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Synthesis of glycosaminoglycan oligosaccharides. Part 4: Synthesis of aza-L-iduronic acid-containing analogs of heparan sulfate oligosaccharides as heparanase inhibitors☆

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ABSTRACT

The synthesis of three azasugar-containing analogs of the disaccharide units of heparan sulfate, which are potential inhibitors of the enzyme heparanase, is reported. Synthetic routes were developed for the preparation of L-*ido*-nojirimycin type glycosyl acceptors with O-4 free. Glycosylation of these acceptors with an O-6 functionalized 2-azido-2-deoxy-D-glucose thioglycoside donor afforded the α-linked disaccharides in good yields. The advantages of using the 4-nitrobenzenesulfonyl group for the protection of the ring nitrogen of azasugars were demonstrated.

1. Introduction

Heparan sulfate proteoglycans (HSPGs) are ubiquitous constituents of the extracellular matrix and of cell membranes.[1] The structure of HSPG consists of a protein core to which linear chains of the glycosaminoglycan, heparan sulfate (HS), are linked by *O*-glycosidic bonds. The carbohydrate backbone of HS is built up of alternating D-glucosamine and hexuronic acid (D-glucuronic acid and L-iduronic acid) units forming →4)-α-L-Ido*p*A-(1→4)-α-D-Glc*p*N-(1→ and →4)-β-D-Glc*p*A-(1→4)-α-D-Glc*p*N-(1→ disaccharides, which are substituted at certain positions. Thus, O-3 and O-6 of the D-glucosamine units, and O-2 of the uronic acid units can be *O*-sulfated, furthermore, the amino group of D-glucosamine can be *N*-acetylated, *N*-sulfated, or remain unsubstituted.[1,2] These variations result in an enormous structural diversity.[3] Heparan sulfate binds to a large number of proteins, thereby influencing a variety of normal and pathological processes including tumor growth and metastasis, tissue repair, angiogenesis, and inflammation.[4] Cleavage of HS chains alters its interaction with proteins and thus influences the above processes.

The most important cleavage enzyme in the catabolism of heparan sulfate chains is heparanase.[5] Heparanase is an *endo*-β-glucuronidase, which specifically cleaves the HS chains at a limited number of sites.[6] It has been recognized that tumor metastasis occurs via complex multistage processes, which involves tumor cell adhesion to various basement membrane components, and degradation of the extracellular matrix and basement membranes. As HS is an important constituent in these structures, cleavage of HS by heparanase plays an important role in cell invasion of some malignant tumors through basement membranes. Heparanase is overexpressed in a number of human tumors.[5b] The expression level of the enzyme is of diagnostic and prognostic value, and has been correlated with the survival time of cancer patients.[5b,7] The inhibition of heparanase forms the basis of potential anti-metastatic cancer therapy, and it has therefore been intensively investigated.[8]

Azasugars are monosaccharide analogs having a nitrogen atom instead of oxygen in the ring, and have received significant attention as carbohydrate mimetics.[9] Compounds of this type, such as 1-deoxynojirimycin, are potent inhibitors of various glycosidases, and are intensely investigated for their therapeutic potential as antidiabetic, antiviral, and anticancer agents. Though monosaccharidic azasugars, in general, show some specificity to inhibit certain types of glycosidases, this specificity is still fairly broad. One way to increase specificity is to use larger size molecules, which are closer mimics of the natural substrates of the enzymes. Thus, oligosaccharides containing an azasugar component have been synthesized for various biological purposes.[10,11]

☆ For Part 3, see Ref. 12.

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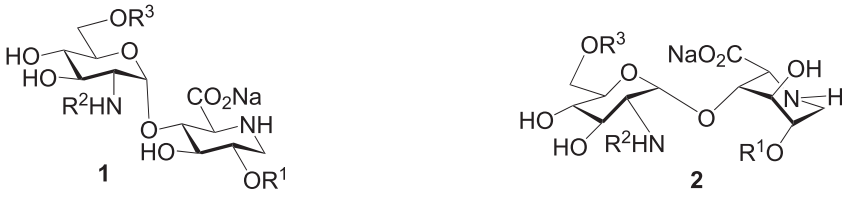
In order to incorporate specificity in azasugars toward heparanase, we have designed azasugar-containing oligosaccharides mimicking the structure of heparin and heparan sulfate (Fig. 1).[12] The synthesis of related aza-analogs of heparan sulfate disaccharides,[13] as well as an interglycosidically *S*-linked oligosaccharide[14] has been reported recently for similar purpose.

2. Results and discussion

2.1. Synthetic design

The target structures **3**–**5** should be available from the 2-azido-2-deoxy-D-glucopyranosyl donor (**7**) and the L-idose

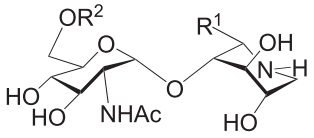


R^1 = H or SO_3Na; R^2 = Ac or SO_3Na; R^3 = H or SO_3Na

Figure 1. Designed azasugar-containing heparan sulfate disaccharides.

Compounds of type **1** and **2** contain a D-glucosamine unit α-(1→4)-linked to an azasugar analog of D-glucuronic acid and L-iduronic acid, respectively. Though heparanase is a β-glucuronidase, compounds of type **2** having an L-*ido*-configured azasugar might also be of interest as potential inhibitors. The rationale for this is that there are several examples reported that azasugars of the 'wrong' configuration are good inhibitors of glycosidases having specificity for a different configuration.[15] Additionally, because of the known conformational mobility of L-idose and L-iduronic acid,[2,16] compounds of type **2** might fit into the active site of the enzyme. It was also of interest, that an L-iduronic acid-type 1-*N*-iminosugar has been reported to have inhibitory activity of cancer metastasis.[17]

Previously only aza-D-glucuronic acid-containing disaccharide inhibitors of heparanase have been reported.[13] As far as we are aware, L-*ido*-configured azasugar-containing oligosaccharides have not been synthesized before, we have recently reported the first compound of this type.[12] We now describe the synthesis of three disaccharides (**3**–**5**) containing azasugar components having L-*ido* configuration, as well as the monosaccharide congener **6** (Fig. 2).



3 R^1 = CH_2OH R^2 = H
4 R^1 = CO_2Na R^2 = H
5 R^1 = CO_2Na R^2 = SO_3Na

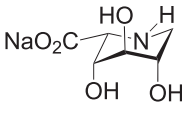


Figure 2. Synthesized azasugar-containing heparan sulfate fragments.

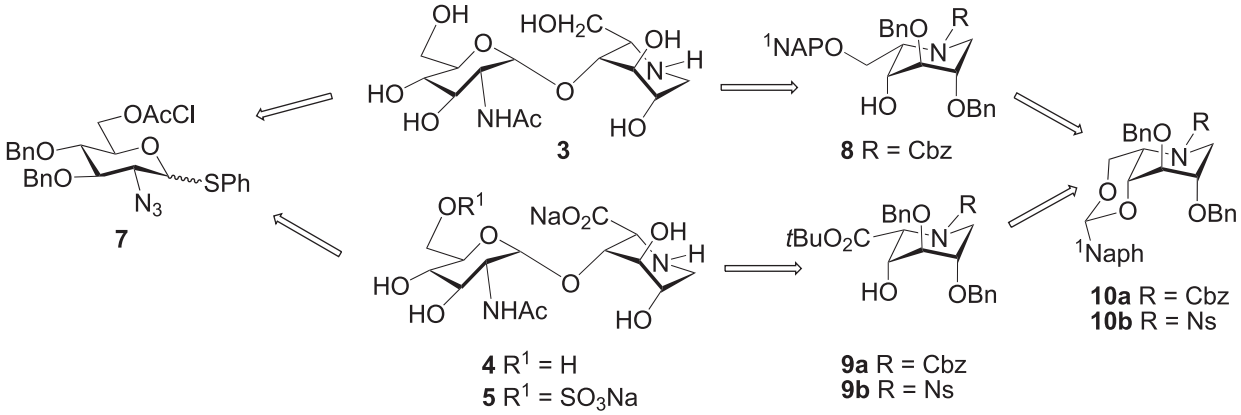
(**8**) and L-iduronic acid (**9**) azasugar glycosyl acceptors (Scheme 1).

In the glycosyl donor **7**, O-6 is masked by the temporary chloroacetyl group, which allows the selective release of O-6 in the synthesis of the *O*-sulfated product (**5**). The carboxyl function in **9** is protected as the *tert*-butyl ester. For the protection of the ring nitrogen in the glycosyl acceptors, the benzyloxycarbonyl group, most commonly used for this purpose in the azasugar field,[10,13] was selected originally. Due to inconveniences and an undesired side reaction recognized during work with the *N*-benzyloxycarbonyl protected derivatives, this group was replaced with the 4-nitrobenzenesulfonyl (Ns) group at a later stage of this work. The synthesis of glycosyl acceptors requires selective manipulations at O-4 and O-6, both **8** and **9** should be available from the (1-naphthyl) methylene acetal **10** by different reductive acetal opening methods giving the readily removable (1-naphthyl)methyl (^{1}NAP) ethers[18] at either O-4 or O-6. The synthesis of the derivatives having L-*ido* configuration was envisioned by S_N2 nucleophilic substitution of *N*-nosyl protected D-*gluco* derivatives in the cyclization step.[19]

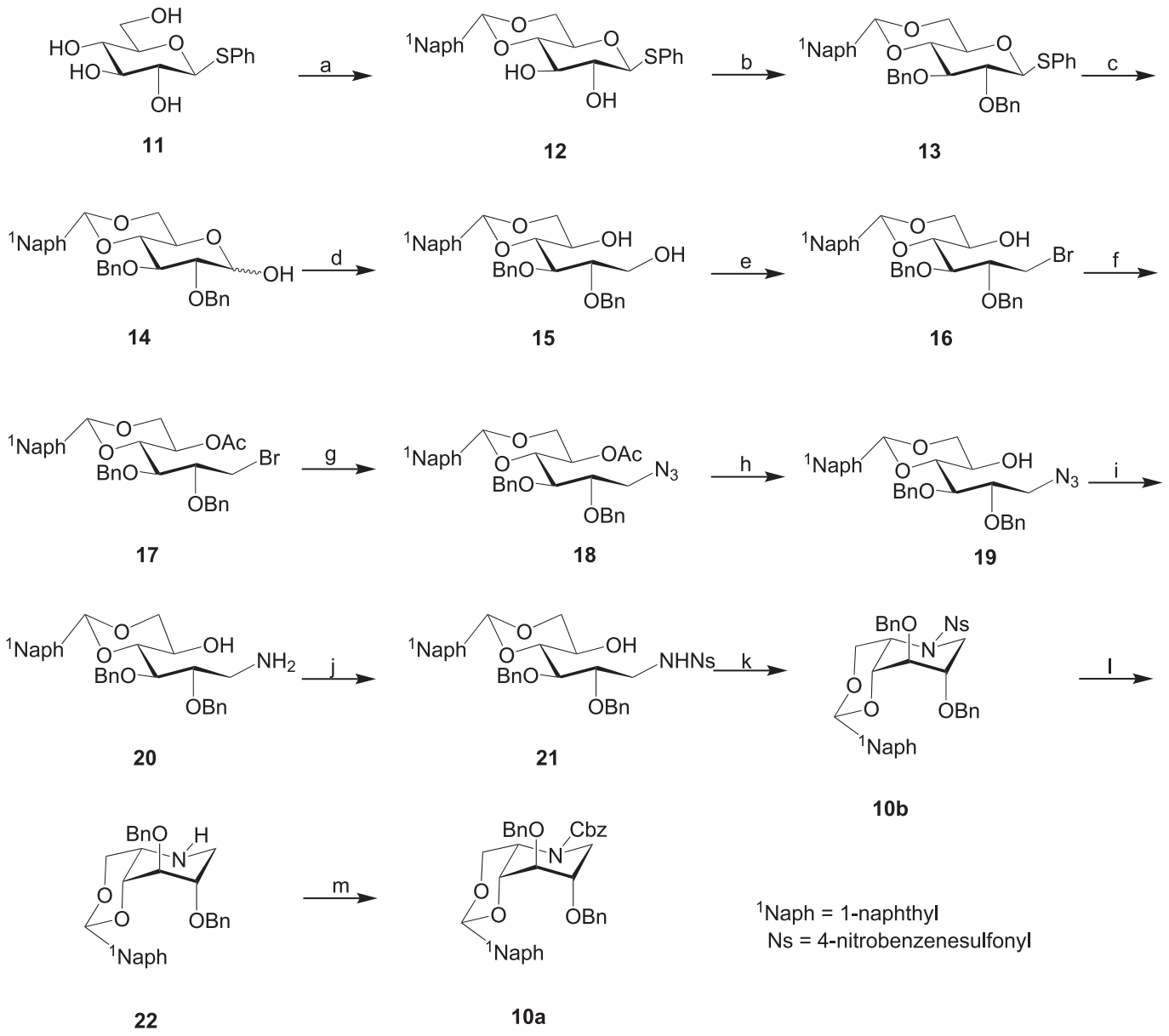
2.2. Oligosaccharide synthesis using *N*-benzyloxycarbonyl protection

2.2.1. Synthesis of the glycosyl acceptors. Phenyl 1-thio-β-D-glucopyranoside (**11**), readily obtained by Zemplén deacetylation of the tetraacetate,[20] was converted into the (1-naphthyl)methylene acetal **12**, which was benzylated to give **13** (Scheme 2).

The hemiacetal was released by reaction with NBS[21] and **14** was reduced to give the alditol **15**. The primary hydroxyl was selectively brominated using Ph_3P and CBr_4[22] to give **16** in excellent yield, then



Scheme 1. Retrosynthesis of heparanase inhibitory disaccharides.

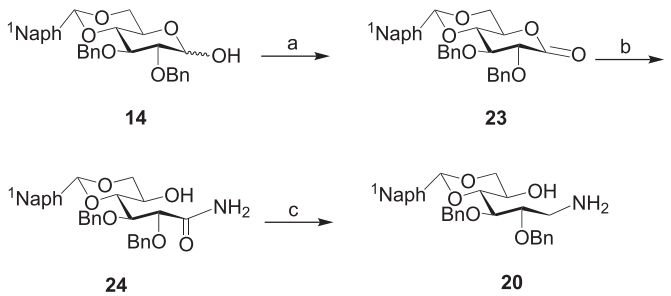


Scheme 2. Reagents and conditions: (a) ^{1}NaphCH(OMe)$_2$, *p*-TSA, MeCN, 98%; (b) BnBr, NaH, DMF, 98%; (c) NBS, CH_2Cl_2, acetone, H_2O, 93%; (d) $NaBH_4$, THF, H_2O, 97%; (e) Ph_3P, CBr_4, pyridine, 98%; (f) Ac_2O, pyridine, 98%; (g) NaN_3, NH_4Cl, DMF, H_2O, 79%; (h) NaOMe, MeOH, 98%; (i) 1,3-propanedithiol, Et_3N, pyridine, H_2O, 96%; or Ph_3P, pyridine, then 25% NH_4OH, 77%; (j) NsCl, Et_3N, CH_2Cl_2, 98%; (k) DEAD, Ph_3P, CH_2Cl_2, 96%; (l) PhSH, K_2CO_3, DMF, 98%; (m) BnOCOCl, $NaHCO_3$, MeOH, 97%.

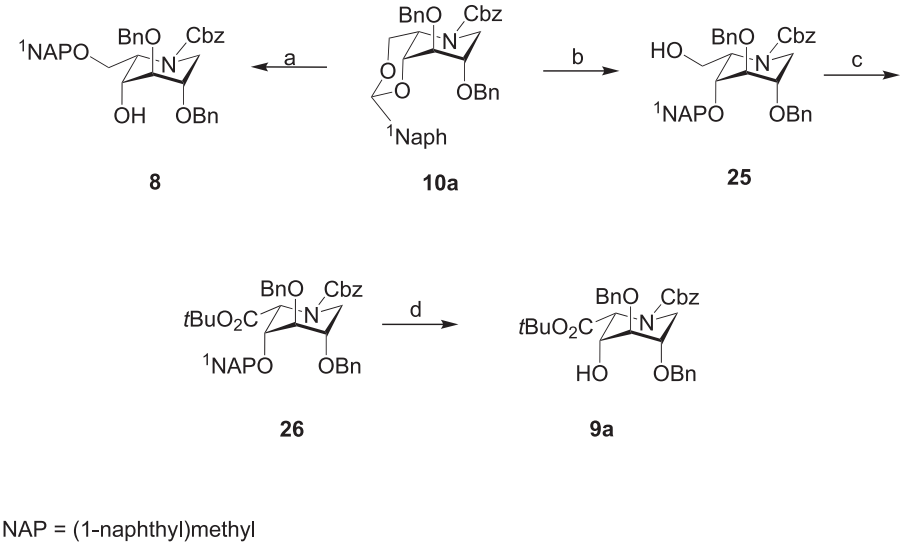
the hydroxyl group was acetylated. Nucleophilic replacement of the bromine in **17** with NaN_3 in DMF and water afforded **18**, which was converted to **19** by Zemplén deacetylation. The azide was reduced to the amine either by 1,3-propanedithiol or by Ph_3P and hydrolysis of the phosphimine, and the resulting **20** was selectively nosylated to the 4-nitrobenzenesulfonamide **21** in excellent yield. Cyclization of **21** using the Mitsunobu reaction took place with configurational inversion at C-5 and provided the L-*ido* derivative **10b** in 96% yield.[19] The 4-nitrobenzenesulfonyl group was exchanged to benzyloxycarbonyl by treating **10b** with PhSH and Et_3N to give **22**, which, in turn, was reacted with benzyl chloroformate to give the central intermediate **10a**.

A shorter route from **14** to **20** involved Dess–Martin oxidation[23] of the hemiacetal to the lactone **23** (Scheme 3). The lactone ring was opened with methanolic ammonia to give the amide **24**, which was reduced with $LiAlH_4$ to give **20**.[24]

The conversion of **10a** to the glycosyl acceptors (**8** and **9a**) was performed in the following ways (Scheme 4). Reductive ring opening of the (1-naphthyl)methylene acetal with $NaBH_3CN$–HCl[25] afforded **8** directly. For the synthesis of **9a**, the 4-*O*-(1-naphthyl)methyl ether was prepared by reduction with $BH_3\cdot$THF–TMSOTf,[26] which gave **25** in 91% yield. One-step oxidation-esterification using pyridinium



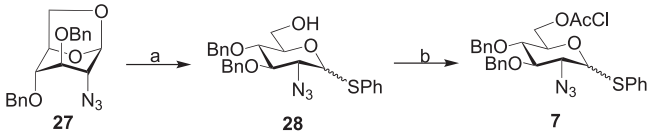
Scheme 3. Reagents and conditions: (a) Dess–Martin periodinane, CH_2Cl_2, 90%; (b) NH_3–MeOH, 65%; (c) $LiAlH_4$, THF, 70%.



Scheme 4. Reagents and conditions: (a) $NaCNBH_3$, HCl–Et_2O, THF, 67%; (b) BH_3·THF, TMSOTf, CH_2Cl_2, 91%; (c) PDC, Ac_2O, *t*-BuOH, CH_2Cl_2, 68%; (d) CAN, MeCN, H_2O, 65%.

dichromate (PDC) in the presence of acetic anhydride and *tert*-butanol[27] afforded the *tert*-butyl uronate **26**. Removal of the (1-naphthyl) methyl group by ceric ammonium nitrate (CAN)[18] then gave **9a**.

2.2.2. Synthesis of the glycosyl donor. Thiolysis of the 1,6-anhydro derivative **27**[28] with $PhSSiMe_3$–ZnI_2 gave the thioglycoside **28**[13] as an about 2:1 α:β anomeric mixture (Scheme 5). Chloroacetylation then afforded **7**, which was used as an anomeric mixture in glycosylation reactions.



Scheme 5. Reagents and conditions: (a) $PhSSiMe_3$, ZnI_2, CH_2Cl_2, 80%; (b) $(ClCH_2CO)_2O$, pyridine, CH_2Cl_2 74%.

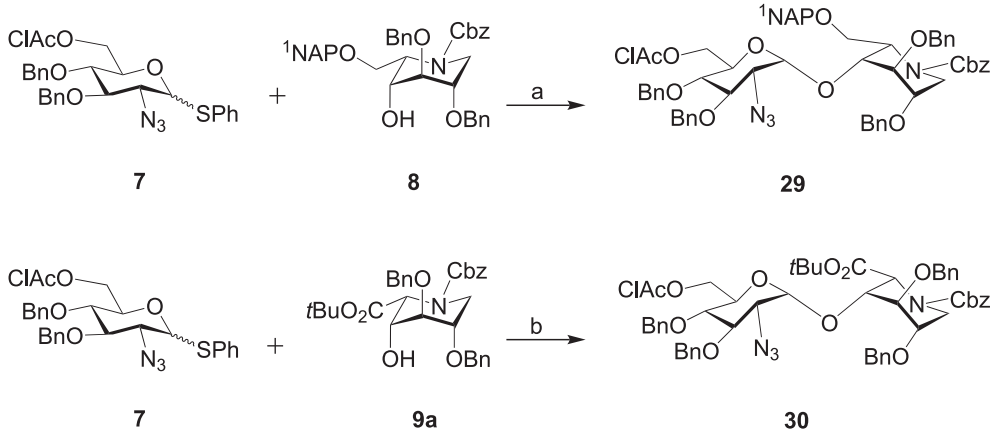
*2.2.3. Synthesis of disaccharides **3** and **4**.* The azasugar derivatives **8** and **9a** proved to be good glycosyl acceptors. Reaction of **7** with **8** using DMTST[29] as promoter in diethyl ether–dichloromethane afforded the α-linked disaccharide in 59% yield (Scheme 6). Reaction of **7** with **9a** was promoted by Me_2S_2–Tf_2O[30] and the α-linked disaccharide **30** was obtained in 80% yield.

The fully protected disaccharide **29** was transformed into the free disaccharide **3** as shown in Scheme 7.

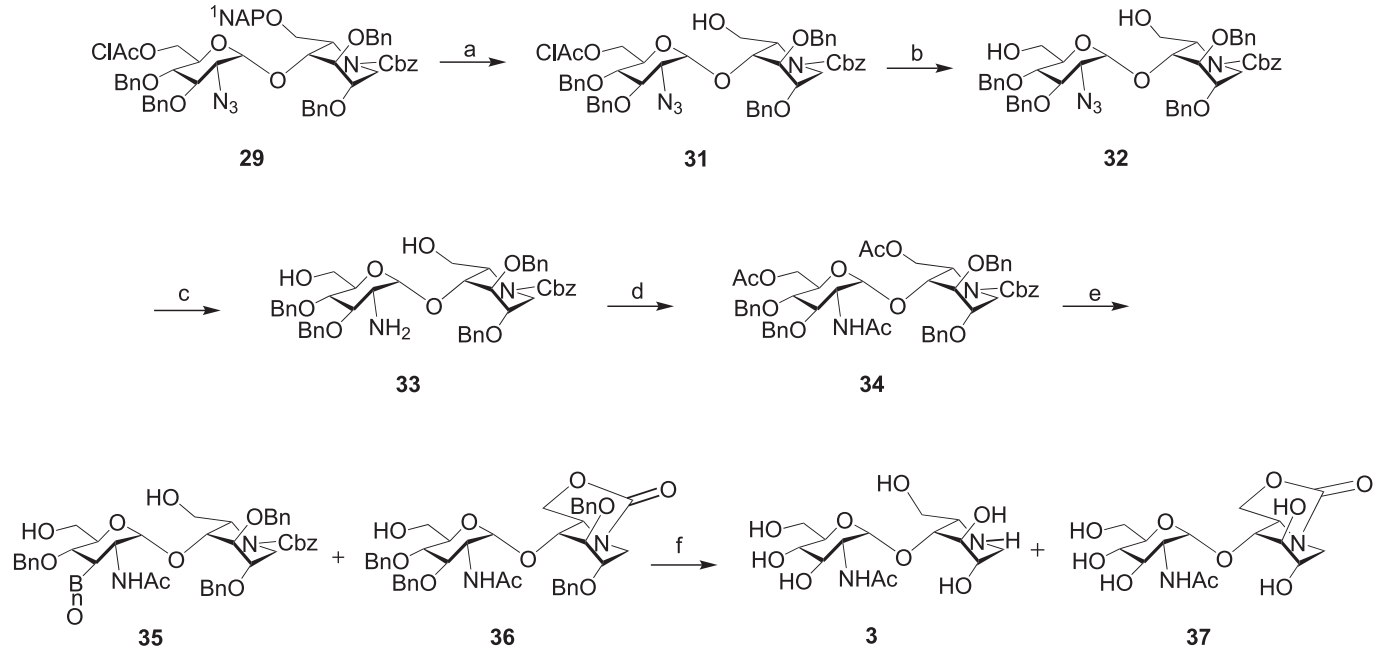
Treatment of **29** with CAN removed the (1-naphthyl)methyl ether and afforded **31** in 71% yield. This product was dechloroacetylated using hydrazinedithiocarbonate (HDTC),[31] and the azido group of **32** was reduced with 1,3-propanedithiol to give the amine **33**. After N,O-acetylation, the *O*-acetyl groups of **34** were removed by Zemplén deacetylation. The resulting product turned out to be a mixture, which in addition to the desired **35** also contained the 6-*O*,*N*-cyclic carbamate derivative **36**. Formation of similar cyclic carbamates from *N*-benzyloxycarbonyl protected azasugars with loss of the benzyl group under basic conditions has been reported earlier.[10f–h,32] The two compounds could not be separated at this stage. For complete deprotection the mixture was subjected to catalytic hydrogenolysis; **3** and **37** were obtained in pure state after careful column chromatographic separation.

For the synthesis of compound **4**, first the chloroacetyl group was removed from **30** as described before, then the azido group of the obtained **38** was reduced with 1,3-propanedithiol to give the amine **39** (Scheme 8). Peracetylation afforded **40**, which was then subjected to Zemplén deacetylation to yield **41**. The *tert*-butyl ester was hydrolyzed by treatment with trifluoroacetic acid (TFA) in dichloromethane, and catalytic hydrogenation of the free acid removed the benzyloxycarbonyl and benzyl groups to provide **4**.

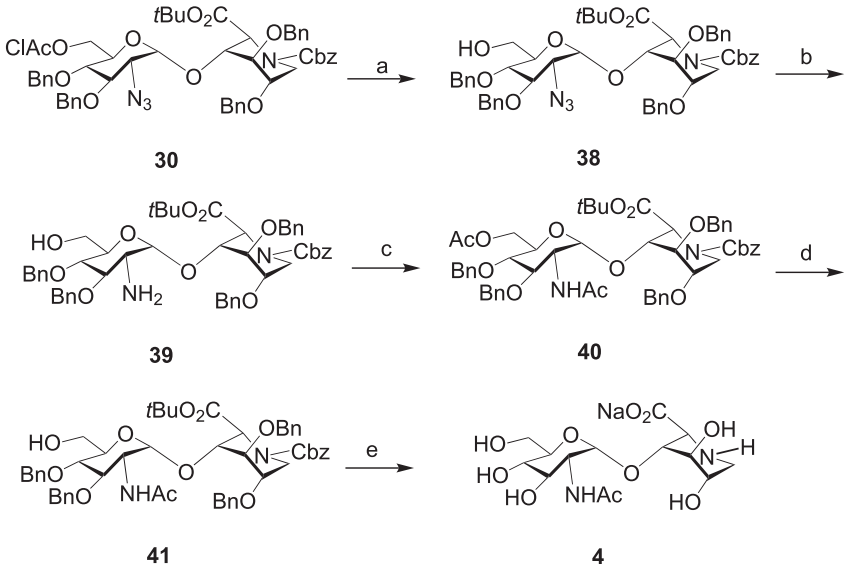
Preparation of the free monosaccharide **6** followed a similar sequence (Scheme 9). Hydrolysis of the uronate **9a** with 20% TFA in CH_2Cl_2 followed by catalytic hydrogenation of **42** afforded **6**.[33]



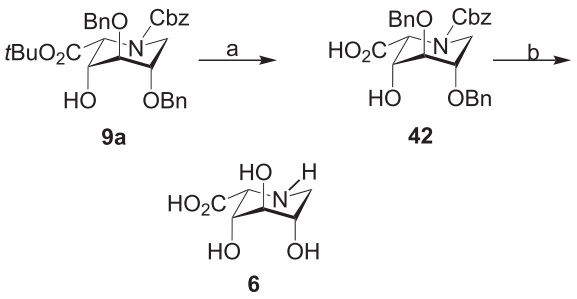
Scheme 6. Reagents and conditions: (a) DMTST, Et_2O, CH_2Cl_2, 59%; (b) Me_2S_2–Tf_2O, Et_2O, CH_2Cl_2, 80%.



Scheme 7. Reagents and conditions: (a) CAN, MeCN, H_2O, 71%; (b) HDTC, DMF, 92%; (c) 1,3-propanedithiol, Et_3N, pyridine, H_2O, 81%; (d) Ac_2O, pyridine, 83%; (e) NaOMe, MeOH, 87%; (f) H_2, Pd/C, THF, H_2O, (**3**) 43%, (**37**) 31%.



Scheme 8. Reagents and conditions: (a) HDTC, DMF, 72%; (b) 1,3-propanedithiol, Et_3N, pyridine, H_2O, 81%; (c) Ac_2O, pyridine, 96%; (d) NaOMe, MeOH, 95%; (e) 1. TFA, CH_2Cl_2, 95%; 2. H_2, Pd/C, THF, H_2O, 88%.



Scheme 9. Reagents and conditions: (a) TFA, CH_2Cl_2, 97%; (b) H_2, Pd/C, THF, H_2O, 79%.

2.3. Oligosaccharide synthesis using *N*-nosyl protection

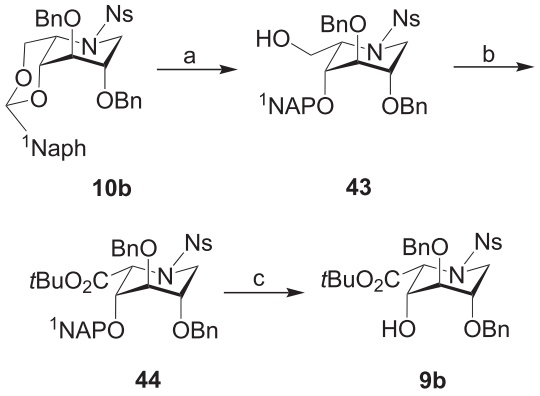
Our original choice for the protection of the ring nitrogen of azasugars was the benzyloxycarbonyl group, which is the most commonly used group for this purpose. During the previous syntheses, however, we have experienced a series of drawbacks associated with the use of this protecting group. A major inconvenience was the doubling of signals in the NMR spectra of the *N*-benzyloxycarbonyl derivatives.[10e,10g,12,32b] This is due to the existence of rotamers around the amide bond, and it necessitated running the measurements at high temperature in DMSO-d_6 to obtain simpler and better-resolved spectra. Another problem with the *N*-benzyloxycarbonyl group was the undesired formation of *O*,*N*-cyclic carbamates (**36** and **37**, Section 2.2.3) during deacetylation. In general, fairly strongly basic conditions are used for the preparation of this type of derivatives,[10f–10h,32] their formation under the mildly basic conditions of Zemplén deacetylation was somewhat unexpected.

On the way to the synthesis of *N*-benzyloxycarbonyl derivatives, it was recognized that the *N*-nosyl intermediates, such as **21** and

10b, gave simpler, better-resolved NMR spectra. As these compounds were intermediates in the preparation of the *N*-benzyloxycarbonyl protected glycosyl acceptors, it was of interest to use the *N*-nosyl protected derivatives in oligosaccharide synthesis to shorten the synthetic route. In our previous communication[12] we have demonstrated that *N*-nosyl protection is fully compatible with the transformations required for oligosaccharide synthesis, therefore *N*-benzyloxycarbonyl protection was abandoned, and compound **5** was synthesized using nosyl protected derivatives.

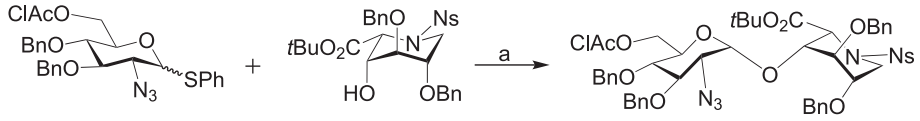
For the synthesis of the glycosyl acceptor the (1-naphthyl) methylene acetal ring of **10b** was cleaved by $BH_3\cdot THF$–TMSOTf to give the 4-*O*-(1-naphthyl)methyl ether **43** (Scheme 10). Reaction with PDC–Ac_2O–*t*-BuOH afforded the *tert*-butyl uronate **44**, from which the 1-(naphthyl)methyl group was removed with CAN to yield the nosyl-protected acceptor **9b**.

Glycosylation of **9b** with **7** was promoted by Me_2S_2–Tf_2O using Et_2O–CH_2Cl_2 as solvent, and the reaction afforded the α-linked disaccharide **45** in 90% yield (Scheme 11).



10b 43 44 9b

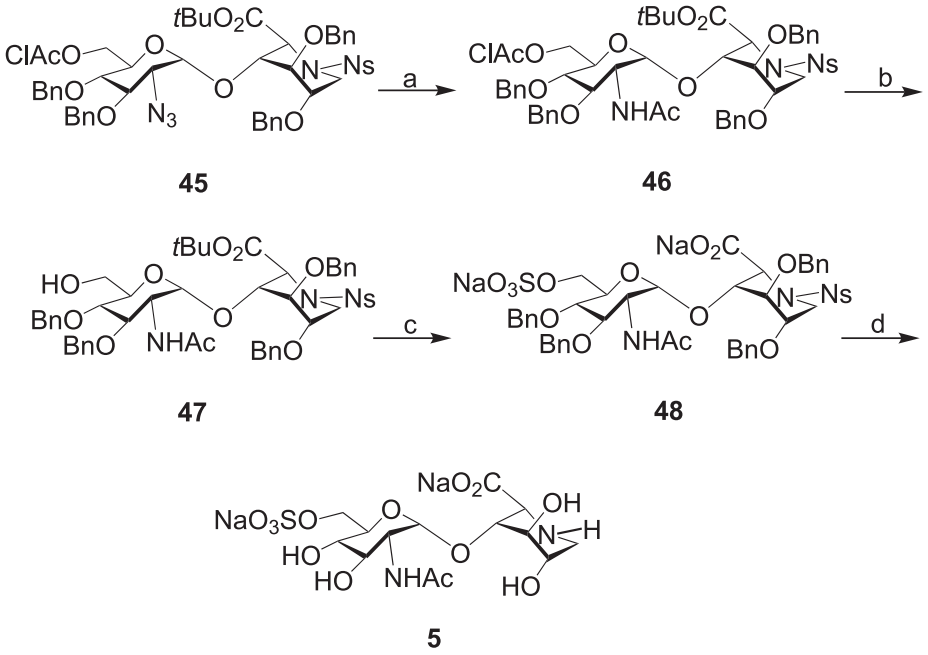
Scheme 10. Reagents and conditions: (a) $BH_3\cdot THF$, TMSOTf, CH_2Cl_2, 93%; (b) PDC, Ac_2O, *t*-BuOH, CH_2Cl_2, 54%; (c) CAN, MeCN, H_2O, 78%.



7 9b 45

Scheme 11. Reagents and conditions: (a) Me_2S_2–Tf_2O, Et_2O, CH_2Cl_2, 90%.

The fully protected disaccharide **45** was converted to the sulfated disaccharide **5** by the sequence shown in Scheme 12. This step was followed by catalytic hydrogenation which gave the target compound **5**.



45 46 47 48 5

Scheme 12. Reagents and conditions: (a) Me_3P, THF, then Ac_2O, 66%; (b) HDTC, DMF, 65%; (c) 1. TFA, CH_2Cl_2; 2. $SO_3\cdot Pyr$, DMF, 94%; (d) 1. PhSH, Et_3N, DMF, 73%; 2. H_2, Pd/C, THF, H_2O, 60%.

Selective reduction of the azido group of **45** in the presence of the nosyl group was accomplished with Me_3P,[12] then the amine was acetylated to give **46**. The primary hydroxyl group was released by HDTC, the *tert*-butyl group of **47** was hydrolyzed, and the free 6′-hydroxyl group was sulfated with $SO_3\cdot Pyr$ to give **48**. Removal of the nosyl group was accomplished with thiophenol and triethylamine without affecting the acid and base sensitive sulfate group.[12]

3. Conclusion

In summary, we have synthesized three azasugar-containing analogs of disaccharide units of heparan sulfate. We have developed synthetic routes for azasugar glycosyl acceptors having L-*ido* configuration. Glycosylation of these acceptors with a 2-azido-2-deoxy-D-glucopyranosyl thioglycoside afforded the α-(1→4)-linked

disaccharides in good yields. The protected disaccharides were transformed to the heparan sulfate analogs.

In addition, we have demonstrated that the 4-nitrobenzenesulfonyl group can be used advantageously for the protection of the ring nitrogen of azasugars.

4. Experimental

4.1. General methods

Organic solutions were dried over $MgSO_4$ and concentrated under reduced pressure at temperatures not exceeding 40 °C. Thin-layer chromatography (TLC) was performed on Silica gel 60 F_{254} plates (E Merck, Darmstadt, Germany); the compounds were detected under UV light and by spraying the plates with a 0.02 M solution of resorcinol in 20% methanolic H_2SO_4 solution followed by heating. For column chromatography, silica gel 60 (0.040–0.063 mm) (E. Merck) was employed. Melting points were determined in capillary tubes on a Griffin melting point apparatus and are uncorrected. Optical rotations were measured at room temperature with a Jasco Optical Activity AA-10R polarimeter. The IR spectra were recorded on a Thermo Nicolet Avatar 320 FT-IR spectrometer. The NMR spectra were recorded on Varian Gemini 2000 (^{1}H: 200 MHz; ^{13}C: 50 MHz), Varian Gemini 3000 (^{1}H: 300 MHz; ^{13}C: 75 MHz) and Varian Unity-Inova 4000 (^{1}H: 400 MHz; ^{13}C: 100 MHz) spectrometers at ambient temperature, unless indicated otherwise. The chemical shifts were referenced to TMS (0.00 ppm for ^{1}H) and to the central line of $CDCl_3$ (77.16 ppm for ^{13}C) for solutions in $CDCl_3$, to the central line of the solvent (3.31 ppm for ^{1}H, 49.00 ppm for ^{13}C) for solutions in CD_3OD, and to the methyl signal of acetone (2.22 ppm for ^{1}H, 30.89 ppm for ^{13}C) for solutions in D_2O, as internal standards. Mass spectrometric measurements were run on an Applied Biosystems 3200QTrap hybrid mass spectrometer in electrospray ionization mode. Elemental analyses were performed with an Elementar Vario EL III instrument at the Analytical Department of the Chemical Research Center, Hungarian Academy of Sciences.

4.2. Phenyl 4,6-*O*-(1-naphthyl)methylene-1-thio-β-D-glucopyranoside (12)

To a solution of **11** (25 g, 91.9 mmol) in dry MeCN (250 mL), 1-naphtaldehyde dimethyl acetal (27 mL, 61.2 mmol, 1.5 equiv) and *p*-toluenesulfonic acid monohydrate (0.9 g, 4.7 mmol, 0.05 equiv) were added. The mixture was stirred at room temperature for 4 h, neutralized with saturated aq $NaHCO_3$ (300 mL), and concentrated. To the residue, hexanes (200 mL) and water (200 mL) were added, and the mixture was stirred intensively. The precipitated crystalline material was filtered off and crystallized from EtOAc–1,2-dichloroethane–hexanes to afford **12** (36.7 g, 98%) as white crystals; mp 217–219 °C; $[\alpha]_D$ −19.2 (*c* 0.7, $CHCl_3$); IR ν_{max} (film): 2956, 966 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$+DMSO-d_6): δ 8.27 (m, 1H, aromatic), 7.28–7.90 (m, 11H, aromatic), 6.06 (s, 1H, ^{1}NaphCH), 5.13 and 5.00 (2d, 2×1H, *J* 4.0 Hz and *J* 4.4 Hz, 2 OH), 4.76 (d, 1H, $J_{1,2}$ 9.9 Hz, H-1), 4.42 (dd, 1H, $J_{6a,6b}$ 10.6 Hz, $J_{5,6b}$ 4.4 Hz, H-6b), 3.89 (dd, 1H, $J_{5,6a}$ 10 Hz, H-6a), 3.76 (dd, 1H, $J_{2,3}\approx J_{3,4}$ 8.8 Hz, H-3), 3.58–3.70 (m, 2H, H-4, H-5), 3.48 (ddd, 1H, H-2); ^{13}C NMR (50 MHz, $CDCl_3$+DMSO-d_6): δ 133.0, 132.3, 132.0, 131.5, 129.8, 129.0, 128.2, 127.7, 126.9, 125.5, 125.0, 124.32, 124.26, 124.0 (aromatic), 100.7 (^{1}NaphCH) 87.7 (C-1), 80.3 (C-4), 74.2 (C-3), 72.6 (C-2), 69.9 (C-5), 68.3 (C-6); MS-ESI: $[M+H]^+$ 410.8, $[M+NH_4]^+$ 427.9, $[M+Na]^+$ 432.9, $[M+K]^+$ 448.8. Anal. Calcd for $C_{23}H_{22}O_5S$: C: 67.30; H: 5.40; S: 7.81. Found: C: 67.25; H: 5.43; S: 7.83.

4.3. Phenyl 2,3-di-*O*-benzyl-4,6-*O*-1-(naphthyl)methylene-1-thio-β-D-glucopyranoside (13)

To a stirred solution of **12** (34.5 g, 84 mmol) in dry DMF (300 mL), 60% NaH suspension (6.9 g, 168 mmol, 2 equiv) was added at 0 °C. After 30 min, benzyl bromide (14 mL, 117.7 mmol, 1.4 equiv) was added dropwise. Stirring was continued for 2 h and then MeOH (20 mL) was added. After 30 min, the mixture was diluted with CH_2Cl_2 (500 mL), washed with water (2×250 mL), dried, and concentrated. The residue was crystallized from EtOAc–hexanes to afford **13** (59.8 g, 98%) as white crystals; mp 155–156 °C; $[\alpha]_D$ +2.1 (*c* 0.2, $CHCl_3$); IR ν_{max} (film): 2869, 2348, 1077 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.13 (m, 1H, aromatic), 7.83 (m, 2H, aromatic), 7.18–7.60 (m, 19H, aromatic), 6.13 (s, 1H, ^{1}NaphCH), 4.77–4.90 (m, 3H, 3×½PhCH$_2$), 4.82 (d, 1H, $J_{1,2}$ 9.9 Hz, H-1), 4.67 (d, 1H, *J* 10.4 Hz, ½PhCH$_2$), 4.49 (dd, 1H, $J_{6a,6b}$ 10.3 Hz, $J_{5,6b}$ 5.0 Hz, H-6b), 3.80–4.00 (m, 4H, H-2, H-3, H-4, H-6a), 3.59 (m, 1H, H-5); ^{13}C NMR (50 MHz, $CDCl_3$): δ 138.24, 138.18, 133.9, 133.2, 132.5, 130.7, 129.9, 129.2, 128.8, 128.5, 128.4, 128.33, 128.31, 128.0, 127.8, 126.4, 125.8, 125.2, 124.2, 123.9 (aromatic), 100.2 (^{1}NaphCH), 88.5 (C-1), 83.1, 82.1 and 80.7 (C-2, C-3, and C-4), 76.0 and 75.4 (2 PhCH$_2$) 70.4 (C-5), 69.1 (C-6); MS-ESI: $[M+H]^+$ 591.2, $[M+NH_4]^+$ 608.2, $[M+Na]^+$ 613.2, $[M+K]^+$ 629.2. Anal. Calcd for $C_{37}H_{34}O_5S$: C: 75.23; H: 5.80; S: 5.43. Found: C: 75.25; H: 5.85; S: 5.40.

4.4. 2,3-Di-*O*-benzyl-4,6-*O*-(1-naphthyl)methylene-α,β-D-glucopyranose (14)

To a solution of **13** (16.5 g, 28 mmol) in a mixture of CH_2Cl_2 (80 mL), acetone (30 mL), and water (12 mL), *N*-bromosuccinimide (19.9 g, 112 mmol, 4 equiv) was added. The mixture was stirred at 0 °C for 1 h, then 10% aq $Na_2S_2O_3$ (20 mL) was added. The mixture was diluted with CH_2Cl_2 (500 mL), and the organic layer was washed with water (2×200 mL), dried, and concentrated. The residue was purified by column chromatography (toluene–acetone, 99:1→4:1) to give syrupy **14** (12.8 g, 93%); R_f (toluene–acetone, 4:1) 0.73; $[\alpha]_D$ +18.5 (*c* 0.3, $CHCl_3$); IR ν_{max} (film): 2923, 1875, 1074 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.14 (m, 1H, aromatic), 7.84 (m, 3H, aromatic), 7.20–7.54 (m, 13H, aromatic), 6.12 and 6.11 (2s, 1H, ^{1}NaphCH), 5.22 (dd, ½H, $J_{1,2}$ 3.7 Hz, $J_{1,OH}$ 2.2 Hz, H-1 α), 4.67–4.96 (m, 4H, PhCH$_2$), 4.42 (2 dd, 1H, H-6b), 3.30–4.25 (m, 5½H, H-1 β, H-2, H-3, H-4, H-5, H-6a), 3.16 (d, 1H, OH); ^{13}C NMR (50 MHz, $CDCl_3$): δ 138.4, 133.9, 132.7, 132.5, 130.7, 129.9, 129.8, 128.74, 128.70, 128.6, 128.4, 128.3, 128.2, 128.0, 127.7, 126.5, 126.4, 125.80, 125.76, 125.2, 124.3, 124.2, 124.0, 123.9 (aromatic), 100.4 and 100.2 (^{1}NaphCH), 98.0 and 92.4 (C-1), 83.3, 82.6, 82.2, 81.0, 79.6 and 78.4 (C-2, C-3, and C-4), 75.5, 75.4, 75.2 and 74.0 (2 PhCH$_2$) 69.5 and 69.1 (C-6), 66.5 and 62.7 (C-5); MS-ESI: $[M+H]^+$ 499.2, $[M+NH_4]^+$516.2, $[M+Na]^+$ 521.2, $[M+K]^+$ 537.4. Anal. Calcd for $C_{31}H_{30}O_6$: C, 74.68; H, 6.07. Found: C, 74.03; H, 6.04.

4.5. 2,3-Di-*O*-benzyl-4,6-*O*-(1-naphthyl)methylene-D-glucitol (15)

To a solution of **14** (4.2 g, 8.6 mmol) in a mixture of THF and water (4:1, 40 mL), $NaBH_4$ (3.24 g, 85.8 mmol, 10 equiv) was added in portions. The mixture was stirred for 2 h at room temperature, and then it was treated with Amberlite IR 120 (H^+) resin (pH ca. 7), filtered, and concentrated. The residue was purified by column chromatography (toluene–acetone, 9:1→7:3) to give **15** (3.4 g, 97%) as a colorless syrup; R_f (toluene–acetone, 4:1) 0.60; $[\alpha]_D$ +21.3 (*c* 0.7, $CHCl_3$); IR ν_{max} (film): 3063, 3031, 2929, 2871, 2361, 1723, 1600, 1454, 1366, 1217, 1104, 1071, 1027 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.13 (m, 1H, aromatic), 7.79 (m, 3H, aromatic), 7.20–7.52 (m, 13H, aromatic), 5.96 (s, 1H, ^{1}NaphCH), 4.74 (d, 1H, *J* 11.7 Hz, ½PhCH$_2$), 4.65 (d, 1H, *J* 11.7 Hz, ½PhCH$_2$), 4.62 (s, 2H, PhCH$_2$), 4.32

(dd, 1H, $J_{6a,6b}$ 10.6 Hz, $J_{5,6b}$ 4.7 Hz, H-6b), 3.78–4.06 (m, 6H, H-1b, H-2, H-3, H-4, H-5, H-6a), 3.65 (dd, 1H, $J_{1a,1b} \approx J_{1a,2}$ 10 Hz, H-1a), 2.84 and 2.37 (2s, 2×1H, 2 OH); ^{13}C NMR (50 MHz, $CDCl_3$): δ 138.1, 137.7, 133.8, 132.8, 130.6, 129.7, 128.7, 128.6, 128.5, 128.1, 126.3, 125.7, 125.1, 124.3, 124.2 (aromatic), 100.3 (^{1}NaphCH), 81.7, 79.8 and 77.1 (C-2, C-3, and C-4), 74.4 and 73.3 (2 $PhCH_2$), 71.2 (C-6), 62.3 (C-5), 61.8 (C-1); MS-ESI: $[M+H]^+$ 501.2, $[M+NH_4]^+$ 518.2, $[M+Na]^+$ 523.1, $[M+K]^+$ 539.2. Anal. Calcd for $C_{31}H_{32}O_6$: C: 74.38; H: 6.44. Found: C: 74.40; H: 6.42.

4.6. 2,3-Di-*O*-benzyl-1-bromo-1-deoxy-4,6-*O*-(1-naphthyl) methylene-D-glucitol (16)

To a solution of **15** (3.4 g, 6.8 mmol) in dry pyridine (30 mL), Ph_3P (3.58 g, 13.6 mmol, 2 equiv) and CBr_4 (3.4 g, 10.2 mmol, 1.5 equiv) were added, and the mixture was stirred at 0 °C for 3 h. MeOH (10 mL) was added and the mixture was diluted with CH_2Cl_2 (250 mL) and washed with 2 M aq HCl (100 mL), saturated aq $NaHCO_3$ (100 mL), and water (100 mL). The organic layer was dried and concentrated. The residue was purified by column chromatography (toluene–acetone, 98:2→9:1) to give **16** (3.8 g, 98%) as a yellowish syrup; R_f (toluene–acetone, 9:1) 0.54; IR ν_{max} (film): 3061, 3031, 2925, 2856, 2361, 1739, 1601, 1454, 1368, 1234, 1107, 1078, 1027 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.12 (m, 1H, aromatic), 7.78 (m, 3H, aromatic), 7.10–7.52 (m, 13H, aromatic), 5.94 (s, 1H, ^{1}NaphCH), 4.73 (d, 1H, *J* 11.4 Hz, ½$PhCH_2$), 4.67 (d, 1H, *J* 11.7 Hz, ½$PhCH_2$), 4.63 (d, 1H, *J* 11.4 Hz, ½$PhCH_2$), 4.59 (d, 1H, *J* 11.7 Hz, ½$PhCH_2$), 4.29 (dd, 1H, $J_{6a,6b}$ 10.3 Hz, $J_{5,6b}$ 4.7 Hz, H-6b), 3.86–4.08 (m, 5H, H-2, H-3, H-4, H-5, H-6a), 3.72 (dd, 1H, $J_{1a,1b}$ 11 Hz, $J_{1b,2}$ 3.6 Hz, H-1b), 3.57 (dd, 1H, $J_{1a,2}$ 7 Hz, H-1a), 2.41 (d, 1H, $J_{5,OH}$ 4 Hz, OH); ^{13}C NMR (50 MHz, $CDCl_3$): δ 137.9, 137.5, 133.8, 132.8, 130.6, 129.7, 129.1, 128.64, 128.61, 128.29, 128.25, 128.21, 126.3, 125.7, 125.4, 125.1, 124.2 (aromatic), 100.2 (^{1}NaphCH), 81.3, 79.6 and 77.3 (C-2, C-3, and C-4), 74.4 and 74.0 (2 $PhCH_2$), 71.1 (C-6), 62.1 (C-5), 32.8 (C-1). Anal. Calcd for $C_{31}H_{31}BrO_5$: C, 66.08; H, 5.55. Found: C, 66.05; H, 5.60.

4.7. 5-*O*-Acetyl-2,3-di-*O*-benzyl-1-bromo-1-deoxy-4,6-*O*-(1-naphthyl)methylene-D-glucitol (17)

To a solution of **16** (3.8 g, 6.8 mmol) in dry pyridine (30 mL), acetic anhydride (6.4 mL, 67.8 mmol, 10 equiv) was added at 0 °C. The mixture was stirred at room temperature overnight, then was quenched with water (10 mL). The mixture was diluted with CH_2Cl_2 (400 mL), washed with 2 M aq HCl (200 mL), saturated aq $NaHCO_3$ (200 mL), and water (200 mL). The organic layer was dried and concentrated. The residue was purified by column chromatography (toluene–acetone, 9:1) to give **17** (4 g, 98%) as a yellowish syrup; R_f (toluene–acetone, 9:1) 0.73; $[\alpha]_D$ +2.6 (*c* 0.4, $CHCl_3$); IR ν_{max} (film): 3030, 2924, 2856, 2361, 1739, 1600, 1454, 1368, 1234, 1107, 1077, 1028 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.14 (m, 1H, aromatic), 7.76 (m, 3H, aromatic), 7.10–7.52 (m, 13H, aromatic), 5.99 (s, 1H, ^{1}NaphCH), 5.22 (ddd, 1H, $J_{4,5} \approx J_{5,6a}$ 9.9 Hz, $J_{5,6b}$ 5.5 Hz, H-5), 4.73 (d, 1H, *J* 11.4 Hz, ½$PhCH_2$), 4.66 (d, 1H, *J* 11.7 Hz, ½$PhCH_2$), 4.57 (d, 1H, *J* 11.7 Hz, ½$PhCH_2$), 4.54 (dd, 1H, $J_{6a,6b}$ 10.6 Hz, H-6b), 4.44 (d, 1H, *J* 11.4 Hz, ½$PhCH_2$), 4.21 (dd, 1H, $J_{3,4}$ 2.0 Hz, H-4), 4.03 (ddd, 1H, $J_{1a,2} \approx J_{1b,2}$ 6.6 Hz, $J_{2,3}$ 2.2 Hz, H-2), 3.62–3.74 (m, 3H, H-1b, H-3, H-6a), 3.55 (dd, 1H, $J_{1a,1b}$ 11.4 Hz, H-1a), 1.92 (s, 3H, OC(O)CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 170.1 (OC(O)CH_3), 138.7, 138.3, 134.5, 133.1, 131.1, 130.5, 129.7, 129.3, 129.2, 129.0, 128.9, 128.8, 128.6, 127.0, 126.4, 126.0, 125.7, 125.2, 124.9 (aromatic), 101.4 (^{1}NaphCH), 79.8, 78.44 and 78.36 (C-2, C-3, and C-4), 74.55 and 74.48 (2 $PhCH_2$), 68.9 (C-6), 63.5 (C-5), 34.6 (C-1), 21.5 (OC(O)CH_3). Anal. Calcd for $C_{33}H_{33}BrO_6$: C, 65.46; H, 5.49. Found: C, 65.45; H, 5.50.

4.8. 5-*O*-Acetyl-1-azido-2,3-di-*O*-benzyl-1-deoxy-4,6-*O*-(1-naphthyl)methylene-D-glucitol (18)

To a solution of **17** (4 g, 6.6 mmol) in a mixture of DMF and water (8:1, 40 mL) NaN_3 (0.6 g, 9.9 mmol, 1.5 equiv) and NH_4Cl (1 g, 19.8 mmol, 3 equiv) were added, and the reaction mixture was heated to reflux for 2 days. The mixture was evaporated, the residue was dissolved in CH_2Cl_2 (400 mL), and washed with water (4×150 mL). The organic layer was dried, the solvent was evaporated, and the residue was purified by column chromatography (hexanes–EtOAc, 9:1→4:1) to give **18** (2.9 g, 79%) as a colorless syrup; R_f (hexanes–EtOAc, 4:1) 0.66; $[\alpha]_D$ +1.4 (*c* 0.7, $CHCl_3$); IR ν_{max} (film): 2923, 2855, 2361, 2099, 1741, 1600, 1454, 1369, 1233, 1107, 1077, 1050, 1027 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.14 (m, 1H, aromatic), 7.85 (m, 2H, aromatic), 7.75 (m, 1H, aromatic), 7.22–7.52 (m, 13H, aromatic), 6.02 (s, 1H, ^{1}NaphCH), 5.21 (ddd, 1H, $J_{4,5} \approx J_{5,6a}$ 9.9 Hz, $J_{5,6b}$ 5.4 Hz, H-5), 4.72 (d, 1H, *J* 11.5 Hz, ½$PhCH_2$), 4.64 (d, 1H, *J* 11.4 Hz, ½$PhCH_2$), 4.58 (d, 1H, *J* 11.5 Hz, ½$PhCH_2$), 4.57 (dd, 1H, $J_{6a,6b}$ 10.4 Hz, H-6b), 4.45 (d, 1H, *J* 11.4 Hz, ½$PhCH_2$), 4.20 (dd, 1H, $J_{3,4}$ 9.9 Hz, $J_{2,3}$ 1.7 Hz, H-4), 3.91 (m, 1H, H-2), 3.65–3.75 (m, 2H, H-3, H-6a), 3.45 (d, 2H, $J_{1,2}$ 4.4 Hz, H-1a, H-1b), 1.96 (s, 3H, OC(O)CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.4 (OC(O)CH_3), 137.9, 137.5, 133.7, 132.4, 130.4, 129.8, 129.0, 128.6, 128.5, 128.4, 128.2, 128.1, 128.0, 127.8, 126.3, 125.7, 125.3, 125.0, 124.4, 124.3, 124.1 (aromatic), 100.5 (^{1}NaphCH), 78.5 (C-2), 77.6 (C-4), 74.1 (C-3), 73.6 and 73.5 (2 $PhCH_2$), 68.2 (C-6), 62.7 (C-5), 52.0 (C-1), 20.8 (OC(O)CH_3); MS-ESI: $[M+H]^+$ 568.3, $[M+NH_4]^+$ 585.2, $[M+Na]^+$ 590.2, $[M+K]^+$ 606.3. Anal. Calcd for $C_{33}H_{33}N_3O_6$: C, 69.83; H, 5.86. Found: C, 69.80; H, 5.89.

4.9. 1-Azido-2,3-di-*O*-benzyl-1-deoxy-4,6-*O*-(1-naphthyl) methylene-D-glucitol (19)

To a solution of **18** (2.9 g, 5.2 mmol) in dry MeOH (30 mL), a catalytic amount of NaOMe was added. The mixture was stirred overnight at room temperature, neutralized with Amberlite IR 120 (H^+) resin (pH ca. 7), filtered, and concentrated to give **19** (2.7 g, 98%) as a colorless syrup; R_f (toluene–acetone, 9:1) 0.38; $[\alpha]_D$ +24.7 (*c* 0.4, $CHCl_3$); IR ν_{max} (film): 2925, 2855, 2362, 2099, 1740, 1601, 1454, 1370, 1233, 1107, 1078, 1028 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.10 (m, 1H, aromatic), 7.80 (m, 3H, aromatic), 7.12–7.52 (m, 13H, aromatic), 5.95 (s, 1H, ^{1}NaphCH), 4.70 (d, 1H, *J* 11.4 Hz, ½$PhCH_2$), 4.67 (d, 1H, *J* 11.7 Hz, ½$PhCH_2$), 4.65 (d, 1H, *J* 11.4 Hz, ½$PhCH_2$), 4.56 (d, 1H, *J* 11.7 Hz, ½$PhCH_2$), 4.30 (dd, 1H, $J_{6a,6b}$ 10.3 Hz, $J_{5,6b}$ 4.7 Hz, H-6b), 3.80–3.94 (m, 4H, H-2, H-3, H-4, H-5), 3.63 (dd, 1H, $J_{5,6a} \approx J_{6a,6b}$ 10.3 Hz, H-6a), 3.50 (d, 2H, $J_{1,2}$ 4.7 Hz, H-1a, H-1b), 2.36 (d, 1H, $J_{5,OH}$ 4.0 Hz, OH); ^{13}C NMR (50 MHz, $CDCl_3$): δ 137.8, 137.4, 133.8, 132.7, 130.6, 129.7, 129.1, 128.7, 128.3, 126.3, 125.7, 125.4, 125.1, 124.2 (aromatic), 100.1 (^{1}NaphCH), 81.5, 79.0 and 76.0 (C-2, C-3, and C-4), 74.3 and 73.7 (2 $PhCH_2$), 71.0 (C-6), 62.0 (C-5), 51.8 (C-1); MS-ESI: $[M+H]^+$ 526.0, $[M+NH_4]^+$ 543.1, $[M+Na]^+$ 548.2, $[M+K]^+$ 563.9. Anal. Calcd for $C_{31}H_{31}N_3O_5$: C, 70.84; H, 5.94. Found: C, 70.88; H, 5.90.

4.10. 1-Amino-2,3-di-*O*-benzyl-1-deoxy-4,6-*O*-(1-naphthyl) methylene-D-glucitol (20)

To a solution of **19** (2.7 g, 5.1 mmol) in a mixture of pyridine and water (9:1, 30 mL) 1,3-propanedithiol (10.3 mL, 102.2 mmol, 20 equiv) and 40 drops of Et_3N (pH ca. 8) were added and the mixture was stirred at room temperature for 3 days. It was then evaporated and co-evaporated with toluene three times. The product was purified by column chromatography (CH_2Cl_2–MeOH, 95:5→4:1) to give **20** (2.4 g, 96%), as white crystals; mp 128–130 °C (from EtOAc–hexanes); R_f (CH_2Cl_2–MeOH, 9:1) 0.33; $[\alpha]_D$ +30.4 (*c* 0.5, $CHCl_3$); IR ν_{max} (film): 3604, 3307, 1642 cm^{-1}; ^{1}H NMR

(200 MHz, $CDCl_3$): δ 8.16 (m, 1H, aromatic), 7.79 (m, 3H, aromatic), 7.18–7.52 (m, 13H, aromatic), 5.98 (s, 1H, ^{1}NaphCH), 4.75 (d, 1H, *J* 11.7 Hz, ½PhCH$_2$), 4.68 (d, 1H, *J* 11.7 Hz, ½PhCH$_2$), 4.66 (d, 1H, *J* 11.4 Hz, ½PhCH$_2$), 4.52 (d, 1H, *J* 11.4 Hz, ½PhCH$_2$), 4.34 (dd, 1H, $J_{5,6b}$ 4.6 Hz, $J_{6a,6b}$ 10.6 Hz, H-6b), 3.86–4.08 and 3.62–3.84 (2 m, 3H and 2H, H-2, H-3, H-4, H-5, H-6a), 3.01 (dd, 1H, $J_{1a,1b}$ 13.4 Hz, $J_{1b,2}$ 3.6 Hz, H-1b), 2.91 (dd, 1H, $J_{1a,2}$ 6.3 Hz, H-1a), 2.82 (br s, 3H, NH_2 and OH); ^{13}C NMR (50 MHz, $CDCl_3$): δ 138.3, 137.9, 133.9 133.0, 130.6, 129.7, 128.8, 128.7, 128.6, 128.4, 128.2, 128.0, 126.2, 125.7, 125.1, 124.4 (aromatic), 100.4 (^{1}NaphCH), 81.9, 80.6 and 77.2 (C-2, C-3, and C-4), 74.6 and 73.5 (2 PhCH$_2$), 71.4 (C-6), 62.2 (C-5), 41.8 (C-1); MS-ESI: $[M+H]^+$ 500.0. Anal. Calcd for $C_{31}H_{33}NO_5$: C, 74.53; H, 6.66. Found: C, 74.55; H, 6.64.

4.11. 2,3-Di-*O*-benzyl-1-deoxy-4,6-*O*-(1-naphthyl)methylene-1-(4-nitro)benzene-sulfonamido-D-glucitol (21)

Et_3N (2.05 mL, 14.7 mmol, 3 equiv) and 4-nitrobenzenesulfonyl chloride (1.35 g, 6.12 mmol, 1.25 equiv) were added to a solution of **20** (2.4 g, 4.9 mmol) in dry CH_2Cl_2 (25 mL) and the mixture was stirred at 0 °C under argon for 10 min. Then, water (40 mL) was added and the mixture was diluted with CH_2Cl_2 (350 mL) and washed with 2 M aq HCl (150 mL), saturated aq $NaHCO_3$ (150 mL), and water (150 mL). The organic layer was dried and concentrated. The residue was purified by column chromatography (toluene–acetone, 95:5→4:1) to give syrupy **21** (3.3 g, 98%); R_f (toluene–acetone, 9:1) 0.25; $[\alpha]_D$ +3.9 (*c* 0.31, $CHCl_3$); IR ν_{max} (film): 2924, 2854, 2283, 1529, 1496, 1348, 1310, 1164, 1103, 1070, 1026, 1013 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.14 (m, 1H, aromatic), 7.78–7.88 (m, 4H, aromatic), 7.64 (m, 1H, aromatic), 7.10–8.18 (m, 15H, aromatic), 5.88 (s, 1H, ^{1}NaphCH), 5.12 (dd, 1H, $J_{NH,H\text{-}1a} \approx J_{NH,H\text{-}1b}$ 6.2 Hz, NH), 4.68 (d, 1H, *J* 11.4 Hz, ½PhCH$_2$), 4.60 (d, 1H, *J* 11.4 Hz, ½PhCH$_2$), 4.54 (d, 1H, *J* 11.6 Hz, ½PhCH$_2$), 4.50 (d, 1H, *J* 11.6 Hz, ½PhCH$_2$), 4.29 (dd, 1H, $J_{5,6b}$ 4.7 Hz, $J_{6a,6b}$ 11.0 Hz, H-6b), 3.80–4.00 and 3.59 (m and t, 5H, H-2, H-3, H-4, H-5, H-6a), 3.29 (ddd, 1H, $J_{1a,1b}$ 12.1 Hz, $J_{1b,2}$ 4.8 Hz, H-1b), 3.10 (ddd, 1H, $J_{1a,2}$ 5.8 Hz, H-1a), 2.07 (s, 1H, OH); ^{13}C NMR (50 MHz, $CDCl_3$): δ 149.6, 145.3, 137.6, 137.4, 133.8, 132.5, 130.4, 129.9, 129.1, 128.8, 128.7, 128.6, 128.44, 128.36, 128.3, 128.1, 127.8, 126.4, 125.9, 125.4, 125.1, 124.7, 124.3, 124.1 (aromatic), 100.8 (^{1}NaphCH), 80.6, 76.7 and 75.3 (C-2, C-3, and C-4), 73.9 and 73.2 (2 PhCH$_2$), 71.3 (C-6), 61.5 (C-5), 43.6 (C-1); MS-ESI: $[M+H]^+$ 685.0, $[M+NH_4]^+$ 702.0, $[M+Na]^+$ 707.2, $[M+K]^+$ 723.0. Anal. Calcd for $C_{37}H_{36}N_2O_9S$: C, 64.90; H, 5.30; N, 4.09; S, 4.68. Found: C, 64.85; H, 5.32; N, 4.11; S, 4.70.

4.12. 2,3-Di-*O*-benzyl-1,5-dideoxy-4,6-*O*-(1-naphthyl) methylene-1,5-imino-*N*-(4-nitro)benzenesulfonyl-L-iditol (10b)

A mixture of **21** (3.3 g, 4.8 mmol), DEAD (1.51 mL, 9.6 mmol, 2 equiv), and Ph_3P (3.77 g, 14.4 mmol, 3 equiv) in dry CH_2Cl_2 (40 mL) was stirred at room temperature under argon for 5 min. The mixture was diluted with EtOAc (400 mL) and it was washed with saturated aq $NaHCO_3$ (2×150 mL), and water (200 mL). The organic layer was dried and concentrated. The residue was purified by column chromatography (hexanes–EtOAc, 9:1→7:3) to give **10b** (3.1 g, 96%) as white crystals; mp 150–151 °C (from EtOAc–hexanes); R_f (hexanes–EtOAc, 4:1) 0.35; $[\alpha]_D$ +6.2 (*c* 0.64, $CHCl_3$); IR ν_{max} (film): 2955, 2925, 2869, 2283, 1529, 1455, 1348, 1162, 1088 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.00–8.06 (m, 21H, aromatic), 6.14 (s, 1H, ^{1}NaphCH), 4.79 (dd, 1H, $J_{5,6b}$ 1.5 Hz, $J_{6a,6b}$ 12.5 Hz, H-6b), 4.52 (m, 1H, $J_{3,4} \approx J_{4,5}$ 3.0 Hz, $J_{2,4}$ 0.8 Hz, H-4), 4.50 (d, 1H, *J* 12.0 Hz, ½PhCH$_2$), 4.46 (d, 1H, *J* 12.0 Hz, ½PhCH$_2$), 4.37 (d, 1H, *J* 11.7 Hz, ½PhCH$_2$), 4.24 (dd, 1H, $J_{5,6a}$ 1.5 Hz, H-6a), 4.18 (d, 1H, *J* 11.7 Hz, ½PhCH$_2$), 3.98 (dd, 1H, $J_{1a,1b}$ 14.0 Hz, $J_{1b,2}$ 6.7 Hz, H-1b), 3.91 (dd, 1H, $J_{1a,2}$ 10.4 Hz, H-1a), 3.79 (ddd, 1H, H-5), 3.74 (dd, 1H, $J_{2,3}$ 2.0 Hz, H-3), 3.30 (ddd, 1H, H-2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.7, 146.0, 137.5, 137.0, 133.7, 132.6, 130.4, 129.9, 128.8, 128.60, 128.58, 128.3, 128.2, 127.9, 127.5, 126.3, 125.7, 125.1, 124.0, 123.3 (aromatic), 99.5 (^{1}NaphCH), 78.5 (C-3), 74.9 (C-4), 74.0 (C-2), 72.0 (C-6), 71.9 and 70.8 (2 PhCH$_2$), 47.8 (C-5), 44.1 (C-1); MS-ESI: $[M+Na]^+$ 689.7. Anal. Calcd for $C_{37}H_{34}N_2O_8S$: C, 66.65; H, 5.14; N, 4.20; S, 4.81. Found: C, 66.67; H, 5.17; N, 4.18; S, 4.85.

4.13. 2,3-Di-*O*-benzyl-1,5-dideoxy-4,6-*O*-(1-naphthyl) methylene-1,5-imino-L-iditol (22)

To a stirred solution of **10b** (3 g, 4.5 mmol) in dry DMF (30 mL), PhSH (0.55 mL, 5.4 mmol, 1.2 equiv) and dry K_2CO_3 (1.9 g, 13.5 mmol, 3 equiv) were added and the mixture was stirred at room temperature for 5 days. It was diluted with CH_2Cl_2 (400 mL) and was washed with water (3×150 mL). The organic layer was dried, the solvent was evaporated, and the residue was purified by column chromatography (CH_2Cl_2–MeOH, 98:2→95:5) to give **22** (2.1 g, 98%) as a pale yellow syrup; R_f (CH_2Cl_2–MeOH, 95:5) 0.25; $[\alpha]_D$ −17.7 (*c* 0.2, $CHCl_3$); IR ν_{max} (film): 2924, 2363, 1879, 1123, 1075 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.18 (m, 1H, aromatic), 7.78 (m, 3H, aromatic), 7.20–7.48 (m, 13H, aromatic), 6.06 (s, 1H, ^{1}NaphCH), 4.67 (d, 1H, *J* 11.7 Hz, ½PhCH$_2$), 4.60 (d, 2H, *J* 13.5 Hz, PhCH$_2$), 4.48 (d, 1H, *J* 11.7 Hz, ½PhCH$_2$), 4.23 (m, 2H), 4.15 (m, 1H), 3.92 (m, 1H), 3.41 (m, 1H), 3.21 (m, 2H) and 2.91 (m, 1H) skeleton protons, 2.77 (br s, 1H, NH); ^{13}C NMR (50 MHz, $CDCl_3$): δ 138.4, 138.0, 134.1, 133.8, 133.5, 130.5, 129.8, 129.5, 128.6, 128.5, 128.3, 128.0, 127.70, 127.66, 127.5, 126.3, 125.6, 125.2, 124.9, 123.9 (aromatic), 100.4 (^{1}NaphCH), 73.9, 73.6 and 72.6 (C-2, C-3, and C-4), 72.3 (C-6), 71.6 and 70.9 (2 PhCH$_2$), 48.9 (C-5), 45.9 (C-1); MS-ESI: $[M+H]^+$ 481.9, $[M+Na]^+$ 504.2. Anal. Calcd for $C_{31}H_{31}NO_4$: C, 77.31; H, 6.49; N, 2.91. Found: C, 77.31; H, 6.51; N, 2.93.

4.14. 2,3-Di-*O*-benzyl-*N*-benzyloxycarbonyl-1,5-dideoxy-1,5-imino-4,6-*O*-(1-naphthyl)methylene-L-iditol (10a)

To a solution of **22** (2.1 g, 4.4 mmol) in dry MeOH (20 mL), benzyl chloroformate (0.74 mL, 5.3 mmol, 1.2 equiv) and $NaHCO_3$ (0.44 g, 5.3 mmol, 1.2 equiv) were added. The mixture was stirred at room temperature for 10 min. Saturated aq $NaHCO_3$ (10 mL) was added, and the mixture was diluted with CH_2Cl_2 (300 mL), washed with 2 M aq HCl (100 mL), saturated aq $NaHCO_3$ (100 mL), and water (100 mL), dried, and concentrated. The residue was purified by column chromatography (hexanes–EtOAc, 95:5→4:1) to give **10a** (2.6 g, 97%) as a colorless syrup; R_f (hexanes–EtOAc, 4:1) 0.36; $[\alpha]_D$ +46.6 (*c* 1.5, $CHCl_3$); IR ν_{max} (film): 2925, 1882, 1701, 1454, 1418, 1347, 1138, 1104, 1074, 1026 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.02 (m, 1H, aromatic), 7.83 (m, 3H, aromatic), 7.20–7.58 (m, 18H, aromatic), 6.12 (s, 1H, ^{1}NaphCH), 5.04–5.24 (m, 2H, C(O)OCH$_2$Ph), 4.32–4.78 (m, 7H, 2 PhCH$_2$ and 3 skeleton protons), 3.60–3.90 (m, 5H, skeleton protons); ^{13}C NMR (50 MHz, $CDCl_3$): δ 155.7 (*C*(O)OCH$_2$Ph) 138.1, 137.8, 136.6, 134.2, 133.8, 133.1, 130.5, 129.7, 128.7, 128.63, 128.58, 128.5, 128.2, 128.01, 128.00, 127.8, 126.4, 125.7, 125.3, 124.1, 123.5 (aromatic), 99.3 (^{1}NaphCH), 80.1, 77.2 and 75.0 (C-2, C-3, and C-4), 71.8 and 71.2 (2 PhCH$_2$), 68.3 (C-6), 67.5 (PhCH$_2$), 46.7 (C-5), 42.1 (C-1); MS-ESI: $[M+H]^+$ 616.0, $[M+NH_4]^+$ 633.0, $[M+Na]^+$ 638.0, $[M+K]^+$ 654.0. Anal. Calcd for $C_{39}H_{37}NO_6$: C, 76.08; H, 6.06; N, 2.27. Found: C, 76.06; H, 6.08; N, 2.28.

4.15. 2,3-Di-*O*-benzyl-4,6-*O*-(1-naphthyl)methylene-D-gluconic amide (24)

A mixture of **14** (0.7 g, 1.4 mmol) and freshly prepared Dess–Martin periodinane[23] (0.65 g, 1.54 mmol, 1.1 equiv) in dry CH_2Cl_2 (10 mL) was stirred at room temperature for 4 h. To the mixture were added saturated aq $NaHCO_3$ (5 mL) and 10% aq $Na_2S_2O_3$ (35 mL), and it was stirred for 30 min. The reaction

mixture was diluted with CH_2Cl_2 (250 mL) and washed with water (2×100 mL). The organic layer was dried and evaporated to give crude **23** (0.63 g, 90%) as a syrup. The crude **23** (0.63 g, 1.3 mmol) was stirred in saturated methanolic ammonia (10 mL) at room temperature for 10 min. The mixture was evaporated and it was purified by column chromatography (CH_2Cl_2–MeOH, 98:2→95:5) to give **24** (0.42 g, 65%) as white crystals; mp 143–144 °C (from EtOAc–hexanes); R_f (CH_2Cl_2–MeOH, 95:5) 0.30; $[\alpha]_D$ +12.4 (*c* 0.7, $CHCl_3$); IR ν_{max} (film): 3448, 1636 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 8.20 (m, 1H, aromatic), 7.72–7.88 (m, 3H, aromatic), 7.24–7.52 (m, 13H, aromatic), 6.68 (d, 1H *J* 3.3 Hz, ½NH_2), 6.04 (m, 2H, ½NH_2 and ^{1}NaphCH), 4.68 (s, 2H, $PhCH_2$), 4.67 (d, 1H, *J* 11.0 Hz, ½$PhCH_2$), 4.57 (d, 1H, *J* 11.0 Hz, ½$PhCH_2$), 4.10–4.40 (m, 4H, H-2, H-3, H-4, H-5), 4.06 (dd, 1H, $J_{6a,6b}$ 10.3 Hz, $J_{5,6a}$ 4.8 Hz, H-6b), 3.68 (t, 1H, $J_{5,6a}$ 9.8 Hz, H-6a), 2.67 (s, 1H, OH); ^{13}C NMR (50 MHz, $CDCl_3$): δ 174.1 (C-1), 137.6, 136.9, 133.9, 132.9, 130.7, 129.8, 128.8, 128.6, 128.4, 128.3, 126.3, 125.7, 125.1, 124.4, 124.3 (aromatic), 100.5 (^{1}NaphCH), 80.7, 79.6 and 79.2 (C-2, C-3, and C-4), 75.2 and 74.1 (2 $PhCH_2$), 71.3 (C-6), 63.1 (C-5); MS-ESI: $[M+H]^+$ 514, $[M+Na]^+$ 536. Anal. Calcd for $C_{31}H_{31}NO_6$: C, 72.50; H, 6.08; N, 2.73. Found: C, 72.45; H, 6.12; N, 2.70.

4.16. 1-Amino-2,3-di-*O*-benzyl-1-deoxy-4,6-*O*-(1-naphthyl) methylene-D-glucitol (20)

To a solution of **24** (0.42 g, 0.8 mmol) in THF (5 mL), $LiAlH_4$ (0.16 g, 4.1 mmol, 5 equiv) was added. The mixture was heated to reflux and stirred for 7 h. To the reaction mixture was added EtOAc (20 mL) and it was stirred for 10 min, then it was treated with cold water (20 mL) and saturated aq $NaHCO_3$ (50 mL). The mixture was filtered, the filtrate was diluted with CH_2Cl_2 (200 mL) and the organic layer was washed with brine (50 mL) and water (50 mL), it was dried and concentrated. The residue was purified by column chromatography (CH_2Cl_2–MeOH, 98:2→4:1) to give **20** (0.3 g, 70%) as white crystals; mp 128–130 °C (from EtOAc–hexanes). The ^1H and ^{13}C NMR spectra were identical with those described in Section 4.10.

4.17. 2,3-Di-*O*-benzyl-*N*-benzyloxycarbonyl-1,5-dideoxy-1,5-imino-6-*O*-(1-naphthyl)methyl-L-iditol (8)

To a mixture of **10a** (1.0 g, 1.6 mmol), $NaBH_3CN$ (1.02 g, 16 mmol, 10 equiv) and 3 Å molecular sieves (1 g) in dry THF (10 mL), an ethereal solution of HCl was added until the pH reached ca. 3. The mixture was stirred at 0 °C under argon for 30 min, then it was filtered, diluted with CH_2Cl_2 (200 mL), and was washed with saturated aq $NaHCO_3$ (2×75 mL) and water (100 mL). The organic layer was dried and was concentrated. The residue was purified by column chromatography (toluene–acetone, 98:2→9:1) to give syrupy **8** (0.67 g, 67%); R_f (toluene–acetone, 9:1) 0.40; $[\alpha]_D$ −6.6 (*c* 0.3, $CHCl_3$); IR ν_{max} (film): 3455, 1636 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.10–7.20 (m, 22H, aromatic), 5.08 (s, 2H, $C(O)OCH_2Ph$), 4.98 (d, 1H, *J* 12.0 Hz, ½$PhCH_2$), 4.90 (d, 1H, *J* 12.0 Hz, ½$PhCH_2$), 4.87 (d, 1H, *J* 12.1 Hz, ½^{1}NaphCH$_2$), 4.66 (ddd, 1H, $J_{5,6a}$ 4.4 Hz, $J_{5,6b}$ 6.5 Hz, $J_{4,5}$ 6.0 Hz, H-5), 4.61 (d, 1H, *J* 11.4 Hz, ½$PhCH_2$), 4.58 (d, 1H, *J* 12.1 Hz, ½^{1}NaphCH$_2$), 4.57 (d, 1H, *J* 11.4 Hz, ½$PhCH_2$), 4.28 (dd, 1H, $J_{1a,1b}$ 13.2 Hz, $J_{1b,2}$ 5.7 Hz, H-1b), 3.86 (dd, 1H, $J_{6a,6b}$ 10.2 Hz, H-6b), 3.82 (dd, 1H, H-6a), 3.69 (dd, 1H, $J_{3,4}$ 9.3 Hz, $J_{4,OH}$ 2.7 Hz, H-4), 3.65 (dd, 1H, $J_{2,3}$ 7.5 Hz, H-3), 3.44 (m, 1H, H-2), 2.98 (dd, 1H, $J_{1a,2}$ 10.6 Hz, H-1a), 2.40 (s, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.7 (*C*(O) OCH_2Ph) 138.6, 138.0, 136.5, 133.8, 133.5, 131.6, 128.5, 127.9, 126.3, 125.8, 125.2, 123.9 (aromatic), 82.5 (C-3), 78.5 (C-2), 75.1 (^{1}NaphCH$_2$), 72.4 and 71.7 (2 $PhCH_2$), 70.6 (C-4), 67.6 ($C(O)OCH_2Ph$), 66.4 (C-6), 53.9 (C-5), 42.6 (C-1); MS-ESI: $[M+H]^+$ 618.1, $[M+Na]^+$ 640.1, $[M+K]^+$ 656.1. Anal. Calcd for $C_{39}H_{39}NO_6$: C, 75.83; H, 6.36; N, 2.27. Found: C, 75.80; H, 6.35; N, 2.29.

4.18. 2,3-Di-*O*-benzyl-*N*-benzyloxycarbonyl-1,5-dideoxy-1,5-imino-4-*O*-(1-naphthyl)methyl-L-iditol (25)

1 M BH_3·THF (8.6 mL, 8.6 mmol, 3 equiv) and TMSOTf (0.062 mL, 0.343 mmol, 0.12 equiv) were added to a solution of **10a** (1.76 g, 2.86 mmol) in dry CH_2Cl_2 (20 mL) and the mixture was stirred at room temperature under argon for 7 h. The mixture was cooled and it was treated with Et_3N (5 mL) and MeOH (5 mL), then it was evaporated and co-evaporated with MeOH (20 mL) three times. The residue was purified by column chromatography (toluene–acetone, 98:2→9:1) to yield **25** (1.6 g, 91%) as a colorless syrup; R_f (toluene–acetone, 9:1) 0.25; $[\alpha]_D$ +1.2 (*c* 0.83, $CHCl_3$); IR ν_{max} (film): 3419, 1636 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 8.04–7.10 (m, 22H, aromatic), 5.10 (m, 5H, $C(O)OCH_2Ph$, 3×½$PhCH_2$), 4.10–4.92 (m, 5H, H-5, H-1b, ½$PhCH_2$, $^1NaphCH_2$), 3.60–4.06 (m, 4H, H-3, H-4, H-6a, H-6b), 3.46 (br s, 1H, H-2), 2.92 (m, 1H, H-1a), 2.41 (br s, 1H, OH); ^{13}C NMR (50 MHz, $CDCl_3$): δ 156.1 and 155.8 ($C(O)OCH_2Ph$) 138.8, 138.0, 136.4, 133.7, 133.3, 131.6, 128.9, 128.6, 128.4, 128.3, 128.1, 127.8, 127.7, 127.5, 126.7, 126.4, 125.9, 125.2, 123.8 (aromatic), 82.1, 79.2 and 78.1 (C-2, C-3, and C-4), 75.4 ($^1NaphCH_2$), 72.9, 71.8 and 71.6 (2 $PhCH_2$), 67.7 ($C(O)OCH_2Ph$), 59.1 (C-6), 54.3 and 54.7 (C-5), 41.9 and 41.6 (C-1); MS-ESI: $[M+H]^+$ 618.1, $[M+Na]^+$ 640.1, $[M+K]^+$ 656.1. Anal. Calcd for $C_{39}H_{39}NO_6$: C, 75.83; H, 6.36; N, 2.27. Found: C, 75.81; H, 6.37; N, 2.32.

4.19. *tert*-Butyl [2,3-di-*O*-benzyl-*N*-benzyloxycarbonyl-1,5-dideoxy-1,5-imino-4-*O*-(1-naphthyl)methyl-L-iditol] uronate (26)

Pyridinium dichromate (1.95 g, 5.18 mmol, 2 equiv), acetic anhydride (2.47 mL, 26 mmol, 10 equiv), and *tert*-butyl alcohol (4.87 mL, 51.8 mmol, 20 equiv) were added to a stirred solution of **25** (1.6 g, 2.6 mmol) in dry CH_2Cl_2 (20 mL). The mixture was stirred for 8 h at room temperature and was then applied on the top of a silica gel column in EtOAc, with a 5 cm layer of EtOAc on top of the gel. The chromium compounds were allowed to precipitate in the presence of EtOAc, and after 30 min the product was eluted with EtOAc. The crude product was purified by column chromatography (hexanes–EtOAc, 95:5→4:1) to give **26** (1.21 g, 68%) as a colorless syrup; R_f (hexanes–EtOAc, 4:1) 0.66; $[\alpha]_D$ −10.3 (*c* 0.58, $CHCl_3$); IR ν_{max} (film): 1753, 1720, 1636 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 8.10–7.10 (m, 22H, aromatic), 5.00–5.40 (m, 4H, 2 $PhCH_2$), 4.55–4.95 (m, 4H, H-5, ½$PhCH_2$, $^1NaphCH_2$), 4.40 (dd, 1H, $J_{1a,1b}$ 13.0 Hz, $J_{1b,2}$ 4.5 Hz, H-1b), 3.90–4.25 (m, 2H, H-3, H-4), 3.25–3.55 (m, 2H, H-2, H-1a), 1.32 (s, 9H, $C(CH_3)_3$); ^{13}C NMR (50 MHz, $CDCl_3$): δ 168.9 and 168.5 (C-6), 155.6 and 155.3 ($C(O)OCH_2Ph$), 138.8, 138.4, 136.4, 133.7, 133.5, 131.6, 128.7, 128.62, 128.56, 128.5, 128.3, 128.2, 128.1, 128.0, 127.8, 127.5, 126.3, 125.8, 125.2, 124.1 (aromatic), 82.1 ($C(CH_3)_3$), 81.1, 80.7, 78.2 and 77.5 (C-2, C-3, and C-4), 75.0, 72.7, 71.7, 71.3 and 67.8 (3 $PhCH_2$ and $^1NaphCH_2$), 57.1 and 56.4 (C-5), 43.3 (C-1), 28.1 ($C(CH_3)_3$); MS-ESI: $[M+H]^+$ 688.4, $[M+NH_4]^+$ 705.6, $[M+Na]^+$ 710.4, $[M+K]^+$ 726.4. Anal. Calcd for $C_{43}H_{45}NO_7$: C, 75.09; H, 6.59; N, 2.04. Found: C, 75.12; H, 6.60; N, 2.08.

4.20. *tert*-Butyl (2,3-di-*O*-benzyl-*N*-benzyloxycarbonyl-1,5-dideoxy-1,5-imino-L-iditol)uronate (9a)

Compound **26** (1.21 g, 1.76 mmol) was dissolved in a mixture of MeCN and water (9:1, 15 mL), CAN (1.93 g, 3.52 mmol, 2 equiv) was added and the mixture was stirred for 3 h at room temperature. It was diluted with chloroform (300 mL) and was washed with saturated aq $NaHCO_3$ (150 mL) and water (100 mL). The aqueous layer was back-extracted with chloroform (200 mL). The combined organic layers were dried and concentrated. Column chromatography of the residue (toluene–acetone, 98:2→9:1) gave syrupy **9a** (0.962 g, 65%); R_f (toluene–acetone, 9:1) 0.43; $[\alpha]_D$ +12 (*c* 0.33,

$CHCl_3$); IR ν_{max} (film): 3125, 3051, 2995, 1754, 1720 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.22–7.48 (m, 15H, aromatic), 4.94–5.26 (m, 3H, $PhCH_2$ and H-5), 4.87 and 4.67 (2 s, 4H, 2 $PhCH_2$), 4.40 (dd, 1H, $J_{1a,1b}$ 12.8 Hz, $J_{1b,2}$ 5.1 Hz, H-1b), 4.12–4.22 and 3.34–3.80 (2 m, 4H, H-1a, H-2, H-3, H-4), 2.19 (s, 1H, OH), 1.39 (s, 9H, $C(CH_3)_3$); ^{13}C NMR (50 MHz, $CDCl_3$): δ 170.0 (C-6), 155.4 (C(O)OCH_2Ph), 138.7, 138.1, 136.3, 128.6, 128.55, 128.50, 128.3, 128.2, 128.0, 127.9, 127.8 (aromatic), 83.5 ($C(CH_3)_3$), 82.6, 77.6 and 73.0 (C-2, C-3, and C-4), 75.3, 71.5 and 67.9 (3 $PhCH_2$), 57.6 (C-5), 43.9 (C-1), 28.1 ($C(CH_3)_3$); MS-ESI: $[M+H]^+$ 548.1, $[M+NH_4]^+$ 565.1, $[M+Na]^+$ 570.1, $[M+K]^+$ 586.1. Anal. Calcd for $C_{32}H_{37}NO_7$: C, 70.18; H, 6.81; N, 2.56. Found: C, 70.22; H, 6.79; N, 2.54.

4.21. Phenyl 2-azido-3,4-di-*O*-benzyl-6-*O*-chloroacetyl-2-deoxy-1-tio-α,β-D-glucopyranoside (7)

To a solution of **27**[28] (19.7 g, 53.7 mmol) in dry CH_2Cl_2 (150 mL), $PhSSiMe_3$ (30.4 mL, 161 mmol, 3 equiv) and ZnI_2 (34.3 g, 107 mmol, 2 equiv) were added. The mixture was stirred at room temperature overnight, then it was filtered through a pad of Celite. The filtrate was diluted with CH_2Cl_2 (500 mL), after which first a solution of HCl in dioxane (20 mL), then water (10 mL) were added. The mixture was stirred at room temperature for 10 min; the organic layer was washed with 2 M aq HCl (200 mL), saturated aq $NaHCO_3$ (200 mL), and water (200 mL), dried, and concentrated. Column chromatography of the residue (toluene–acetone, 98:2→9:1) gave syrupy **28**[13] (20.5 g, 80%) as an about 2:1 mixture of the α and β anomers. A solution of 90% chloroacetic anhydride (3.6 g, 20.9 mmol, 2 equiv) in CH_2Cl_2 (10 mL) was added dropwise to a stirred solution of **28** (5 g, 10.5 mmol) in a mixture of dry CH_2Cl_2 (15 mL) and dry pyridine (25 mL) at −20 °C. After 10 min, the reaction was quenched with water (15 mL) and stirred for 1 h. The mixture was diluted with CH_2Cl_2 (500 mL), washed with 2 M aq HCl (200 mL), saturated aq $NaHCO_3$ (200 mL), and water (200 mL), dried, and concentrated. Column chromatography of the residue (hexanes–EtOAc, 9:1→4:1) gave syrupy **7** (4.1 g, 74%); R_f (hexanes–EtOAc, 4:1) 0.54; IR ν_{max} (film): 2952, 2109, 1764 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.12–7.70 (m, 15H, aromatic), 5.57 (d, 0.7H, $J_{1,2}$ 5.0 Hz, H-1 α), 4.40 (d, 0.3H, $J_{1,2}$ 10.1 Hz, H-1 β), 3.20–5.00 (m, 12H, skeleton protons, C(O)CH_2Cl and 2 $PhCH_2$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.7 (C(O)CH_2Cl), 137.3, 137.2, 133.9, 133.4, 132.9, 132.7, 132.0, 130.6, 129.1, 128.9, 128.8, 128.54, 128.46, 128.1, 128.0, 127.8, 127.7 (aromatic), 86.9 (C-1 α), 86.1 (C-1 β), 85.2, 81.9, 81.3, 76.94, 76.90, 76.1, 76.0, 75.2, 75.1, 70.0, 65.2, 64.41 and 64.38 (C-6), 64.2, 40.7 and 40.6 (C(O)CH_2Cl); MS-ESI: $[M+NH_4]^+$ 571.2. Anal. Calcd for $C_{28}H_{28}ClN_3O_5S$: C, 60.70; H, 5.09; N, 7.58; S, 5.79. Found: C, 61.54; H, 5.23; N, 6.30; S, 5.73.

4.22. (2-Azido-3,4-di-*O*-benzyl-6-*O*-chloroacetyl-2-deoxy-α-D-glucopyranosyl)-(1→4)-[2,3-di-*O*-benzyl-*N*-benzyloxycarbonyl-1,5-dideoxy-1,5-imino-6-*O*-(1-naphthyl) methyl-L-iditol] (29)

A mixture of **8** (0.43 g, 0.78 mmol), **7** (0.67 g, 0.97 mmol, 1.25 equiv), and 4 Å molecular sieves (2 g) was stirred in a mixture of dry diethyl ether and CH_2Cl_2 (4:1, 12 mL) at 0 °C under argon for 30 min, then DMTST (1 g, 3.9 mmol, 5 equiv) was added. After 1 day, the reaction was quenched with Et_3N (2 mL). The mixture was filtered through a pad of Celite, the filtrate was diluted with CH_2Cl_2 (300 mL), and washed with 2 M aq HCl (150 mL), saturated aq $NaHCO_3$ (150 mL), and water (150 mL), dried, and concentrated. The residue was purified by column chromatography (hexanes–EtOAc, 9:1→7:3) to give **29** as a colorless syrup (0.486 g, 59%); R_f (hexanes–EtOAc, 4:1) 0.58; $[\alpha]_D$ +38.6 (*c* 1.04, $CHCl_3$); IR ν_{max} (film): 2926, 2108, 1764 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6, 100 °C): δ 7.19–8.21 (m, 32H, aromatic), 5.26 (d, 1H, $J_{1',2'}$ 3.6 Hz, H-1′), 5.07 (s, 2H, C(O)OCH_2Ph), 5.00 (d, 1H, *J* 12.4 Hz, ½$PhCH_2$), 4.94 (d, 1H, *J* 12.0 Hz, ½$PhCH_2$), 4.80 (d, 1H, *J* 11.0 Hz, ½$PhCH_2$), 4.79 (s, 2H, $^1NaphCH_2$), 4.76 (d, 1H, *J* 12.4 Hz, ½$PhCH_2$), 4.70 (d, 1H, *J* 11.6 Hz, ½$PhCH_2$), 4.61 (d, 1H, *J* 11.6 Hz, ½$PhCH_2$), 4.59 (ddd, 1H, $J_{4,5}$ 11.2 Hz, $J_{5,6a}$ 3.6 Hz, $J_{5,6b}$ 7.6 Hz, H-5), 4.58 (d, 1H, *J* 11.0 Hz, ½$PhCH_2$), 4.55 (d, 1H, *J* 12.0 Hz, ½$PhCH_2$), 4.13–4.29 (m, 5H, H-4, H-6a′, H-6b′, C(O)CH_2Cl), 4.19 (dd, 1H, $J_{1a,1b}$ 13.2 Hz, $J_{1b,2}$ 5.2 Hz, H-1b), 3.95 (dd, 1H, $J_{6a,6b}$ 10.8 Hz, H-6b), 3.85 (dd, 1H, H-6a), 3.84 (ddd, 1H, $J_{4',5'}$ 8.8 Hz, $J_{5',6a'}$ 2.0 Hz, $J_{5',6b'}$ 3.6 Hz, H-5′), 3.80 (dd, 1H, $J_{2',3'}$ 11.0 Hz, $J_{3',4'}$ 10.0 Hz, H-3′), 3.79 (t, 1H, $J_{2,3} \approx J_{3,4}$ 3.2 Hz, H-3), 3.57 (dd, 1H, H-4′), 3.51 (dd, 1H, H-2′), 3.46 (ddd, 1H, $J_{1a,2}$ 11.0 Hz, $J_{1b,2}$ 5.2 Hz, H-2), 2.86 (dd, 1H, H-1a); ^{13}C NMR (100 MHz, DMSO-d_6, 100 °C): δ 167.5 (OC(O)CH_2Cl), 155.2 (C(O)OCH_2Ph), 138.7, 137.9, 137.6, 137.2, 136.5, 133.8, 133.3, 131.6, 128.7, 128.6, 128.4, 128.33, 128.27, 128.1, 127.9, 127.5, 126.5, 126.4, 126.3, 128.2, 125.9, 125.8, 125.24, 125.19, 124.1, 124.0 (aromatic), 98.9 (C-1′), 82.6 (C-3), 80.2 (C-3′), 78.9 (C-2), 77.9 (C-4), 77.2 (C-4′), 75.5 ($^1NaphCH_2$), 75.3, 75.2, 75.0 and 72.7 (4 $PhCH_2$), 70.0 (C-5′), 67.6 (C(O)OCH_2Ph), 66.1 (C-6), 64.5 (C-6′), 63.2 (C-2′), 53.8 (C-5), 42.1 (C-1), 40.9 (C(O)CH_2Cl); MS-ESI: $[M+H]^+$ 1061.5, $[M+NH_4]^+$ 1078.5, $[M+Na]^+$ 1083.5, $[M+K]^+$ 1099.3. Anal. Calcd for $C_{61}H_{61}ClN_4O_{11}$: C, 69.01; H, 5.79; N, 5.28. Found: C, 69.05; H, 5.82; N, 5.25.

4.23. (2-Azido-3,4-di-*O*-benzyl-6-*O*-chloroacetyl-2-deoxy-α-D-glucopyranosyl)-(1→4)-[*tert*-butyl (2,3-di-*O*-benzyl-*N*-benzyloxycarbonyl-1,5-dideoxy-1,5-imino-L-iditol) uronate] (30)

A mixture of **9a** (0.165 g, 0.298 mmol), **7** (0.207 g, 0.373 mmol, 1.25 equiv), and 2,6-di-*tert*-butyl-4-methylpyridine (0.041 g, 0.2 mmol) in a mixture of dry diethyl ether and CH_2Cl_2 (4:1, 6 mL) was stirred with 4 Å molecular sieves (1 g) at −30 °C under argon for 30 min, then a 1 M solution of Me_2S_2–Tf_2O (0.56 mL, 1.5 equiv/donor) in CH_2Cl_2 was added. The mixture was stirred for 5 min, then, it was neutralized with Et_3N, was diluted with CH_2Cl_2 (250 mL), and filtered through a pad of Celite. The filtrate was washed with 2 M aq HCl (100 mL), saturated aq $NaHCO_3$ (100 mL) and water (100 mL). The organic layer was dried and concentrated. The residue was purified by column chromatography (hexanes–EtOAc, 9:1→4:1) to give **30** (0.234 g, 80%) as a colorless syrup; R_f (hexanes–EtOAc, 4:1) 0.60; $[\alpha]_D$ +49.7 (*c* 0.81, $CHCl_3$); IR ν_{max} (film): 2109, 1737, 1699, 1217, 1144 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, 65 °C): δ 7.22–7.37 (m, 25H, aromatic), 5.22 (d, 1H, $J_{1',2'}$ 4.0 Hz, H-1′), 5.14 (d, 1H, *J* 12.4 Hz, ½$PhCH_2$), 5.09 (d, 1H, *J* 12.4 Hz, ½$PhCH_2$), 4.96 (d, 1H, *J* 10.8 Hz, ½$PhCH_2$), 4.90 (d, 1H, *J* 10.8 Hz, ½$PhCH_2$), 4.86 (d, 1H, *J* 11.2 Hz, ½$PhCH_2$), 4.85 (d, 1H, *J* 10.8 Hz, ½$PhCH_2$), 4.81 (d, 1H, *J* 10.8 Hz, ½$PhCH_2$), 4.62 (s, 2H, C(O)CH_2Cl), 4.61 (d, 1H, $J_{4,5}$ 7.0 Hz, H-5), 4.59 (d, 1H, *J* 11.2 Hz, ½$PhCH_2$), 4.06–4.26 (m, 5H, H-1b, H-3, H-5′, H-6a′, H-6b′), 3.95 (dd, 1H, $J_{2',3'}$ 10.4 Hz, $J_{3',4'}$ 8.8 Hz, H-3′), 3.78 (dd, 1H, $J_{3,4}$ 9.2 Hz, H-4), 3.39–3.49 (m, 2H, H-2, H-4′), 3.35 (dd, 1H, $J_{1a,1b}$ 12.4 Hz, $J_{1a,2}$ 11.2 Hz, H-1a), 3.25 (dd, 1H, H-2′), 1.47 (s, 9H, $C(CH_3)_3$); ^{13}C NMR (100 MHz, $CDCl_3$, 65 °C): δ 168.1 (C-6), 166.4 (OC(O)CH_2Cl), 155.1 (C(O)OCH_2Ph), 138.9, 138.1, 137.9, 137.6, 136.2, 128.7, 128.6, 128.53, 128.50, 128.4, 128.2, 128.1, 127.8, 127.7, 127.5 (aromatic), 99.7 (C-1′), 82.7 ($C(CH_3)_3$), 81.3 (C-3), 80.2 (C-3′), 78.4 (C-2), 78.3 (C-4), 75.9 (C-4′), 75.4, 75.1, 75.0 and 72.7 (4 $PhCH_2$), 69.9 (C-5′), 68.0 ($PhCH_2$), 64.4 (C-6′), 63.6 (C-2′), 58.1 (C-5), 43.1 (C-1), 40.6 (OC(O)CH_2Cl), 28.2 ($C(CH_3)_3$); MS-ESI: $[M+NH_4]^+$ 1008.6, $[M+Na]^+$ 1013.5, $[M+K]^+$ 1029.5. Anal. Calcd for $C_{54}H_{59}ClN_4O_{12}$: C, 65.41; H, 6.00; N, 5.65. Found: C, 65.43; H, 6.02; N, 5.60.

4.24. (2-Azido-3,4-di-*O*-benzyl-6-*O*-chloroacetyl-2-deoxy-α-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-benzyl-*N*-benzyloxycarbonyl-1,5-dideoxy-1,5-imino-L-iditol) (31)

Compound **29** (0.48 g, 0.46 mmol) was dissolved in a mixture of MeCN and water (9:1, 10 mL), CAN (0.51 g, 0.92 mmol, 2 equiv)

was added and the mixture was stirred for 2 h at room temperature. It was diluted with chloroform (100 mL) and was washed with saturated aq $NaHCO_3$ (50 mL) and water (50 mL). The aqueous layer was back-extracted with chloroform (50 mL). The combined organic layers were dried and concentrated. Column chromatography of the residue (toluene–acetone, 95:5→9:1) gave syrupy **31** (0.35 g, 71%); R_f (toluene–acetone, 9:1) 0.26; $[\alpha]_D$ +55.2 (*c* 0.36, $CHCl_3$); IR ν_{max} (film): 3446, 2106, 1636 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.10–7.42 (m, 25H, aromatic), 5.33 (d, 1H, $J_{1',2'}$ 3.3 Hz, H-1′), 5.10 (s, 2H, $PhCH_2$), 4.80–5.00 (m, 4H, H-5, 3×½$PhCH_2$), 4.52–4.66 (m, 4H, 2 $PhCH_2$), 4.42 (d, 1H, *J* 11.0 Hz, ½$PhCH_2$), 4.12 (dd, 1H, $J_{1a,1b}$ 13.0 Hz, $J_{1b,2}$ 6.0 Hz, H-1b), 3.40–4.20 (m, 12H, H-2, H-3, H-4, H-6a, H-6b, H-3′, H-4′, H-5′, H-6a′, H-6b′, C(O)CH_2Cl), 3.24 (dd, 1H, $J_{2',3'}$ 10.3 Hz, H-2′), 2.94 (dd, 1H, $J_{1a,2}$ 11.4 Hz, H-1a), 2.00 (br s, 1H, OH); ^{13}C NMR (50 MHz, $CDCl_3$): δ 166.7 (O*C*(O)CH_2Cl), 156.1 (*C*(O)OCH_2Ph), 138.6, 137.8, 137.6, 137.3, 136.3, 129.2, 129.1, 128.8, 128.7, 128.6, 128.5, 128.3, 128.2, 128.1, 128.0, 127.7, 127.6 (aromatic), 99.1 (C-1′), 82.5 (C-3), 80.2 (C-3′), 79.3 (C-2), 78.9 (C-4′), 78.0 (C-4), 75.7, 75.4, 75.34, 75.31 and 72.9 (5 $PhCH_2$), 68.0 (C-5′), 64.5 (C-6), 63.3 (C-2′), 59.0 (C-6′), 56.1 (C-5), 41.8 (C-1), 40.9 (C(O)CH_2Cl); MS-ESI: $[M+H]^+$ 921.4, $[M+Na]^+$ 946.6, $[M+K]^+$ 959.6. Anal. Calcd for $C_{50}H_{53}ClN_4O_{11}$: C, 65.17; H, 5.80; N, 6.08. Found: C, 65.12; H, 5.83; N, 6.10.

4.25. (2-Azido-3,4-di-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-benzyl-*N*-benzyloxycarbonyl-1,5-dideoxy-1,5-imino-L-iditol) (32)

To a solution of **31** (0.3 g, 0.325 mmol) in dry DMF (4 mL) a freshly prepared solution of HDTC[31] (2.24 mL, 0.42 M, 0.935 mmol, 3 equiv) was added and the mixture was stirred at room temperature for 30 min. The mixture was diluted with CH_2Cl_2 (200 mL), and was washed with 2 M aq HCl (75 mL), saturated aq $NaHCO_3$ (75 mL) and water (75 mL), it was dried and evaporated. Column chromatography (toluene–acetone, 95:5→4:1) gave **32** (0.252 g, 92%) as a colorless syrup; R_f (toluene–acetone, 9:1) 0.42; $[\alpha]_D$ +36.4 (*c* 0.41, $CHCl_3$); IR ν_{max} (film): 3441, 2107, 1637 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.12–7.50 (m, 25H, aromatic), 5.31 (d, 1H, $J_{1',2'}$ 3.7 Hz, H-1′), 5.09 (s, 2H, $PhCH_2$), 4.80–4.95 (m, 4H, 2 $PhCH_2$), 4.58–4.68 (m, 4H, 2 $PhCH_2$), 3.34–4.30 (m, 12H, H-1b, H-2, H-3, H-4, H-5, H-6a, H-6b, H-3′, H-4′, H-5′, H-6a′, H-6b′), 3.25 (br m, 1H, H-2′), 2.93 (br m, 1H, H-1a); ^{13}C NMR (50 MHz, $CDCl_3$): δ 156.1 (*C*(O)OCH_2Ph), 138.6, 137.9, 137.8, 137.7, 136.3, 129.1, 128.71, 128.67, 128.6, 128.4, 128.3, 128.1, 128.0, 127.9, 127.8, 127.7 (aromatic), 99.5 (C-1′), 82.2, 80.0, 78.8, 78.2 and 77.2 (C-2, C-3, C-4, C-3′, and C-4′), 75.5, 75.4, 75.3, 73.0 (4 $PhCH_2$), 72.8 (C-5′), 68.0 ($PhCH_2$), 63.5 (C-2′), 61.5 (C-6′), 58.5 (C-6), 56.4 (C-5), 41.7 (C-1); MS-ESI: $[M+H]^+$ 845.6, $[M+Na]^+$ 867.6, $[M+K]^+$ 883.6. Anal. Calcd for $C_{48}H_{52}N_4O_{10}$: C, 68.23; H, 6.20; N, 6.63. Found: C, 68.25; H, 6.22; N, 6.59.

4.26. (2-Amino-3,4-di-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→4)-(2,3-di-*O*-benzyl-*N*-benzyloxycarbonyl-1,5-dideoxy-1,5-imino-L-iditol) (33)

To a solution of **32** (0.25 g, 0.29 mmol) in a mixture of pyridine and water (9:1, 5 mL), 1,3-propanedithiol (0.6 mL, 5.96 mmol, 20 equiv) and six drops of Et_3N (pH ca. 8) were added and the mixture was stirred at room temperature for 2 days. It was then evaporated and co-evaporated with toluene three times. The residue was purified by column chromatography (CH_2Cl_2–MeOH, 98:2→95:5) to give syrupy **33** (0.197 g, 81%); R_f (CH_2Cl_2–MeOH, 95:5) 0.33; $[\alpha]_D$ +40.4 (*c* 0.45, $CHCl_3$); IR ν_{max} (film): 2920, 1695 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.10–7.46 (m, 25H, aromatic), 5.08 (m, 3H, H-1′, $PhCH_2$), 4.91 (d, 1H, *J* 10.0 Hz, ½$PhCH_2$), 4.87 (d, 1H, *J* 10.0 Hz, ½$PhCH_2$), 4.79 (d, 1H, *J* 11.0 Hz, ½$PhCH_2$), 4.69 (d, 1H, *J* 11.4 Hz, ½$PhCH_2$), 4.61 (d, 1H, *J* 11.4 Hz, ½$PhCH_2$), 4.56 (s, 1H, ½$PhCH_2$), 4.53 (d, 1H, *J* 11.0 Hz, ½$PhCH_2$), 4.48 (d, 1H, *J* 11.0 Hz, ½$PhCH_2$), 4.17 (dd, 1H, $J_{1a,1b}$ 13.2 Hz, $J_{1b,2}$ 5.1 Hz, H-1b), 3.34–4.08 (m, 11H, H-2, H-3, H-4, H-5, H-6a, H-6b, H-3′, H-4′, H-5′, H-6a′, H-6b′), 2.96 (dd, 1H, $J_{1a,2}$ 11.3 Hz, H-1a), 2.71 (br m, 1H, H-2′), 2.49 (s, 4H, NH_2 and 2 OH); ^{13}C NMR (50 MHz, $CDCl_3$): δ 156.1 (*C*(O)OCH_2Ph), 138.5, 138.4, 137.9, 137.8, 136.3, 128.61, 128.58, 128.5, 128.4, 128.2, 128.1, 127.9, 127.8, 127.6, 127.5 (aromatic), 101.7 (C-1′), 83.4, 81.2, 78.9, 78.8 and 78.5 (C-2, C-3, C-4, C-3′, and C-4′), 75.6, 75.0, 74.9 and 72.7 (4 $PhCH_2$), 73.8 (C-5′), 67.8 ($PhCH_2$), 61.6 (C-6′), 58.2 (C-6), 56.3 (C-5), 53.4 (C-2′), 41.7 (C-1); MS-ESI: $[M+H]^+$ 819.4, $[M+Na]^+$ 841.6, $[M+K]^+$ 857.6. Anal. Calcd for $C_{48}H_{54}N_2O_{10}$: C, 70.40; H, 6.65; N, 3.42. Found: C, 70.45; H, 6.60; N, 3.45.

4.27. (2-Acetamido-6-*O*-acetyl-3,4-di-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→4)-(6-*O*-acetyl-2,3-di-*O*-benzyl-*N*-benzyloxycarbonyl-1,5-dideoxy-1,5-imino-L-iditol) (34)

To a solution of **33** (0.19 g, 0.24 mmol) in dry pyridine (2 mL), acetic anhydride (0.23 mL, 2.4 mmol, 10 equiv) was added at 0 °C. The mixture was stirred at room temperature overnight, and then the reaction was quenched with water (1 mL). The mixture was diluted with CH_2Cl_2 (200 mL), washed with 2 M aq HCl (2×75 mL), saturated aq $NaHCO_3$ (75 mL), and water (75 mL). The organic layer was dried and concentrated. The residue was purified by column chromatography (toluene–acetone, 9:1→4:1) to give syrupy **34** (0.188 g, 83%); R_f (toluene–acetone, 4:1) 0.36; $[\alpha]_D$ +34.8 (*c* 0.52, $CHCl_3$); IR ν_{max} (film): 3336, 3030, 2926, 1742, 1706, 1236 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.10–7.48 (m, 25H, aromatic), 5.93 (d, 1H, $J_{2',NH}$ 9.1 Hz, NH), 5.23 (d, 1H, *J* 12.1 Hz, ½$PhCH_2$), 5.10 (d, 1H, $J_{1',2'}$ 3.7 Hz, H-1′), 5.03 (d, 1H, *J* 10.6 Hz, ½$PhCH_2$), 4.94 (d, 1H, *J* 11.4 Hz, ½$PhCH_2$), 4.91 (d, 1H, *J* 11.0 Hz, ½$PhCH_2$), 4.83 (d, 1H, *J* 11.0 Hz, ½$PhCH_2$), 4.77 (d, 1H, *J* 11.4 Hz, ½$PhCH_2$), 4.60 (s, 2H, $PhCH_2$), 4.55 (d, 1H, *J* 10.6 Hz, ½$PhCH_2$), 4.49 (d, 1H, *J* 12.1 Hz, ½$PhCH_2$), 3.40–4.70 (m, 13H, H-1b, H-2, H-3, H-4, H-5, H-6a, H-6b, H-2′, H-3′, H-4′, H-5′, H-6a′, H-6b′), 2.91 (dd, 1H, $J_{1a,1b}$ 12.0 Hz, $J_{1a,2}$ 11.0 Hz, H-1a), 2.00 and 1.85 (2s, 6H, 2C(O)CH_3), 1.38 (s, 3H, NHC(O)CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 170.8 (NH*C*(O)CH_3), 170.6 and 170.1 (2 O*C*(O)CH_3), 155.4 (*C*(O)OCH_2Ph), 138.2, 137.9, 137.7, 137.6, 137.5, 136.2, 129.1, 128.72, 128.68, 128.6, 128.5, 128.4, 128.3, 128.23, 128.16, 128.1, 127.9 (aromatic), 100.5 (C-1′), 81.1, 80.8, 78.6, 78.2 and 77.5 (C-2, C-3, C-4, C-3′, and C-4′), 75.5, 75.2 and 75.1 (3 $PhCH_2$), 72.7 (C-5′), 71.1 and 67.8 (2 $PhCH_2$), 62.8 and 62.7 (C-6 and C-6′), 59.2 (C-5), 53.0 and 52.8 (C-2′), 41.7 and 41.3 (C-1), 22.7 (NHC(O)CH_3), 21.5 and 20.7 (2C(O)CH_3); MS-ESI: $[M+H]^+$ 945.6, $[M+Na]^+$ 967.6, $[M+K]^+$ 983.6. Anal. Calcd for $C_{54}H_{60}N_2O_{13}$: C, 68.63; H, 6.40; N, 2.96. Found: C, 68.60; H, 6.42; N, 2.92.

4.28. 2-Acetamido-2-deoxy-α-D-glucopyranosyl-(1→4)-1,5-dideoxy-1,5-imino-L-iditol (3)

To a solution of **34** (0.18 g, 0.2 mmol) in dry MeOH (2 mL), a catalytic amount of NaOMe was added. The mixture was stirred overnight at room temperature, neutralized with Amberlite IR 120 (H^+) resin (pH ca. 7), filtered, and concentrated to give a syrup (0.148 g, 87%), which contained **35** and **36**. The syrup was dissolved in a mixture of THF and water (1:1, 4 mL) and was hydrogenated in the presence of 10% Pd/C catalyst (0.100 g) for 5 days at atmospheric pressure at room temperature. The mixture was filtered through a pad of Celite and the filtrate was concentrated. The residue was separated by column chromatography (2-propanol–acetone–water, 4:2:3) to give **3** (0.042 g, 43%) as a syrup and syrupy **37** (0.022 g, 31%). They were further purified on a column of Sephadex G-25 using water as eluent and then freeze dried to give the products as white foams.

Compound **3**: R_f (2-propanol–acetone–water, 4:1:1) 0.30; $[\alpha]_D$ +56.4 (*c* 0.48, H_2O); ^1H NMR (400 MHz, D_2O): δ 5.04 (d, 1H, $J_{1',2'}$ 3.7 Hz, H-1′), 3.90 (d, 1H, $J_{2,3} \approx J_{3,4}$ 4.5 Hz, H-3), 3.89 (dd, 1H, $J_{2',3'}$

10.0 Hz, H-2′), 3.83 (m, 1H, H-4), 3.78 (dd, 1H, $J_{6a',6b'}$ 12.0 Hz, $J_{6b',5'}$ 4.8 Hz, H-6b′), 3.77 (d, 1H, H-2), 3.75 (s, 2H, H-6), 3.70 (dd, 1H, $J_{6a',5'}$ 2.5 Hz, H-6a′), 3.62 (dd, 1H, $J_{3',4'}$ 9.6 Hz, H-3′), 3.56 (ddd, 1H, $J_{4',5'}$ 9.4 Hz, H-5′), 3.42 (dd, 1H, H-4′), 3.37 (m, 1H, H-5), 3.14 (dd, 1H, $J_{1a,1b}$ 13.2 Hz, $J_{1a,2}$ 4.5 Hz, H-1a), 2.98 (dd, 1H, $J_{1b,2}$ 3.0 Hz, H-1b), 1.93 (s, 3H, NHC(O)CH_3); ^{13}C NMR (100 MHz, D_2O): δ 174.6 (NH*C*(O)CH_3), 96.5 (C-1′), 73.5 (C-4), 73.3 (C-5′), 71.6 (C-3′), 69.9 (C-4′), 68.0 (C-2), 66.9 (C-3), 60.7 (C-6′), 59.0 (C-6), 56.6 (C-5), 53.7 (C-2′), 45.4 (C-1), 22.2 (NHC(O)*C*H_3); MS-ESI: $[M+H]^+$ 367.2, $[M+Na]^+$ 389.2. Anal. Calcd for $C_{14}H_{26}N_2O_9$: C, 45.90; H, 7.15; N, 7.65. Found: C, 45.93; H, 7.13; N, 7.67.

Compound **37**: R_f (2-propanol–acetone–water, 4:1:1) 0.73; $[\alpha]_D$ +35.8 (*c* 0.98, H_2O); ^{1}H NMR (400 MHz, D_2O): δ 5.05 (d, 1H, $J_{1',2'}$ 3.6 Hz, H-1′), 4.45 (dd, 1H, $J_{6a,6b}$ 9.0 Hz, $J_{6b,5}$ 8.8 Hz, H-6b), 4.33 (dd, 1H, $J_{6a,5}$ 4.0 Hz, H-6a), 4.27 (ddd, 1H, $J_{4,5}$ 2.5 Hz, H-5), 4.05 (dd, 1H, $J_{2,3}$ 3.6 Hz, $J_{3,4}$ 3.3 Hz, H-3), 3.88 (dd, 1H, $J_{2',3'}$ 10.5 Hz, H-2′), 3.86 (dd, 1H, $J_{1a,2}$ 2.8 Hz, $J_{1b,2}$ 1.5 Hz, H-2), 3.81 (dd, 1H, $J_{6a',6b'}$ 12.0 Hz, $J_{6b',5'}$ 5.4 Hz, H-6b′), 3.78 (dd, 1H, H-4), 3.71 (dd, 1H, $J_{6a',5'}$ 2.6 Hz, H-6a′), 3.63 (ddd, 1H, $J_{4',5'}$ 9.7 Hz, H-5′), 3.62 (d, 1H, $J_{1a,1b}$ 14.5 Hz, H-1b), 3.57 (dd, 1H, $J_{3',4'}$ 9.2 Hz, H-3′), 3.44 (dd, 1H, H-1a), 3.41 (dd, 1H, H-4′), 1.93 (s, 3H, NHC(O)CH_3); ^{13}C NMR (100 MHz, D_2O): δ 174.7 (NH*C*(O)CH_3), 160.2 (N*C*(O)O), 96.6 (C-1′), 74.0 (C-4), 73.6 (C-5′), 71.6 (C-3′), 69.9 (C-4′), 67.4 (C-2), 65.5 (C-3), 64.9 (C-6), 60.8 (C-6′), 53.7 (C-2′), 53.4 (C-5), 43.6 (C-1), 22.2 (NHC(O)*C*H_3); MS-ESI: $[M+H]^+$ 393.4, $[M+Na]^+$ 415.4. Anal. Calcd for $C_{15}H_{24}N_2O_{10}$: C, 45.92; H, 6.17; N, 7.14. Found: C, 45.90; H, 6.15; N, 7.17.

4.29. (2-Azido-3,4-di-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→4)-[*tert*-butyl (2,3-di-*O*-benzyl-*N*-benzyloxycarbonyl-1,5-dideoxy-1,5-imino-L-iditol)uronate] (38)

To a solution of **30** (0.212 g, 0.25 mmol) in dry DMF (4 mL) a freshly prepared solution of HDTC (1.54 mL, 0.42 M, 0.643 mmol, 3 equiv) was added and the mixture was stirred at room temperature for 10 min. The mixture was diluted with CH_2Cl_2 (200 mL), and was washed with 2 M aq HCl (75 mL), saturated aq $NaHCO_3$ (75 mL), and water (75 mL), it was dried and evaporated. Column chromatography (toluene–acetone, 98:2→9:1) gave **38** (0.141 g, 72%) as a yellowish syrup; R_f (toluene–acetone, 9:1) 0.31; $[\alpha]_D$ +34.8 (*c* 0.43, $CHCl_3$); IR ν_{max} (film): 3446, 2925, 1732 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.10–7.50 (m, 25H, aromatic), 5.23 (br s, 1H, H-1′), 4.56–5.18 (m, 10H, 5 $PhCH_2$), 3.32–4.50 (m, 11H, H-1a, H-1b, H-2, H-3, H-4, H-5, H-3′, H-4′, H-5′, H-6a′, H-6b′), 3.25 (dd, 1H, $J_{1',2'}$ 3.6 Hz, $J_{2',3'}$ 10.2 Hz, H-2′), 1.80 (br s, 1H, OH), 1.45 (s, 9H, C$(CH_3)_3$); ^{13}C NMR (50 MHz, $CDCl_3$): δ 168.2 (C-6), 155.1 (*C*(O)OCH_2Ph), 138.9, 138.3, 138.2, 137.8, 136.2, 129.1, 128.6, 128.54, 128.50, 128.44, 128.41, 128.3, 128.2, 128.0, 127.8, 127.6 (aromatic), 100.0 (C-1′), 82.7 (*C*$(CH_3)_3$), 81.0, 79.9, 78.3, 78.0 and 76.0 (C-2, C-3, C-4, C-3′, and C-4′), 75.4, 75.3, 74.9 and 72.8 (4 $PhCH_2$), 72.1 (C-5′), 68.0 ($PhCH_2$), 63.5 (C-6′), 61.2 (C-2′), 58.0 (C-5), 42.9 (C-1), 28.2 (C$(CH_3)_3$); MS-ESI: $[M+Na]^+$ 937.6. Anal. Calcd for $C_{52}H_{58}N_4O_{11}$: C, 68.25; H, 6.39; N, 6.12. Found: C, 68.23; H, 6.40; N, 6.13.

4.30. (2-Amino-3,4-di-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→4)-[*tert*-butyl (2,3-di-*O*-benzyl-*N*-benzyloxycarbonyl-1,5-dideoxy-1,5-imino-L-iditol) uronate] (39)

To a solution of **38** (0.14 g, 0.15 mmol) in a mixture of pyridine and water (9:1, 5 mL) 1,3-propanedithiol (0.31 mL, 3.08 mmol, 20 equiv) and six drops of Et_3N (pH ca. 8) were added and the mixture was stirred at room temperature for 6 days. It was then evaporated and co-evaporated with toluene three times. The product was purified by column chromatography (CH_2Cl_2–MeOH, 98:2→9:1) to give syrupy **39** (0.111 g, 81%); R_f (CH_2Cl_2–MeOH, 95:5) 0.33; $[\alpha]_D$ +41.4 (*c* 0.41, $CHCl_3$); IR ν_{max} (film): 3430, 1637 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.10–7.48 (m, 25H, aromatic), 5.10 (br s, 1H, H-1′), 4.50–5.00 (m, 10H, 5 $PhCH_2$), 3.10–4.50 (m, 11H, H-1a, H-1b, H-2, H-3, H-4, H-5, H-3′, H-4′, H-5′, H-6a′, H-6b′), 2.73 (m, 1H, H-2′), 1.64 (br s, 3H, OH, NH_2), 1.42 (s, 9H, C$(CH_3)_3$); ^{13}C NMR (50 MHz, $CDCl_3$): δ 168.2 (C-6), 155.1 (*C*(O)OCH_2Ph), 138.8, 138.7, 138.6, 138.1, 136.2, 128.6, 128.53, 128.49, 128.4, 128.3, 128.0, 127.9, 127.8, 127.7, 127.6 (aromatic), 102.0 (C-1′), 82.5 (*C*$(CH_3)_3$), 83.8, 80.7, 78.4, 78.3 and 75.9 (C-2, C-3, C-4, C-3′, and C-4′), 75.6, 75.1, 74.6 and 72.7 (4 $PhCH_2$), 72.5 (C-5′), 67.9 ($PhCH_2$), 61.5 (C-6′), 58.0 (C-5), 56.3 (C-2′), 42.9 (C-1), 28.1 (C(*C*$H_3)_3$); MS-ESI: $[M+H]^+$ 889.6, $[M+Na]^+$ 911.6. Anal. Calcd for $C_{52}H_{60}N_2O_{11}$: C, 70.25; H, 6.80; N, 3.15. Found: C, 70.20; H, 6.83; N, 3.17.

4.31. (2-Acetamido-6-*O*-acetyl-3,4-di-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→4)-[*tert*-butyl (2,3-di-*O*-benzyl-*N*-benzyloxycarbonyl-1,5-dideoxy-1,5-imino-L-iditol)-uronate] (40)

To a solution of **39** (0.11 g, 0.12 mmol) in dry pyridine (2 mL), acetic anhydride (0.12 mL, 1.25 mmol, 10 equiv) was added at 0 °C. The mixture was stirred at room temperature overnight, and then the reaction was quenched with water. The mixture was diluted with CH_2Cl_2 (150 mL), washed with 2 M aq HCl (2×50 mL), saturated aq $NaHCO_3$ (50 mL), and water (50 mL). The organic layer was dried and concentrated. The residue was purified by column chromatography (toluene–acetone, 9:1→4:1) to give **40** (0.117 g, 96%) as a colorless syrup; R_f (toluene–acetone, 4:1) 0.33; $[\alpha]_D$ +48.5 (*c* 0.64, $CHCl_3$); IR ν_{max} (film): 3446, 2360, 1638 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.06–7.34 (m, 25H, aromatic), 5.69 (d, 1H, $J_{2',NH}$ 8.5 Hz, NH), 5.09 (d, 1H, $J_{1',2'}$ 3.6 Hz, H-1′), 4.45–5.05 (m, 10H, 5 $PhCH_2$), 3.30–4.40 (m, 11H, H-1b, H-2, H-3, H-4, H-5, H-2′, H-3′, H-4′, H-5′, H-6a′, H-6b′), 2.99 (m, 1H, H-1a), 1.89 (br s, 3H, OC(O)CH_3), 1.31 (br s, 12H, C$(CH_3)_3$ and NHC(O)CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 170.6 and 169.9 (2 OC(O)CH_3), 167.8 (C-6), 154.8 (*C*(O)OCH_2Ph), 138.2, 138.1, 137.9, 137.6, 136.1, 128.6, 128.5, 128.4, 128.3, 128.2, 127.9, 127.8, 127.7, 127.1 (aromatic), 100.1 (C-1′), 82.7 (*C*$(CH_3)_3$), 80.7, 79.6, 78.0, 77.6 and 76.3 (C-2, C-3, C-4, C-3′, and C-4′), 75.0, 74.8, 74.4 and 72.4 (4 $PhCH_2$), 70.3 (C-5′), 67.9 ($PhCH_2$), 62.5 (C-6′), 57.6 (C-5), 52.4 (C-2′), 42.7 (C-1), 28.0 (C(*C*$H_3)_3$), 22.7 (NHC(O)*C*H_3), 20.7 (OC(O)*C*H_3); MS-ESI: $[M+H]^+$ 973.6, $[M+Na]^+$ 995.4, $[M+K]^+$ 1011.4. Anal. Calcd for $C_{56}H_{64}N_2O_{13}$: C, 69.12; H, 6.63; N, 2.88. Found: C, 69.15; H, 6.62; N, 2.90.

4.32. (2-Acetamido-3,4-di-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→4)-[*tert*-butyl (2,3-di-*O*-benzyl-*N*-benzyloxycarbonyl-1,5-dideoxy-1,5-imino-L-iditol)-uronate] (41)

To a solution of **40** (0.11 g, 0.12 mmol) in dry MeOH (2 mL), a catalytic amount of NaOMe was added. The mixture was stirred overnight at room temperature, neutralized with Amberlite IR 120 (H^+) resin (pH ca. 7), filtered, and concentrated. The residue was purified by column chromatography (CH_2Cl_2–MeOH, 95:5→4:1) to give syrupy **41** (0.106 g, 95%); R_f (CH_2Cl_2–MeOH, 4:1) 0.55; $[\alpha]_D$ +84.4 (*c* 0.26, $CHCl_3$); IR ν_{max} (film): 3446, 2962, 2360, 1638, 1216 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.14–7.32 (m, 25H, aromatic), 5.68 (d, 1H, $J_{2',NH}$ 9.9 Hz, NH), 4.90 (d, 1H, $J_{1',2'}$ 3.3 Hz, H-1′), 4.45–5.05 (m, 10H, 5 $PhCH_2$), 3.20–4.40 (m, 11H, H-1b, H-2, H-3, H-4, H-5, H-2′, H-3′, H-4′, H-5′, H-6a′, H-6b′), 2.97 (dd, 1H, J_1 12.0 Hz, H-1a), 2.40 (br s, 1H, OH), 1.31 (br s, 12H, C$(CH_3)_3$ and NHC(O)CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 170.0 (NH*C*(O)CH_3), 167.8 (C-6), 154.9 (*C*(O)OCH_2Ph), 138.4, 138.3, 138.1, 137.7, 136.1, 128.6, 128.5, 128.44, 128.38, 128.3, 128.0, 127.93, 127.89, 127.7, 127.3 (aromatic), 100.2 (C-1′), 82.8 (*C*$(CH_3)_3$), 80.4, 79.7, 78.1, 77.9 and 76.5 (C-2, C-3, C-4, C-3′, and C-4′), 74.87, 74.86 and 74.6 (3 $PhCH_2$), 72.6 (C-5′), 72.5 and 68.0

(2 $PhCH_2$), 61.5 (C-6′), 57.7 (C-5), 52.6 (C-2′), 42.7 (C-1), 28.1 (C(CH_3)$_3$), 22.8 (NHC(O)CH_3); MS-ESI: $[M+H]^+$ 931.4, $[M+Na]^+$ 953.4, $[M+K]^+$ 969.4. Anal. Calcd for $C_{54}H_{62}N_2O_{12}$: C, 69.66; H, 6.71; N, 3.01. Found: C, 69.70; H, 6.69; N, 3.03.

4.33. (2-Acetamido-2-deoxy-α-D-glucopyranosyl)-(1→4)-[(1,5-dideoxy-1,5-imino-L-iditol)uronic acid] sodium salt (4)

Compound **41** (0.1 g, 0.11 mmol) was dissolved in a solution of TFA in CH_2Cl_2 (20 v/v%, 3 mL) and the solution was stirred for 2 h. The reaction mixture was concentrated and the residue was co-evaporated with toluene twice. The resulting syrup was purified by column chromatography (CH_2Cl_2–MeOH, 98:2→9:1). The material obtained was converted into the sodium salt by stirring with Dowex 50WX8 [Na^+] resin in MeOH, the mixture was filtered and the filtrate was concentrated to give (2-acetamido-3,4-di-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→4)-[(2,3-di-*O*-benzyl-*N*-benzyloxycarbonylamino-1,5-dideoxy-1,5-imino-L-iditol)uronic acid] (0.1 g, 95%) as a syrup; $[\alpha]_D$ +50 (*c* 0.8, $CHCl_3$); MS-ESI: $[M+H]^+$ 875.6, $[M+Na]^+$ 897.6, $[M+K]^+$ 913.6.

To a solution of this syrup (0.091 g, 0.104 mmol) in a mixture of THF and water (1:1, 5 mL) two drops of acetic acid was added, and the mixture was hydrogenated in the presence of 10% Pd/C catalyst (0.050 g) for 3 days at atmospheric pressure at room temperature. The mixture was neutralized with saturated aq $NaHCO_3$, was filtered through a pad of Celite, and the filtrate was concentrated. The residue was purified by column chromatography (2-propanol–acetone–water, 4:1:1) to give a syrup, which was desalted on a column of Sephadex G-25 using water as eluent to afford **4** (0.035 g, 88%) as a white foam; R_f (2-propanol–acetone–water, 4:2:3) 0.36; $[\alpha]_D$ +13.3 (*c* 0.3, H_2O); ^1H NMR (400 MHz, D_2O): δ 5.04 (d, 1H, $J_{1',2'}$ 3.6 Hz, H-1′), 4.09 (dd, 1H, $J_{2,3}$ 2.8 Hz, $J_{3,4}$ 4.2 Hz, H-3), 4.00 (dd, 1H, $J_{4,5}$ 2.6 Hz, H-4), 3.86 (dd, 1H, $J_{2',3'}$ 10.5 Hz, H-2′), 3.74 (d, 2H, H-6a′, H-6b′), 3.72 (ddd, 1H, $J_{1a,2}$ 2.8 Hz, $J_{1b,2}$ 2.5 Hz, H-2), 3.69 (ddd, 1H, $J_{4',5'}$ 10.3 Hz, $J_{5',6'}$ 6.0 Hz, H-5′), 3.68 (d, 1H, H-5), 3.63 (dd, 1H, $J_{3',4'}$ 9.0 Hz, H-3′), 3.42 (dd, 1H, H-4′), 3.08 (dd, 1H, $J_{1a,1b}$ 14.0 Hz, H-1b), 3.00 (dd, 1H, H-1a), 1.94 (s, 3H, NHC(O)CH_3); ^{13}C NMR (100 MHz, D_2O): δ 175.2 (C-6), 174.6 (NH*C*(O)CH_3), 95.0 (C-1′), 72.9 (C-4), 72.3 (C-5′), 71.6 (C-3′), 69.8 (C-4′), 66.9 (C-2), 65.3 (C-3), 60.4 (C-6′), 58.6 (C-5), 53.8 (C-2′), 45.5 (C-1), 22.2 (NHC(O)*C*H_3); MS-ESI: $[M+H]^+$ 381.2, $[M+Na]^+$ 403.2, $[M+K]^+$ 419.2. Anal. Calcd for $C_{14}H_{23}N_2NaO_{10}$: C, 41.79; H, 5.76; N, 6.96. Found: C, 41.82; H, 5.74; N, 6.94.

4.34. (2,3-Di-*O*-benzyl-*N*-benzyloxycarbonyl-1,5-dideoxy-1,5-imino-L-iditol)uronic acid (42)

Compound **9a** (0.078 g, 0.142 mmol) was dissolved in a solution of TFA in CH_2Cl_2 (20 v/v%, 2 mL) and was stirred for 1 h. The reaction mixture was evaporated and co-evaporated with toluene twice. The residue was purified by column chromatography (CH_2Cl_2–MeOH, 95:5→9:1). The material obtained was converted into the sodium salt by stirring with Dowex 50WX8 [Na^+] resin in MeOH, the mixture was filtered, and the filtrate was concentrated to give **42** (0.067 g, 97%) as a colorless syrup; R_f (2-propanol–acetone–water, 4:1:1) 0.26; $[\alpha]_D$ −7.5 (*c* 0.3, $CHCl_3$); IR ν_{max} (film): 3446, 2926, 2360, 1706, 1257 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 6.40–7.60 (m, 15H, aromatic), 2.80–5.50 (m, 12H, 3 $PhCH_2$, H-1a, H-1b, H-2, H-3, H-4, H-5), 1.26 (s, 1H, OH); ^{13}C NMR (50 MHz, $CDCl_3$): δ 176.6 (C-6), 157.1 (*C*(O)OCH_2Ph), 139.2, 138.3, 136.3, 128.5, 128.3, 128.0, 127.8, 127.6, 127.3 (aromatic), 83.0 and 77.6 (C-2 and C-3), 74.9 and 72.6 (2 $PhCH_2$), 71.0 (C-4), 68.1 ($PhCH_2$), 58.6 (C-5), 44.0 (C-1); MS-ESI: $[M+H]^+$ 492.2, $[M+NH_4]^+$ 509.2, $[M+Na]^+$ 514.2, $[M+K]^+$ 530.2. Anal. Calcd for $C_{28}H_{29}NO_7$: C, 68.42; H, 5.95; N, 2.85. Found: C, 68.45; H, 5.93; N, 2.84.

4.35. (1,5-Dideoxy-1,5-imino-L-iditol)uronic acid (6)

A solution of **42** (0.065 g, 0.13 mmol) in a mixture of THF and water (1:1, 3 mL) was hydrogenated in the presence of 10% Pd/C (0.050 g) for 2 days at atmospheric pressure at room temperature. The mixture was filtered through a pad of Celite and the filtrate was concentrated. The residue was purified by column chromatography (2-propanol–acetone–water, 4:1:1) to give a syrup, which was desalted on a column of Sephadex G-25 using water as eluent to afford **6** (0.019 g, 79%) as a white foam; R_f (2-propanol–acetone–water, 4:1:1) 0.36; $[\alpha]_D$ +30.7 (*c* 0.75, H_2O), lit[33] $[\alpha]_D$ +34 (*c* 0.35, H_2O); ^1H NMR (400 MHz, D_2O): δ 4.09 (dd, 1H, $J_{3,4}$ 4.8 Hz, $J_{4,5}$ 2.6 Hz, H-4), 3.87 (dd, 1H, $J_{2,3}$ 3.8 Hz, H-3), 3.83 (m, 1H, H-2), 3.79 (d, 1H, H-5), 3.23 (dd, 1H, $J_{1a,1b}$ 13.5 Hz, $J_{1b,2}$ 2.5 Hz, H-1b), 3.13 (dd, 1H, $J_{1a,2}$ 3.5 Hz, H-1a); ^{13}C NMR (100 MHz, D_2O): δ 173.4 (C-6), 69.2 (C-4), 69.0 (C-3), 66.8 (C-2), 58.3 (C-5), 45.2 (C-1); MS-ESI: $[M+H]^+$ 178.1, $[M+Na]^+$ 200.1. Anal. Calcd for $C_6H_{11}NO_5$: C, 40.68; H, 6.26; N, 7.91. Found: C, 40.70; H, 6.25; N, 7.90.

The ^1H and ^{13}C NMR data are in agreement with those reported.[33]

4.36. 2,3-Di-*O*-benzyl-1,5-dideoxy-1,5-imino-4-*O*-(1-naphthyl)methyl-*N*-(4-nitro)benzenesulfonyl-L-iditol (43)

1 M BH_3·THF (9.0 mL, 9.0 mmol, 3 equiv) and TMSOTf (0.07 mL, 0.39 mmol, 0.13 equiv) were added to a solution of **10b** (2.0 g, 3.0 mmol) in dry CH_2Cl_2 (50 mL) and the mixture was stirred at room temperature under argon for 7 h. The mixture was cooled, Et_3N (5 mL) and MeOH were added, then the mixture was evaporated, and the residue was co-evaporated with MeOH three times. The residue was purified by column chromatography (hexanes–EtOAc, 4:1→7:3) to yield **43** (1.6 g, 93%) as a syrup; R_f (hexanes–EtOAc, 7:3) 0.30; $[\alpha]_D$ +10.5 (*c* 0.95, $CHCl_3$); IR ν_{max} (film): 3446, 2925, 1643, 1529, 1348, 1160, 1087 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.10–8.00 (m, 21H, aromatic), 5.09 (d, 1H, *J* 11.8 Hz, ½$PhCH_2$), 4.91 (d, 1H, *J* 11.8 Hz, ½$PhCH_2$), 4.68 (s, 2H, $^1NaphCH_2$), 4.57 (d, 1H, *J* 11.6 Hz, ½$PhCH_2$), 4.47 (d, 1H, *J* 11.6 Hz, ½$PhCH_2$), 3.99 (m, 1H, $J_{1a,1b}$ 13.5 Hz, $J_{1b,2}$ 7.0 Hz, H-1b), 3.34–3.84 (m, 5H, H-2, H-3, H-4, H-5, H-6b), 3.15 (ddd, 1H, $J_{6a,6b}$ 11.0 Hz, $J_{6a,OH}$ 8.4 Hz, $J_{5,6a}$ 5.5 Hz, H-6a), 2.86 (dd, 1H, $J_{1a,2}$ 11.3 Hz, H-1a), 1.98 (t, 1H, OH); ^{13}C NMR (50 MHz, $CDCl_3$): δ 149.8, 146.0, 138.5, 137.8, 133.8, 133.0, 131.6, 129.2, 128.7, 128.6, 128.4, 128.1, 128.0, 127.8, 127.7, 127.1, 126.6, 126.1, 125.3, 124.3, 123.8 (aromatic), 82.1 (C-3), 78.2 (C-2), 77.3 (C-4), 75.7, 73.2 and 71.9 (2 $PhCH_2$, $^1NaphCH_2$), 58.6 (C-6), 57.0 (C-5), 43.1 (C-1); MS-ESI: $[M+Na]^+$ 691.3. Anal. Calcd for $C_{37}H_{36}N_2O_8S$: C, 66.45; H, 5.43; N, 4.19; S, 4.79. Found: C, 66.46; H, 5.40; N, 4.21; S, 4.75.

4.37. *tert*-Butyl [2,3-di-*O*-benzyl-1,5-dideoxy-1,5-imino-4-*O*-(1-naphthyl)methyl-*N*-(4-nitro)benzenesulfonyl-L-iditol] uronate (44)

Pyridinium dichromate (1.7 g, 4.52 mmol, 2 equiv), acetic anhydride (2.15 mL, 22.6 mmol, 10 equiv), and *tert*-butyl alcohol (4.24 mL, 45.2 mmol, 20 equiv) were added to a stirred solution of **43** (1.5 g, 2.26 mmol) in dry CH_2Cl_2 (20 mL). The mixture was stirred for 19 h at room temperature and was then applied on the top of a silica gel column in EtOAc, with a 5 cm layer of EtOAc on top of the gel. The chromium compounds were allowed to precipitate in the presence of EtOAc, and after 30 min the product was eluted with EtOAc. The crude product was purified by column chromatography (hexanes–EtOAc, 95:5→4:1) to give **44** (0.875 g, 54%) as white crystals; mp 110–111 °C (from EtOAc–hexanes); R_f (hexanes–EtOAc, 4:1) 0.40; $[\alpha]_D$ −24.2 (*c* 0.41, $CHCl_3$); IR ν_{max} (film): 2923, 1730, 1532, 1350, 1165, 1088 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.10–8.30 (m, 21H, aromatic), 5.21 (d, 1H, *J* 11.7 Hz, ½$PhCH_2$), 5.11 (d, 1H, *J* 11.7 Hz, ½$PhCH_2$), 4.80 (d, 1H, $J_{4,5}$ 6.4 Hz, H-5), 4.74 (s, 2H,

^{1}NaphCH$_2$), 4.71 (d, 1H, *J* 11.7 Hz, ½PhCH$_2$), 4.62 (d, 1H, *J* 11.7 Hz, ½PhCH$_2$), 3.84–3.98 (m, 2H, H-1b, H-3), 3.78 (dd, 1H, $J_{2,3}$ 6.7 Hz, $J_{1a,2}$ 9.1 Hz, H-2), 3.42–3.54 (m, 2H, H-4, H-1a), 1.20 (s, 9H, C(CH$_3$)$_3$); ^{13}C NMR (75 MHz, CDCl$_3$): δ 167.3 (C-6), 150.0, 144.8, 138.4, 138.0, 133.6, 132.9, 131.4, 128.8, 128.5, 128.4, 128.3, 128.2, 127.9, 127.8, 127.7, 127.5, 126.5, 126.4, 125.9, 125.1, 124.3, 123.9 (aromatic), 82.9 (*C*(CH$_3$)$_3$), 80.8 (C-3), 78.3 (C-2), 77.3 (C-4), 75.4, 73.2 and 71.4 (2 PhCH$_2$, ^{1}NaphCH$_2$), 57.0 (C-5), 44.2 (C-1), 27.8 (C(*C*H$_3$)$_3$); MS-ESI: [M+Na]$^+$ 761.3. Anal. Calcd for $C_{41}H_{42}N_2O_9S$: C, 66.65; H, 5.73; N, 3.79; S, 4.34. Found: C, 66.60; H, 5.75; N, 3.77; S, 4.39.

4.38. *tert*-Butyl [2,3-di-*O*-benzyl-1,5-dideoxy-1,5-imino-*N*-(4-nitro)benzenesulfonyl-L-iditol]uronate (9b)

Compound **44** (0.850 g, 1.15 mmol) was dissolved in a mixture of MeCN and water (9:1, 10 mL), CAN (1.26 g, 2.3 mmol, 2 equiv) was added and the mixture was stirred for 3 h at room temperature. It was diluted with chloroform (500 mL) and was washed with saturated aq NaHCO$_3$ (200 mL) and water (150 mL). The aqueous layer was back-extracted with chloroform (300 mL). The combined organic layers were dried and concentrated. Column chromatography of the residue (hexanes–EtOAc, 9:1→4:1) gave syrupy **9b** (0.535 g, 78%); R_f (hexanes–EtOAc, 4:1) 0.35; $[\alpha]_D$ +6.4 (*c* 0.47, CHCl$_3$); IR ν_{max} (film): 3448, 2924, 2360, 1728, 1531, 1350, 1144, 1088 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$): δ 8.28 (m, 2H, aromatic), 7.88 (m, 2H, aromatic), 7.20–7.42 (m, 10H, aromatic), 4.90 (d, 1H, *J* 11.4 Hz, ½PhCH$_2$), 4.76 (d, 1H, *J* 11.4 Hz, ½PhCH$_2$), 4.62–4.76 (m, 3H, H-5, PhCH$_2$), 3.91 (ddd, 1H, $J_{1a,1b}$ 12.5 Hz, $J_{1b,2}$ 5.5 Hz, H-1b), 3.60–3.80 (m, 2H, H-3, H-4), 3.50 (ddd, 1H, $J_{2,3}$ 8.1 Hz, $J_{1a,2}$ 10.6 Hz, H-2), 3.20 (dd, 1H, H-1a), 2.84 (d, 1H, $J_{4,OH}$ 4.8 Hz, OH), 1.28 (s, 9H, C(CH$_3$)$_3$); ^{13}C NMR (75 MHz, CDCl$_3$): δ 168.1 (C-6), 150.3, 145.4, 138.4, 137.9, 128.7, 128.5, 128.3, 128.2, 128.1, 128.0, 124.5 (aromatic), 83.9 (*C*(CH$_3$)$_3$), 81.5 (C-3), 77.7 (C-2), 75.4 and 73.3 (2 PhCH$_2$), 71.3 (C-4), 58.4 (C-5), 44.7 (C-1), 28.0 (C(*C*H$_3$)$_3$); MS-ESI: [M+Na]$^+$ 621.2. Anal. Calcd for $C_{30}H_{34}N_2O_9S$: C, 60.19; H, 5.72; N, 4.68; S, 5.36. Found: C, 60.10; H, 5.75; N, 4.65; S, 5.38.

4.39. (2-Azido-3,4-di-*O*-benzyl-6-*O*-chloroacetyl-2-deoxy-α-D-glucopyranosyl)-(1→4)-[*tert*-butyl (2,3-di-*O*-benzyl-1,5-dideoxy-1,5-imino-*N*-(4-nitro)benzenesulfonyl-L-iditol) uronate] (45)

A mixture of **9b** (0.17 g, 0.284 mmol), **7** (0.197 g, 0.355 mmol, 1.25 equiv), and 2,6-di-*tert*-butyl-4-methylpyridine (0.06 g, 0.3 mmol) in a mixture of dry diethyl ether and CH$_2$Cl$_2$ (4:1, 6 mL) was stirred with 4 Å molecular sieves (1 g) at −30 °C under argon for 30 min, then a 1 M solution of Me$_2$S$_2$–Tf$_2$O (0.53 mL, 1.5 equiv/donor) in CH$_2$Cl$_2$ was added. The mixture was stirred for 5 min, then, it was neutralized with Et$_3$N, was diluted with CH$_2$Cl$_2$ (300 mL), and filtered through a pad of Celite. The filtrate was washed with 2 M aq HCl (100 mL), saturated aq NaHCO$_3$ (100 mL), and water (100 mL). The organic layer was dried and concentrated. The residue was purified by column chromatography (hexanes–EtOAc, 9:1→4:1) to give syrupy **45** (0.266 g, 90%); R_f (hexanes–EtOAc, 4:1) 0.38; $[\alpha]_D$ +24.7 (*c* 0.36, CHCl$_3$); IR ν_{max} (film): 2109, 1754, 1722, 1533, 1351, 1328, 1172, 1121 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.02–8.40 (m, 24H, aromatic), 5.23 (d, 1H, $J_{1',2'}$ 3.8 Hz, H-1′), 4.96 (d, 1H, *J* 10.7 Hz, ½PhCH$_2$), 4.89 (2d, 2H, $J \approx 11.0$ Hz, PhCH$_2$), 4.83 (dd, 2H, *J* 10.6 Hz, PhCH$_2$), 4.69 (d, 1H, *J* 11.7 Hz, ½PhCH$_2$), 4.66 (d, 1H, $J_{4,5}$ 6.9 Hz, H-5), 4.63 (d, 1H, *J* 11.7 Hz, ½PhCH$_2$), 4.61 (d, 1H, *J* 10.7 Hz, ½PhCH$_2$), 4.46 (dd, 1H, $J_{5',6b'}$ 1.7 Hz, $J_{6a',6b'}$ 11.5 Hz, H-6b′), 4.22 (dd, 1H, $J_{5',6a'}$ 5.8 Hz, H-6a′), 4.18 (d, 1H, *J* 14.9 Hz, ½C(O)CH$_2$Cl), 4.15 (ddd, 1H, $J_{4',5'}$ 9.7 Hz, H-5′), 4.09 (d, 1H, *J* 14.9 Hz, ½C(O)CH$_2$Cl), 4.04 (dd, 1H, $J_{2,3} \approx J_{3,4}$ 9.4 Hz, H-3), 3.86 (m, 2H, $J_{2',3'}$ 10.5 Hz, $J_{3',4'}$ 8.6 Hz, H-3′ and H-1b), 3.83 (dd, 1H, H-4), 3.54 (ddd, 1H, $J_{1a,2}$ 10.8 Hz, $J_{1b,2}$ 5.6 Hz, H-2), 3.43 (dd, 1H, H-4′), 3.39 (dd, 1H, $J_{1a,1b}$ 12.1 Hz, H-1a), 3.28 (dd, 1H, H-2′), 1.28 (s, 9H, C(CH$_3$)$_3$); ^{13}C NMR (100 MHz, CDCl$_3$): δ 167.4 (O*C*(O)CH$_2$Cl), 166.8 (C-6), 150.2, 145.0, 138.6, 137.8, 137.43, 137.36, 128.6, 128.5, 128.44, 128.40, 128.3, 128.11, 128.07, 128.0, 127.9, 127.6, 127.5, 124.5 (aromatic), 99.8 (C-1′), 83.7 (*C*(CH$_3$)$_3$), 81.0 (C-3), 80.1 (C-3′), 78.3 (C-2), 78.1 (C-4′), 75.9 (C-4), 75.5, 75.4, 75.1 and 73.2 (4 PhCH$_2$), 69.9 (C-5′), 64.7 (C-6′), 63.3 (C-2′), 58.4 (C-5), 43.9 (C-1), 40.9 (C(O)*C*H$_2$Cl), 28.0 (C(*C*H$_3$)$_3$); MS-ESI: [M+Na]$^+$ 1064.2. Anal. Calcd for $C_{52}H_{56}ClN_5O_{14}S$: C, 59.91; H, 5.41; N, 6.72; S, 3.08. Found: C, 59.88; H, 5.39; N, 6.75; S, 3.10.

4.40. (2-Acetamido-3,4-di-*O*-benzyl-6-*O*-chloroacetyl-2-deoxy-α-D-glucopyranosyl)-(1→4)-[*tert*-butyl (2,3-di-*O*-benzyl-1,5-dideoxy-1,5-imino-*N*-(4-nitro)benzenesulfonyl-L-iditol)uronate] (46)

A solution of Me$_3$P in toluene (0.235 mL, 1 M, 0.235 mmol, 1 equiv) was added to a solution of compound **45** (0.235 g, 0.22 mmol) in dry THF (5 mL) at room temperature under argon. After cessation of the nitrogen evolution (~20 min), acetic anhydride (0.021 mL, 0.22 mmol, 1 equiv) was added and the mixture stirred at room temperature for 24 h. It was evaporated and co-evaporated with toluene three times. The product was purified by column chromatography (hexanes–EtOAc, 4:1→3:2) to give **46** (0.156 g, 66%) as a colorless syrup; R_f (hexanes–EtOAc, 3:2) 0.40; $[\alpha]_D$ +42.3 (*c* 0.69, CHCl$_3$); IR ν_{max} (film): 3441, 2924, 1644, 1529, 1456, 1370, 1180, 1027 cm^{-1}; ^{1}H NMR (200 MHz, CDCl$_3$): δ 8.30 (d, 2H, aromatic), 7.90 (d, 2H, aromatic), 7.10–7.42 (m, 20H, aromatic), 5.53 (d, 1H, $J_{2',NH}$ 9.5 Hz, NH), 4.99 (d, 1H, $J_{1',2'}$ 4.0 Hz, H-1′), 4.95 (d, 1H, *J* 12.0 Hz, ½PhCH$_2$), 4.87 (d, 1H, *J* 10.6 Hz, ½PhCH$_2$), 4.77 (d, 1H, *J* 12.0 Hz, ½PhCH$_2$), 4.63 (d, 1H, *J* 11.0 Hz, ½PhCH$_2$), 4.61 (s, 2H, PhCH$_2$), 4.60 (d, 1H, *J* 11.0 Hz, ½PhCH$_2$), 4.57 (d, 1H, *J* 10.6 Hz, ½PhCH$_2$), 4.46 (d, 1H, $J_{6a',6b'}$ 11.0 Hz, H-6b′), 4.30 (dd, 1H, $J_{5',6a'}$ 4.7 Hz, H-6a′), 3.37–4.22 (m, 11H, H-1b, H-2, H-3, H-4, H-5, H-2′, H-3′, H-4′, H-5′ and C(O)CH$_2$Cl), 3.15 (dd, 1H, $J_{1a,1b}$ 12.3 Hz, $J_{1a,2}$ 10.6 Hz, H-1a), 1.38 (s, 3H, NHC(O)CH$_3$), 1.32 (s, 9H, C(CH$_3$)$_3$); ^{13}C NMR (50 MHz, CDCl$_3$): δ 169.9 (NH*C*(O)CH$_3$), 167.4 (O*C*(O)CH$_2$Cl), 166.7 (C-6), 145.3, 138.1, 137.9, 137.8, 137.6, 128.7, 128.6, 128.5, 128.3, 128.2, 128.1, 128.0, 127.1, 124.6 (aromatic), 100.8 (C-1′), 83.7 (*C*(CH$_3$)$_3$), 80.6, 80.1, 78.3, 77.6 and 77.3 (C-2, C-3, C-4, C-3′, and C-4′), 75.2, 75.1, 75.0 and 73.1 (4 PhCH$_2$), 70.5 (C-5′), 64.6 (C-6′), 58.5 (C-5), 52.3 (C-2′), 43.9 (C-1), 40.9 (C(O)*C*H$_2$Cl), 28.1 (C(*C*H$_3$)$_3$), 22.9 (NHC(O)*C*H$_3$); MS-ESI: [M+H]$^+$ 1066.1, [M+Na]$^+$ 1088.2, [M+K]$^+$ 1104.1. Anal. Calcd for $C_{54}H_{60}ClN_3O_{15}S$: C, 61.27; H, 5.71; N, 3.97; S, 3.03. Found: C, 61.30; H, 5.68; N, 3.95; S, 3.05.

4.41. (2-Acetamido-3,4-di-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→4)-[*tert*-butyl (2,3-di-*O*-benzyl-1,5-dideoxy-1,5-imino-*N*-(4-nitro)benzenesulfonyl-L-iditol) uronate] (47)

To a solution of **46** (0.15 g, 0.15 mmol) in dry DMF (3 mL) a freshly prepared solution of HDTC (1.06 mL, 0.42 M, 0.442 mmol, 3 equiv) was added and the mixture was stirred at room temperature for 20 min. The mixture was diluted with CH$_2$Cl$_2$ (300 mL), and was washed with 2 M aq HCl (100 mL), saturated aq NaHCO$_3$ (100 mL), and water (100 mL), it was dried and evaporated. Column chromatography (toluene–acetone, 9:1→7:3) gave **47** (0.094 g, 65%) as a colorless syrup; R_f (toluene–acetone, 9:1) 0.24; $[\alpha]_D$ +37.4 (*c* 0.27, CHCl$_3$); IR ν_{max} (film): 3425, 2924, 1637, 1529, 1370, 1180, 1027 cm^{-1}; ^{1}H NMR (200 MHz, CDCl$_3$): δ 8.28 (d, 2H, aromatic), 7.93 (d, 2H, aromatic), 7.10–7.50 (m, 20H, aromatic), 5.55 (d, 1H, $J_{2',NH}$ 9.5 Hz, NH), 5.01 (d, 1H, $J_{1',2'}$ 3.6 Hz, H-1′), 4.93 (d, 1H, *J* 11.3 Hz, ½PhCH$_2$), 4.85 (d, 1H, *J* 11.0 Hz, ½PhCH$_2$), 4.80 (d, 1H, *J* 11.3 Hz, ½PhCH$_2$), 4.78 (d, 1H, *J* 11.0 Hz, ½PhCH$_2$), 4.64 (d, 1H, *J* 12.1 Hz, ½PhCH$_2$), 4.60 (s, 2H, PhCH$_2$), 4.59 (d, 1H, *J* 12.1 Hz, ½PhCH$_2$), 4.32 (ddd, 1H, $J_{4',5'}$ 10.0 Hz, $J_{5',6a'}$ 3.3 Hz, $J_{5',6b'}$ 3.7 Hz, H-5′), 3.47–4.20 (m, 10H, H-1a, H-2, H-3, H-4, H-5, H-2′, H-3′, H-4′,

H-6a′, H-6b′), 3.15 (dd, 1H, $J_{1a,1b}$ 12.5 Hz, $J_{1a,2}$ 11.4 Hz, H-1a), 2.20 (s, 1H, OH), 1.37 (s, 3H, NHC(O)CH_3), 1.28 (s, 9H, C(CH_3)$_3$); ^{13}C NMR (50 MHz, $CDCl_3$): δ 169.9 (NH*C*(O)CH_3), 166.6, (C-6), 150.2, 145.5, 138.3, 138.1, 137.9, 137.6, 129.1, 128.7, 128.6, 128.5, 128.3, 128.2, 128.03, 127.96, 127.9, 127.8, 127.2, 125.4, 124.4 (aromatic), 100.9 (C-1′), 83.5 (*C*(CH_3)$_3$), 80.5, 80.0, 78.5, 78.2 and 77.6 (C-2, C-3, C-4, C-3′, and C-4′), 75.1, 75.0, 74.8 and 73.1 (4 PhCH_2), 73.0 (C-5′), 62.0 (C-6′), 58.3 (C-5), 52.5 (C-2′), 43.8 (C-1), 27.9 (C(CH_3)$_3$), 22.8 (NHC(O)*C*H_3); MS-ESI: $[M+Na]^+$ 1004.6, $[M+K]^+$ 1020.5. Anal. Calcd for $C_{52}H_{59}N_3O_{14}S$: C, 63.59; H, 6.06; N, 4.28; S, 3.26. Found: C, 63.60; H, 6.09; N, 4.30; S, 3.22.

4.42. (2-Acetamido-3,4-di-*O*-benzyl-2-deoxy-6-*O*-sulfo-α-D-glucopyranosyl)-(1→4)-[(2,3-di-*O*-benzyl-1,5-dideoxy-1,5-imino-*N*-(4-nitro)benzenesulfonyl-L-iditol)uronic acid] (48)

Compound **47** (0.09 g, 0.09 mmol) was dissolved in a solution of TFA in CH_2Cl_2 (20 v/v %, 3 mL) and was stirred at room temperature for 2 h. The reaction mixture was evaporated and co-evaporated with toluene twice. The crude syrup was dissolved in dry DMF (2 mL) and sulfur trioxide pyridine complex (0.03 g, 0.019 mmol, 2 equiv) was added. The mixture was stirred at room temperature for 10 min, the excess of reagent was decomposed with saturated aq $NaHCO_3$, and the mixture was concentrated. The residue was purified by column chromatography (CH_2Cl_2–MeOH, 9:1→4:1). The material obtained was converted into the sodium salt by stirring with Dowex 50WX8 [Na^+] resin in MeOH, the mixture was filtered and the filtrate was concentrated to give **48** (0.091 g, 94%) as a colorless syrup; R_f (CH_2Cl_2–MeOH, 9:1) 0.50; $[\alpha]_D$ +27.2 (*c* 0.41, CH_3OH); IR ν_{max} (film): 3446, 1636 cm^{-1}; ^{1}H NMR (200 MHz, CD_3OD): δ 8.14 (d, 2H, aromatic), 7.92 (d, 2H, aromatic), 7.00–7.40 (m, 20H, aromatic), 4.97 (br s, 1H, H-1′), 4.81 (s, 4H, 2 PhCH_2), 3.66–4.76 and 3.04–3.48 (2 m, 12+4H, H-1a, H-1b, H-2, H-3, H-4, H-5, H-2′, H-3′, H-4′, H-5′, H-6a′, H-6b′, and 2 PhCH_2), 1.56 (s, 3H, NHC(O)CH_3); ^{13}C NMR (50 MHz, CD_3OD): δ 174.9 (C-6), 172.9 (NHC(O)CH_3), 151.4, 146.7, 140.0, 139.7, 139.6, 139.2, 129.7, 129.5, 129.3, 129.24, 129.18, 129.1, 128.9, 128.6, 128.5, 128.2, 125.4 (aromatic), 99.6 (C-1′), 81.9, 80.8, 79.6, 78.0 and 75.6 (C-2, C-3, C-4, C-3′, and C-4′), 76.3, 75.9, 75.0 and 73.0 (4 PhCH_2), 71.9 (C-5′), 67.9 (C-6′), 61.6 (C-5), 54.2 (C-2′), 44.6 (C-1), 22.8 (NHC(O)CH_3); MS-ESI: $[M+H_2NaA]^+$ 1028.34 $[M+HNa_2A]^+$ 1050.4, $[M+HNa_3A]^+$ 1072.4. Anal. Calcd for $C_{48}H_{50}N_3O_{17}S_2$: C, 57.36; H, 5.01; N, 4.18; S, 6.38. Found: C, 57.33; H, 5.05; N, 4.15; S, 6.40.

4.43. (2-Acetamido-2-deoxy-6-*O*-sulfo-α-D-glucopyranosyl)-(1→4)-[(1,5-dideoxy-1,5-imino-L-iditol)uronic acid] disodium salt (5)

PhSH (0.011 mL, 0.11 mmol, 1.2 equiv) and dry Et_3N (10 drops, pH ca. 8) were added to a stirred solution of **48** (0.09 g, 0.09 mmol) in dry DMF (2 mL), and the mixture was stirred for 24 h at room temperature. It was neutralized with saturated aq $NaHCO_3$, concentrated, and the residue was purified by column chromatography (CH_2Cl_2–MeOH, 9:1→7:3) to give the denosylated compound (0.057 g, 73%). To a solution of this syrup (0.057 g, 0.07 mmol) in a mixture of THF and water (1:1, 5 mL) two drops of acetic acid was added, and the mixture was hydrogenated in the presence of 10% Pd/C (0.050 g) for 4 days at atmospheric pressure at room temperature. The mixture was neutralized with saturated aq $NaHCO_3$, was filtered through a pad of Celite, and the filtrate was concentrated. The residue was purified by column chromatography (2-propanol–acetone–water, 4:1:1) to give a syrup, which was desalted on a column of Sephadex G-25 using water as eluent to afford **5** (0.014 g, 60%) as a white foam; R_f (2-propanol–acetone–water, 4:1:1) 0.22; $[\alpha]_D$ +37.5 (*c* 0.2, water); ^{1}H NMR (300 MHz, D_2O): δ 5.02 (d, 1H, $J_{1',2'}$ 3.6 Hz, H-1′), 4.27 (br s, 1H, H-4), 4.23 (dd, 1H, $J_{6a',6b'}$ 11.1 Hz, $J_{5',6b'}$ 3.1 Hz, H-6b′), 4.15 (m, 1H, H-3), 4.09 (dd, 1H, $J_{5',6a'}$ 2.9 Hz, H-6a′), 3.97 (m, 2H, H-2, H-5), 3.89 (dd, 1H, $J_{2',3'}$ 10.1 Hz, H-2′), 3.81 (ddd, 1H, $J_{4',5'}$ 9.2 Hz, H-5′), 3.57 (dd, 1H, $J_{3',4'}$ 9.5 Hz, H-3′), 3.49 (dd, 1H, H-4′), 3.30 (m, 2H, H-1a, H-1b), 1.89 (s, 3H, NHC(O)CH_3); ^{13}C NMR (75 MHz, D_2O): δ 173.3 (C-6), 169.9 (NH*C*(O)CH_3), 93.1 (C-1′), 70.4 (C-3′), 70.0 (C-4), 69.4 (C-5′), 67.9 (C-4′), 65.3 (C-6′), 64.2 (C-2), 61.8 (C-3), 56.7 (C-5), 52.1 (C-2′), 44.2 (C-1), 21.0 (NHC(O)*C*H_3); MS-ESI: $[M-H]^-$ 459.3. Anal. Calcd for $C_{14}H_{22}N_2Na_2O_{13}S$: C, 33.34; H, 4.40; N, 5.55; S, 6.36. Found: C, 33.30; H, 4.43; N, 5.57; S, 6.40.

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Supplementary data

The supplementary data associated with this article can be found in the on-line version at doi:10.1016/j.tet.2010.07.055. These data include MOL files and InChIKeys of the most important compounds described in this article.

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