Pergamon

Bioorganic & Medicinal Chemistry, Vol. 4, No. 11, pp 1989–2001, 1996

PII: S0968-0896(96)00182-2
0968-0896/96 $15.00 + 0.00

Synthesis and Conformational Studies of the Tyvelose Capped, Lewis-x Like Tetrasaccharide Epitope of *Trichinella spiralis*

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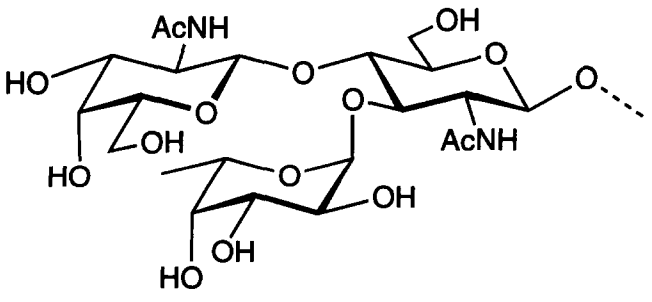
Abstract—Chemical synthesis and high resolution NMR studies are reported for the tetrasaccharide epitope and constituent structures that occur as terminal elements of *Trichinella spiralis* cell surface glycans. The 2-(trimethylsilyl)ethyl and methyl glycosides of Lewis-x type trisaccharides, in which βGalNAc replaces βGal were synthesized from monosaccharide synthons utilizing thioglycoside and halide-ion glycosylation methods. The unique 3,6-dideoxy-β-D-arabinohexopyranosyl residue that caps the structure was introduced to selectively protected 2-(trimethylsilyl)ethyl and methyl trisaccharide glycosides by utilizing an insoluble silver zeolite catalyst and a glycosyl halide. In separate reactions not only were the principal targets obtained but also the corresponding α-linked tetrasaccharides. A comparison of the NMR spectra of the methyl tetrasaccharide glycosides showed that at the site of the α-linked tyvelose structure, specific GalNAc resonances (*C*-1, *C*-2, *C*-3) possess uncharacteristically wide ^{13}C (8–21 Hz) and ^{1}H lines. The β-linked tetrasaccharide glycoside, that represents the native parasite epitope, exhibited only narrow line widths (3 Hz, ^{13}C). Since NOE derived distance constraints for the α-linked tyvelose structure were not consistent with the existence of unusual glycosidic conformers, the origin of the limited number of wide lines was attributed to local rigidity in the GalNAc residue, at the site of tyvelose glycosylation. Copyright © 1996 Elsevier Science Ltd

Introduction

Trichinella spiralis is a parasitic nematode that establishes itself in the intestinal epithelia of any carnivorous animal, including man. During invasion, *T. spiralis* secretes an array of glycoproteins[1] and it has been shown that antibody binding to the glycans of these glycoproteins causes expulsion of larvae from the intestines of rats.[2] The glycans are large tri- and tetra-antennary structures, terminated by a Lewis-x like trisaccharide (**1**), that is capped by tyvelose, a rare sugar (3,6-dideoxy-D-*arabino*-hexose), to produce a tetrasaccharide epitope (**2**).[3,4] This antigenic feature is present on the surfaces of larvae[2] and on glycoproteins called excretory/secretory (ES) antigens disgorged from the esophagus by *Trichinella spiralis* larvae. The tyvelose bearing glycans are highly immunogenic and stimulate high levels of IgG antibodies in parasitized rats, mice and pigs.[2,5] Analysis of the binding specificity of protective rat monoclonal antibodies by synthetic oligosaccharide inhibitors and disaccharide neoglycoconjugates provides strong evidence that tyvelose is β-linked,[6] a structural feature and linkage configuration not observed in any natural product containing this sugar, or any other 3,6-dideoxyhexoses that were previously only seen as α-anomers. The synthesis of the GalNAc trisaccharide analogue of Lewis-x in the form of glycosides **3**, **4** as well as both the β- and α-linked tetrasaccharide glycosides **5**, **6** and **7**, **8** has been completed in order to examine the fine specificity of protective rat monoclonal antibodies and to attempt the co-crystallization of the tetrasaccharide methyl glycoside **6** with antibody Fab for determination of the crystal structure of the carbohydrate-Fab complex. These oligosaccharides also provide valuable probes to (i) establish ^{1}H NMR parameters for use in direct characterization of the tyvelose anomeric configuration in native glycans and (ii) investigate the possible role of surface glycan mediated adherence leading to parasitic infection.



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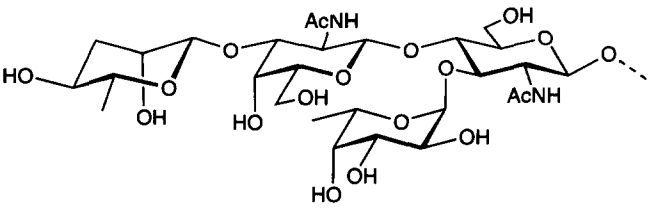

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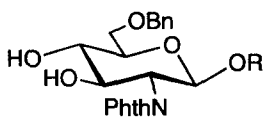
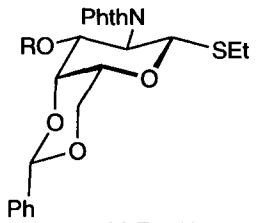
Results and Discussion

Synthetic strategy and preparation of monosaccharide building blocks

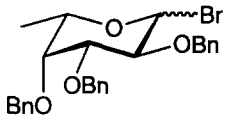
The target oligosaccharides to be synthesized were 2-(trimethylsilyl)ethyl (TMSET)[7] glycosides **3**, **5**, **7** and methyl glycosides **4**, **6**, **8**. In designing the synthesis, a general route was selected that would be amenable to the preparation of oligosaccharide analogues containing either modified or isotopically labeled sugar residues. Therefore, the strategy chosen relies on the stepwise addition of monosaccharides from the reducing terminus of the molecule, with the most valuable sugar, tyvelose, being added last. Elaboration of the oligosaccharides as TMSET glycosides facilitates the eventual derivatization[6,8] with a tether, for covalent attachment to proteins, while the methyl glycosides function as the most convenient forms of simple inhibitors for epitope mapping and crystallography.[9] The monosaccharide synthons **9–14** were selected to facilitate this approach. Selectively protected diols **9**[10] or **10** function in turn as an acceptor to a thioglycoside donor **12**[11] and subsequently the fucopyranosyl halide **13.**[12] Introduction of the tyvelose residues could then be accomplished via the glycosyl chloride **14**,[6,13] a derivative that in combination with a heterogeneous silver salt catalysis[14] would permit, in a single step, the synthesis of both 3,6-dideoxy-D-*arabino*-hexopyranosyl anomers.[6]



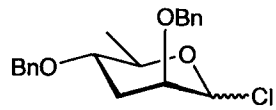
9 R = TMSET
10 R = Me



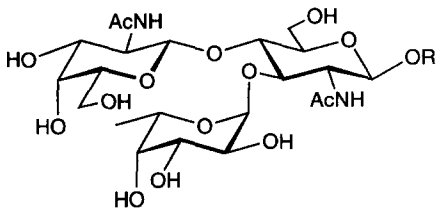
11 R = H
12 R = Bz



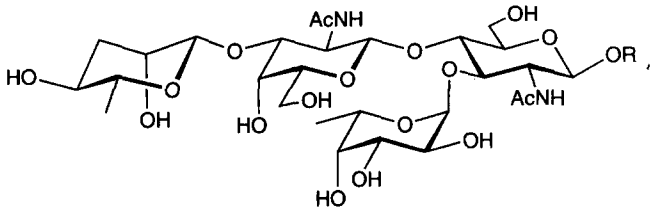
13



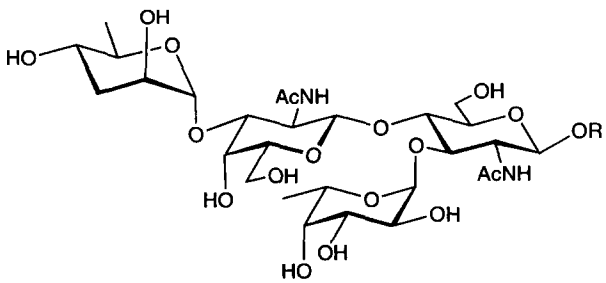
14



3 R = $CH_2CH_2SiMe_3$
4 R = Me



5 R = $CH_2CH_2SiMe_3$
6 R = Me



7 R = $CH_2CH_2SiMe_3$
8 R = Me

The methyl glycoside diol **10** was prepared from methyl 4,6-*O*-benzylidene-2-deoxy-2-phthalimido-β-D-glucopyranoside[15] by the procedure recently reported for the corresponding TMSET glycoside **9**.[10] Ethyl 3,4,6-tri-2O-acetyl-2-deoxy-2-phthalimido-1-thio-β-D-galacto-pyranoside[10] was deacetylated and converted to the benzylidene acetal **11** by treatment with benzaldehyde and formic acid. Benzoylation then gave the thioglycoside donor **12**. The remaining synthons, fucopyranosyl bromide **13** and the tyvelose donor **14**, were prepared according to literature procedures.[12,13]

Assembly of oligosaccharides

Activation of thioglycoside donor **12** by *N*-iodosuccinimide[16,17] and silver triflate[18] in the presence of the selectively protected dihydroxy alcohol **9** gave the TMSET disaccharide glycoside **15** in 81–84% yield. Since the donor/acceptor **9/12** are a mismatched pair[19] for formation of the 1,3 β-linkage at GlcNAc *O*-3, selective glycosylation at *O*-4 of the GlcNAc residue can be anticipated. This outcome was confirmed by a one-dimensional NMR experiment (1D-TROESY) that showed the expected inter-residue NOE (H-1 GalNAc to H-4 GlcNAc). Halide-ion assisted glycosylation[20] of the alcohol **15** was performed with the fucose donor **13** in anhydrous dichloromethane together with tetraethylammonium bromide and DMF to give trisaccharide glycoside **17** in 43–65% yield. Hydrazine hydrate in anhydrous ethanol and toluene removed both phthalimido groups[21] of **17**, as well as the benzoyl ester, and then the resultant, partially deprotected diamino product was *N*-acylated with acetic anhydride in methanol to give trisaccharide **19** in 87–90% yield. Hydrogenation of **19** with 10% palladium on charcoal as catalyst in acetic acid gave the deprotected 'Le^x' analogue **3** in 90% yield. The methyl glycoside **4** was obtained in an analogous manner from trisaccharide

20, which in turn had been assembled from **10** by a series of reactions similar to those used to synthesize the TMSET glycoside **19**.

The trisaccharide alcohol **19** was glycosylated by the tyvelose donor **14** with the heterogeneous promoter, silver zeolite[14] at low temperature. After work-up the protected tetrasaccharides were obtained in 36–49% yield as a mixture of anomers **21** and **22**. Following chromatographic separation a single step hydrogenation in acetic acid with 10% palladium on charcoal gave the target tetrasaccharides **5** and **7** in high yield. The corresponding methyl glycosides **6** and **8** were prepared from **20** in similar yields by a series of reactions, via compounds **23** and **24**, analogous to those described for the TMSET glycosides **5** and **7**. The assignment of anomeric configuration was confirmed in all oligosaccharides by $^{3}J_{H1,H2}$ ^{1}H NMR coupling constants and for the β-*manno*-case by the chemical shift of tyvelose H-5.[6,22] In particular, the observed $^{3}J_{H1,H2}$ values for the tyvelose moiety (<1 and 1.6 Hz, Table 1) are typical of β and α glycosides with the *manno*-configuration.[23] This conclusion was further corroborated by heteronuclear $^{1}J_{C1,H1}$ coupling constants[24] determined for the deprotected tetrasaccharides (Table 2).

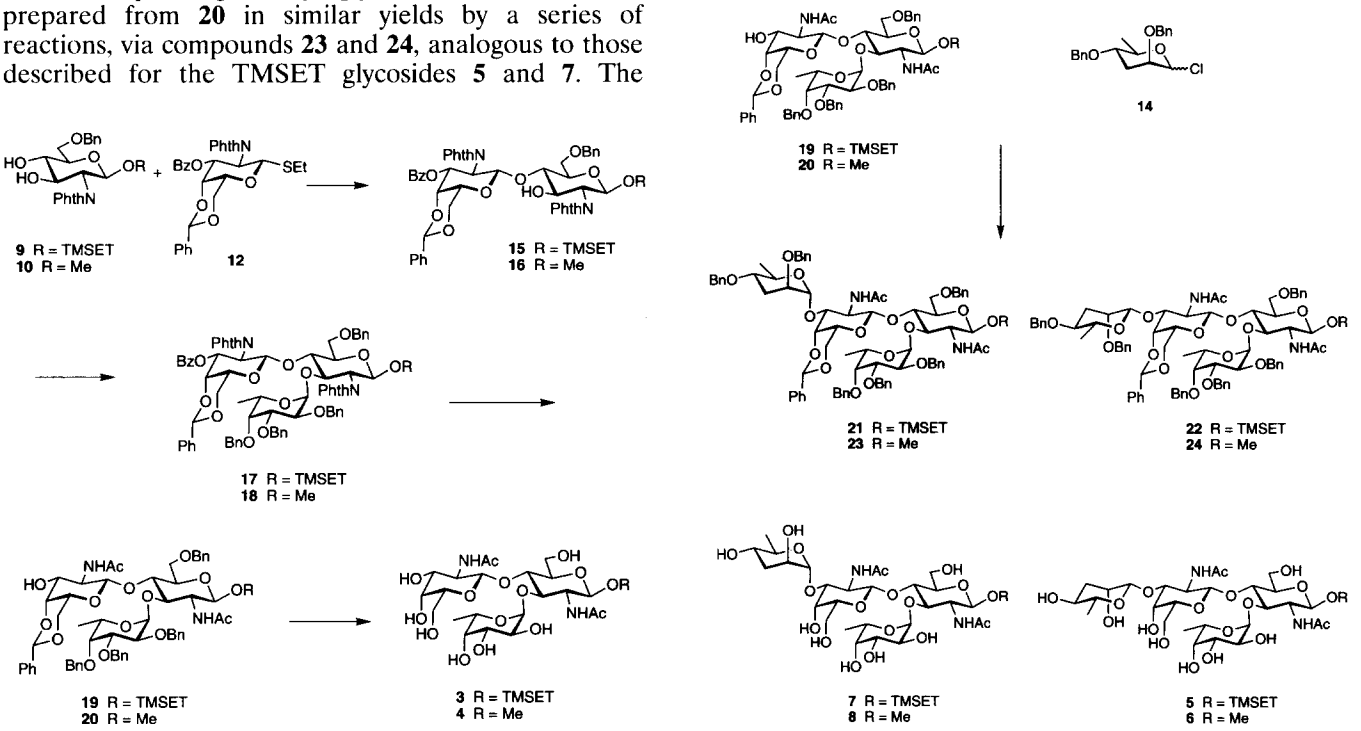


Table 1. Proton NMR data of tetrasaccharides **6** and **8** and trisaccharide **4**[a]

Sugar	H-1	H-2	H-3	H-4	H-5	H-6[b]
β-Tyv(1→3)β-GalNAc (1→4)[α-Fuc(1→3)]β-GlcNAc1→OCH$_3$ **6**[b]						
A GlcNAc[d]	4.43 (8.4)[c]	3.91	3.82	3.90	3.52	3.92, 3.74
B Fuc	5.09 (4.0)	3.69	3.92	3.82	4.84	1.25
C GalNAc[d]	4.52 (8.5)	4.07	3.84	4.09	3.60	3.76, 3.71
D Tyv	4.69 (<1)	3.90	2.16, 1.66	3.55	3.44	1.27
α-Tyv(1→3)β-GalNAc (1→4)[α-Fuc(1→3)]β-GlcNAc1→OCH$_3$ **8**						
A GlcNAc[d]	4.44 (8.2)[c]	3.92	3.83	3.92	3.54	3.93, 3.77
B Fuc	5.11 (4.1)	3.68	3.95	3.83	4.82	1.25
C GalNAc[d]	4.57 (7.8)	4.02	3.79	4.12	3.56	3.79, 3.72
D Tyv	4.76 (1.6)	3.97	2.02, 1.75	3.60	3.59	1.27
β-GalNAc (1→4)[α-Fuc(1→3)]β-GlcNAc1→OCH$_3$ **4**						
A GlcNAc[d]	4.43 (8.2)[c]	3.90	3.87	3.83	3.52	3.90, 3.74
B Fuc	5.10 (4.0)	3.69	3.93	3.83	4.84	1.26
C GalNAc[d]	4.45 (8.4)	3.97	3.71	3.91	3.57	3.77, 3.72

[a]All data were recorded on a Varian Unity spectrometer operating a 500 MHz. Sample concentrations were between 6 and 8 mM in D_2O. The temperature was 30.0±0.1 °C. Chemical shifts in ppm are referenced to external 0.1% acetone at 2.225 ppm recorded under identical experimental conditions.

[b]Geminal protons are not assigned stereospecifically.

[c]Coupling constants of the anomeric protons in Hz.

[d]The chemical shifts of the aglyconic methyl and N-acetyl groups are: 3.49, 2.04 (GalNAc), 2.02 (GlcNAc) (**6**); 3.50, 2.06 (GalNAc), 2.02 (GlcNAc) (**8**) and 3.49, 2.04, 2.02 ppm (**4**).

Table 2. ^{13}C NMR data of tetrasaccharides **6** and **8** and trisaccharide **4**[a]

Sugar[b]		C-1	C-2	C-3	C-4	C-5	C-6	NAc	J_{C1H1}[c]
β-Tyv(1→3)β-GalNAc (1→4)[α-Fuc(1→3)]β-GlcNAc1→OCH_3 **6**									
A GlcNAc	δ (ppm)	102.6	56.4	75.4	74.2	76.2	60.9	23.1	163.3
B Fuc	δ (ppm)	99.4	68.5	70.0	72.9	67.7	16.2	—	171.9
C GalNAc	δ (ppm)	101.1	52.3	79.9	68.5	75.5	62.3	22.9	161.3
D Tyv	δ (ppm)	103.3	68.5	37.2	67.7	76.8	17.9	—	159.7
α-Tyv(1→3)β-GalNAc (1→4)[α-Fuc(1→3)]β-GlcNAc1→OCH_3 **8**									
A GlcNAc	δ (ppm)	102.6	56.4	75.2	74.3	76.2	60.9	23.1[e]	162.5
	$\Delta_{1/2}$ (Hz)[d]	3.0	3.3	3.1	3.1	2.9	3.8	2.8	
	T1 (s)	0.32	0.32	0.37	0.31	0.29	0.22	1.23	
B Fuc	δ (ppm)	99.2	68.5	70.0	72.8	67.7	16.2	—	172.2
	$\Delta_{1/2}$ (Hz)	3.0	2.9	2.9	2.9	3.0	2.6	—	
	T1 (s)	0.30	0.33	0.34	0.32	0.31	0.51	—	
C GalNAc	δ (ppm)	101.2	51.7	75.6	64.3	75.6	62.3	23.0[e]	162.3
	$\Delta\nu_{1/2}$ (Hz)	8.0	11.3	20.9	3.1	3.1	3.1	2.8	
	T1 (s)	0.42	0.44	[f]	0.29	0.33	0.19	1.14	
D Tyv	δ (ppm)	96.0	68.4	34.0	67.5	71.1	17.7	—	168.6
	$\Delta\nu_{1/2}$ (Hz)	2.9	2.7	3.8	2.9	2.8	2.3	—	
	T1 (s)	0.42	0.37	0.23	0.33	0.37	0.60	—	
β-GalNAc (1→4)[α-Fuc(1→3)]β-GlcNAc1→OCH_3 **4**									
A GlcNAc	δ (ppm)	102.6	56.3	75.6	74.3	76.3	60.9	23.1[e]	162.0
B Fuc	δ (ppm)	99.3	68.6	70.0	72.9	67.8	16.2	—	171.6
C GalNAc	δ (ppm)	101.6	53.2	71.6	68.2	75.7	62.3	23.0[e]	161.4

[a]All data were recorded on a Varian Unity 500 spectrometer operating a 125.7 MHz. Sample concentrations were between 30 and 34 mM in D_2O, temperature 30.0±0.1 °C. Chemical shifts in ppm are referenced to external 1% acetone at 31.07 ppm.
[b]The chemical shifts of the aglyconic methyl groups are: 58.0 (**6**), 58.0 (**8**) and 58.0 ppm (**4**); ^{13}C line width and T_1 in **8**: 2.2 Hz, 0.98 s.
[c]Anomeric $^1J_{C1H1}$ coupling constants in Hz.
[d]Peak widths were measured at half peak height by a VNMR-internal routine.
[e]No independent assignment could be made, shifts are too close.
[f]T_1 cannot be determined reliably; lines are too broad.

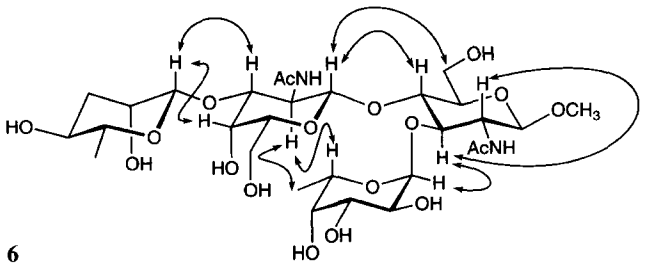
NMR data. The complete ^1H assignments of the methyl glycosides **6** and **8** are summarized in Table 1 based on two-dimensional gradient-enhanced GCOSY experiments carried out as described elsewhere.[25] ^{13}C assignments and $^1J_{C1,H1}$ coupling constants, listed in Table 2, are based on proton-coupled HMQC experiments.[26] To achieve higher precision, the actual values for ^{13}C chemical shifts were measured in one-dimensional DEPT experiments[27] from which the line widths of **6** and **8** were extracted as well. The ^{13}C T_1 relaxation measurement were obtained by the inversion–recovery method.[28] All NMR data are completely consistent with the anomeric configurations shown for glycosides **6** and **8**.

It was observed that the α-linked tetrasaccharide glycoside **8** showed exceptionally wide lines for certain GalNAc resonances: H-1, H-2, H-3 and C-1, C-2 and C-3. In fact, the C-3 resonance was so broad (≈21 Hz) that its presence was initially overlooked. Carbons C-1 and C-2 also exhibit wide lines of 8.0 and 11.3 Hz, respectively, substantially higher than the typical line widths, observed within a very narrow range from 2.7 to 3.3 Hz (Table 2) for the other CH resonances of this tetrasaccharide and all the CH resonances of the β-tyvelose tetrasaccharide glycoside **6** (data not shown).

The presence of wide lines in the proton domain is easily recognized for H-1 and H-2 in one-dimensional spectra. The same effect is present for H-3 but it cannot be readily observed in 1D spectra due to spectral overlap. Precise measurements of proton line widths are not meaningful, of course, as complicated multiplets are present due to vicinal and unresolved long range coupling constants[29] contributing to the line width. The H-3 line-broadening is very evident, however, in all two-dimensional homo- and heteronuclear spectra to the extent that correlations are very difficult to obtain due to the very short T_2 relaxation of this proton.

Carbon-13 T_1 for tetrasaccharide **8** shows typical values although the tyvelose C-1 and GalNAc C-1 and C-2 values are 30% longer than the values for other carbon atoms with one proton attached (Table 2). This suggests that a preferred axis of rotation and overall tumbling motions of the tetrasaccharide are not the source of the selective line broadening.

The conformation of tetrasaccharides **6** and **8** was investigated by examination of NOEs determined from two-dimensional T-ROESY experiments.[30,31] The observed inter-residue ROEs for each structure are presented in Figure 1. The absence of an interaction between tyvelose H-1 and GalNAc H-3 in tetrasaccharide **8** together with the presence of a tyvelose H-1 and GalNAc H-4 is not necessarily surprising. In fact, there is precedence for this type of NOE pattern. In the blood group B trisaccharide, where an α-D-galactopyranose residue substitutes a β-Gal residue at *O*-3, there is only a very weak NOE between α-Gal



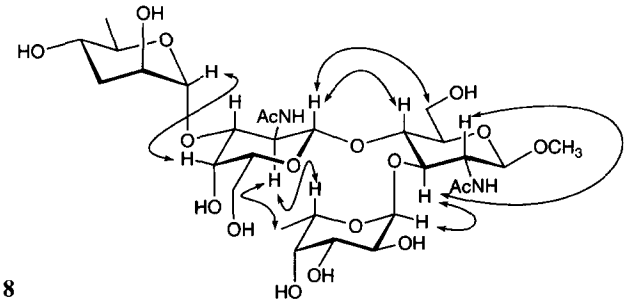


Figure 1. ROEs determined by TROESY experiments for solutions of the tetrasaccharide methyl glycosides **6** and **8** in deuterium oxide.

H-1 and β-Gal H-3.[32] However, it should be emphasized that the absence of this H-1/H-3 NOE in **8** could, in this case be the result of the very short T_2 relaxation of H-3 and not an indication of an unusual linkage orientation.

The inter-proton distances inferred from these measurements are consistent with low energy conformers such as those calculated by the GEGOP[33] forcefield and depicted in Figure 2. These distances for the α-anomer **8** place the electronegative groups Tyv *O*-5 and the acetamido carbonyl oxygen of the GalNAc residue in close proximity (Fig. 2A). The resultant local restriction in flexibility that can arise from the strong repulsion experienced by these electronegative groups appears to be a plausible explanation for the selective broadening of a limited number of GalNAc carbon and proton resonances. In support of this interpretation it is noted that for the β-linked tyvelose structure **6** with only narrow C-13 line widths, the tyvelose *O*-5 is placed toward GalNAc H-4 and away from the acetamido function (Fig. 2B). The appearance of broad resonances can also be rationalized based on a close inspection of inter-atomic distances between the tyvelose *O*-5 and the amide proton of the GalNAc N-acetyl group. In the α-anomer **8**, the lowest energy conformer and three conformers within 1 kcal mol^{-1} of higher energy, show those atoms clearly within hydrogen bond distance (ca. 3.1 Å) and an *O*-5–H-N angle of around 115°, whereas in the β-anomer such an interaction is impossible. The forming and breaking of the hydrogen bond, repulsion of electronegative groups together with the steric crowding, due to consecutive substitution of three GalNAc positions, is likely to reduce flexibility of the $^4C_1$ chair conformation, and slow down the molecular motion *locally* to an extent that interconversion becomes slow or comparable to the NMR time scale. In the β-isomer, on the other hand, the conformational averaging is fast with respect to the NMR time scale as no hydrogen bonding is present, the tyvelose ring is turned away from the crowded area of the GalNAc acetamido function and tyvelose *O*-5 is no longer close to this group, hence the lines are normal in appearance. The broad resonance lines ranging from C-1 to C-3 of GalNAc can therefore be rationalized as the superposition of slightly different conformers with slightly different chemical shifts. Since these effects are seen principally on the GalNAc ring it seems most likely that an altered population of chair conformations causes line broadening, rather than rigidity of inter-glycosidic linkages that would also affect carbon atoms of adjacent pyranose rings.

The involvement of the amide hydrogen atom in a hydrogen bond to tyvelose *O*-5 involves a relatively small (30°) rotation of the plane of the amide nitrogen and carbonyl group away from the normal eclipsed arrangement with H-2. If hydrogen bonded, the amide proton would be expected to show a reduced chemical shift temperature dependence. Studies of such conformational features as well as attempts to study the complex between antibody Fab and oligosaccharide are the subject of continuing studies.

Experimental

General synthetic and analytical methods

Optical rotations were measured at room temperature (20 ± 1 °C) using a Perkin–Elmer model 241 polarimeter. FAB-MS were run in a Cleland and NBA matrix (dithioerythritol: dithiothreitol). TLC were performed on silica gel 60 F_{254} (Merck) precoated glass plates and visualized by charring with 5% H_2SO_4 in ethanol. Unless otherwise stated, flash chromatography (FC) was performed on silica gel 60 (40–63 μm, Merck No. 9385). Itrobeads refers to a beaded silica gel 6RS-8060 manufactured by Iatron Laboratories (Tokyo). Anhydrous dichloromethane was obtained from refluxing with calcium hydride, pyridine was dried over potassium hydroxide and distilled from calcium hydride. Methanol and ethanol were dried with magnesium.[34]

NMR measurements

All spectra whose data are reported in Tables 1 and 2 were recorded on a Varian Unity 500 spectrometer operating at 500 and 125.7 MHz, respectively, while some ^1H data of synthetic intermediates were acquired on a Bruker AM-360 console. Samples were 6–8 mM and 30–34 mM in concentration for ^1H and ^{13}C, respectively. All data in Tables 1 and 2 were recorded under temperature controlled conditions at 30.0 ± 0.1 °C. Chemical shifts for $CDCl_3$ solns are referenced to residual $CHCl_3$ at 7.24 ppm and relative to 0.1% external acetone at 2.225 ppm for solutions in D_2O. Reported coupling constants are first order. The ^{13}C T_1 measurements were carried out with an inversion recovery delay ranging from 0.025 to 6.4 s in nine

increments, 640 scans were acquired per delay with a relaxation delay of 6 s. The data were then analysed by a VNMR-internal exponential analysis (errors 0.02–0.05 s). For the broad lines of GalNAc the errors are naturally larger: 0.11 Hz (C1) and 0.08 Hz (C2). For GalNAc-C3 no reliable measurement could be made. DEPT sequences were acquired with a delay based on a 140 Hz direct carbon–proton coupling constant. In view of the broad lines, a full 3000 scans were acquired for **8** (400 for **6**). Line widths were measured at half-peak height by a VNMR-internal routine. All two-dimensional spectra were recorded at 500 MHz as 4K × 512 (zero-filled to 4K × 1K) data sets, the homonuclear correlations with the aid of gradients (GCOSY, 3 scans per t_1 increment), while the HMQCs were acquired proton-coupled, 8 scans per t_1-increment, without gradients but with a BIRD sequence (delay 0.5 s) and delays based on a 150 Hz coupling constant. Spectral widths were 2500 Hz in F2 and F1 (homonuclear) and 2500 Hz/12 kHz in the HMQC experiments. The T-ROESY experiments were acquired with a 180_x-180_{-x} spin-lock of 200 ms duration and a field strength of 2.3 kHz.

Potential energy calculations

The GEGOP forcefield was used to grid the potential energies of compounds **6** and **8**. The coordinates of the

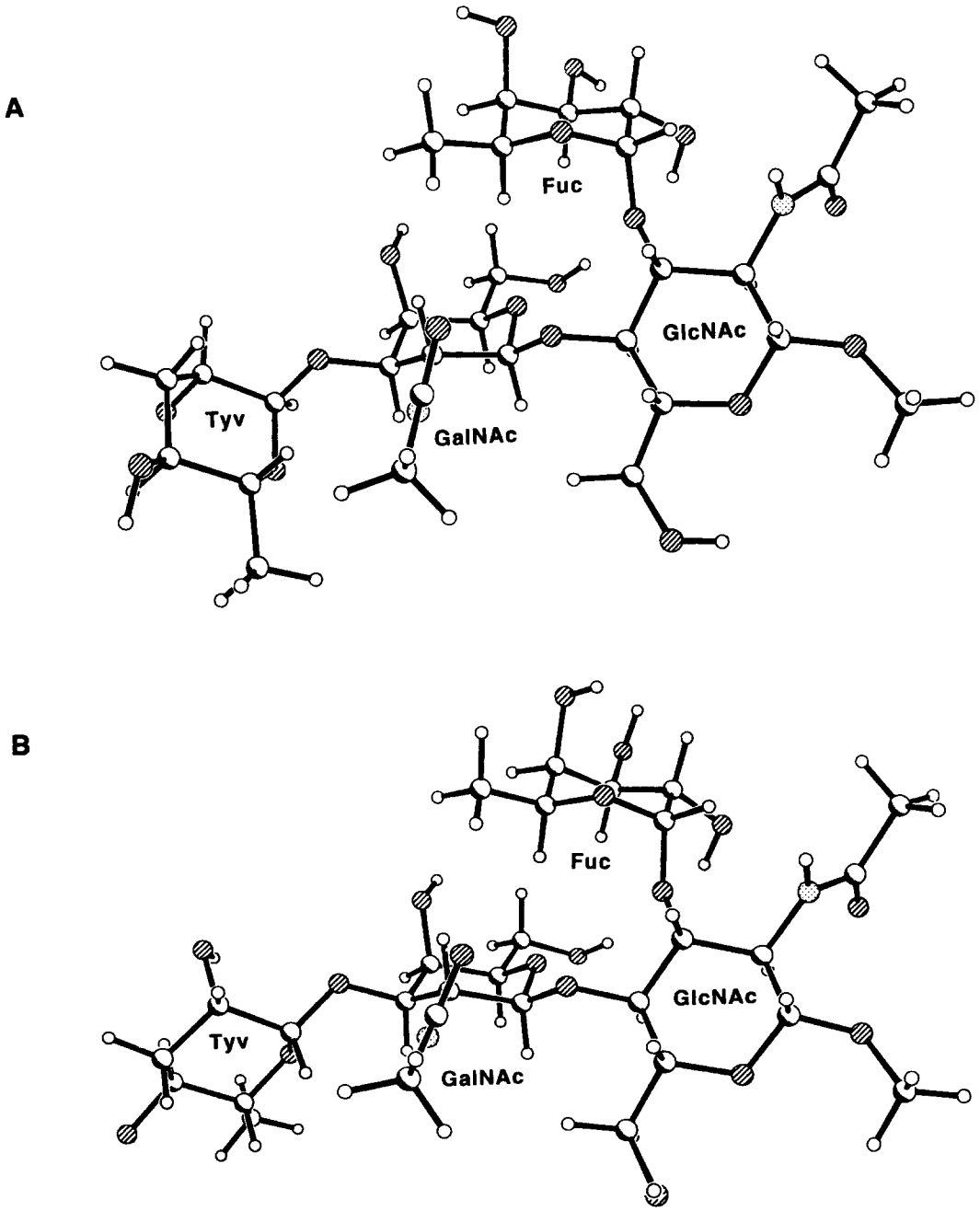


Figure 2. Minimum energy conformations, that are consistent with the observed NOEs, and calculated for compounds **6** (B) and **8** (A) by the GEGOP forcefield.[33]

tyvelose monosaccharide were taken from the published X-ray structure of methyl 3,6-dideoxy-α-D-*arabino*hexopyranoside.[29] Coordinates for 3,6-dideoxy-β-D-*arabino*hexopyranose were constructed from the corresponding α-anomer. The structure was then minimized using the Homan's modification[35] (for carbohydrates) of the AMBER potential.[36] An iterative gradient search technique of the potential energy surface was used to locate the minimum; the process was considered to have converged when the difference in energy between two consecutive iterations was less than 0.001 kcal/mol.

The conformational search for the lowest energy structure of the tetrasaccharides were determined using the GEGOP program.[33] A grid search as a function of the (ϕ,ψ) angles of each glycosidic linkage was executed, followed by an optimization of every structure generated. The ϕ angles were stepped through 360° in 10° intervals and the ψ angles independently varied in 18 steps of 20° each. The closest local minima was ~2 kcal/mol above the lowest energy conformation.

2-(Trimethysilyl)ethyl 6-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (9). A mixture of 2-(trimethysilyl)-ethyl 4,6-*O*-benzylidene-2-deoxy-2-phthalimido-β-D-glucopyranoside[7] (574 mg, 1.15 mmol), $NaBH_3CN$ (370 mg, 5.57 mmol) and 3 Å molecular sieves (300 mg) in anhydrous THF (10 mL) with methyl orange (1 mg) as indicator was stirred at rt for 30 min, then a solution of HCl in ether was added dropwise until the pink color persisted. After stirring for 3 h at room temperature, solid was collected and washed with ethyl acetate. The filtrates were concd and purified by flash chromatography (toluene:AcOEt, 1:1) to give **9** as a white solid (504 mg, 88%). $[\alpha]_D^{22}$ −29.0° (*c* 0.89, $CHCl_3$) [lit[10] $[\alpha]_D^{20}$ −19.6° ($CHCl_3$)]. ^{1}H NMR (360 MHz, $CDCl_3$): δ 7.90–7.60 (4H, m, Phth-H), 7.30 (5H, m, Ph-H), 5.21 (1H, d, $J_{1,2}$ 8.3 Hz, H-1), 4.60 (2H, q, Ph$\underline{CH_2}$O), 4.29 (1H, m, H-5), 4.11 (1H, dd, $J_{2,3}$ = 10.9 Hz, H-2), 3.90 (1H, dt, J = 5.5 Hz, J = 9.8 Hz, O$\underline{CH_2}CH_2$ $SiMe_3$), 3.80 (2H, m, H-3, H-4), 3.62 (2H, m, H-6), 3.47 (1H, dt, J = 6.8 Hz, O$\underline{CH_2}CH_2$, $SiMe_3$), 3.17 (1H, d, J = 2.1 Hz, OH), 2.57 (1H, d, OH), 0.76 (2H, m, O$CH_2\underline{CH_2}$, $SiMe_3$), −0.16 (9H, s, $SiMe_3$).

Methy 6-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (10). A mixture of methyl 4,6-*O*-benzylidene-2-deoxy-2-phthalimido-β-D-glucopyranoside[15] (2.60 g, 6.33 mmol), $NaBH_3CN$ (1.70 g, 25.6 mmol) and 3 Å MS (2.0 g) in anhydrous THF with methyl orange (2 mg) as indicator was stirred at rt for 30 min. Then a soln of HCl in ether was added dropwise until the pink color persisted. After stirring for 3 h at rt, solid was collected and washed with ethyl acetate. The filtrates were concd and purified by flash chromatography to give **10** as a white solid (2.03 g, 78%), $[\alpha]_D^{22}$ −43.3° (*c* 0.97; $CHCl_3$). ^{1}H NMR (360 MHz, $CDCl_3$): δ 7.80–7.60 (4H, m, Phth-H), 7.26 (5H, m, Ph-H), 5.07 (1H, d, $J_{1,2}$ 8.4 Hz, H-1), 4.55 (2H, q, Ph$\underline{CH_2}$O), 4.24 (1H, m, H-5), 4.02 (1H, dd, $J_{2,3}$ = 10.8 Hz, H-2), 3.72 (4H, m, H-3, H-4, OH × 2), 3.56 (2H, m, H-6), 3.36 (3H, s, OCH_3).

Ethyl 4,6-*O*-benzylidene-2-deoxy-2-phthalimido-1-thio-β-D-galactopyranoside (11). A soln of ethyl tri-*O*-acetyl-2-deoxy-2-phthalimido-1-thio-β-D-galactopyranoside[10] (440 mg, 0.92 mmol) in methanol (10 mL) and sodium methoxide (10 mg) was stirred for 2 h at rt (TLC; pentane:EtOAc = 1:1) then dry-ice was added. After concn to dryness the syrup was dissolved in a mixture of formic acid (96%, 5 mL) and benzaldehyde (5 mL). After stirring for 3 h at rt, toluene (10 mL) was added, the mixture was concd and the residue purified by flash chromatography to give a colorless syrup **11** (310 mg, 77%), $[\alpha]_D^{22}$ +13.5° (*c* 1.19; $CHCl_3$). ^{1}H NMR (360 MHz, $CDCl_3$): δ 7.90–7.35 (9H, m, Ar-H), 5.59 (1H, s, Ph-C$\underline{H}O_2$), 5.35 (1H, d, $J_{1,2}$ = 10.0 Hz, H-1), 4.55 (1H, m, H-3), 4.52 (1H, dd, $J_{2,3}$ = 10.4 Hz, H-2), 4.39 (1H, dd, $J_{5,6a}$ = 1.5 Hz, $J_{6a,6b}$ = 12.4 Hz, H-6a), 4.31 (1H, dd, $J_{3,4}$ = 3.2 Hz, $J_{4,5}$ = 1.1 Hz, H-4), 4.09 (1H, m, H-5), 4.07 (1H, dd, $J_{5,6b}$ = 1.8 Hz, H-6b), 3.68 (1H, d, OH), 2.82 (1H, dq, S-CH_2), 2.66 (1H, dq, S-CH_2), 1.24 (3H, t, C-CH_3). Anal. calcd for $C_{23}H_{23}NO_6S$: C, 62.57; H, 5.25; N, 3.17; S, 7.26%; found: C, 62.62; H, 5.04; N, 3.16; S, 7.00%.

Ethyl 3-*O*-benzoyl-4,6-*O*-benzylidene-2-deoxy-2-phthalamido-1-thio-β-D-galactopyranoside (12). Benzoyl chloride (0.2 mL) in anhydrous dichloromethane (2 mL) was added dropwise to a cooled soln of **11** (410 mg, 0.93 mmol) in anhydrous dichloromethane (10 mL) containing pyridine (0.2 mL). The reaction was complete after 5 min (TLC, pentane:EtOAc, 3:1). Methanol (0.4 mL) was added and the stirring continued for 20 min. After concn the residue was purified by flash chromatography to give a white solid **12** (499 mg, 99%). $[\alpha]_D^{22}$ +103.4° (*c* 0.64; $CHCl_3$). ^{1}H NMR (360 MHz, $CDCl_3$): δ 7.95–7.25 (14H, m, Ar-H), 5.99 (1H, dd, $J_{2,3}$ = 10.9 Hz, $J_{3,4}$ = 3.6 Hz, H-3), 5.55 (1H, s, Ph-C$\underline{H}O_2$), 5.53 (1H, d, $J_{1,2}$ = 10.4 Hz, H-1), 5.12 (1H, dd, H-2), 4.66 (1H, d, H-4), 4.41 (1H, dd, $J_{5,6a}$ = 1.6 Hz, $J_{6a,6b}$ = 12.4 Hz, H-6a), 4.09 (1H, dd, $J_{5,6b}$ = 1.6 Hz, H-6b), 3.80 (1H, m, H-5), 2.90 (1H, dq, S-CH_2), 2.72 (1H, dq, S-CH_2), 1.24 (3H, t, C-CH_3). Anal. calcd for $C_{30}H_{27}NO_7S$: C, 66.04; H, 4.99; N, 2.57; S, 5.88%; found: C, 65.98; H, 5.03; N, 2.56; S, 5.735%.

2-(Trimethylsilyl)ethyl 6-*O*-benzyl-2-deoxy-4-*O*-(3-*O*-benzoyl-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-β-D-galactopyranosyl)-2-phthalimido-β-D-glucopyranoside (15). A mixture of **12** (262 mg, 0.48 mmol), **9** (250 mg, 0.50 mmol) and 4 Å molecular sieves (400 mg) in anhydrous dichloromethane (10 mL) was stirred for 30 min under argon at −45°C, then NIS (151 mg, 0.67 mmol, 1.4 equivalent) was added, followed immediately by dropwise addition of AgOTf (50 mg, 0.19 mmol, 0.4 equivalent) dissolved in anhydrous toluene (2 mL). The reaction was complete in 20 min (TLC) and triethylamine (0.3 mL) was added. Solid was collected and washed with dichloromethane. The filtrate was washed with 10% aqueous sodium thiosulphate, water and then dried over Na_2SO_4. After concn the residue was

purified by flash chromatography (toluene:EtOAc, 3:1) to give **15** (398 mg, 84%), $[\alpha]_D^{22}$ +40.5° (*c* 0.86, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 7.90–7.10 (23H, Ar-H), 5.96 (1H, dd, $J_{3',4'}$ = 3.7 Hz, $J_{2',3'}$ = 11.4 Hz, H-3'), 5.51 (1H, d, $J_{1',2'}$ = 8.4 Hz, H-1'), 5.49 (1H, s, Ph-C<u>H</u>O_2), 5.14 (1H, d, $J_{1,2}$ = 8.6 Hz, H-1), 4.95 (1H, dd, H-2'), 4.61 (1H, d, H-4'), 4.41 (1H, ddd, $J_{2,3}$ = 9.4 Hz, $J_{3,4}$ = 8.4 Hz, H-3), 4.31 (1H, d, OH), 4.29 (1H, dd, $J_{5',6'a}$ = 1.5 Hz, $J_{6'a,6'b}$ = 12.6 Hz, H-6'a), 4.13 (2H, q, Ph-C<u>H</u>$_2$-O), 4.12 (1H, dd, H-2), 4.05 (1H, dd, $J_{5',6'b}$ = 1.7 Hz, H-6'b), 3.82 (1H, dt, *J* = 5.6 Hz, *J* = 9.8 Hz, OC<u>H</u>$_2$CH$_2$ SiMe$_3$), 3.79 (1H, m, H-5'), 3.71 (1H, dd, $J_{4,5}$ = 9.7 Hz, H-4), 3.51 (1H, ddd, $J_{5,6a}$ = 2.1 Hz, $J_{5,6b}$ = 3.9 Hz, H-5), 3.43 (1H, dt, *J* = 6.7 Hz, *J* = 9.8 Hz, OC<u>H</u>$_2$CH$_2$ SiMe$_3$), 3.28 (2H, m, H-6), 0.74 (2H, m, OCH$_2$C<u>H</u>$_2$ SiMe$_3$), −0.19 (9H, s, SiMe$_3$) Anal. calcd for $C_{54}H_{54}N_2O_{14}Si$: C, 65.97; H, 5.54; N, 2.85%; found: C, 65.96; H, 5.45; N, 2.83%.

Methyl 6-*O*-benzyl-2-deoxy-4-*O*-(3-*O*-benzoyl-4,6-*O*-benzylidene-2-phthalimido-β-D-galactopyranosyl)-2-phthalimido-β-D-glucopyranoside (16). A mixture of methyl glycoside **10** (1.48 g, 3.58 mmol), and thioglycoside **12** (1.90 g, 3.48 mmol) and 4 Å molecular sieves (2.0 g) in anhydrous dichloromethane (30 mL) was stirred for 30 min under argon at −45°C, then NIS (1.10 g, 4.88 mmol, 1.4 equivalent) was added, followed immediately by dropwise addition of AgOTf (0.36 g, 1.39 mmol, 0.4 equivalent) dissolved in anhydrous toluene (2 mL) dropwise. After 20 min the reaction was complete (TLC, toluene:EtOAc = 3:1) and triethylamine (0.3 mL) was added. Solid was collected and washed with dichloromethane. The filtrate was washed with 10% aqueous sodium thiosulfate, water and then dried over Na_2SO_4. After evaporation the residue was purified by flash chromatography (toluene:EtOAc, 3:1) to afford **16** (2.50 g, 81%), $[\alpha]_D^{22}$ +49.0° (*c* 1.04; $CHCl_3$). ^1H NMR (360 MHz, $CDCl_3$): δ 7.90–7.10 (23H, Ar-H), 5.98 (1H, dd, $J_{2',3'}$ = 11.4 Hz, $J_{3',4'}$ = 3.7 Hz, H-3'), 5.54 (1H, d, $J_{1',2'}$ = 8.5 Hz, H-1'), 5.51 (1H, s, Ph-C<u>H</u>O_2), 5.06 (1H, d, $J_{1,2}$ = 8.5 Hz, H-1), 4.96 (1H, dd, H-2'), 4.62 (1H, d, H-4'), 4.44 (1H, dd, $J_{2,3}$ = 10.9 Hz, $J_{3,4}$ = 8.4 Hz, H-3), 4.34 (1H, s, OH), 4.29 (1H, dd, $J_{5',6'a}$ = 1.2 Hz, $J_{6'a,6'b}$ = 12.6 Hz, H-6'a), 4.15 (2H, q, Ph-CH$_2$-O), 4.12 (1H, dd, H-2), 4.06 (1H, dd, $J_{5',6'b}$ = 1.4 Hz, H-6'b), 3.79 (1H, m, H-5'), 3.76 (1H, dd, $J_{4,5}$ = 9.6 Hz, H-4), 3.53 (1H, ddd, $J_{5,6a}$ = 2.1 Hz, $J_{5,6b}$ = 3.6 Hz, H-5), 3.35 (3H, s, CH_3-O), 3.31 (2H, m, H-6). Anal. calcd for $C_{50}H_{44}N_2O_{14}$: C, 66.96; H, 4.94; N, 3.12%; found: C, 66.97; H, 4.71; N, 3.04%.

2-(Trimethylsilyl)ethyl 6-*O*-benzyl-2-deoxy-3-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-4-*O*-(3-*O*-benzoyl-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-β-D-galactopyranosyl)-2-phthalimido-β-D-glucopyranoside (17). A mixture of selectively protected disaccharide TMS glycoside **15** (360 mg, 0.37 mmol), tetraethylammonium bromide (150 mg, 0.71 mmol) and 4 Å molecular sieves in anhydrous dichloromethane (10 mL) and DMF (1 mL) was stirred for 1 h under argon at rt. Freshly prepared 2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl bromide **13**[12] (430 mg, 0.86 mmol) in anhydrous dichloromethane was added dropwise and the mixture was stirred for 7 days. Methanol (2 mL) was added and stirring was continued for 1 h. Solid was collected and washed with dichloromethane. The combined filtrate and washings were washed with satd aq $NaHCO_3$, water, and dried over Na_2SO_4. Evapn of the soln and chromatography (toluene:EtOAc, 4:1) afforded a white solid **17** (220 mg, 43%), $[\alpha]_D^{22}$ −34.5° (*c* 0.74; $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 7.95–6.85 (38H, m, Ar-H), 5.88 (1H, dd, $J_{2C,3C}$ = 11.4 Hz, $J_{3C,4C}$ = 3.9 Hz, H-3C), 5.51 (1H, s, Ph-C<u>H</u>O_2), 5.45 (1H, d, $J_{1C,2C}$ = 8.5 Hz, H-1C), 4.90 (1H, dd, H-2C), 4.86 (1H, d, $J_{1A,2A}$ = 8.5 Hz, H-1A), 4.80 (1H, q, H-5B), 4.77 (1H, d, Ph-C<u>H</u>$_2$-O), 4.69 (1H, d, Ph-C<u>H</u>$_2$-O), 4.66 (2H, m, H-3A, H-1B), 4.53 (2H, m, Ph-C<u>H</u>$_2$-O), 4.47 (1H, d, H-4C), 4.45 (1H, d, Ph-C<u>H</u>$_2$-O), 4.40 (2H, m, H-2A, H-6Aa), 4.34 (1H, dd, $J_{5C,6Ca}$ = 1.2 Ha, $J_{6Ca,6Cb}$ = 12.5 Hz, H-6Ca), 4.22 (1H, d, Ph-C<u>H</u>$_2$-O), 3.99 (1H, d, Ph-C<u>H</u>$_2$-O), 3.94 (1H, dd, $J_{5C,6Cb}$ = 2.4 Hz, H-6Cb), 3.91 (1H, dd, $J_{2B,3B}$ = 10.4 Hz, $J_{3B,4B}$ = 2.7 Hz, H-3B), 3.76 (1H, dt, OC<u>H</u>$_2$CH$_2$ SiMe$_3$), 3.72 (1H, m, H-4A), 3.58 (1H, dd, $J_{1B,2B}$ = 3.7 Hz, H-2B), 3.38 (1H, d, Ph-C<u>H</u>$_2$-O), 3.36 (1H, m, H-5A), 3.27 (1H, dt, OC<u>H</u>$_2$CH$_2$ SiMe$_3$), 3.08 (1H, d, H-4B), 2.94 (1H, m, H-5C), 1.35 (3H, d, $J_{5B,6B}$ = 6.6 Hz, H-6B), 0.62 (2H, m, OCH$_2$C<u>H</u>$_2$ SiMe$_3$), −0.22 (9H, SiMe$_3$). Anal. calcd for $C_{81}H_{82}N_2O_{18}Si$: C, 69.51; H, 5.90; N, 2.00%; found: C, 69.70; H, 5.96; N, 1.97%.

Methyl 6-*O*-benzyl-2-deoxy-3-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-4-*O*-(3-*O*-benzoyl-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-β-D-galactopyranosyl)-2-phthalimido-β-D-glucopyranoside (18). A mixture of the disaccharide methyl glycoside **16** (1.68 g, 1.88 mmol), tetraethylammonium bromide (590 mg, 2.81 mmol) and 4 Å molecular sieves (2.0 g) in anhydrous dichloromethane (40 mL) and DMF (3.8 mL) was stirred for 30 min under argon at room temperature. Freshly prepared 2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl bromide[12] (2.71 g, 5.45 mmol) in anhydrous dichloromethane (15 mL) was added dropwise and the mixture was stirred for 6 days. Methanol (2 mL) was added and the mixture was stirred for 1 h. Solid was collected and washed with dichloromethane. The combined filtrate and washings were washed with satd aq $NaHCO_3$, water and dried over Na_2SO_4. Evapn of the solvent and chromatography afforded white solid **18** 1.60 g (65%), $[\alpha]_D^{22}$ −59.7° (*c* 1.01; $CHCl_3$). ^1H NMR (360 MHz, $CDCl_3$): δ 7.95–6.85 (38H, m, Ar-H), 5.88(1H, dd, $J_{2C,3C}$ = 11.4 Hz, $J_{3C,4C}$ = 3.8 Hz, H-3C), 5.52 (1H, s, Ph-C<u>H</u>O_2), 5.46 (1H, d, $J_{1C,2C}$ = 8.6 Hz, H-1C), 4.91 (1H, dd, H-2C), 4.80 (3H, m, H-1A, H-5B, Ph-C<u>H</u>$_2$-O), 4.70 (3H, m, H-1B, H-3A, Ph-C<u>H</u>$_2$-O), 4.54 (2H, m, Ph-CH$_2$-O × 2), 4.47 (1H, d, H-4C), 4.44 (2H, m, H-4A, Ph-C<u>H</u>$_2$-O), 4.41 (1H, dd, $J_{2A,3A}$ = 10.4 Hz, H-2A), 4.34 (1H, m, H-6Ca), 4.24 (1H, d, Ph-C<u>H</u>$_2$-O), 3.99 (1H, d, Ph-C<u>H</u>$_2$-O), 3.94 (1H, dd, $J_{5C,6Cb}$ = 1.8 Hz, $J_{6Ca,6Cb}$ = 12.6 Hz , H-6Cb), 3.92 (1H, dd, $J_{2B,3B}$ = 10.5 Hz, $J_{3B,4B}$ = 2.6 Hz, H-3B), 3.74 (2H, m, H-6A), 3.59 (1H, dd, $J_{1B,2B}$ = 3.7 Hz, H-2B), 3.39 (2H, m, H-5A, Ph-C<u>H</u>$_2$-O), 3.27 (3H, s, OCH_3), 3.09 (1H, d, H-4B), 2.89 (1H, m, H-5C), 1.35 (3H, d, $J_{5B,6B}$ = 6.6 Hz, H-6B). Anal. calcd

for $C_{74}H_{72}N_2O_{18}$: C, 70.41; H, 5.53; N, 2.13%; found: C, 70.28; H, 5.37; N, 2.05%.

2-(Trimethylsilyl)ethyl 2-acetamido-6-*O*-benzyl-2-deoxy-3-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-4-*O*-(2-acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-galactopyranosyl)-β-D-glucopyranoside (19). A solution of trisaccharide TMS glycoside **17** (550 mg, 0.39 mmol) in anhydrous ethanol (6 mL), anhydrous toluene (6 mL), and hydrazine hydrate (99%, 0.5 mL) was refluxed for 12 h (TLC, toluene:EtOAc, 3:1). The white precipitate was collected and washed with methanol. The filtrate and methanol washings were concd, the residue dissolved in methanol (10 mL) and acetylated with acetic anhydride (1 mL). After stirring for 4 h at rt, the soln was concd to dryness and chromatographed (toluene:acetone, 1:1) to give a white solid **19** (383 mg, 87%), $[\alpha]_D^{22}$ −63.2° (*c* 0.56, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 7.70–7.10 (25H, m, Ar-H), 6.39 (1H, d, $J_{2C,NH}$ = 5.4 Hz, NHC), 5.62 (1H, s, $PhCHO_2$), 5.58 (1H, d, $J_{2A,NH}$ = 6.6 Hz, NHA), 5.20 (1H, d, $J_{1A,2A}$ = 8.0 Hz, H-1A), 4.92 (1H, d, $PhCH_2O$), 4.86 (1H, d, $J_{1B,2B}$ = 3.5 Hz, H-1B), 4.60 (8H, m, $PhCH_2O \times 5$, OH, H-C, H-5B), 4.31 (1H, dd, $J_{5C,6Ca}$ = 0.8 Hz, $J_{6Ca,6Cb}$ = 11.8 Hz, H-6Ca), 4.27 (1H, dd, $J_{2A,3A}$ = 9.2 Hz, $J_{3A,4A}$ = 9.1 Hz, H-3A), 4.20 (1H, d, $PhCH_2O$), 4.10 (1H, d, $J_{3C,4C}$ = 3.3 Hz, H-4C), 4.05 (1H, dd, $J_{5C,6Cb}$ = 1.2 Hz, H-6Cb), 3.84 (6H, m, H-2B, H-3B, H-2C, H-3C, H-4A, $O\text{-}CH_2CH_2$, $SiMe_3$), 3.73 (2H, m, H-6A), 3.59 (1H, m, H-5A), 3.54 (1H, d, $PhCH_2O$), 3.49 (1H, dt, *J* = 9.9 Hz, *J* = 6.7 Hz, $O\text{-}CH_2CH_2$, $SiMe_3$), 3.18 (2H, m, H-4B, H-5A), 2.94 (1H, m, H-2A), 1.83 (3H, s, Ac), 1.52 (3H, s, Ac), 1.02 (3H, d, $J_{5B,6B}$ = 6.5 Hz, H-6B), 0.86 (2 H, m, $O\text{-}CH_2CH_2$, $SiMe_3$), −0.04 (9H, s, $SiMe_3$). Anal. calcd for $C_{62}H_{78}N_2O_{15}Si$: C, 66.53; H, 7.02; N, 2.50%; found: C, 66.52; H, 7.01; N, 2.48%.

Methyl 6-*O*-benzyl-2-acetamido-2-deoxy-3-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-4-*O*-(2-acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-galactopyranosyl)-β-D-glucopyranoside (20). A soln of trisaccharide methyl glycoside **18** (1.21 g, 0.92 mmol) in a mixture of anhydrous ethanol (10 mL), anhydrous toluene (10 mL), and hydrazine hydrate (99%, 1.0 mL) was refluxed for 12 h (TLC, toluene:EtOAc, 2:1). The white precipitate was collected and washed with methanol. The filtrate and methanol washings were concd, the residue dissolved in methanol (15 mL) and acetylated with acetic anhydride (2 mL). After stirring for 4 h at rt, the reaction soln was concd to dryness and chromatographed (EtOAc:acetone, 1:1) to give **20** as a white solid (860 mg, 90%), $[\alpha]_D^{22}$ −64.8° (*c* 1.57; $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 7.60–7.14 (25H, m, Ar-H), 6.31 (1H, d, $J_{2C,NH}$ = 5.3 Hz, NHC), 5.66 (1H, d, $J_{2A,NH}$ = 6.7 Hz, NHA), 5.61 (1H, s, $PhCHO_2$), 5.10 (1H, d, $J_{1A,2A}$ = 8.0 Hz, H-1A), 4.91 (1H, d, $PhCH_2O$), 4.89 (1H, d, $J_{1B,2B}$ = 3.8 Hz, H-1B), 4.62 (5H, m, $PhCH_2 \times 4$, H-5B), 4.56 (1H, d, $J_{1C,2C}$ = 7.9 Hz, H-1C), 4.51 (1H, d, $PhCH_2O$), 4.31 (1H, dd, $J_{5C,6Ca}$ = 0.6 Hz, $J_{6Ca,6Cb}$ = 12.4 Hz, H-6Ca), 4.22 (2H, m, H-3A, $PhCH_2O$), 4.09 (1H, d, $J_{3C,4C}$ = 3.5 Hz, H-4C), 4.04 (1H, dd, $J_{5C,6Cb}$ = 1.8 Hz, H-6Cb), 3.96 (1H, dd, $J_{2B,3B}$ = 10.4 Hz, H-2B), 3.89 (1H, dd, $J_{3B,4B}$ = 2.6 Hz, H-3B), 3.83 (3H, m, H-2C, H-4A, OH), 3.77 (1H, dd, $J_{2C,3C}$ = 10.7 Hz, $J_{3C,4C}$ = 3.5 Hz, H-3C), 3.75 (2H, m, H-6A), 3.59 (2H, m, H-5A, $PhCH_2O$), 3.41 (3H, s, OCH_3), 3.21 (1H, m, H-4B), 3.15 (1H, m, H-5C), 3.03 (1H, m, H-2A), 1.85 (3H, s, $COCH_3$), 1.56 (3H, s, $COCH_3$), 1.03 (3H, d, $J_{5B,6B}$ = 6.6 Hz, H-6B). Anal. calcd for $C_{58}H_{68}N_2O_{15}$: C, 67.43; H, 6.63; N, 2.71%; found: C, 67.18; H, 6.59; N, 2.65%.

2-(Trimethylsilyl)ethyl 2-acetamido-6-*O*-benzyl-2-deoxy-3-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-4-*O*-[2-acetamido-4,6-*O*-benzylidene-2-deoxy-3-*O*-(2,4-di-*O*-benzyl-3,6-deoxy-α-D-*arabino*-hexopyranosyl)-β-D-galactopyranosyl]-β-D-glucopyranoside (21) and 2-(trimethylsilyl)ethyl 2-acetamido-6-*O*-benzyl-2-deoxy-3-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-4-*O*-[2-acetamido-4,6-*O*-benzylidene-2-deoxy-3-*O*-(2,4-di-*O*-benzyl-3,6-deoxy-β-D-*arabino*-hexopyranosyl)-β-D-galactopyranosyl]-β-D-glucopyranoside (22). Oxalyl chloride (223 mg, 1.75 mmol) in anhydrous dichloromethane was added dropwise to a solution of 2,4-di-*O*-benzyl-D-*arabino*-hexopyranose[13] (160 mg, 0.49 mmol) in anhydrous dichloromethane (6 mL) and DMF (0.1 mL) under argon. After 5 h at rt the mixture was poured into ice-water and the organic layer was washed twice with cold water and dried over Na_2SO_4. The oil **14** obtained by evapn of solvent was dried over high vacuum for 50 min and used immediately in the glycosylation step. A mixture of the trisaccharide alcohol **19** (273 mg, 0.24 mmol), 4 Å molecular sieves (300 mg) and silver zeolite[14] (300 mg) in anhydrous dichloromethane (10 mL) was stirred under argon at −78°C in the dark for 30 min. 2,4-Di-*O*-benzyl-α-D-*arabino*-hexopyranosyl chloride **14** described above and dissolved in anhydrous dichloromethane (4 mL) at −78°C was transferred to the reaction mixture by a cannula. The temperature was allowed to rise to room temperature and the reaction mixture stirred for 40 h. Filtration, concn and flash chromatography (toluene:acetone, 3:2) afforded the α-linked tetrasaccharide **21** (170 mg, 49%) and the β-linked tetrasaccharide **22** (124 mg, 36%). Data for tetrasaccharide **21**: $[\alpha]_D^{22}$ −11.2° (*c* 1.06; $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 7.46–7.14 (35H, m, Ar-H), 5.63 (1H, d, $J_{2A,NHA}$ = 6.6 Hz, NHA), 5.52 (1H, d, $J_{2C,NHC}$ = 7.2 Hz, NHC), 5.42 (1H, s, $PhCHO_2$), 5.14 (1H, d, $J_{1A,2A}$ = 8.1 Hz, H-1A), 5.00 (1H, d, $J_{1C,2C}$ = 8.4 Hz, H-1C), 4.91 (1H, d, $PHCH_2O$), 4.88 (1H, d, $J_{1B,2B}$ = 3.5 Hz, H-1B), 4.83 (1H, s, H-1D), 4.67 (1H, d, $PHCH_2O$), 4.66–4.56 (6H, m, H-5B, $PHCH_2O \times 5$), 4.55 (1H, m, H-3C), 4.09 (3H, m, $PHCH_2O \times 3$), 4.26–4.18 (3H, H-3A, H-6Ca, $PHCH_2O$), 4.06 (2H, m, H-4A, H-4C), 3.93 (1H, dd, $J_{2B,3B}$ = 10.4 Hz, H-2B), 3.88 (3H, m, H-3B, H-6Cb, OCH_2CH_2, $SiMe_3$), 3.76 (2H, m, H-6A), 3.70 (1H, dq, $J_{4D,5D}$ = 9.3 Hz, H-5D), 3.61 (1H, m, H-2D), 3.42–3.50 (4H, m, H-4D, H-5A, $PHCH_2O$, OCH_2CH_2, $SiMe_3$), 3.33 (1H, m, H-2C), 3.11 (1H, m, H-4B), 2.98 (1H, ddd, $J_{2A,3A}$ = 8.2 Hz, H-2A), 2.74 (1H, m, H-5C), 2.23 (1H, ddd, $^2J_{3Dax,3Deq}$ = 13.7 Hz, $J_{3Deq,4D}$ = 4.0 Hz, $J_{2D,3Deq}$ = 3.8 Hz, H-3Deq), 1.92 (3H, s, CH_3CO), 1.74 (1H, ddd, $J_{2D,3Dax}$ = 3.0 Hz, $J_{3Dax,4D}$ = 10.8 Hz, H-3Dax), 1.52 (3H, s, CH_3CO), 1.33 (3H, d, $J_{5D,6D}$ = 6.3 Hz, H-6D), 1.00 (3H, d, $J_{5B,6B}$ = 6.6 Hz,

H-6B), 0.91 (1H, m, $OCH_2C\underline{H}_2$ $SiMe_3$), 0.81 (1H, m, $OCH_2C\underline{H}_2$ $SiMe_3$), −0.001 (9H, s, $SiMe_3$). Anal. calcd for $C_{82}H_{100}N_2O_{18}Si$: C, 68.88; H, 7.05; N, 1.96%; found: C, 68.87; H, 6.99; N, 1.91%.

Data for tetrasaccharide **22**: [α] −43.7° (*c* 0.67, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 7.58–7.13 (35H, m, Ar-H), 5.65 (1H, d, $J_{2A,NHA}$ = 6.7 Hz, NHA), 5.55 (1H, s, $PhC\underline{H}O_2$), 5.46 (1H, d, $J_{2C,NHC}$ = 6.1 Hz, NHC), 5.15 (1H, d, $J_{1A,2A}$ = 7.9 Hz, H-1A), 4.92 (2H, m, H-1C, $PhC\underline{H}_2O$), 4.89 (1H, d, $J_{1B,2B}$ = 3.5 Hz, H-1B), 4.80 (2H, m, $PHC\underline{H}_2O \times 2$), 4.70–4.53 (8H, m, H-1D, H-5B, $PHC\underline{H}_2O \times 6$), 4.50 (1H, dd, $J_{2C,3C}$ = 11.2 Hz, $J_{3C,4C}$ = 3.4 Hz, H-3C), 4.46 (1H, d, $PHC\underline{H}_2O$), 4.18–4.30 (4H, m, H-3A, H-4C, H-6Ca, $PhC\underline{H}_2O$), 4.03 (1H,dd, $J_{3A,4A}$ = 9.2 Hz, $J_{4A,5A}$ = 9.0 Hz, H-4A), 3.95 (1H, dd, $J_{2B,3B}$ = 10.4 Hz, H-2B), 3.91 (2H, m, H-3B, H-6Cb), 3.87 (1H, m, $OCH_2C\underline{H}_2SiMe_3$), 3.68–3.78 (2H, m, H-6A), 3.65 (1H, m, H-2D), 3.54–3.48 (6H, m, H-2C, H-4D, H-5A, H-5D, $PHC\underline{H}_2O$, $OCH_2C\underline{H}_2$ $SiMe_3$), 3.17 (1H, m, H-4B), 2.98 (1H, m, H-2A), 2.84 (1H, m, H-5C), 2.34 (1H, ddd, $^2J_{3Dax,3Deq}$ = 13.2 Hz, $J_{3Deq,4D}$ = 3.9 Hz, $J_{2D,3Deq}$ = 3.6 Hz, H-3Deq), 1.80 (3H, s, CH_3CO), 1.53 (3H, s, CH_3CO), 1.46 (1H, m, H-3Dax), 1.35 (3H, d, $J_{5D,6D}$ = 5.5 Hz, H-6D), 1.07 (3H, d, $J_{5B,6B}$ = 6.4 Hz, H-6B), 0.92 (1H, m, $OCH_2C\underline{H}_2$ $SiMe_3$), 0.82 (1H, m, $OCH_2C\underline{H}_2$ $SiMe_3$), −0.001 (9H, s, $SiMe_3$). FAB-MS calcd for $C_{82}H_{100}N_2O_{18}Si$: [M + Na] 1451.7; found: 1451.0. Anal. calcd for $C_{82}H_{100}N_2O_{18}Si$: C, 68.88; H, 7.05; N, 1.96%; found: C, 68.70; H, 6.90; N, 1.92%.

Methyl 2-acetamido-6-*O*-benzyl-2-deoxy-3-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-4-*O*-[2-acetamido-4,6-*O*-benzylidene-2-deoxy-3-*O*-(2,4-di-*O*-benzyl-3,6-deoxy-α-D-*arabino*-hexopyranosyl)-β-D-galactopyranosyl]-β-D-glucopyranoside (23) and methyl 2-acetamido-6-*O*-benzyl-2-deoxy-3-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-4-*O*-[2-acetamido-4,6-*O*-benzylidene-2-deoxy-3-*O*-(2,4-di-*O*-benzyl-3, 6-deoxy-β-D-arabino-hexopyranosyl)-β-D-galactopyranosyl]-β-D-glucopyranoside (24). Oxalyl chloride (271 mg, 2.0 mmol) in anhydrous dichloromethane was added dropwise to a soln of 2,4-di-*O*-benzyl-α-D-*arabino*-hexopyranose (350 mg, 1.07 mmol) in anhydrous dichloromethane (8 mL) and DMF (0.1 mL) under argon. After 5 h at room temperature, the mixture was poured into ice-water and the organic layer was washed twice cold water and dried over Na_2SO_4. Evapn of the solvent gave an oil, that was dried at high vacuum for 40 min and then used immediately in the next step.

A mixture of trisaccharide alcohol **20** (359 mg, 0.35 mmol), 4 Å MS (1.0 g) and silver zeolite (400 mg) in anhydrous dichloromethane (10 mL) was stirred under argon at −78°C in the dark for 30 min. 2,4-Di-*O*-benzyl-α-D-*arabino*-hexopyranosyl chloride **14** described above and dissolved in anhydrous dichloromethane (6 mL) at −78°C was transferred to the reaction mixture by a canula. The temperature was allowed to rise to rt and the reaction mixture stirred for 30 h. Filtration, concentration and flash chromatography (toluene:acetone, 1:1) afforded α-linked tetrasaccharide **23** (182 mg, 39%) and β-linked tetrasaccharide **24** (194 mg, 42%).

Data for tetrasaccharide **23**: $[\alpha]_D^{22}$ −7.9° (*c* 0.34; $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): 7.46–7.14 (35H, m, Ar-H), 5.71 (1H, d, $J_{2A,NHA}$ = 6.8 Hz, NHA), 5.52 (1H, d, $J_{2C,NHC}$ = 7.2 Hz, NHC), 5.42 (1H, s, $PHC\underline{H}O_2$), 5.06 (1H, d, $J_{1A,2A}$ = 7.8 Hz, H-1A), 5.00 (1H, d, $J_{1C,2C}$ = 8.4 Hz, H-1C), 4.91 (1H, d, $PHC\underline{H}_2O$), 4.90 (1H, d, $J_{1B,2B}$ = 3.6 Hz, H-1B), 4.83 (1H, s, H-1D), 4.68 (1H, d, $PHC\underline{H}_2O$), 4.65–4.56 (4H, m, H-5B, $PHC\underline{H}_2O \times 3$), 4.53 (1H, dd, $J_{2C,3C}$ = 10.7 Hz, $J_{3C,4C}$ = 3.5 Hz, H-3C), 4.48 (5H, m, $PhC\underline{H}_2O \times 5$), 4.25–4.18 (3H, H-3A, H-6Ca, $PhC\underline{H}_2O$), 4.09 (1H, dd, $J_{3A,4A}$ = 10.1 Hz, $J_{4A,5A}$ = 10.1 Hz, H-4A), 4.06 (1H, d, H-4C), 3.95 (1H, dd, $J_{2B,3B}$ = 10.4 Hz, H-2B), 3.92–3.85 (2H, m, H-3B, H-6Cb), 3.78 (2H, m, H-6A), 3.70 (1H, dq, $J_{4D,5D}$ = 9.3 Hz, $J_{5D,6D}$ = 6.3 Hz, H-5D), 3.61 (1H, m, H-2D), 3.53–3.42 (3H, m, H-4D, H-5A, $PhC\underline{H}_2O$), 3.42 (3H, s, OCH_3), 3.34 (1H, m, H-2C), 3.13 (1H, b, H-4B), 3.06 (1H, m, H-2A), 2.73 (1H, m, H-5C), 2.23 (1H, ddd, $^2J_{3Dax,3Deq}$ = 13.5 Hz, $J_{3Deq,4D}$ = 4.0 Hz, $J_{2D,3Deq}$ = 3.8 Hz, H-3Deq), 1.93 (3H, s, CH_3CO), 1.74 (1H, ddd, $J_{2D,3Dax}$ = 3.1 Hz, $J_{3Dax,4D}$ = 10.8 Hz, H-3Dax), 1.55 (3H, s, CH_3CO), 1.34 (3H, d, H-6D), 1.00 (3H, d, $J_{5B,6B}$ = 6.4 Hz, H-6B). Anal. calcd for $C_{78}H_{90}N_2O_{18}$: C, 69.73; H, 6.75; N, 2.08%; found: C, 69.67; H, 6.78; N, 1.98%.

Data for **24**: $[\alpha]_D^{22}$ −40.9° (*c* 0.47; $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 7.57–7.14 (35H, m, Ar-H), 5.73 (1H, d, $J_{2A,NHA}$ = 6.6 Hz, NHA), 5.55 (1H, s, $PHC\underline{H}O_2$), 5.46 (1H, d, $J_{2C,NHC}$ = 6.8 Hz, NHC), 5.07 (1H, d, $J_{1A,2A}$ = 7.8 Hz, H-1A), 4.91 (3H, m, H-1B, H-1C, $PHCH_2O$), 4.80 (2H, m, $PhC\underline{H}_2O \times 2$), 4.65 (5H, m, H-1D, H-5B, $PhC\underline{H}_2O \times 3$), 4.56 (3H, m, $PhC\underline{H}_2O \times 3$), 4.49 (1H, m, H-3C), 4.46 (1H, d, 11.6 Hz, $PhC\underline{H}_2O$), 4.27–4.18 (4H, m, H-3A, H-4C, H-6Ca, $PhC\underline{H}_2O$), 4.06 (1H, dd, $J_{3A,4A}$ = 8.9 Hz, $J_{4A,5A}$ = 8.7 Hz, H-4A), 3.97 (1H, dd, $J_{1B,2B}$ = 3.7 Hz, $J_{2B,3B}$ = 10.2 Hz, H-2B), 3.91 (2H, m, H-3B, H-6Cb), 3.80–3.71 (2H, m, H-6A), 3.65 (1H, m, H-2D), 3.54–3.42 (5H, m, H-2C, H-4D, H-5A, H-5D, $PhC\underline{H}_2O$), 3.41 (3H, s, OCH_3), 3.18 (1H, b, H-4B), 2.96 (1H, m, H-2A), 2.83 (1H, b, H-5C), 2.34 (1H, ddd, $^2J_{3Dax,3Deq}$ = 13.4 Hz, $J_{3Deq,4D}$ = 3.8 Hz, $J_{2D,3Deq}$ = 3.7 Hz, H-3Deq), 1.80 (3H, s, CH_3CO), 1.56 (3H, s, CH_3CO), 1.46 (1H, m, H-3Dax), 1.35 (3H, d, $J_{5D,6D}$ = 5.6 Hz, H-6D), 1.07 (3H, d, $J_{5B,6B}$ = 6.6 Hz, H-6B). Anal. calcd for $C_{78}H_{90}N_2O_{18}$: C, 69.73; H, 6.75; N, 2.08%; found: C, 69.51; H, 6.85; N, 1.98%.

2-(Trimethylsilyl)ethyl 2-acetamido-2-deoxy-3-*O*-(α-L-fucopyranosyl)-4-*O*-(2-acetamido-2-deoxy-β-D-galactopyranosyl)-β-D-glucopyranoside (3). A soln of **19** (44 mg, 0.04 mmol) in acetic acid (5 mL) with 10% palladium on charcoal (50 mg) was hydrogenated at rt for 40 h. The suspension was filtered through celite and the residue was washed with methanol. The combined filtrates were concd and purified by chromatography on Itrobeads (EtOAc:methanol, 2:1) to give a solid which was lyophilized to give a white solid **3** (24 mg, 92%), $[\alpha]_D^{22}$ −62.9° (*c* 0.35; H_2O). ^1H NMR (500 MHz, D_2O): δ 5.10 (1H, d, $J_{1B,2B}$ = 4.0 Hz, H-1B), 4.84 (1H, q, $J_{5B,6B}$ = 6.6 Hz, H-5B), 4.52 (1H, d, $J_{1A,2A}$ = 8.3

Hz, H-1A), 4.46 (1H, d, $J_{1C,2C}$ = 8.4 Hz, H-1C), 4.01 (1H, dt, J = 10.5 Hz, J = 5.1 Hz, $OCH_2CH_2SiMe_3$), 3.97 (1H, dd, $J_{2C,3C}$ = 10.7 Hz, H-2C), 3.93 (1H, dd, $J_{2B,3B}$ = 10.5 Hz, $J_{3B,4B}$ = 3.5 Hz, H-3B), 3.91 (2H, m, H-4C, H-6Aa), 3.87 (2H, m, H-2A, H-4A), 3.83 (2H, m, H-3A, H-4B), 3.76 (2H, m, H-6C), 3.74 (1H, H-6Ab), 3.69 (2H, m, H-2B, H-3C), 3.66 (1H, dt, J = 10.5 Hz, J = 7.2 Hz, $OCH_2CH_2SiMe_3$), 3.57 (1H, dd, $J_{5C,6Ca}$ = 4.3 Hz, $J_{5C,6Cb}$ = 7.9 Hz, H-5C), 3.49 (1H, ddd, $J_{4A,5A}$ = 9.2 Hz, $J_{5A,6Aa}$ = 2.3 Hz, $J_{5A,6Ab}$ = 4.9 Hz, H-5A), 2.04 (3H, s, CH_3CO), 2.01 (3H, s, CH_3CO), 1.26 (3H, d, $J_{5B,6B}$ = 6.6 Hz, H-6B), 0.97 (1H, m, $OCH_2CH_2SiMe_3$), 0.86 (1H, m, $OCH_2CH_2SiMe_3$), −0.001 (9H, s, $SiMe_3$). HR-FABMS calcd for $C_{27}H_{50}N_2O_{15}Si$ (M+Na): 693.2878; found: 693.2887. Anal. calcd for $C_{27}H_{50}N_2O_{15}Si$: C, 48.35; H, 7.51; N, 4.18%; found: C, 48.24; H, 7.48; N, 4.10%.

Methyl 2-acetamido-2-deoxy-3-*O*-(α-L-fucopyranosyl)-4-*O*-(2-acetamido-2-deoxy-β-D-galactopyranosyl)-β-D-glucopyranoside (4). A soln of **20** (140 mg, 0.16 mmol) in acetic acid (8 mL) with 10% palladium on charcoal (90 mg) was hydrogenated at rt for 40 h. The suspension was filtered through celite and the residue was washed with methanol. The combined filtrates were concd and purified by chromatography on Itrobeads (EtOAc:methanol, 2:1) to give a solid which was lyophilized to give **4** (70.4 mg, 89%), $[\alpha]_D^{22}$ −213.3° (*c* 0.30; H_2O). ^1H NMR (500 MHz, D_2O): δ 5.10 (1H, d, $J_{1B,2B}$ = 4.0 Hz, H-1B), 4.84 (1H, q, $J_{5B,6B}$ = 6.6 Hz, H-5B), 4.45 (1H, d, $J_{1C,2C}$ = 8.4 Hz, H-1C), 4.43 (1H, d, $J_{1A,2A}$ = 8.2 Hz, H-1A), 3.94 (1H, dd, $J_{2C,3C}$ = 10.8 Hz, H-2C), 3.95–3.87 (5H, m, H-2A, H-3B, H-4A, H-4C, H-6Aa), 3.86–3.81 (2H, m, H-3A, H-4B), 3.79–3.74 (3H, m, H-6C, H-6Ab), 3.71 (1H, m, H-3C), 3.69 (1H, dd, $J_{2B,3B}$ = 10.5 Hz, H-2B), 3.57 (1H, dd, $J_{5C,6Ca}$ = 4.3 Hz, $J_{5C,6Cb}$ = 8.0 Hz, H-5C), 3.52 (1H, ddd, $J_{4A,5A}$ = 8.9 Hz, $J_{5A,6Aa}$ = 2.4 Hz, $J_{5A,6Ab}$ = 5.2 Hz, H-5A), 3.49 (3H, s, OCH_3), 2.04 (3H, s, CH_3CO), 2.02 (3H, s, CH_3CO), 1.26 (3H, d, H-6B). ^{13}C NMR (125 MHz, D_2O): 102.58 ($J_{C1A,H1A}$ = 162.0 Hz, C-1A), 101.60 ($J_{C1C,H1C}$ = 161.4 Hz, C-1C), 99.30 ($J_{C1B,H1B}$ = 171.6 Hz, C-1B), 76.32 (C-5A), 75.69 (C-5C), 75.72 (C-3A), 74.28 (C-4A), 72.85 (C-4B), 71.58 (C-3C), 70.04 (C-3B), 68.55 (C-2B), 68.20 (C-4C), 67.77 (C-5B), 62.29 (C-6C), 60.89 (C-6A), 57.97 (OCH_3), 56.26 (C-2A), 53.22 (C-2C), 23.06 ($\underline{C}H_3CO$), 23.03 ($\underline{C}H_3CO$), 16.21 (C-6B). HR-FABMS calcd for $C_{23}H_{40}N_2O_{15}$ (M+Na): 607.2326; found: 607.2301.

2-(Trimethylsilyl)ethyl 2-acetamido-2-deoxy-3-*O*-(α-L-fucopyranosyl)-4-*O*-[2-acetamido-2-deoxy-4-*O*-(3,6-dideoxy-β-D-*arabino*-hexopyranosyl)-β-D-galactopyranosyl]-β-D-glucopyranoside (5). A soln of **22** (101 mg, 0.07 mmol) in acetic acid (8 mL) was hydrogenated over 10% palladium on charcoal (100 mg) at rt for 40 h. The suspension was filtered through celite and the residue was washed with methanol. The combined filtrates were concd and purified by chromatography on Itrobeads (EtOAc:methanol, 1:1) to give a solid that was lyophilized to give **5** (51 mg, 91%), [α]-118.8° (*c* 0.32; H_2O). ^1H NMR (500 MHz, D_2O): δ 5.09 (1H, d, $J_{1B,2B}$ = 4.0 Hz, H-1B), 4.84 (1H, q, $J_{5B,6B}$ = 6.5 Hz, H-5B), 4.69 (1H, s, H-1D), 4.53 (1H, d, $J_{1A,2A}$ = 8.4 Hz, H-1A), 4.52 (1H, d, $J_{1C,2C}$ = 8.6 Hz, H-1C), 4.09 (1H, d, $J_{3C,4C}$ = 3.4 Hz, H-4C), 4.07 (1H, dd, $J_{2C,3C}$ = 10.7 Hz, H-2C), 4.01 (1H, dt, J = 10.4 Hz, J = 4.9 Hz, $OCH_2CH_2SiMe_3$), 3.93 (1H, m, H-3B), 3.92–3.88 (4H, m, H-2A, H-2D, H-4A, H-6Aa), 3.86 (1H, m, H-3C), 3.82 (2H, m, H-3A, H-4B), 3.74 (2H, m, H-6Ab, H-6Ca), 3.70 (2H, m, H-2B, H-6Cb), 3.66 (1H, dt, J = 10.4 Hz, J = 7.2 Hz, $OCH_2CH_2SiMe_3$), 3.60 (1H, dd, $J_{5C,6Ca}$ = 4.1 Hz, $J_{5C,6Cb}$ = 8.1 Hz, H-5C), 3.55 (1H, ddd, $J_{3Deq,4D}$ = 4.6 Hz, $J_{3Dax,4D}$ = 11.4 Hz, $J_{4D,5D}$ = 9.3 Hz, H-4D), 3.49 (1H, ddd, $J_{4A,5A}$ = 9.5 Hz, $J_{5A,6Aa}$ = 2.3 Hz, $J_{5A,6Ab}$ = 4.7 Hz, H-5A), 3.44 (1H, dq, $J_{5D,6D}$ = 6.1 Hz, H-5D), 2.17 (1H, ddd, $J_{2D,3Deq}$ = 3.7 Hz, $^2J_{3Deq,3Dax}$ = 13.7 Hz, H-3Deq), 2.03 (3H, s, CH_3CO), 2.01 (3H, s, CH_3CO), 1.65 (1H, ddd, H-3Dax), 1.27 (3H, d, H-6D), 1.25 (3H, d, H-6B), 0.96 (1H, m, $OCH_2CH_2SiMe_3$), 0.86 (1H, m, $OCH_2CH_2SiMe_3$), −0.001 (9H, s, $SiMe_3$). HR-FABMS calcd for $C_{33}H_{60}N_2O_{18}Si$ (M+Na): 823.3508; found: 823.3505.

2-(Trimethylsilyl)ethyl 2-acetamido-2-deoxy-3-*O*-(α-L-fucopyranosyl)-4-*O*-[2-acetamido-2-deoxy-4-*O*-(3,6-dideoxy-α-D-*arabino*-hexopyranosyl)-β-D-galactopyranosyl]-β-D-glucopyranoside (7). A soln of **21** (145 mg, 0.10 mmol) in acetic acid (8 mL) with 10% palladium on charcoal (100 mg) was hydrogenated at rt for 40 h. The suspension was filtered through celite and the residue was washed with methanol. The combined filtrates were concd and purified by chromatography on Itrobeads (EtOAc:methanol, 1:1) to give a solid which was lyophilized to give **7** (74 mg, 91%), $[\alpha]_D^{22}$ −19.4° (*c* 0.36, H_2O). ^1H NMR (500 MHz, D_2O): δ 5.11 (1H, d, $J_{1B,2B}$ = 4.0 Hz, H-1B), 4.82 (1H, q, $J_{5B,6B}$ = 6.6 Hz, H-5B), 4.76 (1H, overlapped by HDO, H-1D), 4.58 (1H, d, $J_{1C,2C}$ = 8.1 Hz, H-1C), 4.53 (1H, d, $J_{1A,2A}$ = 8.2 Hz, H-1A), 4.12 (1H, d, $J_{3C,4C}$ = 3.2 Hz, H-4C), 4.02 (2H, m, H-2C, $OCH_2CH_2SiMe_3$), 3.97 (1H, m, H-2D), 3.94 (2H, m, H-3B, H-6Aa), 3.90 (2H, m, H-2A, H-4A), 3.83 (2H, m, H-3A, H-4B), 3.79 (2H, m, H-3C, H-6Ca), 3.76 (1H, m, H-6Ab), 3.70 (2H, m, H-2B, H-6Cb), 3.66 (1H, dt, J = 10.1 Hz, J = 7.2 Hz, $OCH_2CH_2SiMe_3$), 3.60 (2H, m, H-4D, H-5D), 3.56 (1H, dd, $J_{5C,6Ca}$ = 4.2 Hz, $J_{5C,6Cb}$ = 8.1 Hz, H-5C), 3.51 (1H, ddd, $J_{4A,5A}$ = 9.4 Hz, $J_{5A,6Aa}$ = 2.3 Hz, $J_{5A,6Ab}$ = 4.9 Hz, H-5A), 2.06 (3H, s, CH_3CO), 2.02 (1H, m, H-3Deq), 2.01 (3H, s, CH_3CO), 1.75 (1H, ddd, $^2J_{2D,3Dax}$ = 2.9 Hz, $J_{3Deq,3Dax}$ = 11.3 Hz, $J_{3Dax,4D}$ = 8.4 Hz, H-3Dax), 1.27 (3H, d, $J_{5D,6D}$ = 5.8 Hz, H-6D), 1.25 (3H, d, H-6B), 0.96 (1H, m, $OCH_2CH_2SiMe_3$), 0.86 (1H, m, $OCH_2CH_2SiMe_3$), −0.001 (9H, s, $SiMe_3$). HR-FABMS calcd for $C_{33}H_{60}N_2O_{18}Si$ (M+Na): 823.3508; found: 823.3513.

Methyl 2-acetamido-2-deoxy-3-*O*-(α-L-fucopyranosyl)-4-*O*-[2-acetamido-2-deoxy-4-*O*-(3,6-dideoxy-β-D-*arabino*-hexopyranosyl)-β-D-galactopyranosyl]-β-D-glucopyranoside (6). A soln of **24** (90 mg, 0.07 mmol) in acetic acid (5 mL) was hydrogenated over 10% palladium on charcoal (90 mg) at rt for 40 h. The suspension was filtered through celite and the residue was washed with methanol. The combined filtrates were concd and

chromatographed on Itrobeads (EtOAc:methanol, 1:1) to give a white solid after lyophilization, **6** (42 mg, 88%), $[\alpha]_D^{22}$ −179.5° (*c* 0.30; H_2O). ^1H NMR (500 MHz, D_2O): δ 5.09 (1H, d, $J_{1B,2B}$ = 4.0 Hz, H-1B), 4.84 (1H, q, $J_{5B,6B}$ = 6.7 Hz, H-5B), 4.69 (1H, s, H-1D), 4.52 (1H, d, $J_{1C,2C}$ = 8.6 Hz, H-1C), 4.43 (1H, d, $J_{1A,2A}$ = 8.4 Hz, H-1A), 4.09 (1H, d, $J_{3C,4C}$ = 3.4 Hz, H-4C), 4.07 (1H, dd, $J_{2C,3C}$ = 10.7 Hz, H-2C), 3.93 (2H, m, H-3B, H-6Aa), 3.92–3.88 (3H, m, H-2A, H-2D, H-4A), 3.84 (2H, m, H-3C, H-4B), 3.80 (1H, m, H-3A), 3.77–3.70 (3H, m, H-6Ab, H-6C), 3.69 (1H, dd, $J_{2B,3B}$ = 10.5 Hz, H-2B), 3.60 (1H, dd, $J_{5C,6Ca}$ = 4.0 Hz, $J_{5C,6Cb}$ = 8.0 Hz, H-5C), 3.55 (1H, ddd, $J_{3Deq,4D}$ = 4.7 Hz, $J_{3Dax,4D}$ = 11.5 Hz, $J_{4D,5D}$ = 9.3 Hz, H-4D), 3.52 (1H, ddd, $J_{4A,5A}$ = 9.4 Hz, $J_{5A,6Aa}$ = 2.3 Hz, $J_{5A,6Ab}$ = 5.0 Hz, H-5A), 3.49 (3H, s, OCH_3), 3.44 (1H, dq, $J_{5D,6D}$ = 6.1 Hz, H-5D), 2.16 (1H, ddd, $J_{2D,3Deq}$ = 3.7 Hz, $^2J_{3Deq,3Dax}$ = 13.7 Hz, H-3Deq), 2.04 (3H, s, CH_3CO), 2.02 (3H, s, CH_3CO), 1.66 (1H, ddd, H-3Dax), 1.27 (3H, d, H-6D), 1.25 (3H, d, H-6B). ^{13}C NMR (125 MHz, D_2O): δ 103.33 ($J_{C1D,H1D}$ = 159.7 Hz, C-1D), 102.58 ($J_{C1A,H1A}$ = 163.3 Hz, C-1A), 101.13 ($J_{C1C,H1C}$ = 161.3 Hz, C-1C), 99.36 ($J_{C1B,H1B}$ = 171.9 Hz, C-1B), 79.87 (C-3C), 76.77 (C-5D), 76.17 (C-5A), 75.53 (C-5C), 75.40 (C-3A), 74.16 (C-4A), 72.85 (C-4B), 70.02 (C-3B), 68.54 (C-2B), 68.50 (C-2D), 68.49 (C-4C), 67.71 (C-5B), 67.66 (C-4D), 62.30 (C-6C), 60.85 (C-6A), 57.98 (OCH_3), 56.36 (C-2A), 52.29 (C-2C), 37.21 (C-3D), 23.06 ($\underline{C}H_3CO$), 22.86 ($\underline{C}H_3CO$), 17.94 (C-6D), 16.24(C-6B). HR-FABMS calcd for $C_{29}H_{50}N_2O_{18}$ (M+Na): 737.2956; found: 737.2950.

Methyl 2-acetamido-2-deoxy-3-*O*-(α-L-fucopyranosyl)-4-*O*-[2-acetamido-2-deoxy-4-*O*-(3,6-dideoxy-α-D-*arabino*-hexopyranosyl)-β-D-galactopyranosyl]-β-D-glucopyranoside (8). A soln of **23** (86 mg, 0.06 mmol) in acetic acid (5 mL) was hydrogenated over 10% palladium on charcoal (80 mg) at rt for 40 h. The suspension was filtered through celite and the residue was washed with methanol. The combined filtrates were concd and purified by chromatography on Itrobeads (dichloromethane:methanol, 1:1) to give a solid which was lyophilized to give **8** (41 mg, 89%), $[\alpha]_D^{22}$ −34.1° (*c* 0.41; H_2O). ^1H NMR (500 MHz, D_2O): δ 5.11 (1H, d, $J_{1B,2B}$ = 4.1 Hz, H-1B), 4.82 (1H, q, $J_{5B,6B}$ = 6.6 Hz, H-5B), 4.76 (1H, overlapped by HDO, H-1D), 4.57 (1H, d, $J_{1C,2C}$ = 7.8 Hz, H-1C), 4.53 (1H, d, $J_{1A,2A}$ = 8.2 Hz, H-1A), 4.12 (1H, d, $J_{3C,4C}$ = 3.2 Hz, H-4C), 3.99–4.05 (1H, m, H-2C), 3.97 (1H, m, H-2D), 3.95 (2H, m, H-3B, H-6Aa), 3.92 (2H, m, H-2A, H-4A), 3.83 (2H, m, H-3A, H-4B), 3.80 (2H, m, H-3C, H-6Ca), 3.77 (1H, m, H-6Ab), 3.73 (1H, m, H-6Cb), 3.68 (1H, dd, $J_{2B,3B}$ = 10.4 Hz, H-2B), 3.60 (2H, m, H-4D, H-5D), 3.56 (1H, dd, $J_{5C,6Ca}$ = 4.1 Hz, $J_{5C,6Cb}$ = 8.1 Hz, H-5C), 3.54 (1H, ddd, $J_{4A,5A}$ = 9.3 Hz, $J_{5A,6Aa}$ = 2.4 Hz, $J_{5A,6Ab}$ = 5.2 Hz, H-5A), 2.06 (3H, s, CH_3CO), 2.02 (1H, m, H-3Deq), 2.02 (3H, s, CH_3CO), 1.75 (1H, ddd, $J_{2D,3Dax}$ = 2.9 Hz, $^2J_{3Deq,3Dax}$ = 13.7 Hz, $J_{3Dax,4D}$ = 11.1 Hz, H-3Dax), 1.27 (3H, d, $J_{5D,6D}$ = 5.8 Hz, H-6D), 1.25 (3H, d, H-6B). ^{13}C NMR (125 MHz, D_2O): 102.6 ($J_{C1A,H1A}$ = 162.5 Hz, C-1A), 101.1 ($J_{C1C,H1C}$ = 163.0 Hz, C-1C), 99.1 ($J_{C1B,H1B}$ = 172.2 Hz, C-1B), 95.9 ($J_{C1D,H1D}$ = 168.6 Hz, C-1D), 76.1 (C-5A), 75.4 (C-5C), 75.3 (C-3C), 75.2 (C-3A), 74.2 (C-4A), 72.7 (C-4B), 71.0 (C-5D), 69.8 (C-3B), 68.5 (C-2B), 68.3 (C-2D), 67.6 (C-5B), 67.2 (C-4D), 64.1 (C-4C), 62.2 (C-6C), 60.7 (C-6A), 57.7 (OCH_3), 56.3 (C-2A), 51.6 (C-2C), 32.8 (C-3D), 22.9 ($\underline{C}H_3CO$), 22.8 ($\underline{C}H_3CO$), 17.5 (C-6D), 16.0 9(C-6B). HR-FABMS calcd for $C_{29}H_{50}N_2O_{18}$ (M+Na): 737.2956; found: 737.2946.

Acknowledgments

The research was supported by a Natural Sciences and Engineering Research Council of Canada research grant to DRB and in part by USPHS Grant AI 14490 to Dr J.A. Appleton, Cornell University, that provided partial support for a University of Alberta Postdoctoral Fellowship to JZ. The authors thank Dr J.A. Appleton for valuable discussions. Dr Shah Nilar is acknowledged for performing the potential energy calculations.

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(*Received in U.S.A.* 7 *March* 1996; *accepted* 17 *May* 1996)