were added to a cooled (0 °C) solution of **35** (6.5 μmol) in dry MeOH (2.0 mL). The mixture was stirred for 3 h at room temperature, then triethylamine (0.3 mL) was added, and the mixture was coevaporated with toluene and methanol. The residue was purified by Sephadex LH-20 chromatography (MeOH/CH_2Cl_2, 1:1) to give **36** as its triethylammonium salt. The sodium salt of **36** (6.2 mg, 90%) was obtained by treatment with Amberlite IR-120 (H^+) resin in MeOH (pH ca. 3), followed by filtration, treatment with NaOH (0.04 M; pH ca. 7), and concentration. ^1H NMR (500 MHz, [D$_4$]methanol, data for sodium salt): δ = 7.58 (m, 2 H, Ar), 7.44 (m, 2 H, Ar), 7.34–7.20 (m, 6 H, Ar), 6.98 (m, 2 H, Ar), 6.82 (m, 2 H, Ar), 5.05 [d, J_{gem} = 10.3 Hz, 1 H, CH_2(Bn)], 4.93 (d, $J_{1,2}$ = 8.5 Hz, 1 H, 1A-H), 4.88 [m, 2 H, CH_2(Bn)], 4.72 [d, J_{gem} = 10.3 Hz, 1 H, CH_2(Bn)], 4.62 (d, $J_{1,2}$ = 8.5 Hz, 1 H, 1C-H), 4.43 (m, 2 H, 1B-H and 1D-H), 4.27 (dd, $J_{1,2}$ = 8.5, $J_{2,3}$ = 10.7 Hz, 1 H, 2A-H), 4.19–4.12 (m, 3 H, 2C-H, 4C-H and 4A-H), 3.96 (m, 1 H, 4B-H), 3.86–3.76 (m, 4 H, 3A-H and 3 6A-H or 6C-H), 3.74 (s, 3 H, OCH_3), 3.72–3.56 (m, 6 H, 5B-H, 6A-H or 6C-H, 3C-H, 5A-H or 5C-H, 4D-H, and 5D-H), 3.51 (m, 1 H, 5A-H or 5C-H), 3.46 (m, 2 H, 2B-H and 3B-H), 3.41 (m, 2 H, 2D-H and 3D-H), 2.05 (s, 3 H, NHCO$\mathit{C}H_3$), 2.05 (s, 3 H, NHCO$\mathit{C}H_3$) ppm. ^{13}C NMR (100 MHz, [D$_4$]methanol, selected data from HSQC experiment): δ = 128.5–113.7 (Ar), 104.2 (C-1B and C-1D), 100.6 (C-1A), 100.0 (C-1C), 84.1 (C-3D), 82.6 (C-3C), 82.5 (C-3B), 80.6 (C-3A), 77.6 (C-4B), 76.4 (C-5B), 75.8 (C-5A or C-5C), 75.2 (2 C: C-4D or C-5D or C-5A or C-5C), 75.0 [CH_2(Bn)], 74.0 [CH_2(Bn)], 73.0 (C-2D), 72.7 (C-2B), 72.0 (C-4D or C-5D or C-5A or C-5C), 67.6 (C-4A and C-4C), 61.1 (C-6A and C-6C), 54.4 ($CO\mathit{C}H_3$), 51.5 (C-2C), 51.2 (C-2A), 22.1 (NHCO$\mathit{C}H_3$), 21.6 (NHCO$\mathit{C}H_3$) ppm. HRMS: calcd. for $C_{49}H_{60}N_2O_{24}$ $[M]^{2-}$ 530.1773; found 530.1775.

Compound **36** (6 mg, 5.4 μmol) and sulfur trioxide–trimethylamine complex (26 mg, 0.19 mmol) were dissolved in dry DMF (1.5 mL), and the mixture was heated at 100 °C for 2 h using microwave irradiation (20 W average power). The reaction vessel was cooled, and Et_3N (150 μL) and MeOH (1 mL) were added. The solution was loaded onto a Sephadex LH-20 chromatography column, which was eluted with MeOH to give **37** as its triethylammonium salt. The residue was converted into the sodium salt by elution from a column of Dowex 50WX4-Na^+ with MeOH/H_2O, 9:1 (5 mg, 56%). ^1H NMR (500 MHz, D_2O, 40 °C, data for sodium salt): δ = 7.62 (m, 2 H, Ar), 7.50–7.36 (m, 8 H, Ar), 7.12 (m, 2 H, Ar), 7.00 (m, 2 H, Ar), 5.31 (d, $J_{1,2}$ = 8.5 Hz, 1 H, 1A-H), 4.96 (m, 2 H, 4A-H and 4C-H), 4.93–4.85 [m, 4 H, 1B-H or 1D-H, 4D-H and CH_2(Bn)], 4.80–4.71 [m, 4 H, 1C-H, 1D-H or 1B-H, and CH_2(Bn)], 4.41 (m, 2 H, 2B-H and 2D-H), 4.36–4.23 (m, 5 H, 3D-H or 5D-H, 3A-H and 3 6A-H or 6C-H), 4.20 (m, 2 H, 3D-H or 5D-H, and 5A-H or 5C-H), 4.15 (m, 2 H, 4B-H and 3C-H), 4.10 (m, 1 H, 6A-H or 6C-H), 3.99 (m, 2 H, 2C-H and 2A-H), 3.93 (m, 1 H, 5A-H or 5C-H), 3.88 (pt, 1 H, 3B-H), 3.83 (s, 3 H, OCH_3), 3.81 (m, 1 H, 5B-H), 2.09 (NHCO$\mathit{C}H_3$), 2.08 (NHCO$\mathit{C}H_3$) ppm. ^{13}C NMR (125 MHz, D_2O, 40 °C, selected data from HSQC experiment): δ = 130.6–116.4 (Ar), 103.8 (C-1D or C-1B), 102.4 (C-1B or C-1D), 101.6 (C-1A), 101.4 (C-1C), 81.6 (C-3B), 80.0 (C-2B and 2D), 80.0 (C-5A or C-5C or C-3D or C-5D) 79.5 (C-3D or C-5D), 78.7 (C-5B), 78.6 (C-3C and C-4B), 77.9 (C-3A), 77.2 (C-4D), 76.9 (C-4A and C-4C), 75.1 [CH_2(Bn)], 74.2 [CH_2(Bn)], 74.1 (C-5A or C-5C or C-3D or C-5D), 73.4 (C-5A or C-5C), 69.3 (C-6A or C-6C), 68.6 (C-6A or C-6C), 57.2 (OCH_3), 53.9 (C-2A and C-2C), 23.9 (2 NHCO$\mathit{C}H_3$) ppm.

4-Methoxyphenyl *O*-(2,4-Di-*O*-sulfo-β-D-glucopyranosyluronic Acid)-(1→3)-*O*-(2-acetamido-2-deoxy-4,6-di-*O*-sulfo-β-D-galactopyranosyl)-(1→4)-*O*-(2-*O*-sulfo-β-D-glucopyranosyluronic Acid)-(1→3)-2-acetamido-2-deoxy-4,6-di-*O*-sulfo-β-D-galactopyranoside (38): A solution of **37** (4.0 mg, 2.5 μmol, sodium salt) in H_2O/MeOH (3.6 mL/0.4 mL) was hydrogenated at 1.5 bar pressure in the presence of $Pd(OH)_2$ (12 mg). After 24 h, the suspension was filtered through Celite, and the filtrate was concentrated to give **38** after lyophilization (3.4 mg, 97%). ^1H NMR (500 MHz, D_2O, data for sodium salt): δ = 7.10 (m, 2 H, Ar), 6.99 (m, 2 H, Ar), 5.22 (d, $J_{1,2}$ = 8.5 Hz, 1 H, 1A-H), 4.95 (d, $J_{3,4}$ = 2.6 Hz, 1 H, 4A-H), 4.93 (d, $J_{3,4}$ = 2.4 Hz, 1 H, 4C-H), 4.77 (m, 2 H, 1C-H and 1D-H), 4.71 (d, $J_{1,2}$ = 7.9 Hz, 1 H, 1B-H), 4.51 (pt, 1 H, 4D-H), 4.36–4.31 (m, 2 H, 2 6A-H or 6C-H), 4.28–4.21 (m, 6 H, 2 6A-H or 6C-H, 5A-H or 5C-H, 2D-H, 3A-H, and 2B-H), 4.16–4.08 (m, 3 H, 3C-H, 5A-H or 5C-H, and 2A-H), 4.03 (pt, 1 H, 3D-H), 3.98 (d, $J_{4,5}$ = 8.5 Hz, 1 H, 5D-H), 3.93 (m, 2 H, 4B-H and 2C-H), 3.85–3.81 (m, 4 H, 3B-H and OCH_3), 3.72 (d, $J_{4,5}$ = 9.6 Hz, 1 H, 5B-H), 2.07 (NHCO$\mathit{C}H_3$), 2.06 (NHCO$\mathit{C}H_3$) ppm. ^{13}C NMR (125 MHz, D_2O, selected data from HSQC experiment): δ = 119.6 (Ar), 116.2 (Ar), 103.8 (C-1B), 102.9 (C-1D), 102.6 (C-1C), 101.7 (C-1A), 81.5 (C-4B), 80.7 (C-2B and C-2D), 79.0 (C-4D), 77.9 (C-3A), 77.8 (C-5B), 77.5 (C-3C and C-5D), 77.0 (C-4A and C-4C), 74.4 (C-3B), 74.2 (C-3D), 73.9 (C-5A or C-5C), 73.5 (C-5A or C-5C), 69.0 (C-6A or C-6C), 68.7 (C-6A or C-6C), 56.8 (OCH_3), 53.3 (C-2A), 23.7 (2 NHCO$\mathit{C}H_3$) ppm. MS (ESI): calcd. for $C_{35}H_{41}N_2O_{45}S_7Na_7$ $[M + 7Na]^{2-}$ 796.9; found 796.7.

4-Methoxyphenyl 3-*O*-(Methyl 3-*O*-Benzyl-2,4-di-*O*-pivaloyl-α-L-idopyranosyluronate)-2-deoxy-4,6-*O*-di-*tert*-butylsilylene-2-trifluoroacetamido-β-D-galactopyranoside (40): Compound **39** (427 mg, 0.428 mmol) was dissolved in CH_2Cl_2 (8.5 mL), and hydrazine monohydrate (0.5 M solution in pyridine/AcOH, 3:2; 3.42 mL) was added. The mixture was stirred at room temperature for 3 h, the reaction mixture was quenched with acetone (5.0 mL). The mixture was diluted with CH_2Cl_2 and washed with HCl (1 M aq.), saturated aqueous $NaHCO_3$, and H_2O. The organic layer was dried ($MgSO_4$), filtered, and concentrated in vacuo to give the corresponding diol, which was used in the next step without further purification [TLC (toluene/EtOAc, 1:2): R_f = 0.20].

This diol was dissolved in pyridine (9 mL). Pivaloyl chloride (2.5 mL) and DMAP (21 mg, 0.17 mmol) were added, and the solution was stirred at room temperature. After 45 h, the mixture was diluted with CH_2Cl_2, washed with HCl (1 M aq.), saturated aqueous $NaHCO_3$, and H_2O, dried ($MgSO_4$), filtered, and concentrated in vacuo. The residue was purified by flash column chromatography (toluene/EtOAc, 6:1) to give **40** (363 mg, 87% over two steps). TLC

(toluene/EtOAc, 4:1): R_f = 0.40. $[\alpha]_D^{20}$ = –19 (c = 1.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.26 (m, 5 H, Ar), 6.94 (m, 2 H, Ar), 6.79 (m, 2 H, Ar), 6.66 (d, $J_{2,NH}$ = 7.2 Hz, 1 H, NH), 5.31 (d, $J_{1,2}$ = 8.4 Hz, 1 H, 1A-H), 5.29 (m, 1 H, 4B-H), 5.15 (d, $J_{4,5}$ = 2.0 Hz, 1 H, 5B-H), 5.04 (br. s, 1 H, 1B-H), 4.86 (m, 1 H, 2B-H), 4.79 [2 d, 2 H, CH_2(Bn)], 4.53 (d, $J_{3,4}$ = 2.8 Hz, 1 H, 4A-H), 4.39 (dd, $J_{2,3}$ = 11.0 Hz, 1 H, 3A-H), 4.20 (m, 2 H, 6aA-H, 6bA-H), 3.98 (dt, 1 H, 2A-H), 3.76 [s, 3 H, Me(OMP) or COOMe], 3.74 [m, 4 H, 3B-H, Me(OMP) or COOMe], 3.47 (br. s, 1 H, 5A-H), 1.19, 1.17, 1.08, 0.97 [4 s, 36 H, C(CH_3)$_3$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.9, 177.6 [CO(Piv)], 169.1 (COOMe), 157.9 (q, $J_{C,F}$ = 37.2 Hz, $COCF_3$), 156.0, 151.2, 137.9 (Ar C), 128.5, 127.7, 127.5, 120.0 (Ar-CH), 115.6 (q, $J_{C,F}$ = 288.4 Hz, $COCF_3$), 114.6 (Ar-CH), 101.4 (C-1B), 99.2 (C-1A), 78.8 (C-3A), 74.0 (C-3B), 72.7 (C-4A), 72.5 [CH_2(Bn)], 71.3 (C-5A), 67.7 (C-4B), 67.5 (C-2B), 67.0 (C-6A), 66.9 (C-5B), 55.7 [COOMe or Me(OMP)], 54.1 (C-2A), 52.4 [COOMe or Me(OMP)], 39.1, 38.8 [$C(CH_3)_3$, Piv], 27.8, 27.4, 27.3, 27.1 [C(CH_3)$_3$], 23.3, 21.0 [$C(CH_3)_3$] ppm. HRMS: calcd. for $C_{47}H_{66}F_3NO_{15}SiNa$ [M + Na]$^+$ 992.4052; found 992.4087.

4-Methoxyphenyl 3-*O*-(Methyl 3-*O*-Benzyl-2,4-di-*O*-pivaloyl-α-L-idopyranosyluronate)-2-deoxy-4,6-di-*O*-levulinoyl-2-trifluoroacetamido-β-D-galactopyranoside (41): An excess of $(HF)_n$·Py (1.85 mL, 71.1 mmol) was added to a solution of **40** (363 mg, 0.374 mmol) in dry THF (8.0 mL) at 0 °C under an argon atmosphere. After 24 h at 0 °C, the mixture was diluted with CH_2Cl_2 and washed with H_2O and saturated aq. $NaHCO_3$ until it reached neutral pH. The organic layers were dried ($MgSO_4$), filtered, and concentrated in vacuo to give the corresponding diol (290 mg), which was used for the next step without further purification [TLC (toluene/EtOAc, 1:6): R_f = 0.45].

LevOH (0.72 mL, 7.0 mmol) was added at 0 °C to a solution of 1,3-dicyclohexylcarbodiimide (721 mg, 3.5 mmol) in CH_2Cl_2 (6 mL). The mixture was stirred for 5 min at room temperature, then it was cooled, filtered, and concentrated to give levulinic anhydride quantitatively (Lev_2O, 3.5 mmol).

A solution of the diol (290 mg) in dry pyridine (10 mL) was added to a flask containing Lev_2O (3.5 mmol) and DMAP (44 mg, 0.35 mmol) under an argon atmosphere. The mixture was stirred for 26 h at room temperature, then it was diluted with CH_2Cl_2 and washed with HCl (1 M aqueous), saturated aqueous $NaHCO_3$, and brine. The organic layers were dried ($MgSO_4$), filtered, and concentrated in vacuo. To complete the reaction, this residue was redissolved in dry pyridine (10 mL), and this solution was added to a flask containing additional Lev_2O (3.5 mmol) and DMAP (44 mg, 0.35 mmol) under an argon atmosphere. The mixture was stirred for 26 h at room temperature, then it was diluted with CH_2Cl_2 and washed with HCl (1 M aq.), saturated aqueous $NaHCO_3$, and brine. The organic layers were dried ($MgSO_4$), filtered, and concentrated in vacuo. The residue was purified by column chromatography (toluene/EtOAc, 2:1) to give **41** (311 mg, 81%). TLC (toluene/EtOAc, 1:1): R_f = 0.30. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.36–7.26 (m, 5 H, Ar), 6.95 (m, 2 H, Ar), 6.79 (m, 3 H, NH, Ar), 5.41 (d, $J_{3,4}$ = 3.2 Hz, 1 H, 4A-H), 5.26 (m, 2 H, 4B-H, 1A-H), 4.98 (br. s, 1 H, 1B-H), 4.86 (d, $J_{4,5}$ = 2.4 Hz, 1 H, 5B-H), 4.83 (br. t, 1 H, 2B-H), 4.71 [m, 2 H, CH_2(Bn)], 4.50 (dd, $J_{2,3}$ = 10.9, $J_{3,4}$ = 3.3 Hz, 1 H, 3A-H), 4.16 (dd, $J_{5,6a}$ = 7.4, $J_{6a,6b}$ = 11.4 Hz, 1 H, 6aA-H), 4.09 (dd, $J_{5,6a}$ = 5.8 Hz, 1 H, 6bA-H), 3.98 (m, 1 H, 2A-H), 3.93 (br. t, 1 H, 5A-H), 3.76 [s, 6 H, Me(OMP), COOMe], 3.69 (br. t, 1 H, 3B-H), 2.72–2.23 [m, 8 H, CH_2(Lev)], 2.16, 2.08 [2 s, 6 H, CH_3(Lev)], 1.18, 1.14 [2 s, 18 H, CH_3(Piv)] ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 206.8, 206.3 [CO(Lev)], 177.8, 177.5, 172.2, 172.1 [CO(Lev, Piv)], 168.9 (COOMe), 158.0 (q, $J_{C,F}$ = 37.3 Hz, $COCF_3$), 155.9, 151.1, 137.6 (Ar-C), 128.0, 127.9, 119.0 (Ar-CH), 115.7 (q, $J_{C,F}$ = 288.2 Hz, $COCF_3$), 114.7 (Ar-CH), 100.9 (C-1B), 99.2 (C-1A), 75.4 (C-3A), 74.4 (C-3B), 72.6 [CH_2(Bn)], 71.4 (C-5A), 68.6 (C-4A), 68.0 (C-2B), 67.8 (C-4B), 67.1 (C-5B), 61.9 (C-6A), 55.7 [COOMe or Me(OMP)], 54.7 (C-2A), 52.4 [COOMe or Me(OMP)], 39.0, 38.7 [$C(CH_3)_3$ (Piv)], 38.0, 37.9 [CH_2(Lev)], 29.9, 29.7 [CH_3(Lev)], 27.9, 27.8 [CH_2(Lev)], 27.2, 27.0 [C(CH_3)$_3$ (Piv)] ppm. HRMS: calcd. for $C_{49}H_{62}F_3NO_{19}Na$ [M + Na]$^+$ 1048.3766; found 1048.3790.

3-*O*-(Methyl 3-*O*-Benzyl-2,4-di-*O*-pivaloyl-α-L-idopyranosyluronate)-2-deoxy-4,6-di-*O*-levulinoyl-2-trifluoroacetamido-α,β-D-galactopyranose (42): CAN (0.63 M solution in H_2O; 1.6 mL) was added to a solution of **41** (346 mg, 0.337 mmol) in CH_2Cl_2/MeCN (1:2; 15 mL). The mixture was stirred for 1 h 30 min at room temperature, then it was diluted with EtOAc, and washed with H_2O, saturated aqueous $NaHCO_3$, and H_2O. The organic phase was dried ($MgSO_4$), filtered, and concentrated to dryness. The residue was purified by column chromatography (toluene/acetone, 7:2) to give **42** (218 mg, 70%) as a mixture of α/β anomers. TLC (toluene/acetone, 7:2): R_f = 0.20 and 0.11. ^1H NMR (300 MHz, $CDCl_3$) (data for α anomer): δ = 7.40–7.26 (m, 5 H, Ar), 6.65 (d, $J_{2,NH}$ = 9.5 Hz, 1 H, NH), 5.35 (m, 2 H, 4A-H, 1A-H), 5.20 (br. t, 1 H, 4B-H), 5.02 (br. s, 1 H, 1B-H), 4.80 (d, $J_{4,5}$ = 2.4 Hz, 1 H, 5B-H), 4.76 (m, 1 H, 2B-H), 4.74–4.62 [2 d, 2 H, CH_2(Bn)], 4.53 (dt, $J_{1,2}$ = 3.5, $J_{2,3}$ = 10.6 Hz, 1 H, 2A-H), 4.34 (dd, $J_{5,6a}$ = 3.7, $J_{5,6b}$ = 8.8 Hz, 1 H, 5A-H), 4.22 (dd, $J_{6a,6b}$ = 11.5 Hz, 1 H, 6aA-H), 4.10 (dd, $J_{3,4}$ = 3.1 Hz, 1 H, 3A-H), 3.95 (dd, 1 H, 6bA-H), 3.77 (s, 3 H, COOMe), 3.70 (br. t, 1 H, 3B-H), 2.82–2.26 [m, 8 H, CH_2(Lev)], 2.19, 2.05 [2 s, 6 H, CH_3(Lev)], 1.18, 1.15 [2 s, 18 H, $(CH_3)_3$ (Piv)] ppm. ^{13}C NMR (75 MHz, $CDCl_3$, data for α anomer): δ = 208.5, 206.7 [CO(Lev)], 177.8, 177.6, 172.3 [CO(Lev, Piv)], 169.0 (COOMe), 157.7 (q, $J_{C,F}$ = 37.2 Hz, $COCF_3$), 137.5 (Ar-C), 128.5, 128.1, 128.0 (Ar-CH), 115.9 (q, $J_{C,F}$ = 288.0 Hz, $COCF_3$), 101.1 (C-1B), 91.7 (C-1A), 75.5 (C-3A), 73.7 (C-3B), 72.4 [CH_2(Bn)], 69.4 (C-4A), 67.9 (C-4B), 67.5 (C-2B), 67.0 (C-5B), 66.9 (C-5A), 62.7 (C-6A), 52.4 (COOMe), 50.2 (C-2A), 39.0, 38.7 [$C(CH_3)_3$ (Piv)], 38.3, 37.9 [CH_2(Lev)], 29.9, 29.7 [CH_3(Lev)], 28.1, 27.7 [CH_2(Lev)], 27.2, 27.1 [C(CH_3)$_3$ (Piv)] ppm. HRMS: calcd. for $C_{42}H_{56}F_3NO_{18}Na$ [M + Na]$^+$ 942.3347; found 942.3311.

***O*-[3-*O*-(Methyl 3-*O*-Benzyl-2,4-di-*O*-pivaloyl-α-L-idopyranosyluronate)-2-deoxy-4,6-di-*O*-levulinoyl-2-trifluoroacetamido-α,β-D-galactopyranosyl] Trichloroacetimidate (43):** Trichloroacetonitrile (162 μL, 1.6 mmol) and catalytic DBU (0.084 M solution in dry CH_2Cl_2; 80 μL) were added to a solution of **42** (60 mg, 65 μmol) in dry CH_2Cl_2 (1.3 mL). The mixture was stirred for 10 h at room temperature, then it was concentrated to dryness. The residue was purified by flash chromatography (toluene/acetone, 5:1 + 1% Et_3N) to give **43** (54 mg, 78%) as a mixture of α/β anomers. TLC (toluene/acetone, 3:1): R_f = 0.45 (for α anomer). ^1H NMR (400 MHz, $CDCl_3$, data for α anomer): δ = 8.81 [s, 1 H, NH(TCA)], 7.35–7.26 (m, 5 H, Ar), 6.78 [d, $J_{2,NH}$ = 8.5 Hz, 1 H, NH(TFA)], 6.47 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1A-H), 5.52 (br. d, 1 H, 4A-H), 5.24 (br. t, 1 H, 4B-H), 5.11 (br. s, 1 H, 1B-H), 4.85 (d, $J_{4,5}$ = 2.6 Hz, 1 H, 5B-H), 4.75–4.67 [m, 4 H, 2B-H, 2A-H, CH_2(Bn)], 4.29 (t, $J_{5,6a}$ = $J_{5,6b}$ = 6.5 Hz, 1 H, 5A-H), 4.23 (dd, $J_{2,3}$ = 11.0, $J_{3,4}$ = 3.1 Hz, 1 H, 3A-H), 4.08 (m, 2 H, 6aA-H, 6bA-H), 3.77 (s, 3 H, COOMe), 3.72 (br. t, 1 H, 3B-H), 2.71–2.17 [m, 8 H, CH_2(Lev)], 2.16, 2.08 [2 s, 6 H, CH_3(Lev)], 1.18, 1.14 [2 s, 18 H, $(CH_3)_3$(Piv)] ppm. ^{13}C NMR (100 MHz, $CDCl_3$, data for α anomer): δ = 206.5, 206.1 [CO(Lev)], 178.0, 177.7, 172.2, 172.0 [CO(Lev, Piv)], 168.9 (COOMe), 160.3 (C=NH), 157.9 (q, $J_{C,F}$ = 37.9 Hz, $COCF_3$), 137.3 (Ar-C), 128.6, 128.1, 128.0 (Ar-CH), 115.7 (q, $J_{C,F}$ = 289.0 Hz, $COCF_3$), 101.3 (C-1B), 94.8 (C-1A), 90.7 (CCl_3), 75.2 (C-3A), 73.9 (C-3B), 72.7

[CH_2(Bn)], 70.0 (C-5A), 68.9 (C-2B), 68.4 (C-4A), 67.6 (C-4B), 67.5 (C-5B), 61.8 (C-6A), 52.5 (COOMe), 49.9 (C-2A), 39.1, 38.8 [*C*(CH_3)$_3$ (Piv)], 37.9 [CH_2(Lev)], 29.9, 29.7 [CH_3(Lev)], 27.9, 27.8 [CH_2(Lev)], 27.2, 27.1 [C(*C*H_3)$_3$ (Piv)] ppm. MS (ESI): calcd. for $C_{44}H_{56}Cl_3F_3N_2O_{18}Na$ [M + Na]$^+$ 1085.2; found 1085.5.

4-Methoxyphenyl *O*-(Methyl 3-*O*-Benzyl-2,4-di-*O*-pivaloyl-α-L-idopyranosyluronate)-(1→3)-*O*-(2-deoxy-4,6-di-*O*-levulinoyl-2-trifluoroacetamido-β-D-galactopyranosyl)-(1→4)-*O*-(benzyl 2-*O*-Benzoyl-3-*O*-benzyl-β-D-glucopyranosyluronate)-(1→3)-2-deoxy-4,6-*O*-di-*tert*-butylsilylene-2-trifluoroacetamido-β-D-galactopyranoside (44): Donor **43** (168 mg, 0.158 mmol) and acceptor **32** (103 mg, 0.105 mmol) were dissolved in dry CH_2Cl_2 (3.0 mL) in the presence of freshly activated 4 Å molecular sieves. The mixture was stirred for 30 min at 0 °C, then TMSOTf (0.092 M solution in dry CH_2Cl_2; 343 μL) was added under an argon atmosphere. The mixture was stirred for 30 min at 0 °C, then it was neutralized with Et_3N, filtered, and concentrated to dryness. The residue was purified by column chromatography (toluene/acetone, 7:1) to give **44** (106 mg, 53%). TLC (toluene/acetone, 3:1): R_f = 0.55. $[\alpha]_D^{20}$ = –2 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.92 (d, 2 H, Ar), 7.56 (t, 1 H, Ar), 7.49–7.22 (m, 12 H, Ar), 7.07 (m, 5 H, Ar), 6.95 (d, $J_{2,NH}$ = 6.5 Hz, 1 H, NH), 6.90 (m, 2 H, Ar), 6.78 (m, 2 H, Ar), 6.68 (d, $J_{2,NH}$ = 8.9 Hz, 1 H, NH), 5.37 (d, $J_{1,2}$ = 8.2 Hz, 1 H, 1A-H), 5.30 (d, $J_{1,2}$ = 7.9 Hz, 1 H, 1B-H), 5.28 [m, 2 H, CH_2(Bn)], 5.24 (m, 1 H, 4D-H), 5.21 (t, 1 H, 2B-H), 5.17 (d, $J_{3,4}$ = 3.1 Hz, 1 H, 4C-H), 4.95 (br. s, 1 H, 1D-H), 4.91 (d, $J_{4,5}$ = 2.2 Hz, 1 H, 5D-H), 4.84 [d, 1 H, CH_2(Bn)], 4.77 (br. s, 1 H, 2D-H), 4.72–4.66 [2 d, 2 H, CH_2(Bn)], 4.57 (br. s, 1 H, 4A-H), 4.51 [d, 1 H, CH_2(Bn)], 4.36 (br. d, $J_{2,3}$ = 11.3 Hz, 1 H, 3A-H), 4.24 (d, $J_{1,2}$ = 8.5 Hz, 1 H, 1C-H), 4.17–3.98 (m, 4 H, 2C-H, 6aA-H, 4B-H, 6bA-H), 3.97–3.93 (m, 2 H, 2A-H, 5B-H), 3.87 (m, 2 H, 6aC-H, 6bC-H), 3.78, 3.75 [2 s, 6 H, Me(OMP), COOMe], 3.68 (m, 2 H, 3B-H, 3D-H), 3.57 (dd, $J_{2,3}$ = 10.5 Hz, 1 H, 3C-H), 3.45 (t, $J_{5,6a}$ = $J_{5,6b}$ = 6.5 Hz, 1 H, 5C-H), 3.32 (m, 1 H, 5A-H), 2.68 [m, 2 H, CH_2(Lev)], 2.48–2.16 [m, 8 H, CH_2(Lev), CH_3(Lev) (2.17)], 2.10–2.04 [m, 1 H, CH_2(Lev)], 1.96 [s, 3 H, CH_3(Lev)], 1.20, 1.18, 1.05, 1.01 [4 s, 36 H, C(CH_3)$_3$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 206.9, 206.1 [CO(Lev)], 177.9, 177.3, 172.2, 172.0, 169.1, 168.9, 165.1 [CO(Lev), CO(Piv), CO(Bz), COOBn, COOMe], 158.2 (q, $J_{C,F}$ = 37.1 Hz, *C*O*C*F_3), 157.7 (q, $J_{C,F}$ = 36.8 Hz, *C*O*C*F_3), 156.0, 151.1, 137.8, 137.6, 134.6 (Ar-C), 133.4, 129.9, 129.7, 129.5, 129.4, 129.3, 128.5, 128.2, 128.0, 127.7, 120.3 (Ar-C, Ar-CH), 116.0 (q, $J_{C,F}$ = 288.3 Hz, CO*C*F_3), 115.5 (q, $J_{C,F}$ = 288.6 Hz, CO*C*F_3), 114.6 (Ar-CH), 100.4 (C-1D), 100.2, 100.1 (C-1B, C-1C), 99.3 (C-1A), 80.2 (C-3B), 78.3 (C-4B), 76.5 (C-3C), 75.3 [CH_2(Bn)], 75.2 (C-3A), 74.2 (C-3D), 74.1 (C-5B), 73.4 (C-4A), 72.5 [CH_2(Bn)], 72.4 (C-2B), 71.4 (C-5A), 71.2 (C-5C), 68.5 [CH_2(Bn)], 68.1 (C-4C), 67.8 (C-4D, C-2D), 67.6 (C-6A), 67.0 (C-5D), 61.4 (C-6C), 55.7 [COOMe or Me(OMP)], 54.1 (C-2A), 53.3 (C-2C), 52.4 [COOMe or Me(OMP)], 39.1, 38.7 [*C*(CH_3)$_3$ (Piv)], 38.0, 37.8 [CH_2(Lev)], 29.9, 29.6 [CH_3(Lev)], 28.0, 27.7 [CH_2(Lev)], 27.6, 27.3, 27.1 [C(*C*H_3)$_3$], 23.4, 20.8 [*C*(CH_3)$_3$ (DBSi)] ppm. HRMS: calcd. for $C_{92}H_{112}F_6N_2O_{31}SiNa$ [M + Na]$^+$ 1905.6820; found 1905.6755.

4-Methoxyphenyl *O*-(Methyl 3-*O*-Benzyl-2,4-di-*O*-pivaloyl-α-L-idopyranosyluronate)-(1→3)-*O*-(2-deoxy-2-trifluoroacetamido-β-D-galactopyranosyl)-(1→4)-*O*-(benzyl 2-*O*-Benzoyl-3-*O*-benzyl-β-D-glucopyranosyluronate)-(1→3)-2-deoxy-4,6-*O*-di-*tert*-butylsilylene-2-trifluoroacetamido-β-D-galactopyranoside (45): Compound **44** (105 mg, 0.056 mmol) was dissolved in CH_2Cl_2 (1.5 mL), and hydrazine monohydrate (0.5 M solution in pyridine/AcOH, 3:2; 0.45 mL) was added. The mixture was stirred at room temperature for 3 h, then it was quenched with acetone (0.7 mL). The mixture was diluted with CH_2Cl_2 and washed with HCl (1 M aq.), saturated aqueous $NaHCO_3$, and H_2O. The organic layer was dried ($MgSO_4$), filtered, and concentrated in vacuo. The residue was purified by flash column chromatography (toluene/EtOAc, 6:1) to give **45** (82 mg, 87%). TLC (toluene/EtOAc, 3:2): R_f = 0.32. $[\alpha]_D^{20}$ = –7 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97 (d, 2 H, Ar), 7.57 (t, 1 H, Ar), 7.46–7.33 (m, 12 H, Ar), 7.13 (m, 5 H, Ar), 6.91 (m, 2 H, Ar), 6.80 (m, 3 H, Ar, NH), 6.52 (d, $J_{2,NH}$ = 8.4 Hz, 1 H, NH), 5.38 (d, $J_{1,2}$ = 8.3 Hz, 1 H, 1A-H), 5.30–5.20 [m, 5 H, 1B-H, 2B-H, CH_2(Bn), 4D-H], 5.08 (br. d, 1 H, 1D-H), 4.94 (d, $J_{4,5}$ = 2.7 Hz, 1 H, 5D-H), 4.86 [d, 1 H, CH_2(Bn)], 4.85 (br. d, 1 H, 2D-H), 4.79–4.68 [2 d, 2 H, CH_2(Bn)], 4.58 (br. s, 1 H, 4A-H), 4.54 [d, 1 H, CH_2(Bn)], 4.38 (br. d, $J_{2,3}$ = 11.1 Hz, 1 H, 3A-H), 4.27 (d, $J_{1,2}$ = 8.5 Hz, 1 H, 1C-H), 4.24 (m, 1 H, 2C-H), 4.11 (d, $J_{6a,6b}$ = 12.3 Hz, 1 H, 6aA-H), 4.05 (t, $J_{3,4}$ = $J_{4,5}$ = 9.5 Hz, 1 H, 4B-H), 3.99 (m, 1 H, 6bA-H), 3.98–3.91 (m, 3 H, 5B-H, 2A-H, 4C-H), 3.76–3.75 [2 s, 6 H, COOMe, Me(OMP)], 3.70 (m, 2 H, 3D-H, 3B-H), 3.56–3.45 (m, 3 H, 6aC-H, 6bC-H, 3C-H), 3.32 (m, 1 H, 5A-H), 3.12 (m, 1 H, 5C-H), 1.20, 1.18, 1.06, 1.02 [4 s, 36 H, C(CH_3)$_3$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.6, 177.4, 169.0, 168.7, 165.1 [CO(Piv), CO(Bz), COOBn, COOMe], 157.9 (q, $J_{C,F}$ = 36.9 Hz, *C*O*C*F_3), 157.7 (q, $J_{C,F}$ = 36.7 Hz, *C*O*C*F_3), 156.0, 151.1, 137.7, 137.2, 134.7 (Ar-C), 133.5, 129.9, 129.5, 129.4, 129.2, 129.1, 128.6, 128.5, 128.3, 128.1, 128.0, 127.8, 120.3 (Ar-C, Ar-CH), 116.0 (q, $J_{C,F}$ = 288.3 Hz, CO*C*F_3), 115.5 (q, $J_{C,F}$ = 288.3 Hz, CO*C*F_3), 114.6 (Ar-CH), 100.4 (C-1B), 100.2 (C-1C), 99.6 (C-1D), 99.3 (C-1A), 80.6 (C-3B), 79.0 (C-3C), 78.0 (C-4B), 75.8 [CH_2(Bn)], 75.5 (C-3A), 74.6 (C-5C), 74.1 (C-5B), 73.7 (C-3D), 73.3 (C-4A), 72.6 (C-2B), 72.4 [CH_2(Bn)], 71.4 (C-5A), 68.3 [CH_2(Bn), C-4C], 68.2 (C-2D), 67.8 (C-5D), 67.0 (C-4D, C-6A), 62.3 (C-6C), 55.7 [COOMe or Me(OMP)], 54.1 (C-2A), 52.5 [COOMe or Me(OMP)], 52.3 (C-2C), 39.1, 38.8 [*C*(CH_3)$_3$ (Piv)], 27.6, 27.3, 27.1 [C(*C*H_3)$_3$], 23.4, 20.8 [*C*(CH_3)$_3$ (DBSi)] ppm. HRMS: calcd. for $C_{82}H_{100}F_6N_2O_{27}SiNa$ [M + Na]$^+$ 1709.6085; found 1709.6031.

4-Methoxyphenyl *O*-(Methyl 3-*O*-Benzyl-2,4-di-*O*-pivaloyl-α-L-idopyranosyluronate)-(1→3)-*O*-(2-deoxy-2-trifluoroacetamido-β-D-galactopyranosyl)-(1→4)-*O*-(benzyl 2-*O*-Benzoyl-3-*O*-benzyl-β-D-glucopyranosyluronate)-(1→3)-2-deoxy-2-trifluoroacetamido-β-D-galactopyranoside (46): An excess of $(HF)_n$·Py (223 μL, 8.6 mmol) was added to a solution of **45** (75 mg, 0.044 mmol) in dry THF (4.0 mL) at 0 °C under an argon atmosphere. After 24 h at 0 °C, the mixture was diluted with CH_2Cl_2, and then washed with H_2O and saturated $NaHCO_3$ solution until it reached neutral pH. The organic layers were dried ($MgSO_4$), filtered, and concentrated in vacuo to give **46** (67 mg, 97%). TLC (toluene/EtOAc, 1:2): R_f = 0.20. $[\alpha]_D^{20}$ = –3 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (d, 2 H, Ar), 7.56 (t, 1 H, Ar), 7.44–7.26 (m, 13 H, Ar, NH), 7.10–7.03 (m, 5 H, Ar), 6.83 (m, 2 H, Ar), 6.72 (m, 2 H, Ar), 6.64 (m, 1 H, NH), 5.37 (m, 1 H, 1A-H), 5.29 (m, 1 H, 2B-H), 5.22 [m, 3 H, 4D-H, CH_2(Bn)], 5.06 (br. d, 1 H, 1D-H), 4.93 (d, $J_{4,5}$ = 2.8 Hz, 1 H, 5D-H), 4.87 [d, 1 H, CH_2(Bn)], 4.84 (m, 1 H, 2D-H), 4.81 (d, $J_{1,2}$ = 7.4 Hz, 1 H, 1B-H), 4.77–4.56 [3 d, 3 H, CH_2(Bn)], 4.48 (m, 2 H, 1C-H, 3A-H), 4.31 (t, $J_{3,4}$ = $J_{4,5}$ = 8.8 Hz, 1 H, 4B-H), 4.16 (m, 1 H, 2C-H), 4.14 (br. s, 1 H, 4A-H), 4.06 (br. d, 1 H, 5B-H), 3.93 (br. d, $J_{3,4}$ = 2.6 Hz, 1 H, 4C-H), 3.88 (m, 1 H, 2A-H), 3.83–3.70 [m, 9 H, 6aA-H, 3B-H, 3D-H, Me(OMP), COOMe], 3.59 (m, 4 H, 6bA-H, 6aC-H, 3C-H, 5A-H), 3.48 (dd, $J_{5,6b}$ = 2.8, $J_{6a,6b}$ = 12.1 Hz, 1 H, 6bC-H), 3.26 (m, 1 H, 5C-H), 2.29 (m, 4 H, OH), 1.19, 1.18 [2 s, 18 H, C(CH_3)$_3$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$, selected data from HSQC experiment): δ = 133.7, 130.2, 129.7–127.6, 119.1, 114.7 (Ar-CH), 101.7 (C-1B), 100.1 (C-1C), 99.6 (C-1D), 98.7 (C-1A), 80.5 (C-3B), 78.8 (C-3C), 78.6 (C-3A), 77.4 (C-4B), 75.9 [CH_2(Bn)], 75.2 (C-5C), 74.5 (C-5A), 74.2 (C-5B), 74.1 (C-3D), 72.8 (C-2B), 72.7 [CH_2(Bn)], 68.8 [CH_2(Bn)], 68.6

(C-4A, C-4C, C-2D), 68.0 (C-5D), 67.6 (C-4D), 62.7 (C-6C), 62.5 (C-6A), 55.9 [COOMe or Me(OMP)], 54.5 (C-2A), 52.8 [C-2C, COOMe or Me(OMP)], 27.5 [C(CH_3)$_3$] ppm. HRMS: calcd. for $C_{74}H_{84}F_6N_2O_{27}Na$ [M + Na]$^+$ 1569.5063; found 1569.5101.

4-Methoxyphenyl *O*-(Methyl 3-*O*-Benzyl-2,4-di-*O*-pivaloyl-α-L-idopyranosyluronate)-(1→3)-*O*-(2-deoxy-4,6-di-*O*-sulfo-2-trifluoroacetamido-β-D-galactopyranosyl)-(1→4)-*O*-(benzyl 2-*O*-Benzoyl-3-*O*-benzyl-β-D-glucopyranosyluronate)-(1→3)-2-deoxy-4,6-di-*O*-sulfo-2-trifluoroacetamido-β-D-galactopyranoside (47): Compound **46** (16 mg, 10 μmol) and sulfur trioxide–trimethylamine complex (58 mg, 0.41 mmol) were dissolved in dry DMF (1.5 mL), and the mixture was heated at 100 °C for 30 min using microwave irradiation (23 W average power). The reaction vessel was cooled, and Et_3N (300 μL), MeOH (1 mL), and CH_2Cl_2 (1 mL) were added. The solution was loaded onto a Sephadex LH-20 chromatography column, which was eluted with CH_2Cl_2/MeOH (1:1) to give **47** as its triethylammonium salt (23 mg, quantitative). TLC (EtOAc/Py/H_2O/AcOH 12:5:3:1): R_f = 0.14. ^{1}H NMR (500 MHz, CD_3OD/$CDCl_3$, 7:1): δ = 7.94 (d, 2 H, Ar), 7.62 (t, 1 H, Ar), 7.54–7.05 (m, 17 H, Ar), 6.97 (d, 2 H, Ar), 6.82 (d, 2 H, Ar), 5.68 (d, $J_{4,5}$ = 2.7 Hz, 1 H, 5D-H), 5.43 [d, J = 11.8 Hz, 1 H, CH_2(Bn)], 5.34 (dd, 1 H, 4D-H), 5.26–5.22 [m, 2 H, 2B-H, CH_2(Bn)], 5.05 (d, $J_{1,2}$ = 2.4 Hz, 1 H, 1D-H), 5.02–4.97 [m, 2 H, 2D-H, CH_2(Bn)], 4.90 (d, $J_{1,2}$ = 7.8 Hz, 1 H, 1B-H), 4.85–4.80 (m, 3 H, 1A-H, 4A-H, 4C-H), 4.76 (d, $J_{1,2}$ = 8.4 Hz, 1 H, 1C-H), 4.70 [m, 2 H, CH_2(Bn)], 4.52–4.43 [m, 3 H, CH_2(Bn), 2 6A-H or 6C-H], 4.40–4.35 (m, 2 H, 4B-H, 6A-H or 6C-H), 4.33–4.25 (m, 2 H, 6A-H or 6C-H, 2C-H), 4.20–4.08 (m, 3 H, 2A-H, 3A-H, 5B-H), 4.01 (dd, $J_{2,3}$ = 11.0, $J_{3,4}$ = 3.0 Hz, 1 H, 3C-H), 3.97–3.94 (m, 2 H, 5A-H, 5C-H), 3.85 (dd, 1 H, 3B-H), 3.78–3.74 [2 s, 6 H, Me(OMP), COOMe], 3.61 (dd, 1 H, 3D-H), 3.16 (q, 24 H, Et_3NH^+), 1.28 (t, 36 H, Et_3NH^+), 1.18, 1.14 [2 s, 18 H, C(CH_3)$_3$] ppm. ^{13}C NMR (125 MHz, CD_3OD/$CDCl_3$, 7:1, selected data from HSQC experiment): δ = 128.3–114.1 (Ar-CH), 101.6 (C-1B), 101.1 (C-1D), 100.7 (C-1C), 99.3 (C-1A), 79.9 (C-3B), 76.9 (C-3A), 75.8 (C-4B), 75.4–75.1 (C-4A, C-4C, C-3C), 74.9 (C-3D), 74.6–74.5 [C-5B, CH_2(Bn)], 73.4 (C-5A, C-5C), 72.6 (C-2B), 71.4 [CH_2(Bn)], 69.2 (C-4D), 68.8 (C-2D), 68.0–67.5 [CH_2(Bn), C-6C, C-6A, C-5D], 54.6 [COOMe or Me(OMP)], 53.0 (C-2A), 51.8 (C-2C), 51.5 [COOMe or Me(OMP)], 26.3 [C(CH_3)$_3$] ppm. MS (ESI): calcd. for $C_{74}H_{81}F_6N_2O_{39}S_4Na$ [M + Na + H]$^{2-}$ 943.2; found 943.3.

4-Methoxyphenyl *O*-(3-*O*-Benzyl-α-L-idopyranosyluronic Acid)-(1→3)-*O*-(2-acetamido-2-deoxy-4,6-di-*O*-sulfo-β-D-galactopyranosyl)-(1→4)-*O*-(3-*O*-benzyl-β-D-glucopyranosyluronic Acid)-(1→3)-2-acetamido-2-deoxy-4,6-di-*O*-sulfo-β-D-galactopyranoside (49): H_2O_2 (30%; 0.19 mL) and an aqueous solution of LiOH (0.7 M; 0.12 mL) were added at 0 °C to a solution of **47** (11 mg, 4.8 μmol) in THF (0.5 mL). The mixture was stirred for 24 h at room temperature, then MeOH (1.0 mL), H_2O (0.3 mL), and NaOH (4 M aq.; 0.24 mL) were added. The mixture was stirred for 72 h at room temperature, then it was neutralized with Amberlite IR-120 (H^+) resin, filtered, and concentrated to give **48** {MS (ESI): calcd. for $C_{45}H_{54}N_2O_{34}S_4Na_2$: 670.0; found 669.9 [M + 2Na + 2H]$^{2-}$}.

Triethylamine (9 μL, 64 μmol) and acetic anhydride (9 μL, 97 μmol) were added to a cooled (0 °C) solution of **48** in dry MeOH (1.5 mL). The mixture was stirred for 2 h at room temp., then Et_3N (200 μL) was added, and the mixture was concentrated to dryness. The residue was purified by Sephadex LH-20 chromatography (MeOH) to give **49**.

This compound was then dissolved in H_2O (2 mL), and Amberlite IR-120 H^+ resin was added (pH = 3.3). The mixture was filtered, treated with NaOH (0.04 M aq.; pH = 7.5) and lyophilized. The white solid was then eluted through a column of Dowex 50WX4-Na^+ (H_2O/MeOH, 9:1) to give **49** as its sodium salt (6 mg, 86%) after lyophilization. TLC (EtOAc/pyridine/H_2O/AcOH, 6:5:3:1): R_f = 0.17. ^{1}H NMR (500 MHz, D_2O): δ = 7.57–7.36 (m, 10 H, Ar), 7.09 (d, 2 H, Ar), 6.97 (d, 2 H, Ar), 5.03 (d, $J_{1,2}$ = 8.5 Hz, 1 H, 1A-H), 4.96 [d, J = 10.5 Hz, 1 H, CH_2(Bn)], 4.85 (d, $J_{3,4}$ = 2.5 Hz, 1 H, 4A-H), 4.84–4.77 [m, 6 H, CH_2(Bn), 5D-H (4.83), 1D-H (4.80), 4C-H (4.76)], 4.70 (d, $J_{1,2}$ = 8.0 Hz, 1 H, 1C-H), 4.55 (d, $J_{1,2}$ = 7.5 Hz, 1 H, 1B-H), 4.35–4.29 (m, 2 H, 2A-H, 6A-H or 6C-H), 4.26–4.19 (m, 3 H, 5A-H or 5C-H, 2 6A-H or 6C-H), 4.16 (dd, 1 H, 3A-H), 4.14–4.04 (m, 4 H, 6A-H or 6C-H, 4D-H, 2C-H, 4B-H), 3.99 (m, 1 H, 5A-H or 5C-H), 3.95 (m, 1 H, 3C-H), 3.81 [s, 3 H, Me(OMP)], 3.76 (d, $J_{4,5}$ = 9.5 Hz, 1 H, 5B-H), 3.67–3.53 (m, 4 H, 2D-H, 3B-H, 2B-H, 3D-H), 2.04, 2.03 (2 s, 6 H, NHAc) ppm. ^{13}C NMR (125 MHz, D_2O, selected data from HSQC experiment): δ = 130.1–116.1 (Ar-CH), 105.3 (C-1D), 104.9 (C-1B), 101.6 (C-1A), 101.3 (C-1C), 82.9 (C-3D), 82.4 (C-3B), 78.4 (C-4B), 77.8 (C-5B), 77.6 (C-4C, C-3C), 76.9 (C-4A), 75.9 (C-3A), 74.7, 74.4 [CH_2(Bn)], 73.8–73.4 (C-5A, C-5C, C-4D), 72.6 (C-2B), 71.8 (C-2D), 68.9, 68.5 (C-6A, C-6C), 56.8 [Me(OMP)], 52.9, 52.6 (C-2A, C-2C), 23.6 (NAc) ppm. MS (ESI): calcd. for $C_{49}H_{58}N_2O_{36}S_4Na_3$ [M + 3Na + 2H]$^-$ 1447.1; found 1447.0.

4-Methoxyphenyl *O*-(α-L-Idopyranosyluronic Acid)-(1→3)-*O*-(2-acetamido-2-deoxy-4,6-di-*O*-sulfo-β-D-galactopyranosyl)-(1→4)-*O*-(β-D-glucopyranosyluronic Acid)-(1→3)-2-acetamido-2-deoxy-4,6-di-*O*-sulfo-β-D-galactopyranoside (50): A solution of **49** (5.8 mg, 3.8 μmol, sodium salt) in H_2O/MeOH (4.5 mL/0.5 mL) was hydrogenated in the presence of $Pd(OH)_2$ (12 mg). After 24 h, the suspension was filtered through Celite, concentrated, and lyophilized to give **50** as its sodium salt (5.1 mg, quantitative). ^{1}H NMR (500 MHz, D_2O): δ = 7.09 (d, 2 H, Ar), 6.98 (d, 2 H, Ar), 5.02 (d, $J_{1,2}$ = 8.5 Hz, 1 H, 1A-H), 4.85 (d, $J_{3,4}$ = 2.6 Hz, 1 H, 4A-H), 4.83 (d, $J_{1,2}$ = 4.5 Hz, 1 H, 1D-H), 4.76 (d, 1 H, 4C-H), 4.67 (d, $J_{1,2}$ = 8.1 Hz, 1 H, 1C-H), 4.63 (d, $J_{4,5}$ = 3.6 Hz, 1 H, 5D-H), 4.53 (d, $J_{1,2}$ = 7.8 Hz, 1 H, 1B-H), 4.34–4.21 [m, 6 H, 2A-H (4.31), 2 6A-H, 2 6C-H, 5A-H or 5C-H (4.23)], 4.17–4.15 (m, 2 H, 5A-H or 5C-H, 3A-H), 4.09–4.02 (m, 2 H, 2C-H, 3C-H), 3.93 (dd, 1 H, 4D-H), 3.81 [s, 3 H, Me(OMP)], 3.78 (dd, 1 H, 4B-H), 3.69 (d, $J_{4,5}$ = 9.7 Hz, 1 H, 5B-H), 3.63–3.59 (m, 2 H, 3B-H, 3D-H), 3.49 (dd, $J_{2,3}$ = 7.5 Hz, 1 H, 2D-H), 3.44 (dd, 1 H, 2B-H), 2.05, 2.03 (2 s, 6 H, NHAc) ppm. ^{13}C NMR (125 MHz, D_2O, selected data from HSQC experiment): δ = 119.6–116.2 (Ar), 104.7 (C-1B), 104.1 (C-1D), 102.6 (C-1C), 101.8 (C-1A), 83.4 (C-4B), 77.8 (C-5B), 77.0 (C-4C, C-4A), 76.5 (C-3C), 76.0 (C-3A), 75.0 (C-3B or C-3D), 73.7, 73.5 (C-5A, C-5C), 73.4 (C-3B or C-3D), 73.1 (C-2B), 72.7 (C-4D), 72.3 (C-5D), 71.4 (C-2D), 68.9–68.8 (C-6A, C-6C), 56.9 [Me(OMP)], 52.7 (C-2A, C-2C), 23.5 (NAc) ppm. MS (ESI): calcd. for $C_{35}H_{46}N_2O_{36}S_4Na_3$ [M + 3Na + 2H]$^-$ 1267.0; found 1266.9.

Fluorescence Polarization Assay: Fluorescence polarization measurements were performed in 384-well microplates (black polystyrene, nontreated, Corning) using a TRIAD multimode reader (Dynex). The fluorescent probe (a fluorescent heparin-like hexasaccharide) and inhibitors were dissolved in PBS buffer (phosphate-buffered saline; 10 mM, pH 7.4). Recombinant human FGF-2 (Peprotech) was dissolved in PBS buffer (10 mM, pH 7.4) containing BSA (bovine serum albumin; 1%). For the inhibition assay, probe solution (10 μL) and protein (20 μL) at fixed concentration (40 nM and 145 nM, respectively) were mixed with inhibitor solution (10 μL; 100 μM). The total sample volume in each well was 40 μL. Therefore, all measurements were done in PBS + 0.5% BSA, and the final concentrations of inhibitor, fluorescent probe and FGF-2 in each well were 25 μM, 10 nM, and 73 nM, respectively. After stirring for 5 min in the dark, fluorescence polarization was recorded.

Two control wells were included in the study. The first one contained only the fluorescent probe; the second one contained FGF-2 and the probe, without any inhibitor. Blank wells contained FGF-2 solution (20 μL) and PBS buffer (20 μL), and their measurements were subtracted from all values. All samples were measured in triplicate.

Supporting Information (see footnote on the first page of this article): Copies of the NMR spectra of new compounds.

Acknowledgments

The authors thank the Spanish Ministry of Economy and Competitiveness (grants CTQ2009-07168 and CTQ2012-32605), the Spanish National Research Council (CSIC) (grant 201180E021) and the European Union (FEDER support) for financial support.

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Received: March 7, 2014
Published Online: May 19, 2014

