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Synthesis of modified *Trichinella spiralis* disaccharide epitopes and a comparison of their recognition by chemical mapping and saturation transfer difference NMR

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ABSTRACT

A rat monoclonal antibody 9D4 raised against the cell surface *N*-glycan of the parasite *Trichinella spirallis* protects rats against further infection. The terminal disaccharide β-D-Tyv*p*(1→3)β-D-GalNAc*p* (**2**) represents the immunodominant portion of the antigenic determinant. Chemical mapping of the antibody binding site by functional group modification employing monodeoxy and mono-*O*-methyl congeners identified key polar contacts and topography of the bound disaccharide. We report here a comparison of the chemical mapping studies with the antigen topography inferred from saturation transfer difference (STD) NMR experiments. During chemical mapping several congeners of compound **2** showed substantially enhanced binding. Pairing of these functional group modifications to create derivatives **6** and **7** did not show additive free energy gains and STD NMR data point to small variations in mode of binding as a probable cause. Improved syntheses of disaccharides **2**–**7** are reported.

1. Introduction

The monoclonal antibody (mAb) IgG 9D4 raised against *Trichinella spiralis*, a pathogenic nematode that causes trichinosis, exhibits high affinity for the terminal tetrasaccharide **1** of the cell surface *N*-glycan of the pathogen (Fig. 1).[1,2] The binding site of the antibody contacts all four sugar moieties, while the majority of its binding energy is focused around the rare dideoxyhexose containing disaccharide β-D-Tyv*p*-(1→3)-β-D-Gal*p*NAc **2**.[2–4] The recognition surface of **2** that is accepted in the IgG 9D4 antibody binding site was identified by a chemical mapping study.[5] The activity changes accompanying monodeoxy and mono-O-methylation of each hydroxyl group of **2** established that polar contacts involved the tyvelose and GalNAc C-4 hydroxyl groups, with tyvelose C2 and GalNAc C4 and C6 hydroxyl group sitting close to or at the periphery of the binding site. The acetamido group of the GalNAc moiety is not crucial to binding, as its replacement by a hydroxyl group has only a subtle effect on activity. It should also be noted that a disaccharide in which a GlcNAc residue replaces GalNAc is inactive indicating steric constraints at the C4 position of GalNAc.

During the course of functional group modification several substantial gains in affinity were observed. The free amino sugar derivative **3** is a sixfold better binder than the native disaccharide **2**. The hydroxyl group at C-6 is clearly at the periphery of the binding site, as deoxygenation has little impact on the binding, while O-methylation (compound **4**) provides an 18-fold affinity gain, most likely by the introduction of new van der Waals' interactions on the edge of the binding pocket. A similar situation occurs for the 2-*O*-methyl derivative of the tyvelose residue (disaccharide **5**), with a ninefold activity gain.

Saturation transfer difference (STD) NMR reveals the relative proximity of each proton of the ligand to the protein, thus providing a complementary approach to epitope mapping.[6] In this paper, STD NMR experiments were carried out to analyze the interaction between mAb 9D4 and a series of disaccharide ligands **2**–**7**, for which a concise and improved synthetic strategy was developed. The results from STD NMR studies are compared with the previous chemical mapping studies.[5] In addition, paired functional group modifications in disaccharides **6** and **7** (Fig. 1) were investigated by competitive inhibition and STD NMR.

2. Results and discussion

2.1. Synthesis of disaccharides 2–7

To get easy access to a library of ligands containing the rare sugar tyvelose and a challenging 1,2-*cis* β glycosidic linkage, an

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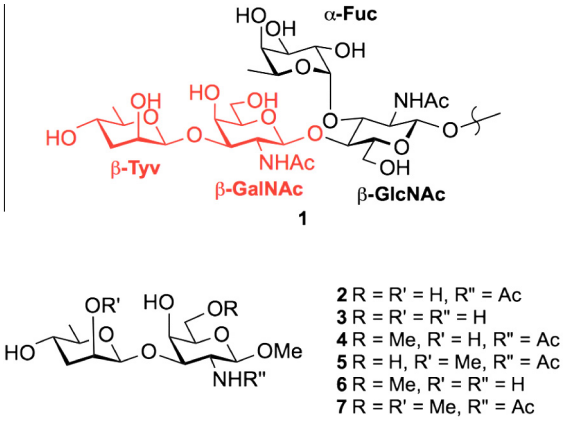
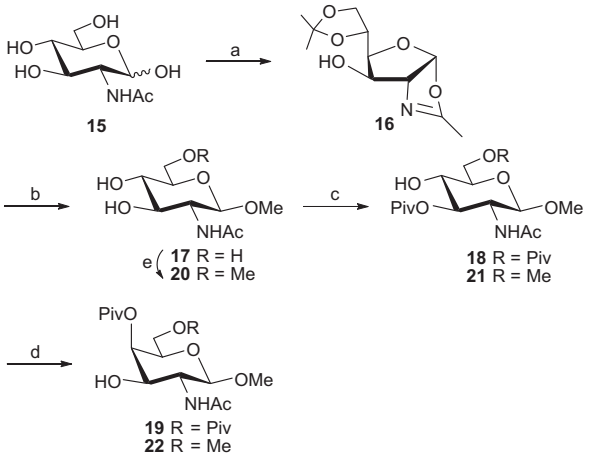


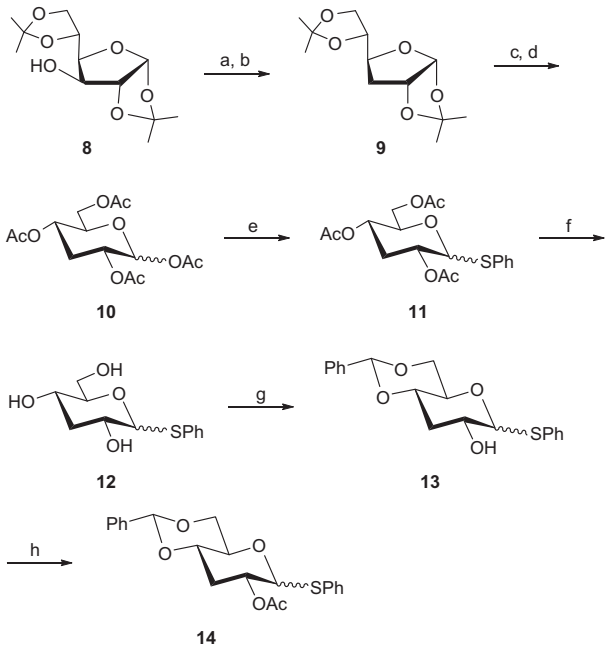
Figure 1. Structure of native terminal tetrasaccharide of the *N*-glycan expressed on the cell surface of *Trichinella spiralis* parasite, and its disaccharide congener **2**. Synthetic disaccharide targets, native terminal disaccharide **2**, disaccharides (**3**, **4**, and **5**) with higher affinity to IgG 9D4 than **2** based on the previous chemical mapping study, and disaccharides with paired functional group modification (**6** and **7**).



Scheme 2. Synthesis of acceptors. Reaction conditions: (a) $FeCl_3$, acetone, reflux, 20 min; (b) MeOH, *p*-TsOH, rt, 81% over two steps; (c) PivCl, pyridine, 90%; (d) Tf_2O, pyridine, then H_2O, reflux, 89%; (e) $(Bu_3Sn)_2O$, toluene, reflux; then MeI, 80% over two steps.

efficient and concise synthetic strategy is desirable. The target disaccharides **2**–**7** were synthesized using the new approach that started from acetonides of glucofuranose and 2-acetamido-2-deoxy glucofuranose (Schemes 1–3).

Synthesis of the tyvelose moiety was envisaged as proceeding via a 3-deoxy glucose donor with manipulation of stereochemistry at C2 and functionality at C6 conducted on disaccharide derivatives. Barton–McCombie deoxygenation[7] of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose **8** gave 3-deoxy furanose **9** (Scheme 1). Hydrolysis of the isopropylidene protecting groups and acetylation gave an anomeric mixture ($\alpha/\beta = 1/2$) of pyranose **10**,[8] This tetraacetate was converted to thiophenyl glycoside **11** by reaction with boron trifluoride and thiophenol.[9,10] Transesterification gave **12** and subsequently 4,6-*O*-benzylidene acetal was installed to afford **13**. The glycosyl donor **14** was obtained following acetylation of **13**. Compounds **11** to **14** could be isolated to obtain α and β separately; however, a mixture of α/β isomers ($\alpha/\beta = 1/2$) of the donor **14** was employed for the glycosylation.[11]



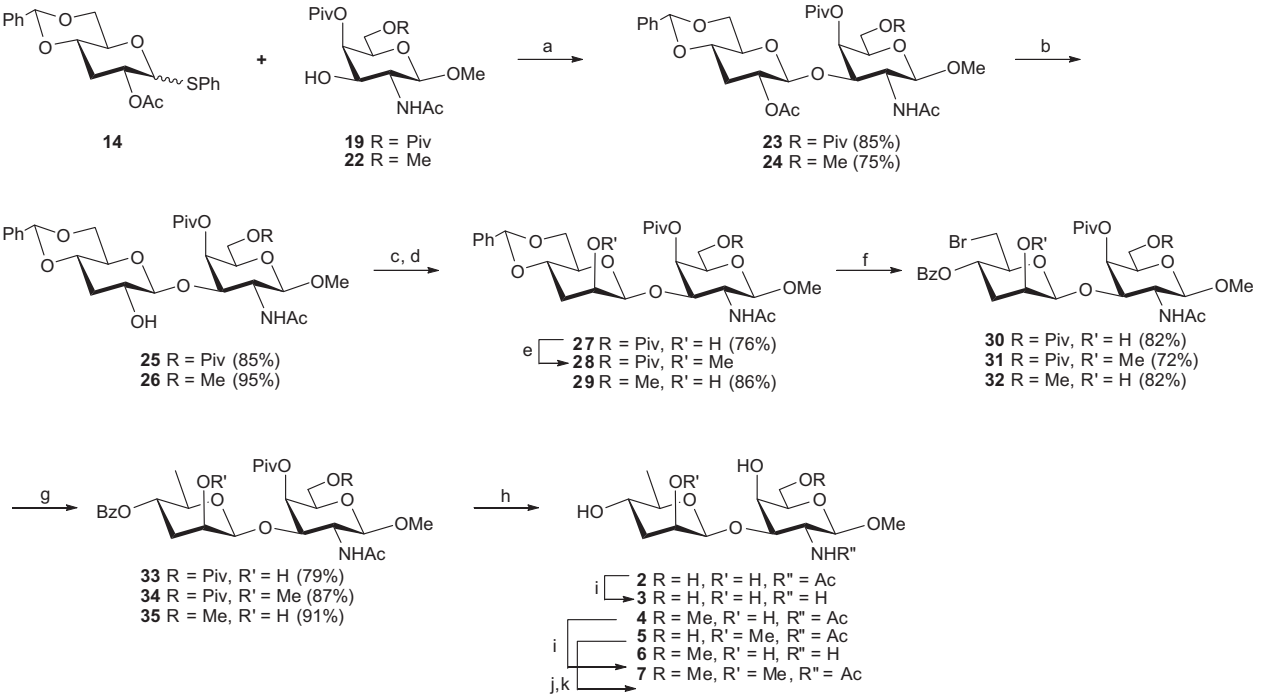
Scheme 1. Synthesis of donor. Reaction conditions: (a) NaH, imidazole, then CS_2, then MeI; (b) Bu_3SnH, AIBN, 75% over two steps; (c) 60% HOAc–H_2O, 80 °C; (d) Ac_2O, pyridine, 93% over two steps; (e) PhSH, $BF_3{\cdot}OEt_2$, 79%; (f) NaOMe, MeOH, quantitative; (g) $PhCH(OMe)_2$, CSA, 96%; (h) Ac_2O, pyridine, 98%.

Previously, the selectively protected GalNAc acceptor was synthesized from 2-acetamido-2-deoxy-D-galactose by formation of a 4,6-*O*-benzylidene acetal.[5] However, further modifications of the disaccharides were low yielding. A facile synthesis of 2-acetamido-2-deoxy-β-D-glucopyranosides from 2-acetamido-2-deoxy-D-glucose via a furanosyl oxazoline was reported by our group,[12] and here we adopted the methodology to provide an inexpensive and convenient route to GalNAc acceptors. Briefly, **15** was stirred with anhydrous ferric chloride in acetone at reflux to give oxazoline **16**,[13] and methyl pyranoside **17** was generated after treatment with a stoichiometric amount of *p*-toluenesulfonic acid in methanol (Scheme 2). The 3- and 6-hydroxyl groups of compound **17** were protected selectively as pivaloate esters[14] to afford **18** (Scheme 2). Treatment with triflic anhydride provided a 4-*O*-triflate, which reacted in situ with water to achieve a configurational change from glucose to galactose and a convenient migration of pivaloyl group from *O*-3 to *O*-4.[15,16]

In order to increase the reactivity of the acceptor and to limit modifications performed on disaccharides, methylation of the 6-hydroxyl group of the GalNAc moiety was performed on compound **17**. Treatment of **17** with bistributyltin oxide[17] under azeotropic conditions generated a tributylstannyl ether, which was subsequently displaced by methyl iodide to obtain the desired methylation product **20** (Scheme 2). The reactions to transform compound **20** to **22** resembled those employed for the transformation of compound **17** to **19**.

Thiolglycoside **14** was activated by *N*-iodosuccinimide/triflic acid,[9,10] and glycosylation of **19** and **22** gave disaccharides **23** and **24** in good yield (Scheme 3). Selective removal of the 2′-*O*-acetyl group in the presence of the pivaloyl group was achieved by stirring compounds **23** and **24** in a methanolic solution of guanidine and sodium methoxide to generate disaccharides **25** and **26**.[18]

Disaccharides **25** and **26** were each oxidized by Swern-type oxidation,[19,20] followed by reduction of the respective ketones using L-selectride[21] in THF to give the epimers **27** and **29**. Methylation of **27** by treatment of MeI/NaH gave the methylated tyvelose derivative **28**. A Hanessian–Hullar reaction converted compounds **27**, **28**, and **29** to the corresponding 6-bromo-6-deoxy disaccharides



Scheme 3. Synthesis of the disaccharides **2**–**7**. Reaction conditions: (a) NIS, TfOH, MS 4 Å; (b) NaOMe, Guanidine; (c) DMSO, Ac_2O; (d) L-selectride; (e) NaH, MeI; (f) NBS, CCl_4; (g) Bu_3SnH, AIBN, Toluene; (h) NaOMe, MeOH; (i) KOH, EtOH; (j) Bu_2SnO, MeOH; (k) MeI, CsF, DMF.

30, **31**, and **32**,[22–24] which were then subjected to tributyltin hydride/AIBN mediated radical reaction to afford 6′-deoxy disaccharides **33**, **34**, and **35**.[25] Transesterification gave the final disaccharides **2**, **5**, and **4**, respectively. The amino disaccharide derivatives **3** and **6** were produced in quantitative yields after stirring compounds **2** and **4** in ethanolic KOH solution at reflux. Methylation of compound **5** via stannyl acetal formation with dibutyltin oxide in dry methanol, followed by addition of MeI, gave the di-*O*-methylated disaccharide **7**.[26]

2.2. Binding of disaccharides 2–7 to antibody IgG 9D4

Competitive enzyme linked immunosorbent assay (ELISA) was used to determine IC_{50} values of disaccharides **2**–**7** for binding by mAb 9D4.[5] Briefly, the ELISA plate was coated with a synthetic [β-D-Tyv*p*-(1→3)-β-D-Gal*p*NAc]$_8$-BSA glycoconjugate, and antibody was added to antigen coated plates in the presence of increasing concentrations of synthetic disaccharide ligands. Bound antibody was revealed by incubation with a horseradish peroxidase (HRP)-labeled goat anti-rat IgG. Percent inhibition was calculated by comparison with control wells without synthetic inhibitor. Compared with the previously identified tighter binding ligands **3**, **4**, and **5** (IC_{50} values in Fig. 3), containing single site modifications, compounds **6** and **7** with IC_{50} values of 8 μM and 10 μM (Fig. 2) did not result in increased binding affinity, despite pairing of the favorable functional group changes.

In the STD NMR experiments, we wish to compare the binding results of disaccharides **2**–**7**, to see whether the differences in binding activities measured by ELISA could be reflected by STD effects. The STD NMR spectrum and its reference spectrum for each of the disaccharides **2** to **7** were obtained using similar parameters. Only the resonances that could be unambiguously assigned were used for calculating amplification factors η, the ratio of the intensity of the signal in the difference spectrum (I_{STD}) and the corresponding signal in the reference spectrum (I_0), multiplied by ligand excess.

$$\eta = I_{STD}/I_0 \times \text{ligand excess}$$

The amplification factor η is normalized by using the proton with the highest saturation transfer set to 100% (Tyv H-6 protons in this case), and all the amplification factors of other signals are scaled to its percentage values. Greater η value indicates stronger STD effect and closer contact with the protein. The STD epitope mapping of all six compounds **2** to **7** in normalized η values is presented in Fig. 3 and Table 1,

2.3. STD effects observed for the tyvelose residue

The tyvelose residue is mostly buried in the binding site. While the whole sugar experiences moderate to high STD effects at all positions, H-6′ and H-5′ protons appear to be the closest to the protein binding pocket. The weak saturation transfer to the methoxyl group at C-2′ is consistent with the positioning of this group at the rim of the binding site. Tyvelose H-4′ of compound **2** displays strong saturation transfer, indicating its close proximity to the antibody. Chemical mapping studies showed the 4-hydroxyl group was an essential polar contact. Thus the hydroxyl group at C-4′ forms a hydrogen bond with the binding site, and on the other hand, the H-4′ is in close contact with a hydrophobic pocket in the antibody. The H-5′ and H-6′ of tyvelose ring also display strong STD effects in all six compounds, suggesting both H-5′ and H-6′ are involved in hydrophobic interactions with the binding site. Together with H-4′ and 4′-hydroxyl group, H-5′ and H-6′ are envisaged to be buried in the binding site. H-1′, H-2′, and H-3′ atoms of the tyvelose epitope show moderate to strong STD effects indicating close proximity to the surface of the site even though this part of the tyvelose ring is not buried as deeply as the other half. The antibody displayed ninefold higher affinity for the 2-O-methylated derivative **5** as compared to the affinity for the native ligand **2**, thus clearly suggesting the peripheral position of its 2-hydroxyl group. From this evidence it is concluded that the H-1′, H-2′, and H-3′ of tyvelose lie along a hydrophobic surface in the binding

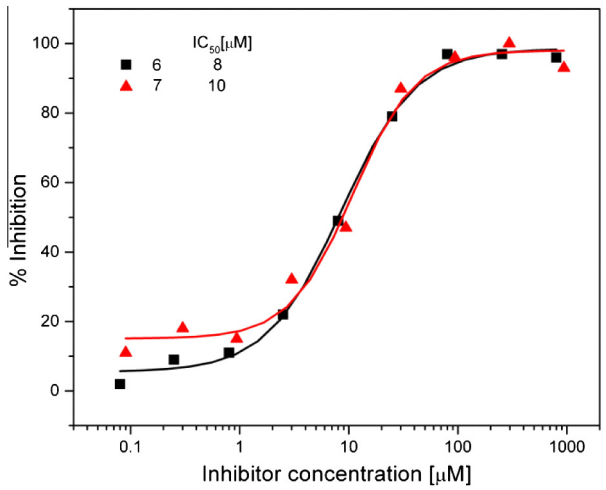


Figure 2. Inhibition curve of disaccharides **6** and **7** with rat monoclonal antibody IgG 9D4. Each point was the average of triplicate measurements and the standard deviation on each point was ±5% or better.

pocket, while the 2-hydroxyl group stretches out of the binding site, the edge of which is lipophilic, as inferred from the increased binding affinity via the introduction of a 2-methoxy group.

2.4. STD effects observed for the GalNAc residue

The GalNAc moiety exhibits weak to moderate saturation transfer effects. Since H-4 is in close contact with the protein, this group experiences the strongest STD effect. All H-4 protons of the GalNAc moiety of the six disaccharides demonstrate strong STD effects, suggesting its close contact with the binding site. This is consistent with the result from chemical mapping that steric clash at C-4 occurred when it was epimerized or O-methylated. The majority of the binding energy at C-4 is therefore inferred to derive from van der Waals' interaction between H-4 and the binding site. This is also supported by the chemical mapping, where the 4-deoxy GalNAc derivative did not show a significant reduction in binding.

All six compounds experience moderate saturation transfer at the H-6 of GalNAc, and the methyl groups at O-6 of compounds **4**, **6**, and **7** experience moderate to strong STD effects. Chemical mapping inferred that C-6 is located at the periphery of the binding site and STD effects support this conclusion. The enhancement in binding energy by methylation at O-6 is realized by the introduction of hydrophobic interaction at the edge of the binding pocket. The 6-*O*-methyl derivative **4** consistently shows stronger STD effects at most hydrogen atoms of the GalNAc ring and also C-3′ of tyvelose. This suggests that either disaccharide **4** binds more deeply or in an altered orientation. Since nearly all protons experience moderate to strong STD effects, disaccharide **4** must be bound in an orientation that results in greater contact with binding site.

In the GalNAc epitope, the 2-acetamido group shows weak to moderate STD effects in most of the compounds **2** to **7**, which is indicative that this group is not in close contact with the antibody. Removal of the *N*-acetyl group resulted in a better ligand **3**, as revealed by chemical mapping. This leads to the conclusion that the 2-acetamido group of the native disaccharide ligand **2** is exposed to bulk solvent, and its free amino sugar congener **3** achieves better binding with the antibody possibly via water-mediated hydrogen

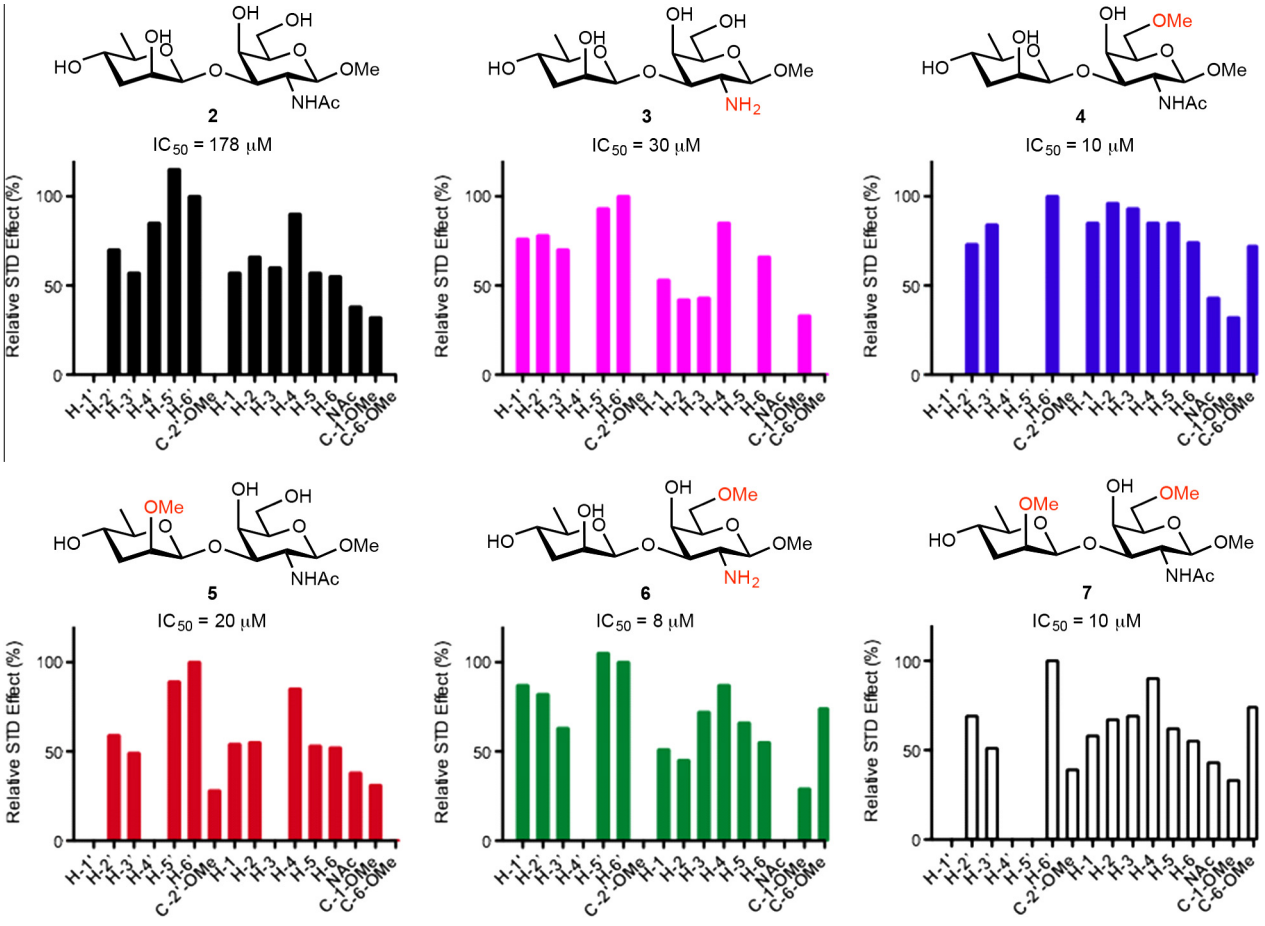


Figure 3. Relative STD effects for disaccharides **2**–**7** interacting with monoclonal antibody IgG 9D4.

Table 1
Relative STD effects for disaccharides **2** to **7** interacting with mAb IgG 9D4

Proton position	Tyvelose residue							GlcNAc residue								
	H-1′	H-2′	H-3′	H-4′	H-5′	H-6′	C-2′-OMe	H-1	H-2	H-3	H-4	H-5	H-6	NAc	C-1-OMe	C-6-OMe
Compound **2**	—	70	57	85	115	100	NA	57	66	60	90	57	55	38	32	NA
Compound **3**	76	78	70	—	93	100	NA	53	42	43	85	—	66	NA	33	NA
Compound **4**	—	73	84	—	—	100	NA	85	96	93	85	85	74	43	32	72
Compound **5**	—	59	49	—	89	100	28	54	55	—	85	53	52	38	31	NA
Compound **6**	87	82	63	—	105	100	NA	51	45	72	87	66	55	NA	29	74
Compound **7**	—	69	51	—	—	100	39	58	67	69	90	62	55	43	33	74

Protons that are not available in the molecule are labeled as NA; protons whose STD effects cannot be calculated due to spectral overlapping are labeled as '—'.

bonding. Other hydrogens of the GalNAc ring exhibit moderate STD effects in all six compounds.

Combination of functional group modifications in compounds **6** and **7** did not result in additive free energy gains. STD NMR suggested that could be explained by small relative movement of the tyvelose and GalNAc residues. This probable conformational alteration was also observed for compound **4**, as all of its hydrogens along the GalNAc ring experience distinct and stronger STD effects as compared to the other five compounds. However, without coordinates for the protein residues of the binding site, it is impossible to develop a quantitative interpretation of the data.

2.5. Conclusions

A concise synthetic strategy to obtain disaccharides **2**–**7** was developed. The binding studies of compounds **2**–**7** revealed the disaccharide epitope is bound quite deeply in the antibody site, and nearly all protons experience moderate to strong STD effects. Chemical mapping showed mAb 9D4 recognizes the disaccharide via H-bond with tyvelose O-4′ and the 6′-deoxy group buried in the binding site with the C-2 position at the periphery of the site. For the GalNAc residue there are no crucial polar contacts, but C-4 and C-5 are in close contact with the protein and C-6 is located at the periphery of the site and the 4-OH group likely accepts a hydrogen bond from a solvent exposed binding site amino acid.

3. Experimental

3.1. General methods

All chemical reagents were of analytical grade, and used as supplied. Organic solvents in reactions were dried according to common literature protocols. All non-hydrolytic reactions were conducted under a positive pressure of argon. Analytical thin layer chromatography (TLC) was performed on silica gel 60-F_{254} (Merck). Plates were visualized by ultraviolet (UV) light, or treatment with ethanolic solution of sulfuric acid containing anisaldehyde, followed by heating. Molecular sieves were stored in an oven (>170 °C), and flame-dried in a flask under vacuum before use. Column chromatography used silica gel (SiliCycle, F60, 40–63 μm, 60 Å) and solvents were of reagent grade, and used as supplied. High performance liquid chromatography (HPLC) was performed using a Waters 2487 Dual λ UV absorbance detector and separations were done on a Beckman C_{18} silica column. ^{1}H NMR spectra were recorded at 400, 500, or 600 MHz and ^{13}C NMR spectra were recorded at 100 or 125 MHz. First order chemical shifts are reported in δ (ppm) using residual solvent signals from deuterated solvents as references. For samples in D_2O, the chemical shifts are referenced to external acetone (0.1% v/v) at δ 2.225. Signals in ^{1}H and ^{13}C NMR spectra were assigned with the aid of two dimensional COSY, HMQC. and HMBC spectra. NMR data reported here are labeled as IUPAC nomenclature for carbohydrate molecules. For some signals in ^{1}H NMR spectra, the coupling patterns were reported as multiplets due to high order coupling or signal overlap. Mass spectrometry was performed under positive/negative-mode electrospray ionization (ESI) on a Micromass ZabSpec Hybrid Sector-TOF. Microanalyses were performed by the analytical services of the Department of Chemistry in University of Alberta. Optical rotations were measured in a 10 cm cell with a Perkin-Elmer 241 polarimeter at 22 ± 2 °C and specific rotation $[\alpha]_D$ values are given in units of 10^{-1} deg cm^2 g^{-1}, and the concentrations are recorded in units of g (100 mL)$^{-1}$.

3.2. Enzyme-linked immunosorbent assays (ELISA)

Enzyme immunoassays were performed in triplicate in a 96-well microtiter plate with monoclonal antibody IgG 9D4.(1) The microtiter plates were coated by incubation with the disaccharide glycoconjugate, [β-D-Tyv*p*-(1→3)-β-D-GalNAc*p*]$_8$-BSA (100 μL/well, 1 μg/mL) at 4 °C overnight (18 h), then washed five times with tween-PBS solution. Plates were patted dry, and blocked with a phosphate buffered saline (PBS) solution of 2% BSA (100 μL/well) for 1 h at rt. After washing the plate, a fixed volume of antibody IgG 9D4 solution (100 μL/well, at 1.0×10^{-4} dilution of ascites fluid) containing increasing concentrations of disaccharide ligands **2** to **7** were added, and control wells containing no inhibitor were used to establish the reference for IgG inhibition. After 24-hour incubation at rt, the plate was washed, and a solution of goat anti-rat IgG antibody conjugated with horse radish peroxidase (100 μL, 1:5000 dilution/well) was added and incubated for 1 h at rt. The labeled secondary antibody was detected according to the manufacturer's suggestions (Kirkegaard and Perry Lab, Mandel, Guelph, ON). The plate was washed, and 3,3′,5,5′-tetramethylbenzidine solution (TMB, 100 μL/well) was added. The color reaction was stopped after 2 min by addition of phosphoric acid (100 μL/well, 1 M), and the blue solutions turned yellow. Absorbance was detected at 450 nm, and percentage inhibition was calculated, using wells without ligand as the reference for zero inhibition. Inhibition curves and reported IC_{50} values were obtained with the Microsoft Origin software, applying a four-parameter logistic function fitting.

3.3. Saturation transfer difference (STD) NMR

An aqueous buffer solution of mAb IgG 9D4 was subjected to repeated ultrafiltration against PBS buffer made in D_2O (pH 7.2). The mAb in deuterated buffer was concentrated to 2.98 mg/mL as determined by UV absorption (OD_{280}). The protein solution (700 μL, 2.98 mg/mL) and ligand solution (50 μL, 100-fold excess) in PBS–D_2O buffer were used throughout the NMR studies. The STD NMR 1D experiments were done with a Varian Inova three-channel 600 MHz spectrometer at 27 °C. The STD NMR epitope mapping for the disaccharide ligands was achieved by applying a series of equally spaced 50 ms Gaussian pulse for saturation, with

1 ms delay between pulses. The total saturation time was 1.53 s. The frequency for protein irradiation was set to 7.8 ppm (absolute frequency = 1650 Hz). The off-resonance irradiation was set at 33.0 ppm. Free induction decay (FID) values with on and off resonance protein saturation were recorded alternatively, and their subtraction was performed after each scan by phase cycling. Protein resonances were suppressed by applying a protein $T_{1\rho}$ filter, a 0.03 s low power spin-lock pulse after the saturation pulse. The resonance of residual HOD was reduced by a WATERGATE W5 pulse.[27] The frequency of this irradiation was selected by an array experiment. The saturation difference spectra were recorded over 2–4 k scans, while the reference spectra were recorded by 1–2 k scans. The relative STD effect values were calculated by dividing the intensities of signals in the difference spectrum by those in the reference spectrum.

3.4. 1,2:5,6-di-*O*-Isopropylidene-3-*O*-[(methylthio)thiocarbonyl]-α-D-glucofuranose (8a)

1,2:5,6-di-*O*-Isopropylidene-α-D-glucofuranose (40.00 g, 0.15 mol) was dissolved in dry THF (400 mL), followed by addition of sodium hydride (15.00 g, 60% dispersion in mineral oil, 0.37 mol) and imidazole (5.20 g, 0.075 mol). Vigorous bubbling occurred when imidazole was added. The reaction was stirred for 2 h at rt, and the colorless solution turned yellow. Carbon disulfide (18.00 g, 0.30 mol) was then added and the reaction mixture was kept at rt for 4 h, during which time it turned brownish yellow. Iodomethane (19.2 mL, 0.30 mol) was added and the reaction was completed in 1.5 h with formation of a white precipitate. THF was then removed by evaporation. The residue dissolved in ethyl acetate was extracted with water, dried over anhydrous sodium sulfate, and evaporated to dryness to afford a brownish yellow syrup. Column chromatography (1:30 ethyl acetate:hexanes) gave clear syrup (53.80 g, 100%): $[\alpha]_D^{22}$ −23.6 (*c* 8.1, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 5.92 (app. d, 2H, J = 3.4 Hz, H-1, H-3), 4.68 (d, 1H, J = 3.9 Hz, H-2), 4.34 (dd, 1H, $J_{4,5}$ = 7.5 Hz, $J_{4,3}$ = 2.8 Hz, H-4), 4.31 (ddd, 1H, $J_{5,6a}$ = 5.5 Hz, $J_{5,6b}$ = 5.5 Hz, H-5), 4.11 (dd, 1H, $J_{6a,6b}$ = 8.8 Hz, H-6a), 4.06 (dd, 1H, H-6b), 2.60 (s, 3H, SCH_3), 1.54 (s, 3H, $(CH_3)_2C$), 1.42 (s, 3H, $(CH_3)_2C$), 1.33 (s, 3H, $(CH_3)_2C$), 1.32 (s, 3H, $(CH_3)_2C$). ^{13}C NMR (125 MHz, $CDCl_3$): δ 214.8 (CH_3SCS–), 112.4 ($(CH_3)_2C$), 109.3 ($(CH_3)_2C$), 105.0 (C-1), 84.2 (C-2), 82.8 (C-4), 79.8 (C-5), 72.4 (C-3), 67.0 (C-6), 26.8 ($(CH_3)_2C$), 26.7($(CH_3)_2C$), 26.3($(CH_3)_2C$), 25.3($(CH_3)_2C$), 19.3(SCH_3). Anal. Calcd for $C_{14}H_{22}O_6S_2$(350.50): C, 47.98; H, 6.33; S, 18.30. Found: C, 47.67; H, 6.11; S, 18.08.

3.5. 3-Deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-ribo-hexofuranose (9)

To a solution of compound **8a** (50.52 g, 0.14 mol) in toluene (500 mL) was added a catalytic amount of azobisisobutyronitrile (AIBN) and tributyltin hydride (45.8 mL, 0.17 mol). The reaction was heated at reflux for 5 h. The solution was concentrated by distillation, and the residue was loaded on a silica gel column, which was eluted first with hexanes to remove the tin derivatives. Column chromatography (1:10 acetone:hexanes) afforded the deoxy sugar as a clear syrup (26.41 g, 75%): $[\alpha]_D^{22}$ −7.6 (*c* 1.8, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 5.78 (d, 1H, $J_{1,2}$ = 3.7 Hz, H-1), 4.72 (dd, 1H, $J_{2,3a}$ = 4.3 Hz, H-2), 4.14–4.05 (m, 3H, H-4, H-5, H-6a), 3.79 (dd, 1H, $J_{6b,6a}$ = 7.5, $J_{6b,5}$ = 4.8 Hz, H-6b), 2.15 (dd, 1H, $J_{3e,3a}$ = 13.4 Hz, $J_{3e,4}$ = 4.4 Hz, H-3e), 1.73 (ddd, 1H, $J_{3a,4}$ = 10.3 Hz, H-3a), 1.48 (s, 3H, $(CH_3)_2C$), 1.39 (s, 3H, $(CH_3)_2C$), 1.32 (s, 3H, $(CH_3)_2C$), 1.28 (s, 3H, $(CH_3)_2C$). ^{13}C NMR (125 MHz, $CDCl_3$): δ 111.3 ($(CH_3)_2C$), 109.6 ($(CH_3)_2C$), 105.6 (C-1), 80.4 (C-2), 78.6 (C-4), 76.8 (C-5), 67.2 (C-6), 35.3 (C-3), 26.8 ($(CH_3)_2C$), 26.5($(CH_3)_2C$), 26.1($(CH_3)_2C$), 25.2($(CH_3)_2C$). Anal. Calcd for $C_{12}H_{20}O_5$ (244.30): C, 59.00; H, 8.25. Found: C, 58.73; H, 8.41.

3.6. Phenyl 2,4,6-tri-*O*-acetyl-3-deoxy-1-thio-α,β-D-glucopyranoside (11)

A solution of deoxy sugar **9** (16.50 g, 0.068 mol) in aqueous acetic acid (60%, 200 mL) was warmed at 80 °C for 2 h and evaporated to dryness. The residue was then dissolved in pyridine (80 mL) and acetic anhydride (80 mL). The solution was stirred at rt. for 3 h and concentrated to a syrup under reduced pressure. The syrup was dissolved in ethyl acetate and extracted with water. The ethyl acetate layer was dried over sodium sulfate, filtered, and evaporated to give a clear syrup. The syrup in dichloromethane (200 mL) solution was cooled to 0 °C, followed by addition of thiophenol (11.2 mL, 0.11 mol) and $BF_3{\cdot}OEt_2$ (12.5 mL, 0.10 mmol). The reaction reached completion after 3 h and was neutralized by addition of triethylamine. Column chromatography afforded thioglycoside **11** (α:β = 1:1.3) as clear syrup (18.98 g, 73%, 3 steps). Data for the α isomer: $[\alpha]_D^{22}$ +254.3 (*c* 2.6, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ 7.50–7.46 (m, 2H, PhH), 7.33–7.25 (m, 3H, PhH), 5.80 (d, 1H, $J_{1,2}$ = 5.2 Hz, H-1), 5.10 (ddd, 1H, $J_{2,3a}$ = 12.9 Hz, $J_{2,3e}$ = 4.9 Hz, H-2), 4.86 (ddd, 1H, $J_{4,3a}$ = 11.0 Hz, $J_{4,5}$ = 11.0 Hz, $J_{4,3e}$ = 4.9 Hz, H-4), 4.46 (ddd, 1H, $J_{5,6a}$ = 5.7 Hz, $J_{5,6b}$ = 2.3 Hz, H-5), 4.25 (dd, 1H, $J_{6a,6b}$ = 12.1 Hz, H-6a), 4.12 (dd, 1H, H-6b), 2.39 (ddd, 1H, $J_{3e,3a}$ = 11.9 Hz, H-3e), 2.11(s, 3H, $OCOCH_3$), 2.08 (s, 3H, $OCOCH_3$), 2.02 (s, 3H, $OCOCH_3$), 1.93 (ddd, 1H, H-3a). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.7 ($OCOCH_3$), 169.8 ($OCOCH_3$), 169.6 ($OCOCH_3$), 133.0 (Ph), 131.9 (Ph), 129.0 (Ph), 127.5 (Ph), 85.9 (C-1), 68.6 (C-5), 67.9 (C-2), 66.0 (C-4), 62.5 (C-6), 30.9 (C-3), 20.9 ($OCOCH_3$), 20.8 ($OCOCH_3$), 20.7 ($OCOCH_3$). Anal. Calcd for $C_{18}H_{22}O_7S$ (382.43): C, 56.53; H, 5.80; S, 8.38. Found: C, 56.38; H, 5.98; S, 8.27. Data for the β isomer: $[\alpha]_D^{22}$ −9.2 (*c* 4.0, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ 7.54–7.49 (m, 2H, PhH), 7.33–7.29 (m, 3H, PhH), 4.84–4.78 (m, 2H, H-2, H-4), 4.67 (d, 1H, $J_{1,2}$ = 9.8 Hz, H-1), 4.25 (dd, 1H, $J_{6a,6b}$ = 12.1 Hz, $J_{6a,5}$ = 2.5 Hz, H-6a), 4.12 (dd, 1H, $J_{6b,5}$ = 6.0 Hz, H-6b), 4.46 (ddd, 1H, $J_{5,4}$ = 9.8 Hz, H-5), 2.39 (ddd, 1H, $J_{3e,3a}$ = 12.0 Hz, $J_{3e,2}$ = 5.0 Hz, $J_{3e,4}$ = 5.0 Hz, H-3e), 2.10(s, 3H, $OCOCH_3$), 2.08 (s, 3H, $OCOCH_3$), 2.04 (s, 3H, $OCOCH_3$), 1.93 (ddd, 1H, $J_{3a,2}$ = 11.6 Hz, $J_{3a,4}$ = 11.6 Hz, H-3a). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.7 ($OCOCH_3$), 169.4 ($OCOCH_3$), 169.2 ($OCOCH_3$), 132.6 (Ph), 132.5 (Ph), 128.8 (Ph), 128.0 (Ph), 87.3 (C-1), 78.0 (C-5), 67.2 (C-2), 65.9 (C-4), 62.8 (C-6), 35.2 (C-3), 20.9 ($OCOCH_3$), 20.8 ($OCOCH_3$), 20.7 ($OCOCH_3$). Anal. Calcd for $C_{18}H_{22}O_7S$ (382.43): C, 56.53; H, 5.80; S, 8.38. Found: C, 56.69; H, 5.92; S, 8.49.

3.7. Phenyl 4,6-*O*-benzylidene-3-deoxy-1-thio-α,β-D-glucopyranoside (13)

The α/β mixture of compound **11** (α:β = 1:1.3, 10.00 g, 0.026 mol) was suspended in dry methanol (100 mL). Sodium methoxide in methanol solution (1.7 M, 3.1 mL, 5.2 mmol) was added, and the reaction mixture was stirred at rt. for 1 h. Dowex 50WX4-50 H^+ resin was added to neutralize the solution, and the resin was removed by filtration. The filtrate was evaporated to dryness and the residue was dissolved in dry distilled acetonitrile (60 mL), followed by addition of benzaldehyde dimethylacetal (7.8 mL, 0.052 mol) and toluenesulfonic acid (0.90 g, 5.2 mmol). After stirring at rt for 6 h, the reaction was neutralized by addition of triethylamine. The residue after evaporation was dissolved in ethyl acetate and extracted with water. Column chromatography (1:50 acetone/toluene) gave **13** (α:β = 1:1.3) as a white solid (8.60 g, 96%, 2 steps). Data for the α isomer: $[\alpha]_D^{22}$ +322.0 (*c* 2.4, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 7.56–7.50 (m, 4H, PhH), 7.41–7.29 (m, 6H, PhH), 5.56 (s, 1H, PhCH), 5.52 (d, 1H, $J_{1,2}$ = 5.0 Hz, H-1), 4.32 (dd, 1H, $J_{6e,6a}$ = 10.3 Hz, $J_{6e,5}$ = 4.9 Hz,

H-6e), 4.19 (ddd, 1H, $J_{5,4}$ = 9.7 Hz, $J_{5,6a}$ = 9.7 Hz, H-5), 4.11 (m, 1H, H-2), 3.77 (dd, 1H, H-6a), 3.62 (ddd, 1H, $J_{4,3a}$ = 13.4 Hz, $J_{4,3e}$ = 4.1 Hz, H-4), 2.42 (ddd, 1H, $J_{3e,2}$ = 4.2 Hz, $J_{3e,3a}$ = 11.7 Hz, H-3e), 2.26 (d, 1H, $J_{OH,2}$ = 10.1 Hz, OH), 1.78 (ddd, 1H, $J_{3a,2}$ = 11.8 Hz, H-3a). ^{13}C NMR (125 MHz, $CDCl_3$): δ 137.2 (Ph), 133.8 (Ph), 132.2 (Ph), 129.2 (Ph), 128.4 (Ph), 127.8 (Ph), 126.2 (Ph), 101.9 (PhCH), 93.5 (C-1), 76.1 (C-4), 69.1 (C-6), 67.8 (C-2), 65.9 (C-5), 35.3 (C-3). Anal. Calcd for $C_{19}H_{20}O_4S$ (344.43): C, 66.26; H, 5.85; S, 9.31. Found: C, 66.01; H, 5.92; S, 9.42. Data for the β isomer: $[\alpha]_D^{22}$ −43.0 (*c* 1.6, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.56–7.53 (m, 2H, PhH), 7.50–7.47 (m, 2H, PhH), 7.39–7.33 (m, 6H, PhH), 5.54 (s, 1H, PhCH), 4.57 (d, 1H, $J_{1,2}$ = 9.5 Hz, H-1), 4.75 (dd, 1H, $J_{6e,6a}$ = 10.6 Hz, $J_{6e,5}$ = 4.9 Hz, H-6e), 3.78 (dd, 1H, $J_{5,6a}$ = 10.3 Hz, H-6a), 3.62–3.58 (m, 2H, H-2, H-4), 3.49 (ddd, 1H, $J_{5,4}$ = 9.8 Hz, H-5), 2.59 (ddd, 1H, $J_{3e,3a}$ = 11.9 Hz, $J_{3e,2}$ = 4.6 Hz, $J_{3e,4}$ = 4.6 Hz, H-3e), 2.45 (d, 1H, $J_{OH,2}$ = 2.1 Hz, OH), 1.78 (ddd, 1H, $J_{3a,2}$ = 11.6 Hz, $J_{3a,4}$ = 11.6, H-3a). ^{13}C NMR (125 MHz, $CDCl_3$): δ 137.2 (Ph), 132.7 (Ph), 131.7 (Ph), 129.2 (Ph), 129.1 (Ph), 128.3 (Ph), 126.2 (Ph), 101.8 (PhCH), 91.6 (C-1), 75.9 (C-4), 74.0 (C-5), 69.0 (C-6), 67.5 (C-2), 36.7 (C-3). Anal. Calcd for $C_{19}H_{20}O_4S$ (344.43): C, 66.26; H, 5.85; S, 9.31. Found: C, 66.19; H, 6.03; S, 9.40.

3.8. Phenyl 2-*O*-acetyl-4,6-*O*-benzylidene-3-deoxy-1-thio-α,β-D-glucopyranoside (14)

The α/β mixture of compound **13** (α:β = 1:1.3, 2.00 g, 5.8 mmol) was dissolved in pyridine: acetic anhydride solution (20 mL, 1:1). After 1 h, the pyridine and acetic anhydride were co-evaporated with toluene, and the residue was loaded on a silica gel column and eluted with acetone/hexanes (1:10) to afford a white solid **14** (α:β = 1:1.3, 2.20 g, 98%). Data for the α isomer: $[\alpha]_D^{22}$ +264.5 (*c* 4.6, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.55–7.45 (m, 4H, PhH), 7.40–7.28 (m, 6H, PhH), 5.81 (d, 1H, $J_{1,2}$ = 5.3 Hz, H-1), 5.57 (s, 1H, PhCH), 5.16 (ddd, 1H, $J_{2,3a}$ = 12.3 Hz, $J_{2,3e}$ = 4.9 Hz, H-2), 4.32 (ddd, 1H, $J_{5,6a}$ = 9.9 Hz, $J_{5,4}$ = 9.9 Hz, $J_{5,6e}$ = 4.8 Hz, H-5), 4.22 (dd, 1H, $J_{6e,6a}$ = 10.3 Hz, H-6e), 3.75 (dd, 1H, H-6a), 3.70 (ddd, 1H, $J_{4,3a}$ = 11.8 Hz, $J_{4,3e}$ = 4.3 Hz, H-4), 2.33 (ddd, 1H, $J_{3e,3a}$ = 11.5 Hz, H-3e), 2.13 (s, 3H, $OCOCH_3$), 2.13 (ddd, 1H, H-3a). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.0 ($OCOCH_3$), 137.2 (Ph), 133.2 (Ph), 132.2 (Ph), 129.2 (Ph), 129.1 (Ph), 128.4 (Ph), 127.5 (Ph), 126.2 (Ph), 101.9 (PhCH), 86.6 (C-1), 76.1 (C-4), 69.0 (C-6), 68.8 (C-2), 65.0 (C-5), 31.2 (C-3), 21.0 ($OCOCH_3$). Anal. Calcd for $C_{21}H_{22}O_5S$ (386.46): C, 65.27; H, 5.74; S, 8.30. Found: C, 65.29; H, 5.56; S, 8.77. Data for the β isomer: $[\alpha]_D^{22}$ −25.3 (*c* 14.8, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.55–7.42 (m, 4H, PhH), 7.40–7.28 (m, 6H, PhH), 5.54 (s, 1H, PhCH), 4.88 (ddd, 1H, $J_{2,3a}$ = 10.9 Hz, $J_{2,1}$ = 9.9 Hz, $J_{2,3e}$ = 5.0 Hz, H-2), 4.75 (d, 1H, H-1), 4.37 (dd, 1H, $J_{6e,6a}$ = 10.6 Hz, $J_{6e,5}$ = 4.9 Hz, H-6e), 3.78 (dd, 1H, $J_{6a,5}$ = 10.4 Hz, H-6a), 3.63 (ddd, 1H, $J_{4,3a}$ = 11.8 Hz, $J_{4,5}$ = 9.1 Hz, $J_{4,3e}$ = 4.2 Hz, H-4), 3.50 (ddd, 1H, H-5), 2.59 (ddd, 1H, $J_{3e,3a}$ = 11.6 Hz, H-3e), 2.12 (s, 3H, $OCOCH_3$), 1.81 (ddd, 1H, H-3a). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.0 ($OCOCH_3$), 137.2 (Ph), 133.2 (Ph), 132.2 (Ph), 129.2 (Ph), 129.1 (Ph), 128.4 (Ph), 127.5 (Ph), 126.2 (Ph), 101.9 (PhCH), 86.6 (C-1), 76.1 (C-4), 69.0 (C-6), 68.8 (C-2), 65.0 (C-5), 31.2 (C-3), 21.0 ($OCOCH_3$). Anal. Calcd for $C_{21}H_{22}O_5S$ (386.46): C, 65.27; H, 5.74; S, 8.30. Found: C, 65.27; H, 5.75; S, 8.45.

3.9. Methyl 2-acetamido-2-deoxy-β-D-glucopyranoside (17)

Anhydrous iron(III) chloride (90.00 g, 0.56 mol) was added to a suspension of 2-acetamido-2-deoxy-D-glucose (60.00 g, 0.27 mol) in dry distilled acetone (1.2 L). The mixture was stirred and heated at reflux for 20 min under argon. The solution was cooled to 0 °C, and Et_3N (294 mL) and acetone (800 mL) were added with stirring. The reaction was quenched with a solution of Na_2CO_3 (800 mL, 1.5 M), concentrated, and extracted with ethyl ether. The organic layer was dried over Na_2SO_4, filtered, and the ethyl ether was evaporated to give oxazoline as a brown syrup. The resulting intermediate (66 g, 0.26 mol) was redissolved in dry methanol (400 mL), and the pH of the solution was adjusted to 2 with *p*-toluenesulfonic acid. The reaction mixture was stirred for 4 h, and neutralized with Et_3N. Methanol was evaporated, and column chromatography (1:10 methanol/dichloromethane) gave a white solid (51.44 g, 81%): $[\alpha]_D^{22}$ −30.8 (*c* 5.6, CH_3OH). ^{1}H NMR (500 MHz, D_2O): δ 4.45 (d, 1H, $J_{1,2}$ = 8.5 Hz, H-1), 3.94 (dd, 1H, $J_{6a,6b}$ = 12.3 Hz, $J_{6a,5}$ = 1.9 Hz, H-6a), 3.75 (dd, 1H, $J_{6b,5}$ = 5.6 Hz, H-6b), 3.69 (dd, 1H, $J_{2,3}$ = 10.3 Hz, H-2), 3.54 (dd, 1H, $J_{3,4}$ = 8.6 Hz, H-3), 3.51 (s, 3H, OCH_3), 3.42–3.48 (m, 2H, H-4, H-5), 2.04 (s, 3H, $NHCOCH_3$). ^{13}C NMR (125 MHz, $CDCl_3$): δ 175.6 ($NHCOCH_3$), 102.8 (C-1), 76.8 (C-3), 74.8 (C-5), 70.8 (C-4), 61.6 (C-6), 57.9 (OCH_3), 56.3 (C-2), 23.0 ($NHCOCH_3$). ES HRMS calcd for $C_9H_{17}NO_6Na$ (M+Na): 258.0948, found: 258.0949.

3.10. Methyl 2-acetamido-2-deoxy-3,6-di-*O*-pivaloyl-β-D-glucopyranoside (18)

To a solution of compound **17** (4.30 g, 18 mmol) in dry dichloromethane (20 mL) and pyridine (20 mL) at 0 °C was added pivaloyl chloride (3 mL, 54 mmol) dropwise over 10 min. The reaction mixture was stirred at 0 °C for 2 h, and evaporated to dryness. Column chromatography (1:8 acetone/toluene) gave **18** as a white solid (6.66 g, 90%): $[\alpha]_D^{22}$ −43.07 (*c* 0.95, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.68 (d, 1H, $J_{NH,2}$ = 7.6 Hz, $NHCOCH_3$), 5.04 (dd, 1H, $J_{3,4}$ = 10.6 Hz, $J_{3,2}$ = 8.7 Hz, H-3), 4.44–4.36 (m, 3H, H-1, H-6a, H-6b), 3.97 (ddd, 1H, $J_{2,1}$ = 8.8 Hz, H-2), 3.57–3.49 (m, 2H, H-4, H-5), 3.47 (s, 3H, OCH_3), 1.94 (s, 3H, $NHCOCH_3$), 1.24 ($(CH_3)_3CCO$–), 1.20 ($(CH_3)_3CCO$–). ^{13}C NMR (125 MHz, $CDCl_3$): δ 179.9 ($(CH_3)_3CCO$–), 179.2 ($(CH_3)_3CCO$–), 170.0 ($NHCOCH_3$), 102.0 (C-1), 75.0 (C-3), 74.3 (C-5), 69.4 (C-4), 63.2 (C-6), 56.4 (OCH_3), 53.7 (C-2), 39.0 ($(CH_3)_3CCO$–), 38.9 ($(CH_3)_3CCO$–), 27.2 ($(CH_3)_3CCO$–), 27.0 ($(CH_3)_3CCO$–), 23.3 ($NHCOCH_3$). Anal. Calcd for $C_{19}H_{33}NO_8$ (403.47): C, 56.56; H, 8.24; N, 3.47. Found: C, 56.17; H, 8.18; N, 3.85.

3.11. Methyl 2-acetamido-2-deoxy-4,6-dipivaloyl-*O*-β-D-galactopyranoside (19)

Compound **18** (3.70 g, 9.2 mmol) was dissolved in dry distilled dichloromethane (37 mL), and dry pyridine (3.7 mL) was added. The solution was then cooled to −35 °C, and trifluoromethanesulfonic anhydride (1.7 mL, 10 mmol) was added dropwise. The mixture was then allowed to warm to rt. over 1 h, and water (6.3 mL) was added. The reaction was refluxed for 4 h, and stirred at rt overnight. After concentration, column chromatography (1:8 acetone/toluene) afforded compound **19** as a white solid (3.3 g, 89%): $[\alpha]_D^{22}$ −28.0 (*c* 2.10, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.69 (d, 1H, $J_{NH,2}$ = 4.2 Hz, $NHCOCH_3$), 5.31 (d, 1H, $J_{4,3}$ = 3.3 Hz, H-4), 4.45 (d, 1H, $J_{1,2}$ = 8.2 Hz, H-1), 4.18 (dd, 1H, $J_{6a,6b}$ = 11.2 Hz, $J_{6a,5}$ = 7.4 Hz, H-6a), 4.11 (dd, 1H, $J_{6b,5}$ = 6.1 Hz, H-6b), 4.00 (dd, 1H, $J_{3,2}$ = 10.4 Hz, H-3), 3.90 (dd, 1H, H-5), 3.67 (ddd, 1H, H-2), 3.53 (s, 3H, OCH_3), 2.07 (s, 3H, $NHCOCH_3$), 1.27 ($(CH_3)_3CCO$–), 1.20 ($(CH_3)_3CCO$–). ^{13}C NMR (125 MHz, $CDCl_3$): δ 178.0 ($(CH_3)_3CCO$–), 177.8 ($(CH_3)_3CCO$–), 173.1 ($NHCOCH_3$), 101.2 (C-1), 72.1 (C-3), 71.5 (C-5), 68.3 (C-4), 61.9 (C-6), 56.7 (OCH_3), 55.8 (C-2), 39.2 ($(CH_3)_3CCO$–), 38.7 ($(CH_3)_3CCO$–), 27.2 ($(CH_3)_3CCO$–), 27.1 ($(CH_3)_3CCO$–), 23.5 ($NHCOCH_3$). ES HRMS calcd for $C_{19}H_{34}NO_8Na$ (M+Na): 404.2279, found: 404.2269.

3.12. Methyl 2-acetamido-2-deoxy-6-*O*-methyl-β-D-glucopyranoside (20)

Compound **17** (5.00 g, 0.021 mol) was suspended in dry toluene (200 mL), and bis(tributyltin) oxide (20 mL, 0.034 mol) was added

slowly. The reaction mixture was heated at reflux for 2 h, and the solution turned clear, indicating complete consumption of starting material. The solvent was then evaporated under reduced pressure to afford a brownish syrup, to which methyl iodide (50 mL) was added. The solution was stirred at reflux for 48 h and concentrated. Column chromatography (2:1 acetone/toluene) produced compound **20** as a white solid (4.08 g, 78%): $[\alpha]_D^{22}$ −24.7 (*c* 3.11, CH_3OH). ^1H NMR (600 MHz, CD_3OD): δ 4.29 (d, 1H, $J_{1,2}$ = 8.4 Hz, H-1), 3.72 (dd, 1H, $J_{6a,6b}$ = 10.9 HzHHH, $J_{6a,5}$ = 2.1 Hz, H-6a), 3.61 (dd, 1H, $J_{2,3}$ = 10.4 Hz, H-2), 3.58 (dd, 1H, $J_{6b,5}$ = 5.8 Hz, H-6b), 3.43 (s, 3H, C-1-OCH_3), 3.41 (dd, 1H, $J_{3,4}$ = 8.7 Hz, H-3), 3.39 (s, 3H, C-6-OCH_3), 3.36 (ddd, 1H, $J_{5,4}$ = 9.9 Hz, H-5), 3.30 (m, 1H, H-4), 1.96 (s, 3H, NHCO*CH*$_3$). ^{13}C NMR (125 MHz, CD_3OD): δ 170.4 (NH*C*OCH$_3$), 100.2 (C-1), 73.5 (C-3), 72.8 (C-5), 69.8 (C-6), 68.8 (C-4), 56.3 (C-6-O*C*H$_3$), 53.9 (C-2), 53.6 (C-1-O*C*H$_3$), 20.0 (NHCO*C*H$_3$). Anal. Calcd for $C_{10}H_{19}NO_6$ (249.12): C, 48.19; H, 7.68; N, 5.62. Found: C, 47.76; H, 7.50; N, 5.62.

3.13. Methyl 2-acetamido-2-deoxy-6-*O*-methyl-3-*O*-pivaloyl-β-D-glucopyranoside (21)

Compound **20** (2.00 g, 8.0 mmol) was dissolved in dichloromethane:pyridine (20 mL, 1:1), the solution was cooled to 0 °C, and pivaloyl chloride (1.1 mL, 8.8 mmol) was added. The reaction mixture was allowed to warm to ambient temperature over 2 h, and then evaporated to dryness. Column chromatography (1:2 acetone/toluene) afforded **21** as a white solid (2.29 g, 86%): $[\alpha]_D^{22}$ −61.83 (*c* 2.10, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 5.37 (d, 1H, $J_{NH,2}$ = 9.6 Hz, N*H*COCH$_3$), 4.98 (dd, 1H, $J_{3,2}$ = 10.7 Hz, $J_{3,4}$ = 9.1 Hz, H-3), 4.39 (d, 1H, $J_{2,1}$ = 8.3 Hz, H-1), 4.01 (ddd, 1H, H-2), 3.79–3.72 (m, 2H, H-4, H-6a), 3.68 (dd, 1H, $J_{6b,6a}$ = 10.2 Hz, $J_{6b,5}$ = 4.8 Hz, H-6b), 3.50 (ddd, 1H, $J_{5,4}$ = 10.4 Hz, $J_{5,6a}$ = 4.8 Hz, H-5), 3.49 (s, 3H, C-1-OCH_3), 3.43 (s, 3H, C-6-OCH_3), 1.94 (s, 3H, NHCO*CH*$_3$), 1.21 ((*CH*$_3$)$_3$CCO–). ^{13}C NMR (125 MHz, $CDCl_3$): δ 179.8 ((CH$_3$)$_3$*C*CO–), 170.2 (NH*C*OCH$_3$), 102.0 (C-1), 75.4 (C-3), 74.3 (C-5), 72.2 (C-6), 70.7 (C-4), 59.6 (C-6-O*C*H$_3$), 56.5 (C-1-O*C*H$_3$), 53.6 (C-2), 39.0 ((CH$_3$)$_3$*C*CO–), 27.0 ((*C*H$_3$)$_3$CCO–), 23.2 (NHCO*C*H$_3$). Anal. Calcd for $C_{15}H_{27}NO_7$ (333.38): C, 54.04; H, 8.16; N, 4.20. Found: C, 53.85; H, 8.12; N, 4.07.

3.14. Methyl 2-acetamido-2-deoxy-6-*O*-methyl-4-*O*-pivaloyl-β-D-galactopyranoside (22)

Compound **21** (1.00 g, 3.0 mmol) was dissolved in dry distilled dichloromethane (10 mL), and dry pyridine (1.0 mL) was added. The solution was then cooled to −35 °C, and trifluoromethanesulfonic anhydride (0.56 mL, 3.3 mmol) was added dropwise. The mixture was then allowed to warm to rt. over 1 h, and water (1.0 mL) was added. The reaction was refluxed for 4 h, and stirred at rt. for 18 h. After concentration, column chromatography (1:2 acetone/toluene) afforded compound **22** as a white solid (0.92 g, 92%): $[\alpha]_D^{22}$ −10.5 (*c* 0.76, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ 5.73 (d, 1H, $J_{NH,2}$ = 3.0 Hz, N*H*COCH$_3$), 5.30 (d, 1H, $J_{4,3}$ = 3.2 Hz, H-4), 4.44 (d, 1H, $J_{1,2}$ = 8.4 Hz, H-1), 3.96 (dd, 1H, $J_{3,2}$ = 10.4 Hz, H-3), 3.80 (dd, 1H, $J_{5,6a}$ = 5.8 Hz, $J_{5,6b}$ = 5.8 Hz, H-5), 3.71 (ddd, 1H, H-2), 3.55 (s, 3H, C-1-OCH_3), 4.50 (dd, 1H, $J_{6a,6b}$ = 10.2 Hz, H-6a), 3.46 (dd, 1H, H-6b), 3.35 (s, 3H, C-1-OCH_3), 2.07 (s, 3H, NHCO*CH*$_3$), 1.28 ((*CH*$_3$)$_3$CCO–). ^{13}C NMR (125 MHz, $CDCl_3$): δ 178.1 ((CH$_3$)$_3$*C*CO–), 173.1 (NH*C*OCH$_3$), 101.2 (C-1), 73.1 (C-5), 72.3 (C-3), 71.3 (C-6), 69.2 (C-4), 59.3 (C-6-O*C*H$_3$), 56.6 (C-1-O*C*H$_3$), 55.5 (C-2), 39.3 ((CH$_3$)$_3$*C*CO–), 27.3 ((*C*H$_3$)$_3$CCO–), 23.4 (NHCO*C*H$_3$). Anal. Calcd for $C_{15}H_{27}NO_7$ (333.38): C, 54.04; H, 8.16; N, 4.20. Found: C, 53.99; H, 8.18; N, 4.08.

3.15. Methyl 2-acetamido-3-*O*-(2-*O*-acetyl-4,6-*O*-benzylidene-3-deoxy-β-D-ribo-hexopyranosyl)-2-deoxy-4,6-di-*O*-pivaloyl-β-D-galactopyranoside (23)

Monosaccharide acceptor **19** (2.0 g, 5.0 mmol) and thioglycoside donor **14** (α:β = 1:1.3, 2.5 g, 6.4 mmol) were dissolved in dry dichloromethane (100 mL). Molecular sieves (20.00 g, 4 Å) were added and the mixture was stirred overnight at room temperature under argon. To the stirred solution was added N-iodosuccinimide (1.7 g, 7.5 mmol) and the reaction was cooled to 0 °C. After addition of triflic acid (0.25 mL) over 5 min, the reaction mixture turned red, and was then stirred for 2 h at 0 °C at which point the reaction reached completion. Triethylamine (1 mL) was then added to neutralize the solution. Column chromatography (1:4 acetone/toluene) gave the title disaccharide **23** as a white solid (β only, 2.9 g, 85%): $[\alpha]_D^{22}$ +1.1 (*c* 2.14, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 7.44–7.43 (m, 2H, PhH), 7.39–7.32 (m, 3H, PhH), 5.59 (d, 1H, $J_{NH,2}$ = 7.1 Hz, N*H*COCH$_3$), 5.52 (s, 1H, PhC*H*), 5.40 (d, 1H, $J_{4,3}$ = 3.2 Hz, H-4), 4.96 (d, 1H, $J_{1,2}$ = 8.3 Hz, H-1), 4.72 (ddd, 1H, $J_{2',3a'}$ = 10.0 Hz, $J_{2',1'}$ = 8.3 Hz, $J_{2',3e'}$ = 5.5 Hz, H-2′), 4.67 (dd, 1H, $J_{3,2}$ = 10.8 Hz, H-3), 4.62 (d, 1H, H-1′), 4.29 (dd, 1H, $J_{6e',6a'}$ = 10.6 Hz, $J_{6e',5'}$ = 4.9 Hz, H-6e′), 4.12 (dd, 1H, $J_{6a,6b}$ = 11.0 Hz, $J_{6a,5}$ = 5.6 Hz, H-6a), 4.04 (dd, 1H, $J_{6b,5}$ = 7.4 Hz, H-6b), 3.92 (dd, 1H, H-5), 3.73 (dd, 1H, $J_{6a',5'}$ = 10.4 Hz, H-6a′), 3.61 (ddd, 1H, $J_{4',3a'}$ = 11.5 Hz, $J_{4',5'}$ = 9.1 Hz, $J_{4',3e'}$ = 4.4 Hz, H-4′), 3.51 (s, 3H, OCH_3), 3.44 (ddd, 1H, H-5′), 3.26 (ddd, 1H, H-2), 2.47 (ddd, 1H, $J_{3e',3a'}$ = 11.5 Hz, H-3e′), 2.07 (s, 3H, OCO*CH*$_3$), 2.01 (s, 3H, NHCO*CH*$_3$), 1.68 (ddd, 1H, H-3a′), 1.23 (s, 9H, (*CH*$_3$)$_3$CCO–), 1.21 (s, 9H, (*CH*$_3$)$_3$CCO–). ^{13}C NMR (125 MHz, $CDCl_3$): δ 177.9 ((CH$_3$)$_3$*C*CO–), 176.9 ((CH$_3$)$_3$*C*CO–), 170.8 (NH*C*OCH$_3$), 169.3 (O*C*OCH$_3$), 137.2 (Ph), 129.1 (Ph), 128.3 (Ph), 126.1 (Ph), 102.1 (C-1′), 101.6 (Ph*C*H), 100.2 (C-1), 75.0 (C-4′), 74.4 (C-3), 71.4 (C-5), 70.1 (C-5′), 70.0 (C-2′), 69.0 (C-6′), 68.6 (C-4), 62.2 (C-6), 57.0 (OCH_3), 55.1 (C-2), 39.1 ((CH$_3$)$_3$*C*CO–), 38.7 ((CH$_3$)$_3$*C*CO–), 33.2 (C-3′), 27.2 ((*C*H$_3$)$_3$CCO–), 27.1 ((*C*H$_3$)$_3$CCO–), 23.7 (NHCO*C*H$_3$), 21.0 (OCO*C*H$_3$). ES HRMS calcd for $C_{34}H_{49}NO_{13}Na$ (M+Na): 702.30961, found: 702.30965. Anal. Calcd for $C_{34}H_{49}NO_{13}$(679.32): C, 60.08; H, 7.27; N, 2.06. Found: C, 59.97; H, 7.50; N, 2.25.

3.16. Methyl 2-acetamido-3-*O*-(2-*O*-acetyl-4,6-*O*-benzylidene-3-deoxy-β-D-ribo- hexopyranosyl)-2-deoxy-6-*O*-methyl-4-*O*-pivaloyl-β-D-galactopyranoside (24)

Monosaccharide acceptor **22** (0.50 g, 1.5 mmol) and thioglycoside donor **14** (α:β = 1:1.3, 1.16 g, 3.0 mmol) were dissolved in dry dichloromethane (15 mL). Molecular sieves (3.00 g, 4 Å) were added and the mixture was stirred overnight at room temperature under argon. To the stirred solution was added *N*-iodosuccinimide (0.71 g, 3.2 mmol) and the reaction was cooled to 0 °C. After addition of triflic acid (40 μL) over 3 min, the reaction mixture turned red, and was stirred for 3 h at 0 °C. Triethylamine was added to neutralize the solution, and the mixture was applied to column chromatography (1:4 acetone/toluene) to give the title disaccharide **24** as a white solid (β only, 0.69 g, 75%): $[\alpha]_D^{22}$ +1.64 (*c* 2.14, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 7.50–7.43 (m, 2H, PhH), 7.40–7.32 (m, 3H, PhH), 5.61 (d, 1H, $J_{NH,2}$ = 7.2 Hz, N*H*COCH$_3$), 5.51 (s, 1H, PhC*H*), 5.38 (d, 1H, $J_{4,3}$ = 3.3 Hz, H-4), 4.94 (d, 1H, $J_{1,2}$ = 8.4 Hz, H-1), 4.73 (ddd, 1H, $J_{2',3a'}$ = 10.8 Hz, $J_{2',1'}$ = 7.3 Hz, $J_{2',3e'}$ = 5.6 Hz, H-2′), 4.62 (d, 1H, H-1′), 4.60 (dd, 1H, $J_{3,2}$ = 10.8 Hz, H-3), 4.31 (dd, 1H, $J_{6e',6a'}$ = 10.6 Hz, $J_{6e',5'}$ = 5.0 Hz, H-6e′), 3.82 (dd, 1H, $J_{5,6a}$ = 5.8 Hz, $J_{5,6b}$ = 5.8 Hz, H-5), 3.72 (dd, 1H, $J_{6a',5'}$ = 10.3 Hz, H-6a′), 3.60 (ddd, 1H, $J_{4',3a'}$ = 11.5 Hz, $J_{4',5'}$ = 10.2 Hz, $J_{4',3e'}$ = 4.6 Hz, H-4′), 3.53 (s, 3H, C-1-OCH_3), 3.50–3.39 (m, 3H, H-5′, H-6a, H-6b), 3.35 (s, 3H, C-6-OCH_3), 3.34–3.30 (m, 1H, H-2), 2.47 (ddd, 1H, $J_{3e',3a'}$ = 11.8 Hz, H-3e′), 2.07 (s, 3H, OCO*CH*$_3$), 2.00 (s, 3H, NHCO*CH*$_3$), 1.68 (ddd, 1H,

H-3a′), 1.23 (s, 9H, (CH_3)$_3$CCO–). ^{13}C NMR (125 MHz, $CDCl_3$): δ 177.1 ((CH$_3$)$_3$CCO–), 170.7 (NHCOCH$_3$), 169.4 (OCOCH$_3$), 137.2 (Ph), 129.1 (Ph), 128.3 (Ph), 126.1 (Ph), 101.9 (C-1′), 101.6 (PhCH), 100.3 (C-1), 75.0 (C-3), 74.7 (C-4′), 72.9 (C-5), 71.5 (C-6), 70.2 (C-5′), 79.9 (C-2′), 69.1 (C-4), 69.0 (C-6′), 59.3 (C-6-OCH$_3$), 57.0 (C-1-OCH$_3$), 55.3 (C-2), 39.1 ((CH$_3$)$_3$CCO–), 33.3 (C-3′), 27.3 ((CH$_3$)$_3$CCO–), 23.7 (NHCOCH$_3$), 21.0 (OCOCH$_3$). Anal. Calcd for $C_{30}H_{43}NO_{12}$(609.66): C, 59.10; H, 7.11; N, 2.30. Found: C, 59.54; H, 7.49; N, 2.30.

3.17. Methyl 2-acetamido-3-*O*-(4,6-*O*-benzylidene-3-deoxy-β-D-ribo-hexopyranosyl)-2- deoxy-4,6-di-*O*-pivaloyl-β-D-galactopyranoside (25)

Compound **23** (2.1 g, 3.1 mmol) was dissolved in guanidine solution (20 mL), and was stirred for 48 h under argon. The reaction was monitored by TLC, and the solution was evaporated to dryness. Column chromatography (1:4 acetone/toluene) gave a white solid **25** (1.7 g, 2.6 mmol, 85%): $[\alpha]_D^{22}$ +2.3 (*c* 1.03, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.52–7.48 (m, 2H, PhH), 7.40–7.31 (m, 3H, PhH), 5.66 (d, 1H, $J_{NH,2}$ = 7.4 Hz, NHCOCH$_3$), 5.51 (s, 1H, PhCH), 5.37 (d, 1H, $J_{4,3}$ = 3.1 Hz, H-4), 4.69 (d, 1H, $J_{1,2}$ = 8.2 Hz, H-1), 4.37 (d, 1H, $J_{1',2'}$ = 7.5 Hz, H-1′), 4.67 (dd, 1H, $J_{3,2}$ = 10.6 Hz, H-3), 4.26 (dd, 1H, $J_{6e',6a'}$ = 10.6 Hz, $J_{6e',5'}$ = 4.9 Hz, H-6e′), 4.14 (dd, 1H, $J_{6a,6b}$ = 10.4 Hz, $J_{6a,5}$ = 6.0 Hz, H-6a), 4.10 (dd, 1H, $J_{6b,5}$ = 7.3 Hz, H-6b), 3.92 (dd, 1H, H-5), 3.76–3.65 (m, 1H, H-6a′, H-2), 3.57–3.53 (m, 1H, H-4′), 3.51 (s, 3H, OCH$_3$), 3.49 (ddd, 1H, $J_{2',3a'}$ = 12.3 Hz, $J_{2',3e'}$ = 4.8 Hz, H-2′), 3.39 (ddd, 1H, $J_{5',4'}$ = 9.7, $J_{5',6a'}$ = 9.7 Hz, H-5′), 2.42 (ddd, 1H, $J_{3e',3a'}$ = 11.8 Hz, $J_{3e',4'}$ = 4.7 Hz, H-3e′), 2.02 (s, 3H, NHCOCH$_3$), 1.68 (ddd, 1H, $J_{4',3a'}$ = 11.8 Hz, H-3a′), 1.25 (s, 9H, (CH$_3$)$_3$CCO–), 1.21 (s, 9H, (CH$_3$)$_3$CCO–). ^{13}C NMR (125 MHz, $CDCl_3$): δ 177.9 ((CH$_3$)$_3$CCO–), 177.2 ((CH$_3$)$_3$CCO–), 171.6 (NHCOCH$_3$), 137.2 (Ph), 129.1 (Ph), 128.3 (Ph), 126.1 (Ph), 105.6 (C-1′), 101.7 (PhCH), 100.9 (C-1), 75.8 (C-4′), 75.5 (C-3), 71.3 (C-5), 70.6 (C-5′), 68.9 (C-6′), 68.7 (C-4), 68.6 (C-2′), 62.0 (C-6), 56.7 (OCH$_3$), 54.1 (C-2), 39.1 ((CH$_3$)$_3$CCO–), 38.7 ((CH$_3$)$_3$CCO–), 33.0 (C-3′), 27.2 ((CH$_3$)$_3$CCO–), 27.0 ((CH$_3$)$_3$CCO–), 23.8 (NHCOCH$_3$). Anal. Calcd for $C_{32}H_{47}NO_{12}$(637.72): C, 60.27; H, 7.43; N, 2.20. Found: C, 59.86; H, 7.55; N, 2.21.

3.18. Methyl 2-acetamido-3-*O*-(4,6-*O*-benzylidene-3-deoxy-β-D-erythro-hexos-2-ulosyl)-2- deoxy-4,6-di-*O*-pivaloyl-β-D-galactopyranoside (25a)

Disaccharide **25** (1.30 g, 2.0 mmol) was dissolved in a mixture of dry distilled dimethylsulfoxide (6.0 mL) and acetic anhydride (3.0 mL) under argon, and the reaction stirred for 96 h. Evaporation of the solvents gave a yellowish syrup **25a**, which can be used directly in the next step. It was purified by column chromatography (acetone/toluene, 1:5) for characterization purpose only: $[\alpha]_D^{22}$ +2.86 (*c* 2.1, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.52–7.48 (m, 2H, PhH), 7.40–7.16 (m, 3H, PhH), 5.76 (d, 1H, $J_{NH,2}$ = 6.9 Hz, NHCOCH$_3$), 5.66 (s, 1H, PhCH), 5.49 (d, 1H, $J_{4,3}$ = 3.0 Hz, H-4), 5.00 (d, 1H, $J_{1,2}$ = 8.3 Hz, H-1), 4.82 (s, 1H, H-1′), 4.80 (dd, 1H, $J_{3,2}$ = 10.8 Hz, H-3), 4.37 (dd, 1H, $J_{6e',6a'}$ = 10.6 Hz, $J_{6e',5'}$ = 5.0 Hz, H-6e′), 4.21 (ddd, 1H, $J_{4',3a'}$ = 11.6 Hz, $J_{4',5'}$ = 9.7 Hz, $J_{4',3e'}$ = 6.1 Hz, H-4′), 4.12–4.08 (m, high order, 2H, H-6a, H-6b), 3.92–3.98 (m, 2H, H-6a′, H-5), 3.73 (ddd, 1H, $J_{5',6a'}$ = 9.7 Hz, H-5′), 3.52 (s, 3H, OCH$_3$), 3.21 (ddd, 1H, H-2), 3.00 (dd, 1H, $J_{3e',3a'}$ = 17.1 Hz, H-3e′), 2.53 (dd, 1H, H-3a′), 2.02 (s, 3H, NHCOCH$_3$), 1.25 (s, 9H, (CH$_3$)$_3$CCO–), 1.22 (s, 9H, (CH$_3$)$_3$CCO–). ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.8 (C-2′), 177.7 ((CH$_3$)$_3$CCO–), 177.0 ((CH$_3$)$_3$CCO–), 171.5 (NHCOCH$_3$), 136.9 (Ph), 129.1 (Ph), 128.3 (Ph), 128.2 (Ph), 126.0 (Ph), 101.1 (PhCH), 100.5 (C-1′), 100.1 (C-1), 74.4 (C-5′), 73.2 (C-4′), 71.0 (C-5), 69.7 (C-3), 68.9 (C-6′), 68.5 (C-4), 61.5 (C-6), 57.0 (OCH$_3$), 55.8 (C-2), 42.5 (C-3′), 39.0 ((CH$_3$)$_3$CCO–), 38.6 ((CH$_3$)$_3$CCO–), 27.1 ((CH$_3$)$_3$CCO–), 27.0 ((CH$_3$)$_3$CCO–), 23.6 (NHCOCH$_3$). ES HRMS calcd for $C_{32}H_{45}NO_{12}Na$ (M+Na): 658.2834, found: 658.2838.

3.19. Methyl 2-acetamido-3-*O*-(4,6-*O*-benzylidene-3-deoxy-β-D-ribo-hexopyranosyl)- 2-deoxy-6-*O*-methyl-4-*O*-pivaloyl-β-D-galactopyranoside (26)

Compound **24** (0.30 g, 0.49 mmol) was dissolved in guanidine solution (3.0 mL), and was stirred for 24 h under argon. The solution was evaporated to dryness, followed by column chromatography (acetone/toluene, 1:3) to give a white solid (0.27 g, 0.47 mmol, 95%): $[\alpha]_D^{22}$ +5.2 (*c* 1.80, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.50–7.45 (m, 2H, PhH), 7.40–7.32 (m, 3H, PhH), 5.74 (d, 1H, $J_{NH,2}$ = 7.5 - Hz, NHCOCH$_3$), 5.50 (s, 1H, PhCH), 5.35 (d, 1H, $J_{4,3}$ = 3.0 Hz, H-4), 4.65 (d, 1H, $J_{1,2}$ = 8.3 Hz, H-1), 4.37 (d, 1H, $J_{1',2'}$ = 7.5 Hz, H-1′), 4.28 (dd, 1H, $J_{6e',6a'}$ = 10.6 Hz, $J_{6e',5'}$ = 5.0 Hz, H-6e′), 4.26 (dd, 1H, $J_{3,2}$ = 10.6 Hz, H-3), 3.84–3.70 (m, 3H, H-4′, H-2, H5), 3.53 (s, 3H, C-1-OCH$_3$), 3.52–3.43 (m, 4H, H-6a′, H-2′, H-6a, H-6b), 3.39 (ddd, 1H, $J_{5',4'}$ = 9.6 Hz, $J_{5',6a'}$ = 9.6 Hz, H-5′), 3.35 (s, 3H, C-6-OCH$_3$), 2.41 (ddd, 1H, $J_{3e',3a'}$ = 11.8 Hz, $J_{3e',2'}$ = 4.7 Hz, $J_{3e',4'}$ = 4.7 Hz, H-3e′), 2.01 (s, 3H, NHCOCH$_3$), 1.67 (ddd, 1H, $J_{3a',2'}$ = 11.8 Hz, $J_{3a',4'}$ = 11.8 Hz, H-3a′), 1.26 (s, 9H, (CH$_3$)$_3$CCO–). ^{13}C NMR (125 MHz, $CDCl_3$): δ 177.6 ((CH$_3$)$_3$CCO–), 171.7 (NHCOCH$_3$), 137.3 (Ph), 129.1 (Ph), 128.3 (Ph), 126.2 (Ph), 105.7 (C-1′), 101.7 (PhCH), 101.1 (C-1), 75.9 (C-3), 72.9 (C-4′), 71.3 (C-6), 70.7 (C-5′), 69.4 (C-5), 69.3 (C-4), 69.0 (C-6′), 68.6 (C-2′), 59.3 (C-6-OCH$_3$), 56.7 (C-1-OCH$_3$), 53.7 (C-2), 39.2 ((CH$_3$)$_3$CCO–), 35.1 (C-3′), 27.3 ((CH$_3$)$_3$CCO–), 23.8 (NHCOCH$_3$). Anal. Calcd for $C_{28}H_{41}NO_{11}$(667.63): C, 59.25; H, 7.28; N, 2.47. Found: C, 59.13; H, 7.60; N, 2.46.

3.20. Methyl 2-acetamido-3-*O*-(4,6-*O*-benzylidene-3-deoxy-β-D-arabino-hexopyranosyl)- 2-deoxy-4,6-di-*O*-pivaloyl-β-D-galactopyranoside (27)

After drying under vacuum for 18 h, the syrup of crude **25a** was dissolved in dry distilled THF (10 mL), and the reaction mixture was cooled at 0 °C under argon. A solution of L-selectride in THF (5.0 mL, 1.0 M) was added slowly by syringe, and the reaction was quenched with methanol immediately when bubbling ceased. Evaporation of the solvents and purification by column chromatography (acetone/toluene, 1:5) afforded the compound **27** as a white solid (0.99 g, 76% over 2 steps): $[\alpha]_D^{22}$ −2.27 (*c* 22.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.49–7.45 (m, 2H, PhH), 7.39–7.32 (m, 3H, PhH), 5.69 (d, 1H, $J_{NH,2}$ = 7.1 Hz, NHCOCH$_3$), 5.55 (s, 1H, PhCH), 5.38 (d, 1H, $J_{4,3}$ = 3.2 Hz, H-4), 4.91 (d, 1H, $J_{1,2}$ = 8.2 Hz, H-1), 4.86 (dd, 1H, $J_{3,2}$ = 11.0 Hz, H-3), 4.68 (s, 1H, H-1′), 4.26 (dd, 1H, $J_{6e',6a'}$ = 10.6 Hz, $J_{6e',5'}$ = 4.9 Hz, H-6e′), 4.16–4.08 (m, high order, 2H, H-6a, H-6b), 3.99 (ddd, 1H, $J_{4',3a'}$ = 11.5 Hz, $J_{4',5'}$ = 9.4 Hz, $J_{4',3e'}$ = 4.5 Hz, H-4′), 3.96 (dd, 1H, $J_{5,6a}$ = 6.7 Hz, $J_{5,6b}$ = 6.7 Hz, H-5), 3.90 (app. s, 1H, H-2′), 3.80 (dd, 1H, $J_{6a',5'}$ = 10.3 Hz, H-6a′), 3.52 (s, 3H, OCH$_3$), 3.42 (ddd, 1H, H-5′), 3.29 (ddd, 1H, H-2), 2.33 (ddd, 1H, $J_{3e',3a'}$ = 13.3 Hz, $J_{3e',2'}$ = 4.0 Hz, H-3e′), 2.00 (s, 3H, NHCOCH$_3$), 1.70 (ddd, 1H, $J_{3a',2'}$ = 3.0 Hz, H-3a′), 1.25 (s, 9H, (CH$_3$)$_3$CCO–), 1.20 (s, 9H, (CH$_3$)$_3$CCO–). ^{13}C NMR (125 MHz, $CDCl_3$): δ 178.1 ((CH$_3$)$_3$CCO–), 177.9 ((CH$_3$)$_3$CCO–), 171.0 (NHCOCH$_3$), 137.5 (Ph), 129.0 (Ph), 128.3 (Ph), 126.2 (Ph), 102.0 (PhCH), 101.1 (C-1′), 100.3 (C-1), 73.3 (C-3), 72.9 (C-4′), 71.0 (C-5 or C-5′), 70.8 (C-5′ or C-5), 69.5 (C-4), 68.9 (C-6′), 67.6 (C-2′), 61.7 (C-6), 57.1 (OCH$_3$), 55.5 (C-2), 39.3 ((CH$_3$)$_3$CCO–), 38.7 ((CH$_3$)$_3$CCO–), 34.1 (C-3′), 27.2 ((CH$_3$)$_3$CCO–), 27.1 ((CH$_3$)$_3$CCO–), 23.8 (NHCOCH$_3$). ES HRMS calcd for $C_{32}H_{47}NO_{12}Na$ (M+Na): 660.2991, found: 660.2993.

3.21. Methyl 2-acetamido-3-*O*-(4,6-*O*-benzylidene-3-deoxy-2-*O*-methyl-β-D-arabino- hexopyranosyl)-2-deoxy-4,6-di-*O*-pivaloyl-β-D-galactopyranoside (28)

To a solution of compound **28** (104 mg, 0.16 mmol) and methyl iodide (52 μL, 0.80 mmol) in dry DMF (1 mL) was added sodium hydride (20 mg, 60% dispersion in mineral oil, 0.48 mmol). The

reaction mixture was stirred at rt. for 1 h, and water was added to quench the reaction. The solution was evaporated to dryness, and column chromatography (acetone/toluene, 1:5) gave the methylated product (35 mg, 0.054 mmol, 33%): $[\alpha]_D^{22}$ +7.7 (*c* 0.43, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 7.48–7.42 (m, 2H, PhH), 7.37–7.30 (m, 3H, PhH), 5.66 (d, 1H, $J_{NH,2}$ = 7.3 Hz, N*H*COCH$_3$), 5.52 (s, 1H, PhC*H*), 5.43 (d, 1H, $J_{4,3}$ = 2.8 Hz, H-4), 4.86 (d, 1H, $J_{1,2}$ = 8.4 Hz, H-1), 4.68 (d, 1H, $J_{1',2'}$ = 1.4 Hz, H-1′), 4.61 (dd, 1H, $J_{3,2}$ = 10.9 Hz, H-3), 4.21 (dd, 1H, $J_{6e',6a'}$ = 10.5 Hz, $J_{6e',5'}$ = 4.9 Hz, H-6e′), 4.10 (dd, 1H, $J_{6a,6b}$ = 11.4 Hz, $J_{6a,5}$ = 6.1 Hz, H-6a), 4.04 (dd, 1H, $J_{6b,5}$ = 7.3 Hz, H-6b), 3.92–3.84 (m, 2H, H-4′, H-5), 3.79 (dd, 1H, $J_{6a',5'}$ = 10.3 Hz, H-6a′), 3.58 (ddd, 1H, $J_{2',3a'}$ = 4.1 Hz, $J_{2',3e'}$ = 4.1 Hz, H-2′), 3.49 (s, 3H, C-1-OCH$_3$), 3.48–3.42 (m, 1H, H-5′), 3.41 (s, 3H, C-6-OCH$_3$), 3.38–3.31 (m, 1H, H-2), 2.28 (ddd, 1H, $J_{3e',3a'}$ = 12.3 Hz, $J_{3e',4'}$ = 4.8 - Hz, H-3e′), 1.97 (s, 3H, NHCOC*H*$_3$), 1.71 (ddd, 1H, $J_{3a',4'}$ = 11.1 Hz, H-3a′), 1.23 (s, 9H, (C*H*$_3$)$_3$CCO–), 1.18 (s, 9H, (C*H*$_3$)$_3$CCO–). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.8 ((CH$_3$)$_3$CCO–), 177.0 ((CH$_3$)$_3$CCO–), 170.7 (NHCOCH$_3$), 137.4 (Ph), 128.9 (Ph), 128.2 (Ph), 126.0 (Ph), 101.6 (PhCH), 101.4 (C-1′), 100.6 (C-1), 76.1 (C-2′), 74.0, 73.1, 71.3, 70.5 (C-4), 68.9 (C-6′), 68.4, 62.0 (C-6), 57.9 (C-2′-OCH$_3$), 56.8 (C-1-OCH$_3$), 55.1 (C-2), 39.3 ((CH$_3$)$_3$CCO–), 38.7 ((CH$_3$)$_3$CCO–), 31.3 (C-3′), 27.2 ((*C*H$_3$)$_3$CCO–), 27.0 ((*C*H$_3$)$_3$CCO–), 23.7 (NHCOCH$_3$). ES HRMS calcd for $C_{33}H_{49}NO_{12}Na$ (M+Na): 674.3147, found: 674.3142.

3.22. Methyl 2-acetamido-3-*O*-(4,6-*O*-benzylidene-3-deoxy-β-D-arabino-hexopyranosyl)- 2-deoxy-6-*O*-methyl-4-*O*-pivaloyl-β-D-galactopyranoside (29)

Compound **26** (0.18 g, 0.31 mmol) was dissolved in a mixture of dry distilled dimethylsulfoxide (1.4 mL) and acetic anhydride (0.7 mL) under argon, and the reaction was stirred for 48 h. Evaporation of the solvents gave a yellowish syrup, which was dissolved in dry distilled THF (2 mL), and the reaction mixture was cooled at −20 °C under argon. A solution of L-selectride in THF (0.8 mL, 1.0 M) was added slowly by syringe, and the reaction was quenched with methanol after 1 min. Evaporation of the solvents and purification by column chromatography (acetone/toluene, 1:2) afforded compound **29** as a white solid (0.15 g, 86% over 2 steps): $[\alpha]_D^{22}$ +0.92 (*c* 6.4, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ 7.50–7.45 (m, 2H, PhH), 7.40–7.32 (m, 3H, PhH), 5.66 (d, 1H, $J_{NH,2}$ = 7.4 Hz, N*H*COCH$_3$), 5.54 (s, 1H, PhC*H*), 5.38 (d, 1H, $J_{4,3}$ = 3.2 Hz, H-4), 4.86 (d, 1H, $J_{1,2}$ = 8.4 Hz, H-1), 4.77 (dd, 1H, $J_{3,2}$ = 11.0 Hz, H-3), 4.67 (s, 1H, H-1′), 4.28 (dd, 1H, $J_{6e',6a'}$ = 10.6 Hz, $J_{6e',5'}$ = 5.0 Hz, H-6e′), 3.98 (ddd, 1H, $J_{4',3a'}$ = 11.6 Hz, $J_{4',5'}$ = 9.5 Hz, $J_{4',3e'}$ = 4.5 Hz, H-4′), 3.90 (app. s, 1H, H-2′), 3.85 (dd, 1H, $J_{5,6a}$ = 6.5 Hz, $J_{5,6b}$ = 6.5 Hz, H-5), 3.82 (dd, 1H, $J_{6a',5'}$ = 10.4 Hz, H-6a′), 3.54 (s, 3H, C-1-OCH$_3$), 3.48 (dd, 1H, $J_{6a,6b}$ = 10.1 Hz, H-6a), 3.44 (dd, 1H, H-6b), 3.44–3.36 (m, 2H, H-5′, H-2), 3.35 (s, 3H, C-6-OCH$_3$), 2.41 (ddd, 1H, $J_{3e',3a'}$ = 13.3 Hz, $J_{3e',2'}$ = 4.0 Hz, H-3e′), 2.00 (s, 3H, vNHCOC*H*$_3$), 1.73–1.68 (m, 1H, H-3a′), 1.26 (s, 9H, (C*H*$_3$)$_3$CCO–). ^{13}C NMR (125 MHz, $CDCl_3$): δ 177.9 ((CH$_3$)$_3$CCO–), 171.0 (NHCOCH$_3$), 137.5 (Ph), 129.0 (Ph), 128.3 (Ph), 126.2 (Ph), 101.9 (PhCH), 100.9 (C-1′), 100.5 (C-1), 73.3 (C-4′), 73.2 (C-3), 72.6 (C-5), 71.2 (C-6), 70.8 (C-5′), 70.0 (C-4), 69.0 (C-6′), 67.6 (C-2′), 59.3 (C-6-OCH$_3$), 57.0 (C-1-OCH$_3$), 55.2 (C-2), 39.1 ((CH$_3$)$_3$CCO–), 34.0 (C-3′), 27.2 ((*C*H$_3$)$_3$CCO–), 23.7 (NHCOCH$_3$). ES HRMS calcd for $C_{28}H_{41}NO_{11}Na$ (M+Na): 590.2572, found: 590.2570.

3.23. Methyl 2-acetamido-3-*O*-(4-*O*-benzoyl-6-bromo-3,6-dideoxy-β-D-arabino- hexopyranosyl)-2-deoxy-4,6-di-*O*-pivaloyl-β-D-galactopyranoside (30)

To a solution of **27** (222 mg, 0.35 mmol) in carbon tetrachloride (2.0 mL), *N*-bromosuccinimide (119 mg, 0.53 mmol) and barium carbonate (151 mg, 0.70 mmol) were added. The reaction mixture was heated at reflux under argon for 1 h, and then cooled. During the bromination, the solution turned orange, and the reaction reached completion when the orange color disappeared. The reaction mixture was applied directly to a column and chromatographed (acetone/toluene, 1:5) to give compound **30** as a white solid (186 mg, 74%): $[\alpha]_D^{22}$ +16.8 (*c* 3.5, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ 8.01–8.00 (m, 2H, PhH), 7.60–7.58 (m, 1H, PhH), 7.47–7.44 (m, 2H, PhH), 5.71 (d, 1H, $J_{NH,2}$ = 7.5 Hz, N*H*COCH$_3$), 5.54 (d, 1H, $J_{4,3}$ = 3.0 Hz, H-4), 5.25 (ddd, 1H, $J_{4',3a'}$ = 10.2 Hz, $J_{4',5'}$ = 10.2 Hz, $J_{4',3e'}$ = 4.9 Hz, H-4′), 4.86 (dd, 1H, $J_{3,2}$ = 11.1 Hz, H-3), 4.81 (d, 1H, $J_{1,2}$ = 8.6 Hz, H-1), 4.79 (s, 1H, H-1′), 4.20 (dd, 1H, $J_{6a,6b}$ = 11.1 Hz, $J_{6a,5}$ = 6.9 Hz, H-6a), 4.10 (dd, 1H, $J_{6b,5}$ = 7.1 Hz, H-6b), 4.00 (dd, 1H, H-5), 3.87 (app. s, 1H, H-2′), 3.82 (ddd, 1H, $J_{5',6a'}$ = 9.1 Hz, $J_{5',6b'}$ = 2.6 Hz, H-5′), 3.58 (dd, 1H, $J_{6b',6a'}$ = 11.1 Hz, H-6b′), 3.55–3.50 (m, 2H, H-2, H-6a′), 3.53 (s, 3H, OCH$_3$), 2.50 (ddd, 1H, $J_{3e',3a'}$ = 13.6 Hz, $J_{3e',2'}$ = 4.5 Hz, H-3e′), 2.03 (s, 3H, NHCOC*H*$_3$), 1.70 (ddd, 1H, $J_{3a',2'}$ = 2.7 Hz, H-3a′), 1.26 (s, 9H, (C*H*$_3$)$_3$CCO–), 1.21 (s, 9H, (C*H*$_3$)$_3$CCO–). ^{13}C NMR (125 MHz, $CDCl_3$): δ 178.4 ((CH$_3$)$_3$CCO–), 177.9 ((CH$_3$)$_3$CCO–), 171.0 (NHCOCH$_3$), 165.2 (PhCO–), 133.4 (Ph), 129.7 (Ph), 129.5 (Ph), 128.5 (Ph), 100.9 (C-1), 100.5 (C-1′), 72.9 (C-4′), 70.9 (C-5), 69.4 (C-4), 67.9 (C-3), 66.7 (C-2′), 61.4 (C-6), 57.0 (OCH$_3$), 54.7 (C-2), 39.4 ((CH$_3$)$_3$CCO–), 38.8 ((CH$_3$)$_3$CCO–), 34.1 (C-3′), 32.3 (C-6′), 27.2 ((*C*H$_3$)$_3$CCO–), 27.1 ((*C*H$_3$)$_3$CCO–), 23.8 (NHCOCH$_3$). ES HRMS calcd for $C_{32}H_{46}NO_{12}BrNa$ (M+Na): 738.2096, found: 738.2093.

3.24. Methyl 2-acetamido-3-*O*-(4-*O*-benzoyl-6-bromo-3,6-dideoxy-2-*O*-methyl-β-D- arabino-hexopyranosyl)-2-deoxy-4,6-di-*O*-pivaloyl-β-D-galactopyranoside (31)

Compound **28** (35 mg, 0.054 mmol) was dissolved in carbon tetrachloride (1.0 mL), followed by addition of *N*-bromosuccinimide (18 mg, 0.081 mmol) and barium carbonate (24 mg, 0.70 mmol). The reaction mixture was refluxed under argon for 70 min, cooled to ambient temperature and applied directly to a column and chromatographed (acetone/toluene, 1:5) to produce compound **31** as a white solid (27 mg, 72%): $[\alpha]_D^{22}$ +11.0 (*c* 5.5, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 8.01–8.00 (m, 2H, PhH), 7.61–7.58 (m, 1H, PhH), 7.48–7.46 (m, 2H, PhH), 5.80 (d, 1H, $J_{NH,2}$ = 6.8 Hz, N*H*COCH$_3$), 5.57 (d, 1H, $J_{4,3}$ = 2.9 Hz, H-4), 5.17 (ddd, 1H, $J_{4',3a'}$ = 9.4 Hz, $J_{4',5'}$ = 9.4 Hz, $J_{4',3e'}$ = 4.6 Hz, H-4′), 4.82 (s, 1H, H-1′), 4.65 (d, 1H, $J_{1,2}$ = 8.3 Hz, H-1), 4.60 (dd, 1H, $J_{3,2}$ = 11.0 Hz, H-3), 4.13 (dd, 1H, $J_{6a,6b}$ = 11.5 Hz, $J_{6a,5}$ = 7.3 Hz, H-6a), 4.05 (dd, 1H, $J_{6b,5}$ = 6.2 Hz, H-6b), 3.92 (dd, 1H, H-5), 3.91–3.88 (m, 1H, H-5′), 3.72 (ddd, 1H, H-2), 3.62–3.59 (m, 1H, H-2′), 3.58–3.54 (m, 1H, H-6a′, H-6b′), 3.51 (s, 3H, C-1-OCH$_3$), 3.46 (s, 3H, C-2′-OCH$_3$), 2.56 (ddd, 1H, $J_{3e',3a'}$ = 13.6 Hz, $J_{3e',2'}$ = 4.9 Hz, H-3e′), 2.04 (s, 3H, NHCOC*H*$_3$), 1.67 (ddd, 1H, $J_{3a',2'}$ = 2.6 Hz, H-3a′), 1.26 (s, 9H, (C*H*$_3$)$_3$CCO–), 1.21 (s, 9H, (C*H*$_3$)$_3$CCO–). ^{13}C NMR (125 MHz, $CDCl_3$): δ 178.0 ((CH$_3$)$_3$CCO–), 177.3 ((CH$_3$)$_3$CCO–), 170.8 (PhCO–), 165.3 (NHCOCH$_3$), 133.5 (Ph), 129.6 (Ph), 129.5 (Ph), 128.5 (Ph), 101.7 (C-1), 100.0 (C-1′), 77.0 (C-5′), 75.5 (C-2′), 73.5 (C-3), 71.4 (C-5), 68.3 (C-4), 67.9 (C-4′), 62.1 (C-6), 57.5 (C-2′-OCH$_3$), 56.7 (C-1-OCH$_3$), 53.9 (C-2), 39.1 ((CH$_3$)$_3$CCO–), 38.7 ((CH$_3$)$_3$CCO–), 32.3 (C-6′), 30.3 (C-3′), 27.3 ((*C*H$_3$)$_3$CCO–), 27.1 ((*C*H$_3$)$_3$CCO–), 23.9 (NHCOCH$_3$). ES HRMS calcd for $C_{33}H_{48}NO_{12}BrNa$ (M+Na): 752.2252, found: 752.2251.

3.25. Methyl 2-acetamido-3-*O*-(4-*O*-benzoyl-6-bromo-3,6-dideoxy-β-D-arabino-hexopyranosyl)-2-deoxy-6-*O*-methyl-4-*O*-pivaloyl-β-D-galactopyranoside (32)

To a solution of **29** (75 mg, 0.13 mmol) in carbon tetrachloride (1 mL), *N*-bromosuccinimide (44 mg, 0.20 mmol) and barium carbonate (56 mg, 0.26 mmol) were added. The reaction mixture was kept at reflux under argon for 1 h, and then cooled. During the bromination, the solution turned orange, and the reaction reached completion when the orange color disappeared. The crude

mixture was applied directly to a column and chromatographed (acetone/toluene, 1:5) to produce compound **32** as a white solid (69 mg, 82%): $[\alpha]_D^{22}$ +5.0 (*c* 11.5, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 8.01–7.99 (m, 2H, PhH), 7.61–7.57 (m, 1H, PhH), 7.46–7.42 (m, 2H, PhH), 5.68 (d, 1H, $J_{NH,2}$ = 7.9 Hz, N*H*COCH$_3$), 5.53 (d, 1H, $J_{4,3}$ = 2.7 Hz, H-4), 5.25 (ddd, 1H, $J_{4',3a'}$ = 10.3 Hz, $J_{4',5'}$ = 10.3 Hz, $J_{4',3e'}$ = 4.9 Hz, H-4′), 4.78 (s, 1H, H-1′), 4.77 (dd, 1H, $J_{3,2}$ = 10.8 Hz, H-3), 4.74 (d, 1H, $J_{1,2}$ = 8.3 Hz, H-1), 3.89–3.84 (m, 2H, H-5, H-2′), 3.81 (ddd, 1H, $J_{5',6a'}$ = 8.4 Hz, $J_{5',6b'}$ = 8.4 Hz, H-5′), 3.62–3.51 (m, 3H, H-2, H-6a′, H-6b′), 3.54 (s, 3H, C-1-OCH$_3$), 3.51–3.44 (m, 2H, H-6a, H-6b), 3.36 (s, 3H, C-6-OCH$_3$), 2.49 (ddd, 1H, $J_{3e',3a'}$ = 13.7 Hz, $J_{3e',2'}$ = 4.4 Hz, H-3e′), 2.03 (s, 3H, NHCOC*H*$_3$), 1.70 (ddd, 1H, $J_{3a',2'}$ = 2.9 - Hz, H-3a′), 1.26 (s, 9H, (C*H*$_3$)$_3$CCO–). ^{13}C NMR (125 MHz, $CDCl_3$): δ 178.4 ((CH$_3$)$_3$CCO–), 170.8 (NH*C*OCH$_3$), 165.2 (Ph*C*O–), 133.4 (Ph), 129.7 (Ph), 129.5 (Ph), 128.5 (Ph), 101.0 (C-1′), 100.4 (C-1), 77.4 (C-5′), 73.2 (C-3), 72.6 (C-5), 71.3 (C-6), 70.1 (C-4), 67.9 (C-4′), 66.7 (C-2′), 59.3 (C-6-O*C*H$_3$), 56.9 (C-1-O*C*H$_3$), 54.5 (C-2), 39.1 ((CH$_3$)$_3$ *C*CO–), 33.9 (C-3′), 32.4 (C-6′), 27.2 ((*C*H$_3$)$_3$CCO–), 23.9 (NHCOC*H*$_3$). ES HRMS calcd for $C_{28}H_{40}BrNO_{11}Na$ (M+Na): 668.1677, found: 668.1680.

3.26. Methyl 2-acetamido-3-*O*-(4-*O*-benzoyl-3,6-dideoxy-β-D-arabino-hexopyranosyl)- 2-deoxy-4,6-di-*O*-pivaloyl-β-D-galactopyranoside (33)

Compound **30** (35 mg, 0.049 mmol) was dissolved in dry toluene (1 mL). After tributyltin hydride (25 μL, 0.059 mmol) and azobisisobutyronitrile (AIBN) (catalytic amount) were added, the reaction mixture was refluxed for 1 h. The reaction mixture was cooled, applied directly to a column and chromatographed (acetone/toluene, 1:4) to give the 3,6-dideoxy sugar **33** as a white solid (32 mg, 100%): $[\alpha]_D^{22}$ +15.5 (*c* 2.5, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ 8.01–7.99 (m, 2H, PhH), 7.60–7.55 (m, 1H, PhH), 7.45–7.42 (m, 2H, PhH), 5.71 (d, 1H, $J_{NH,2}$ = 7.1 Hz, N*H*COCH$_3$), 5.45 (d, 1H, $J_{4,3}$ = 3.3 Hz, H-4), 5.09 (ddd, 1H, $J_{4',3a'}$ = 10.6 Hz, $J_{4',5'}$ = 10.6 Hz, $J_{4',3e'}$ = 4.9 Hz, H-4′), 4.96 (d, 1H, $J_{1,2}$ = 8.3 Hz, H-1), 4.89 (dd, 1H, $J_{3,2}$ = 11.0 Hz, H-3), 4.68 (s, 1H, H-1′), 4.15 (dd, 1H, $J_{6a,6b}$ = 11.2 Hz, $J_{6a,5}$ = 7.5 Hz, H-6a), 4.11 (dd, 1H, $J_{6b,5}$ = 7.5 Hz, H-6b), 3.97 (dd, 1H, H-5), 3.86 (app. d, 1H, $J_{2',OH}$ = 2.2 Hz, H-2′), 3.68 (dq, 1H, $J_{5',6'}$ = 6.2 Hz, H-5′), 3.52 (s, 3H, OCH$_3$), 3.25 (ddd, 1H, H-2), 2.56 (d, 1H, C-2′-OH), 2.48 (ddd, 1H, $J_{3e',3a'}$ = 13.5 Hz, $J_{3e',2'}$ = 4.4 Hz, H-3e′), 2.01 (s, 3H, NHCOC*H*$_3$), 1.63 (m, 1H, H-3a′), 1.28 (d, 1H, C-6′), 1.25 (s, 9H, (C*H*$_3$)$_3$CCO–), 1.20 (s, 9H, (C*H*$_3$)$_3$CCO–). ^{13}C NMR (125 MHz, $CDCl_3$): δ 178.0 ((CH$_3$)$_3$C*C*O–), 177.9 ((CH$_3$)$_3$*C*CO–), 171.0 (NH*C*OCH$_3$), 165.4 (Ph*C*O–), 133.0 (Ph), 130.1 (Ph), 129.6 (Ph), 128.4 (Ph), 100.8 (C-1′), 100.4 (C-1), 73.9 (C-5′), 72.6 (C-3), 71.1 (C-5), 70.1 (C-4′), 69.3 (C-4), 67.2 (C-2′), 61.7 (C-6), 57.1 (OCH$_3$), 55.6 (C-2), 39.3 ((CH$_3$)$_3$CCO–), 38.7 ((CH$_3$)$_3$CCO–), 34.4 (C-3′), 27.2 ((*C*H$_3$)$_3$CCO–), 27.1 ((*C*H$_3$)$_3$CCO–), 23.8 (NHCO*C*H$_3$), 18.0 (C-6′). ES HRMS calcd for $C_{32}H_{47}NO_{12}Na$ (M+Na): 660.2991, found: 660.2991.

3.27. Methyl 2-acetamido-3-*O*-(4-*O*-benzoyl-3,6-dideoxy-2-*O*-methyl-β-D-arabino-hexopyranosyl)- 2-deoxy-4,6-di-*O*-pivaloyl-β-D-galactopyranoside (34)

Compound **31** (19 mg, 0.026 mmol) was dissolved in dry toluene (1 mL). Tributyltin hydride (15 μL, 0.032 mmol) and azobisisobutyronitrile (AIBN) (catalytic amount) were added, the reaction mixture was refluxed for 50 min, cooled, applied directly to a column and chromatographed (acetone/toluene, 1:5) to give compound **34** as a white solid (15 mg, 0.023 mmol, 87%): $[\alpha]_D^{22}$ +19.0 (*c* 4.5, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ 8.01–8.00 (m, 2H, PhH), 7.60–7.56 (m, 1H, PhH), 7.44–7.40 (m, 2H, PhH), 5.78 (d, 1H, $J_{NH,2}$ = 6.8 Hz, N*H*COCH$_3$), 5.48 (d, 1H, $J_{4,3}$ = 3.2 Hz, H-4), 4.93 (ddd, 1H, $J_{4',3a'}$ = 10.0 Hz, $J_{4',5'}$ = 10.4 Hz, $J_{4',3e'}$ = 4.8 Hz, H-4′), 4.72 (d, 1H, $J_{1,2}$ = 8.5 Hz, H-1), 4.69 (s, 1H, H-1′), 4.60 (dd, 1H, $J_{3,2}$ = 11.0 Hz, H-3), 4.14 (dd, 1H, $J_{6a,6b}$ = 11.2 Hz, $J_{6a,5}$ = 6.2 Hz, H-6a), 4.09 (dd, 1H, $J_{6b,5}$ = 7.2 Hz, H-6b), 3.91 (dd, 1H, H-5), 3.78 (dq, 1H, $J_{5',6'}$ = 6.2 Hz, H-5′), 3.62 (app. s, 1H, H-2′), 3.55–3.50 (m, 1H, H-2), 3.51 (s, 3H, C-1-OCH$_3$), 3.47 (s, 3H, C-2′-OCH$_3$), 2.41 (ddd, 1H, $J_{3e',3a'}$ = 13.8 Hz, $J_{3e',2'}$ = 4.4 Hz, H-3e′), 2.00 (s, 3H, NHCOC*H*$_3$), 1.56 (ddd, 1H, $J_{3a',2'}$ = 2.4 Hz, H-3a′), 1.31 (d, 3H, H-6′), 1.25 (s, 9H, (C*H*$_3$)$_3$CCO–), 1.20 (s, 9H, (C*H*$_3$)$_3$CCO–). ^{13}C NMR (125 MHz, $CDCl_3$): δ 177.9 ((CH$_3$)$_3$CCO–), 177.4 ((CH$_3$)$_3$CCO–), 170.8 (NH*C*OCH$_3$), 165.6 (Ph*C*O–), 133.1 (Ph), 130.0 (Ph), 129.6 (Ph), 128.4 (Ph), 101.5 (C-1), 99.9 (C-1′), 76.0 (C-2′), 74.5 (C-5′), 73.0, 71.4, 70.4, 67.8 (C-4), 62.3 (C-6), 57.0 (C-2′-O*C*H$_3$), 56.8 (C-1-O*C*H$_3$), 54.2 (C-2), 39.1 ((CH$_3$)$_3$*C*CO–), 38.7 ((CH$_3$)$_3$CCO–), 30.5 (C-3′), 27.3 ((*C*H$_3$)$_3$CCO–), 27.1 ((*C*H$_3$)$_3$CCO–), 23.8 (NHCO*C*H$_3$), 18.4 (C-6′). ES HRMS calcd for $C_{33}H_{49}NO_{12}Na$ (M+Na): 674.3147, found: 674.3145.

3.28. Methyl 2-acetamido-3-*O*-(4-*O*-benzoyl-3,6-dideoxy-β-D-arabino-hexopyranosyl)- 2-deoxy-6-*O*-methyl-4-*O*-pivaloyl-β-D-galactopyranoside (35)

Compound **32** (36 mg, 0.056 mmol) was dissolved in dry toluene (1 mL). After tributyltin hydride (33 μL, 0.067 mmol) and azobisisobutyronitrile (AIBN) (catalytic amount) were added, the reaction mixture was refluxed for 1 h. The reaction mixture was cooled, applied directly to a column and chromatographed (acetone/toluene, 1:4) to give compound **35** as a white solid (29 mg, 91%): $[\alpha]_D^{22}$ +11.8 (*c* 12.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 8.00–7.96 (m, 2H, PhH), 7.59–7.50 (m, 1H, PhH), 7.43–7.37 (m, 2H, PhH), 5.65 (d, 1H, $J_{NH,2}$ = 7.0 Hz, N*H*COCH$_3$), 5.41 (d, 1H, $J_{4,3}$ = 3.1 Hz, H-4), 5.06 (ddd, 1H, $J_{4',3a'}$ = 10.7 Hz, $J_{4',5'}$ = 10.7 Hz, $J_{4',3e'}$ = 4.6 Hz, H-4′), 4.90 (d, 1H, $J_{1,2}$ = 8.4 Hz, H-1), 4.80 (dd, 1H, $J_{3,2}$ = 11.1 Hz, H-3), 4.65 (s, 1H, H-1′), 3.86–3.84 (m, 2H, H-5, H-2′), 3.65 (dq, 1H, $J_{5',6'}$ = 6.2 Hz, H-5′), 3.52 (s, 3H, C-1-OCH$_3$), 3.47–3.43 (m, 2H, H-6a, H-6b), 3.32 (s, 3H, C-6-OCH$_3$), 3.32–3.28 (m, 1H, H-2), 2.45 (ddd, 1H, $J_{3e',3a'}$ = 13.7 Hz, $J_{3e',2'}$ = 4.3 Hz, H-3e′), 1.99 (s, 3H, NHCOC*H*$_3$), 1.62–1.55 (m, 1H, H-3a′), 1.27 (d, 3H, H-6′), 1.23 (s, 9H, (C*H*$_3$)$_3$CCO–). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.9 ((CH$_3$)$_3$CCO–), 170.8 (NH*C*OCH$_3$), 165.2 (Ph*C*O–), 132.9 (Ph), 130.0 (Ph), 129.4 (Ph), 128.2 (Ph), 100.5 (C-1′), 100.3 (C-1), 73.8 (C-5′), 72.7 (C-5), 72.6 (C-3), 71.2 (C-6), 70.0 (C-4), 69.8 (C-4′), 67.1 (C-2′), 59.2 (C-6-O*C*H$_3$), 57.0 (C-1-O*C*H$_3$), 55.4 (C-2), 39.4 ((CH$_3$)$_3$*C*CO–), 34.1 (C-3′), 27.1 ((*C*H$_3$)$_3$CCO–), 23.7 (NHCO*C*H$_3$), 18.0 (C-6′). ES HRMS calcd for $C_{28}H_{41}NO_{11}Na$ (M+Na): 590.2572, found: 590.2573.

3.29. Methyl 2-acetamido-3-*O*-(3,6-dideoxy-β-D-arabino-hexopyranosyl)-2-deoxy- β-D-galactopyranoside (2)

Compound **33** (26 mg, 0.041 mmol) was dissolved in dry distilled methanol (1 mL) under argon. Sodium methoxide in methanol solution (1.7 M, 29 μL) was added, and the reaction mixture was stirred at rt. for 22 h. Dowex 50WX4-50 H^+ resin was added to neutralize the solution, and the resin was removed by filtration. The filtrate was evaporated to dryness and the residue was purified by HPLC using a Beckman C_{18} silica column. MeOH–H_2O gradient elution afforded the native disaccharide **2** (15 mg, 100%): $[\alpha]_D^{22}$ −27.5 (*c* 0.50, CH_3OH). ^1H NMR (600 MHz, CD_3OD): δ 4.55 (d, 1H, $J_{1',2'}$ = 1.0 Hz, H-1′), 4.34 (d, 1H, $J_{1,2}$ = 8.4 Hz, H-1), 4.04 (d, 1H, $J_{4,3}$ = 2.5 Hz, H-4), 4.01 (dd, 1H, $J_{2,3}$ = 10.7 Hz, H-2), 3.78–3.72 (m, 3H, H-2′, H-3, H-6a, H-6b), 3.52–3.46 (m, 2H, H-5, H-4′), 3.45 (s, 3H, OCH$_3$), 3.26 (dd, 1H, $J_{5',4'}$ = 9.2 Hz, $J_{5',6'}$ = 6.1 Hz, H-5′), 2.12 (ddd, 1H, $J_{3e',3a'}$ = 13.7 Hz, $J_{3e',4'}$ = 4.7 Hz, $J_{3e',2'}$ = 3.3 Hz, H-3e′), 1.94 (s, 3H, NHCOC*H*$_3$), 1.51 (ddd, 1H, $J_{3a',4'}$ = 11.4 Hz, $J_{3a',2'}$ = 2.7 Hz, H-3a′), 1.26 (d, 3H, H-6′). ^{13}C NMR (125 MHz, CD_3OD): δ 173.7 (NH*C*OCH$_3$), 104.1 (C-1′), 103.6 (C-1), 81.0 (C-3), 77.5 (C-4′), 76.3

(C-5), 69.8 (C-4), 69.2 (C-2′), 68.1 (C-5′), 62.4 (C-6), 56.9 (OCH_3), 52.9 (C-2), 38.9 (C-3′), 23.0 ($NHCOCH_3$), 18.4 (C-6′). ES HRMS calcd for $C_{15}H_{27}NO_9Na$ (M+Na): 388.1578, found: 388.1576.

3.30. Methyl 2-acetamido-3-*O*-(3,6-dideoxy-2-*O*-methyl-β-D-arabino-hexopyranosyl)- 2-deoxy- β-D-galactopyranoside (5)

Compound **34** (15 mg, 0.023 mmol) was suspended in dry distilled methanol (1 mL) under argon. A methanolic solution of sodium methoxide (1.7 M, 29 μL) was added, and the reaction mixture was stirred at rt for 6 h. Dowex 50WX4-50 H^+ resin was added to neutralize the solution, and the resin was removed by filtration. The filtrate was evaporated to dryness and the residue was purified by HPLC using a Beckman C_{18} silica column. Gradient elution with MeOH–H_2O afforded the final disaccharide **5** (8.7 mg, 0.017 mmol, 100%): $[\alpha]_D^{22}$ −23.7 (*c* 0.50, CH_3OH). ^1H NMR (600 MHz, D_2O): δ 4.73 (s, 1H, H-1′), 4.43 (d, 1H, $J_{1,2}$ = 8.6 Hz, H-1), 4.12 (d, 1H, $J_{4,3}$ = 3.1 Hz, H-4), 4.01 (dd, 1H, $J_{2,3}$ = 10.7 Hz, H-2), 3.82 (dd, 1H, $J_{6a,6b}$ = 11.8 Hz, $J_{6a,5}$ = 8.0 Hz, H-6a), 3.80 (dd, 1H, H-3), 3.76 (dd, 1H, $J_{6b,5}$ = 4.3 Hz, H-6b), 3.69 (dd, 1H, H-5), 3.57 (dd, 1H, $J_{2',3a'}$ = 3.1 Hz, $J_{2',3e'}$ = 3.1 Hz, H-2′), 3.51 (s, 3H, C-1-OCH_3), 3.47–3.42 (m, 2H, H-4′, H-5′), 3.41 (s, 3H, C-2′-OCH_3), 2.36 (ddd, 1H, $J_{3e',3a'}$ = 13.9 Hz, $J_{3e',4'}$ = 3.6 Hz, H-3e′), 2.02 (s, 3H, $NHCOCH_3$), 1.53 (ddd, 1H, $J_{3a',4'}$ = 11.0 Hz, H-3a′), 1.25 (d, 3H, $J_{6',5'}$ = 5.2 Hz, H-6′). ^{13}C NMR (125 MHz, D_2O): δ 175.3 ($NHCOCH_3$), 103.9 (C-1′), 102.9 (C-1), 81.0 (C-3), 77.9 (C-2′), 77.0 (C-5′), 75.7 (C-5), 68.7 (C-4), 67.8 (C-4′), 61.9 (C-6), 58.3 (C-2′-OCH_3), 57.8 (C-1-OCH_3), 52.0 (C-2), 34.6 (C-3′), 23.0 ($NHCOCH_3$), 18.0 (C-6′). ES HRMS calcd for $C_{16}H_{29}NO_9Na$ (M+Na): 402.1735, found: 402.1733.

3.31. Methyl 2-acetamido-3-*O*-(3,6-dideoxy-β-D-arabino-hexopyranosyl)-2-deoxy- 6-*O*-methyl-β-D-galactopyranoside (4)

Compound **35** (15 mg, 0.026 mmol) was dissolved in dry distilled methanol (1 mL) under argon. Sodium methoxide in methanol solution (1.7 N, 29 μL) was added, and the reaction mixture was stirred at rt for 6 h. Dowex 50WX4-50 H^+ resin was added to neutralize the solution, and the resin was removed by filtration. The filtrate was evaporated to dryness and the residue was purified by HPLC using a Beckman C_{18} silica column with a MeOH-H_2O gradient to afford the final compound **4** (10 mg, 100%): $[\alpha]_D^{22}$ −21.0 (*c* 0.30, CH_3OH). ^1H NMR (600 MHz, D_2O): δ 4.68 (s, 1H, H-1′), 4.44 (d, 1H, $J_{1,2}$ = 8.6 Hz, H-1), 4.09 (d, 1H, $J_{4,3}$ = 1.1 Hz, H-4), 4.01 (dd, 1H, $J_{2,3}$ = 10.6 Hz, H-2), 3.89 (dd, 1H, $J_{2',3a'}$ = 3.1 Hz, $J_{2',3e'}$ = 3.1 - Hz, H-2′), 3.86 (dd, 1H, H-3), 3.82 (dd, 1H, $J_{5,6a}$ = 7.7 Hz, $J_{5,6b}$ = 4.1 Hz, H-5), 3.71 (dd, 1H, $J_{6a,6b}$ = 11.0 Hz, H-6a), 3.68 (dd, 1H, H-6b), 3.55 (ddd, 1H, $J_{4',3a'}$ = 11.8 Hz, $J_{4',5'}$ = 10.0 Hz, $J_{4',3e'}$ = 4.7 - Hz, H-4′), 3.56 (s, 3H, C-1-OCH_3), 3.45–3.42 (m, 1H, H-5′), 3.42 (s, 3H, C-6-OCH_3), 2.16 (ddd, 1H, $J_{3e',3a'}$ = 14.0 Hz, H-3e′), 2.02 (s, 3H, $NHCOCH_3$), 1.65 (ddd, 1H, H-3a′), 1.27 (d, 3H, $J_{6',5'}$ = 6.2 Hz, H-6′). ^{13}C NMR (125 M Hz, $CDCl_3$): δ 175.6 ($NHCOCH_3$), 103.4 (C-1′), 102.9 (C-1), 80.0 (C-3), 76.8 (C-5′), 74.0 (C-5), 72.5 (C-6), 69.3 (C-4), 68.5 (C-2′), 67.7 (C-4′), 59.4 (C-6-OCH_3), 57.9 (C-1-OCH_3), 52.1 (C-2), 37.3 (C-3′), 23.0 ($NHCOCH_3$), 18.0 (C-6′). ES HRMS calcd for $C_{16}H_{29}NO_9Na$ (M+Na): 402.1735, found: 402.1730.

3.32. Methyl 2-amino-3-*O*-(3,6-dideoxy-β-D-arabino-hexopyranosyl)-2-deoxy- 6-*O*-methyl-β-D-galactopyranoside (3)

Compound **2** (5.7 mg, 0.016 mmol) was dissolved in an ethanolic solution of potassium hydroxide (1 mL, 4 M) and the solution was heated to reflux for 24 h. The reaction was stopped by removal of heat, and ethanol was evaporated. The crude solid was applied to a C_{18} Sep-Pak cartridge, followed by HPLC on C_{18} silica column eluted with methanol–water system to afford the amino sugar **3** as a white solid (4.8 mg, 100% after recovery of starting material): $[\alpha]_D^{22}$ −26.3 (*c* 0.32, CH_3OH). ^1H NMR (600 MHz, D_2O): δ 4.78 (s, 1H, H-1′), 4.24 (d, 1H, $J_{1,2}$ = 8.1 Hz, H-1), 4.10 (app. s, 1H, H-4), 4.08 (app. s, 1H, H-2′), 3.80 (dd, 1H, $J_{6a,6b}$ = 11.4 Hz, $J_{6a,5}$ = 8.0 Hz, H-6a), 3.75 (dd, 1H, $J_{6b,5}$ = 4.1 Hz, H-6b), 3.68 (dd, 1H, H-5), 3.65 (dd, 1H, $J_{3,2}$ = 10.7 Hz, $J_{3,4}$ = 3.0 Hz, H-3), 3.56 (s, 3H, OCH_3), 3.58–3.52 (m, 1H, H-4′), 3.49–3.43 (m, 1H, H-5′), 2.91 (dd, 1H, H-2), 2.18 (ddd, 1H, $J_{3e',3a'}$ = 13.8 Hz, $J_{3e',2'}$ = 4.1 Hz, $J_{3e',4'}$ = 4.1 Hz, H-3e′), 1.68 (ddd, 1H, $J_{3a',4'}$ = 11.4 Hz, $J_{3a',2'}$ = 2.6 Hz, H-3a′), 1.27 (d, $J_{6',5'}$ = 6.2 Hz, H-6′). ^{13}C NMR (125 MHz, CD_3OD): δ 175.6 ($NHCOCH_3$), 104.8 (C-1), 103.8 (C-1′), 82.9 (C-5), 77.7 (C-5′), 76.4 (C-4′), 69.1 (C-4), 68.8 (C-2′), 68.0 (C-3), 62.4 (C-6), 57.3 (OCH_3), 53.6 (C-2), 39.0 (C-3′), 18.4 (C-6′). ES HRMS calcd for $C_{13}H_{25}NO_8Na$ (M+Na): 346.1472, found: 346.1472.

3.33. Methyl 2-amino-3-*O*-(3,6-dideoxy-β-D-arabino-hexopyranosyl)-2-deoxy-6-*O*-methyl- β-D-galactopyranoside (6)

Compound **4** (4.0 mg, 0.011 mmol) was dissolved in an ethanolic solution of potassium hydroxide (1 mL, 4 N) and the solution was refluxed for 64 h. The reaction was stopped by evaporating the ethanol, and the crude mixture was applied to a Sep-Pak cartridge, followed by HPLC with a C_{18} silica column eluted by methanol–water to afford amino sugar **6** as a white solid (3.5 mg, 100% after recovery of s.m.): $[\alpha]_D^{22}$ −20.0 (*c* 0.10, CH_3OH). ^1H NMR (600 MHz, D_2O): δ 4.78 (s, 1H, H-1′), 4.24 (d, 1H, $J_{1,2}$ = 8.1 Hz, H-1), 4.09 (app. s, 1H, H-4), 4.09 (app. s, 1H, H-2′), 3.82 (dd, 1H, $J_{5,6a}$ = 7.8 Hz, $J_{5,6b}$ = 4.1 Hz, H-5), 3.69 (dd, 1H, $J_{6a,6b}$ = 11.0 Hz, H-6a), 3.66 (dd, 1H, H-6b), 3.66 (dd, 1H, $J_{3,2}$ = 10.8 Hz, $J_{3,4}$ = 3.1 Hz, H-3), 3.59–3.54 (m, 1H, H-4′), 3.56 (s, 3H, C-1-OCH_3), 3.46 (dq, 1H, $J_{5',4'}$ = 9.5 Hz, $J_{5',6'}$ = 6.1 Hz, H-5′), 3.41 (s, 3H, C-6-OCH_3), 2.92 (dd, 1H, H-2), 2.18 (ddd, 1H, $J_{3e',3a'}$ = 14.0 Hz, $J_{3e',2'}$ = 4.1 Hz, $J_{3e',4'}$ = 4.1 Hz, H-3e′), 1.68 (ddd, 1H, $J_{3a',4'}$ = 11.8 Hz, $J_{3a',2'}$ = 2.8 Hz, H-3a′), 1.27 (d, 3H, H-6′). ^{13}C NMR (125 MHz, $CDCl_3$): δ 106.1 (C-1), 104.0 (C-1′), 83.9 (C-3), 77.6 (C-5′), 74.7 (C-5), 73.1 (C-6), 69.4, 68.8, 68.1, 59.4 (C-6-OCH_3), 57.3 (C-1-OCH_3), 53.5 (C-2), 39.0 (C-3′), 18.4 (C-6′). ES HRMS calcd for $C_{14}H_{27}NO_8Na$ (M+Na): 360.1629, found: 360.1625.

3.34. Methyl 2-acetamido-3-*O*-(3,6-dideoxy-2-*O*-methyl-β-D-arabino-hexopyranosyl) -2-deoxy- 6-*O*-methyl-β-D-galactopyranoside (7)

A milky suspension of compound **5** (8 mg, 0.020 mmol) and dibutyltin oxide (6 mg, 0.024 mmol) in dry distilled methanol (2 mL) was refluxed for 2 h until the reaction mixture became clear. The methanol was then evaporated, the syrup was co-evaporated with toluene, until a dry white residue was obtained. After drying the white solid under vacuo, it was dissolved in dry DMF (1 mL). Cesium fluoride salt (9.3 mg, 0.060 mmol) and iodomethane (3.7 μL, 0.060 mmol) were added to the solution, which was heated at 50 °C for 18 h. DMF was evaporated under high vacuo, and the mixture was purified by HPLC using a Beckman C_{18} silica column with a MeOH–H_2O gradient to afford final compound **7** as a white solid (3.5 mg, 42%) and starting material **5** was recovered (4.0 mg, 50%). The data for compound **7**: $[\alpha]_D^{22}$ −17.3 (*c* 1.6, CH_3OH). ^1H NMR (600 MHz, D_2O): δ 4.75 (s, 1H, H-1′), 4.44 (d, 1H, $J_{1,2}$ = 8.7 Hz, H-1), 4.10 (d, 1H, $J_{4,3}$ = 3.0 Hz, H-4), 4.01 (dd, 1H, $J_{2,3}$ = 10.8 Hz, H-2), 3.82 (dd, 1H, $J_{5,6a}$ = 7.4 Hz, $J_{5,6b}$ = 3.2 Hz, H-5), 3.80 (dd, 1H, H-3), 3.72 (dd, 1H, $J_{6a,6b}$ = 10.9 Hz, H-6a), 3.68 (dd, 1H, H-6b), 3.58 (dd, 1H, $J_{2',3a'}$ = 2.6 Hz, $J_{2',3e'}$ = 2.6 Hz, H-2′), 3.51 (s, 3H, C-1-OCH_3), 3.45–3.43 (m, 2H, H-4′, H-5′), 3.42 (s, 3H, C-6-OCH_3), 3.41 (s, 3H, C-2′-OCH_3), 2.36 (ddd, 1H, $J_{3e',3a'}$ = 14.1 Hz, $J_{3e',4'}$ = 3.4 Hz, H-3e′), 2.02 (s, 3H, $NHCOCH_3$), 1.53 (ddd, 1H, $J_{3a',4'}$ = 2.7 Hz, H-3a′), 1.26 (d, 3H, $J_{6',5'}$ = 5.7 Hz, H-6′). ^{13}C NMR (125 MHz, $CDCl_3$): δ 175.3 ($NHCOCH_3$), 103.9 (C-1′), 102.9 (C-1), 80.9 (C-3), 77.9 (C-2′), 77.0 (C-5′), 73.9 (C-5), 72.6 (C-6), 69.0

(C-4), 67.8 (C-4′), 59.4 (C-1-OCH_3), 58.3 (C-2′-OCH_3), 57.9 (C-6-OCH_3), 51.9 (C-2), 34.6 (C-3′), 23.0 (NHCOCH_3), 18.0 (C-6′). ES HRMS calcd for $C_{17}H_{31}NO_9Na$ (M+Na): 416.1891, found: 416.1891.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.carres.2013.10.012.

References

1. Appleton, J. A.; Schain, L. R.; McGregor, D. D. *Immunology* **1988**, *65*, 487–492.
2. Appleton, J.; Dell, A.; Nitz, M.; Bundle, D. *Trends Glycosci. Glycotechnol.* **2001**, *13*, 481–492.
3. Nitz, M.; Bundle, D. R. *J. Org. Chem.* **2000**, *65*, 3064–3073.
4. Zhang, J.; Otter, A.; Bundle, D. R. *Bioorg. Med. Chem.* **1996**, *4*, 1989–2001.
5. Zhang, P.; Appleton, J.; Ling, C. C.; Bundle, D. R. *Can. J. Chem.* **2002**, *80*, 1141–1161.
6. Meyer, B.; Peters, T. *Angew. Chem., Int. Ed.* **2003**, *42*, 864–890.
7. Barton, D. H. R.; McCombie, S. W. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1574–1585.
8. Lemieux, R. U. *Adv. Carbohydr. Chem.* **1954**, *9*, 1–57.
9. Ferrier, R. J.; Furneaux, R. H. *Carbohydr. Res.* **1976**, *52*, 63–68.
10. Fugedi, P.; Garegg, P. J.; Lonn, H.; Norberg, T. *Glycoconjugate J.* **1987**, *4*, 97–108.
11. Wallace, J. E.; Schroeder, L. R. *J. Chem. Soc., Perkin Trans. 2* **1977**, 795–802.
12. Cai, Y.; Ling, C. C.; Bundle, D. R. *Org. Lett.* **2005**, *7*, 4021–4024.
13. Mack, H.; Basabe, J. V.; Brossmer, R. *Carbohydr. Res.* **1988**, *175*, 311–316.
14. Haines, A. *Adv. Carbohydr. Chem. Biochem.* **1976**, *33*, 11–109.
15. Deslongchamps, P. *Stereoelectronic Effects in Organic Chemistry*; Pergamon Press: Oxford, 1983.
16. Bouvet, V. R.; Ben, R. N. *J. Org. Chem.* **2006**, *71*, 3619–3622.
17. Ogawa, T.; Takahashi, Y.; Matsui, M. *Carbohydr. Res.* **1982**, *102*, 207–215.
18. Kunesch, N.; Miet, C.; Poisson, J. *Tetrahedron Lett.* **1987**, *28*, 3569–3572.
19. Albright, J. D.; Goldman, L. *J. Am. Chem. Soc.* **1967**, *89*, 2416–2423.
20. Albright, J.; Goldman, L. *J. Am. Chem. Soc.* **1965**, *87*, 4214–4216.
21. Knight, S. D.; Overman, L. E.; Pairaudeau, G. *J. Am. Chem. Soc.* **1993**, *115*, 9293–9294.
22. Hanessian, S.; Plessas, N. R. *J. Org. Chem.* **1969**, *34*, 1045–1053.
23. Hanessian, S. *Carbohydr. Res.* **1966**, *2*, 86–88.
24. Failla, D. L.; Hullar, T. L.; Siskin, S. B. *Chem. Commun.* **1966**, 716–717.
25. Smith, A. B.; Hale, K. J.; Vaccaro, H. A.; Rivero, R. A. *J. Am. Chem. Soc.* **1991**, *113*, 2112–2122.
26. Wolfrom, M. L. *Methods Carbohydr. Chem.* **1963**, *2*, 215–222.
27. McGavin, R. S. Ph.D. Thesis, University of Alberta, 2006.