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Synthesis of variously sulfated biotinylated oligosaccharides from the linkage region of proteoglycans

Katia Aït-Mohand, Chrystel Lopin-Bon, Jean-Claude Jacquinet *

Institut de Chimie Organique et Analytique, UMR 7311 CNRS et Université d'Orléans, Pôle de Chimie, Université d'Orléans, BP 6759, 45067 Orléans Cedex 2, France

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ABSTRACT

The synthesis of a collection, as biotinylated conjugates, of various sulfoforms of the trisaccharide β-D-Glc*p*A-(1→3)-β-D-Gal*p*-(1→3)-β-D-Gal*p*, structures encountered in the linkage region of proteoglycans, is reported herein for the first time. An efficient and stereocontrolled preparation was achieved using common key intermediates in a divergent manner. These molecules should be useful probes to study the substrate specificity of the glycosyltransferases involved at the bifurcation point in the biosynthesis of proteoglycans.

1. Introduction

Proteoglycans (PGs) are biologically important macromolecules composed of glycosaminoglycan (GAG) chains covalently linked to a core protein. They are widespread on the cell surface and in the extracellular matrix, and are involved in many biological processes and pathologies,[1] thus having a great potential as pharmacological targets. PG assembly starts in the Golgi apparatus with the attachment of D-Xylose to a L-serine residue within the protein core. The stepwise addition of two D-Galactose units (D-Gal^{I} and D-Gal^{II}) then one D-Glucuronic acid (D-GlcA) unit provides the so-called common tetrasaccharide intermediate.

At this point, a possible divergence in the biosynthetic pathway may occur (Fig. 1).[2] Transfer of an α-D-GlcNAc residue at O-4 of the terminal non-reducing D-GlcA unit initiates the formation of *gluco*saminoglycans (heparin, heparan sulfate), whereas those of a β-D-GalNAc residue lead to *galacto*saminoglycans (chondroitin sulfate and dermatan sulfate). GAG chains consist of hexosamines and uronic acids arranged in alternating sequences, and these repeating units are variously substituted by sulfate groups creating a great degree of structural and functional diversity. The current hypothesis that the linkage region should be common to all GAG species strongly contrasts with the structural heterogeneity of the GAG region. However, it has been reported that this linkage region may be modified by sulfation at C-4 or C-6 of both D-Gal units, and/or by phosphorylation at C-2 of the D-Xyl unit.[3] The biological significance of these unique substitutions is not yet fully understood, though they could act as biosynthetic signals.[4] Phosphorylation of the D-Xyl unit was demonstrated to be a transient phenomenon involved in the early steps of the biosynthesis.[5,6] Specific sulfation at C-6 of Gal^{I} was found to strongly accelerate the transfer of the D-GlcA unit.[6] But the exact role of these sulfate substituents at the bifurcation of the biosynthesis of PGs has not yet been clarified.

To address this issue, several syntheses of various glycoconjugates of the linkage region containing or not sulfate and/or phosphate groups have been reported,[7] but no clear-cut biological results were obtained with these synthetic molecules. Since phosphorylation or not on the D-Xyl unit apparently has no effect at the divergence level in the biosynthesis, and to shed light on the exact role of the sulfate substituents, we now report for the first time a systematic preparation of all possible sulfoforms of the truncated structure β-D-Glc*p*A-(1→3)-β-D-Gal*p*-(1→3)-β-D-Gal*p* conjugated to biotin to serve as potential substrates for the hexosaminyl transferases involved at the bifurcation point in the biosynthesis of PGs.

2. Results and discussion

For the synthesis of the non-sulfated target molecule **1** and the four possible sulfoforms **2**–**5** (Fig. 2), two common key trisaccharide intermediates **6** and **7** were designed. Diol **6** may be a precursor of **1** and of the two species **2** and **3** sulfated at C-4 and C-6 on Gal^{I}, whereas diol **7** may lead to the two corresponding species **4** and **5** sulfated on Gal^{II}. These later may be in turn prepared by stereoselective assembly of two donors **8** and **9**, which differ in their

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* Corresponding author. Tel.: +33 238 417072; fax: +33 238 417281.
E-mail address: Jean-Claude.Jacquinet@univ-orleans.fr (J.-C. Jacquinet).

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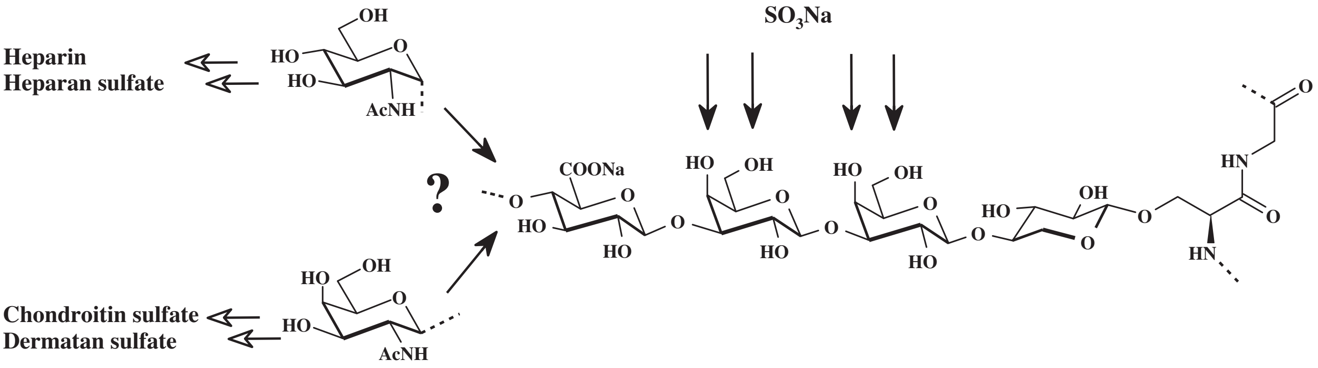


Figure 1. The linkage region of proteoglycans and the bifurcation in their biosynthesis. The arrows indicate possible substitutions with sulfate groups.

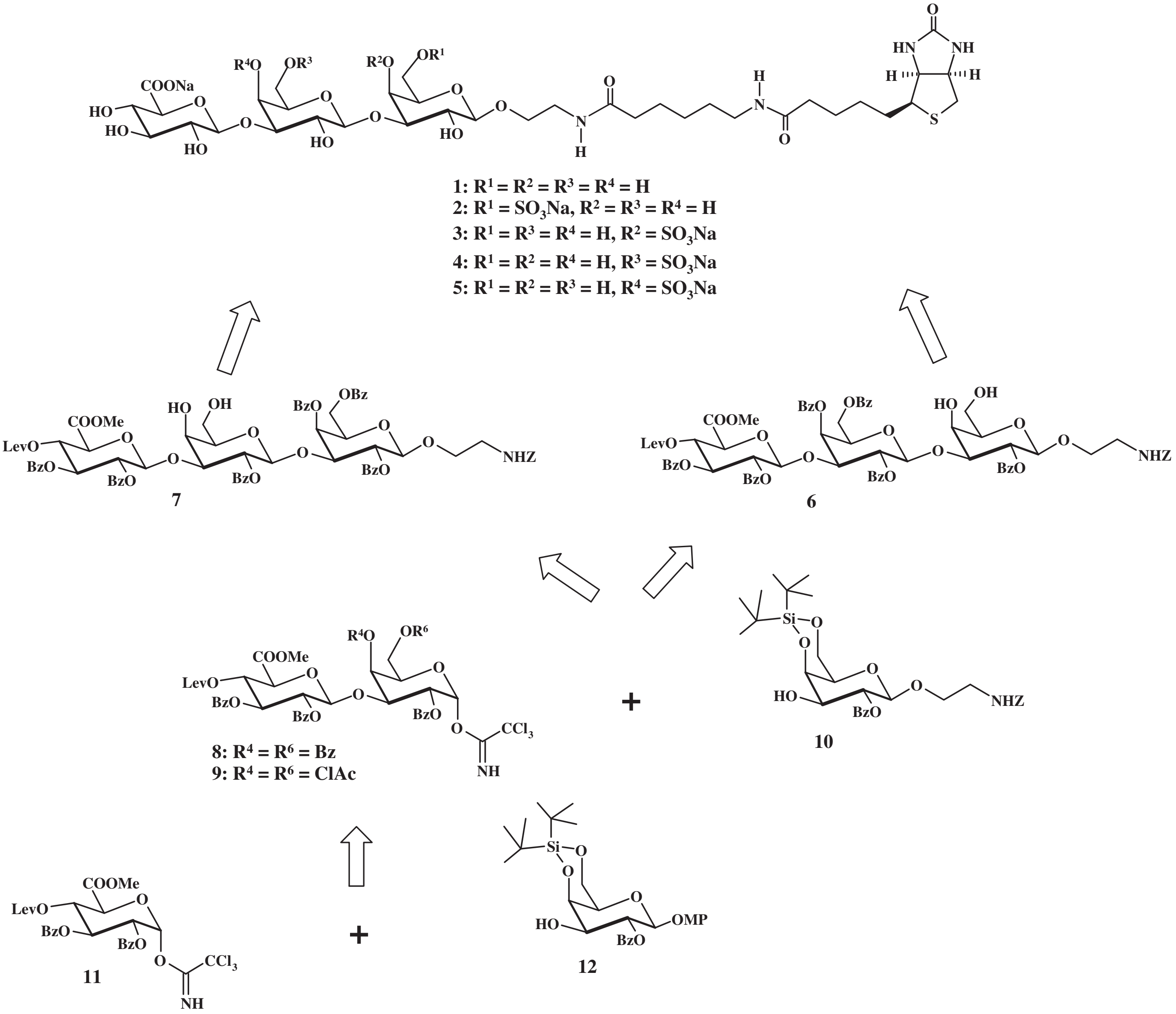
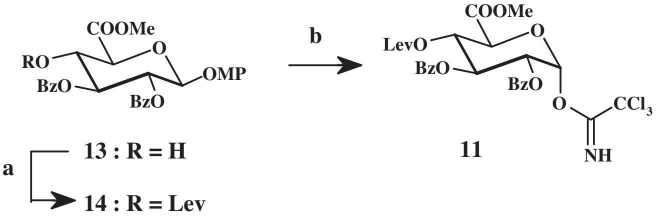


Figure 2. Retrosynthesis for target molecules **1–5**.

substitution pattern at C-4 and C-6 of the D-Gal unit, with acceptor **10** still possessing a masked amine linker to allow further coupling with biotin. These two donors may be obtained by stereoselective coupling of donor **11** and acceptor **12**. The β-selectivity in forming all glycosidic linkages would rely on neighboring group assistance by benzoyl groups, which serve also as permanent protective groups. All glycosylation reactions will be performed using Schmidt's trichloroacetimidate procedure.[8] As a prelude for further

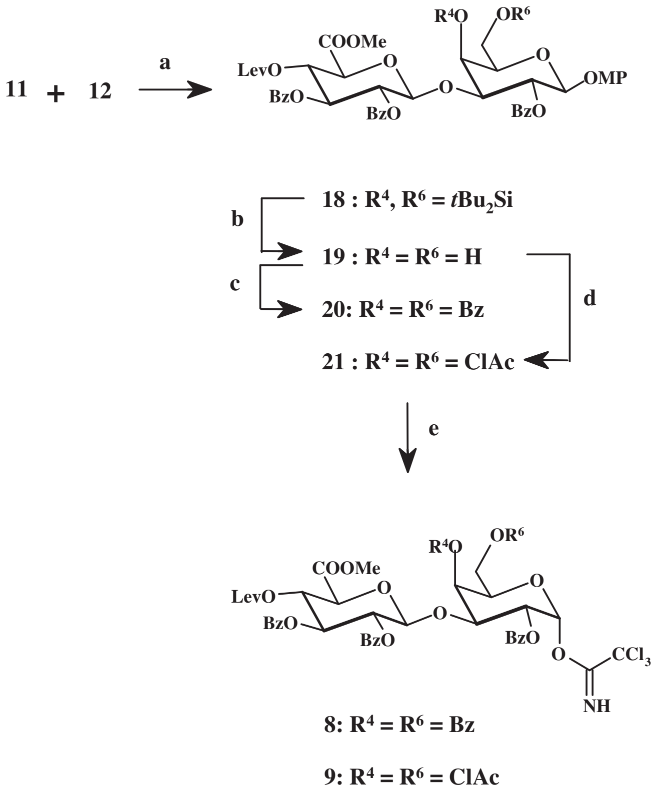


Scheme 1. Reagents and conditions: (a) LevOH, DCC, DMAP, CH_2Cl_2, rt, 1 h; (b) CAN, toluene/MeCN/H_2O, rt, 30 min; then Cl_3CCN, DBU, CH_2Cl_2, rt, 30 min.

possible chain elongation at C-4 of the D-GlcA moiety, an orthogonal levulinoyl group was installed on this position from the beginning of the synthesis.

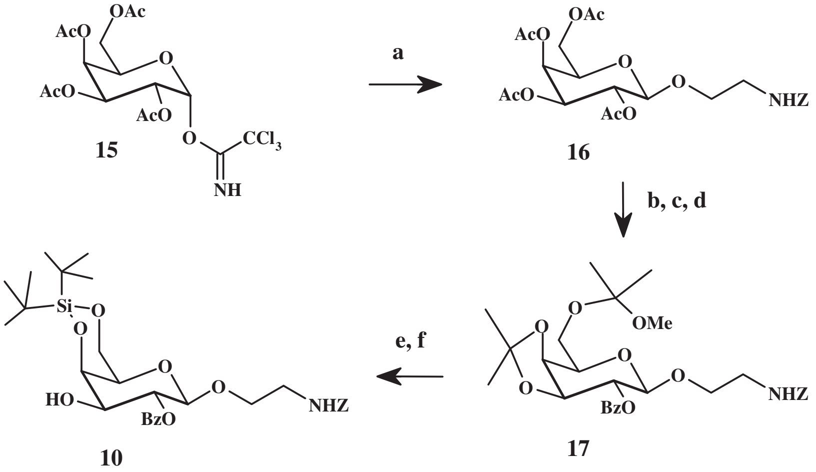
Preparation of the D-glucuronyl donor **11** was achieved as follows (Scheme 1). Known alcohol **13**,[9] easily prepared in multigram quantities by tin-mediated selective dibenzoylation of the corresponding triol, was treated with levulinic acid, 1,3-dicyclohexylcarbodiimide (DCC), and 4-dimethylaminopyridine (DMAP) in dichloromethane to give **14** in 91% yield. Introduction of the trichloroacetimidoyl group at C-1 was then achieved through oxidative removal of the 4-methoxyphenyl group with Cerium(IV) diammonium hexanitrate (CAN) followed by imidoylation of the intermediate hemiacetal with trichloroacetonitrile and 1,8-diazabicyclo[5,4,0]-undec-7-ene (DBU) in dichloromethane to afford the α-imidate **11** in 74% overall yield, for which physical data matched those reported for the preparation of **11** following another route.[10]

The precursor of the central D-Gal^{II} unit **12** was prepared as reported previously,[11] and the reducing D-Gal^{I} moiety was synthesized following a similar route (Scheme 2). Coupling reaction of known[12] 2,3,4,6-tetra-*O*-acetyl-1-*O*-trichloroacetimidoyl-α-D-galactopyranose **15** with 2-benzyloxycarbonylaminoethanol in the presence of trimethylsilyl triflate (TMSOTf) in dichloromethane gave **16** in 91% yield. Zemplèn transesterification of **16** gave quantitatively the corresponding tetrol, which was directly treated with 2,2-dimethoxypropane and 10-camphorsulfonic acid (CSA) under thermodynamic control[13] to give the intermediate 3,4,6-trisubstituted bis-acetal that was benzoylated to afford the crystalline ester **17** in 76% overall yield. Acid hydrolysis of **17** gave the corresponding triol derivative which was treated with di-*tert*-butylsilyl ditriflate (DTBS ditriflate) and *sym*-collidine in dichloromethane to provide alcohol **10** in 90% overall yield. The convenience of the silylene acetal in oligosaccharide synthesis compared to its 4,6-benzylidene congener was previously demonstrated.[14]

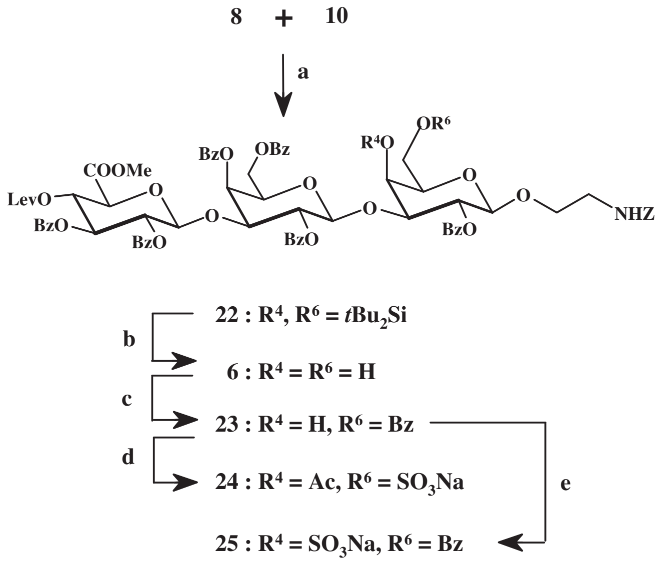


Scheme 3. Reagents and conditions: (a) Compound **11** (1.3 equiv), TMSOTf, 4 Å mol. sieves, CH_2Cl_2, rt, 40 min; (b) $Et_3N{\cdot}3HF$, THF, 0 °C, 3 h; (c) PhCOCl, pyridine/CH_2Cl_2, 0 °C, 2 h; (d) $(ClAc)_2O$, pyridine/CH_2Cl_2, 0 °C, 1 h; (e) CAN, toluene/MeCN/H_2O, rt, 30 min; then Cl_3CCN, DBU, CH_2Cl_2, rt, 30 min.

Preparation of the activated disaccharide derivatives **8** and **9** was then achieved as follows (Scheme 3). Condensation of imidate **11** (1.3 equiv) with alcohol **12** in dichloromethane in the presence of TMSOTf gave **18** (85%). The 1,2-*trans* configuration of the interglycosidic linkage was deduced from its ^{1}H NMR spectrum ($J_{1,2}$ 8.0 Hz, GlcA H-1). Treatment of **18** with triethylamine–trihydrofluoride complex in tetrahydrofuran afforded the crystalline diol **19** in



Scheme 2. Reagents and conditions: (a) 2-Benzyloxycarbonylaminoethanol, TMSOTf, CH_2Cl_2, 0 °C, 30 min; (b) MeONa, MeOH, rt, 1 h; (c) 2,2-dimethoxypropane (neat), CSA, rt, 60 h; (d) PhCOCl, pyridine/CH_2Cl_2, 0 °C, 1 h; (e) 90% TFA, rt, 10 min; (f) DTBS ditriflate, *sym*-collidine, CH_2Cl_2, 0 °C, 90 min.

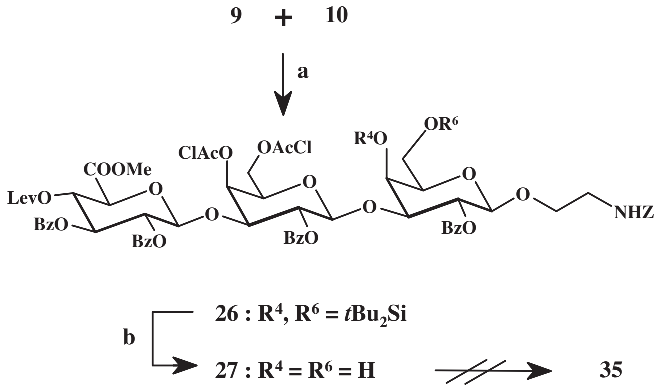


Scheme 4. Reagents and conditions: (a) Compound **10** (1.5 equiv), TMSOTf, 4 Å mol. sieves, CH_2Cl_2, rt, 40 min; (b) $Et_3N{\cdot}3HF$, THF, 0 °C, 3 h; (c) PhCOCN, pyridine, rt, 16 h; (d) $Me_3N{\cdot}SO_3$, DMF, 40 °C, 10 h; then Ac_2O, pyridine, rt, 16 h; (e) $Me_3N{\cdot}SO_3$, DMF, 60 °C, 16 h.

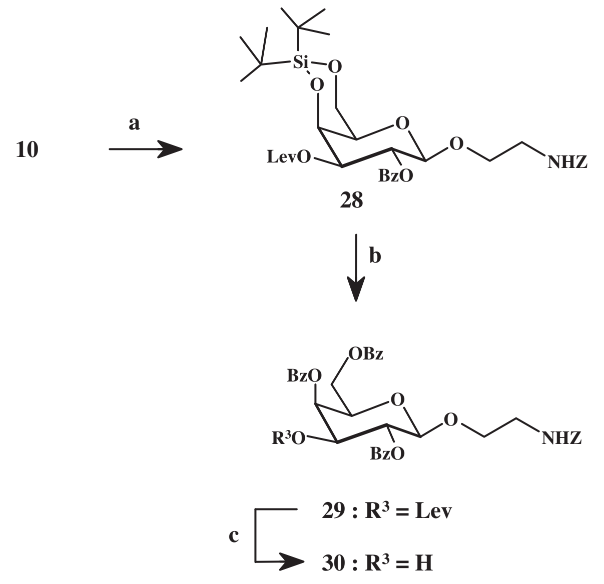
83% yield. At this point, diol **19** can either be benzoylated to give crystalline **20** in 86% yield, the precursor of species non-sulfated on Gal^{II}, or chlororacetylated to give crystalline **21** in 90% yield, those of species sulfated on Gal^{II}. Disaccharide derivatives **20** and **21** were transformed, as reported for the preparation of **11**, into the corresponding α-imidates **8** and **9**.

Next was undertaken the preparation of intermediates selectively O-sulfonated at C-4 and C-6 on Gal^{I} (Scheme 4). Coupling reaction between donor **8** and acceptor **10** (1.5 equiv), as described for the preparation of **18**, proceeded readily and afforded **22** in 67% yield, the structure of which was deduced from its ^{1}H NMR spectrum ($J_{1,2}$ 8.0 Hz, Gal^{II} H-1). Desilylation of **22**, as reported for the preparation of **19**, gave the crystalline diol **6** in 82% yield, the key intermediate for the preparation of target molecules **1**–**3**. Treatment of **6** with benzoyl cyanide in pyridine afforded regioselectively the crystalline 6-benzoate **23** in 77% yield, the precursor of the 4-sulfated species. Controlled regioselective 6-O-sulfonation of diol **6** with sulfur trioxide–trimethylamine complex in *N*,*N*-dimethylformamide (DMF) at 40 °C,[15] followed by direct acetylation and ion-exchange, gave the sodium salt **24** in 71% yield. The ^{1}H NMR spectrum of **24** showed the expected[16] downfield shift $\Delta\delta \sim 0.4$ ppm of the signals for Gal^{I} H-6a, 6b in **24** compared with those of its non-sulfated precursor **6**, and the presence of a telling signal at δ 5.57 ppm (Gal^{I} H-4). Sulfation of the low-reactive alcohol **23** required excess of reagent and higher temperature to go to completion, and the sodium salt **25** was isolated in 83% yield. Comparison of the ^{1}H NMR spectra of **25** and those of its precursor **23** showed the expected[16] downfield shift $\Delta\delta \sim 1$ ppm of the signal for Gal^{I} H-4 in **25**.

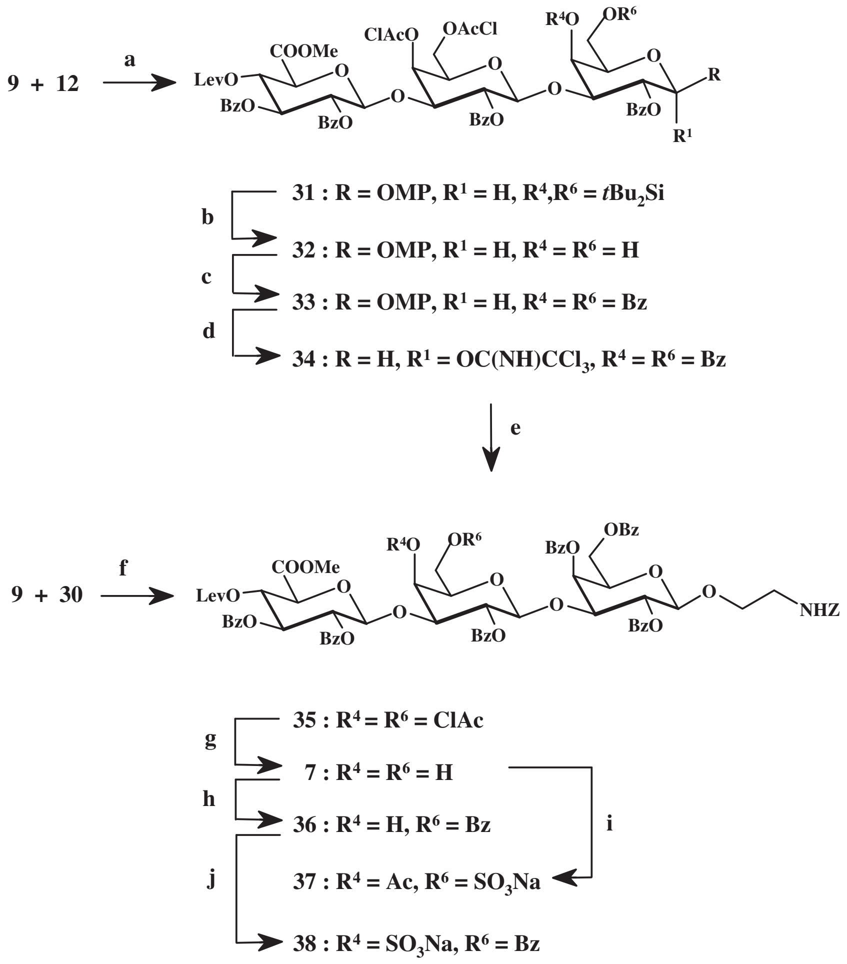
The preparation of species selectively O-sulfonated at C-4 and C-6 of Gal^{II} unexpectedly was more problematical (Scheme 5). Coupling reaction between imidate **9** and alcohol **10** (1.5 equiv), as reported for the preparation of **18**, gave trisaccharide **26** in 49% yield, along with ~15% of a corresponding orthoester derivative that could not be rearranged into **26** by addition of more catalyst. Desilylation of **26** afforded readily the crystalline diol **27** in 81% yield, that was fully resistant to benzoylation or acetylation. Changes of acylating reagent, catalyst, or temperature did not allow the obtention of **35** in acceptable yields. These frustrating results, probably due to a dramatic change of the conformation of **27** in solution, prompt us to design a new strategy for the preparation of the key intermediate **7**. To achieve this goal, two possible routes were explored. The first one involved a change in the protective groups pattern in the acceptor (Scheme 6). To this end, alcohol **10** was transformed into alcohol **30** through levulinoylation at *O*-3 to give **28**, followed by desilylation and benzoylation to afford **29**, and finally delevulinoylation with hydrazine acetate to provide alcohol **30** in excellent overall yield. Coupling reactions between disaccharide imidate **9** and alcohol **30** (1.5 equiv), as reported above, afforded the crystalline trisaccharide derivative **35** in 48% yield, the ^{1}H NMR spectrum of which was in full agreement with the expected structure. The second route involved the preparation of the trisaccharide imidate **34** and coupling with the spacer (Scheme 7). Thus, coupling reaction between imidate **9** and alcohol **12** (1.5 equiv) gave trisaccharide **31** in 61% yield, the structure of which was deduced from its ^{1}H NMR spectrum. Desilylation of **31** gave diol **32** in 88% yield, that was benzoylated to afford the crystalline ester **33** in 83% yield. Derivative **33** was transformed, as reported for the preparation of **11**, into α-imidate **34** in 38% overall yield. Coupling reaction between trisaccharide imidate **34** and 2-benzyloxycarbonylaminoethanol, as reported above, provided **35** in 56% yield, whose



Scheme 5. Reagents and conditions: (a) Compound **10** (1.5 equiv), TMSOTf, 4 Å mol. sieves, CH_2Cl_2, rt, 40 min; (b) $Et_3N{\cdot}3HF$, THF, 0 °C, 3 h.



Scheme 6. Reagents and conditions: (a) LevOH, DCC, DMAP, CH_2Cl_2, rt, 1 h; (b) $Et_3N{\cdot}3HF$, THF, 0 °C, 3 h; then PhCOCl, pyridine/CH_2Cl_2, 0 °C, 1 h; (c) hydrazine acetate, pyridine, rt, 8 min.



Scheme 7. Reagents and conditions: (a) Compound **12** (1.5 equiv), TMSOTf, 4 Å mol. sieves, CH_2Cl_2, rt, 40 min; (b) $Et_3N{\cdot}3HF$, THF, 0 °C, 3 h; (c) PhCOCl, pyridine/CH_2Cl_2, 0 °C, 1 h; (d) CAN, toluene/MeCN/H_2O, rt, 30 min; then Cl_3CCN, DBU, CH_2Cl_2, rt, 30 min; (e) 2-benzyloxycarbonylaminoethanol, TMSOTf, CH_2Cl_2, 0 °C, 30 min; (f) compound **30** (1.5 equiv), TMSOTf, 4 Å mol. sieves, CH_2Cl_2, rt, 40 min; (g) thiourea, pyridine/EtOH, 80 °C, 2 h; (h) PhCOCN, pyridine, rt, 16 h; (i) $Me_3N{\cdot}SO_3$, DMF, 40 °C, 6 h; then Ac_2O, pyridine, rt, 16 h; (j) $Me_3N{\cdot}SO_3$, DMF, 60 °C, 16 h.

physical data matched those of compound prepared by the first route. Treatment of **35** with thiourea in pyridine/ethanol gave the key diol **7** in 77% yield, which upon regioselective benzoylation at *O*-6, as reported for the preparation of **23**, afforded alcohol **36** in 80% yield. Controlled regioselective 6-O-sulfonation on **7**, followed by acetylation and ion-exchange, as reported for the preparation of **24**, gave the sodium salt **37** in 76% yield, the ^{1}H NMR spectrum of which showed the same characteristic features as those reported for **24**. Sulfation of alcohol **36** at C-4 provided the sodium salt **38** in 77% yield, the ^{1}H NMR spectrum of which was in full agreement with the expected structure.

Access to the target molecules **1**–**5** was then achieved as follows (Scheme 8). For the deprotections of diol **6** and sulfoforms **24**, **25**, **37,** and **38**, a two-step saponification process avoiding β-elimination reaction at the D-GlcA moiety,[17] with lithium hydroperoxide followed by sodium hydroxide, provided the non-sulfated **39** in 69% yield, and the disodium salts **40**–**43** in 80–88% yields, respectively. The ^{1}H and ^{13}C NMR spectra for **39**–**43** showed high purity, and were fully consistent with the expected structures. Finally, catalytic hydrogenation of **39**–**43** in water led to the corresponding free amine derivatives, which were readily treated with 6-biotinylamidohexanoic acid *N*-hydroxysuccinimidoyl ester and triethylamine in *N,N*-dimethylformamide/water to afford, after purification on Sephadex LH-20 in water, the target molecules **1**–**5** in 60–79% yields. For all biotinylated molecules, the ^{13}C NMR spectra clearly showed the downfield shifts $\Delta\delta \sim 9$ ppm for the signals for Gal C-4 in 4-sulfated units, and those $\Delta\delta \sim 7$ ppm for the signals of Gal C-6 in 6-sulfated units, compared with those of the non-sulfated units.

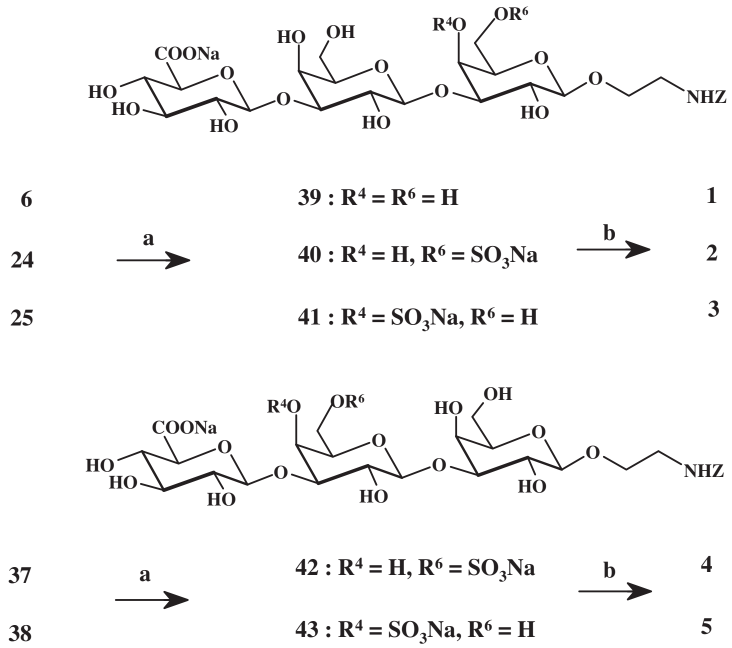
3. Conclusion

In conclusion, we have reported for the first time a stereocontrolled approach toward the preparation of a set of sulfoforms of biotinylated structures from the linkage region of proteoglycans. Common precursors were used in a divergent manner which allowed the obtention of target molecules with high purity. These structures will be useful to check the substrate specificity of the hexosaminyltransferases involved in the chain elongation and sorting of proteoglycans. All these molecules are currently being investigated in biological assays, the results of which will be reported elsewhere in due course.

4. Experimental

4.1. General methods

Solvents were dried by standard methods, and molecular sieves were activated prior to use by heating for 4 h at 500 °C. Melting points were determined in capillary tubes with a Büchi apparatus



Scheme 8. Reagents and conditions: (a) LiOH/H$_2$O$_2$, THF/H$_2$O, −10 °C → rt, 8 h; then 4 M NaOH, rt, 16 h; (b) H$_2$, Pd/C, H$_2$O, rt, 16 h; then 6-biotinylamidohexanoic acid *N*-hydroxysuccinimidoyl ester, Et$_3$N, DMF/H$_2$O, rt, 1 h.

and are uncorrected. Optical rotations were measured at 20 °C with a Perkin–Elmer 341 polarimeter. ^{1}H and ^{13}C NMR spectra were recorded at 25 °C with a Bruker Advance II 400 instrument, with Me$_4$Si as internal standard, unless otherwise stated. Assignments were based on homo- and heteronuclear correlations using the supplier's software. In the NMR data for oligomers, Gal^{I} (with roman numeral superscript) refer to 'reducing' D-galactose residue, and Gal^{II} to non-reducing residue, respectively. Low-resolution mass spectra (ISMS) were obtained on a Perkin–Elmer SCIEX API 300 spectrometer operating in the ion-spray mode or on a Micromass Quattro Ultima spectrometer equipped with a Z-spray ionization source operating in the negative mode. High-resolution mass spectra (HRESIMS) were performed on a Bruker maXis mass spectrometer by the 'Fédération de Recherche ICOA/CBM (FR 2708) platform. Flash-silica chromatography was performed on Silica Gel 60 (0.040–0.063 mm, Merck, Darmstadt). The reactions were monitored by TLC on coated aluminium sheets (Silica Gel 60 GF$_{254}$, Merck), and spots were detected under UV light and by charring with a 95/5 mixture of ethanol and sulfuric acid. Elemental analyses were carried out at the Service Central d'Analyse du CNRS (Institut des Sciences Analytique, Solaize, France).

4.2. Methyl (4-methoxyphenyl 2,3-di-*O*-benzoyl-4-*O*-levulinoyl-β-D-glucopyranosid)uronate (14)

A mixture of methyl (4-methoxyphenyl 2,3-di-*O*-benzoyl-β-D-glucopyranosid)uronate **13**[9] (3.13 g, 6 mmol), levulinic acid (0.88 g, 7.5 mmol) and DMAP (122 mg, 1 mmol) in anhyd CH$_2$Cl$_2$ (40 mL) was treated in portions with DCC (1.55 g, 7.5 mmol), and the mixture was stirred for 1 h at rt. The precipitated DCU was filtered off, washed with CH$_2$Cl$_2$, and the filtrate was washed with cold 0.1 M HCl, satd aq NaHCO$_3$, and water, dried (MgSO$_4$), and concentrated. The solid residue was recrystallized from hot acetone to give **14** (3.39 g, 91%) as a white cotton: mp 169–170 °C; $[\alpha]_D^{20}$ +58 (*c* 1, CHCl$_3$); ^{1}H NMR (CDCl$_3$, 400 MHz): δ 8.0–6.80 (m, 14H, Ar-*H*), 5.76 (dd, 1H, $J_{2,3} = J_{3,4} = 9.0$ Hz, H-3), 5.68 (dd, 1H, $J_{1,2}$ 7.0 Hz, H-2), 5.58 (dd, 1H, $J_{4,5}$ 9.5 Hz, H-4), 5.23 (d, 1H, H-1), 4.32 (d, 1H, H-5), 3.78, 3.76 (2s, 6H, OC*H*$_3$, COOC*H*$_3$), 2.70–2.40 (m, 4H, C*H*$_2$CO), 2.08 (s, 3H, COC*H*$_3$); ISMS: *m/z* 643 [M+Na]$^+$. Anal. Calcd for C$_{33}$H$_{32}$O$_{12}$: C, 63.87; H, 5.35. Found: C, 63.71; H, 5.40.

4.3. Methyl 2,3-di-*O*-benzoyl-4-*O*-levulinoyl-1-*O*-trichloroacetimidoyl-α-D-glucopyranuronate (11)

A mixture of **14** (2.92 g, 4.7 mmol) and CAN (13.7 g, 25 mmol) in 1:1.5:1 toluene/MeCN/H$_2$O (140 mL) was stirred for 30 min at rt, then was poured into ice-cold water (300 mL) and extracted with EtOAc (3 × 50 mL). The organic layer was washed with brine, and water, dried (MgSO$_4$), and concentrated. Flash silica chromatography (5:4 EtOAc/petroleum ether) gave the corresponding hemiacetal as a yellow foam. A mixture of the hemiacetal, Cl$_3$CCN (4.5 mL, 45 mmol), and DBU (165 μL, 1.1 mmol) in anhyd CH$_2$Cl$_2$ (20 mL) was stirred for 30 min at rt, then was concentrated. Flash silica chromatography (3:2 petroleum ether/EtOAc, containing 0.1% of Et$_3$N) gave imidate **11** (2.28 g, 74%) as a white foam: $[\alpha]_D^{20}$ +120 (*c* 1, CHCl$_3$), lit.[10] +113.3, ^{1}H NMR spectral data matched that reported.

4.4. 2-Benzyloxycarbonylaminoethyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranoside (16)

A mixture of imidate **15**[12] (4.93 g, 10 mmol), 2-benzyloxycarbonylaminoethanol (3.12 g, 16 mmol) and powdered 4 Å molecular sieves (1 g) in anhyd CH$_2$Cl$_2$ (50 mL) was stirred at 0 °C under dry Ar. A solution of Me$_3$SiOTf in anhyd toluene (1 M, 1.6 mL) was added, and the mixture was stirred for 30 min at 0 °C. Triethylamine (1 mL) was added, and the mixture was filtered, and concentrated. Flash silica chromatography (1:1 petroleum ether/EtOAc, containing 0.1% of Et$_3$N) gave **16** (4.79 g, 91%) as a white foam: $[\alpha]_D^{20}$ −3 (*c* 1, CHCl$_3$); ^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.40–7.30 (m, 5H, Ar-*H*), 5.38 (dd, 1H, $J_{3,4}$ 3.5, $J_{4,5}$ <1 Hz, H-4), 5.17 (dd, 1H, $J_{1,2}$ 8.0, $J_{2,3}$ 11.0 Hz, H-2), 5.15 (br s, 1H, N*H*), 5.10 (s, 2H, C*H*$_2$-Ar), 4.99 (dd, 1H, H-3), 4.45 (d, 1H, H-1), 4.15–4.10 (m, 2H, H-6a,6b), 3.91–3.87 (m, 2H, H-5, OC*H*$_2$), 3.70–3.66 (m, 1H, OC*H*$_2$), 3.42–3.38 (m, 2H, C*H*$_2$N), 2.16, 2.10, 2.08, 2.07 (4s, 12H, OCOC*H*$_3$); ISMS:

m/z 548 [M+Na]$^+$. Anal. Calcd for $C_{24}H_{31}NO_{12}$: C, 54.85; H, 5.95; N, 2.66. Found: C, 54.73; H, 5.99; N, 2.49.

4.5. 2-Benzyloxycarbonylaminoethyl 2-*O*-benzoyl-3,4-*O*-isopropylidene-6-*O*-(2-methoxy-2-propyl)-β-D-galactopyranoside (17)

A solution of **16** (4.20 g, 8 mmol) in MeOH (30 mL) was treated for 1 h with methanolic sodium methoxide (1 M, 1 mL), then was deionized with Amberlite IR-120 [H$^+$] resin, filtered, and concentrated to give quantitatively the corresponding tetrol. A mixture of the tetrol and CSA (120 mg) in 2,2-dimethoxypropane (120 mL) was stirred for 60 h at rt. Triethylamine (2 mL) was added, and the mixture was concentrated. Flash silica chromatography (3:1 EtOAc/petroleum ether, containing 0.2% of Et_3N) gave the corresponding bis-acetal (3.08 g, 82%) as a colorless glass. Benzoyl chloride (1.56 mL, 13 mmol) was added dropwise at 0 °C to a solution of the above isolated alcohol in anhyd pyridine (7 mL) and anhyd CH_2Cl_2 (20 mL), and the mixture was stirred for 1 h at 0 °C. Methanol (1 mL) was added, and the mixture was diluted with CH_2Cl_2 (100 mL), washed with water, satd aq $NaHCO_3$, and water, dried ($MgSO_4$), and concentrated. Crystallization of the residue from hot petroleum ether gave **17** (3.49 g, 76% from **16**): mp 117–118 °C; $[\alpha]_D^{20}$ +22 (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): δ 8.10–7.20 (m, 10H, Ar-*H*), 5.51 (br s, 1H, N*H*), 5.21 (dd, 1H, $J_{1,2}$ 8.0, $J_{2,3}$ 7.0 Hz, H-2), 5.02 (ABq, 2H, CH_2-Ar), 4.47 (d, 1H, H-1), 4.32 (dd, 1H, $J_{3,4}$ 5.5 Hz, H-3), 4.23 (dd, 1H, $J_{4,5}$ 2.0 Hz, H-4), 3.96–3.94 (m, 1H, H-5), 3.87–3.83 (m, 1H, OCH_2), 3.80–3.70 (m, 3H, H-6a,6b, OCH_2), 3.40–3.30 (m, 2H, CH_2N), 3.19 (s, 3H, OCH_3), 1.62, 1.35, 1.31 (3s, 12H, $(CH_3)_2C$); ISMS: *m/z* 596 [M+Na]$^+$. Anal. Calcd for $C_{30}H_{39}NO_{10}$: C, 62.81; H, 6.85; N, 2.44. Found: C, 62.71; H, 6.92; N, 2.31.

4.6. 2-Benzyloxycarbonylaminoethyl 2-*O*-benzoyl-4,6-*O*-di-*tert*-butylsilylene-β-D-galactopyranoside (10)

A solution of **17** (2.17 g, 3.78 mmol) in TFA/H_2O (9:1, 10 mL) was stirred for 10 min at rt, then was diluted with water (20 mL), concentrated, evaporated with water (3 × 10 ml), and dried in vacuo to give quantitatively the corresponding triol. Di-*tert*-butylsilyl ditriflate (1.53 mL, 4.5 mmol) was added at 0 °C to a suspension of the triol and *sym*-collidine (1.25 mL, 9.5 mmol) in anhyd CH_2Cl_2 (15 mL), and the mixture was stirred for 90 min at 0 °C. The clear solution was washed with water, satd aq $NaHCO_3$, and water, dried ($MgSO_4$), and concentrated. Flash silica chromatography (3:2 petroleum ether/EtOAc, containing 0.1% of Et_3N) gave alcohol **10** (2.05 g, 90% from **17**) as a white foam: $[\alpha]_D^{20}$ +10 (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): δ 8.10–7.20 (m, 10H, Ar-*H*), 5.34 (dd, 1H, $J_{1,2}$ 8.0, $J_{2,3}$ 11.0 Hz, H-2), 5.21 (br s, 1H, N*H*), 5.02 (ABq, 2H, CH_2-Ar), 4.54 (d, 1H, H-1), 4.45 (dd, 1H, $J_{3,4}$ 3.5, $J_{4,5}$ 0.8 Hz, H-4), 4.30–4.26 (m, 2H, H-6a,6b), 3.87–3.84 (m, 1H, OCH_2), 3.74–3.68 (m, 2H, H-3, OCH_2), 3.51–3.49 (m, 1H, H-5), 3.36–3.30 (m, 2H, CH_2N), 2.68 (d, 1H, $J_{3,OH}$ 3.5 Hz, *H*O-3), 1.09, 1.06 (2s, 18H, $(CH_3)_3C$); ISMS: *m/z* 624 [M+Na]$^+$. Anal. Calcd for $C_{31}H_{43}NO_9Si$: C, 61.87; H, 7.20; N, 2.33. Found: C, 61.65; H, 7.11; N, 2.21.

4.7. 4-Methoxyphenyl *O*-(methyl 2,3-di-*O*-benzoyl-4-*O*-levulinoyl-β-D-glucopyranosyluronate)-(1→3)-2-*O*-benzoyl-4,6-*O*-di-*tert*-butylsilylene-β-D-galactopyranoside (18)

A mixture of imidate **11** (428 mg, 0.65 mmol), alcohol **12** (265 mg, 0.5 mmol) and powdered 4 Å molecular sieves (0.2 g) in anhyd CH_2Cl_2 (6 mL) was stirred for 40 min at rt under dry Ar. A solution of Me_3SiOTf in anhyd toluene (1 M, 0.12 mL) was added, and the mixture was stirred for 40 min at rt. Triethylamine (0.14 mL) was added, and the mixture was filtered, and concentrated. Flash silica chromatography (2:1 petroleum ether/EtOAc, containing 0.1% of Et_3N) gave **18** (430 mg, 85%) as a white foam: $[\alpha]_D^{20}$ +66.5 (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): δ 7.85–6.67 (m, 19H, Ar-*H*), 5.76 (dd, 1H, $J_{1,2}$ 8.0, $J_{2,3}$ 10.0 Hz, Gal H-2), 5.55 (dd, 1H, $J_{2,3} = J_{3,4}$ = 9.0 Hz, GlcA H-3), 5.49–5.42 (m, 2H, GlcA H-2,4), 5.08 (d, 1H, $J_{1,2}$ 8.0 Hz, GlcA H-1), 4.87 (d, 1H, Gal H-1), 4.72 (dd, 1H, $J_{3,4}$ 3.0, $J_{4,5}$ <1 Hz, Gal H-4), 4.29–4.27 (m, 2H, Gal H-6a,6b), 4.15 (d, 1H, $J_{4,5}$ 10.0 Hz, GlcA H-5), 3.99 (dd, 1H, Gal H-3), 3.77 (s, 3H, $COOCH_3$), 3.70 (s, 3H, OCH_3), 3.53 (s, 1H, Gal H-5), 2.63–2.46 (m, 3H, CH_2CO), 2.39–2.32 (m, 1H, CH_2CO), 2.04 (s, 3H, $COCH_3$), 1.08, 1.07 (2s, 18H, $(CH_3)_3C$); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 205.60 (1C, $COCH_3$), 171.02, 167.00, 165.53, 164.67, 164.61 (5C, GlcA C-6, C=O), 155.49-114.22 (24C, Ar-*C*), 101.1 (1C, Gal C-1), 101.36 (1C, GlcA C-1), 79.46 (1C, Gal C-3), 72.84 (1C, GlcA C-5), 72.62 (1C, Gal C-4), 72.35 (1C, GlcA C-3), 71.68 (1C, GlcA C-2), 71.52 (1C, Gal C-5), 70.66 (1C, Gal C-2), 69.61 (1C, GlcA C-4), 66.87 (1C, Gal C-6), 55.51 (1C, OCH_3), 52.96 (1C, $COOCH_3$), 37.58 (1C, CH_2CO), 29.52 (1C, $COCH_3$), 27.64 (1C, CH_2CO), 27.43, 27.38, 27.28, 27.20, 23.34, 20.70 (6C, $(CH_3)_3C$); HRESIMS: Calcd for $C_{54}H_{63}O_{18}Si$ [M+H]$^+$: *m/z* 1027.37782. Found: 1027.37759. Anal. Calcd for $C_{54}H_{62}O_{18}Si$: C, 63.14; H, 6.08. Found: C, 63.24; H, 6.60.

4.8. 4-Methoxyphenyl *O*-(methyl 2,3-di-*O*-benzoyl-4-*O*-levulinoyl-β-D-glucopyranosyluronate)-(1→3)-2-*O*-benzoyl-β-D-galactopyranoside (19)

A mixture of **18** (3.19 g, 3.1 mmol) and $Et_3N\cdot 3HF$ (1.12 mL, 6.8 mmol) in anhyd THF (35 mL) was stirred for 3 h at 0 °C, then was concentrated. A solution of the residue in CH_2Cl_2 (200 mL) was washed with water, satd aq $NaHCO_3$, and water, dried ($MgSO_4$), and concentrated. Flash silica chromatography (19:1 CH_2Cl_2/MeOH) gave diol **19** (2.29 g, 83%) as a white solid: mp 215–216 °C (from hot EtOH); $[\alpha]_D^{20}$ +66 (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): δ 7.82–6.68 (m, 19H, Ar-*H*), 5.68 (dd, 1H, $J_{1,2}$ 8.0, $J_{2,3}$ 10.0 Hz, Gal H-2), 5.61 (dd, 1H, $J_{2,3} = J_{3,4}$ = 9.0 Hz, GlcA H-3), 5.45 (dd, 1H, $J_{4,5}$ 10.0 Hz, GlcA H-4), 5.41 (dd, 1H, $J_{1,2}$ 7.0 Hz, GlcA H-2), 5.02 (d, 1H, GlcA H-1), 4.95 (d, 1H, Gal H-1), 4.230–4.28 (m, 1H, Gal H-4), 4.26 (d, 1H, GlcA H-5), 4.11–4.09 (m, 1H, Gal H-5), 4.05 (dd, 1H, $J_{3,4}$ 3.0, $J_{4,5}$ <1 Hz, Gal H-3), 3.92–3.88 (m, 1H, Gal H-6a), 3.79 (s, 3H, $COOCH_3$), 3.78–3.74 (m, 1H, Gal H-6b), 3.69 (s, 3H, OCH_3), 3.26 (s, 1H, Gal *H*O-4), 2.66–2.48 (m, 3H, CH_2CO), 2.41–2.33 (m, 2H, Gal *H*O-6, CH_2CO), 2.03 (s, 3H, $COCH_3$); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 206.41 (1C, $COCH_3$), 171.11, 167.38, 165.23, 164.83, 164.75 (5C, GlcA C-6, C=O), 154.85–113.81 (24C, Ar-*C*), 101.15 (1C, GlcA C-1), 100.87 (1C, Gal C-1), 80.92 (1C, Gal C-3), 74.75 (1C, Gal C-5), 71.69, 71.46 (2C, Gal C-2,4), 71.07 (1C, GlcA C-4), 70.36 (1C, GlcA C-3), 69.09 (1C, GlcA C-2), 67.95 (1C, GlcA C-5), 60.60 (1C, Gal C-6), 47.75 (1C, OCH_3), 47.54 (1C, $COOCH_3$), 36.86 (1C, CH_2CO), 28.56 (1C, $COCH_3$), 27.08 (1C, CH_2CO); HRESIMS: Calcd for $C_{46}H_{46}NaO_{18}$ [M+Na]$^+$: *m/z* 909.25764. Found: 909.25813. Anal. Calcd for $C_{46}H_{46}O_{18}$: C, 62.30; H, 5.23. Found: C, 62.24; H, 5.60.

4.9. 4-Methoxyphenyl *O*-(methyl 2,3-di-*O*-benzoyl-4-*O*-levulinoyl-β-D-glucopyranosyluronate)-(1→3)-2,4,6-tri-*O*-benzoyl-β-D-galactopyranoside (20)

A mixture of diol **19** (0.56 g, 0.63 mmol) and benzoyl chloride (0.29 mL, 2.5 mmol) in anhyd pyridine and CH_2Cl_2 (1:1, 10 mL) was stirred for 2 h at 0 °C. Methanol (1 mL) was added, and the mixture was diluted with CH_2Cl_2 (50 mL), washed with water, satd aq $NaHCO_3$, and water, dried ($MgSO_4$), and concentrated. Flash silica chromatography (1:1 EtOAc/petroleum ether) gave **20** (590 mg, 86%) as a white solid: mp 183–184 °C (from EtOAc/petroleum ether); $[\alpha]_D^{20}$ +83.5 (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): δ

8.15–6.53 (m, 29H, Ar-*H*), 5.90 (dd, 1H, $J_{3,4}$ 3.0, $J_{4,5}$ <1 Hz, Gal H-4), 5.82 (dd, 1H, $J_{1,2}$ 8.0, $J_{2,3}$ 10.0 Hz, Gal H-2), 5.50–5.39 (m, 2H, GlcA H-3,4), 5.26 (dd, 1H, $J_{1,2}$ 7.0, $J_{2,3}$ 9.0 Hz, GlcA H-2), 5.00 (d, 1H, Gal H-1), 4.98 (d, 1H, GlcA H-1), 4.61 (dd, 1H, $J_{5,6a}$ 4.5, $J_{6a,6b}$ 12.0 Hz, Gal H-6a), 4.46 (dd, 1H, $J_{5,6b}$ 8.0 Hz, Gal H-6b), 4.39 (dd, 1H, Gal H-3), 4.27–4.24 (m, 1H, Gal H-5), 4.14 (d, 1H, $J_{4,5}$ 10.0 Hz, GlcA H-5), 3.73 (s, 3H, COOC*H*$_3$), 3.64 (s, 3H, OC*H*$_3$), 2.61–2.29 (m, 4H, C*H*$_2$CO), 2.01 (s, 3H, COC*H*$_3$); ^{13}C NMR (CDCl$_3$, 100 MHz): δ 205.59 (1C, *C*OCH$_3$), 170.88, 166.80, 166.05, 165.74, 165.47, 164.52, 164.26 (7C, GlcA C-6, C=O), 155.43–114.26 (36C, Ar-*C*), 100.96, 100.80 (2C, Gal C-1, GlcA C-1), 76.80 (1C, Gal C-3), 72.79 (1C, GlcA C-5), 72.10 (2C, GlcA C-3, Gal C-5), 71.52 (1C, GlcA C-2), 71.39 (1C, Gal C-2), 69.59 (1C, Gal C-4), 69.29 (1C, GlcA C-4), 62.90 (1C, Gal C-6), 55.46 (1C, O*C*H$_3$), 52.96 (1C, COO*C*H$_3$), 37.61 (1C, *C*H$_2$CO), 29.50 (1C, CO*C*H$_3$), 27.61 (1C, *C*H$_2$CO). HRESIMS: Calcd for $C_{60}H_{55}O_{20}$ [M+H]$^+$: *m/z* 1095.32812. Found: 1095.32863. Anal. Calcd for $C_{60}H_{54}O_{20}$: C, 65.81; H, 4.97. Found: C, 65.64; H, 4.75.

4.10. 4-Methoxyphenyl *O*-(methyl 2,3-di-*O*-benzoyl-4-*O*-levulinoyl-β-D-glucopyranosyluronate)-(1→3)-2-*O*-benzoyl-4,6-di-*O*-chloroacetyl-β-D-galactopyranoside (21)

A mixture of diol **19** (709 mg, 0.8 mmol) and freshly recrystallized chloroacetic anhydride (547 mg, 3.2 mmol) in anhyd pyridine and CH$_2$Cl$_2$ (1:1, 10 mL) was stirred for 1 h at 0 °C, then was poured into ice-cold water (100 mL) and extracted with CH$_2$Cl$_2$. The organic layer was washed with water, satd aq NaHCO$_3$, and water, dried (MgSO$_4$), and concentrated. Flash silica chromatography (22:1 CH$_2$Cl$_2$/acetone) gave **21** (749 mg, 90%) as a white solid: mp 234–236 °C (from EtOAc/petroleum ether); $[\alpha]_D^{20}$ +76 (*c* 1, CHCl$_3$); ^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.83–6.69 (m, 19H, Ar-*H*), 5.63–5.58 (m, 2H, Gal H-2,4), 5.23 (dd, 1H, $J_{2,3}$ 9.0 Hz, $J_{3,4}$ 9.5 Hz, GlcA H-3), 5.43 (dd, 1H, $J_{4,5}$ 10.0 Hz, GlcA H-4), 5.30 (dd, 1H, $J_{1,2}$ 7.0 Hz, GlcA H-2), 4.94 (d, 1H, $J_{1,2}$ 8.0 Hz, Gal H-1), 4.88 (d, 1H, GlcA H-1), 4.38–4.34 (m, 3H, Gal H-6a,6b, C*H*$_2$Cl), 4.27–4.23 (m, 2H, Gal H-3, C*H*$_2$Cl), 4.12 (d, 1H, GlcA H-5), 4.09 (s, 2H, C*H*$_2$Cl), 4.10–4.07 (m, 1H, Gal H-5), 3.82 (s, 3H, COOC*H*$_3$), 3.71 (s, 3H, OC*H*$_3$), 2.64–2.45 (m, 3H, C*H*$_2$CO), 2.38–2.31 (m, 1H, C*H*$_2$CO), 2.03 (s, 3H, COC*H*$_3$); ^{13}C NMR (CDCl$_3$, 100 MHz): δ 205.57 (1C, *C*OCH$_3$), 170.96, 167.04, 166.84, 166.72, 165.48, 164.56, 164.35 (7C, GlcA C-6, C=O), 155.67–114.39 (24C, Ar-*C*), 100.83, 100.80 (2C, Gal C-1, GlcA C-1), 76.04 (1C, Gal C-3), 72.73, 71.82 (2C, GlcA C-3,5), 71.42, 70.97, 70.69, 70.53 (4C, Gal C-2,4,5, GlcA C-2), 69.31 (1C, GlcA C-4), 63.46 (1C, Gal C-6), 55.55 (1C, O*C*H$_3$), 53.18 (1C, COO*C*H$_3$), 40.74, 40.53 (2C, *C*H$_2$Cl), 37.57 (1C, *C*H$_2$CO), 29.51 (1C, CO*C*H$_3$), 27.57 (1C, *C*H$_2$CO). HRESIMS: Calcd for $C_{50}H_{49}Cl_2O_{20}$ [M+H]$^+$: *m/z* 1039.21888. Found: 1039.21743. Anal. Calcd for $C_{50}H_{48}Cl_2O_{20}$: C, 57.75; H, 4.65. Found: C, 57.50; H, 4.62.

4.11. *O*-(Methyl 2,3-di-*O*-benzoyl-4-*O*-levulinoyl-β-D-glucopyranosyluronate)-(1→3)-2,4,6-tri-*O*-benzoyl-1-*O*-trichloroacetimidoyl-β-D-galactopyranose (8)

Compound **20** (2.16 g, 1.97 mmol) was treated as described for the preparation of **11**. Flash silica chromatography (2:1 petroleum ether/EtOAc, containing 0.1% of Et$_3$N) gave imidate **8** (1.40 g, 62% from **20**) as a white foam: mp 110–115 °C (from petroleum ether/EtOAc); $[\alpha]_D^{20}$ +114 (*c* 1, CHCl$_3$); ^{1}H NMR (CDCl$_3$, 400 MHz): δ 8.48 (s, 1H, C=N*H*), 8.10–7.04 (m, 25H, Ar-*H*), 6.74 (d, 1H, $J_{1,2}$ 3.5 Hz, Gal H-1), 6.05 (dd, 1H, $J_{3,4}$ 3.0, $J_{4,5}$ <1 Hz, Gal H-4), 5.72 (dd, 1H, $J_{2,3}$ 10.0 Hz, Gal H-2), 5.55 (dd, 1H, $J_{2,3}$ 9.0, $J_{3,4}$ 10.0 Hz, GlcA H-3), 5.45 (dd, 1H, $J_{4,5}$ 10.0 Hz, GlcA H-4), 5.27 (dd, 1H, $J_{1,2}$ 7.0 Hz, GlcA H-2), 5.12 (d, 1H, GlcA H-1), 4.72–4.68 (m, 2H, Gal H-3,5), 4.52 (dd, 1H, $J_{5,6a}$ 5.0, $J_{6a,6b}$ 12.0 Hz, Gal H-6a), 4.41 (dd, 1H, $J_{5,6b}$ 7.5 Hz, Gal H-6b), 4.26 (d, 1H, GlcA H-5), 3.77 (s, 3H, COOC*H*$_3$), 2.62–2.33 (m, 4H, C*H*$_2$CO), 2.03 (s, 3H, COC*H*$_3$); ^{13}C NMR (CDCl$_3$, 100 MHz): δ 205.60 (1C, *C*OCH$_3$), 170.92, 166.95, 166.01, 165.54, 165.46, 164.99, 164.26, 160.30 (8C, GlcA C-6, C=O, C=N), 133.37–127.99 (30C, Ar-*C*), 100.89 (1C, GlcA C-1), 93.56 (1C, Gal C-1), 90.76 (1C, *C*Cl$_3$), 73.27 (1C, Gal C-3), 72.86 (1C, GlcA C-5), 72.03 (1C, GlcA C-3), 71.76 (1C, GlcA C-2), 70.30 (1C, Gal C-4), 69.92 (1C, Gal C-5), 69.85 (1C, Gal C-2), 69.21 (1C, GlcA C-4), 62.87 (1C, Gal C-6), 53.01 (1C, COO*C*H$_3$), 37.63 (1C, *C*H$_2$CO), 29.51 (1C, CO*C*H$_3$), 27.64 (1C, *C*H$_2$CO). HRESIMS: Calcd for $C_{55}H_{48}Cl_3NNaO_{19}$ [M+Na]$^+$: *m/z* 1154.17783. Found: 1154.17922. Anal. Calcd for $C_{55}H_{48}Cl_3NO_{19}$: C, 58.29; H, 4.27; N, 1.24. Found: C, 58.15; H, 4.36; N, 0.88.

4.12. *O*-(Methyl 2,3-di-*O*-benzoyl-4-*O*-levulinoyl-β-D-glucopyranosyluronate)-(1→3)-2-*O*-benzoyl-4,6-di-*O*-chloroacetyl-1-*O*-trichloroacetimidoyl-β-D-galactopyranoside (9)

Compound **21** (2.05 g, 1.97 mmol) was treated as described for the preparation of **11**. Flash silica chromatography (3:2 petroleum ether/EtOAc, containing 0.1% of Et$_3$N) gave imidate **9** (1.40 g, 62% from **21**) as a white solid: mp 180–181 °C (from petroleum ether/EtOAc); $[\alpha]_D^{20}$ +107 (*c* 1, CHCl$_3$); ^{1}H NMR (CDCl$_3$, 400 MHz): δ 8.54 (s, 1H, C=N*H*), 7.83–7.09 (m, 15H, Ar-*H*), 6.59 (d, 1H, $J_{1,2}$ 3.5 Hz, Gal H-1), 5.75 (dd, 1H, $J_{3,4}$ 3.0, $J_{4,5}$ <1 Hz, Gal H-4), 5.57 (dd, 1H, $J_{2,3}$ 9.0, $J_{3,4}$ 10.0 Hz, GlcA H-3), 5.49 (dd, 1H, $J_{2,3}$ 10.0 Hz, Gal H-2), 5.45 (dd, 1H, $J_{4,5}$ 10.0 Hz, GlcA H-4), 5.31 (dd, 1H, $J_{1,2}$ 7.0 Hz, GlcA H-2), 5.01 (d, 1H, GlcA H-1), 4.55–4.52 (m, 2H, Gal H-3,5), 4.35 (dd, 1H, $J_{5,6a}$ 5.0 Hz, $J_{6a,6b}$ 11.0 Hz, Gal H-6a), 4.28–4.19 (m, 4H, GlcA H-5, Gal H-6b, C*H*$_2$Cl), 4.07 (s, 2H, C*H*$_2$Cl), 3.84 (s, 3H, COOC*H*$_3$), 2.65–2.47 (m, 3H, C*H*$_2$CO), 2.41–2.33 (m, 1H, C*H*$_2$CO), 2.04 (s, 3H, COC*H*$_3$); ^{13}C NMR (CDCl$_3$, 100 MHz): δ 205.57 (1C, *C*OCH$_3$), 171.00, 166.81, 165.47, 164.74, 164.56, 160.23 (8C, GlcA C-6, C=O, C=N), 133.46–128.13 (18C, Ar-*C*), 100.95 (1C, GlcA C-1), 93.32 (1C, Gal C-1), 90.65 (1C, *C*Cl$_3$), 72.82 (1C, Gal C-3), 72.73 (1C, GlcA C-5), 71.77, 71.56 (2C, GlcA C-2,3), 70.90 (1C, Gal C-4), 69.32, 69.13, 69.07 (3C, Gal C-2,5, GlcA C-4), 63.32 (1C, Gal C-6), 53.19 (1C, COO*C*H$_3$), 40.61, 40.49 (2C, *C*H$_2$Cl), 37.59 (1C, *C*H$_2$CO), 29.52 (1C, CO*C*H$_3$), 27.60 (1C, *C*H$_2$CO). HRESIMS: Calcd for $C_{43}H_{41}Cl_2NaO_{19}$ [M−Cl$_3$CC(NH)+Na]$^+$): *m/z* 955.15896. Found: 955.15969. Anal. Calcd for $C_{45}H_{42}Cl_5NO_{19}$: C, 50.13; H, 3.93; N, 1.30. Found: C, 50.09; H, 4.10; N, 0.86.

4.13. 2-Benzyloxycarbonylaminoethyl *O*-(methyl 2,3-di-*O*-benzoyl-4-*O*-levulinoyl-β-D-glucopyranosyluronate)-(1→3)-(2,4,6-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-2-*O*-benzoyl-4,6-*O*-di-*tert*-butylsilylene-β-D-galactopyranoside (22)

A mixture of imidate **8** (681 mg, 0.6 mmol) and alcohol **10** (542 mg, 0.9 mmol) was treated as described for the preparation of **18**. Flash silica chromatography (18:1 CH$_2$Cl$_2$/acetone containing 0.1% of Et$_3$N) gave **22** (632 mg, 67%) as a white foam: $[\alpha]_D^{20}$ +62 (*c* 1, CHCl$_3$); ^{1}H NMR (CDCl$_3$, 400 MHz): δ 8.09–6.91 (m, 35H, Ar-*H*), 5.83 (dd, 1H, $J_{3,4}$ 3.0, $J_{4,5}$ <1 Hz, Gal$^{\text{II}}$ H-4), 5.51 (dd, 1H, $J_{1,2}$ 8.0, $J_{2,3}$ 10.0 Hz, Gal$^{\text{II}}$ H-2), 5.39–5.37 (m, 3H, Gal$^{\text{I}}$ H-2, GlcA H-3,4), 5.16 (dd, 1H, $J_{1,2}$ 7.0, $J_{2,3}$ 8.5 Hz, GlcA H-2), 5.05 (br s, 1H, N*H*), 4.95 (ABq, 2H, C*H*$_2$-Ar), 4.92 (d, 1H, Gal$^{\text{II}}$ H-1), 4.79 (d, 1H, GlcA H-1), 4.69 (dd, 1H, $J_{3,4}$ 3.0, $J_{4,5}$ <1 Hz, Gal$^{\text{I}}$ H-4), 4.74–4.39 (m, 2H, Gal$^{\text{II}}$ H-6a,b), 4.34–4.31 (m, 1H, Gal$^{\text{II}}$ H-3), 4.31 (d, 1H, $J_{1,2}$ 7.5 Hz, Gal$^{\text{I}}$ H-1), 4.16–4.06 (m, 2H, Gal$^{\text{II}}$ H-5, Gal$^{\text{I}}$ H-6a), 4.08 (d, 1H, $J_{4,5}$ 9.0 Hz, GlcA H-5), 4.02–3.98 (m, 1H, Gal$^{\text{I}}$ H-6b), 3.74–3.68 (m, 5H, Gal$^{\text{I}}$ H-3, OC*H*$_2$, COOC*H*$_3$), 3.52–3.47 (m, 1H, OC*H*$_2$), 3.21–3.17 (m, 3H, Gal$^{\text{I}}$ H-5, NC*H*$_2$), 2.60–2.41 (m, 3H, C*H*$_2$CO), 2.34–2.26 (m, 1H, C*H*$_2$CO), 2.01 (s, 3H, COC*H*$_3$), 1.01, 0.95 (2s, 18H, (C*H*$_3$)$_3$C); ^{13}C NMR (CDCl$_3$, 100 MHz): δ 205.63 (1C, *C*OCH$_3$), 170.86, 166.89, 165.87, 165.49, 165.41, 164.64, 164.14, 164.11, 156.29 (9C, GlcA C-6, C=O), 133.67–127.75 (42C, Ar-*C*), 102.26 (1C, Gal$^{\text{II}}$ C-1), 101.52 (1C, Gal$^{\text{I}}$ C-1), 100.51 (1C, GlcA C-1), 80.16 (1C, Gal$^{\text{I}}$ C-3), 75.83 (1C, Gal$^{\text{II}}$ C-3), 72.68 (1C, Gal$^{\text{I}}$ C-4), 72.63 (1C, GlcA C-5), 72.08, 71.96, 71.64, 71.52, 71.37, 70.51, 69.70, 69.25 (8C, Gal$^{\text{I}}$ C-2,5, Gal$^{\text{II}}$ C-2,4,5, GlcA C-2,3,4), 68.65 (1C, O*C*H$_2$), 66.69 (1C, Gal$^{\text{I}}$ C-6), 66.28 (1C, *C*H$_2$-Ar), 62.85 (1C, Gal$^{\text{II}}$ C-6), 52.93 (1C, COO*C*H$_3$), 40.84 (1C, N*C*H$_2$), 37.57 (1C, *C*H$_2$CO), 29.51 (1C, CO*C*H$_3$), 27.58 (1C, *C*H$_2$CO), 27.38, 27.25 (4C, (*C*H$_3$)$_3$C), 23.18, 20.59 (2C, (CH$_3$)$_3$*C*). HRESIMS: Calcd for $C_{84}H_{89}NNaO_{27}Si$ [M+Na]$^+$: *m/z* 1594.52834. Found: 1594.52825. Anal. Calcd for $C_{84}H_{89}NO_{27}Si$: C, 64.15; H, 5.70; N, 0.89. Found: C, 64.15; H, 5.83; N, 0.81.

4.14. 2-Benzyloxycarbonylaminoethyl *O*-(methyl 2,3-di-*O*-benzoyl-4-*O*-levulinoyl-β-D-glucopyranosyluronate)-(1→3)-(2,4,6-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-2-*O*-benzoyl-β-D-galactopyranoside (6)

Compound **22** (1.03 g, 0.65 mmol) was treated as described for the preparation of **19**. The solid residue was recrystallized from EtOAc/petroleum ether to give diol **6** (771 mg, 82%); mp 194–195 °C; $[\alpha]_D^{20}$ +56 (*c* 1, CHCl$_3$); ^{1}H NMR (CDCl$_3$, 400 MHz): δ 8.10–6.99 (m, 35H, Ar-*H*), 5.81 (dd, 1H, $J_{3,4}$ 3.0, $J_{4,5}$ <1 Hz, Gal$^{\text{II}}$ H-4), 5.51 (dd, 1H, $J_{1,2}$ 8.0, $J_{2,3}$ 10.0 Hz, Gal$^{\text{II}}$ H-2), 5.37–5.29 (m, 3H, Gal$^{\text{I}}$ H-2, GlcA H-3,4), 5.16–5.12 (m, 2H, GlcA H-2, N*H*), 4.92 (ABq, 2H, C*H*$_2$-Ar), 4.82 (d, 1H, $J_{1,2}$ 7.0 Hz, GlcA H-1), 4.76 (d, 1H, Gal$^{\text{II}}$ H-1), 4.62 (dd, 1H, $J_{5,6a}$ 4.0, $J_{6a,6b}$ 12.0 Hz, Gal$^{\text{II}}$ H-6a), 4.44 (dd, 1H, $J_{5,6b}$ 8.0 Hz, Gal$^{\text{II}}$ H-6b), 4.33 (d, 1H, $J_{1,2}$ 8.5 Hz, Gal$^{\text{I}}$ H-1), 4.27 (dd, 1H, Gal$^{\text{II}}$ H-3), 4.18 (m, 1H, Gal$^{\text{II}}$ H-5), 4.05–4.03 (m, 2H, Gal$^{\text{I}}$ H-4, GlcA H-5), 3.78 (dd, 1H, $J_{2,3}$ 10.0, $J_{3,4}$ 3.0 Hz, Gal$^{\text{I}}$ H-3), 3.82–3.70 (m, 5H, Gal$^{\text{I}}$ H-6a, OC*H*$_2$, COOC*H*$_3$), 3.57–3.47 (m, 2H, Gal$^{\text{I}}$ H-6b, OC*H*$_2$), 3.96–3.92 (m, 1H, Gal$^{\text{I}}$ H-5), 3.23–3.20 (m, 2H, NC*H*$_2$), 2.19 (s, 1H, Gal$^{\text{I}}$ *H*O-4), 2.60–2.41 (m, 3H, C*H*$_2$CO), 2.34–2.23 (m, 2H, Gal$^{\text{I}}$ *H*O-6, C*H*$_2$CO), 2.00 (s, 3H, COC*H*$_3$); ^{13}C NMR (CDCl$_3$, 100 MHz): δ 205.61 (1C, *C*OCH$_3$), 170.84, 166.80, 166.07, 165.84, 165.35, 164.11, 164.08 (9C, GlcA C-6, C=O), 133.48–127.86 (42C, Ar-*C*), 101.65 (1C, Gal$^{\text{II}}$ C-1), 101.44 (1C, Gal$^{\text{I}}$ C-1), 100.52 (1C, GlcA C-1), 80.66 (1C, Gal$^{\text{I}}$ C-3), 75.66 (1C, Gal$^{\text{II}}$ C-3), 74.39 (1C, Gal$^{\text{I}}$ C-5), 72.66 (1C, GlcA C-5), 72.13, 71.89, 71.29, 71.25, 70.53, 69.74, 69.17 (7C, Gal$^{\text{I}}$ C-2, Gal$^{\text{II}}$ C-2,4,5, GlcA C-2,3,4), 68.79 (1C, Gal$^{\text{I}}$ C-4), 68.68 (1C, O*C*H$_2$), 66.36 (1C, *C*H$_2$-Ar), 62.74 (1C, Gal$^{\text{II}}$ C-6), 62.03 (1C, Gal$^{\text{I}}$ C-6), 52.96 (1C, COO*C*H$_3$), 40.82 (1C, N*C*H$_2$), 37.52 (1C, *C*H$_2$CO), 29.46 (1C, CO*C*H$_3$), 27.52 (1C, *C*H$_2$CO). HRESIMS: Calcd for $C_{76}H_{74}NO_{27}$ [M+H]$^+$: *m/z* 1432.44427. Found: 1432.44471. Anal. Calcd for $C_{76}H_{73}NO_{27:}$ C, 63.73; H, 5.14; N, 0.98. Found: C, 62.10; H, 5.13; N, 0.88.

4.15. 2-Benzyloxycarbonylaminoethyl *O*-(methyl 2,3-di-*O*-benzoyl-4-*O*-levulinoyl-β-D-glucopyranosyluronate)-(1→3)-(2,4,6-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-2,6-di-*O*-benzoyl-β-D-galactopyranoside (23)

A mixture of **6** (250 mg, 0.17 mmol) and benzoyl cyanide (46 mg, 0.35 mmol) in anhyd pyridine (5 mL) was stirred for 16 h at rt. Methanol (1 mL) was added, and the mixture was concentrated. Flash silica chromatography (12:1 CH$_2$Cl$_2$/acetone) gave alcohol **23** (207 mg, 77%) as a white solid: mp 192–193 °C (from EtOAc/petroleum ether); $[\alpha]_D^{20}$ +66.5 (*c* 1, CHCl$_3$); ^{1}H NMR (CDCl$_3$, 400 MHz): δ 8.10–7.03 (m, 40H, Ar-*H*), 5.81 (dd, 1H, $J_{3,4}$ 3.5, $J_{4,5}$ <1 Hz, Gal$^{\text{II}}$ H-4), 5.52 (dd, 1H, $J_{1,2}$ 8.0, $J_{2,3}$ 10.0 Hz, Gal$^{\text{II}}$ H-2), 5.36–5.31 (m, 3H, Gal$^{\text{I}}$ H-2, GlcA H-3,4), 5.15 (dd, 1H, $J_{1,2}$ 7.0, $J_{2,3}$ 9.0 Hz, GlcA H-2), 5.0 (br s, 1H, N*H*), 4.87 (ABq, 2H, C*H*$_2$-Ar), 4.83 (d, 1H, GlcA H-1), 4.78 (d, 1H, Gal$^{\text{II}}$ H-1), 5.58 (dd, 1H, $J_{5,6a}$ 4.5 Hz, $J_{6a,6b}$ 12.0 Hz, Gal$^{\text{II}}$ H-6a), 4.50–4.41 (m, 2H, Gal$^{\text{I}}$ H-6a, Gal$^{\text{II}}$ H-6b), 4.37–4.33 (m, 1H, Gal$^{\text{I}}$ H-6b), 4.33 (d, 1H, $J_{1,2}$ 8.0 Hz, Gal$^{\text{I}}$ H-1), 4.26 (dd, 1H, Gal$^{\text{II}}$ H-3), 4.19–4.16 (m, 1H, Gal$^{\text{II}}$ H-5), 4.13 (dd, 1H, $J_{3,4}$ 3.0, $J_{4,5}$ <1 Hz, Gal$^{\text{I}}$ H-4), 4.04 (d, 1H, $J_{4,5}$ 10.0 Hz, GlcA H-5), 3.82 (dd, 1H, $J_{2,3}$ 10.0 Hz, Gal$^{\text{I}}$ H-3), 3.73 (s, 3H, COOC*H*$_3$), 3.72–3.67 (m, 2H, Gal$^{\text{I}}$ H-5, OC*H*$_2$), 3.51–3.46 (m, 1H, OC*H*$_2$), 3.26–3.13 (m, 2H, NC*H*$_2$), 2.30 (s, 1H, Gal$^{\text{I}}$ *H*O-4), 2.60–2.41 (m, 3H, C*H*$_2$CO), 2.35–2.27 (m, 1H, C*H*$_2$CO), 2.01 (s, 3H, COC*H*$_3$); ^{13}C NMR (CDCl$_3$, 100 MHz): δ 205.56 (1C, *C*OCH$_3$), 170.82, 166.76, 166.10, 166.02, 165.81, 165.35, 164.60, 164.11, 164.06, 156.21 (10C, GlcA C-6, C=O), 133.36–127.80 (48C, Ar-*C*), 101.51 (1C, Gal$^{\text{II}}$ C-1), 101.15, 100.53 (2C, Gal$^{\text{I}}$ C-1, GlcA C-1), 80.15 (1C, Gal$^{\text{I}}$ C-3), 75.69 (1C,Gal$^{\text{II}}$ C-3), 72.69 (1C, GlcA C-5), 72.22, 72.14, 71.92, 71.31, 71.28, 70.54, 69.65, 69.19 (8C, Gal$^{\text{I}}$ C-2,5, Gal$^{\text{II}}$ C-2,4,5, GlcA C-2,3,4), 68.54 (1C, O*C*H$_2$), 68.29 (1C, Gal$^{\text{I}}$ C-4), 66.26 (1C, *C*H$_2$-Ar), 63.59 (1C, Gal$^{\text{I}}$ C-6), 62.68 (1C, Gal$^{\text{II}}$ C-6), 52.94 (1C, COO*C*H$_3$), 40.72 (1C, N*C*H$_2$), 37.54 (1C, *C*H$_2$CO), 29.47 (1C, CO*C*H$_3$), 27.54 (1C, *C*H$_2$CO). HRESIMS: Calcd for $C_{24}H_{26}NaO_{10}$ [M+Na]$^+$: *m/z* 1558.45243. Found: 1558.45225. Anal. Calcd for $C_{24}H_{26}O_{10}$: C, 64.88; H, 5.05; N, 0.91. Found: C, 64.67; H, 5.07; N, 0.84.

4.16. 2-Benzyloxycarbonylaminoethyl *O*-(methyl 2,3-di-*O*-benzoyl-4-*O*-levulinoyl-β-D-glucopyranosyluronate)-(1→3)-(2,4,6-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-4-*O*-acetyl-2-*O*-benzoyl-6-*O*-sodium sulfonato-β-D-galactopyranoside (24)

A mixture of diol **6** (199 mg, 0.14 mmol) and Me$_3$N·SO$_3$ (39 mg, 0.28 mmol) in anhyd DMF (5 mL) was stirred for 6 h at 40 °C. More reagent (19.5 mg, 0.14 mmol) was then added, and the mixture was stirred for 4 h at 40 °C, then was cooled. Methanol (1 mL) was added, and the mixture was concentrated. A mixture of the residue, pyridine (4 mL), and Ac$_2$O (2 mL) was stirred overnight at rt, then was concentrated. Flash silica chromatography (9:1 CH$_2$Cl$_2$/MeOH) followed by elution from a column (1.5 × 30 cm) of Sephadex SP-C25 [Na$^+$] with 9:5:1 CH$_2$Cl$_2$/MeOH/water gave the sodium salt **24** (156 mg, 71%) as a white powder: $[\alpha]_D^{20}$ +58 (*c* 1, MeOH); ^{1}H NMR (CD$_3$OD/CDCl$_3$, 400 MHz): δ 8.09–6.94 (m, 35H, Ar-*H*), 5.86 (dd, 1H, $J_{3,4}$ 3.0, $J_{4,5}$ <1 Hz, Gal$^{\text{II}}$ H-4), 5.57 (dd, 1H, $J_{3,4}$ 3.0, $J_{4,5}$ <1 Hz, Gal$^{\text{I}}$ H-4), 5.43–5.38 (m, 2H, Gal$^{\text{II}}$ H-2, GlcA H-3), 5.29 (dd, 1H, $J_{3,4} = J_{4,5}$ = 10.0 Hz, GlcA H-4), 5.18 (dd, 1H, $J_{1,2}$ 8.0, $J_{2,3}$ 10.0 Hz, Gal$^{\text{I}}$ H-2), 5.10 (dd, 1H, $J_{1,2}$ 7.5, $J_{2,3}$ 9.0 Hz, GlcA H-2), 4.95 (d, 1H, GlcA H-1), 4.84 (d, 1H, $J_{1,2}$ 8.0 Hz, Gal$^{\text{II}}$ H-1), 4.84 (ABq, 2H, C*H*$_2$-Ar), 4.50 (dd, 1H, $J_{5,6a}$ 6.5, $J_{6a,6b}$ 12.0 Hz, Gal$^{\text{II}}$ H-6a), 4.44 (d, 1H, Gal$^{\text{I}}$ H-1), 4.40 (dd, 1H, $J_{5,6b}$ 8.0 Hz, Gal$^{\text{II}}$ H-6b), 4.28 (dd, 1H, $J_{2,3}$ 10.0 Hz, Gal$^{\text{II}}$ H-3), 4.22–4.18 (m, 2H, Gal$^{\text{II}}$ H-5, GlcA H-5), 4.12–4.06 (m, 2H, Gal$^{\text{I}}$ H-3,6a), 3.97–3.90 (m, 2H, Gal$^{\text{I}}$ H-5,6b), 3.79–3.73 (m, 1H, OC*H*$_2$), 3.65 (s, 3H, COOC*H*$_3$), 3.52–3.47 (m, 1H, OC*H*$_2$), 3.15–3.12 (m, 2H, NC*H*$_2$), 2.58–2.54 (m, 2H, C*H*$_2$CO), 2.44–2.26 (m, 2H, C*H*$_2$CO), 2.06 (s, 3H, COC*H*$_3$), 1.97 (s, 3H, OCOC*H*$_3$); ^{13}C NMR (CD$_3$OD/CDCl$_3$, 100 MHz): δ 207.99 (1C, *C*OCH$_3$), 172.31, 171.36, 168.36, 167.44, 167.00, 166.51, 165.66, 165.60, 158.04 (10C, GlcA C-6, C=O), 134.23–128.41 (42C, Ar-*C*), 102.24 (1C, Gal$^{\text{II}}$ C-1), 101.99 (1C, Gal$^{\text{I}}$ C-1), 101.57 (1C, GlcA C-1), 78.25 (1C, Gal$^{\text{II}}$ C-3), 77.68 (1C, Gal$^{\text{I}}$ C-3), 73.37, 73.18, 73.01, 72.42, 72.33, 72.27, 72.13 (7C, Gal$^{\text{I}}$ C-2,5, Gal$^{\text{II}}$ C-2,5, GlcA C-2,3,5), 71.11, 71.01 (2C, Gal$^{\text{I}}$ C-4, Gal$^{\text{II}}$ C- 4), 70.33 (1C, GlcA C-4), 69.14 (1C, O*C*H$_2$), 67.16 (1C, *C*H$_2$-Ar), 67.09 (1C, Gal$^{\text{I}}$ C-6), 63.32 (1C, Gal$^{\text{II}}$ C-6), 53.40 (1C, COO*C*H$_3$), 41.31 (1C, N*C*H$_2$), 38.14 (1C, *C*H$_2$CO), 29.55 (1C, CO*C*H$_3$), 28.42 (1C, *C*H$_2$CO), 20.85 (1C, OCO*C*H$_3$). HRESIMS: Calcd for $C_{78}H_{74}NO_{31}S$ [M−Na]$^-$: *m/z* 1552.39710. Found: 1552.40024.

4.17. 2-Benzyloxycarbonylaminoethyl *O*-(methyl 2,3-di-*O*-benzoyl-4-*O*-levulinoyl-β-D-glucopyranosyluronate)-(1→3)-(2,4,6-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-2,6-di-*O*-benzoyl-4-*O*-sodium sulfonato-β-D-galactopyranoside (25)

A mixture of alcohol **23** (189 mg, 0.12 mmol) and Me$_3$N·SO$_3$ (171 mg, 1.2 mmol) in anhyd DMF (3 mL) was stirred overnight at 60 °C, then was cooled. Methanol (2 mL) was added, and the mixture was directly eluted from a column (3 × 80 cm) of

Sephadex LH-20 with 1:1 CH_2Cl_2/MeOH. Fractions containing the product were submitted to flash silica chromatography (12:1 CH_2Cl_2/MeOH) followed by elution from a column (1.5 × 30 cm) of Sephadex SP-C25 [Na$^+$] with 9:5:1 CH_2Cl_2/MeOH/water to give the sodium salt **25** (177 mg, 83%) as a white powder: $[\alpha]_D^{20}$ +49 (*c* 1, MeOH); ^{1}H NMR ($CD_3OD/CDCl_3$, 400 MHz): δ 8.27–6.96 (m, 40H, Ar-*H*), 5.91 (dd, 1H, $J_{3,4}$ 3.2, $J_{4,5}$ <1 Hz, Gal^{II} H-4), 5.91 (dd, 1H, $J_{1,2}$ 8.0, $J_{2,3}$ 9.0 Hz, Gal^{II} H-2), 5.45 (dd, 1H, $J_{2,3} = J_{3,4}$ = 9.0 Hz, GlcA H-3), 5.36 (dd, 1H, $J_{4,5}$ 10.0 Hz, GlcA H-4), 5.19 (dd, 1H, $J_{1,2}$ 7.5, $J_{2,3}$ 10.0 Hz, Gal^{I} H-2), 5.14–5.10 (m, 2H, Gal^{I} H-4, GlcA H-2), 4.97 (d, 1H, $J_{1,2}$ 7.5 Hz, GlcA H-1), 4.88–4.80 (m, 3H, Gal^{II} H-1, C*H*$_2$-Ar), 4.69–4.52 (m, 3H, Gal^{I} H-6a,6b, Gal^{II} H-6a), 4.47–4.42 (m, 2H, Gal^{I} H-1, Gal^{II} H-6b), 4.32 (dd, 1H, Gal^{II} H-3), 4.26–4.21 (m, 2H, Gal^{II} H-5, GlcA H-5), 4.02 (dd, 1H, $J_{3,4}$ 2.0 Hz, Gal^{I} H-3), 3.81–3.78 (m, 1H, Gal^{I} H-5), 3.69 (s, 3H, COOC*H*$_3$), 3.69–3.64 (m, 1H, OC*H*$_2$), 3.54–3.48 (m, 1H, OC*H*$_2$), 3.14–3.10 (m, 2H, NC*H*$_2$), 2.59–2.28 (m, 3H, C*H*$_2$CO), 2.47–2.39 (m, 1H, C*H*$_2$CO), 1.98 (s, 3H, COC*H*$_3$); ^{13}C NMR ($CD_3OD/CDCl_3$, 100 MHz): δ 206.48 (1C, *C*OCH$_3$), 170.83, 166.86, 166.08, 165.92, 165.65, 165.55, 165.23, 165.12, 164.31 (10C, GlcA C-6, C=O), 133.02–127.22 (48C, Ar-*C*), 101.57 (1C, Gal^{II} C-1), 100.63 (2C, Gal^{I} C-1, GlcA C-1), 76.78, 76.74 (2C, Gal^{I} C-3, Gal^{II} C-3), 75.49 (1C, Gal^{I} C-4), 72.22 (1C, Gal^{I} C-5), 71.93, 71.86, 71.54 (3C, Gal^{II} C-5, GlcA C-2,5), 71.34 (1C, Gal^{I} C-2), 70.41, 69.22 (2C, Gal^{II} C-2, GlcA C-3), 68.70 (1C, Gal^{II} C-4), 68.11 (1C, GlcA C-4), 68.07 (1C, O*C*H$_2$), 65.95 (1C, *C*H$_2$-Ar), 63.38 (1C, Gal^{I} C-6), 62.00 (1C, Gal^{II} C-6), 52.39 (1C, COO*C*H$_3$), 40.11 (1C, N*C*H$_2$), 37.02 (1C, *C*H$_2$CO), 28.68 (1C, CO*C*H$_3$), 27.14 (1C, *C*H$_2$CO). HRESIMS: Calcd for $C_{83}H_{76}NNaO_{31}S$ [M−Na]$^-$: *m/z* 1614.41275. Found: 1614.41347.

4.18. 2-Benzyloxycarbonylaminoethyl *O*-(methyl 2,3-di-*O*-benzoyl-4-*O*-levulinoyl-β-D-glucopyranosyluronate)-(1→3)-(2-*O*-benzoyl-4,6-di-*O*-chloroacetyl-β-D-galactopyranosyl)-(1→3)-2-*O*-benzoyl-4,6-*O*-di-*tert*-butylsilylene-β-D-galactopyranoside (26)

A mixture of imidate **9** (158 mg, 0.15 mmol) and alcohol **10** (133 mg, 0.22 mmol) was treated as described for the preparation of **18**. Flash silica chromatography (15:1 CH_2Cl_2/acetone containing 0.1% of Et_3N) gave **26** (68 mg, 49%) as a white solid: $[\alpha]_D^{20}$ +53 (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.78–6.97 (m, 25H, Ar-*H*), 5.51 (dd, 1H, $J_{3,4}$ 3.5, $J_{4,5}$ <1 Hz, Gal^{II} H-4), 5.43–5.33 (m, 3H, Gal^{I} H-2, GlcA H-3,4), 5.30 (dd, 1H, $J_{1,2}$ 8.0, $J_{2,3}$ 10.5 Hz, Gal^{II} H-2), 5.20 (dd, 1H, $J_{1,2}$ 7.0, $J_{2,3}$ 8.5 Hz, GlcA H-2), 5.07 (br s, 1H, N*H*), 4.94 (ABq, 2H, C*H*$_2$-Ar), 4.92 (d, 1H, Gal^{II} H-1), 4.69 (d, 1H, GlcA H-1), 4.61 (dd, 1H, $J_{3,4}$ 3.0, $J_{4,5}$ <1 Hz, Gal^{I} H-4), 4.38 (d, 1H, $J_{1,2}$ 8.0 Hz, Gal^{I} H-1), 4.26–4.05 (m, 9H, Gal^{I} H-6a,6b, Gal^{II} H-3,6a,6b, C*H*$_2$Cl), 4.02 (d, 1H, $J_{4,5}$ 10.0 Hz, GlcA H-5), 3.91 (dd, 1H, $J_{5,6a}$ 6.0, $J_{5,6b}$ 7.0 Hz, Gal^{II} H-5), 3.79 (s, 3H, COOC*H*$_3$), 3.78–3.70 (m, 2H, Gal^{I} H-3, OC*H*$_2$), 3.54–3.49 (m,1H, OC*H*$_2$), 3.39–3.36 (m, 1H, Gal^{I} H-5), 3.23–3.20 (m, 2H, NC*H*$_2$), 2.62–2.27 (m, 4H, C*H*$_2$CO), 2.02 (s, 3H, COC*H*$_3$), 1.02, 0.99 (2s, 18H, (C*H*$_3$)$_3$C); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 205.59 (1C, *C*OCH$_3$), 170.88, 166.85, 166.68, 165.38, 164.69, 164.43, 163.97, 156.25 (9C, GlcA C-6, C=O), 136.57–127.69 (30C, Ar-*C*), 101.52 (1C, Gal^{I} C-1), 101.23 (1C, Gal^{II} C-1), 100.63 (1C, GlcA C-1), 79.13 (1C, Gal^{I} C-3), 75.86 (1C, Gal^{II} C-3), 72.74 (1C, Gal^{I} C-4), 72.52 (1C, GlcA C-5), 71.74, 71.42, 71.23, 70.97, 70.76, 70.72, 69.43, 69.23 (8C, Gal^{I} C-2,5, Gal^{II} C-2,4,5, GlcA C-2,3,4), 68.70 (1C, O*C*H$_2$), 66.72 (1C, Gal^{II} C-6), 66.25 (1C, *C*H$_2$-Ar), 66.46 (1C, Gal^{I} C-6), 52.07 (1C, COO*C*H$_3$), 40.77, 40.60, 40.57 (3C, *C*H$_2$Cl, N*C*H$_2$), 37.47 (1C, *C*H$_2$CO), 29.45 (1C, CO*C*H$_3$), 27.49 (1C, *C*H$_2$CO), 27.40, 27.17 (6C, (*C*H$_3$)$_3$C), 23.20, 20.51 (2C, (CH$_3$)$_3$*C*). ISMS: *m/z* 1518.5 [M+H]$^+$. Anal. Calcd for $C_{74}H_{83}Cl_2NO_{27}Si$: C, 58.57; H, 5.51; N, 0.92. Found: C, 58.43; H, 5.39; N, 0.87.

4.19. 2-Benzyloxycarbonylaminoethyl *O*-(methyl 2,3-di-*O*-benzoyl-4-*O*-levulinoyl-β-D-glucopyranosyluronate)-(1→3)-(2-*O*-benzoyl-4,6-di-*O*-chloroacetyl-β-D-galactopyranosyl)-(1→3)-2-*O*-benzoyl-β-D-galactopyranoside (27)

Compound **26** (473 mg, 0.31 mmol) was treated as described for the preparation of **19**. The residue was crystallized from hot EtOH to give **27** (348 mg, 81%): mp 230–232 °C; $[\alpha]_D^{20}$ +48 (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.78–7.01 (m, 25H, Ar-*H*), 5.54 (dd, 1H, $J_{3,4}$ 3.0, $J_{4,5}$ <1 Hz, Gal^{II} H-4), 5.42–5.34 (m, 2H, GlcA H-3,4), 5.32–5.27 (m, 2H, Gal^{I} H-2, Gal^{II} H-2), 5.20–5.13 (m, 2H, GlcA H-2, N*H*), 4.93 (ABq, 2H, C*H*$_2$-Ar), 4.73, 4.71 (2d, 2H, $J_{1,2}$ 7.0 Hz, Gal^{II} H-1, GlcA H-1), 4.41 (d, 1H, $J_{1,2}$ 8.0 Hz, Gal^{I} H-1), 4.35–4.26 (m, 2H, Gal^{II} H-6a,6b), 4.26 (ABq, 2H, C*H*$_2$Cl), 4.13 (s, 2H, C*H*$_2$Cl), 4.13–4.10 (m, 2H, Gal^{I} H-4, Gal^{II} H-3), 4.05–3.92 (m, 3H, Gal^{I} H-6a, Gal^{II} H-5, GlcA H-5), 3.84 (dd, 1H, $J_{2,3}$ 9.5, $J_{3,4}$ 3.0 Hz, Gal^{I} H-3), 3.79 (s, 3H, COOC*H*$_3$), 3.79–3.70 (m, 2H, Gal^{I} H-6b, OC*H*$_2$), 3.62–3.52 (m, 2H, Gal^{I} H-5, OC*H*$_2$), 3.26–3.17 (m, 2H, NC*H*$_2$), 2.80 (s, 1H, Gal^{I} *H*O-4), 2.63–2.43 (m, 4H, Gal^{I} *H*O-6, C*H*$_2$CO), 2.34–2.27 (m, 1H, C*H*$_2$CO), 2.01 (s, 3H, COC*H*$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 206.30 (1C, *C*OCH$_3$), 170.95, 167.07, 166.97, 166.84, 165.36, 164.75, 164.49, 164.47 (9C, GlcA C-6, C=O), 156.55–127.47 (30C, Ar-*C*), 101.45, 101.18, 100.42 (3C, Gal^{I} C-1, Gal^{II} C-1, GlcA C-1), 80.26 (1C, Gal^{I} C-3), 75.35 (1C, Gal^{II} C-3), 74.47 (1C, Gal^{I} C-5), 72.18, 71.86, 71.58, 71.09, 70.69, 70.65, 70.50, 69.05 68.36, (9C, Gal^{I} C-2,4, Gal^{II} C-2,4,5, GlcA C-2,3,4,5), 68.25 (1C, O*C*H$_2$), 66.14 (1C, *C*H$_2$-Ar), 63.08 (1C, Gal^{II} C-6), 60.87 (1C, Gal^{I} C-6), 52.92 (1C, COO*C*H$_3$), 40.45, 40.35, 40.29 (3C, *C*H$_2$Cl, N*C*H$_2$), 37.21 (1C, *C*H$_2$CO), 29.10 (1C, CO*C*H$_3$), 27.26 (1C, *C*H$_2$CO). HRESIMS: Calcd for $C_{66}H_{68}Cl_2NO_{27}$ [M+H]$^+$: *m/z* 1376.33503. Found: 1376.33502. Anal. Calcd for $C_{66}H_{67}Cl_2NO_{27}$: C, 57.56; H, 4.90; N, 1.02. Found: C, 57.31; H, 4.93; N, 0.94.

4.20. 2-Benzyloxycarbonylaminoethyl 2-*O*-benzoyl-4,6-*O*-di-*tert*-butylsilylene-3-*O*-levulinoyl-β-D-galactopyranoside (28)

Compound **10** (1.0 g, 1.66 mmol) was treated as described for the preparation of **14**. Flash silica chromatography (2:1 petroleum ether/EtOAc) gave **28** (1.09 g, 94%) as a white foam: $[\alpha]_D^{20}$ +32 (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.01–7.31 (m, 10H, Ar-*H*), 5.62 (dd, 1H, $J_{1,2}$ 8.0, $J_{2,3}$ 10.0 Hz, H-2), 5.21 (br s, 1H, N*H*), 5.01 (ABq, 2H, C*H*$_2$-Ar), 4.94 (dd, 1H, $J_{2,3}$ 11.0, $J_{3,4}$ 3.0 Hz, H-3), 4.66 (dd, 1H, H-4), 4.57 (d, 1H, H-1), 4.29–4.23 (m, 2H, H-6a, H-6b), 3.86–3.82 (m, 1H, OC*H*$_2$), 3.71–3.32 (m, 1H, OC*H*$_2$), 3.54–3.52 (m, 1H, H-5), 3.35–3.31 (m, 2H, NC*H*$_2$), 2.59–2.55 (m, 4H, C*H*$_2$CO), 2.04 (s, 3H, COC*H*$_3$), 1.10, 1.04 (2s, 18H, (C*H*$_3$)$_3$C). HRESIMS: Calcd for $C_{36}H_{50}NO_{11}Si$ [M+H]$^+$: *m/z* 700.31476. Found: 700.31471. Anal. Calcd for $C_{36}H_{49}NO_{11}Si$: C, 61.78; H, 7.06; N, 2.00. Found: C, 61.48; H, 7.15; N, 2.09.

4.21. 2-Benzyloxycarbonylaminoethyl 2,4,6-tri-*O*-benzoyl-3-*O*-levulinoyl-β-D-galactopyranoside (29)

Compound **28** (1.07 g, 1.53 mmol) was treated as described for the preparation of **19** to give the crude intermediate diol (0.83 g, 96%) as a white foam: HRESIMS: Calcd for $C_{28}H_{34}O_{11}N$ [M+H]$^+$: *m/z* 560.21264. Found: 560.21235. A mixture of the above isolated diol (284 mg, 0.51 mmol) and benzoyl chloride (235 μL, 2.04 mmol) in anhyd pyridine and CH_2Cl_2 (1:1, 6 mL) was stirred at 0 °C for 1 h. Methanol (1 mL) was added, and the mixture was diluted with CH_2Cl_2 (30 mL), washed with water, satd aq $NaHCO_3$, and water, dried ($MgSO_4$), and concentrated. Flash silica chromatography (3:2 petroleum ether/EtOAc) gave **29** (366 mg, 94% from **28**) as a white foam: $[\alpha]_D^{20}$ +24 (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ

8.15–7.28 (m, 20H, Ar-*H*), 5.82 (dd, 1H, $J_{3,4}$ 3.0, $J_{4,5}$ <1 Hz, H-4), 5.56 (dd, 1H, $J_{1,2}$ 7.5, $J_{2,3}$ 10.0 Hz, H-2), 4.35 (dd, 1H, H-3), 5.14 (br s, 1H, N*H*), 4.97 (ABq, 2H, CH_2-Ar), 4.71 (d, 1H, H-1), 4.39 (dd, 1H, $J_{5,6a}$ 7.0, $J_{6a,6b}$ 12.0 Hz, H-6a), 4.39 (dd, 1H, $J_{5,6b}$ 6.5 Hz, H-6b), 4.22–4.20 (m, 1H, H-5), 3.97–3.93 (m, 1H, OCH_2), 3.73–3.68 (m, 1H, OCH_2), 3.46–3.30 (m, 2H, NCH_2), 2.62–2.31 (m, 4H, CH_2CO), 1.92 (s, 3H, $COCH_3$). HRESIMS: Calcd for $C_{42}H_{43}$ NO_{13} $[M+H]^+$: *m/z* 768.26507. Found: 768.26602. Anal. Calcd for $C_{42}H_{42}NO_{13}$: C, 65.70; H, 5.38; N, 1.82. Found: C, 65.21; H, 5.51; N, 1.74.

4.22. 2-Benzyloxycarbonylaminoethyl 2,4,6-tri-*O*-benzoyl-β-D-galactopyranoside (30)

A solution of **29** (320 mg, 0.42 mmol) in pyridine (3 mL) was treated for 8 min at rt with 12:8:1 pyridine/AcOH/hydrazine hydrate (9 mL), then was diluted with CH_2Cl_2 (30 mL), washed with water, satd aq $NaHCO_3$, and water, dried ($MgSO_4$), and concentrated. Flash silica chromatography (3:2 petroleum ether/EtOAc) gave alcohol **30** (263 mg, 94%) as a white foam: $[\alpha]_D^{20}$ +13.5 (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): δ 8.16–7.29 (m, 20H, Ar-*H*), 5.76 (dd, 1H, $J_{3,4}$ 3.0, $J_{4,5}$ <1 Hz, H-4), 5.34 (dd, 1H, $J_{1,2}$ 8.0, $J_{2,3}$ 10.0 Hz, H-2), 5.15 (br s, 1H, N*H*), 4.98 (ABq, 2H, CH_2-Ar), 4.69 (d, 1H, H-1), 4.56 (dd, 1H, $J_{5,6a}$ 7.0, $J_{6a,6b}$ 12.0 Hz, H-6a), 4.44 (dd, 1H, $J_{5,6b}$ 6.0 Hz, H-6b), 4.16–4.09 (m, 2H, H-3,5), 3.98–3.93 (m, 1H, OCH_2), 3.76–3.71 (m, 1H, OCH_2), 3.46–3.30 (m, 2H, NCH_2), 2.70 (d, 1H, $J_{3,OH}$ 6.0 Hz, *H*O-3). HRESIMS: Calcd for $C_{37}H_{36}NO_{11}$ $[M+H]^+$: *m/z* 670.22829. Found: 670.22879. Anal. Calcd for $C_{37}H_{35}NO_{11}$: C, 66.36; H, 5.27; N, 2.09. Found: C, 66.15; H, 5.37; N, 2.07.

4.23. 4-Methoxyphenyl *O*-(methyl 2,3-di-*O*-benzoyl-4-*O*-levulinoyl-β-D-glucopyranosyluronate)-(1→3)-(2-*O*-benzoyl-4,6-di-*O*-chloroacetyl-β-D-galactopyranosyl)-(1→3)-2-*O*-benzoyl-4,6-*O*-di-*tert*-butylsilylene-β-D-galactopyranoside (31)

A mixture of imidate **9** (1.34 g, 1.24 mmol) and alcohol **12** (1.0 g, 1.88 mmol) was treated as described for the preparation of **18**. Flash silica chromatography (22:1 CH_2Cl_2/acetone containing 0.1% of Et_3N) gave **31** (1.10 g, 61%) as a white foam: $[\alpha]_D^{20}$ +64.5 (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): δ 7.87–6.65 (m, 24H, Ar-*H*), 5.63 (dd, 1H, $J_{1,2}$ 8.0, $J_{2,3}$ 9.5 Hz, Gal^I H-2), 5.52 (dd, 1H, $J_{3,4}$ 3.0, $J_{4,5}$ <1 Hz, Gal^{II} H-4), 5.43–5.31 (m, 3H, Gal^{II} H-2, GlcA H-3,4), 5.20 (dd, 1H, $J_{1,2}$ 7.5, $J_{2,3}$ 9.0 Hz, GlcA H-2), 4.94 (d, 1H, $J_{1,2}$ 7.5 Hz, Gal^{II} H-1), 4.81 (d, 1H, Gal^I H-1), 4.70 (d, 1H, GlcA H-1), 4.66 (dd, 1H, $J_{3,4}$ 2.5, $J_{4,5}$ <1 Hz, Gal^I H-4), 4.25–4.20 (m, 4H, Gal^I H-6a,6b, Gal^{II} H-6a,6b), 4.15 (ABq, 2H, CH_2Cl), 4.10 (s, 2H, CH_2Cl), 4.07 (dd, 1H, $J_{2,3}$ 10.0 Hz, Gal^{II} H-3), 4.01 (d, 1H, $J_{4,5}$ 9.0 Hz, GlcA H-5), 3.94–3.91 (m, 1H, Gal^{II} H-5), 3.87 (dd, 1H, Gal^I H-3), 3.79 (s, 3H, $COOCH_3$), 3.69 (s, 3H, OCH_3), 3.47–3.44 (m, 1H, Gal^I H-5), 2.62–2.43 (m, 3H, CH_2CO), 2.35–2.27 (m, 1H, CH_2CO), 2.01 (s, 3H, $COCH_3$), 1.04, 1.03 (2s, 18H, $(CH_3)_3C$); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 205.56 (1C, $COCH_3$), 170.91, 166.89, 166.72, 166.70, 165.41, 164.56, 164.48, 164.02 (8C, GlcA C-6, C=O), 155.45–114.19 (30C, Ar-*C*), 101.70 (1C, Gal^I C-1), 101.27 (1C, Gal^{II} C-1), 100.65 (1C, GlcA C-1), 79.22 (1C, Gal^I C-3), 75.84 (1C, Gal^{II} C-3), 72.73, 72.57 (2C, Gal^I C-4, GlcA C-5), 71.79, 71.49, 71.27, 71.03, 70.82, 70.77, 69.27 (8C, Gal^I C-2,5, Gal^{II} C-2,4,5, GlcA C-2,3,4), 66.84, 63.48 (2C, Gal^I C-6, Gal^{II} C-6), 55.49 (1C, OCH_3), 53.09 (1C, $COOCH_3$), 40.60 (2C, CH_2Cl), 37.51 (1C, CH_2CO), 29.49 (1C, $COCH_3$), 27.53 (1C, CH_2CO), 27.41, 27.30 (6C, $(CH_3)_3C$), 23.25, 20.63 (2C, $(CH_3)_3C$). HRESIMS: Calcd for $C_{71}H_{79}Cl_2O_{26}Si$ $[M+H]^+$: *m/z* 1445.40004. Found: 1445.40082. Anal. Calcd for $C_{71}H_{78}Cl_2O_{26}Si$: C, 58.96; H, 5.44. Found: 58.57; H, 5.68.

4.24. 4-Methoxyphenyl *O*-(methyl 2,3-di-*O*-benzoyl-4-*O*-levulinoyl-β-D-glucopyranosyluronate)-(1→3)-(2-*O*-benzoyl-4,6-di-*O*-chloroacetyl-β-D-galactopyranosyl)-(1→3)-2-*O*-benzoyl-β-D-galactopyranoside (32)

Compound **31** (1.10 g, 0.76 mmol) was treated as described for the preparation of **19**. Flash silica chromatography (22:1 CH_2Cl_2/MeOH) gave **32** (0.87 g, 88%) as a white foam: $[\alpha]_D^{20}$ +66 (*c* 1, $CHCl_3$); ^1H NMR ($CD_3OD/CDCl_3$, 400 MHz): δ 7.79–6.65 (m, 24H, Ar-*H*), 5.54 (dd, 1H, $J_{1,2}$ 8.0, $J_{2,3}$ 9.5 Hz, Gal^I H-2), 5.52 (dd, 1H, $J_{3,4}$ 3.0, $J_{4,5}$ <1 Hz, Gal^{II} H-4), 5.42–5.36 (m, 2H, GlcA H-3,4), 5.33 (dd, 1H, $J_{1,2}$ 8.0, $J_{2,3}$ 10.0 Hz, Gal^{II} H-2), 5.18 (dd, 1H, $J_{1,2}$ 7.5, $J_{2,3}$ 9.0 Hz, GlcA H-2), 4.87 (d, 1H, Gal^I H-1), 4.75 (d, 1H, Gal^{II} H-1), 4.71 (d, 1H, GlcA H-1), 4.33–4.28 (m, 2H, Gal^{II} H-6a,6b), 4.27 (ABq, 2H, CH_2Cl), 4.17 (dd, 1H, $J_{3,4}$ 3.0, $J_{4,5}$ <1 Hz, Gal^I H-4), 4.14 (s, 2H, CH_2Cl), 4.12 (dd, 1H, Gal^{II} H-3), 4.04–4.01 (m, 2H, Gal^{II} H-5, GlcA H-5), 3.98 (dd, 1H, $J_{5,6a}$ 4.5, $J_{6a,6b}$ 12.5 Hz, Gal^I H-6a), 3.90 (dd, 1H, Gal^I H-3), 3.89–3.81 (m, 2H, Gal^I H-5,6b), 3.79 (s, 3H, $COOCH_3$), 3.68 (s, 3H, OCH_3), 2.96 (s, 1H, Gal^I *H*O-4), 2.63–2.42 (m, 3H, CH_2CO), 2.36–2.27 (m, 2H, CH_2CO, Gal^I *H*O-6), 2.01 (s, 3H, $COCH_3$); ^{13}C NMR ($CD_3OD/CDCl_3$, 100 MHz): δ 206.46 (1C, $COCH_3$), 171.09, 167.99, 167.92, 167.04, 165.19, 164.84, 164.65, 164.44 (8C, GlcA C-6, C=O), 151.0–113.85 (30C, Ar-*C*), 101.32 (1C, GlcA C-1), 100.92 (1C, Gal^I C-1), 100.19 (1C, Gal^{II} C-1), 80.31 (1C, Gal^I C-3), 74.66, 71.89, 70.97, 70.51, 70.34, 70.18, 67.99 (11C, Gal^I C-2,4,5, Gal^{II} C-2,3,4,5, GlcA C-2,3,4,5), 63.01 (1C, Gal^{II} C-6), 60.41 (1C, Gal^I C-6), 54.83 (1C, OCH_3), 52.55 (1C, $COOCH_3$), 40.12, 40.04 (2C, CH_2Cl), 36.93 (1C, CH_2CO), 28.60 (1C, $COCH_3$), 27.06 (1C, CH_2CO). HRESIMS: Calcd for $C_{63}H_{62}Cl_2NaO_{26}$ $[M+Na]^+$: *m/z* 1327.27986. Found: 1327.28076. Anal. Calcd for $C_{63}H_{62}Cl_2O_{26}$: C, 57.94; H, 4.78. Found: C, 57.64; H, 4.60.

4.25. 4-Methoxyphenyl *O*-(methyl 2,3-di-*O*-benzoyl-4-*O*-levulinoyl-β-D-glucopyranosyluronate)-(1→3)-(2-*O*-benzoyl-4,6-di-*O*-chloroacetyl-β-D-galactopyranosyl)-(1→3)-2,4,6-tri-*O*-benzoyl-β-D-galactopyranoside (33)

Compound **32** (153 mg, 0.12 mmol) was benzoylated as described for the preparation of **29**. Flash silica chromatography (19:1 CH_2Cl_2/acetone) gave **33** (143 mg, 83%) as a white solid: mp 179–180 °C (from EtOAc/petroleum ether); $[\alpha]_D^{20}$ +58 (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): δ 8.09–6.48 (m, 34H, Ar-*H*), 5.79 (dd, 1H, $J_{3,4}$ 3.0, $J_{4,5}$ <1 Hz, Gal^I H-4), 5.69 (dd, 1H, $J_{1,2}$ 8.0, $J_{2,3}$ 9.0 Hz, Gal^I H-2), 5.45 (dd, 1H, $J_{3,4}$ 3.0, $J_{4,5}$ <1 Hz, Gal^{II} H-4), 5.39–5.30 (m, 2H, GlcA H-3,4), 5.20–5.12 (m, 2H, Gal^{II} H-2, GlcA H-2), 4.94 (d, 1H, Gal^I H-1), 4.77 (d, 1H, $J_{1,2}$ 7.5 Hz, Gal^{II} H-1), 4.69–4.65 (m, 1H, Gal^I H-6a), 4.66 (d, 1H, $J_{1,2}$ 7.0 Hz, GlcA H-1), 4.42–4.35 (m, 1H, Gal^I H-6b), 4.22–4.16 (m, 4H, Gal^I H-3, Gal^{II} H-5,6a,6b), 4.16 (s, 2H, CH_2Cl), 4.04 (dd, 1H, $J_{2,3}$ 10.0 Hz, Gal^{II} H-3), 3.99 (d, 1H, $J_{4,5}$ 9.0 Hz, GlcA H-5), 3.97 (ABq, 2H, CH_2Cl), 3.91 (dd, 1H, $J_{5,6a}$ 6.0, $J_{5,6b}$ 6.5 Hz, Gal^I H-5), 3.77 (s, 3H, $COOCH_3$), 3.63 (s, 3H, OCH_3), 2.61–2.41 (m, 3H, CH_2CO), 2.34–2.25 (m, 1H, CH_2CO), 2.01 (s, 3H, $COCH_3$); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 205.56 (1C, $COCH_3$), 170.89, 166.94, 166.82, 166.69, 166.06, 166.02, 165.40, 164.44, 164.39 (10C, GlcA C-6, C=O), 155.36–114.19 (42C, Ar-*C*), 101.11 (1C, Gal^{II} C-1), 100.85 (1C, Gal^I C-1), 100.53 (1C, GlcA C-1), 77.35 (1C, Gal^{II} C-3), 75.55 (1C, Gal^I C-3), 72.58 (1C, GlcA C-5), 72.20 (1C, Gal^I C-5), 71.76, 71.27, 71.15, 70.77, 70.71, 70.60, 69.97, 69.23 (8C, Gal^I C-2,4, Gal^{II} C-2,4,5, GlcA C-2,3,4), 63.29 (2C, Gal^I C-6, Gal^{II} C-6), 55.44 (1C, OCH_3), 53.10 (1C, $COOCH_3$), 40.75, 40.49 (2C, CH_2Cl), 37.53 (1C, CH_2CO), 29.49 (1C, $COCH_3$), 27.53 (1C, CH_2CO). HRESIMS: Calcd for $C_{77}H_{71}Cl_2O_{28}$ $[M+H]^+$: *m/z* 1513.35034. Found: 1513.34906. Anal. Calcd for $C_{77}H_{70}Cl_2O_{28}$: C, 61.07; H, 4.66. Found: C, 61.39; H, 4.62.

4.26. *O*-(Methyl 2,3-di-*O*-benzoyl-4-*O*-levulinoyl-β-D-glucopyranosyluronate)-(1→3)-(2-*O*-benzoyl-4,6-di-*O*-chloroacetyl-β-D-galactopyranosyl)-(1→3)-2,4,6-tri-*O*-benzoyl-1-*O*-trichloroacetimidoyl-α-D-galactopyranose (34)

Compound **33** (143 mg, 0.1 mmol) was treated as described for the preparation of **11**. Flash silica chromatography (1:1 EtOAc/petroleum ether, containing 0.1% of Et_3N) gave imidate **34** (94 mg, 38%) as a white powder: mp 187–189 °C (from EtOAc/petroleum ether); $[\alpha]_D^{20}$ +69 (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): δ 8.43 (s, 1H, C=N*H*), 8.05–6.91 (m, 30H, Ar-*H*), 6.65 (d, 1H, $J_{1,2}$ 3.5 Hz, Gal$^{\mathrm{I}}$ H-1), 5.94 (dd, 1H, $J_{3,4}$ 3.0, $J_{4,5}$ <1 Hz, Gal$^{\mathrm{I}}$ H-4), 5.63 (dd, 1H, $J_{2,3}$ 10.0 Hz, Gal$^{\mathrm{I}}$ H-2), 5.50 (dd, 1H, $J_{3,4}$ 3.0, $J_{4,5}$ <1 Hz, Gal$^{\mathrm{II}}$ H-4), 5.39–5.32 (m, 2H, GlcA H-3,4), 5.20–5.12 (m, 2H, Gal$^{\mathrm{II}}$ H-2, GlcA H-2), 4.88 (d, 1H, $J_{1,2}$ 8.0 Hz, Gal$^{\mathrm{II}}$ H-1), 4.69 (d, 1H, $J_{1,2}$ 7.0 Hz, GlcA H-1), 4.64–4.61 (m, 1H, $J_{5,6a}$ 7.0, $J_{5,6b}$ 4.5 Hz, Gal$^{\mathrm{I}}$ H-5), 4.56 (dd, 1H, $J_{6a,6b}$ 12.0 Hz, Gal$^{\mathrm{I}}$ H-6a), 4.48 (dd, 1H, Gal$^{\mathrm{I}}$ H-3), 4.34 (dd, 1H, Gal$^{\mathrm{I}}$ H-6b), 4.26–4.22 (m, 2H, Gal$^{\mathrm{II}}$ H-6a,6b), 4.16 (s, 2H, CH_2Cl), 4.07–3.99 (m, 3H, Gal$^{\mathrm{II}}$ H-3,5, GlcA H-5), 4.00 (ABq, 2H, CH_2Cl), 3.79 (s, 3H, $COOCH_3$), 2.64–2.42 (m, 3H, CH_2CO), 2.34–2.27 (m, 1H, CH_2CO), 2.01 (s, 3H, $COCH_3$); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 205.55 (1C, $COCH_3$), 170.88, 166.99, 166.83, 166.69, 166.04, 165.82, 165.39, 164.82, 164.36, 163.60, 160.127 (11C, GlcA C-6, C=O, C=N), 133.35–127.96 (36C, Ar-*C*), 101.26 (1C, Gal$^{\mathrm{II}}$ C-1), 100.58 (1C, GlcA C-1), 93.51 (1C, Gal$^{\mathrm{I}}$ C-1), 75.67 (1C, Gal$^{\mathrm{II}}$ C-3), 74.07 (1C, Gal$^{\mathrm{I}}$ C-3), 72.61, 71.74, 71.30, 70.84, 70.75, 70.57, 70.49, 70.30, 69.19, 69.13 (10C, Gal$^{\mathrm{I}}$ C-2,4,5, Gal$^{\mathrm{II}}$ C-2,4,5, GlcA C-2,3,4,5), 63.34, 63.23 (2C, Gal$^{\mathrm{I}}$ C-6, Gal$^{\mathrm{II}}$ C-6), 53.13 (1C, $COOCH_3$), 40.70, 40.50 (2C, CH_2Cl), 37.53 (1C, CH_2CO), 29.49 (1C, $COCH_3$), 27.52 (1C, CH_2CO). HRESIMS: Calcd for $C_{72}H_{64}Cl_5NNaO_{27}$ $[M+Na]^+$: *m/z* 1572.20006. Found: 1572.19878. Anal. Calcd for $C_{72}H_{64}Cl_5NO_{27}$: C, 55.70; H, 4.15; N, 0.90. Found: C, 55.31; H, 4.11; N, 0.81.

4.27. 2-Benzyloxycarbonylaminoethyl *O*-(methyl 2,3-di-*O*-benzoyl-4-*O*-levulinoyl-β-D-glucopyranosyluronate)-(1→3)-(2-*O*-benzoyl-4,6-di-*O*-chloroacetyl-β-D-galactopyranosyl)-(1→3)-2,4,6-tri-*O*-benzoyl-β-D-galactopyranoside (35)

4.27.1. Procedure A

A mixture of disaccharide imidate **9** (129 mg, 0.12 mmol) and alcohol **30** (130 mg, 0.19 mmol) was treated as described for the preparation of **18**. Flash silica chromatography (3:2 EtOAc/petroleum ether, containing 0.1% of Et_3N) gave **35** (92 mg, 48%) as a white solid: mp 166–168 °C (from EtOAc/petroleum ether); $[\alpha]_D^{20}$ +48.5 (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): δ 8.05–6.96 (m, 35H, Ar-*H*), 5.76 (dd, 1H, $J_{3,4}$ 3.0, $J_{4,5}$ <1 Hz, Gal$^{\mathrm{I}}$ H-4), 5.45 (dd, 1H, $J_{3,4}$ 3.0, $J_{4,5}$ <1 Hz, Gal$^{\mathrm{II}}$ H-4), 5.42 (dd, 1H, $J_{1,2}$ 8.0, $J_{2,3}$ 9.5 Hz, Gal$^{\mathrm{I}}$ H-2), 5.36–5.33 (m, 2H, GlcA H-3,4), 5.16–5.11 (m, 2H, Gal$^{\mathrm{II}}$ H-2, GlcA H-2), 4.98 (br s, 1H, N*H*), 4.88 (ABq, 2H, CH_2-Ar), 4.74 (d, 1H, $J_{1,2}$ 8.0 Hz, Gal$^{\mathrm{II}}$ H-1), 4.65 (d, 1H, $J_{1,2}$ 7.5 Hz, GlcA H-1), 4.56 (dd, 1H, $J_{5,6a}$ 5.0, $J_{6a,6b}$ 12.0 Hz, Gal$^{\mathrm{I}}$ H-6a), 4.51 (d, 1H, Gal$^{\mathrm{I}}$ H-1), 4.37 (dd, 1H, $J_{5,6b}$ 6.0 Hz, Gal$^{\mathrm{I}}$ H-6b), 4.20–4.17 (m, 2H, Gal$^{\mathrm{II}}$ H-6a,6b), 4.14 (s, 2H, CH_2Cl), 4.11–4.05 (m, 2H, Gal$^{\mathrm{I}}$ H-5, Gal$^{\mathrm{II}}$ H-3), 4.03–3.98 (m, 2H, Gal$^{\mathrm{I}}$ H-3, GlcA H-5), 3.97 (ABq, 2H, CH_2Cl), 3.93–3.90 (m, 1H, Gal$^{\mathrm{II}}$ H-5), 3.80–3.76 (m, 1H, OCH_2), 3.77 (s, 3H, $COOCH_3$), 3.55–3.50 (m, 1H, OCH_2), 3.29–3.14 (m, 2H, NCH_2), 2.63–2.61 (m, 3H, CH_2CO), 2.33–2.26 (m, 1H, CH_2CO), 2.00 (s, 3H, $COCH_3$); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 205.57 (1C, $COCH_3$), 170.87, 166.935, 166.82, 166.69, 166.17, 165.88, 165.38, 164.59, 164.36, 163.57, 156.19 (11C, GlcA C-6, C=O), 136.51–127.85 (42C, Ar-*C*), 101.36 (1C, GlcA C-1), 101.03 (1C, Gal$^{\mathrm{I}}$ C-1), 100.52 (1C, Gal$^{\mathrm{II}}$ C-1), 77.02 (1C, Gal$^{\mathrm{I}}$ C-3), 75.52 (1C, Gal$^{\mathrm{II}}$ C-3), 72.55 (1C, GlcA C-5), 72.02, 71.73 (2C, Gal$^{\mathrm{I}}$ C-2,5), 71.29, 71.24, 70.72, 70.69 (4C, Gal$^{\mathrm{II}}$ C-2,4,5, GlcA C-2), 70.57 (1C, Gal$^{\mathrm{I}}$ C-4), 70.07, 69.20 (2C, GlcA C-3,4), 68.92 (1C, OCH_2), 66.34 (1C, CH_2-Ar), 63.25, 63.13 (2C, Gal$^{\mathrm{I}}$ C-6, Gal$^{\mathrm{II}}$ C-6), 53.10 (1C, $COOCH_3$), 40.71 (2C, CH_2Cl), 40.48 (1C, NCH_2), 37.50 (1C, CH_2CO), 29.47 (1C, $COCH_3$), 27.50 (1C, CH_2CO). HRESIMS: Calcd for $C_{80}H_{75}Cl_2NNaO_{29}$ $[M+Na]^+$: *m/z* 1606.36940. Found: 1606.37004. Anal. Calcd for $C_{80}H_{75}Cl_2NO_{29}$: C, 60.61; H, 4.77; N, 0.88. Found: C, 60.60; H, 4.73; N, 0.87.

4.27.2. Procedure B

A mixture of trisaccharide imidate **34** (79 mg, 52 μmol) and 2-benzyloxycarbonylaminoethanol (20.5 mg, 105 μmol) was treated as described for the preparation of **18**. Flash silica chromatography (12:1 CH_2Cl_2/acetone, containing 0.1% of Et_3N) gave **35** (46.5 mg, 56%) as a white solid. Physical data matched those reported above.

4.28. 2-Benzyloxycarbonylaminoethyl *O*-(methyl 2,3-di-*O*-benzoyl-4-*O*-levulinoyl-β-D-glucopyranosyluronate)-(1→3)-(2-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-2,4,6-tri-*O*-benzoyl-β-D-galactopyranoside (7)

A mixture of **35** (639 mg, 0.4 mmol) and thiourea (123 mg, 1.6 mmol) in pyridine and EtOH (1:1, 9 mL) was stirred for 2 h at 80 °C, then was cooled. The mixture was concentrated and diluted with CH_2Cl_2, washed with water, brine, and water, dried ($MgSO_4$), and concentrated. Flash silica chromatography (5:1 CH_2Cl_2/acetone) gave diol **7** (443 mg, 77%) as a white foam: mp 188–190 °C (from EtOAc/petroleum ether); $[\alpha]_D^{20}$ +44 (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): δ 8.11–6.88 (m, 35H, Ar-*H*), 5.9 (dd, 1H, $J_{3,4}$ 3.0, $J_{4,5}$ <1 Hz, Gal$^{\mathrm{I}}$ H-4), 5.49 (dd, 1H, $J_{1,2}$ 8.0, $J_{2,3}$ 9.5 Hz, Gal$^{\mathrm{I}}$ H-2), 5.42 (dd, 1H, $J_{2,3} = J_{3,4} = 9.0$ Hz, GlcA H-3), 5.34 (dd, 1H, $J_{4,5}$ 9.0 Hz, GlcA H-4), 5.24–5.20 (m, 2H, Gal$^{\mathrm{II}}$ H-2, GlcA H-2), 5.01–4.91 (m, 2H, N*H*, CH_2-Ar), 4.82–4.79 (m, 2H, Gal$^{\mathrm{II}}$ H-1, CH_2-Ar), 4.72 (d, 1H, $J_{1,2}$ 8.0 Hz, GlcA H-1), 4.52–4.48 (m, 2H, Gal$^{\mathrm{I}}$ H-1,6a), 4.340–4.36 (m, 1H, Gal$^{\mathrm{I}}$ H-6b), 4.10 (d, 1H, GlcA H-5), 4.09–4.03 (m, 3H, Gal$^{\mathrm{I}}$ H-3,5, Gal$^{\mathrm{II}}$ H-4), 3.88–3.83 (m, 2H, Gal$^{\mathrm{II}}$ H-3,6a), 3.80–3.77 (m, 1H, OCH_2), 3.72 (s, 3H, $COOCH_3$), 3.67–3.64 (m, 1H, Gal$^{\mathrm{II}}$ H-6b), 3.60–3.58 (m, 1H, Gal$^{\mathrm{II}}$ H-5), 3.53–3.48 (m, 1H, OCH_2), 3.27–3.15 (m, 2H, NCH_2), 2.98 (br s, 1H, Gal$^{\mathrm{II}}$ *H*O-4), 2.63–2.43 (m, 4H, Gal$^{\mathrm{II}}$ *H*O-6, CH_2CO), 2.35–2.28 (m, 1H, CH_2CO), 2.01 (s, 3H, $COCH_3$); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 205.60 (1C, $COCH_3$), 171.03, 167.22, 167.13, 166.11, 165.33, 164.74, 164.54, 163.85, 156.18 (9C, GlcA C-6, C=O), 136.51–127.72 (42C, Ar-*C*), 101.96 (1C, GlcA C-1), 101.55 (1C, Gal$^{\mathrm{I}}$ C-1), 100.81 (1C, Gal$^{\mathrm{II}}$ C-1), 80.21 (1C, Gal$^{\mathrm{II}}$ C-3), 78.38 (1C, Gal$^{\mathrm{I}}$ C-3), 72.27 (1C, Gal$^{\mathrm{II}}$ C-5), 72.27 (1C, GlcA C-5), 71.73, 71.58, 71.24, 70.95 (4C, Gal$^{\mathrm{I}}$ C-2, Gal$^{\mathrm{II}}$ C-2, GlcA C-2,3), 70.23 (1C, Gal$^{\mathrm{I}}$ C-4), 69.11, 69.02, 68.95 (3C, Gal$^{\mathrm{I}}$ C-5, Gal$^{\mathrm{II}}$ C-4, GlcA C-4), 66.30 (1C, OCH_2), 62.88 (1C, CH_2-Ar), 62.82 (1C, Gal$^{\mathrm{I}}$ C-6), 62.63 (1C, Gal$^{\mathrm{II}}$ C-6), 53.76 (1C, $COOCH_3$), 40.65 (1C, NCH_2), 37.46 (1C, CH_2CO), 29.48 (1C, $COCH_3$), 27.51 (1C, CH_2CO). HRESIMS: Calcd for $C_{76}H_{73}NNaO_{27}$ $[M+Na]^+$: *m/z* 1454.42622. Found: 1454.42746. Anal. Calcd for $C_{76}H_{73}NO_{27}$: C, 63.73; H, 5.14; N, 0.98. Found: C, 63.79; H, 5.07; N, 0.89.

4.29. 2-Benzyloxycarbonylaminoethyl *O*-(methyl 2,3-di-*O*-benzoyl-4-*O*-levulinoyl-β-D-glucopyranosyluronate)-(1→3)-(2,6-di-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-2,4,6-tri-*O*-benzoyl-β-D-galactopyranoside (36)

Compound **7** (202 mg, 0.14 mmol) was treated as described for the preparation of **23**. Flash silica chromatography (12:1 CH_2Cl_2/acetone) gave alcohol **36** (175 mg, 80%) as a white solid: mp 148–150 °C (from EtOAc/petroleum ether);); $[\alpha]_D^{20}$ +47.5 (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): δ 8.09–6.91 (m, 40H, Ar-*H*), 5.80 (dd, 1H, $J_{3,4}$ 3.0, $J_{4,5}$ <1 Hz, Gal$^{\mathrm{I}}$ H-4), 5.46–5.33 (m, 3H, Gal$^{\mathrm{I}}$ H-2, GlcA H-3,4), 5.30–5.21 (m, 2H, Gal$^{\mathrm{II}}$ H-2, GlcA H-2), 4.99 (br s, 1H, N*H*), 4.88 (ABq, 2H, CH_2-Ar), 4.81 (d, 1H, $J_{1,2}$ 7.0 Hz, Gal$^{\mathrm{II}}$

H-1), 4.70 (d, 1H, $J_{1,2}$ 8.0 Hz, GlcA H-1), 4.62–4.59 (m, 2H, Gal^{I} H-6a, Gal^{II} H-6a), 4.46–4.38 (m, 3H, Gal^{I} H-1, Gal^{I} H-6b, Gal^{II} H-6b), 4.20–4.16 (m, 2H, Gal^{I} H-3, Gal^{II} H-4), 4.09 (d, 1H, $J_{4,5}$ 10.0 Hz, GlcA H-5), 3.96–3.93 (m, 1H, Gal^{I} H-5), 3.86–3.75 (m, 3H, Gal^{II} H-3,5, OC*H*$_2$), 3.66 (s, 3H, COOC*H*$_3$), 3.52–3.47 (m, 1H, OC*H*$_2$), 3.25–3.13 (m, 2H, NC*H*$_2$), 2.89 (br s, 1H, Gal^{II} *H*O-4), 2.63–2.44 (m, 3H, C*H*$_2$CO), 2.36–2.29 (m, 1H, C*H*$_2$CO), 2.02 (s, 3H, COC*H*$_3$); ^{13}C NMR (CDCl$_3$, 100 MHz): δ 205.60 (1C, *C*OCH$_3$), 167.01, 166.23, 166.04, 165.55, 165.36, 164.58, 164.51, 163.88, 156.21 (10C, GlcA C-6, C=O), 136.54–127.77 (48C, Ar-*C*), 101.46 (1C, Gal^{I} C-1), 100.99, 100.90 (2C, Gal^{II} C-1, GlcA C-1), 80.27 (1C, Gal^{II} C-3), 75.30 (1C, Gal^{I} C-3), 72.27 (1C, GlcA C-5), 72.15, 71.96, 71.63 (3C, Gal^{I} C-5, Gal^{II} C-5, GlcA C-3), 71.19, 70.43 (2C, Gal^{II} C-2, GlcA C-2), 69.97 (1C, Gal^{I} C-4), 69.15 (2C, Gal^{I} C-2, GlcA C-4), 68.88 (1C, O*C*H$_2$), 68.17 (1C, Gal^{II} C-4), 66.33 (1C, *C*H$_2$-Ar), 62.99, 62.78 (2C, Gal^{I} C-6, Gal^{II} C-6)), 53.03 (1C, COO*C*H$_3$), 40.68 (1C, N*C*H$_2$), 37.48 (1C, *C*H$_2$CO), 29.51 (1C, CO*C*H$_3$), 27.53 (1C, *C*H$_2$CO). HRESIMS: Calcd for $C_{83}H_{77}NNaO_{28}$ [M+Na]$^+$: *m/z* 1558.45243. Found: 1558.45250. Anal. Calcd for $C_{83}H_{77}NO_{28}$: C, 64.88; H, 5.05; N, 0.91. Found: C, 64.61; H, 4.99; N, 0.80.

4.30. 2-Benzyloxycarbonylaminoethyl *O*-(methyl 2,3-di-*O*-benzoyl-4-*O*-levulinoyl-β-D-glucopyranosyluronate)-(1→3)-(4-*O*-acetyl-2-*O*-benzoyl-6-*O*-sodium sulfonato-β-D-galactopyranosyl)-(1→3)-2,4,6-tri-*O*-benzoyl-β-D-galactopyranoside (37)

Compound **7** (174 mg, 0.12 mmol) was treated as described for the preparation of **24** to give the sodium salt **37** (145 mg, 76%) as a white powder: $[\alpha]_D^{20}$ +53.5 (*c* 1, CHCl$_3$); ^{1}H NMR (CD$_3$OD/CDCl$_3$, 400 MHz): δ 8.01–6.94 (m, 35H, Ar-*H*), 5.82 (dd, 1H, $J_{3,4}$ 3.0, $J_{4,5}$ <1 Hz, Gal^{I} H-4), 5.49 (dd, 1H, $J_{3,4}$ 3.0, $J_{4,5}$ <1 Hz, Gal^{II} H-4), 5.45–5.37 (m, 2H, Gal^{I} H-2, GlcA H-3), 5.25 (dd, 1H, $J_{3,4}$ 9.5, $J_{4,5}$ 10.0 Hz, GlcA H-4), 5.13–5.09 (m, 2H, Gal^{II} H-2, GlcA H-2), 4.84 (ABq, 2H, C*H$_2$*-Ar), 4.78, 4.76 (2d, 2H, $J_{1,2}$ 7.5 Hz, Gal^{II} H-1, GlcA H-1), 4.63 (d, 1H, $J_{1,2}$ 8.0 Hz, Gal^{I} H-1), 4.50–4.46 (m, 1H, Gal^{I} H-6a), 4.40–4.35 (m, 2H, Gal^{I} H-3,6b), 4.24–4.21 (m, 1H, Gal^{I} H-5), 4.14 (d, 1H, GlcA H-5), 4.10–4.03 (m, 3H, Gal^{II} H-5,6a,6b), 3.97 (dd, 1H, $J_{2,3}$ 10.0 Hz, Gal^{II} H-3), 3.80–3.75 (m, 4H, OC*H*$_2$, COOC*H*$_3$), 3.56–3.53 (m, 1H, OC*H*$_2$), 3.18–3.16 (m, 2H, NC*H*$_2$), 2.59–2.28 (m, 4H, C*H*$_2$CO), 1.99 (s, 6H, COC*H*$_3$, OCOC*H*$_3$); ^{13}C NMR (CD$_3$OD/CDCl$_3$, 100 MHz): δ 207.68 (1C, *C*OCH$_3$), 172.25, 171.95, 168.75, 167.30, 167.14, 166.28, 166.02, 165.56, 165.03 (10C, GlcA C-6, C=O), 137.20–128.27 (42C, Ar-*C*), 102.08 (1C, Gal^{I} C-1), 101.91, 101.39 (2C, Gal^{II} C-1, GlcA C-1), 78.03 (1C, Gal^{II} C-3), 76.88 (1C, Gal^{I} C-3), 72.87, 72.74, 72.57 (3C, Gal^{I} C-5, Gal^{II} C-5, GlcA C-5), 72.51, 72.42 (2C, Gal^{I} C-2, GlcA C-3), 72.04 (1C, Gal^{I} C-4), 71.99, 71.53 (2C, Gal^{II} C-2, GlcA C-2), 70.30 (1C, GlcA C-4), 70.14 (1C, Gal^{II} C-4), 69.37 (1C, O*C*H$_2$), 66.98 (1C, *C*H$_2$-Ar), 66.25 (1C, Gal^{II} C-6), 64.07 (1C, Gal^{I} C-6), 53.62 (1C, COO*C*H$_3$), 41.20 (1C, N*C*H$_2$), 37.98 (1C, *C*H$_2$CO), 29.59 (1C, CO*C*H$_3$), 28.22 (1C, *C*H$_2$CO), 20.65 (1C; OCO*C*H$_3$). HRESIMS: Calcd for $C_{78}H_{74}NO_{31}S$ [M−Na]$^-$: *m/z* 1552.39710. Found: 1552.39847.

4.31. 2-Benzyloxycarbonylaminoethyl *O*-(methyl 2,3-di-*O*-benzoyl-4-*O*-levulinoyl-β-D-glucopyranosyluronate)-(1→3)-(2,6-di-*O*-benzoyl-4-*O*-sodium sulfonato-β-D-galactopyranosyl)-(1→3)-2,4,6-tri-*O*-benzoyl-β-D-galactopyranoside (38)

Compound **36** (148 mg, 98 μmol) was treated as described for the preparation of **25** to give the sodium salt **38** (122 mg, 77%) as a white powder: $[\alpha]_D^{20}$ +48 (*c* 1, MeOH); ^{1}H NMR (CD$_3$OD/CDCl$_3$, 400 MHz): δ 8.18–6.97 (m, 40H, Ar-*H*), 5.81 (dd, 1H, $J_{3,4}$ 3.0, $J_{4,5}$ <1 Hz, Gal^{I} H-4), 5.34 (dd, 1H, $J_{2,3}$ 9.0, $J_{3,4}$ 9.5 Hz, GlcA H-3), 5.44 (dd, 1H, $J_{4,5}$ 10.0 Hz, GlcA H-4), 5.41–5.37 (m, 2H, Gal^{I} H-2, GlcA H-2), 5.17–5.12 (m, 2H, Gal^{II} H-2,4), 4.99 (d, 1H, $J_{1,2}$ 7.5 Hz, GlcA H-1), 4.87–4.77 (m, 4H, Gal^{I} H-6a, Gal^{II} H-1, C*H*$_2$-Ar), 4.64 (dd, 1H, $J_{5,6b}$ 4.5, $J_{6a,6b}$ 12.0 Hz, Gal^{I} H-6b), 4.58 (d, 1H, $J_{1,2}$ 8.0 Hz, Gal^{I} H-1), 4.36 (d, 1H, GlcA H-5), 4.33 (dd, 1H, $J_{2,3}$ 11.0 Hz, Gal^{I} H-3), 4.26–4.13 (m, 4H, Gal^{I} H-5, Gal^{II} H-3,6a,6b), 3.99–3.96 (m, 1H, Gal^{II} H-5), 3.74–3.70 (m, 4H, OC*H*$_2$, COOC*H*$_3$), 3.54–3.49 (m, 1H, OC*H*$_2$), 3.12–3.09 (m, 2H, NC*H*$_2$), 2.59–2.55 (m, 2H, C*H*$_2$CO), 2.46–2.38 (m, 1H, C*H*$_2$CO), 2.35–2.28 (m, 1H, C*H*$_2$CO), 1.95 (s, 3H, COC*H*$_3$); ^{13}C NMR (CD$_3$OD/CDCl$_3$, 100 MHz): δ 208.38 (1C, *C*OCH$_3$), 172.89, 169.40, 167.75, 167.48, 167.11, 166.84, 166.80, 166.61, 166.35, 158.46 (10C, GlcA C-6, C=O), 138.12–128.65 (48C, Ar-*C*), 102.97 (1C, Gal^{II} C-1), 102.63, 102.57 (2C, Gal^{I} C-1, GlcA C-1), 78.98 (1C, Gal^{II} C-3), 78.12 (1C, Gal^{I} C-3), 78.09 (1C, Gal^{II} C-4), 77.06 (1C, Gal^{I} C-5), 73.85 (1C, GlcA C-3), 73.32, 73.09 (2C, Gal^{II} C-5, GlcA C-5), 73.06, 73.01 (2C, Gal^{I} C-2, GlcA C-2), 72.41 (1C, Gal^{I} C-4), 72.09 (1C, Gal^{II} C-2), 70.60 (1C, GlcA C-4), 69.54 (1C, O*C*H$_2$), 67.28 (1C, *C*H$_2$-Ar), 65.11 (1C, Gal^{I} C-6), 64.30 (1C, Gal^{II} C-6), 53.59 (1C, COO*C*H$_3$), 41.59 (1C, N*C*H$_2$), 38.29 (1C, *C*H$_2$CO), 29.47 (1C, CO*C*H$_3$), 28.73 (1C, *C*H$_2$CO). HRESIMS: Calcd for $C_{83}H_{76}NO_{31}S$ [M−Na]$^-$: *m/z* 1614.41275. Found: 1614.41567.

4.32. 2-Benzyloxycarbonylaminoethyl *O*-(sodium β-D-glucopyranosyluronate)-(1→3)-(β-D-galactopyranosyl)-(1→3)-β-D-galactopyranoside (39)

A solution of **6** (191 mg, 0.13 mmol) in THF/water (3:1, 3 mL) was treated at −10 °C with a freshly prepared mixture of H_2O_2 (30 wt % in water, 0.35 mL) and LiOH (1 M, 0.7 mL), and the mixture was stirred for 8 h at rt, then was cooled to 0 °C. Sodium hydroxide (4 M, 2.3 mL) was added, and the mixture was stirred overnight at rt, then was adjusted to pH 3.5 (pH meter monitoring) with Amberlite IR-120 [H$^+$] resin, filtered, concentrated, and dried. The residue was extracted several times with EtOH, then was taken up in water (2 mL), and the pH of the solution was adjusted to pH 8.5 with 0.1 M NaOH. The solution was eluted from a column (3 × 80 cm) of Sephadex LH-20 with water to give the sodium salt **39** (66 mg, 69%) as a white powder: *R* = 0.42 (4:2:1 EtOAc/MeOH/water); $[\alpha]_D^{20}$ −4 (*c* 1, water); ^{1}H NMR (D$_2$O, internal HOD, δ_H 4.79, 400 MHz): δ 7.48–7.40 (m, 5H, Ar-*H*), 5.14 (s, 2H, C*H*$_2$-Ar), 4.69 (d, 1H, $J_{1,2}$ 8.0 Hz, GlcA H-1), 4.67 (d, 1H, $J_{1,2}$ 8.0 Hz, Gal^{II} H-1), 4.43 (d, 1H, $J_{1,2}$ 7.5 Hz, Gal^{I} H-1), 4.21, 4.19 (2dd, 2H, $J_{3,4}$ 2.0, $J_{4,5}$ <1 Hz, Gal^{I} H-4, Gal^{II} H-4), 3.98–3.93 (m, 1H, OC*H*$_2$), 3.84–3.80 (m, 2H, Gal^{I} H-3, Gal^{II} H-3), 3.80–3.65 (m, 10H, Gal^{I} H-2,5,6a,6b, Gal^{II} H-2,5,6a,6b, GlcA H-5, OC*H*$_2$), 3.54–3.52 (m, 2H, GlcA H-3,4), 3.44 (dd, 1H, $J_{2,3}$ 9.0 Hz, GlcA H-2), 3.42–3.37 (m, 2H, NC*H*$_2$); ^{13}C NMR (D$_2$O, internal acetone, δ_C 30.83, 100 MHz): δ 176.55 (1C, GlcA C-6), 159.02 (1C, NH*C*(O)O), 137.11–128.38 (6C, Ar-C), 104.60 (1C, Gal^{II} C-1), 104.19 (1C, GlcA C-1), 103.31 (1C, Gal^{I} C-1), 83.01, 82.89 (2C, Gal^{I} C-3, Gal^{II} C-3), 76.80, 75.94, 75.41, 75.36, 73.78, 72.39, 70.78, 70.51 (8C, Gal^{I} C-2,5, Gal^{II} C-2,5, GlcA C-2,3,4,5), 69.50 (1C, O*C*H$_2$), 69.00, 68.65 (2C, Gal^{I} C-4, Gal^{II} C-4), 67.55 (1C, *C*H$_2$-Ar), 61.57, 61.48 (2C, Gal^{I} C-6, Gal^{II} C-6), 41.16 (1C, N*C*H$_2$). HRESIMS: Calcd for $C_{28}H_{41}NNaO_{19}$ [M+H]$^+$: *m/z* 718.21650. Found: 718.21580.

4.33. 2-Benzyloxycarbonylaminoethyl *O*-(sodium β-D-glucopyranosyluronate)-(1→3)-(β-D-galactopyranosyl)-(1→3)-6-*O*-sodium sulfonato-β-D-galactopyranoside (40)

Compound **24** (203 mg, 0.13 mmol) was treated as described for the preparation of **39** to give the disodium salt **40** (91 mg, 86%) as a white powder: *R* = 0.27 (4:2:1 EtOAc/MeOH/water); $[\alpha]_D^{20}$ −34 (*c* 1, water); ^{1}H NMR (D$_2$O, internal HOD, δ_H 4.79, 400 MHz): δ 7.46–7.42 (m, 5H, Ar-*H*), 5.15 (s, 2H, C*H*$_2$-Ar), 4.70 (d, 1H, $J_{1,2}$ 7.5 Hz, GlcA H-1), 4.67 (d, 1H, $J_{1,2}$ 7.5 Hz, Gal^{II} H-1), 4.45 (d, 1H, $J_{1,2}$ 8.0 Hz, Gal^{I} H-1), 4.25, 4.21 (2dd, 2H, $J_{3,4}$ 3.0, $J_{4,5}$ <1 Hz, Gal^{I} H-4, Gal^{II} H-4), 4.24–4.19 (m, 2H, Gal^{I} H-6a,6b), 3.98–3.90 (m, 2H, Gal^{I} H-3,

OCH_2), 3.85–3.65 (m, 9H, Gal^{I} H-2,5, Gal^{II} H-2,3,5,6a,6b, GlcA H-5, OCH_2), 3.57–3.51 (m, 2H, GlcA H-3,4), 3.46 (dd, 1H, $J_{2,3}$ 9.0 Hz, GlcA H-2), 3.42–3.36 (m, 2H, NCH_2); ^{13}C NMR (D_2O, internal acetone, δ_C 30.83, 100 MHz): δ 176.52 (1C, GlcA C-6), 150.02 (1C, NHC(O)O), 137.16–128.40 (6C, Ar-C), 104.66 (1C, Gal^{II} C-1), 104.21 (1C, GlcA C-1), 103.24 (1C, Gal^{I} C-1), 83.04, 82.71 (2C, Gal^{I} C-3, Gal^{II} C-3), 75.94, 75.40, 73.78, 72.99, 72.39, 70.83, 70.78, 70.39 (8C, Gal^{I} C-2,5, Gal^{II} C-2,5, GlcA C-2,3,4,5), 69.56 (1C, OCH_2), 68.76, 68.65 (2C, Gal^{I} C-4, Gal^{II} C-4), 67.75 (1C, Gal^{I} C-6), 67.54 (1C, CH_2-Ar), 61.54 (1C, Gal^{II} C-6), 41.20 (1C, NCH_2). HRESIMS: Calcd for $C_{28}H_{39}NNaO_{22}S$ $[M-Na]^-$: *m/z* 796.15876. Found: 796.15841.

4.34. 2-Benzyloxycarbonylaminoethyl *O*-(sodium β-D-glucopyranosyluronate)-(1→3)-(β-D-galactopyranosyl)-(1→3)-4-*O*-sodium sulfonato-β-D-galactopyranoside (41)

Compound **25** (167 mg, 0.1 mmol) was treated as described for the preparation of **39** to give the disodium salt **41** (68 mg, 80%) as a white powder: *R* = 0.28 (4:2:1 EtOAc/MeOH/water); $[\alpha]_D^{20}$ −14 (*c* 1, water); ^{1}H NMR (D_2O, internal HOD, δ_H 4.79, 400 MHz): δ 7.47–7.42 (m, 5H, Ar-*H*), 5.14 (s, 2H, CH_2-Ar), 4.86 (dd, 1H, $J_{3,4}$ 3.0, $J_{4,5}$ <1 Hz, Gal^{I} H-4), 4.70 (d, 1H, $J_{1,2}$ 7.5 Hz, GlcA H-1), 4.69 (d, 1H, $J_{1,2}$ 7.5 Hz, Gal^{II} H-1), 4.46 (d, 1H, $J_{1,2}$ 7.5 Hz, Gal^{I} H-1), 4.18 (dd, 1H, $J_{3,4}$ 2.0, $J_{4,5}$ <1 Hz, Gal^{II} H-4), 4.03–3.94 (m, 2H, Gal^{I} H-3, OCH_2), 3.85–3.68 (m, 11H, Gal^{I} H-2,5,6a,6b, Gal^{II} H-2,3,5,6a,6b, GlcA H-5, OCH_2), 3.56–3.51 (m, 2H, GlcA H-3,4), 3.45 (dd, 1H, $J_{2,3}$ 9.0 Hz, GlcA H-2), 3.42–3.39 (m, 2H, NCH_2); ^{13}C NMR (D_2O, internal acetone, δ_C 30.83, 100 MHz): δ 176.63 (1C, GlcA C-6), 159.12 (1C, NHC(O)O), 137.21–128.40 (6C, Ar-C), 104.65, 104.37 (2C, Gal^{II} C-1, GlcA C-1), 103.45 (1C, Gal^{I} C-1), 83.03 (1C, Gal^{I} C-3), 79.13 (1C, Gal^{II} C-3), 78.11 (1C, Gal^{I} C-4), 76.88, 75.99, 75.61, 75.18, 73.83, 72.47, 71.07, 70.84 (8C, Gal^{I} C-2,5, Gal^{II} C-2,5, GlcA C-2,3,4,5), 69.75 (1C, OCH_2), 69.08 (1C, Gal^{II} C-4), 67.62 (CH_2-Ar), 62.76, 62.61 (2C, Gal^{I} C-6, Gal^{II} C-6), 42.18 (1C, NCH_2). HRESIMS: Calcd for $C_{28}H_{39}NNaO_{22}S$ $[M-Na]^-$: 796.15876. Found: 796.15884.

4.35. 2-Benzyloxycarbonylaminoethyl *O*-(sodium β-D-glucopyranosyluronate)-(1→3)-(6-*O*-sodium sulfonato-β-D-galactopyranosyl)-(1→3)-β-D-galactopyranoside (42)

Compound **37** (135 mg, 85 μmol) was treated as described for the preparation of **39** to give the disodium salt **42** (56.5 mg, 80%) as a white powder: *R* = 0.32 (4:2:1 EtOAc/MeOH/water); $[\alpha]_D^{20}$ +5 (*c* 1, water); ^{1}H NMR (D_2O, internal HOD, δ_H 4.79, 400 MHz): δ 7.46–7.42 (m, 5H, Ar-*H*), 5.14 (s, 2H, CH_2-Ar), 4.69 (d, 1H, $J_{1,2}$ 8.0 Hz, GlcA H-1), 4.65 (d, 1H, $J_{1,2}$ 7.0 Hz, Gal^{II} H-1), 4.42 (d, 1H, $J_{1,2}$ 7.5 Hz, Gal^{I} H-1), 4.26–4.25 (m, 2H, Gal^{I} H-4, Gal^{II} H-4), 4.22–4.20 (m, 2H, Gal^{II} H-6a,6b), 3.98–3.92 (m, 2H, Gal^{II} H-5, OCH_2), 3.86–3.65 (m, 9H, Gal^{I} H-2,3,5,6a,6b, Gal^{II} H-2,3, GlcA H-5, OCH_2), 3.54–3.52 (m, 2H, GlcA H-3,4), 3.45 (dd, 1H, $J_{2,3}$ 9.0 Hz, GlcA H-2), 3.42–3.36 (m, 2H, NCH_2); ^{13}C NMR (D_2O, internal acetone, δ_C 30.83, 100 MHz): δ 172.55 (1C, GlcA C-6), 159.02 (1C, NHC(O)O), 138.39–129.35 (6C, Ar-C), 104.41, 104.23 (2C, Gal^{II} C-1, GlcA C-1), 103.25 (1C, Gal^{I} C-1), 83.33, 82.82 (2C, Gal^{I} C-3, Gal^{II} C-3), 75.95, 75.63, 73.80, 73.16, 72.42, 70.66, 70.37, 70.11 (8C, Gal^{I} C-2,5, Gal^{II} C-2,5, GlcA C-2,3,4,5), 69.49 (1C, OCH_2), 69.08, 68.58 (2C, Gal^{I} C-4, Gal^{II} C-4), 68.49 (1C, Gal^{II} C-6), 67.57 (1C, CH_2-Ar), 61.86 (1C, Gal^{I} C-6), 41.05 (1C, NCH_2). HRESIMS: Calcd for $C_{28}H_{41}NNaO_{22}S$ $[M-Na+2H]^+$: *m/z* 798.17331. Found: 798.17149.

4.36. 2-Benzyloxycarbonylaminoethyl *O*-(sodium β-D-glucopyranosyluronate)-(1→3)-(4-*O*-sodium sulfonato-β-D-galactopyranosyl)-(1→3)-β-D-galactopyranoside (43)

Compound **38** (113.5 mg, 70 μmol) was treated as described for the preparation of **39** to give the disodium salt **43** (50 mg, 88%) as a white powder: *R* = 0.28 (4:2:1 EtOAc/MeOH/water); $[\alpha]_D^{20}$ −63 (*c* 1, water); ^{1}H NMR (D_2O, internal HOD, δ_H 4.79, 400 MHz): δ 7.50–7.44 (m, 5H, Ar-*H*), 5.13 (s, 2H, CH_2-Ar), 4.79–4.77 (m, 2H, Gal^{I} H-1, Gal^{II} H-4), 4.68 (d, 1H, $J_{1,2}$ 7.5 Hz, Gal^{II} H-1), 4.42 (d, 1H, $J_{1,2}$ 7.5 Hz, GlcA H-1), 4.17 (dd, 1H, $J_{3,4}$ 2.0, $J_{4,5}$ <1 Hz, Gal^{I} H-4), 4.06 (dd, 1H, $J_{2,3}$ 10.0, $J_{3,4}$ 3.0 Hz, Gal^{II} H-3), 3.96–3.92 (m, 1H, OCH_2), 3.85–3.66 (m, 11H, Gal^{I} H-2,3,5,6a,6b, Gal^{II} H-2,5,6a,6b, GlcA H-5, OCH_2), 3.57–3.49 (m, 2H, GlcA H-3,4), 3.42 (dd, 1H, $J_{2,3}$ 9.0 Hz, GlcA H-2), 3.40–3.33 (m, 2H, NCH_2); ^{13}C NMR (D_2O, internal acetone, δ_C 30.83, 100 MHz): δ 176.55 (1C, GlcA C-6), 159.02 (1C, NHC(O)O), 137.09–128.32 (6C, Ar-C), 104.71 (1C, Gal^{II} C-1), 103.71, 103.29 (2C, Gal^{I} C-1, GlcA C-1), 83.00 (1C, Gal^{II} C-3), 77.81 (1C, Gal^{II} C-4), 77.16 (1C, Gal^{I} C-3), 76.77, 75.96, 75.35, 75.07, 73.69, 72.46, 71.62, 70.50 (8C, Gal^{I} C-2,5, Gal^{II} C-2,5, GlcA C-2,3,4,5), 69.48 (1C, OCH_2), 68.90 (1C, Gal^{I} C-4), 67.52 (1C, CH_2-Ar), 61.52, 61.48 (2C, Gal^{I} C-6, Gal^{II} C-6), 41.12 (1C, NCH_2). HRESIMS: Calcd for $C_{28}H_{39}NNaO_{22}S$ $[M-Na]^-$: *m/z* 796.15876. Found: 796.15886.

4.37. 2-(6-Biotinylamidohexanoyl)aminoethyl *O*-(sodium β-D-glucopyranosyluronate)-(1→3)-(β-D-galactopyranosyl)-(1→3)-β-D-galactopyranoside (1)

A solution of **39** (23.5 mg, 33 mol) in water (8 mL) was hydrogenated in the presence of 10% Pd/C catalyst (20 mg) overnight at rt. The catalyst was removed by filtration through a Celite pad, and the filtrate was concentrated to give the intermediate amine. A solution of the amine and 6-biotinylamidohexanoic acid *N*-hydroxysuccinimidoyl ester (45 mg, 98 mol) in DMF/water (9:1, 0.85 mL) was stirred for 1 h at rt, then was concentrated. The resulting solid was washed several times with absolute EtOH, and a solution of the residue in water (2 mL) was eluted from a column (3 × 80 cm) of Sephadex LH-20 with water and lyophilized to afford biotinylated **1** (19.3 mg, 64%) as a white powder: *R* = 0.32 (2:1:1 EtOAc/MeOH/water); $[\alpha]_D^{20}$ +17 (*c* 1, water); ^{1}H NMR (D_2O, internal HOD, δ_H 4.79, 400 MHz): δ 4.70 (d, 1H, $J_{1,2}$ 8.0 Hz, Gal^{II} H-1), 4.68 (d, 1H, $J_{1,2}$ 8.0 Hz, GlcA H-1), 4.62 (ddd, 1H, $J_{b,c}$ 8.0 $J_{c,d}$ <1.0, $J_{c,d'}$ 5.0 Hz, H-c), 4.48 (d, 1H, $J_{1,2}$ 8.0 Hz, Gal^{I} H-1), 4.44 (dd, 1H, $J_{b,e}$ 4.5 Hz, H-b), 4.22–4.20 (m, 2H, Gal^{I} H-4, Gal^{II} H-4), 4.02–3.97 (m, 1H, OCH_2), 3.86–3.69 (m, 12 H, Gal^{I} H-2,3,5,6a,6b, Gal^{II} H-2,3,5,6a,6b, GlcA H-5, OCH_2), 3.54–3.52 (m, 2H, GlcA H-3,4), 3.48–3.43 (m, 3H, GlcA H-2, NCH_2), 3.38–3.34 (m, 1H, H-e), 3.21–3.18 (m, 2H, NCH_2), 3.01 (dd, 1H, $J_{d,d'}$ 13.0 Hz, H-d′), 2.80 (dd, 1H, H-d), 2.31–2.28 (m, 4H, CH_2CO), 1.79–1.29 (m, 12H, CCH_2); ^{13}C NMR (D_2O, internal acetone, δ_C 30.83, 100 MHz): δ 177.75, 177.24, 176.54, (3C, GlcA C-6, C=O), 165.96 (1C, C-a), 104.62, 104.23 (2C, Gal^{I} C-1, Gal^{II} C-1), 103.25 (1C, GlcA C-1), 83.04, 82.96 (2C, Gal^{I} C-3, Gal^{II} C-3), 76.88, 76.00, 75.48, 73.83, 72.45, 70.85 (8C, Gal^{I} C-2,5, Gal^{II} C-2,5, GlcA C-2,3,4,5), 69.11 (1C, OCH_2), 69.08, 68.70, (2C, Gal^{I} C-4, Gal^{II} C-4), 62.77 (1C, C-b), 61.63 (2C, Gal^{I} C-6, Gal^{II} C-6), 60.93 (1C, C-c), 56.08 (1C, C-e), 40.39 (1C, C-d), 39.98, 39.78 (2C, NCH_2), 36.30, 36.22 (2C, CH_2CO), 28.72, 28.54, 28.37, 26.24, 25.91, 25.65 (6C, CCH_2). HRESIMS: Calcd for $C_{36}H_{59}N_4O_{20}S$ $[M-Na]^-$: *m/z* 899.34488. Found: 899.34481.

4.38. 2-(6-Biotinylamidohexanoyl)aminoethyl *O*-(sodium β-D-glucopyranosyluronate)-(1→3)-(β-D-galactopyranosyl)-(1→3)-6-*O*-sodium sulfonato-β-D-galactopyranoside (2)

Compound **40** (32.8 mg, 40 μmol) was treated as described for the preparation of **1** to give biotinylated **2** (29.2 mg, 71%) as a white powder: *R* = 0.39 (3:2:1 EtOAc/MeOH/water); $[\alpha]_D^{20}$ +19 (*c* 1, water); ^{1}H NMR (D_2O, internal HOD, δ_H 4.79, 400 MHz): δ 4.70 (d, 1H, $J_{1,2}$ 8.0 Hz, Gal^{II} H-1), 4.68 (d, 1H, $J_{1,2}$ 8.0 Hz, GlcA H-1), 4.63 (ddd, 1H, $J_{c,d}$ <1.0, $J_{c,d'}$ 5.0, $J_{b,c}$ 8.00 Hz, H-c), 4.50 (d, 1H, $J_{1,2}$ 8.0 Hz, Gal^{I} H-1), 4.44 (dd, 1H, $J_{b,e}$ 4.5 Hz, H-b), 4.27 (dd, 1H, $J_{3,4}$ 3.0, $J_{4,5}$ <1 Hz, Gal^{I} H-4), 4.24 (dd, 1H, $J_{3,4}$ 3.0, $J_{4,5}$ <1 Hz, Gal^{II}

H-4), 4.23–4.21 (m, 2H, Gal^{I} H-6a,6b), 3.99-3.96 (m, 2H, Gal^{I} H-5, OCH_2), 3.88–3.69 (m, 9 H, Gal^{I} H-2,3, Gal^{II} H-2,3,5,6a,6b, GlcA H-5, OCH_2), 3.55–3.53 (m, 2H, GlcA H-3,4), 3.48–3.43 (m, 3H, GlcA H-2, NCH_2), 3.36–3.33 (m, 1H, H-e), 3.22–3.18 (m, 2H, NCH_2), 3.02 (dd, 1H, $J_{d,d'}$ 13.0 Hz, H-d′), 2.80 (dd, 1H, H-d), 2.31–2.25 (m, 4H, CH_2CO), 1.79–1.32 (m, 12H, CCH_2); ^{13}C NMR (D_2O, internal acetone, δ_C 30.83, 100 MHz): δ 177.67, 177.18 (3C, GlcA C-6, C=O), 165.88 (1C, C-a), 104.57, 104.14 (2C, Gal^{II} C-1, GlcA C-1), 103.12 (1C, Gal^{I} C-1), 82.96, 82.67 (2C, Gal^{I} C-3, Gal^{II} C-3), 75.86, 75.33, 73.70, 73.00, 72.32, 70.71, 70.32 (8C, Gal^{I} C-2,5, Gal^{II} C-2,5, GlcA C-2,3,4,5), 69.24 (1C, OCH_2), 68.73, 68.57 (2C, Gal^{I} C-4, Gal^{II} C-4), 67.87 (1C, Gal^{I} C-6), 62.64 (1C, C-b), 61.47 (1C, Gal^{II} C-6), 60.81 (1C, C-c), 55.93 (1C, C-e), 40.27 (1C, C-d), 39.92, 39.65 (2C, NCH_2), 36.18, 36.10 (2C, CH_2CO), 28.55, 28.40, 28.23, 26.09, 25.79, 25.43 (6C, CCH_2). HRESIMS: Calcd for $C_{36}H_{58}N_4O_{23}S_2$ $[M-2Na]^{2-}$: *m/z* 489.14721. Found: 489.14818.

4.39. 2-(6-Biotinylamidohexanoyl)aminoethyl *O*-(sodium β-D-glucopyranosyluronate)-(1→3)-(β-D-galactopyranosyl)-(1→3)-4-*O*-sodium sulfonato-β-D-galactopyranoside (3)

Compound **41** (32.8 mg, 40 μmol) was treated as described for the preparation of **1** to give biotinylated **3** (32.5 mg, 79%) as a white powder: *R* = 0.24 (3:2:1 EtOAc/MeOH/water); $[\alpha]_D^{20}$ +16 (*c* 1, water); ^{1}H NMR (D_2O, internal HOD, δ_H 4.79, 400 MHz): δ 4.88 (dd, 1H, $J_{3,4}$ 2.5, $J_{4,5}$ <1 Hz, GalI H-4), 4.71 (d, 1H, $J_{1,2}$ 8.0 Hz, GlcA H-1), 4.69 (d, 1H, $J_{1,2}$ 8.0 Hz, Gal^{II} H-1), 4.63 (ddd, 1H, $J_{c,d}$ <1.0, $J_{c,d'}$ 5.5, $J_{b,c}$ 7.5 Hz, H-c), 4.50 (d, 1H, $J_{1,2}$ 8.0 Hz, Gal^{I} H-1), 4.45 (dd, 1H, $J_{b,e}$ 4.5 Hz, H-b), 4.18 (dd, 1H, $J_{3,4}$ 2.0, $J_{4,5}$ <1 Hz, Gal^{II} H-4), 4.04 (dd, 1H, $J_{2,3}$ 10.0 Hz, Gal^{I} H-3), 4.03–3.97 (m, 1H, OCH_2), 3.85–3.68 (m, 11H, Gal^{I} H-2,5,6a,6b, Gal^{II} H-2,3,5,6a,6b, GlcA H-5, OCH_2), 3.55–3.52 (m, 2H, GlcA H-3,4), 3.47–3.41 (m, 3H, GlcA H-2, NCH_2), 3.36–3.33 (m, 1H, H-e) 3.24–3.16 (m, 2H, NCH_2), 3.02 (dd, 1H, $J_{d',c}$ 5.0, $J_{d,d'}$ 13.0 Hz, H-d′), 2.81 (dd, 1H, H-d), 2.31–2.25 (m, 4H, CH_2CO), 1.77–1.31 (m, 12H, CCH_2); ^{13}C NMR (D_2O, internal acetone, δ_C 30.83, 100 MHz): δ 177.65, 177.12, 176.50 (3C, GlcA C-6, C=O), 165.85 (1C, C-a), 104.50, 104.22 (2C, Gal^{II} C-1, GlcA C-1), 103.16 (1C, Gal^{I} C-1), 82.89 (1C, Gal^{II} C-3), 79.03 (1C, Gal^{I} C-3), 77.99 (1C, Gal^{I} C-4), 75.84, 75.45, 75.06, 73.66, 72.31, 70.94, 70.69 (8C, Gal^{I} C-2,5, Gal^{II} C-2,5, GlcA C-2,3,4,5), 69.07 (1C, OCH_2), 68.92 (1C, Gal^{II} C-4), 62.64 (1C, C-b), 61.61, 61.53 (2C, Gal^{I} C-6, Gal^{II}C-6), 60.80 (1C, C-c), 55.95 (1C, C-e), 40.27 (1C, C-d), 39.82, 39.64 (2C, NCH_2), 36.17, 36.08 (2C, CH_2CO), 28.57, 28.41, 28.23, 26.08, 25.77, 25.51 (6C, CCH_2). HRESIMS: Calcd for $C_{36}H_{58}N_4NaO_{23}S_2$ $[M-Na]^{-}$: *m/z* 1001.28364. Found: 1001.28269.

4.40. 2-(6-Biotinylamidohexanoyl)aminoethyl *O*-(sodium β-D-glucopyranosyluronate)-(1→3)-(6-*O*-sodium sulfonato-β-D-galactopyranosyl)-(1→3)-β-D-galactopyranoside (4)

Compound **42** (33.9 mg, 41 μmol) was treated as described for the preparation of **1** to give biotinylated **4** (27.4 mg, 65%) as a white powder: *R* = 0.37 (3:2:1 EtOAc/MeOH/water); $[\alpha]_D^{20}$ +15 (*c* 1, water); ^{1}H NMR (D_2O, internal HOD, δ_H 4.79, 400 MHz): δ 4.70 (d, 1H, $J_{1,2}$ 8.0 Hz, Gal^{II} H-1), 4.67 (d, 1H, $J_{1,2}$ 7.5 Hz, GlcA H-1), 4.62 (ddd, 1H, $J_{c,d}$ <1.0, $J_{c,d'}$ 5.0, $J_{b,c}$ 8.0 Hz, H-c), 4.48 (d, 1H, $J_{1,2}$ 8.0 Hz, Gal^{I} H-1), 4.44 (dd, 1H, $J_{b,e}$ 4.5 Hz, H-b), 4.28, 4.24 (2dd, 2H, $J_{3,4}$ 2.5, $J_{4,5}$ <1 Hz, Gal^{I} H-4, Gal^{II} H-4), 4.22–4.20 (m, 2H, Gal^{II} H-6a,6b), 4.02–3.97 (m, 1H, OCH_2), 3.95–3.92 (m, 1H, $J_{5,6a}$ 5.5, $J_{5,6b}$ 6.0 Hz, Gal^{II} H-5), 3.87–3.68 (m, 9H, Gal^{I} H-2,3,5,6a,6b, Gal^{II} H-2,3, GlcA H-5, OCH_2), 3.55–3.52 (m, 2H, GlcA H-3,4), 3.48–3.41 (m, 3H, GlcA H-2, NCH_2), 3.36–3.33 (m, 1H, H-e), 3.21–3.17 (m, 2H, NCH_2), 3.01 (dd, 1H, $J_{d,d'}$ 13.0 Hz, H-d′), 2.80 (dd, 1H, H-d), 2.30–2.24 (m, 4H, CH_2CO), 1.77–1.30 (m, 12H, CCH_2); ^{13}C NMR (D_2O, internal acetone, δ_C 30.83, 100 MHz): δ 177.70, 177.1 (3C, GlcA C-6, C=O), 165.90 (1C, C-a), 104.38, 104.22 (2C, Gal^{II} C-1, GlcA C-1), 103.16 (1C, Gal^{I} C-1), 83.34, 82.85 (2C, Gal^{I} C-3, Gal^{II} C-3), 75.88, 75.60, 73.71, 73.08, 72.32, 70.59, 70.32, 70.25 (8C, Gal^{I} C-2,5, Gal^{II} C-2,5, GlcA C-2,3,4,5), 69.01 (1C, OCH_2), 68.50 (2C, Gal^{I} C-4, Gal^{II} C-4), 68.38 (1C, Gal^{II} C-6), 62.68 (1C, C-b), 61.86 (1C, Gal^{I} C-6), 60.84 (1C, C-c), 55.98 (1C, C-e), 40.30 (1C, C-d), 39.90, 39.68 (2C, NCH_2), 36.20, 36.12 (2C, CH_2CO), 28.61, 28.45, 28.27, 26.14, 25.81, 25.55 (6C, CCH_2). HRESIMS: Calcd for $C_{36}H_{58}N_4NaO_{23}S_2$ $[M-Na]^{-}$: *m/z* 1001.28364. Found: 1001.28399.

4.41. 2-(6-Biotinylamidohexanoyl)aminoethyl *O*-(sodium β-D-glucopyranosyluronate)-(1→3)-(4-*O*-sodium sulfonato-β-D-galactopyranosyl)-(1→3)-β-D-galactopyranoside (5)

Compound **43** (33.4 mg, 40.7 μmol) was treated as described for the preparation of **1** to give biotinylated **5** (25 mg, 60%) as a white powder: *R* = 0.30 (3:2:1 EtOAc/MeOH/water); $[\alpha]_D^{20}$ +12 (*c* 1, water); ^{1}H NMR (D_2O, internal HOD, δ_H 4.79, 400 MHz): δ 4.81 (dd, 1H, $J_{3,4}$ 2.0, $J_{4,5}$ <1 Hz, Gal^{II} H-4), 4.79 (d, 1H, $J_{1,2}$ 7.5 Hz, GlcA H-1), 4.70 (d, 1H, $J_{1,2}$ 8.0 Hz, Gal^{II} H-1), 4.62 (ddd, 1H, $J_{c,d}$ <1.0, $J_{c,d'}$ 5.0, $J_{b,c}$ 7.5 Hz, H-c), 4.47 (d, 1H, $J_{1,2}$ 8.0 Hz, Gal^{I} H-1), 4.43 (dd, 1H, $J_{b,e}$ 5.0 Hz, H-b), 4.19 (dd, 1H, $J_{3,4}$ 2.0, $J_{4,5}$ <1 Hz, Gal^{I} H-4), 4.06 (dd, 1H, $J_{2,3}$ 10.0, Gal^{II} H-3), 4.00–3.95 (m, 1H, OCH_2), 3.85-3.69 (m, 11H, Gal^{I} H-2,3,5,6a,6b, Gal^{II} H-2,5,6a,6b, GlcA H-5, OCH_2), 3.58–3.49 (m, 2H, GlcA H-3,4), 3.48–3.36 (m, 3H, GlcA H-2, NCH_2), 3.35–3.33 (m, 1H, H-e), 3.20–3.16 (m, 2H, NCH_2), 3.00 (dd, 1H, $J_{d,d'}$ 13.0 Hz, H-d′), 2.79 (dd, 1H, H-d), 2.29–2.24 (m, 4H, CH_2CO), 1.77–1.29 (m, 12H, CCH_2). ^{13}C NMR (D_2O, internal acetone, δ_C 30.83, 100 MHz): δ 177.72, 177.69, 176.51 (3C, GlcA C-6, C=O), 165.89 (1C, C-a), 104.69 (1C, Gal^{II} C-1), 103.42 (1C, GlcA C-1), 103.19 (1C, Gal^{I} C-1), 83.06 (1C, Gal^{I} C-3), 77.79 (1C, Gal^{II} C-4), 77.16 (1C, Gal^{II} C-3), 76.76, 75.95, 75.38, 75.05, 73.68, 72.45, 71.62, 70.49 (8C, Gal^{I} C-2,5, Gal^{II} C-2,5, GlcA C-2,3,4,5), 69.00 (1C, Gal^{I} C-4), 68.90 (1C, OCH_2), 62.68 (1C, C-b), 61.59, 61.53 (2C, Gal^{I} C-6, Gal^{II} C-6), 60.84 (1C, C-c), 55.98 (1C, C-e), 40.30 (1C, C-d), 39.88, 39.68 (2C, NCH_2), 36.20, 36.11 (2C, CH_2CO), 28.61, 28.43, 28.27, 26.14, 25.81, 25.55 (6C, CCH_2). HRESIMS: Calcd for $C_{36}H_{58}N_4NaO_{23}S_2$ $[M-Na]^{-}$: *m/z* 1001.28364. Found: 1001.28430.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.carres.2012.03.039.

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