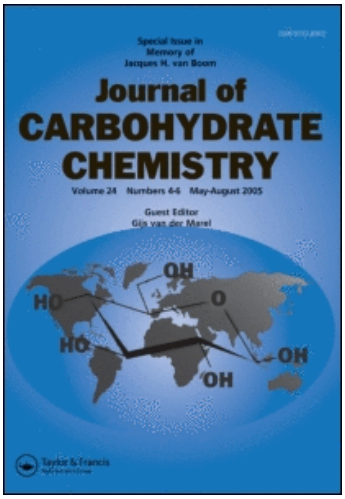

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SYNTHESIS OF A SINGLE REPEAT UNIT OF TYPE VIII GROUP B *STREPTOCOCCUS* CAPSULAR POLYSACCHARIDE[1]

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ABSTRACT

We have synthesized a single repeat unit of type VIII Group B *Streptococcus* capsular polysaccharide, the structure of which is {L-Rhap(ß1→4)-D-Glcp(ß1→4)[Neu5Ac(α2→3)]-D-Galp(ß1→4)}$_n$. The synthesis presented three significant synthetic challenges namely: the L-Rhap(ß1→4)-D-Glcp bond, the Neu5Ac(α2→3)-D-Galp bond and 3,4-D-Galp branching. The L-Rhap bond was constructed in 60% yield (α:ß 1:1.2) using 4-*O*-acetyl-2,3-di-*O*-benzoyl-α-L-rhamnopyranosyl bromide **6** as donor, silver silicate as promotor and 6-*O*-benzyl-2,3-di-*O*-benzoyl-1-thio-ß-D-glucopyranoside as acceptor to yield disaccharide **18**. The Neu5Ac(α2→3) linkage was synthesized in 66% yield using methyl [phenyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-2-thio-D-glycero-D-galacto-nonulopyranosid]onate as donor and triol 2-(trimethylsilyl) ethyl 6-*O*-benzyl-ß-D-galactopyranoside as acceptor to give disaccharide **21**. The 3,4-D-Galp branching was achieved by regioselective glycosylation of disaccharide diol **21** by disaccharide **18** in 28% yield to give protected tetrasaccharide **22**. Tetrasaccharide **22** was deprotected to give as its 2-(trimethylsilyl)ethyl glycoside the title compound **1a**. In addition the 2-(trimethylsilyl)ethyl group was cleaved and the tetrasaccharide coupled by glycosylation (via tetrasaccharide trichloroacetimidate) to a linker suitable for conjugation.

INTRODUCTION

Group B *Streptococcus* (GBS) has long been recognized as a major cause of neonatal sepsis and meningitis.[2] Strains (I-VIII) of GBS are classified into serotypes on the basis of their type specific capsular polysaccharides. Type VIII has been identified

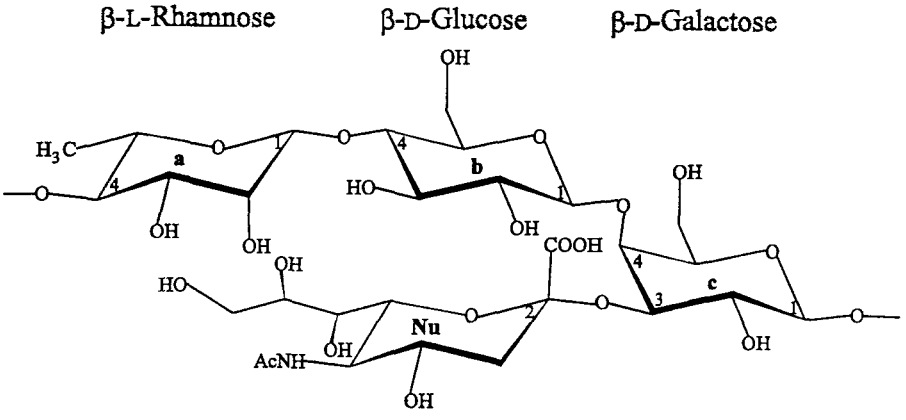
among disease-causing isolates in Japan where it is now a prevalent strain.[3] The structure (Scheme 1) of its capsular polysaccharide has been determined and consists of a branched tetrasaccharide repeat unit {L-Rhap(ß1→4)-D-Glcp(ß1→4)[Neu5Ac(α2→3)]-D-Galp(ß1→4)}$_n$.[4]

A common feature of sialic acid containing capsular polysaccharides is that protective antibodies often recognize extended epitopes which contain more than one repeat unit.[5] "Molecular mimicry" by the bacteria of the host's natural cell surface oligosaccharides has been suggested as the cause of this phenomenon. It is supposed that antibodies to a single repeat unit of the polysaccharide could trigger auto-immune responses and are therefore selected against. In this case, the Type VIII GBS oligosaccharide bears resemblance to common ganglioside structures. As part of a program to develop vaccines for GBS infections, we have synthesized a single repeat unit of the type VIII capsular polysaccharide. This synthesis is sufficiently flexible that future developments will allow for the synthesis of multiple repeat units. We have synthesized the glycoside **1a** and an analogue **1b** with a linker at the reducing terminus suitable for attachment to a vaccine carrier for the preparation of antibodies.[6]

Synthesis of this tetrasaccharide presents three significant synthetic challenges; namely, the L-Rhap(ß1→4)-D-Glcp bond, the Neu5Ac(α2→3)-D-Galp bond and the 3,4 D-Galp branching. Each of these is elaborated below.

RESULTS AND DISCUSSION

ß-L-Rhamnose - Formation of the *cis*-equatorial linkage of ß-L-rhamnosyl or ß-D-mannosyl glycosides remains a challenge for carbohydrate chemistry.[7] Classical methods have used glycosyl halides as donors and insoluble supported heavy metal salts as catalysts.[8] A plausible mechanism for this class of reactions is that a glycosyl carbenium ion-insoluble support ion pair is formed after activation of the donor. Subsequent attack by the nucleophilic hydroxyl then occurs preferentially from the now least hindered ß-face, leading to the *cis*-glycoside. Other approaches include using intramolecular tethers followed by intramolecular glycosylation,[9] inversion at C-2 by oxidation-reduction[10] or S_N2 methods[11] and direct glycosylation with 2-ulosyl donors followed by stereospecific reduction.[12] However, in our case, we need a temporary protecting group at C-4 in order to build molecules with more than one repeat unit (Scheme 1) and it is not a simple task to find a protecting group strategy compatible with these newer glycosylation

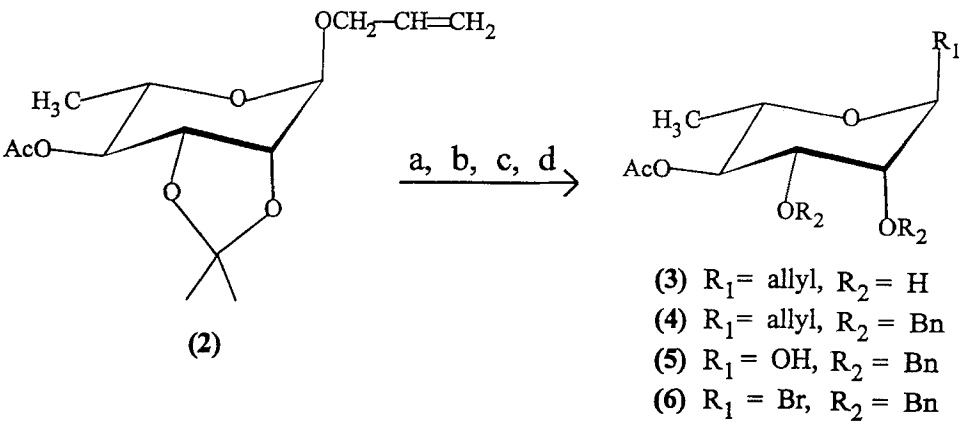


Scheme 1. Single repeat unit of the type VIII group B *Streptococcus* capsular polysaccharide.

strategies. Thus, we choose to use the proven silver silicate method[13] and rhamnosyl bromide **6** with the temporary acetate group at C-4.

This donor was synthesized from the 4-*O*-acetyl derivative **2**, which was prepared from known allyl 2,3-*O*-isopropylidene-α-L-rhamnopyranoside,[14] in four steps in 35% overall yield (Scheme 2). The benzylation of diol **3** to dibenzylderivative **4** required acid catalyzed conditions to avoid acetyl migration.[15] Also, the reaction was best terminated while some of both monobenzyl derivatives were still present due to the formation of unidentified decomposition products with prolonged exposure to the acidic reaction conditions. The preparation of hemi-acetal **5** has been described but required more steps.[16]

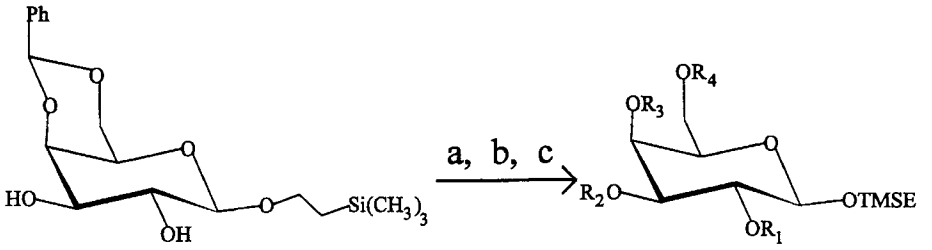
One of our goals was to develop a synthesis that would allow the introduction of various substituents including sialic acids on a 3-*O*-D-Galp position. Thus, we prepared a D-Glcp(ß1→4)-D-Galp disaccharide having the 4'-*O*-position unprotected and the 3-*O*-position with the selectively cleavable allyl group. For this purpose the D-Galp acceptor **9** was prepared from the known 2-(trimethylsilyl)ethyl 4,6-*O*-benzylidene-ß-D-galactopyranoside[17] by a 3-*O*-selective allylation followed by 2-*O*-benzylation and a reductive opening sequence in 27% overall yield (Scheme 3). The acceptor **9** was then glycosylated under NIS/TfOH conditions[18] with known donor **10**[19] to give the (ß1→4) linked disaccharide **11** in 47% yield (Scheme 4). The 4,6-*O*-benzylidene group was



(2)

(3) R_1= allyl, R_2 = H
(4) R_1= allyl, R_2 = Bn
(5) R_1 = OH, R_2 = Bn
(6) R_1 = Br, R_2 = Bn

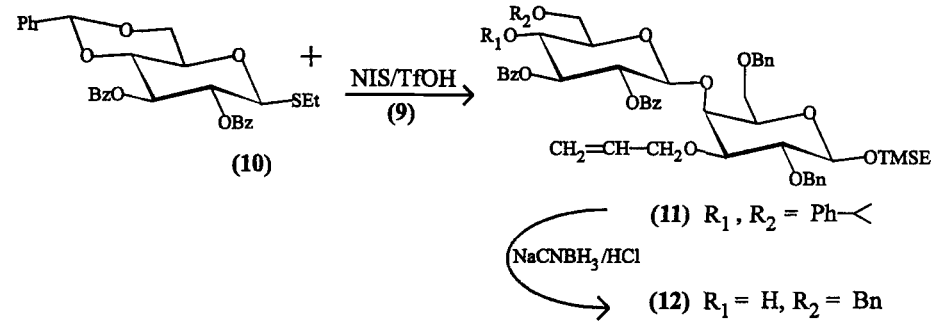
Scheme 2. Preparation of the L-rhamnopyranosyl donor: a) 80% acetic acid 80 °C; b) benzyl trichloroacetimidate/cyclohexane/CH_2Cl_2/TfOH; c) Rh catalyst EtOH/H_2O; d) oxalyl bromide/DMF.



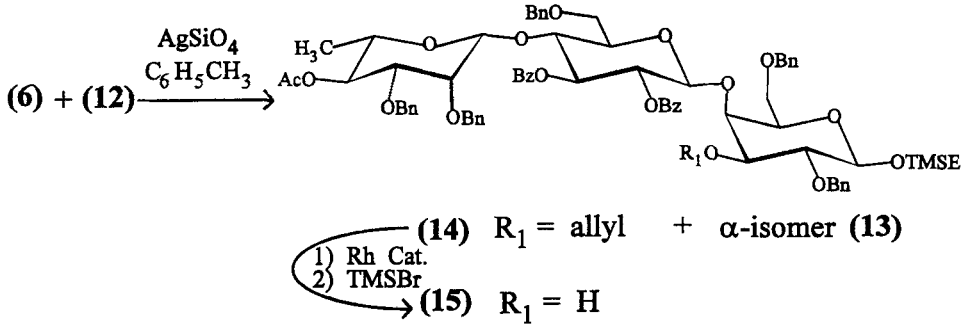
(7) R_1= H, R_2= allyl, R_3, R_4 = Ph–≺
(8) R_1= Bn, R_2= allyl, R_3, R_4 = Ph–≺
(9) R_1= Bn, R_2= allyl, R_3= H, R_4= Bn

Scheme 3. Preparation of the D-galactopyranosyl acceptor: a) dibutyltin oxide/allyl bromide/TBAB/benzene; b) benzyl bromide/NaH/DMF; c) $NaCNBH_3$/HCl.

reductively opened with $NaCNBH_3$ and HCl to give the 4'-OH derivative **12** in 73% yield. Subsequent coupling with L-Rhap donor **6** gave the (ß1→4) linked trisaccharide **14** in 35% yield along with its (α1→4) linked isomer **13** in 34% yield (Scheme 5). The allyl group of **14** was readily cleaved to give acceptor **15** by isomerization with Wilkinson's Rh catalyst followed by hydrolysis with TMSBr.[20] However, all attempts to sialylate the 3-OH of **15** were unsuccessful under a variety of known glycosylation conditions.



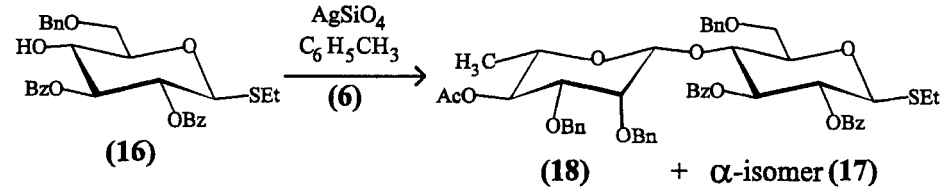
Scheme 4. Preparation of a disaccharide acceptor D-Glcp(ß1→4)-D-Galp.



Scheme 5. Preparation of trisaccharide acceptor L-Rhap(ß1→4)-D-Glcp(ß1→4)-D-Galp.

Therefore, an alternative strategy was used involving the coupling of two disaccharides to make the tetrasaccharide.[21] The L-Rhap(ß1→4)-D-Glcp disaccharide was prepared first by converting glucose donor **10** into the known acceptor **16** by reductive opening of the 4,6-*O*-benzylidene group.[19] Acceptor **16** was then glycosylated with L-Rhap donor **6** promoted by silver silicate to yield the (ß1→4) linked disaccharide **18** in 33% yield along with its (α1→4) linked isomer **17** in 27% yield (Scheme 6). The anomeric configurations were determined by the chemical shifts of H-1, H-3 and H-5 of the L-Rhap unit (α downfield compared to ß, see experimental for values) and by the values of $J_{C\text{-}H}$ for C-1 of 172 Hz for **17** and 156 Hz for **18**.[22]

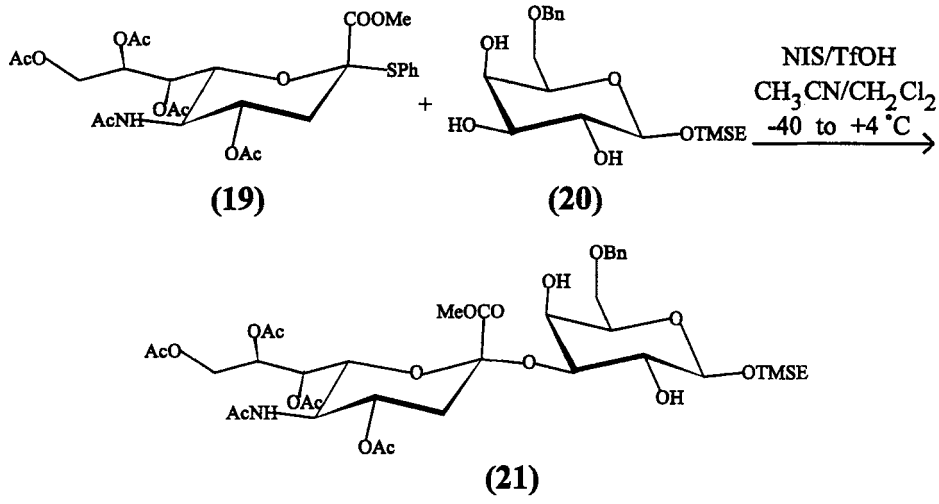
Sialylation of 3-*O*-Galactose - A second disaccharide acceptor Neu5Ac(α2→3)-D-Galp with a free O-4 was necessary for reaction with donor disaccharide **18**. Several approaches to the synthesis of Neu5Ac containing oligosaccharides have been reported including chemical and enzymatic methods.[23] In this case, the desialylated polysaccharide



Scheme 6. Preparation of disaccharide donor L-Rhap(ß1→4)-D-Glcp.

could not be resialylated with sialyl-CMP and a α2→3 transferase. Thus, chemical methods were necessary. Among the many chemical methods reported, the use of methyl[24] and phenyl thioglycosides[25] of Neu5Ac or the corresponding phosphites[26] have been among the most successful methods. Preliminary experiments with all three of these donors led us to use methyl [phenyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-2-thio-D-glycero-D-galacto-nonulopyranosid]onate **19** as donor. Donor **19** was synthesized by the phase transfer method from the corresponding chloride.[27] The D-Galp acceptor triol **20** was synthesized from the known 2,3-di-*O*-benzoate.[17] Similar regioselective and stereoselective (α2→3) glycosylations of 2,3,4-triols of galactose derivatives have been previously reported.[28] Thus, sialylation of triol **20** using donor **19** and NIS/TfOH as promoter (Scheme 7) proceeded regioselectively and stereoselectively to yield acceptor disaccharide **21** in 66% yield.[29] No other products were isolated in sufficient quantity to identify except the known Neu5Ac elimination product the 2,3 glycal.[30] The regiochemistry was deduced from the ^1H-^1H COSY connectivities between the hydroxyl proton at 2.57 ppm and Gal H-4c as well as between the other hydroxyl proton at 2.39 ppm and Gal H-2c. The α-anomeric configuration was determined by observing a measurable long range $J_{C\text{-}1,H\text{-}3eq}$ of J = 3.5 - 4.0 Hz, which is only possible for α-anomers.[31]

Galactose 3,4-Branching - Much synthetic effort has been directed towards glycolipid gangliosides.[32] Most of these gangliosides have (α2→3) sialic acid at C-3 and (ß1→4) GalpNAc at position C-4 of a D-Galp. Most syntheses have constructed the sialic acid linkage first, although a recent report has accomplished this branching in the other order.[33] Our initial attempts at adding the sialic acid residue last were prompted by the desire to make the synthesis flexible enough to allow the addition of sialic acid analogues. However, the failure of this approach prompted us to study the elaboration of diol disaccharide **21**. We could have attempted to regioselectively protect the diol at D-Galp

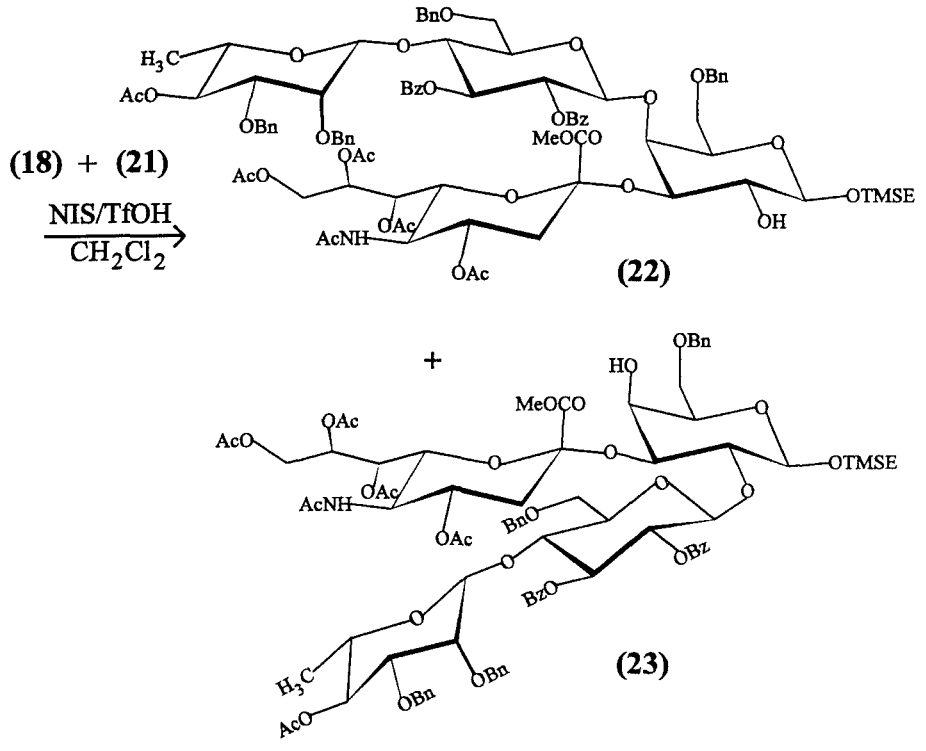


Scheme 7. Preparation of disaccharide acceptor Neu5Ac(α2→3)-D-Galp.

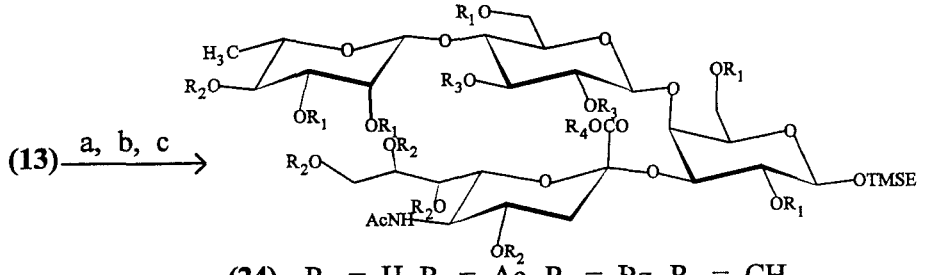
C-2 but, we first investigated regioselective glycosylation. Glycosylation with disaccharide **18** under NIS/TfOH catalysis gave in 28% yield the protected tetrasaccharide **22** along with its 2-*O*-regioisomer **23** in 15% yield (Scheme 8). The new linkage was established as ß from the size of D-Glcp J_{12} (7.9 Hz). The connectivity was 1→4 because the only OH at 2.21 ppm is coupled to D-Galp H-2 at 3.35 ppm. Interestingly in regioisomer **23**, the signals of the Neu5Ac proton H-3eq and of the COOMe methyl are shielded, appearing at 2.19 ppm and 3.43 ppm respectively, in comparison with "normal" values in **22** for H-3eq of 2.67 ppm and for Me of 3.73 ppm.

CONCLUSION

Linker Addition and Deprotection. - Tetrasaccharide **22** was hydrogenolyzed to remove the benzyl protecting groups giving **24** and then perbenzoylated to give the peracyl glycoside **25** (Scheme 9). The relatively low yield, 52%, may be due to steric hindrance for some hydroxyls but only one main component was observed by TLC. The acyl groups and the methyl ester of the sialic acid were readily cleaved by basic hydrolysis to give as its 2-(trimethylsilyl)ethyl glycoside the title compound **1a**. The ^1H NMR spectrum of this tetrasaccharide was fully assigned and is entirely consistent with its structure, notably, H-1a 4.86 vs. 4.86 ppm; H-1b 4.83 vs. 4.82 ppm, H-3c 4.20 vs. 4.17 ppm and



Scheme 8. Regioselective tetrasaccharide formation.



(24) R_1 = H, R_2 = Ac, R_3 = Bz, R_4 = CH_3

(25) R_1 = Bz, R_2 = Ac, R_3 = Bz, R_4 = CH_3

(1a) $R_1 = R_2 = R_3$ = H, R_4 = Na^+

Scheme 9. Deprotection of tetrasaccharide: a) 10% Pd/C acetic acid; b) benzoyl chloride/pyridine; c) sodium methoxide then NaOH.

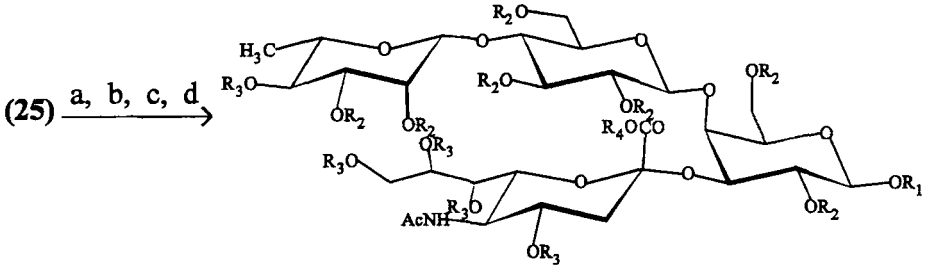
H-3Nu 2.73 vs. 2.71 ppm,[4] in comparison with the signals of the natural polysaccharide having this repeating unit. In addition, the 2-(trimethylsilyl)ethyl group of **25** was cleaved with trifluoroacetic acid to give the hemi-acetal **26**[34] which was subsequently converted to trichloroacetimidate **27** with CCl_3CN/DBU.[35] This tetrasaccharide donor was then coupled with the azido alcohol linker, 3-azido propan-1-ol,[36] to give **28** which was hydrolysed to **1b** by the same procedure as for **1a** (Scheme 10). The ^1H and ^{13}C NMR spectra of **1b** were fully assigned and the ^1H spectrum is shown in Figure 1.

The linker in tetrasaccharide **1b** is suitable (after reduction to the amine) for conjugation to carrier proteins by reductive amination in order to prepare antibodies. The results of biological testing and the subsequent modifications of this synthetic procedure to produce multiple repeat units will be reported in future communications.

EXPERIMENTAL METHODS

Materials and General Methods. Optical rotations were measured (λ = 589 nm) at room temperature using a Perkin-Elmer 243 polarimeter in a 10 cm 1 mL cell. The ^1H and ^{13}C NMR spectra were recorded at 500 MHz and 125 MHz on a Bruker AMX-500 spectrometer, respectively in either deuteriochloroform or deuterium oxide. ^1H NMR spectra in $CDCl_3$ were referenced to residual $CHCl_3$ at 7.24 ppm, and ^{13}C NMR spectra to the central peak of $CDCl_3$ 77.0 ppm. In D_2O spectra were referenced to internal acetone at 2.225 ppm and 31.55 ppm, for ^1H and ^{13}C NMR spectra, respectively. Assignments were made by standard ^1H-^1H-COSY and ^1H-coupled ^{13}C-^1H-COSY experiments. For **1a** and **1b** additional ^1H-decoupled ^{13}C-^1H-COSY, ^1H-^1H-TOCSY and ^1H-^1H-ROESY measurements were made at 300 K. For **21** additional ^1H-coupled ^{13}C and long range ^{13}C-^1H correlation measurements were made at 300 K. For NMR assignments, all carbohydrate residues in products larger than monosaccharides have been designated as follows: rhamnose a, glucose b, galactose c and neuraminic acid Nu.

The mass spectra were recorded on a Fisons VG-Quattro spectrometer in the loop injection mode using 50:50 acetonitrile:water with 0.4 % acetic acid as matrix in the negative ion mode. TLC was performed on Merck Silica gel 60 F_{254} plates and preparative Silica gel chromatography used Merck Silica gel 60 (70-230 mesh) and MPLC used Merck Silica gel 60 (230-400 mesh). Detection was effected by examination under UV light and by charring with 5% sulfuric acid in water. Solutions were concentrated at or below 40 °C at aspirator pressure. Microanalyses were carried out by the analytical services of this



(26) R_1 = H, R_2 = Bz, R_3 = Ac, R_4 = CH_3

(27) R_1 = $C(=NH)CCl_3$, R_2 = Bz, R_3 = Ac, R_4 = CH_3

(28) R_1 = $CH_2CH_2CH_2N_3$, R_2 = Bz, R_3 = Ac, R_4 = CH_3

(1b) R_1 = $CH_2CH_2CH_2N_3$, R_2 = R_3 = H, R_4 = Na^+

Scheme 10. Deprotection and attachment of linker: a) trifluoroacetic acid; b) CCl_3CN/DBU; c) 3-azidopropan-1-ol/$BF_3{\cdot}OEt_2$; d) sodium methoxide then NaOH.

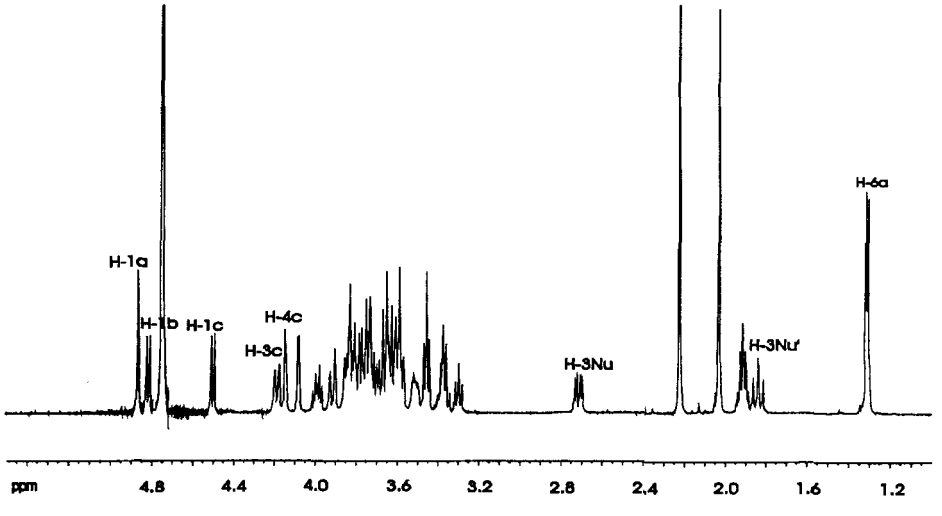


Figure 1. ^{1}H NMR Spectrum of **1b** in D_2O ref. acetone.

department and all samples submitted for elemental analyses were dried overnight under vacuum with phosphorus pentoxide at 56 °C (refluxing acetone).

Allyl 4-*O*-Acetyl-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (2). Allyl 2,3-*O*-isopropylidene-α-L-rhamnopyranoside[14] (73.0 g, 0.3 mol), was dissolved in pyridine (400 mL) and the solution under nitrogen was chilled to 0 °C. To this solution, acetic anhydride (100 mL) was added dropwise, and the mixture while stirring was left to warm up to room temperature overnight. The solution was concentrated and then reconcentrated twice with toluene. The residue was purified by chromatography on a large open column, using 1:4 ethyl acetate:hexanes as an eluant to yield **2**, (65.5 g, 76.5%) as a light syrup: $[\alpha]_D$ -24.8° (*c* 1.2, chloroform); ^{1}H NMR ($CDCl_3$) δ 5.92 - 5.84 (m, 1H, CH_2CHCH_2), 5.30 (dd, 1H, J=1.4 and 17.2 Hz, CH_2CH) 5.26 (dd, 1H, J=0.9 and 10.4 Hz, CH_2CH), 5.02 (s, 1H, H-1), 4.84 (dd, 1H, J=7.1 and 10.1 Hz, H-4), 4.17 - 4.13 (m, 3H, CH-CH_2O, H-2, H-3), 3.98 (dd, 1H, J=6.1 and 12.9 Hz, CH-CH_2O), 3.74 (m, 1H, H-5), 2.02 (s, 3H, OAc), 1.54 (s, 3H, CH_3C), 1.33 (s, 3H, CH_3C), 1.14 (d, 3H, J=6.3 Hz, H-6).

Anal. Calcd for $C_{14}H_{22}O_6$(286.3): C, 58.73; H, 7.74. Found: C, 58.51; H, 7.81.

Allyl 4-*O*-Acetyl-α-L-rhamnopyranoside (3). To compound **2** (54.5 g, 0.19 mol) was added 80% acetic acid (500 mL) and the mixture was heated to 80 °C with an oil bath. After 90 min, the reaction mixture was cooled to room temperature, the solvents were concentrated and the residue reconcentrated twice with toluene. The semi-solid residue was triturated overnight with hexanes, and **3** was obtained as a white solid (37.7 g, 72%): $[\alpha]_D$ -105.6° (*c* 0.66, chloroform); ^{1}H NMR ($CDCl_3$) δ 5.9 - 5.82 (m, 1H, CH_2CHCH_2), 5.27 (dd, 1H, J=1.5 and 17.2 Hz, CH_2 CH), 5.18 (dd, 1H, J=1.3 and 10.4 Hz, CH_2 CH), 4.84 (bs, 1H, H-1), 4.78 (t, 1H, J=9.6 Hz, H-4), 4.15 (dd, 1H, J=5.1 and 13.0 Hz, $CHCH_2O$), 3.93 (dd, 1H, J=6.1 and 12.9 Hz, $CHCH_2O$), 3.98 (bs, 1H, H-2), 3.88 (m, 1H, H-3), 3.79 (m, 1H, H-5), 2.95 (d, 1H, J=6.9 Hz, OH-3), 2.60 (d, 1H, J=4.6 Hz, OH-2), 2.17 (s, 3H, OAc), 1.19 (d, 3H, J=6.2 Hz, H-6).

Anal. Calcd for $C_{11}H_{18}O_6$(246.2): C, 53.65, H, 7.36. Found: C, 53.55; H, 7.37.

Allyl 4-*O*-Acetyl-2,3-di-*O*-benzyl-α-L-rhamnopyranoside (4). Compound **3** (12.3 g, 0.05 mol) was dissolved in dichloromethane (100 mL) and cyclohexane (200 mL). To this stirred solution under nitrogen was added benzyl trichloroacetimidate (37 mL, 0.20 mol) followed by trifluoromethanesulfonic acid (TfOH, 0.6 mL). Some solid material precipitated out shortly after the addition started. After 2 h, pyridine (10 mL) and more dichloromethane were added until all the solids dissolved. This solution was then washed

with water and a saturated sodium chloride solution, dried over magnesium sulfate, and concentrated. The residue was purified by chromatography using 3:1 hexanes:ethyl acetate as eluant to obtain **4** (12.1 g, 57%): $[\alpha]_D$ -30.8° (*c* 1.18, chloroform); ^{1}H NMR ($CDCl_3$) δ 7.35-7.23 (m, 10H, 2*Ph*CH_2), 5.86-5.80 (m, 1H, CH_2*CH*CH_2), 5.23 (bs, 1H, H-4), 5.19 (bd, 1H, J=8.4 Hz, *CH*$_2$CHCH$_2$O), 5.15 (bd, H, J=10.4 Hz, *CH*$_2$CHCH$_2$O), 4.83 (s, 1H, H-1), 4.77 (d, 1H, J=12.5 Hz, *CH*$_2$Ph), 4.67 (d, 1H, J=12.4 Hz, *CH*$_2$Ph), 4.57 (d, 1H, J=12.1 Hz, *CH*$_2$Ph), 4.43 (d, 1H, J=12.1 Hz, *CH*$_2$Ph), 4.16 (dd, 1H, J=4.3 and 12.5 Hz, CH$_2$CH*CH*$_2$O), 3.91 (dd, 1H, J=5.9 and 13.1 Hz, CH$_2$CH*CH*$_2$O), 3.78 (m, 2H, H-2 and H-3), 3.70 (m, 1H, H-5), 1.99 (s, 3H, OAc), 1.19 (d, 3H, J=6.2 Hz, H-6).

Anal. Calcd for $C_{25}H_{30}O_6$(426.5): C, 70.40; H, 7.09. Found: C, 70.42; H, 7.06.

4-*O*-Acetyl-2,3-di-*O*-benzyl-α-L-rhamnopyranose (5). Tris(trichlorophenylphosphine)rhodium(I) chloride (300 mg, 0.3 mmol) was added to a solution of the allyl glycoside **4** (1.8 g, 4.22 mmol) in 9:1 ethanol:water (100 mL), followed by a few crystals of diazabicyclooctane (DABCO) and the mixture was heated at reflux for 18 h under nitrogen. The solution was filtered and concentrated. The residual yellow oil was dissolved in 9:1 acetone:water (100 mL), and the solution was stirred while yellow mercury(II)oxide (0.92 g, 4.22 mmol) was added, followed by the dropwise addition of a solution of mercury(II) chloride (11.2 mL of an 8.2% solution in 9:1 acetone:water), followed by 9:1 acetone:water (60 mL). This mixture was stirred for 2.5 h, the solvents were concentrated and the resulting syrup dissolved in ethyl acetate. Following filtration through Celite, the filtrate was washed successively with saturated aqueous potassium iodide (2x), aqueous sodium thiosulfate (2x), and water (2x). The organic layer was dried ($MgSO_4$), filtered and concentrated. The residue was purified by chromatography with 4:1 hexanes:ethyl acetate as eluant to give pure deallylated **5** as an oil (1.4 g, 86%): $[\alpha]_D$ -13.2° (*c* 2.62, chloroform), lit. $[\alpha]_D$ -13.0°; ^{1}H NMR ($CDCl_3$) δ 7.3-7.1 (m, 10H, 2*Ph*CH_2), 5.21 (t, 1H, J=9.6 Hz, H-4), 5.17 (bs, 1H, H-1), 4.77 (d, 1H, J=12.4 Hz, *CH*$_2$Ph), 4.67 (d, 1H, J=12.4 Hz, *CH*$_2$Ph), 4.58 (d, 1H, J=12.2 Hz, *CH*$_2$Ph), 4.47 (d, 1H, J=12.2 Hz, *CH*$_2$Ph), 3.93 (m, 1H, H-5), 3.83 (dd, 1H, J=2.9 and 9.6 Hz, H-3), 3.79 (m, 1H, H-2), 2.56 (d, 1H, J=3.4 Hz, OH-1), 1.97 (s, 3H, OAc), 1.18 (d, 3H, J=6.2 Hz, H-6).

Anal. Calcd for $C_{22}H_{26}O_6$(386.4): C, 68.38; H, 6.78. Found: C, 66.39; H, 6.82.

2-(Trimethylsilyl)ethyl 3-*O*-Allyl-4,6-*O*-benzylidene-ß-D-galactopyranoside (7). A suspension of 2-(trimethylsilyl)ethyl 4,6-*O*-benzylidene-ß-D-galacto-pyranoside[17] (5.1 g, 0.014 mol) and dibutyltin oxide (4.2 g, 0.0168 mol) in benzene (100 mL) was refluxed

with azeotropic removal of water for 24 h. Allyl bromide (22 mL, 0.25 mol) and tetrabutylammonium bromide (TBAB, 2.25 g, 0.007 mol) were added and the mixture refluxed for another 3 h and then concentrated. The residue was purified by column chromatography using 1:3 ethyl acetate:hexanes as eluant to give **7** (3.52 g, 62%) as an amorphous solid: $[\alpha]_D$ +16.3° (*c* 0.6, chloroform); ^{1}H NMR ($CDCl_3$) δ 7.50-7.23 (m, 5H, Ph), 5.97-5.92 (m, 1H, CH_2CHCH_2), 5.51 (s, 1H, *CH*Ph), 5.30 (bd, 1H, J=17.2 Hz, CH_2CHCH_2O), 5.18 (bd, 1H, J=10.4 Hz, CH_2CHCH_2O), 4.33-4.30 (m, 2H, H-1 and H-6), 4.21-4.18 (m, 3H, H-4 and CH_2CHCH_2O), 4.06-4.01 (m, 2H, H-6 and CH_2CH_2Si), 3.93 (bt, 1H, J=7.9 Hz, H-2), 3.56 (m, 1H, CH_2CH_2Si), 3.45 (dd, 1H, J=9.8 and 3.6 Hz, H-3), 3.38 (bs, 1H, H-5), 2.39 (bs, 1H, OH-2), 1.04-0.99 (m, 2H, CH_2CH_2Si), -0.004 (bs, 9H, $(CH_3)_3Si$).

Anal. Calcd for $C_{21}H_{32}O_6Si$ (408.57): C, 61.73; H, 7.89. Found C, 61.61; H, 7.84.

2-(Trimethylsilyl)ethyl 3-*O*-Allyl-2-*O*-benzyl-4,6-*O*-benzylidene-ß-D-galactopyranoside (8). To a stirred solution of **7** (1.1 g, 2.7 mmol) in DMF (80 mL) under nitrogen was added (petroleum ether washed) 50% sodium hydride (230 mg, 4.8 mmol), followed by benzyl bromide (0.48 mL, 4 mmol) at 0 °C. The reaction was complete in 1 h. After methanol (2 mL) was added, the suspension was stirred for another 1 h, then the mixture was poured over ice water (300 mL). A white solid precipitated which was filtered off and dried to obtain **8** (1.15 g, 85%): $[\alpha]_D$ +22.8° (*c* 0.4, chloroform); ^{1}H NMR ($CDCl_3$) δ 7.53-7.24 (m, 10H, 2Ph), 5.97-5.89 (m, 1H, CH_2CHCH_2O), 5.52 (s, 1H, *CH*Ph), 5.36 (dd, 1H, J=17.2 and 1.5 Hz, CH_2CHCH_2O), 5.26 (bd, 1H, J=10.3 Hz, CH_2CHCH_2O), 4.90 (d, 1H, J=10.8 Hz, CH_2Ph), 4.74 (d, 1H, J=10.8 Hz, CH_2Ph), 4.39 (d, 1H, J=7.7 Hz, H-1), 4.31 (bd, 1H, J=12.3 Hz, CH_2CHCH_2O), 4.22-4.18 (m, 3H, CH_2CH_2Si, H-6 and H-4), 4.07-4.01 (m, 2H, CH_2CHCH_2O, and H-6), 3.77 (dd, 1H, J=9.7 and 7.8 Hz, H-2), 3.60-3.55 (m, 1H, CH_2CH_2Si), 3.49 (dd, 1H, J=9.7 and 3.6 Hz, H-3), 3.35 (bs, 1H, H-5), 1.05-1.01 (m, 2H, CH_2CH_2Si), -0.01 (s, 9H, $(CH_3)_3Si$).

Anal. Calcd for $C_{28}H_{38}O_6Si$ (498.69): C, 67.44; H, 7.68. Found C, 67.62; H, 7.78.

2-(Trimethylsilyl)ethyl 3-*O*-Allyl-2,6-di-*O*-benzyl-ß-D-galactopyranoside (9). To a stirred suspension of **8** (1.1 g, 2.2 mmol), $NaCNBH_3$ (1.4 g, 22 mmol), and powdered molecular sieves (3Å, 1.5 g) in dry tetrahydrofuran (30 mL) at room temperature, a saturated solution of HCl in diethyl ether was added dropwise until the pH

was 2. After 1 h, more diethyl ether was added, the suspension was filtered through Celite, and the filtrate was washed with a saturated aqueous sodium hydrogen carbonate solution and water, dried ($MgSO_4$), and concentrated. Only one main sugar component was observed by TLC of the reaction mixture. The residue was purified by chromatography using 1:3 ethyl acetate:hexanes as eluant to give compound **9** as a light syrup (0.56 g, 52 %): $[\alpha]_D$ +2.3° (*c* 0.6, chloroform); ^{1}H NMR ($CDCl_3$) δ 7.35-7.22 (m, 10H, 2 Ph), 5.92 (m, 1H, CH_2CHCH_2), 5.29 (bd, 1H, J=16.2 Hz, CH_2CHCH_2), 5.16 (bd, 1H, J=10.2 Hz, CH_2CHCH_2), 4.87 (bd, 1H, J=11.1 Hz, CH_2Ph), 4.70 (bd, 1H, J=11.1 Hz, CH_2Ph), 4.57 (s, 2H, CH_2Ph), 4.33 (d, 1H, J=7.8 Hz, H-1), 4.17 (m, 2H, CH_2CHCH_2O), 4.03 (m, 2H, H-4 and OCH_2CH_2), 3.79 (dd, 1H, J=6.0 and 9.8 Hz, H-6), 3.72 (dd, 1H, J=6.0 and 9.9 Hz, H-6'), 3.60-3.53 (m, 3H, H-2, H-5 and OCH_2CH_2), 3.38 (dd, 1H, J= 3.4 and 9.3 Hz, H-3), 2.43 (bs, 1H, OH-4), 1.02 (m, 2H, CH_2CH_2Si), 0.01 (s, 9H, $(CH_3)_3Si$).

Anal. Calcd for $C_{28}H_{40}O_6Si$ (500.71): C, 67.16; H, 8.05. Found C, 67.29; H, 8.19.

2-(Trimethylsilyl)ethyl 3-*O*-Allyl-2,6-di-*O*-benzyl-4-*O*-(2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-ß-D-glucopyranosyl)-ß-D-galactopyranoside (11). Compound **9** (1.70 g, 3.39 mmol) and ethyl 2,3-di-*O*-benzoyl-4,6-*O*-benzylidene 1-thio-ß-D-glucopyranoside[19] **10** (1.76 g, 3.39 mmol) were dissolved in dry dichloromethane (120 mL), and powdered molecular sieves (4Å, 20 g, freshly activated) were added. The mixture was stirred for 2 h at room temperature, then *N*-iodosuccinimide (1.90 g, 8.47 mmol) was added and the suspension stirred for 10 min before a saturated solution of triflic acid in dichloromethane (ca 0.13 M) was added rapidly dropwise. After the addition of 0.15 equiv of acid, all the thioglycoside had been consumed. The reaction was quenched with triethylamine, further diluted with dichloromethane and filtered through Celite. The filtrate was washed with a saturated solution of $NaHCO_3$, 10% $Na_2S_2O_3$, water and a saturated NaCl solution. After evaporation of the solvent, purification of the residue by chromatography using 4:1 hexanes:ethyl acetate as eluant gave disaccharide **11** (1.52 g, 47%) as a glassy solid: $[\alpha]_D$ +16.3° (*c* 0.67, chloroform); ^{1}H NMR ($CDCl_3$) δ 8.01-7.01 (m, 25H, 5Ph), 5.88 (m, 1H, CH_2CHCH_2), 5.77 (t, 1H, J=9.5 Hz, H-3b), 5.50 (m, 2H, H-2b, *CH*Ph), 5.28 (dd, 1H, J=7.3 and J= <1 Hz, CH_2CHCH_2), 5.19 (m, 2H, CH_2CHCH_2) and H-1b), 4.55 (bs, 2H, CH_2Ph), 4.30 (d, 1H, J=11.1 Hz, CH_2Ph), 4.27 (m, 1H, H-6b), 4.20 (d, 1H, J=7.6 Hz, H-1c), 4.10-4.04 (m, 3H, H-4c and $CHCH_2O$), 3.92 (m, 2H, OCH_2CH_2 and H-4b), 3.79 (m, 2H, H-6c and H-6b'), 3.66 (m, 3H, H-5b, H-6c' and CH_2Ph), 3.50 (m, 2H, H-5c and

OCH_2CH_2), 3.27 (dd, 1H, J=9.8 and 2.5 Hz, H-3c), 3.21 (bd, 1H, J=7.7 Hz, H-2c), 0.96-0.85 (m, 2H, CH_2CH_2Si), 0.01 (s, 9H, $(CH_3)_3Si$); ^{13}C NMR ($CDCl_3$) δ 101.40 (J=165.7 Hz, CHPh), 102.10 (J=167.5 Hz, CH-1b), 103.13 (J=160.2, CH-1c).

Anal. Calcd for $C_{55}H_{62}O_{13}Si$ (959.185): C, 68.87; H, 6.51. Found C, 68.47; H, 6.35.

2-(Trimethylsilyl)ethyl 3-*O*-Allyl-4-*O*-(2,3-di-*O*-benzoyl-6-*O*-benzyl-ß-D-glucopyranosyl)-2,6-di-*O*-benzyl-ß-D-galactopyranoside (12). Disaccharide **11** (1.5 g, 1.56 mmol), $NaCNBH_3$ (1.2 g, 20 mmol) and molecular sieves (3Å, 1.5 g) were suspended in dry tetrahydrofuran (60 mL). Saturated etheral HCl was added dropwise at room temperature until gas evolution ceased and TLC showed complete consumption of **11**. The mixture was neutralized with solid $NaHCO_3$, further diluted and filtered through Celite and the filtrate concentrated. The residue was purified by chromatography column using 1:4 ethyl acetate:hexanes as eluant to give **12** (1.1 g, 73%) as a syrup: $[\alpha]_D$ +38.7° (*c* 0.4, chloroform); ^1H NMR ($CDCl_3$) δ 8.08 - 7.09 (m, 25H, 5Ph), 5.84 (m, 1H, CH_2CHCH_2), 5.36 (m, 2H, H-2b and H-3b), 5.25 (bd, 1H, J=17.2 Hz, CH_2CH), 5.13 (bd, 1H, J=10.5 Hz, CH_2CH), 5.02 (bd, 1H, J=7.2 Hz, H-1b), 4.55 - 4.74 (m, 4H, $2CH_2Ph$), 4.33 (d, 1H, J=10.8 Hz, CH_2Ph), 4.21 (d, 1H, J=7.6 Hz, H-1c), 4.15 (dd, 1H, J=5.2 and 12.9 Hz, $CHCH_2O$), 4.10 (m, 2H, $CHCH_2O$, and H-4c), 3.93 (m, 3H, H-4b, H-6b and OCH_2CH_2), 3.86 (m, 1H, H-6c), 3.78 (bd, 1H, H-6b'), 3.72 (m, 2H, CH_2Ph and H-6c'), 3.65 (m, 1H, H-5b), 3.53 (m, 2H, H-5c and OCH_2CH_2), 3.38 (d, 1H, J=3.2 Hz, OH-4b), 3.31 (dd, 1H, J=9.5 and 2.5 Hz, H-3c), 3.22 (bd, 1H, J=7.8 Hz, H-2c), 0.88 (m, 2H, CH_2Si), -0.01 (s, 9H, $(CH_3)_3Si$), ^{13}C NMR ($CDCl_3$) δ 101.43 (J=166.2 Hz, C-H-1b), 103.12 (J=160.7 Hz, C-H-1c).

Anal. Calcd for $C_{55}H_{64}O_{13}Si$ (961.20): C, 68.72; H, 6.71. Found C, 68.38; H, 6.68.

2-(Trimethylsilyl)ethyl 4-*O*-[(4-*O*-Acetyl-2,3-di-*O*-benzyl α-(13) and ß-L-rhamnopyranosyl)-2,3-di-*O*-benzoyl-6-*O*-benzyl-ß-D-glucopyranosyl]-3-*O*-allyl-2,6-di-*O*-benzyl-ß-D-galactopyranoside (14). 4-*O*-Acetyl-2,3-di-*O*-benzyl-α-L-rhamnopyranose **5** (1.2 g, 3.1 mmol) was dissolved in dichloromethane (50 mL), containing *N,N'*-dimethylformamide (240 μL, 3.0 mmol). While the solution was stirred under nitrogen, oxalyl bromide (880 μL, 9.0 mmol) was added dropwise by syringe. After stirring at room temperature for 4 h the solution was concentrated, and the solid residue suspended in 1:1 ethyl acetate:hexanes and filtered through freshly baked silica gel. The filtrate was concentrated and reconcentrated twice with toluene, then the crude rhamnosyl bromide **6**

was dissolved in toluene and used as such in the glycosylation reaction below. A suspension of **12** (0.92 g, 0.95 mmol) and freshly activated molecular sieves (4Å, 10 g) in dry dichloromethane (100 mL) was stirred under an argon atmosphere for 2 h, before silver silicate (2 g) was added. This mixture was further stirred for 15 min, then the suspension chilled to 0 °C. Rhamnosyl bromide **6** (1.2 g, 3.1 mmol) in toluene (30 mL) was added dropwise to the chilled suspension. The reaction was allowed to come to room temperature overnight. More dichloromethane was added and suspension filtered through Celite. The filtrate was concentrated and the residue purified by chromatography using 9:1 toluene:ethyl acetate as eluant to obtain **13** (437 mg, 34%) and **14** (0.445 mg, 35%) as light syrups: **13** $[\alpha]_D$ +2.6° (*c* 0.47, chloroform); ^{1}H NMR ($CDCl_3$) δ 8.05 - 6.95 (m, 35H, 7Ph), 5.89 (m, 1H, $CH_2CH_2CH_2$), 5.63 (t, 1H, J=9.4 Hz, H-3b), 5.35 (t, 1H, J=9.4 Hz, H-2b), 5.30 (bd, 1H, J=17.0 Hz, CH_2CHCH_2), 5.19 (bd, 1H, J=10.8 Hz, CH_2CHCH_2), 5.07 (d, 1H, J=7.8 Hz, H-1b), 4.98 (bt, 1H, H-4a), 4.92 (s, 1H, H-1a), 4.61 - 4.30 (m, 9H, CH_2Ph), 4.19 (d, 1H, J=7.3 Hz, H-1c), 4.16 - 4.04 (m, 4H, $CHCH_2O$, H-4b and H-4c), 3.91 (m, 1H, OCH_2CH_2), 3.85 (m, 1H, H-6b), 3.69 (m, 2H, H-6c and CH_2Ph), 3.59 (m, 3H, H-2a, H-3a and H-6c'), 3.51-3.44 (m, 5H, OCH_2CH_2, H-5a, H-5b, H-5c, H-6b'), 3.26 (m, 1H, H-3c), 3.19 (t, 1H, J=8.3 Hz, H-2c), 1.98 (s, 3H, OAc), 1.00 (m, 2H, CH_2Si), 0.71 (d, 3H, J=6.1 Hz, H-6a), 0.01 (s, 9H, $(CH_3)_3Si$); ^{13}C NMR ($CDCl_3$) δ 99.0 (J=173.5, CH-1a), 101.5 (J=163.6, CH-1b), 103.1 (J=159.4, CH-1c).

Anal. Calcd for $C_{77}H_{88}O_{18}Si$(1329.64): C, 69.55; H, 6.67. Found C, 69.63; H, 6.59.

14 $[\alpha]_D$ +44.6° (*c* 0.42, chloroform); ^{1}H NMR ($CDCl_3$) δ 8.15-6.88 (m, 35H, 7Ph), 5.91 (m, 1H, CH_2CHCH_2), 5.69 (t, 1H, J=9.5 Hz, H-3b), 5.37 (m, 2H, H-2b and CH_2CHCH_2), 5.21 (d, 1H, J=10.5 Hz, CH_2CHCH_2), 5.10 (d, 1H, J=7.7 Hz, H-1b), 4.98 (m, 1H, H-4a), 4.79 (d, 1H, J=12.2 Hz, CH_2Ph), 4.62 (d, 1H, J=12.3 Hz, CH_2Ph), 4.54 - 4.45 (m, 5H, CH_2Ph), 4.40 (s, 1H, H-1a), 4.34 (d, 1H, J=10.8 Hz, CH_2Ph), 4.21 (d, 1H, J=7.4 Hz, H-1c), 4.12 - 3.88 (m, 8H, CH_2CHCH_2O, H-4b, H-4c, OCH_2CH_2, H-6b, H-6c, CH_2Ph), 3.76-3.71 (m, 3H, CH_2Ph, H-6b', H-6c'), 3.67 (m, 1H, H-5b), 3.53 - 3.45 (m, 3H, OCH_2CH_2, H-2a and H-5c), 3.28 (m, 1H, H-3c), 3.23 (t, 1H, J=8.4 Hz, H-2c), 3.18 (m, 1H, H-5a), 2.83 (bd, 1H, H-3a), 1.91 (s, 3H, OAc), 1.13 (d, 3H, J=5.8 Hz, H-6a), 0.93 (m, 2H, CH_2Si), -0.03 (s, 9H, $(CH_3)_3Si$); ^{13}C NMR ($CDCl_3$) δ 101.28 (J=165.6 Hz, C-H-1b), 102.59 (J=155.9 Hz, C-H-1a), 103.09 (J=157.6 Hz, C-H-1c).

Anal. Calcd for $C_{77}H_{88}O_{18}Si$(1329.64): C, 69.55; H, 6.67. Found C, 69.84; H, 6.81.

2-(Trimethylsilyl)ethyl 4-*O*-[(4-*O*-acetyl-2,3-di-*O*-benzyl-ß-L-rhamnopyranosyl)-2,3-di-*O*-benzoyl-6-*O*-benzyl-ß-D-glucopyranosyl]-2,6-di-*O*-benzyl ß-D-galactopyranoside (15). To a solution of **14** (310 mg, 0.23 mmol) in EtOH/toluene/H_2O 8:3:1 (10 mL) was added DABCO (26 mg, 0.23 mmol), and $(Ph_3)_3RhCl$ (20 mg) and the suspension was refluxed for 4 h. The mixture was cooled and filtered through a plug of Celite and a short column, using 1:1 ethyl acetate:hexanes as eluant. The filtrate was concentrated and the residue dissolved in dichloromethane (10 mL). Molecular sieves (4Å, 300 mg) were added and the suspension chilled to 0 °C before Me_3SiBr (91 μL, 0.69 mmol) was added. The mixture was stirred at 0 °C for 2 h, then overnight at 4 °C, and filtered through Celite. The filtrate was washed with cold $NaHCO_3$, H_2O and brine, dried over $MgSO_4$, filtered and concentrated. The residue was purified by chromatography using hexanes:ethyl acetate 3:1 as eluant to afford a glassy solid **15** (212 mg, 70%): $[\alpha]_D$ +26.3° (*c* 1.06, dichloromethane); ^1H NMR ($CDCl_3$) δ 7.97-6.82 (m, 35H, 7Ph), 5.65 (t, 1H, J=9.7 Hz, H-3b), 5.32 (t, 1H, J=8.1 Hz, H-2b), 5.05 (d, 1H, J=8.0 Hz, H-1b), 4.91 (t, 1H, J=9.7 Hz, H-4a), 4.70 (d, 1H, J=12.3 Hz, CH_2Ph), 4.53 (d, 1H, J=12.3 Hz, CH_2Ph), 4.48-4.37 (m, 5H, CH_2Ph), 4.32 (s, 1H, H-1a), 4.14 (d, 1H, J=7.7 Hz, H-1c), 4.00 (bs, 1H, H-4c), 3.95 (t, 1H, J=9.4 Hz, H-4b), 3.88 (m, 1H, CH_2CH_2Si), 3.84-3.80 (m, 3H, H-6b, H-6c, and CH_2Ph), 3.71-3.65 (m, 2H, H-6b' and H-6c'), 3.63 (m, 1H, H-5b), 3.53-3.40 (m, 6H, H-5c, H-3c, $2CH_2$Ph, H-2a and CH_2CH_2Si), 3.08 (dt, 1H, J=5.9 and 6.1 Hz, H-5a), 3.02 (dd, 1H, J=7.9 and 9.6 Hz, H-2c), 2.73 (dd, 1H, J=2.9 and 9.8 Hz, H-3a), 2.22 (d, 1H, J=4.0 Hz, OH-3a), 1.82 (s, 3H, OAc), 1.05 (d, 3H, J=6.1 Hz, H-6a), 0.93-0.79 (m, 2H, CH_2CH_2Si), -0.01 (s, 9H, $(CH_3)_3Si$); ^{13}C NMR ($CDCl_3$) δ 101.51 (J=165.8 Hz, CH-1b), 102.52 (J=157.4 Hz, CH-1a), 102.90 (J=159.1 Hz, CH-1c).

Anal. Calcd for $C_{74}H_{84}O_{18}Si$(1289.57): C, 68.92; H, 6.56. Found C, 68.95; H, 6.52.

Ethyl 4-*O*-(4-*O*-Acetyl-2,3-di-*O*-benzyl-α-(17) and ß-L-rhamnopyranosyl)-2,3-di-*O*-benzoyl-6-*O*-benzyl-1-thio-ß-D-glucopyranoside(18). Ethyl 2,3-di-*O*-benzoyl-6-*O*-benzyl-1-thio-ß-D-glucopyranoside[19] **16** (520 mg, 1 mmol) was dissolved in dry dichloromethane (15 mL), and silver silicate (1 g) and activated molecular sieves (4Å, 1 g) were added. This suspension was stirred under a nitrogen atmosphere for 1 h, then chilled to 0 °C. Then rhamnosyl bromide **6** (prepared as above, 1.55 mmol) was added dropwise by syringe, the mixture stirred for 1 h at 0 °C, then for 2 h at room temperature before all of the bromide was consumed. Triethylamine (1 mL) was added to terminate

the reaction. The suspension was diluted with more dichloromethane, and filtered through Celite. The filtrates were washed with 10% sodium hydrogen carbonate and water, dried ($MgSO_4$), filtered and concentrated. The residue was purified by chromatography using toluene:ethyl acetate 95:5 as eluant to obtain α isomer **17** (240 mg, 27%), and ß isomer **18** (289 mg, 33%) as viscous syrups: **17** $[\alpha]_D$ -2.62° (*c* 1.4, chloroform); ^1H NMR ($CDCl_3$) δ 7.95 - 6.80 (m, 25 H, 5Ph), 5.60 (t, 1H, J=9.3 Hz, H-3b), 5.37 (t, 1H, J=9.5 Hz, H-2b), 4.98 (t, 1H, J=9.5 Hz, H-4a), 4.93 (s, 1H, H-1a), 4.63-4.39 (m, 7H, H-1b and 6 CH_2Ph), 4.13 (t, 1H, J=9.3 Hz, H-4b), 3.67-3.42 (m, 6H, H-2a, H-3a, H-5a, H-5b, H-6b and H-6b'), 2.75 (m, 2H, CH_3CH_2S), 1.80 (s, 3H, OAc), 1.24 (t, 3H, CH_3CH_2S), 0.60 (d, 3H, J=6.1 Hz, H-6a); ^{13}C NMR ($CDCl_3$) δ 99.14 J=172.0 Hz, C-H-1a), 83.40 (J=154.0, C-H-1b).

Anal. Calcd for $C_{51}H_{54}O_{12}S$(891.05): C, 68.72; H, 6.11. Found C, 68.41; H, 6.01.

18 $[\alpha]_D$ +68.6° (*c* 0.9, chloroform); ^1H NMR ($CDCl_3$) δ 7.95-6.80 (m, 25H, 5Ph), 5.71 (t, 1H, J=9.5 Hz, H-3b), 5.38 (t, 1H, J=9.8 Hz, H-2b), 4.98 (t, 1H, J=9.8 Hz, H-4a), 4.77 (d, 1H, J=12.2 Hz, CH_2Ph), 4.72 (d, 1H, J=10.1 Hz, H-1b), 4.60-4.50 (m, 3H, 3 CH_2Ph), 4.38 (s, 1H, H-1a), 4.02-3.96 (m, 2H, H-6b and H-4b), 3.90 (d, 1H, J=12.3 Hz, CH_2Ph), 3.78-3.72 (m, 2H, H-6b' and H-5b), 3.60 (d, 1H, J=12.4 Hz, CH_2Ph), 3.50 (d, 1H, J=2.7 Hz, H-2a), 3.15 (dt, 1H, J=6.3 and 6.1 Hz, H-5a), 2.81 (dd, 1H, J=9.9 and 2.9 Hz, H-3a), 2.77 (m, 2H, CH_3CH_2S), 1.90 (s, 3H, OAc), 1.26 (t, 3H, J=7.4 Hz, CH_3CH_2S), 1.13 (d, 3H, J=6.2 Hz, H-6a); ^{13}C NMR ($CDCl_3$) δ 102.84 (J=155.6 Hz, C-H-1a), 83.34 (J=154.7 Hz, C-H-1b).

Anal. Calcd for $C_{51}H_{54}O_{12}S$(891.05): C, 68.72; H, 6.11. Found C, 68.40; H, 6.03.

2-(Trimethylsilyl)ethyl 6-*O*-Benzyl-ß-D-galactopyranoside (20). 2-(Trimethylsilyl)ethyl 2,3-di-*O*-benzoyl-6-*O*-benzyl-ß-D-galactopyranoside[17] (4.2 g, 7.25 mmol) was dissolved in dry methanol (150 mL), and 1M sodium methoxide in methanol (1 mL) was added. The mixture was stirred at room temperature overnight, then neutralized with REXYN 101 (H^+) ion exchange resin and concentrated. Only one sugar component was observed by TLC of the reaction mixture. The residue was purified by chromatography using MPLC with ethyl acetate:hexanes 70:30 as eluant to obtain a white amorphous material **20** (1.77 g, 66%): $[\alpha]_D$ -31.3° (*c* 0.68, chloroform); ^1H NMR ($CDCl_3$) δ 7.30-7.20 (m, 5H, Ph), 4.57 (s, 2H, CH_2Ph), 4.22 (d, 1H, J=7.3 Hz, H-1), 4.01 (m, 2H, CH_2CH_2O, and H-4), 3.75 (m, 2H, H-6 and H-6'), 3.63-3.55 (m, 4H, H-2, H-3, H-5, and CH_2CH_2O), 2.60 (d, 1H, J=3.8 Hz, OH-4), 2.57 (d, 1H, J=5.7 Hz, OH-3), 2.37 (d, 1H, 1.9 Hz, OH-2), 1.05-0.94 (m, 2H, $SiCH_2CH_2$), -0.01 (s, 9H, Si $(CH_3)_3$).

Anal. Calcd for $C_{18}H_{30}O_6Si$(370.52): C, 58.35; H, 8.16. Found C, 58.21; H, 8.18.

2-(Trimethylsilyl)ethyl *O*-(Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-6-*O*-benzyl-ß-D-galactopyranoside (21). To a stirred mixture of 2-(trimethylsilyl)ethyl 6-*O*-benzyl-ß-D-galactopyranoside **20** (333 mg, 0.9 mmol), and phenyl (methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-2-thio-D-glycero-α-D-galacto-2-nonulopyranoside)onate **19** (876 mg, 1.5 mmol), and freshly baked molecular sieves (3Å, 1.5 g), in 10:1 acetonitrile-dichloromethane (42 mL) at -40 °C, powdered NIS was added (672 mg, 3 mmol), followed by TfOH (0.3 mmol). This mixture was stirred at -40 °C for 6 h, then at +4 °C overnight. Triethylamine was used to neutralize the reaction. A precipitate was filtered off through a plug of Celite and washed with more dichloromethane. The filtrate and washings were combined, successively washed with 5% $Na_2S_2O_3$, saturated $NaHCO_3$, water, dried ($MgSO_4$) and concentrated. The residue after chromatography using 3:1 ethyl acetate:hexanes as eluant, afforded **21** (505 mg, 66%) as a foamy solid: $[\alpha]_D$ -119.0° (*c* 0.75, chloroform); ^1H NMR ($CDCl_3$) δ 7.30-7.21 (m, 5H, Ph), 5.37 (m, 1H, H-8Nu), 5.25 (dd, 1H, J=1.6 and 8.9 Hz, H-7Nu), 5.07 (d, 1H, J=9.7 Hz, NH), 4.87 (m, 1H, H-4Nu), 4.49 (s, 2H, CH_2Ph), 4.34 (d, 1H, J=7.6 Hz, H-1c), 4.21 (dd, 1H, J=2.6 and 12.5 Hz, H-9Nu), 4.07-3.92 (m, 5H, H-9Nu', OCH_2CH_2, H-5Nu, H-6Nu, H-3c), 3.72-3.57 (m, 9H, OCH_3, OCH_2CH_2, H-2c, H-4c, H-5c, H-6c and H-6c'), 2.65 (dd, 1H, J=4.6 and 13.0 Hz, H-3Nu), 2.57 (bs, 1H, OH-4c), 2.39 (d, 1H, J=3.6 Hz, OH-2c), 2.04 (s, 3H, OAc), 2.02 (s, 3H, OAc), 1.96 (s, 6H, 2 OAc), 1.99 (t, 1H, J=12.8 Hz, H-3Nu'), 1.80 (s, 3H, NAc), 0.95 (m, 2H, CH_2CH_2Si), -0.06 (s, 9H, $Si(CH_3)_3$); ^{13}C NMR ($CDCl_3$); δ 168.3 *CO*OMe, 102.47, (J=159.4 Hz, C-1c).

Anal. Calcd for $C_{38}H_{57}NO_{18}Si$ (843.96): C, 54.08; H, 6.80; N, 1.66. Found C, 54.35; H, 6.74; N, 1.98.

2-(Trimethylsilyl)ethyl *O*-(4-*O*-Acetyl-2,3-di-*O*-benzyl-ß-L-rhamnopyranosyl)-(1→4)-*O*-(2,3-di-*O*-benzoyl-6-*O*-benzyl-ß-D-glucopyranosyl)-(1→4)-*O*-[(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)]-6-*O*-benzyl-ß-D-galactopyranoside (22) and 2-(Trimethylsilyl)ethyl *O*-(4-*O*-Acetyl-2,3-di-*O*-benzyl-ß-L-rhamnopyranosyl)-(1→4)-*O*-(2,3-di-*O*-benzoyl-6-*O*-benzyl-ß-D-glucopyranosyl)-(1→2)-*O*-[(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)]-6-*O*-benzyl-ß-D-galactopyranoside (23). A suspension of **18** (100 mg, 0.112 mmol), **21** (100 mg, 0.117 mmol) and activated molecular sieves (4Å, 300 mg) in dichloromethane (10 mL) was stirred at room temperature for 2 h under an argon

atmosphere, before NIS (63 mg, 0.28 mmol) was added. After the reaction mixture was stirred for 10 min, a solution of TfOH (0.35 mL in 10 mL of dichloromethane) was added 100 μL at a time and the reaction followed by TLC. A total of 300 μL was added before TLC showed total consumption of the thioglycoside **18**. Triethylamine (0.5 mL) was added to neutralize the reaction and after further dilution with dichloromethane (30 mL), some solids were filtered off through Celite. The filtrate was washed (2x water, 10% $Na_2S_2O_4$, $NaHCO_3$, brine), dried ($MgSO_4$), filtered and concentrated. The residue was purified by chromatography using 6:4 ethyl acetate-hexanes as eluant to give as viscous oils **22** (54 mg, 28%), and **23** (28 mg, 15%). **22** $[\alpha]_D$ +36.5° (*c* 0.48, chloroform); ^{1}H NMR ($CDCl_3$) δ 7.95-6.80 (m, 30H, 6Ph), 5.63 (t, 1H, J=9.6 Hz, H-3b), 5.37 (m, 1H, H-8Nu), 5.22 (bd, 1H, J=9.0 Hz, H-7Nu), 5.20 (t, 1H, J=8.9 Hz, H-2b), 5.07 (d, 1H, J=9.8 Hz, NH), 5.05 (d, 1H, J=7.9 Hz, H-1b), 4.95-4.89 (m, 2H, H-4a, and H-4Nu), 4.76 (d, 1H, J=12.2 Hz, *CH*$_2$Ph), 4.59 (d, 1H, J=12.2 Hz, *CH*$_2$Ph), 4.51 (s, 2H, *CH*$_2$Ph), 4.39 (s, 2H, *CH*$_2$Ph), 4.33 (s, 1H, H-1a), 4.30 (d, 1H, J=7.7 Hz, H-1c), 4.15 (dd, 1H, J=2.3 and 12.5 Hz, H-9Nu), 4.00 (dd, 1H, J=12.6 and 5.0 Hz, H-9Nu'), 3.98-3.52 (m, 18H, H-4b, H-5Nu, H-6Nu, H-3c, H-4c, H-5c, *CH*$_2$CH$_2$Si; *CH*$_2$Ph, OMe; H-6c, H-6c'; H-5b; H-6b; H-6b'), 3.47 (d, 1H, J=2.7 Hz, H-2a), 3.35 (t, 1H, J=8.7 Hz, H-2c), 3.12 (dt, 1H, J=6.1 and 6.3 Hz, H-5a), 2.79 (dd, 1H, J=2.8 and 9.7 Hz, H-3a), 2.66 (dd, 1H, J=4.5 and 13.1 Hz, H-3Nu), 2.21 (brs, 1H, OH-2c), 2.04 (s, 3H, OAc), 2.036 (s, 3H, OAc), 2.026 (s, 3H, OAc), 1.99 (s, 3H, OAc), 1.87 (s, 3H, OAc), 1.85 (s, 3H, NAc), 1.81 (t, 1H, J=12.9 Hz, H-3Nu'), 1.09 (d, 3H, J=6.1 Hz, H-6a), 1.01-0.87 (m, 2H, CH$_2$*CH*$_2$Si), -0.01 (s, 9H, Si(CH$_3$)$_3$); ^{13}C NMR($CDCl_3$): δ 100.87 (J=163.9 Hz, C-H-1b); 102.45 (J=158.0 Hz, C-H-1c); 102.90 (J=161.1 Hz, C-H-1a).

Anal. Calcd for $C_{87}H_{105}NO_{30}Si$(1672.87): C, 62.46; H, 6.32; N, 0.84. Found C, 62.38; H, 6.42; N, 0.71.

23 $[\alpha]_D$ +21.8° (*c* 0.52, chloroform); ^{1}H NMR ($CDCl_3$) δ 7.92-7.15 (m, 30H, 6Ph), 5.58 (t, 1H, J=9.5 Hz, H-3b), 5.34 (m, 2H, H-8Nu, H-2b), 5.27 (d, 1H, J=7.9 Hz, H-1b), 5.21 (bd, 1H, J=9.0 Hz, H-7Nu), 5.05 (d, 1H, J=9.6 Hz, NH), 4.97 (t, 1H, J =9.6 Hz, H-4a), 4.90 (m, 1H, H-4Nu), 4.75 (d, 1H, J=12.4 Hz, *CH*$_2$Ph), 4.65 (d, 1H, J=12.4 Hz, *CH*$_2$Ph), 4.57-4.52 (m, 9H, *CH*$_2$Ph, H-1c), 4.41 (bs, 1H, H-1a), 4.16 (dd, 1H, J=2.5 and 12.4 Hz, H-9Nu), 4.12 (t, 1H, J=9.5 Hz, H-4b), 4.06 (dd, 1H, J=3.1 and 12.4 Hz, H-9Nu'), 4.03-3.59 (m, 13H, H-3c, *CH*$_2$Ph, H-5Nu, H-6Nu, H-5c, H-6c, H-6c', *CH*$_2$CH$_2$Si, *CH*$_2$Ph, H-6b, H-6b', H-5b, *CH*$_2$CH$_2$Si), 3.50 (d, 1H, J=2.8 Hz, H-2a), 3.43 (s, 3H, OMe), 3.15 (m, 1H, H-5a), 2.84 (dd, 1H, J=3.0 and 9.9 Hz, H-3a), 2.36 (bs, 1H, OH-

4c), 2.19-2.16 (m, 4H, H-3Nu and OAc), 2.02 (s, 3H, OAc), 2.00 (s, 3H, OAc), 1.95 (s, 3H, OAc), 1.89 (s, 3H, OAc), 1.84 (s, 3H, NAc), 1.82 (t, 1H, J=12.3 Hz, H-3Nu'), 1.11 (d, 3H, J=6.1 Hz, H-6a), 1.04-0.96 (m, 2H, CH_2CH_2Si), -0.01 (s, 9H, $Si(CH_3)_3$); ^{13}C NMR ($CDCl_3$) δ 102.82 (J=157.4 Hz, C-H-1a), 102.36 (J=158.9 Hz, C-H-1c), 100.10 (J=167.8 Hz C-H-1b);

Anal. Calcd for $C_{87}H_{105}NO_{30}Si$(1672.87): C, 62.46; H, 6.32; N, 0.84. C, 62.88; H, 6.31; N, 0.72.

2-(Trimethylsilyl)ethyl *O*-(4-*O*-Acetyl-ß-L-rhamnopyranosyl)-(1→4)-*O*-(2,3-di-*O*-benzoyl-ß-D-glucopyranosyl)-(1→4)-*O*-[(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)]-ß-D-galactopyranoside (24). Tetrasaccharide **22** (280 mg, 0.166 mmol), in glacial acetic acid (20 mL) was hydrogenated over 10% Pd/C (200 mg). After filtration through Celite and evaporation of the filtrates the residue was purified by chromatography using 95:5 ethyl acetate:ethanol as an eluant to yield **24** (158 mg, 72%) as a viscous oil: $[\alpha]_D$ +38.5° (*c* 0.8, chloroform); ^1H NMR ($CDCl_3$) δ 7.94 (bd, 2H, J=7.5 Hz, Bz_{ortho}), 7.88 (bd, 2H, J=7.5 Hz, Bz_{ortho}), 7.57-7.32 (m, 6H, 2Ph), 5.70 (bd, 1H, J=8.7 Hz, NH), 5.63 (t, 1H, J=9.6 Hz, H-3b), 5.40 (m, 1H, H-8Nu), 5.27 (m, 2H, H-2b and H-7Nu), 5.05 (d, 1H, J=8.0 Hz, H-1b), 4.98 (m, 1H, H-4Nu), 4.72 (t, 1H, J=9.6 Hz, H-4a), 4.43 (s, 1H, H-1a), 4.26 (d, 1H, J=7.7 Hz, H-1c), 4.22 (dd, 1H, J=12.5 and 2.7 Hz, H-9Nu), 4.03 (dd, 1H, J=12.4 and 5.9 Hz, H-9Nu'), 4.01-3.89 (m, 11H, H-5Nu, H-6Nu, H-4b, H-3c, H-4c, OMe, CH_2CH_2Si, H-6b and H-6c), 3.72-3.69 (m, 3H, H-6c', H-5c, and H-2a), 3.64 (m, 1H, H-6b'), 3.53 (m, 2H, CH_2CH_2Si and OH-6), 3.46 (m, 1H, H-5b), 3.36 (t, 1H, J=8.7 Hz, H-2c), 3.29 (m, 1H, H-5a), 3.20 (m, 1H, OH-6'), 3.12 (m, 1H, H-3a), 2.91 (d, 1H, J=10.2 Hz, OH-3a), 2.71 (bs, 1H, OH-2a), 2.64 (dd, 1H, J=13.0 and 4.5 Hz, H-3Nu), 2.23 (s, 1H, OH-2c), 2.10 (s, 3H, OAc), 2.08 (s, 3H, OAc), 2.07 (s, 3H, OAc), 2.06 (s, 3H, OAc), 2.05 (s, 3H, OAc), 1.86 (m, 4H, NAc and H-3Nu'), 1.23 (d, 3H, J=6.1 Hz, H-6a), 1.02-0.84 (m, 2H, CH_2CH_2Si), -0.01 (s, 9H, $Si(CH_3)_3$); ^{13}C NMR ($CDCl_3$) δ 102.55 (J=161.0 Hz, C-H-1c), 101.34 (J=167.0 Hz, C-H-1b), 99.88 (J=161.0 Hz, C-H-1a).

Anal. Calcd for $C_{59}H_{81}NO_{30}Si$(1312.37): C, 53.99; H, 6.22; N, 1.06. Found C, 53.93; H, 6.16; N, 1.03.

2-(Trimethylsilyl)ethyl *O*-(4-*O*-Acetyl-2,3-di-*O*-benzoyl-ß-L-rhamnopyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-benzoyl-ß-D-glucopyranosyl)-(1→4)-*O*-[(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-

(2→3)]-2,6-di-*O*-benzoyl-ß-D-galactopyranoside (25). To a solution of **24** (148 mg, 0.113 mmol) in pyridine (5 mL) at 0 °C under argon, was added dropwise benzoyl chloride (0.26 mL, 2.2 mmol). This mixture was stirred at 0 °C for 4 h, then allowed to come to room temperature overnight. A few drops of methanol were added to terminate the reaction, then the reaction mixture was concentrated and reconcentrated twice with toluene. The residue was purified by chromatography using 1:1 ethyl acetate:hexanes to obtain **25** (108 mg, 52%) as a viscous oil; $[\alpha]_D$ +51.1° (*c* 0.6, chloroform); ^{1}H NMR ($CDCl_3$) δ 8.09-7.25 (m, 35H, 7Ph), 5.65 (t, 1H, J=9.6 Hz, H-3b), 5.56 (d, 1H, J=3.6 Hz, H-2a), 5.40-5.35 (m, 2H, H-2b and H-8Nu), 5.16-5.12 (m, 3H, H-2c, H-4a, H-7Nu), 5.08 (d, 1H, J=7.8 Hz, H-1b), 4.95 (d, 1H, J=10.2 Hz, NH), 4.91 (dd, 1H, J=3.3 and 10.1 Hz, H-3a), 4.82-4.79 (m, H-1a, and H-4Nu), 4.64 (dd, 1H, J=5.2 and 12.2 Hz, H-6c), 4.58-4.54 (m, 2H, H-1c and H-6b), 4.44-4.40 (m, 2H, H-6b' and H-6c'), 4.35-4.28 (m, 2H, H-4b and H-3c), 4.03 (dd, 1H, J=2.4 and 12.3 Hz, H-9Nu), 3.91-3.88 (m, 2H, H-4c, and H-9Nu'), 3.86-3.78 (m, 4H, H-5b, H-5c, H-5Nu and CH_2CH_2Si), 3.67 (s, 3H, OMe), 3.63 (dd, 1H, J=10.6 and 2.2 Hz, H-6Nu), 3.46 (m, 1H, CH_2CH_2Si), 3.37 (m, 1H, H-5a), 2.28 (dd, 1H, J=4.7 and 13.0 Hz, H-3Nu), 1.99 (s, 3H, OAc), 1.94 (s, 3H, OAc), 1.89 (s, 3H, OAc), 1.83 (s, 3H, OAc), 1.79 (s, 3H, OAc), 1.76 (t, 1H, J=12.4 Hz, H-3Nu') 1.66 (s, 3H, NAc), 1.03 (d, 3H, J=6.1 Hz, H-6a), 0.78-0.66 (m, 2H, OCH_2CH_2), -0.01 (s, 9H, $Si(CH_3)_3$); ^{13}C (NMR), ($CDCl_3$) δ 100.89 (J=166.7 Hz, C-H-1b), 100.74, (J=161.0 Hz, C-H-1c), 98.10 (J=160.0 Hz, C-H-1a).

Anal. Calcd for $C_{94}H_{101}NO_{35}Si$(1832.92): C, 61.59; H, 5.54; N, 0.76. Found C, 61.60; H, 5.55; N, 0.94.

2-(Trimethylsilyl)ethyl O-(ß-L-Rhamnopyranosyl)-(1→4)-O-(ß-D-glucopyranosyl)-(1→4)-*O*-[(5-acetamido-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonic acid)-(2→3)]-ß-D-galactopyranoside (1a). To a solution of **25** (25 mg, 0.0136 mmol) in methanol (4 mL) was added 1M sodium methoxide (1 mL). This solution was stirred at room temperature for 24 h, then chilled to 0 °C and water (0.5 mL) was added and mixture further stirred for 24 h at 4 °C. To complete the reaction, 2 drops of 1M sodium hydroxide were added and 24 h later the reaction was terminated. More methanol was added, and mixture neutralized with REXYN 101(H^+) ion exchange resin, filtered and the filtrate concentrated. The residue was placed on a Bio-Gel P-2 column and eluted with water. The fractions were monitored by RI detection. Freeze drying of the pure fractions gave **1a** (7.8 mg, 65% yield) as its sodium salt: $[\alpha]_D$ +10.1° (*c* 0.25, water); ^{1}H NMR ($CDCl_3$) δ 4.86 (s, 1H, H-1a), 4.82 (d, 1H, J=8.0 Hz, H-1b), 4.51 (d, 1H, J=8.0 Hz,

H-1c), 4.17 (bd, 1H, J=8.9 Hz, H-3c), 4.13 (bs, 1H, H-4c), 4.08 (d, 1H, J=3.1 Hz, H-2a), 4.04 (m, 1H, CH_2CH_2Si), 3.92 (bd, 1H, J=11.4 Hz, H-6b), 3.85 (m, H-9Nu), 3.83 (m, H-5Nu), 3.82 (m, H-6b'), 3.80 (m, H-8Nu), 3.76 (m, H-6c), 3.76 (m, CH_2CH_2Si), 3.71 (m, H-5c), 3.70 (m, H-6c'), 3.70 (m, H-4Nu), 3.67 (m, H-3b), 3.63 (m, H-2c), 3.63 (m, H-4b), 3.63 (m, H-9Nu'), 3.60 (m, H-7Nu), 3.59 (m, H-6Nu), 3.59 (m, H-3a), 3.52 (m, 1H, H-5b), 3.37 (m, 2H, H-4a and H-5a), 3.30 (t, 1H, J 8.6 Hz, H-2b), 2.71 (dd, 1H, J= 12.2 and 4.2 Hz, H-3Nu), 2.03 (s 3H, NAc), 1.84 (bt, 1H, J=12.3 Hz, H-3Nu'), 1.31 (d, 3H, J=5.2 Hz, H-6a), 1.07-0.96 (m, 2H, CH_2CH_2Si), -0.01 (s, 9H, $Si(CH_3)_3$); ^{13}C NMR (D_2O): δ 175.88 (N-C=O), 174.33 (C-1Nu), 103.51 (J=165.6 Hz, C-H-1b), 102.60 (J=162.1 Hz, C-H-1c), 101.44 (J=161.8 Hz, C-H-1a), 77.48 (C-4b), 76.36 (C-3b), 76.26 (C-3c), 75.73 (C-4c), 74.98 (C-5c), 74.92 (C-5b), 74.19 (C-2b), 73.74 (C-6Nu), 73.44 (C-3a), 73.02 (C-5a), 72.89 (C-4a), 72.80 (C-8Nu), 71.47 (C-2a), 70.19 (C-2c), 69.30 (C-4Nu), 69.03 (OCH_2CH_2Si), 68.91 (C-7Nu), 63.51 (C-9Nu), 61.80 (C-6b), 61.44 (C-6c), 52.51 (C-5Nu), 39.35 (C-3Nu), 22.87 ($CH_3C=O(N)$), 18.40 (OCH_2CH_2Si), 17.48 (C-6a), -1.69 ($Si(CH_3)_3$); MS - Electrospray -ve ion. Calcd for $C_{34}H_{61}NO_{23}Si$ (879.944) obs. 878.4 (M-1).

***O*-(4-*O*-Acetyl-2,3-di-*O*-benzoyl-ß-L-rhamnopyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-benzoyl-ß-D-glucopyranosyl)-(1→4)-*O*-[(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)]-2,6-di-*O*-benzoyl-D-galactopyranosyl Trichloroacetimidate (27).** A solution of **25** (68 mg, 0.037 mmol) in dry dichloromethane (0.9 mL) was cooled to 0 °C under an argon atmosphere and trifluoroacetic acid (0.1 mL) was added. TLC indicated that the reaction was complete after it had been stirred for 1 h at 0 °C. Ethyl acetate (1 mL) was added, and the reaction concentrated, then coconcentrated twice more with ethyl acetate. Purification by column chromatography of the residue with ethyl acetate as an eluant gave *O*-(4-*O*-acetyl-2,3-di-*O*-benzoyl-ß-L-rhamnopyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-benzoyl-ß-D-glucopyranosyl)-(1→4)-*O*-[(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2→3)]-2,6-di-*O*-benzoyl-D-galactopyranose **26** (58 mg, 91 %) as an amorphous solid. To a solution of **26** (55 mg, 0.031 mmol) in dichloromethane (1 mL) and trichloroacetonitrile (0.2 mL) was added 1,8-diazabicyclo [5.4.0] undec-7-ene (DBU, 5 mg) at −5 °C, and the mixture stirred for 2 h at 0 °C and then concentrated. Purification of the residue by column chromatography using 7:3 ethyl acetate:hexanes as eluant gave **27** (45 mg, 75%) as an amorphous solid. ^1H NMR ($CDCl_3$) δ 8.32 (s 1H, C=NH), 8.07-7.05 (m, 35H, 7 Ph), 5.62 (d, 1H, J=3.3 Hz, H-1c), 5.59 (m, 2H, H-3b

and H-2a), 5.41 (dd, 1H, J=7.9, 8.1 and 9.7 Hz, H-2b), 5.23 (m, 2H, H-7Nu and H-8Nu), 5.16-5.10 (m, 4H, H-2c, H-1b, H-4a, and NH), 5.00 (m, 1H, H-4Nu), 4.59 (dd, 1H, J=3.1 and 9.9 Hz, H-3a), 4.82 (s 1H, H-1a), 4.80 (dd, 1H, J=2.7, 2.4 and 10.9 Hz, H-3c), 4.67 (dd, 1H, J=4.3 and 11.8 Hz, H-6c), 4.59 (dd, 1H, J=3.0, 2.8 and 12.0 Hz, H-6b), 4.48-4.36 (m, 5H, H-6c', H-6b', H-5c, H-4b and H-5b), 4.05-3.78 (m, 8H, H-5b, H-5Nu, H-6Nu, H-9Nu, O*CH*$_3$, H-9Nu'), 3.36 (m, 1H, H-5a), 2.63 (dd, 1H, J =.8 and 13.3 Hz, H-3Nu), 2.07 (s 3H, OAc), 1.97 (m, 4H, H-3Nu' and OAc), 1.86 (s 3H, OAc), 1.82 (bs, 9H, 2OAc and NAc), 1.01 (d, 3H, J=6.0 Hz, H-6a); ^{13}C NMR ($CDCl_3$) δ 94.17 (J=182.6 Hz, C-H-1c), 97.97 (J=158.0 Hz, C-H-1a), 101.14 (J=161.5 Hz, C-H-1b).

3-Azidopropyl *O*-(*4-O*-Acetyl-2,3-di-*O*-benzoyl-ß-L-rhamnopyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-benzoyl-ß-D-glucopyranosyl)-(1→4)-*O*-[(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-nonulopyranosylonate-(2→3)]-2,6-di-*O*-benzoyl-ß-D-galactopyranoside (28). To a solution of **27** (45 mg, 0.024 mmol) and 3-azidopropan-1-ol[36] (6 mg, 0.06 mmol), in dry dichloromethane (3 mL) were added molecular sieves (4Å, 130 mg) and the mixture was stirred at room temperature for 1.5 h, then cooled to 0 °C under an argon atmosphere. Boron trifluoride etherate (35 μL) was added and after the mixture had been stirred for 1 ½ h at 0 °C, the reaction was complete. Triethylamine (0.1 mL) was added, and the suspension was further diluted with dichloromethane, then filtered through Celite. The filtrate was concentrated and the syrupy residue purified by chromatography using 75:25 ethyl acetate:hexanes as an eluant to obtain **28** (35 mg, 80%) as a thick syrup: ^{1}H NMR ($CDCl_3$) δ 8.03-7.25 (m, 30H, 6Ph), 5.65 (t, 1H, J=9.6 Hz, H-3b), 5.56 (d, 1H, J=2.9 Hz, H-2a), 5.41-5.36 (m, 2H, H-2b and H-8Nu), 5.17-5.10 (m, 3H, H-2c, H-4a and H-7Nu), 5.07 (d, 1H, J=7.7 Hz, H-1b), 4.96 (d, 1H, J=10.2 Hz, NH), 4.92 (dd, 1H, J=10.0 and 3.2 Hz, H-3a), 4.80 (m, 2H, H-1a and H-4Nu), 4.63 (dd, 1H, J=11.6 and 5.2 Hz, H-6c), 4.56 (m, 2H, H-1c and H-6b), 4.42 (m, 2H, H-6b' and H-6c'), 4.33 (m, 2H, H-3c and H-4b), 4.05 (dd, 1H, J=12.4 and 2.1 Hz, H-9Nu), 3.89 (m, 2H, H-4c and H-9Nu'), 3.84-3.74 (m, 4H, H-5Nu, H-5b, H-5c and *OCH*$_2$CH$_2$CH$_2$N), 3.67 (s 3H, OMe), 3.63 (dd, 1H, J=10.8 and 2.1, H-6Nu), 3.46 (m, 1H, *OCH*$_2$CH$_2$CH$_2$N$_3$), 3.37 (m, 1H, H-5a), 3.03 (m, 2H, *CH*$_2$N$_3$), 2.30 (dd, 1H, J=12.9 and 4.6 Hz, H-3Nu), 1.99 (s 3H, OAc), 1.94 (s 3H, OAc), 1.91 (s 3H, OAc), 1.83 (s 3H, OAc), 1.79 (s 3H, OAc), 1.72 (t, 1H, J=12.6 Hz, H-3Nu'), 1.63 (s 3H, NAc), 1.56 (bs, 2H, CH$_2$*CH*$_2$CH$_2$), 1.04 (d, 3H, J=6.1 Hz, H-6a); ^{13}C NMR ($CDCl_3$) δ 101.30, (J=161.1 Hz, C-H-1c), 100.85, (J=165.8 Hz, C-H-1b), 98.10, (J=157.7 Hz, C-H-1a).

3-Azidopropyl *O*-(ß-L-Rhamnopyranosyl)-(1→4)-*O*-(ß-D-glucopyranosyl)-(1→4) -*O*-[(5-acetamido-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonic acid)-(2→3)]-ß-D-galactopyranoside (1b). To a solution of **28** (30 mg, 0.0165 mmol) in 3methanol (4 mL) was added 1M sodium methoxide in methanol (1 mL). This solution was stirred at room temperature overnight, then chilled to 0 °C and water (0.5 mL) was added followed by 2 drops of 1M sodium hydroxide. This solution was stirred at 4 °C for 24 h, further diluted with methanol and the reaction was neutralized with REXYN 101 (H^+) ion exchange resin, and concentrated. The residue was placed on a Bio-Gel P2 column and eluted with water. The fractions were monitored by RI detection. Freeze drying of the pure fractions gave **1b** (7.8 mg, 61%) as its sodium salt: $[\alpha]_D$ +15.5° (*c* 0.42, water); ^{1}H NMR (D_2O) δ 4.87 (s 1H, H-1a), 4.82 (d, 1H, J=7.7 Hz, H-1b), 4.50 (d, 1H, J=8.0 Hz, H-1c), 4.19 (dd, 1H, J=2.9 and 9.8 Hz, H-3c), 4.14 (d, 1H, J=2.7 Hz, H-4c), 4.08 (d, 1H, J=3.2 Hz, H-2a), 3.99 (dt, 1H, J=2.3, 4.1 and 10.4 Hz, O*CH*$_2$), 3.92 (dd, 1H, J=2.0 and 12.2 Hz, H-6b), 3.85 (m, H-9Nu), 3.83 (m, H-5Nu), 3.82 (m, H-6b'), 3.80 (m, H-8Nu), 3.77 (m, H-5c), 3.76 (m, H-6c), 3.76 (m, O*CH*$_2$), 3.73 (m, H-6c'), 3.70 (m, H-4Nu), 3.67 (m, H-3b), 3.65 (m, H-2c), 3.64 (m, H-9Nu'), 3.63 (m, H-4b), 3.61 (m, H-7Nu), 3.59 (m, H-3a), 3.58 (m, H-6Nu), 3.51 (m, 1H, H-5b), 3.45 (t, 2H, *CH*$_2$N$_3$), 3.39-3.32 (m, 2H, H-4a, H-5a), 3.29 (t, 1H, J=8.5 Hz, H-2b), 2.71 (dd, 1H, J=4.7 and 12.6 Hz, H-3Nu), 2.03 (s 3H, NAc), 1.94 (dt, 2H, J=6.7 and 13.4 Hz, CH$_2$*CH*$_2$CH$_2$), 1.83 (t, 1H, J=12.2 Hz, H-3Nu'), 1.31 (d, 3H, J=5.5 Hz, H-6a); ^{13}C NMR (D_2O) δ 175.9 (N-C=O), 174.34 (C-1Nu), 101.41 (C-2Nu), 101.46 (J=162.4 Hz, C-H-1a), 103.33 (J=154.5 Hz, C-H-1c), 103.46 (J=158.9 Hz, C-H-1b) 77.46 (C-4b), 76.37 (C-3b), 76.12 (C-3c), 75.67 (C-4c), 75.04 (C-5b), 74.99 (C-5c) 74.21 (C-2b), 73.75 (C-6Nu), 73.45 (C-3a), 73.03 (C-5a), 72.89 (C-8Nu), 72.81 (C-4a), 71.48 (C-2a), 70.24 (C-2c), 69.33 (C-4Nu), 68.89 (C-7Nu), 68.11 (O*CH*$_2$), 63.48 (C-9Nu), 61.79 (C-6b), 61.55 (C-6c), 52.51 (C-5Nu), 48.78 (*CH*$_2$N), 39.36 (C-3Nu), 29.09 (OCH$_2$*CH*$_2$CH$_2$N), 22.88 (*CH*$_3$C=O(N)), 17.48 (C-6a); MS - Electrospray -ve ion Calcd for $C_{32}H_{54}N_4O_{23}$ (862.80) obs. 861.3 (M-1).

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