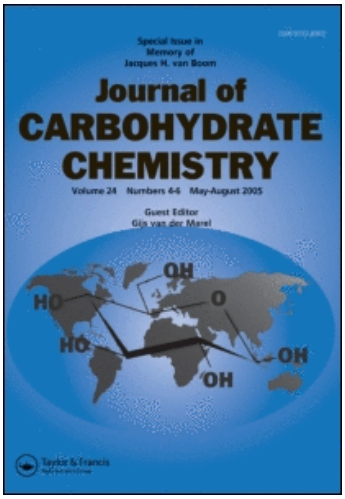

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SYNTHETIC STUDIES ON SIALOGLYCOCONJUGATES 16: α-PREDOMINANT GLYCOSIDE SYNTHESIS OF N-ACETYLNEURAMINIC ACID WITH THE PRIMARY HYDROXYL GROUP IN CARBOHYDRATES USING DIMETHYL(METHYLTHIO)SULFONIUM TRIFLATE AS A GLYCOSYL PROMOTER

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ABSTRACT

Coupling of the primary hydroxyl group in the suitably protected 2-(trimethylsilyl)ethyl glycosides of D-glucopyranose (3), N-acetyl-D-glucosamine (7), N-acetyl-D-galactosamine (9), D-lactose (10), and N-acetylneuraminic acid (11), with methyl (methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-2-thio-D-glycero-α-D-galacto-2-nonulopyranosid)onate (12) as the glycosyl donor in acetonitrile in the presence of dimethyl(methylthio)sulfonium triflate (DMTST) as a glycosyl promoter and molecular sieves 3A, gave predominantly the corresponding α-glycosides 13, 15, 17, 25, and 29 of N-acetylneuraminic acid in 43-71% yields, respectively, together with the β-glycosides (13-24%).

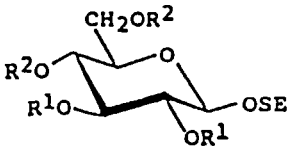
INTRODUCTION

Sialic acids[1-3] are well known as constituents of glycoproteins and glycolipids of cell membranes, and they are associated with the functions of sialoglycoconjugates. It is also known that sialic acids are linked in the α-configuration at O-3 of galactose and N-

acetylgalactosamine, and at O-6 of glucose, galactose, N-acetylglucosamine, and N-acetylgalactosamine, and at O-8 or O-9 of sialic acid, in sialoglycoconjugates. In view of these facts, a facile regio- and α-selective glycoside synthesis of N-acetylneuraminic acid (Neu5Ac) is critically important, in order to investigate the functions of such sialoglycoconjugates as glycoproteins and glycolipids at the molecular level. Previously, we demonstrated[4] a new, efficient α-glycosidation of sialic acid at O-3 of galactose and at O-3' of lactose by use of dimethyl(methylthio)sulfonium triflate (DMTST) as the glycosyl promoter and synthesized[5,6] a variety of gangliosides and their analogs using the α-sialyl-(2→3)-galactose and α-sialyl-(2→3')-lactose as the building units. As a part of our continuing efforts on the synthesis of sialoglycoconjugates, we describe here a synthesis of the α-glycosides of Neu5Ac with the primary hydroxyl group in a variety of sugar acceptors (3, 7, 9, 10, and 11) by use of DMTST[7] as a glycosyl promotor, and the methyl α-2-thioglycoside (12) of Neu5Ac as the glycosyl donor.

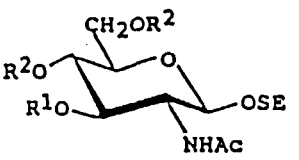
RESULTS AND DISCUSSION

The suitably protected glycosyl acceptors, in which the anomeric hydroxyl group was protected by a 2-(trimethylsilyl)ethyl group, were prepared as follows. Treatment of 2-(trimethylsilyl)ethyl β-D-glucopyranoside[8] (1) with 2-methoxypropene in N,N-dimethylformamide in the presence of p-toluenesulfonic acid monohydrate gave the 4,6-O-isopropylidene derivative which was converted, by O-acetylation and subsequent O-deisopropylidenation, into 2-(trimethylsilyl)-ethyl 2,3-di-O-acetyl-β-D-glucopyranoside (3). The observed chemical shifts and coupling constants for H-2 (δ 4.83, $J_{1,2}$ = 8.1 Hz, $J_{2,3}$ = 9.5 Hz) and for H-3 (δ 5.06, $J_{2,3}$ = $J_{3,4}$ = 9.5 Hz) are consistent with structure 3. O-Deacetylation of 2-(trimethylsilyl)-ethyl 2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranoside[9] (4) and subsequent isopropylidenation with 2,2-dimethoxypropane gave the 4,6-O-isopropylidene derivative 5 in 87% yield as crystals, which, on 3-O-benzoylation and O-deisopropylidenation according to the procedure described for 3, afforded 2-(trimethylsilyl)ethyl 2-



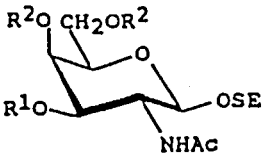
1 $R^1=R^2=H$
2 $R^1=Ac$, $R^2=Me_2C<$
3 $R^1=Ac$, $R^2=H$

SE=$Me_3SiCH_2CH_2$-



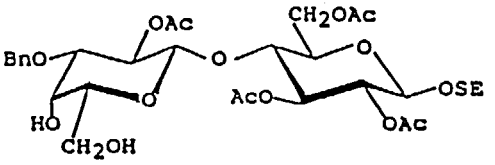
4 $R^1=R^2=Ac$
5 $R^1=H$, $R^2=Me_2C<$
6 $R^1=Bz$, $R^2=Me_2C<$
7 $R^1=Bz$, $R^2=H$

Bz=benzoyl



8 $R^1=R^2=Ac$
9 $R^1=Bn$, $R^2=H$

Bn=benzyl



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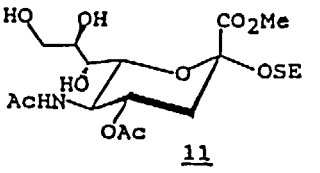

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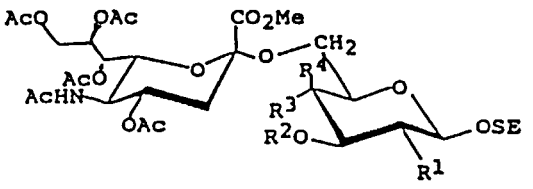
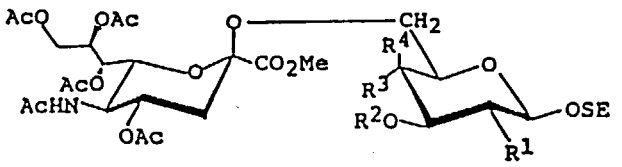
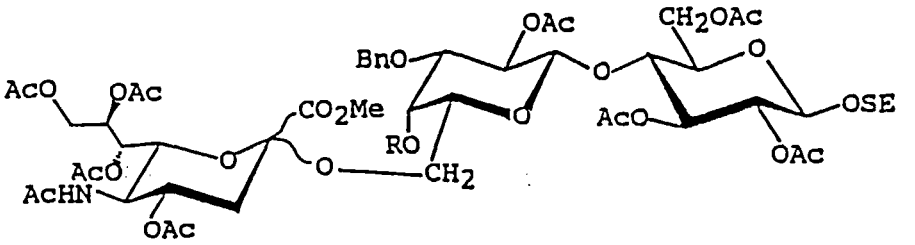


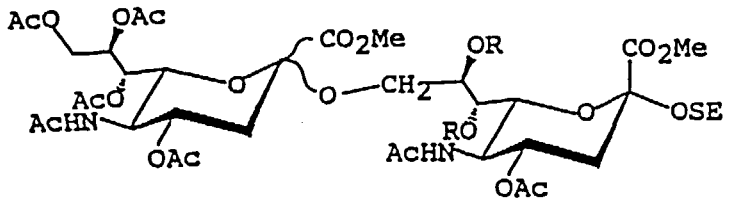
13 $R^1=OAc$, $R^2=Ac$, $R^3=OH$, $R^4=H$
14 $R^1=R^3=OAc$, $R^2=Ac$, $R^4=H$
15 $R^1=NHAc$, $R^2=Bz$, $R^3=OH$, $R^4=H$
16 $R^1=NHAc$, $R^2=Bz$, $R^3=OAc$, $R^4=H$
17 $R^1=NHAc$, $R^2=Bn$, $R^3=H$, $R^4=OH$
18 $R^1=NHAc$, $R^2=Bn$, $R^3=H$, $R^4=OAc$



19 $R^1=OAc$, $R^2=Ac$, $R^3=OH$, $R^4=H$
20 $R^1=R^3=OAc$, $R^2=Ac$, $R^4=H$
21 $R^1=NHAc$, $R^2=Bz$, $R^3=OH$, $R^4=H$
22 $R^1=NHAc$, $R^2=Bz$, $R^3=OAc$, $R^4=H$
23 $R^1=NHAc$, $R^2=Bn$, $R^3=H$, $R^4=OH$
24 $R^1=NHAc$, $R^2=Bn$, $R^3=H$, $R^4=OAc$



25 α : R=H
26 R=Ac
27 β : R=H
28 R=Ac



29 α : R=H
30 R=Ac
31 β : R=H
32 R=Ac

acetamido-3-O-benzoyl-2-deoxy-β-D-glucopyranoside (7) as crystals. Treatment of 2-acetamido-1,3,4,6-tetra-O-acetyl-2-deoxy-D-galactopyranose with trimethylsilyl trifluoromethanesulfonate[10] in dichloromethane gave the oxazoline derivative, which, on treatment with 2-(trimethylsilyl)ethanol in the presence of sulfuric acid afforded 2-(trimethylsilyl)ethyl 2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-galactopyranoside (8) in 96% yield. O-Deacetylation of 8, and subsequent selective benzylation[11] at O-3, using dibutyltin oxide, tetrabutylammonium bromide, and benzyl bromide gave compound 9 in 76% yield. Other glycosyl acceptors, 2-(trimethylsilyl)ethyl O-(2-O-acetyl-3-O-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-O-acetyl-β-D-glucopyranoside[12] (10) and methyl [2-(trimethylsilyl)-ethyl 5-acetamido-4-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-

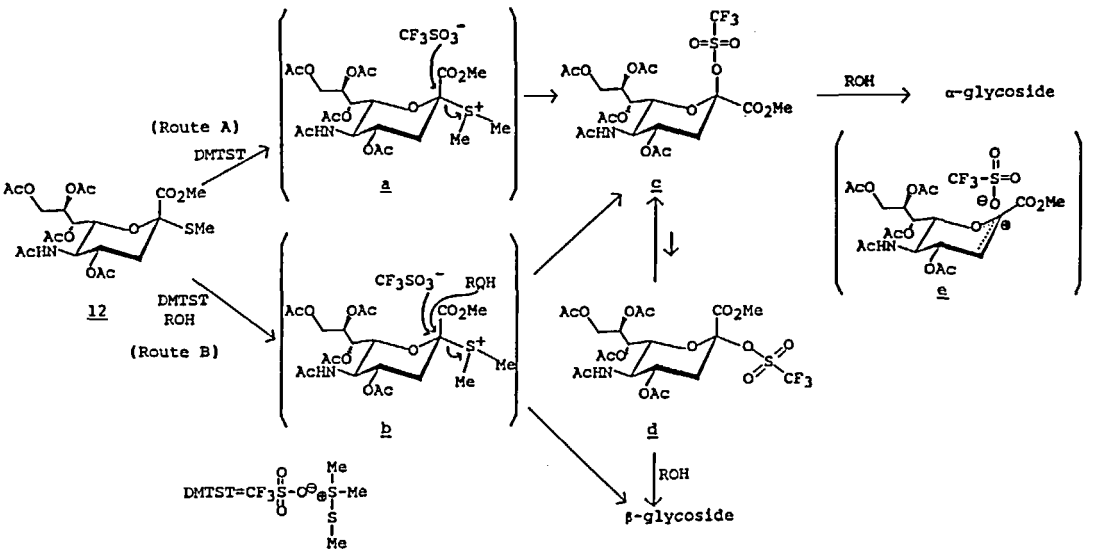


Fig.1

nonulopyranosid]onate (11) were, respectively, prepared according to the method[13] described before. Glycosylation of 3 with methyl (methyl 5-acet- amido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-2-thio-D-glycero-α-D-galacto-2-nonulopyranosid)onate[5a] (12, 2.0 equiv. to the glycosyl acceptor) in acetonitrile for 24 h at -15 °C in the presence of DMTST (4.0 equiv. to the glycosyl donor) and molecular sieves 3A, according to the procedure[5a,b] demonstrated by us for the regio and α-stereoselective glycosidation of Neu5Ac with the secondary hydroxyl groups of sugar derivatives, unexpectedly gave the desired α-glycoside 13 (45%), together with a substantial amount of the β-glycoside 19 (20%). A reasonable reaction mechanism, for the glycosidation of the methyl α-2-thio-glycoside (12) of Neu5Ac using DMTST as a glycosyl promoter is illustrated as shown in Fig.1. When compound 12 was treated with DMTST for 5 min in acetonitrile at -40 °C (Route A, Fig. 1), to form the glycosyl intermediates (c, d, and e), via a, and then 3 was added, the α/β ratio of the glycosides obtained was 58:13, with an incleased amount of α-glycoside of Neu5Ac. When the reactive alcohol (primary hydroxyl compound) was

applied with the glycosyl donor and DMTST at the same time (Route B), formation of c and β-glycoside, via b, occurred competitively corresponding to an increased amount of the β-glycoside. The structures of the glycosides (13 and 19) and their acetyl derivatives (14 and 20) were proved by ^{1}H NMR spectroscopy. The observed chemical shifts and coupling constants of the Neu5Ac unit in the glycosides for H-3e (δ 2.46, $J_{3a,3e}$ = 13.2 Hz, $J_{3e,4}$ = 4.4 Hz, 13; δ 2.61, $J_{3a,3e}$ = 12.8 Hz, $J_{3e,4}$ = 4.4 Hz, 14; δ 2.45, $J_{3a,3e}$ = 12.8 Hz, $J_{3e,4}$ = 4.8 Hz, 19; δ 2.42, $J_{3a,3e}$ = 12.8 Hz, $J_{3e,4}$ = 4.4 Hz, 20), H-4 (δ 4.95, 13; 4.88, 14; 5.32, 19; 5.17, 20), and of the glucose unit for H-4 (δ 5.32, $J_{3,4}$ = 8.8 Hz, $J_{4,5}$ = 9.9 Hz, 14; δ 5.29, $J_{3,4}$ = $J_{4,5}$ = 8.8 Hz, 20), clearly indicate the anomeric configurations of the glycosidic linkages[4-6,14] and the linked positions. In the same way reaction of 12 with the glycosyl acceptors (7, 9, 10, and 11) yielded the α-predominant glycoside mixtures of Neu5Ac, in good yields respectively. The yields and the ratio of α and β anomers are summarized in TABLE 1. The glycosides 15, 17, 21, 23, 25, 27, 29, and 31 of Neu5Ac obtained were acetylated to compounds 16, 18, 22, 24, 26, 28, 30, and 32, respectively, and characterized by ^{1}H NMR spectroscopy. In conclusion, regio and α-predominant glycosidation of Neu5Ac with the primary hydroxyl groups of carbohydrates which are constituents of sialoglycoconjugates was achieved by use of the methyl α-2-thioglycoside of Neu5Ac (12) as the glycosyl donor and the suitably protected acceptors 3, 7, 9, 10, and 11 with DMTST in acetonitrile under controlled conditions. The α-glycosides 14, 16, 18, 26, and 30 of Neu5Ac obtained here could be used as suitable intermediates for the sialoglycoconjugates syntheses.

EXPERIMENTAL

General Procedures. Melting points were determined with a Yanagimoto micro melting point apparatus and are uncorrected. Specific rotations were determined with a Union PM-201 polarimeter

TABLE 1

DMTST-Promoted Glycosylation of the Methyl α-2-Thioglycoside (12) of N-Acetylneuraminic Acid with the Primary Hydroxyl Group of Carbohydrates.

Glycosyl Acceptors (ROH)	α-Glycosides	Yields[a] (%)	β-Glycosides	Yields[a] (%)
3	13	58	19	13
7	15	71	21	22
9	17	63	23	14
10	25	51	27	19
11	29	43	31	24

a. Yields based on the weight of acceptor employed.

at 25 °C, and the IR spectra were recorded with a JASCO IRA-100 spectrophotometer. ^{1}H NMR spectra were recorded with a JEOL JNM-GX 270 spectrometer. Preparative chromatography was performed on silica gel (Wako Co., 200 mesh) with the solvent systems specified. Concentrations were conducted in vacuo.

2-(Trimethylsilyl)ethyl 2,3-Di-O-acetyl-4,6-O-isopropylidene-β-D-glucopyranoside (2). To a solution of 2-(trimethylsilyl)ethyl β-D-glucopyranoside[8] (1, 910 mg, 3.3 mmol) in dry N,N-dimethylformamide (DMF, 20 mL), cooled to 0 °C, was added 2-methoxypropene (0.47 mL, 4.9 mmol), and pH of the mixture was adjusted to 3 by adding p-toluenesulfonic acid monohydrate (20 mg). The mixture was stirred for 3 h at 0 °C, and sodium hydrogen carbonate (3 g) was added. The precipitate was filtered off, and washed with DMF (5 mL). The filtrate and washings were combined, and concentrated to a syrup, which was acetylated with acetic anhydride (3 mL)-pyridine (5 mL). The product was purified by chromatography on a column of silica gel (100 g) with 1:10 ethyl acetate-hexane to give 2 (1.2 g, 91%) as a syrup: $[\alpha]_D$ -52.4° (c 1.3, chloroform); ^{1}H NMR ($CDCl_3$) δ 0.91 (m,

2H, $Me_3SiCH_2CH_2$), 1.37, 1.45 (2s, 6H, Me_2C), 2.03 (2s, 6H, 2AcO), 3.33 (ddd, 1H, $J_{5,6}$ = 9.9 Hz, H-5), 3.52, 3.92 (2m, 2H, Me_3SiCH_2-CH_2), 3.75 (m, 2H, H-6,6'), 4.53 (d, 1H, $J_{1,2}$ = 7.9 Hz, H-1), 4.91 (dd, 1H, $J_{2,3}$ = 9.2 Hz, H-2), and 5.11 (dd, 1H, $J_{3,4}$ = 9.2 Hz, H-3).

Anal. Calcd for $C_{18}H_{32}O_8Si$ (404.5): C, 53.44; H, 7.97. Found: C, 53.45; H, 8.13.

2-(Trimethylsilyl)ethyl 2,3-Di-O-acetyl-β-D-glucopyranoside (3). A solution of 2 (700 mg, 1.7 mmol) in 80% aqueous acetic acid (10 mL) was heated for 1 h at 40 °C, and concentrated to a syrup, which was chromatographed on a column of silica gel (80 g) with ethyl acetate to give 3 (480 mg, 76%) as an amorphous mass: $[\alpha]_D$ -31.8° (c 0.79, chloroform); ^1H NMR ($CDCl_3$) δ 0.85-0.96 (m, 2H, $Me_3SiCH_2CH_2$), 2.02, 2.06 (2s, 6H, 2AcO), 3.40 (m, 1H, H-5), 3.55, 3.96 (m, 2H, $Me_3SiCH_2CH_2$), 3.72-3.80 (m, 2H, H-6,6'), 4.53 (d, 1H, $J_{1,2}$ = 8.1 Hz, H-1), 4.83 (dd, 1H, $J_{2,3}$ = 9.5 Hz, H-2), and 5.06 (t, 1H, $J_{3,4}$ = 9.5 Hz, H-3).

Anal. Calcd for $C_{15}H_{28}O_8Si$ (364.5): C, 49.43; H, 7.74. Found: C, 49.29; H, 7.91.

2-(Trimethylsilyl)ethyl 2-Acetamido-2-deoxy-4,6-O-isopropylidene-β-D-glucopyranoside (5). De-O-acetylation of 2-(trimethylsilyl)-ethyl 2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranoside[9] (4, 895 mg, 2 mmol) with sodium methoxide (50 mg) in methanol (100 mL) in the usual way gave the de-O-acetyl derivative. To a DMF (10 mL) solution of 2-(trimethylsilyl)ethyl 2-acetamido-2-deoxy-β-D-glucopyranoside obtained above were added 2,2-dimethoxypropane (3 mL) and p-toluenesulfonic acid monohydrate (30 mg), and the mixture was stirred for 1 h at room temperature, and then treated with Amberlite 1R-410 (OH^-) resin to remove the acid. The solution was concentrated to a syrup, which was chromatographed on a column of silica gel (100 g) with 50:1 dichloromethane-methanol to give 5 (630 mg, 87%). Crystallization from ether gave needles: mp 123-124 °C, $[\alpha]_D$ -74.0° (c 0.8, chloroform); IR (KBr) 3600-3350 (OH, NH), 1660 and 1540 (amide), 860 and 840 (TMS, Me_2C), and 750 and 690 cm^{-1} (Ph).

Anal. Calcd for $C_{16}H_{31}NO_6Si$ (361.5): C, 53.16; H, 8.64; N, 3.87. Found: C, 53.09; H, 8.66; N, 3.74.

2-(Trimethylsilyl)ethyl 2-Acetamido-3-O-benzoyl-2-deoxy-4,6-O-isopropylidene-β-D-glucopyranoside (6). To a solution of 5 (500 mg, 1.38 mmol) in pyridine (10 mL), cooled to -20 °C, was added benzoyl chloride (280 mg), and the mixture was stirred for 2 h at -10 °C. Methanol (1 mL) was added to the mixture, and the mixture was concentrated to a syrup, which was chromatographed on a column of silica gel (60 g) with 100:1 dichloromethane-methanol to give crystalline 6 (592 mg, 92%). Recrystallization from ether gave needles: mp 147-148 °C; $[\alpha]_D$ -34.5° (c 0.62, chloroform); ^{1}H NMR ($CDCl_3$) δ 0.95 (m, 2H, $Me_3Si\underline{CH_2}CH_2$), 1.37, 1.51 (2s, 6H, Me_2C), 1.89 (s, 3H, AcN), 3.56, 4.00 (2m, 2H, $Me_3SiCH_2\underline{CH_2}$), 3.96 (m, 3H, H-4,5,6), 4.31 (dd, 1H, $J_{1,2}$ = 8.1 Hz, $J_{2,3}$ = 9.9 Hz, H-2), 4.65 (d, 1H, H-1), 5.48 (t, 1H, $J_{3,4}$ = 9.9 Hz, H-3), 6.40 (d, 1H, $J_{NH,2}$ = 9.5 Hz, NH), and 7.46-8.04 (m, 5H, Ph).

Anal. Calcd for $C_{23}H_{35}NO_7Si$ (465.6): C, 59.33; H, 7.58; N, 3.01. Found: C, 59.41; H, 7.48; N, 3.03.

2-(Trimethylsilyl)ethyl 2-Acetamido-3-O-benzoyl-2-deoxy-β-D-glucopyranoside (7). A solution of 6 (430 mg, 0.92 mmol) in 80% aqueous acetic acid (10 mL) was heated, with stirring, for 2 h at 45 °C, and concentrated. The residue was chromatographed on a column of silica gel (60 g) with 40:1 dichloromethane-methanol to give 7 (358 mg, 91%). Crystallization from ether-hexane gave needles: mp 85-88 °C; $[\alpha]_D$ +1.8° (c 0.3, chloroform); ^{1}H NMR ($CDCl_3$) δ 0.88 (m, 2H, $Me_3Si\underline{CH_2}CH_2$), 1.80, (s, 3H, AcN), 3.50, 3.94 (m, 2H, $Me_3SiCH_2\underline{CH_2}$), 3.54 (m, 1H, H-6), 3.83 (m, 2H, H-2,6'), 3.95 (dd, 1H, $J_{3,4}$ = 9.5 Hz, $J_{4,5}$ = 8.8 Hz, H-4), 4.12 (m, 1H, H-5), 4.66 (d, 1H, $J_{1,2}$ = 8.4 Hz, H-1), 5.39 (dd, 1H, $J_{2,3}$ = 9.9 Hz, H-3), 6.34 (broad s, 1H, NH), and 7.35-8.05 (m, 5H, Ph).

Anal. Calcd for $C_{20}H_{31}NO_7Si$ (425.6): C, 56.45; H, 7.34; N, 3.30. Found: C, 56.21; H, 7.48; N, 3.31.

2-(Trimethylsilyl)ethyl 2-Acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-galactopyranoside (8). Acetylation of 2-acetamido-2-deoxy-D-galactose (15 g) with acetic anhydride (70 mL)-pyridine (100 mL) overnight at 35 °C gave crystalline peracetate (25.2 g, 95%). To a solution of the peracetate (10 g, 25.7 mmol) in dry dichloromethane

(100 mL) was added trimethylsilyl trifluoromethanesulfonate (12 g, 54 mmol), and the mixture was stirred for 5 h at 40 °C, and then cooled. Dichloromethane (200 mL) was added to the mixture, and this was washed with M sodium carbonate, dried (sodium sulfate), and concentrated. To a solution of the residue in dry dichloromethane (150 mL) were added 2-(trimethylsilyl)ethanol (4.5 g, 38 mmol) and concd sulfuric acid (7 drops), and the mixture was stirred for 20 h at 40 °C, and then successively washed with M sodium carbonate, water, dried (sodium sulfate), and concentrated. The residue was chromatographed on a column of silica gel (200 g) with 1:1 ethyl acetate-hexane to give 8 (11 g, 96%) as an amorphous mass: $[\alpha]_D$ -26.5° (c 0.66, chloroform); ^{1}H NMR ($CDCl_3$) δ 0.95 (m, 2H, Me_3Si-$\underline{CH_2}CH_2$), 1.94 (s, 3H, AcN), 1.98, 2.03, 2.12 (3s, 9H, 3AcO), 3.55, 3.92 (m, 2H, $Me_3SiCH_2\underline{CH_2}$), 3.86-4.02 (m, 2H, H-2,5), 4.13 (dd, 1H, $J_{5,6}$ = 8.1 Hz, $J_{6,6'}$ = 11.4 Hz, H-6), 4.20 (dd, 1H, $J_{5,6'}$ = 5.1 Hz, H-6'), 4.75 (d, 1H, $J_{1,2}$ = 8.4 Hz, H-1), 5.31-5.35 (m, 2H, H-3,4), and 5.58 (broad d, 1H, NH).

Anal. Calcd for $C_{19}H_{33}NO_9Si$ (447.6): C, 50.99; H, 7.43; N, 3.13. Found: C, 51.14; H, 7.49; N, 3.20.

2-(Trimethylsilyl)ethyl 2-Acetamido-3-O-benzyl-2-deoxy-β-D-galactopyranoside (9). To a solution of 8 (10.0 g, 22 mmol) in methanol (100 mL) was added sodium methoxide (200 mg); after 10 min, the reaction was complete. The usual work-up gave crystalline 2-(trimethylsilyl)ethyl 2-acetamido-2-deoxy-β-D-galactopyranoside in quantitative yield [mp 192-193 °C, $[\alpha]_D$ -5.2° (c 0.57, chloroform); ^{1}H NMR (CD_3OD) δ 0.91 (m, 2H, $Me_3Si\underline{CH_2}CH_2$), 1.99 (s, 3H, AcN), 3.48, 3.98 (m, 2H, $Me_3Si\underline{CH_2}CH_2$), 3.50 (dd, 1H, $J_{1,2}$ = 8.4 Hz, $J_{2,3}$ = 11.7 Hz, H-2), 3.56 (dd, 1H, $J_{3,4}$ = 2.6 Hz, H-3), 3.61 (m, 1H, H-5), 3.78 (dd, 2H, H-6,6'), 3.86 (dd, 1H, $J_{4,5}$ = 9.9 Hz, H-4), and 4.41 (d, 1H, H-1)]. A suspension of the glycoside (3.2 g, 10 mmol) obtained above and molecular sieves 4A (MS-4A, 3 g) in dry benzene (80 mL) was stirred for 2 h at 80 °C, and dibutyltin oxide (3.75g, 15 mmol) was added to the mixture. The mixture was refluxed with stirring for 4 h, and tetrabutylammonium bromide (1.6 g, 5 mmol) and benzyl bromide (8.5 g, 50 mmol) were added. The mixture was stirred for

another 3 h at 80 °C and the precipitate was filtered off, and the solution was concentrated to a syrup, which was chromatographed on a column of silica gel (200 g) with dichloromethane and 50:1 dichloromethane-methanol. The latter eluent gave 9 (3.1 g, 76%) as crystals. Recrystallization from ether gave needles: mp 150-152 °C, $[\alpha]_D$ +14.5° (c 0.47, chloroform); ^{1}H NMR ($CDCl_3$) δ 0.95 (m, 2H, $Me_3Si\underline{CH_2}CH_2$), 1.94 (s, 3H, AcN), 3.30 (near t, 1H, H-5), 3.46-3.60 (m, 2H, H-2, one-proton in $Me_3SiCH_2\underline{CH_2}$), 3.91 (m, 1H, one-proton in $Me_3SiCH_2\underline{CH_2}$), 3.93 (dd, 1H, $J_{2,3}$ = 9.9 Hz, $J_{3,4}$ = 4.0 Hz, H-3), 3.98 (dd, 1H, $J_{4,5}$ = 5.5 Hz, H-4), 4.10-4.20 (m, 2H, H-6,6'), 4.53, 4.69 (2d, 2H, J_{gem} = 11.7 Hz, $Ph\underline{CH_2}$), 4.90 (d, 1H, $J_{1,2}$ = 8.4 Hz, H-1), 5.96 (d, 1H $J_{NH,2}$ = 7.7 Hz, NH), and 7.28-7.37 (m, 5H, Ph).

Anal. Calcd for $C_{20}H_{33}NO_7Si$ (411.6): C, 58.37; H, 8.08; N, 3.40. Found: C, 58.61; H, 8.25; N, 3.38.

Methyl [2-(Trimethylsilyl)ethyl 5-Acetamido-4-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosid]onate (11). To a solution of methyl [2-(trimethylsilyl)ethyl 5-acetamido-3,5-dideoxy-8,9-O-isopropylidene-D-glycero-α-D-galacto-2-nonulopyranosid]onate[13a] (440 mg, 0.95 mmol) in pyridine (10 mL), cooled to -35 °C, was added dropwise a solution of acetyl chloride (0.09 mL) in dichloromethane (1 mL), and the mixture was stirred for 2 h at -30 °C. Methanol (0.2 mL) was added to the mixture, and the mixture was concentrated to a syrup, which was chromatographed on a column of silica gel (50 g) with 75:1 dichloromethane-methanol, to give the 4-O-acetyl derivative [$[\alpha]_D$ -11° (c 0.8, dichloromethane)] in quantitative yield. A solution of the 4-O-acetyl derivative in 70 % aqueous acetic acid (10 mL) was heated for 3 h at 45 °C while the progress of the reaction was monitored by TLC. The solution was concentrated to a syrup which was chromatographed on a column of silica gel (50 g) with 50:1 dichloromethane-methanol to give 11 (420 mg, 95%) as an amorphous mass: $[\alpha]_D$ -22.7° (c 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 0.88 (m, 2H, $Me_3Si\underline{CH_2}CH_2$), 1.99 (s, 3H, AcN), 2.11 (s, 3H, AcO), 2.68 (dd, 1H, $J_{3a,3e}$ = 12.8 Hz, $J_{3e,4}$ = 4.8 Hz, H-3e), 3.86 (s, 3H, MeO), 4.17 (q, 1H, $J_{4,5} = J_{5,6} = J_{5,NH}$ = 10.5 Hz, H-5), 4.90 (ddd, 1H, $J_{3a,4}$ = 11.5 Hz, H-4), and 5.93 (d, 1H, NH).

Anal. Calcd for $C_{19}H_{35}NO_{10}Si$ (465.6): C, 49.02; H, 7.58; N, 3.01. Found: C, 49.22; H, 7.62; N, 2.91.

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→6)-2,3-di-O-acetyl-β-D-glucopyranoside (13) and 2-(Trimethylsilyl)ethyl O-(Methyl 5-Acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-β-D-galacto-2-nonulopyranosylonate)-(2→6)-2,3-di-O-acetyl-β-D-glucopyranoside (19). To a solution of 3 (179 mg, 0.84 mmol) in dry acetonitrile (2 mL) was added molecular sieves 3 A (MS-3A, 200 mg), and the mixture was stirred for 6 h at room temperature, and cooled to -40 °C (mixture A). On the other hand, a mixture of methyl (methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-2-thio-D-glycero-α-D-galacto-2-nonulopyranosid)onate[4a,5a] (12, 521 mg, 1.0 mmol) and MS-3A (200 mg) in dry acetonitrile (2 mL) was stirred for 6 h at room temperature and cooled to -40 °C (mixture B). To the stirred mixture A was added a mixture (1.7 g, 60 % DMTST by weight) of dimethyl(methylthio)sulfonium triflate[7a] (DMTST) and MS-3A, and the mixture was stirred for 5 min at -40 °C, and then the mixture B was added at -40 °C. The combined mixture was stirred for 24 h at -15 - -20 °C; the progress of the reaction was monitored by TLC. The precipitate was filtered off, and washed with dichloromethane. The filtrate and washings were combined, and this was successively washed with M sodium carbonate and water, dried (sodium sulfate), and concentrated to a syrup that was chromatographed on a column of silica gel (60 g) with 100:1 dichloromethane-methanol as the eluent. Compound 19 (51 mg, 12.6 %) was obtained as a faster-moving component, and compound 13 (235 mg, 58.2%) appeared as a slower-moving component.

Compound 13 had $[\alpha]_D$ -25.0° (c 1.3, chloroform); ^1H NMR ($CDCl_3$) Neu5Ac unit δ 1.90 (s, 3H, AcN), 2.64 (dd, 1H, $J_{3a,3e}$ = 13.2 Hz, $J_{3e,4}$ = 4.4 Hz, H-3e), 3.80 (s, 3H, MeO), 4.05-4.18 (m, 3H, H-5, 6,9), 4.35 (dd, 1H, H-9'), 4.95 (ddd, 1H, $J_{3a,4}$ = 10.3 Hz, $J_{4,5}$ = 9.9 Hz, H-4), 5.36 (m, 2H, H-7,8), and 5.56 (d, 1H, NH); Glc unit δ 0.92 (m, 2H, $Me_3SiCH_2CH_2$), 3.39-3.56 (m, 2H, H-5, one of proton in $Me_3SiCH_2CH_2$), 3.85-3.99 (m, 3H, H-4,6, and one of proton in Me_3Si-

$CH_2\underline{CH_2}$), 4.45 (d, 1H, $J_{1,2}$ = 7.7 Hz, H-1), 4.93 (dd, 1H, $J_{2,3}$ = 9.5 Hz, H-2), and 5.08 (t, 1H, $J_{3,4}$ = 9.5 Hz, H-3); O-acetyl groups δ 2.03, 2.04 (2), 2.05 (2), and 2.12 (6s, 18H, 6AcO).

Anal. Calcd for $C_{35}H_{55}NO_{22}Si$ (837.9): C, 50.17; H, 6.62; N, 1.67. Found: C, 50.09; H 6.51; N, 1.73.

Compound 19 had $[\alpha]_D$ -13.7° (c 0.97, chloroform); ^1H NMR ($CDCl_3$) Neu5Ac unit δ 1.86 (s, 3H, AcN), 2.45 (dd, 1H, $J_{3a,3e}$ = 12.8 Hz, $J_{3e,4}$ = 4.8 Hz, H-3e), 3.79 (s, 3H, MeO), 3.95-4.15 (m, 3H, H-5,6,9), 4.85 (dd, 1H, $J_{8,9'}$ = 2.2. Hz, H-9'), 5.23 (m, 1H, H-8), 5.39 (near d, 1H, H-7), 5.32 (m, 1H, $J_{3e,4}$ = 4.8 Hz, H-4), and 5.81 (d, 1H, NH); Glc unit δ 0.92 (m, 2H, $Me_3Si\underline{CH_2}CH_2$), 3.50 (m, 1H, H-5), 3.51, 3.79 (m, 2H, $Me_3SiCH_2\underline{CH_2}$), 3.65 (dd, 1H, $J_{5,6}$ = 4.0 Hz, $J_{6,6'}$ = 10.6 Hz, H-6), 3.80 (m, 2H, H-4,6'), 4.48 (d, 1H, $J_{1,2}$ = 8.1 Hz, H-1), 4.86 (dd, 1H, $J_{2,3}$ = 9.9 Hz, H-2), and 5.30 (t, 1H, $J_{3,4}$ = 10.0 Hz, H-3); O-acetyl groups δ 2.00, 2.01, 2.02 (2), 2.03, and 2.08 (6s, 18H, 6AcO).

Found: C, 50.25; H, 6.79; N, 1.58.

A sample of compound 13 (230 mg, 0.28 mmol) was acetylated with acetic anhydride (1 mL) in pyridine (4 mL) in the usual way, to give 14 (220 mg, 91%) as an amorphous mass: $[\alpha]_D$ -5.4° (c 2.2, chloroform); ^1H NMR ($CDCl_3$) Neu5Ac unit δ 1.86 (s, 3H, AcN), 2.61 (dd, 1H, $J_{3a,3e}$ = 12.8 Hz, $J_{3e,4}$ = 4.4 Hz, H-3e), 3.78 (s, 3H, MeO), 3.87-4.10 (m, 3H, H-5,6 9), 4.29 (dd, 1H, $J_{8,9'}$ = 2.2 Hz, $J_{9,9'}$ = 12.5 Hz, H-9'), 4.88 (ddd, 1H, $J_{3a,4}$ = 10.2 Hz, $J_{4,5}$ = 8.4 Hz, H-4), 5.33 (m, 2H, H-7,8), and 5.55 (d, 1H, $J_{NH,5}$ = 8.1 Hz, NH); Glc unit δ 0.85-0.97 (m, 2H, $Me_3Si\underline{CH_2}CH_2$), 3.56, 3.95 (m, 2H, $Me_3SiCH_2\underline{CH_2}$), 4.03 (m, 2H, H-6,6'), 4.45 (d, 1H, $J_{1,2}$ = 7.7 Hz, H-1), 4.93 (dd, 1H, $J_{2,3}$ = 9.5 Hz, H-2), 5.14 (dd, 1H, $J_{3,4}$ = 8.8 Hz, H-3), and 5.32 (dd, 1H, $J_{4,5}$ = 9.9 Hz, H-4); O-acetyl groups δ 1.99, 2.02 (2), 2.03, 2.05, 2.12, and 2.13 (7s, 21H, 7AcO).

Anal. Calcd for $C_{37}H_{57}NO_{21}Si$ (880.0): C, 50.50; H, 6.53; N, 1.59. Found: C, 50.46; H, 6.71; N, 1.55.

A sample of 19 (50 mg, 0.06 mmol) was acetylated with acetic anhydride (1 mL)-pyridine (2 mL) in the usual way, to give 20 (50

mg, quantitative) as an amorphous mass: $[\alpha]_D$ -10.1° (c 0.9, chloroform); ^{1}H NMR ($CDCl_3$) Neu5Ac unit δ 1.87 (s, 3H, AcN), 2.42 (dd, 1H, $J_{3a,3e}$ = 12.8 Hz, $J_{3e,4}$ = 4.4 Hz, H-3e), 3.80 (s, 3H, MeO), 4.12 (m, 2H, H-5,6), 4.15 (dd, 1H, $J_{8,9}$ = 9.9 Hz, $J_{9,9'}$ = 14.1 Hz, H-9), 4.79 (dd, 1H, $J_{8,9'}$ = 4.8 Hz, H-9'), 5.17 (m, 2H, H-4,8), and 5.40 (broad s, 1H, H-7); Glc unit δ 0.93 (m, 2H, $Me_3Si\underline{CH_2}CH_2$), 3.57 (m, 3H, H-6,6', one-proton in $Me_3SiCH_2\underline{CH_2}$), 4.51 (d, 1H, $J_{1,2}$ = 7.7 Hz, H-1), 4.94 (dd, 1H, $J_{2,3}$ = 9.5 Hz, H-2), 5.20 (dd, 1H, $J_{3,4}$ = 8.8 Hz, H-3), and 5.29 (t, 1H, H-4); O-acetyl groups δ 2.00, 2.03 (2), 2.05, 2.06, 2.13, and 2.14 (7s, 21H, 7 AcO).

Found: C, 50.39; H, 6.70; N, 1.58.

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→6)-2-acetamido-3-O-benzoyl-2-deoxy-β-D-glucopyranoside (15) and 2-(Trimethylsilyl)ethyl O-(Methyl 5-Acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-β-D-galacto-2-nonulopyranosylonate)-(2→6)-2-acetamido-3-O-benzoyl-2-deoxy-β-D-glucopyranoside (21). Glycosylation of compound 7 (165 mg, 0.39 mmol) with 12 (400 mg, 0.77 mmol) in dry acetonitrile (5 mL) using DMTST (1.6 g, 3.2 mmol), as described for 13, gave 15 (244 mg, 70.8%) and 21 (77 mg, 22.4%), respectively.

Compound 15 had $[\alpha]_D$ -4.9° (c 0.67, chloroform), ^{1}H NMR ($CDCl_3$) Neu5Ac unit δ 2.65 (dd, 1H, $J_{3a,3e}$ = 13.2 Hz, $J_{3e,4}$ = 4.8 Hz, H-3e), 3.52 (q, 1H, $J_{4,5} = J_{5,6} = J_{5,NH}$ = 10.0 Hz, H-5), 3.90-4.32 (m, 2H, H-6,9), 4.30 (dd, 1H, $J_{8,9'}$ = 2.2 Hz, $J_{9,9'}$) = 12.5 Hz, H-9'), 4.98 (ddd, 1H, $J_{3a,4}$ = 9.5 Hz, H-4), 5.25-5.36 (m, 2H, H-7,8), and 5.72 (d, 1H, NH); GlcNAc unit δ 0.92 (m, 2H, $Me_3Si\underline{CH_2}CH_2$), 3.49-3.58 (m, 2H, H-5, one of proton in $Me_3SiCH_2\underline{CH_2}$), 3.90-4.20 (m, 5H, H-2,4,6,6' and one-proton in $Me_3SiCH_2\underline{CH_2}$), 4.55 (d, 1H, $J_{1,2}$ = 8.4 Hz, H-1), 5.30 (dd, 1H, H-3), 6.03 (d, 1H, $J_{2,NH}$ = 9.2 Hz, NH), and 7.18-8.04 (m, 5H, Ph); other groups δ 1.81, 1.84 (2s, 6H, 2AcN) and 1.88, 2.00, 2.04, 2.09 (4s, 12H, 4AcO).

Anal. Calcd for $C_{40}H_{58}N_2O_{19}Si$ (899.0): C, 53.44; H, 6.50; N, 3.12. Found: C, 53.40; H, 6.63; N, 3.08.

Compound 21 had $[\alpha]_D$ -5.9° (c 1.2, chloroform); ^{1}H NMR ($CDCl_3$) Neu5Ac unit δ 2.51 (dd, 1H, $J_{3a,3e}$ = 12.8 Hz, $J_{3e,4}$ = 4.8 Hz, H-3e), 3.79 (s, 3H, MeO), 4.00-4.15 (m, 3H, H-5,6,9), 4.87 (dd, 1H, $J_{8,9'}$ = 2.2 Hz, $J_{9,9'}$ = 12.5 Hz, H-9'), and 5.29 (m, 2H, H-4,8), and 5.42 (broad s, 1H, H-7); GlcNAc unit δ 0.91 (m, 2H, $Me_3Si\underline{CH_2}CH_2$), 3.52-3.64 (m, 3H, H-4,5, and one proton in $Me_3SiCH_2\underline{CH_2}$), 3.95 (m, 2H, H-6, one proton in $Me_3SiCH_2\underline{CH_2}$), 4.60 (d, 1H, $J_{1,2}$ = 8.4 Hz, H-1), 5.31 (t, 1H, $J_{2,3} = J_{3,4}$ = 9.2 Hz, H-3), and 7.41-8.02 (m, 5H, Ph); other groups δ 1.78, 1.81 (2s, 6H, 2AcN), and 1.94, 1.98, 2.00 (2) and 2.13 (5s, 15H, 5AcO), and 6.37, 6.58 (2d, 2H, 2NH).

Found: C, 53.42; H, 6.78; N, 3.00.

A sample of 15 (55 mg, 0.062 mmol) was acetylated with acetic anhydride (0.5 mL)-pyridine (1 mL) overnight at room temperature, to give 16 (56 mg, 97%) as an amorphous mass; $[\alpha]_D$-14.7° (c 1.5, chloroform); ^{1}H NMR ($CDCl_3$) Neu5Ac unit δ 2.63 (dd, 1H, $J_{3a,3e}$ = 12.8 Hz, $J_{3e,4}$ = 4.4 Hz, H-3e), 4.31 (dd, 1H, $J_{8,9'}$ = 1.9 Hz, $J_{9,9'}$ = 12.1 Hz, H-9'), 4.89 (ddd, 1H, $J_{3a,4}$ = 10.5 Hz, $J_{4,5}$ = 8.1 Hz, H-4), 5.28-5.36 (m, 1H, H-8), and 5.42 (m, 1H, H-7); GlcNAc unit δ 0.89 (m, 2H, $Me_3Si\underline{CH_2}CH_2$), 3.50-3.60 (m, 3H, H-2,5, and one proton in $Me_3SiCH_2\underline{CH_2}$), 3.92 (m, 1H, one proton in $Me_3SiCH_2\underline{CH_2}$), 4.87 (d, 1H, $J_{1,2}$ = 8.4 Hz, H-1), 5.33 (dd, 1H, $J_{3,4}$ = 9.9 Hz, $J_{4,5}$ = 9.5 Hz, H-4), 5.46 (t, 1H, $J_{2,3}$ = 9.9 Hz, H-3), 7.38-8.02 (m, 5H, Ph); other groups δ 1.82, 1.84 (2, 6H, 2AcN), 5.45, 5.93 (2d, 2H, 2NH), and 1.96, 2.02 (2), 2.10, 2.13 (5s, 15H, 5AcO).

Anal. Calcd for $C_{42}H_{60}N_2O_{20}Si$ (941.0): C, 53.61; H, 6.43; N, 2.98. Found: C, 53.44; H, 6.48; N, 3.05.

A sample of compound 21 (45 mg, 0.05 mmol) was acetylated as described for 16, to give 22 (45 mg, quantitative) as an amorphous mass: $[\alpha]_D$ -15.0° (c 0.9, chloroform); ^{1}H NMR ($CDCl_3$) Neu5Ac unit δ 2.44 (dd, 1H, $J_{3a,3e}$ = 12.8 Hz, $J_{3e,4}$ = 4.8 Hz, H-3e), 3.76 (s, 3H, MeO), 4.15 (m, 3H, H-5,6,9), 4.82 (broad d, 1H, H-9'), 5.20 (m, 2H, H-4,8), and 5.41 (broad s, 1H, H-7); GlcNAc unit δ 0.91 (m, 2H, $Me_3Si\underline{CH_2}CH_2$), 3.59-4.02 (m, 2H, $Me_3SiCH_2\underline{CH_2}$), 3.61 (m, 2H, H-6,6'), 4.04 (ddd, 1H, $J_{4,5}$ = 9.9 Hz, $J_{5,6}$ = 9.7 Hz, H-5), 4.07 (dd, 1H, $J_{1,2}$ = 8.4 Hz, $J_{2,3}$ = 10.3 Hz, H-2), 4.77 (d, 1H, H-1), 5.33 (t, 1H,

$J_{3,4}$ = 9.9 Hz, H-4), 5.54 (dd, 1H, H-3), and 7.38-8.02 (m, 5H, Ph); other groups δ 1.81, 1.85 (2s, 6H, 2AcN), 1.92, 1.99, 2.01, 2.06, and 2.12 (5s, 15H, 5AcO)

Found: 53.49; H, 6.53; N, 2.92.

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→6)-2-acetamido-3-O-benzyl-2-deoxy-β-D-galactopyranoside (17) and 2-(Trimethylsilyl)ethyl O-(Methyl 5-Acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-β-D-galacto-2-nonulopyranosylonate)-(2→6)-2-acetamido-3-O-benzyl-2-deoxy-β-D-galactopyranoside (23). Glycosylation of 9 (206 mg, 0.5 mmol) with 12 (521 mg, 1.0 mmol) in dry acetonitrile (5 mL) using DMTST (2.0 g, 4 mmol) in the presence of MS-3A (500 mg) as described for 13, afforded compound 17 (281 mg, 63.4%) and 23 (60 mg, 13.6%) as an amorphous mass, respectively.

Compound 17 had $[\alpha]_D$ -25.7° (c 0.28, chloroform); ^{1}H NMR ($CDCl_3$) Neu5Ac unit δ 2.61 (dd, 1H, $J_{3a,3e}$ = 13.2 Hz, $J_{3e,4}$ = 4.3 Hz, H-3e), 3.50-4.19 (m, 3H, H-5,6,9), 3.82 (s, 3H, MeO), 4.38 (dd, 1H, $J_{8,9'}$ = 2.2 Hz, $J_{9,9'}$ = 12.8 Hz, H-9'), 4.90 (ddd, 1H, $J_{3a,4}$ = 10.5 Hz, $J_{4,5}$ = 8.1 Hz, H-4), 5.25-5.39 (m, 2H, H-7,8); GalNAc unit δ 0.88 (m, 2H, $Me_3Si\underline{CH_2}CH_2$), 3.38-3.57 (m, 2H, H-5, one proton in $Me_3SiCH_2\underline{CH_2}$), 3.47 (t, 1H, $J_{1,2}$ = $J_{2,3}$ = 9.2 Hz, H-2), 3.64-4.19 (m, 5H, H-3,4,6,6', and one proton in $Me_3SiCH_2\underline{CH_2}$), 4.53 (d 1H, H-1), 7.34 (s, 5H, Ph); other groups δ 1.82, 1.88 (2s, 6H, 2AcN), 2.02, 2.04, 2.12, 2.14 (4s, 12H, 4AcO) and 5.35, 5.84 (2d, 2H, 2NH).

Anal. Calcd for $C_{40}H_{60}N_2O_{18}Si$ (885.0): C, 54.29; H, 6.83; N, 3.17. Found: C, 54.15; H, 6.99; N, 3.06.

Compound 23 had $[\alpha]_D$ -7.0° (c 0.4, chloroform); ^{1}H NMR ($CDCl_3$) Neu5Ac unit δ 2.49 (dd, 1H, $J_{3a,3e}$ = 12.5 Hz, $J_{3e,4}$ = 4.4 Hz, H-3e), 3.83 (s, 3H, MeO), 4.03-4.24 (m, 3H, H-5,6,9), 4.31 (dd, 1H, $J_{8,9'}$ = 2.9 Hz, $J_{9,9'}$ = 8.1 Hz, H-9'), 5.00 (m, 1H, H-5), 5.30 (m, 1H, H-4), 5.35 (m, 2H, H-7,8); GalNAc unit δ 0.92 (m, 2H, $Me_3Si\underline{CH_2}CH_2$), 3.28-3.64 (m, 3H, H-5,6', one proton in $Me_3SiCH_2\underline{CH_2}$), 3.88 (m, 2H, H-6,6'), 3.95 (m, 1H, one proton in $Me_3SiCH_2\underline{CH_2}$), and 4.72 (d, 1H, $J_{1,2}$ = 11.0 Hz, H-1), and 7.34 (s, 5H, Ph); other groups δ 1.90, 1.93 (2s, 6H, 2AcN), 2.03, 2.04, 2.08, 2.16 (4s, 12H, 4AcO), and 5.48, 5.97 (2d, 2H, 2NH).

Found: C, 54.18; H, 6.99; N, 3.24.

A sample of 17 (35 mg, 0.04 mmol) was acetylated as described for 16, to give 18 (36 mg, quantitative) as an amorphous mass: $[\alpha]_D$ -3.5° (c 1.2, chloroform); ^{1}H NMR ($CDCl_3$) Neu5Ac unit δ 2.59 (dd, 1H, $J_{3a,3e}$ = 12.8 Hz, $J_{3e,4}$ = 4.8 Hz, H-3e), 3.45 (q, 1H, H-5), 3.80 (s, 3H, MeO), 3.88-4.09 (m, 2H, H-6,9), 4.18 (dd, 1H, $J_{8,9'}$ = 3.3 Hz, $J_{9,9'}$ = 10.6 Hz, H-9'), 4.90 (m, 1H, $J_{3a,4}$ = 10.0 Hz, $J_{4,5}$ = 8.4 Hz, H-4), 5.27 (ddd, $J_{7,8}$ = 9.9 Hz, H-8), and 5.35 (m, 1H, H-7); GalNAc unit δ 0.90 (m, 2H, $Me_3Si\underline{CH_2}CH_2$), 3.39-3.64 (m, 2H, H-5, one proton in $Me_3SiCH_2\underline{CH_2}$), 3.88-4.09 (m, 4H, H-2,3,6,6'), 4.35 (d, 1H, $J_{1,2}$ = 10.6 Hz, H-1), 4.74, 4.89 (2d, 2H, J_{gem} = 11.0 Hz, $Ph\underline{CH_2}$), 5.62 (broad d, 1H, H-4), and 7.30 (s, 5H, Ph); other groups δ 1.88, 1.90 (2s, 6H, 2AcN), and 2.02 (2), 2.11 (2), 2.13 (5s, 15H, 5AcO).

Anal. Calcd for $C_{42}H_{62}N_2O_{19}Si$ (927.1): C, 54.52; H, 6.74; N, 3.02. Found: C, 54.55; H, 6.80; N, 3.14.

A sample of 23 (40 mg, 0.045 mmol) was acetylated with acetic anhydride (0.5 mL)-pyridine (1 mL) as described for 16, to give 24 (42 mg, quantitative) as an amorphous mass: $[\alpha]_D$ +1.5° (c 0.7, chloroform); ^{1}H NMR ($CDCl_3$) Neu5Ac unit δ 2.49 (dd, 1H, $J_{3a,3e}$ = 12.5 Hz, $J_{3e,4}$ = 4.4 Hz, H-3e), 3.82 (s, 3H, MeO), 3.96 (m, 1H, H-5), 4.32 (dd, 1H, $J_{8,9'}$ = 2.2 Hz, $J_{9,9'}$ = 11.4 Hz, H-9'), 5.08 (m, 1H, H-8), 5.33 (ddd, 1H, $J_{3a,4}$ = 11.2 Hz, $J_{4,5}$ = 9.9 Hz, H-4), and 5.37 (m, 1H, H-8); GalNAc unit δ 0.90 (m, 2H, $Me_3Si\underline{CH_2}CH_2$), 3.53-3.94 (m, 2H, $Me_3SiCH_2\underline{CH_2}$), 4.02 (dd, 1H, H-3), 4.22 (m, 1H, H-2), 4.38, 4.72 (2d, 2H, J_{gem} = 11.2 Hz, $Ph\underline{CH_2}$), 4.72 (d, 1H, $J_{1,2}$ = 9.8 Hz, H-1), and 5.38 (m, 1H, H-4), 7.33-7,38 (m, 5H, Ph); other groups δ 1.90, 1.93 (2s, 6H, 2AcN), and 2.03, 2.04, 2.08 (2), 2.16 (5s, 15H, 5AcO).

Found: C, 54.49; H, 6.79; N, 2.86.

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→6)-O-(2-O-acetyl-3-O-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-O-acetyl-β-D-glucopyranoside (25) and 2-(Trimethylsilyl)ethyl O-(Methyl 5-Acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-β-

D-galacto-2-nonulopyranosylonate)-(2→6)-O-(2-O-acetyl-3-O-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-O-acetyl-β-D-glucopyranoside (27). Glycosylation of 2-(trimethylsilyl)ethyl O-(2-O-acetyl-3-O-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-O-acetyl-β-D-glucopyranoside[12] (10, 275 mg, 0.41 mmol) with 12 (430 mg, 0.77 mmol) in dry acetonitrile (5 mL) at -15 - -20 °C using DMTST (1.5 g, 3 mmol) in the presence of MS-3A (500 mg), as described for 13, gave the α-glycoside 25 (238 mg, 51%) and the corresponding β-glycoside 27 (87 mg, 19%), respectively.

Compound 25 had $[\alpha]_D$ -16.7° (c 1.3, chloroform); ^{1}H NMR (CD_3OD) Neu5Ac unit δ 1.89 (s, 3H, AcN), 2.61 (dd, 1H, $J_{3a,3e}$ = 12.8 Hz, $J_{3e,4}$ = 4.4 Hz, H-3e), 3.82 (s, 3H, MeO), 4.04-4.18 (m, 3H, H-5,6,9), 4.87 (ddd, 1H, $J_{3a,4}$ = 11.5 Hz, $J_{4,5}$ = 8.1 Hz, H-4), 5.33 (m, 2H, H-7,8), and 5.40 (d, 1H, $J_{NH,5}$ = 9.5 Hz, NH); lactose unit δ 0.90 (m, 2H, $Me_3SiCH_2CH_2$), 3.92 (t, 1H, $J_{3,4} = J_{4,5}$ = 9.9 Hz, H-4), 4.36 (d, 1H, $J_{1,2}$ = 8.1 Hz, H-1), 4.48 (d, 1H, $J_{1',2'}$ = 8.2 Hz, H-1'), 4.51, 4.72 (2d, 2H, J_{gem} = 12.1 Hz, $PhCH_2$), 4.88 (dd, 1H, $J_{2,3}$ = 9.5 Hz, H-2), 5.09 (dd, 1H, $J_{2',3'}$ = 9.9 Hz, H-2'), 5.13 (dd, 1H, $J_{3,4}$ = 9.2 Hz, H-3), 7.28-7.39 (m, 5H, Ph); O-acetyl groups δ 2.01, 2.02, 2.03, 2.04 (2), 2.07, 2.14, 2.15 (8s, 24H, 8AcO).

Anal. Calcd for $C_{52}H_{75}NO_{27}Si$ (1174.3): C, 53.19; H, 6.44; N, 1.20. Found: C, 53.01; H, 6.54; N, 1.18.

Compound 27 had $[\alpha]_D$ -0.7° (c 1.5, chloroform); ^{1}H NMR ($CDCl_3$) Neu5Ac unit δ 1.88 (s, 3H, AcN), 2.50 (dd, 1H, $J_{3a.3e}$ = 12.5 Hz, $J_{3e,4}$ = 4.4 Hz, H-3e), 3.83 (s, 3H, MeO), 5.30 (m, 1H, H-4), 5.36 (broad s, 1H, H-7), 5.46 (m, 1H, H-8), 5.94 (m, 1H, $J_{NH,5}$ = 8.8. Hz, NH); lactose unit δ 0.90 (m, 2H, $Me_3SiCH_2CH_2$), 3.85, 3.92 (m, 2H, $Me_3SiCH_2CH_2$), 7.35 (s, 5H, Ph); O-acetyl groups δ 1.98, 2.02, 2.03, 2.04, 2.06, 2.08, 2.09, 2.15 (8s, 24H, 8AcO).

Found: C, 53.01; H, 6.62; N, 1.19.

A sample of compound 25 (70 mg, 0.06 mmol) was acetytated with acetic anhydride (0.5 mL)-pyridine (0.5 mL) as described for 16, to give 26 (63 mg, 87%) as an amorphous mass: $[\alpha]_D$ -0.6° (c 1.2, chloroform); ^{1}H NMR ($CDCl_3$) Neu5Ac unit δ 1.89 (s, 3H, AcN), 2.59 (dd, 1H, $J_{3a,3e}$ = 12.5 Hz, $H_{3e,4}$ = 4.5 Hz, H-3e), 3.82 (s, 3H, MeO),

4.14-4.17 (m, 3H, H-5,6,9), 4.37 (dd, 1H, $J_{8,9'}$ = 2.6 Hz, $J_{9,9'}$ = 12.1 Hz, H-9'), 4.87 (ddd, 1H, $J_{3a,4}$ = 9.5 Hz, $J_{4,5}$ = 7.7 Hz, H-4), 5.31 (m, 2H, H-7,8), 5.55 (d, 1H, NH); lactose unit δ 0.89 (m, 2H, $Me_3SiCH_2CH_2$), 3.35, 3.93 (2m, 2H, $Me_3SiCH_2CH_2$), 3.72-3.82 (2m, 2H, H-6,6'), 4.42 (d, 1H, $J_{1',2'}$ = 8.1 Hz, H-1'), 4.47 (d, 1H, $J_{1,2}$ = 7.7 Hz, H-1), 4.73 (2d, 2H, J_{gem} = 11.7 Hz, $PhCH_2$), 4.99 (dd, 1H, $J_{2',3'}$ = 10.3 Hz, H-2'), 5.18 (dd, 1H, $J_{2,3}$ = 9.5 Hz, $J_{3,4}$ = 9.2 Hz, H-3), 5.31 (broad s, 1H, H-4'), and 7.23-7.33 (m, 5H, Ph); O-acetyl groups δ 2.00, 2.03, 2.04 (2), 2.05, 2.06, 2.08, 2.14 (2) (9s, 27H, 9AcO).

Anal. Calcd for $C_{52}H_{77}NO_{28}Si$ (1216.3): C, 53.33; H, 6.38; N, 1.15. Found: C, 53.41; H, 6.36; N, 1.09.

A sample of 27 (35 mg, 0.03 mmol) was acetylated with acetic anhydride (0.5 mL)-pyridine (1 mL) as described for 16, to give 28 (35 mg, 97%) as an amorphous mass: $[\alpha]_D$ +1.1° (c 1.9, chloroform); ^1H NMR ($CDCl_3$) Neu5Ac unit δ 1.93 (s, 3H, AcN), 2.48 (dd, 1H, $J_{3a,3e}$ = 12.5 Hz, H-3e), 3.85 (s, 3H, MeO), 3.85-4.08 (m, 2H, H-5,9), 4.11 (dd, 1H, $J_{5,6}$ = 9.5 Hz, $J_{6,7}$ = 2.1 Hz, H-6), 4.42 (dd, 1H, $J_{8,9'}$ = 2.9 Hz, $J_{9,9'}$ = 12.5 Hz, H-9'), 5.25 (m, 1H, H-4),5.30 (m, 1H, H-8), 5.39 (broad s, 1H, H-7), 5.94 (d, 1H, $J_{NH,5}$ = 8.8 Hz, NH); lactose unit δ 0.91 (m, 2H, $Me_3SiCH_2CH_2$), 4.19 (t, 1H, $J_{2',3'} = J_{3',4'}$ = 10.3 Hz, H-3'), 4.48 (d, 1H, $J_{1,2}$ = 7.7 Hz, H-1), 4.69 (2d, 2H, J_{gem} = 11.7 Hz, $PhCH_2$), 4.83 (t, 1H, $J_{1,2} = J_{2,3}$ = 7.7 Hz, H-2), 5.08 (dd, 1H, $J_{1',2'}$ = 7.5 Hz, $J_{2',3'}$ = 8.5 Hz, H-2'), 5.16 (t, 1H, $J_{3,4}$ = 8.0 Hz, H-3), 5.33 (broad d, 1H, H-4'); O-acetyl groups δ 1.97, 2.00, 2.01, 2.02, 2.04, 2.05, 2.07, 2.08, 2.19 (9s, 27H, 9AcO).

Found: C, 53.44; H, 6.49; N, 1.21.

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→9)-(methyl 5-acetamido-4-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosid)onate (29) and 2-(Trimethylsilyl)ethyl O-(Methyl 5-Acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-β-D-galacto-2-nonulopyranosylonate)-(2→9)-(methyl 5-acetamido-4-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosid)onate (31). Glycosylation of 11 (340 mg, 0.73 mmol) with 12 (766 mg, 1.5

mmol) in dry acetonitrile (5 mL) in the presence of DMTST (2.0 g) and MS-3A (700 mg) as described for 13, gave the α-glycoside 29 (295 mg, 42.8%) and the β-glycoside 31 (165 mg, 23.9%) as an amorphous mass.

Compound 29 had $[\alpha]_D$ -25.2° (c 0.82, chloroform); ^{1}H NMR ($CDCl_3$) 0.87 (m, 2H, $Me_3Si\underline{CH_2}CH_2$), 1.86, 1.91 (2s, 6H, 2AcO), 2.02, 2.05, 2.08, 2.13, 2.14 (5s, 15H, 5AcO), 2.63 (dd, 1H, $J_{3a',3e'}$ = 12.6 Hz, $J_{3'e,4'}$ = 4.4.Hz, H-3'e), 2.70 (dd, 1H, $J_{3a,3e}$ = 12.6 Hz, $J_{3e,4}$ = 4.8 Hz, H-3e), 3.82, 3.85 (2s, 6H, 2MeO), 4.87-4.97 (m, 2H, H-4,4'), 5.30-5.43 (m, 2H, H-7',8').

Anal. Calcd for $C_{39}H_{62}N_2O_{22}Si$ (939.0): C, 49.88; H, 6.66; N, 2.98. Found: C, 49.61; H, 6.85; N, 2.84.

Compound 31 had $[\alpha]_D$ -22.6° (c 0.4, chloroform); ^{1}H NMR ($CDCl_3$) δ 0.87 (m, 2H, $Me_3Si\underline{CH_2}CH_2$), 1.88, 2.00 (2s, 6H, 2AcN), 2.03 (2), 2.10, 2.13, 2.15 (5s, 15H, 5AcO), 2.51 (dd, 1H, $J_{3'a,3'e}$ = 12.8 Hz, $J_{3'e,4'}$ = 4.8 Hz, H-3'e), 2.67 (dd, 1H, $J_{3a,3e}$ = 12.8 Hz, $J_{3e,4}$ = 4.8 Hz, H-3e), 3.79, 3.86 (2s, 6H, 2MeO), 4.76 (dd, 1H, H-9), 4.95 (dt, 1H, $J_{3a,4} = J_{4,5}$ = 10.3 Hz, H-4), 5.29-5.35 (m, 3H, H-4',8,8'), and 5.40 (broad s, 1H, H-7').

Found: C, 49.67; H, 6.81; N, 2.95.

A sample of 29 (380 mg, 0.4 mmol) was acetylated with acetic anhydride (4 mL)-pyridine (5 mL) as described for 16, to give 30 (411 mg, quantitative) as an amorphous mass: $[\alpha]_D$ -12.5° (c 0.56, chloroform); ^{1}H NMR ($CDCl_3$) δ 0.90 (m, 2H, $Me_3Si\underline{CH_2}CH_2$), 1.70, 1.88 (2s, 6H, 2AcN), 1.91, 2.03, 2.05, 2.07, 2.13, 2.15, 2.16 (7s, 21H, 7AcO), 2.56, 2.61 (2dd, 2H, H-3e, H-3'e), 3.80, 3.81 (2s, 6H, 2MeO), 4.87 (2m, 2H, H-4,4'), 5.28 (d, 1H, $J_{5,NH}$ = 8.4 Hz, NH), 5.30-5.43 (m, 5H, H-7,7',8,8', NH).

Anal. Calcd for $C_{43}H_{66}N_2O_{24}$ (1023.1): C, 50.48; H, 6.50; N, 2.74. Found: C, 50.24; H, 6.51; N,2.68.

A sample of 31 (130 mg, 0.14 mmol) was acetylated with acetic anhydride (0.5 mL)-pyridine (2 mL) as described for 16, to give 32 (133 mg, 94%) as an amorphous mass: $[\alpha]_D$ -21.6° (c 0.9, chloroform); ^{1}H NMR ($CDCl_3$) δ 0.90 (m, 2H, $Me_3Si\underline{CH_2}CH_2$), 1.90, 1.91 (2s, 6H, 2AcN), 2.01, 2.03, 2.10 (2), 2.15, 2.18, 2.19 (7s, 21H, 7AcO), 2.40,

(dd, 1H, H-3'e), 2.56 (dd, 1H, H-3e), 3.79, (2s, 6H, 2MeO), 4.86 (ddd, 1H, H-4), 5.10 (ddd, 1H, H-4'), 5.24-5.39 (m, 4H, H-7,7',8, 8'), 5.49, 5.82 (2d, 2H, $J_{5,NH}$ = 9.9 Hz, 2NH).

Found: C, 50.48; H, 6.69; N,2.69.

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