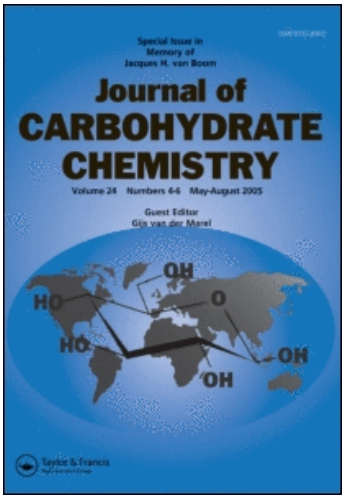

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Synthetic Studies on Sialoglycoconjugates 18: Synthesis of 7-O-, 7,9-Di-O-, and 7,8,9-Tri-O-Acetyl-N-Acetyl-Neuraminic Acid Derivatives

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SYNTHETIC STUDIES ON SIALOGLYCOCONJUGATES 18: SYNTHESIS OF 7-O-, 7,9-DI-O-, AND 7,8,9-TRI-O-ACETYL-N-ACETYL-NEURAMINIC ACID DERIVATIVES

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ABSTRACT

7-O-, 7,9-Di-O-, and 7,8,9-tri-O-acetyl derivatives of N-acetyl-neuraminic acid were synthesized starting from benzyl [2-(trimethylsilyl)-ethyl 5-acetamido-3,5-dideoxy-8,9-O-isopropylidene-D-glycero-α-D-galacto-2-nonulopyranosid]onate (1).

INTRODUCTION

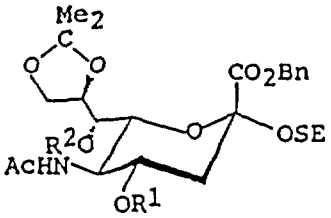
Sialic acids are essential constituents of many glycoproteins and glycolipids, and involved in a variety of the biological functions[1] of the sialoglycoconjugates. Recently,[2,3] it has been shown that influenza C virus utilizes 9-O-acetyl-sialic acids as the primary receptor determinant for attaching to cell surface receptors. In a previous paper[4] we described the synthesis of the partially O-acetylated N-acetylneuraminic acids. To continue the investigation aimed at elucidating the role of the O-acetyl group at the sialic acid moiety of the ganglioside molecule for biological functions, we report here the synthesis of the 7-O-, 7,9-di-O-, and 7,8,9-tri-O-acetyl-sialic acid derivatives.

RESULTS AND DISCUSSION

Treatment of benzyl [2-(trimethylsilyl)ethyl 5-acetamido-3,5-dideoxy-8,9-O-isopropylidene-D-glycero-α-D-galacto-2-nonulopyranosid]onate[4] (1) with t-butyldimethylsilyl chloride in pyridine gave the 4-O-t-butyldimethylsilyl derivative (3) quantitatively, which was acetylated to give 4. Hydrolysis of the 8,9-O-isopropylidene and 4-O-t-butyldimethylsilyl groups in compound 4 with 80% aqueous acetic acid afforded benzyl [2-(trimethylsilyl)ethyl 5-acetamido-7-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosid]onate (8) in 64% yield. Significant signals in the ^{1}H NMR spectrum of 8 were a one-proton doublet of doublets at δ 5.10 ($J_{6,7}$ = 1.0 Hz, $J_{7,8}$ = 9.2 Hz, H-7) and two sharp singlets, each integrating for three protons, at δ 2.07 and 2.16 which showed the presence of one N-acetyl and one O-acetyl group; other ^{1}H NMR data are consistent with structure 8.

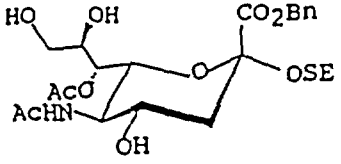
When treated with chloroacetic anhydride in pyridine at -40 °C, compound 1 gave the 4-O-chloroacetyl derivative 5 in 90% yield, which was acetylated to 6. There were three significant signals in the ^{1}H NMR spectrum of 5, two three-proton singlets at δ1.38 and 1.47 (Me_2C), a three-proton singlet at δ 2.06 (N-acetyl), and a one-proton doublet of triplets at δ 5.17 ($J_{3a,4} = J_{4,5}$ = 10.6 Hz, $J_{3e,4}$ = 5.1 Hz, H-4), indicating the structure assigned.

Treatment of 1 with 2-(trimethylsilyl)ethoxymethyl chloride in dichloromethane in the presence of N,N-diisopropylethylamine afforded the 4-O-SEM derivative 7 in 87% yield, which was used for the preparation of 7,8,9-tri-O-acetyl-N-acetylneuraminic acid derivatives. O-Deisopropylidenation of compounds 5-7 by mild, acid hydrolysis gave 9, 11, and 13 in good yields, respectively. The structures of compounds 9, 11, and 13 were unambiguously proved by 270-MHz ^{1}H NMR spectroscopy. Acetylation of 9 gave the 7,8,9-tri-O-acetyl derivative 10, which could be used as the glycosyl donor for the synthesis of 7,8,9-tri-O-acetyl-sialyl glycoconjugates after conversion[5,6] of the 2-(trimethylsilyl)ethoxy group to the S-methyl group. Selective 9-O-acetylation of 11 with acetyl chloride in pyridine-dichloromethane at -40 °C gave the 7,9-di-O-acetyl derivative 12 in 84% yield. Acetylation of 13 gave the 7,8,9-tri-O-acetyl derivative 14, which was converted, *via* selective removal[7] of the 2-(trimethylsilyl) ethyl and 2-(trimethylsilyl)ethoxymethyl groups by treatment with boron

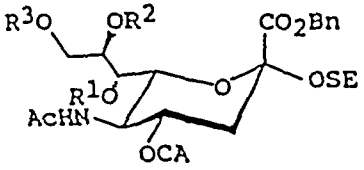


1 $R^1=R^2=H$
2 $R^1=R^2=Ac$
3 $R^1=TBDMS, R^2=H$
4 $R^1=TBDMS, R^2=Ac$
5 $R^1=CA, R^2=H$
6 $R^1=CA, R^2=Ac$
7 $R^1=SEM, R^2=H$

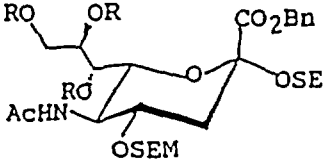
Bn=benzyl
SE=$Me_3SiCH_2CH_2$-
TBDMS=$Me_3C(Me)_2Si$-
CA=$ClCH_2CO$-
SEM=$Me_3SiCH_2CH_2OCH_2$-



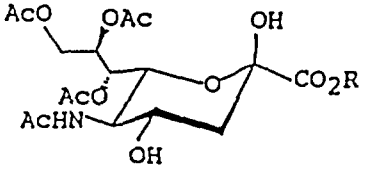
8



9 $R^1=R^2=R^3=H$
10 $R^1=R^2=R^3=Ac$
11 $R^1=Ac, R^2=R^3=H$
12 $R^1=R^3=Ac, R^2=H$



13 R=H
14 R=Ac



15 R=Bn
16 R=H

trifluoride etherate in dichloromethane for 8 h at 0 °C and subsequent hydrogenolytic removal of the benzyl group into 5-acetamido-7,8,9-tri-O-acetyl-3,5-dideoxy-D-glycero-ß-D-galacto-2-nonulopyranosonic acid (16) in good yield.

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 at 25 °C, and IR spectra were recorded with a JASCO A-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.

Benzyl [2-(Trimethylsilyl)ethyl 5-Acetamido-4,7-di-O-acetyl-8,9-O-isopropylidene-D-glycero-α-D-galacto-2-nonulopyranosid]onate (2). To a solution of benzyl [2-(trimethylsilyl)ethyl 5-acetamido-3,5-dideoxy-8,9-O-isopropylidene-D-glycero-α-D-galacto-2-nonulopyranosid]onate[4] (1; 400 mg, 0.74 mmol) in pyridine (5 mL) was added acetic anhydride (3 mL), and the mixture was kept overnight at room temperature, and concentrated to a syrup, which was chromatographed on a column of silica gel (60 g) with 100:1 dichloromethane-methanol to give 2 (445 mg, 96%) as an amorphous mass: $[\alpha]_D$ -20.5° (c 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 0.87 (m, 2H, $Me_3SiCH_2CH_2$), 1.32, 1.34 (2s, 6H, Me_2C), 1.90 (s, 3H, AcN), 2.05, 2.15 (2s, 6H, 2AcO), 2.71 (dd, 1H, $J_{3a,3e}$ = 12.8 Hz, $J_{3e,4}$ = 4.9 Hz, H-3e), 3.40, 3.79 (2m, 2H, $Me_3SiCH_2CH_2$), 3.85 (dd, 1H, $J_{5,6}$ = 10.3 Hz, $J_{6,7}$ = 2.2 Hz, H-6), 3.96-4.08 (m, 3H, H-5,9,9'), 4.26 (td, 1H, $J_{8,9'}$ = 2.9 Hz, H-8), 4.94 (ddd, 1H, $J_{4,5}$ = 10.3 Hz, H-4), 5.23, 5.30 (2d, 2H, J_{gem} = 11.9 Hz, $PhCH_2$), 5.29 (d, 1H, $J_{NH,5}$ = 9.7 Hz, NH), 5.43 (dd, 1H, $J_{7,8}$ = 8.5 Hz, H-7), and 7.41 (s, 5H, Ph).

Anal. Calcd for $C_{30}H_{45}NO_{11}Si$ (623.8): C, 57.77; H, 7.27; N, 2.25. Found: C, 57.69; H, 7.30; N, 2.14.

Benzyl [2-(Trimethylsilyl)ethyl 5-Acetamido-4-O-t-butyldimethylsilyl-3,5-dideoxy-8,9-O-isopropylidene-D-glycero-α-D-galacto-2-nonulopyranosid]onate (3). To a solution of 1 (300 mg, 0.56 mmol) in pyridine (7 mL), cooled to -10 °C, was added, with stirring, t-butyldimethylsilyl chloride (500 mg), and the mixture was stirred for 3 days at room temperature.

Methanol (1 mL) was added to the mixture and this was stirred for 1 h at room temperature, and concentrated. The residue was chromatographed on a column of silica gel (50 g) with 100:1 dichloromethane-methanol, to give 3 (360 mg, quantitative) as a syrup: $[\alpha]_D$ +1.2° (c 0.37, chloroform); IR (film) 3600-3350 (OH, NH), 1740 and 1250 (ester), 1640 and 1550 (amide), 830 (TMS), and 690 cm^{-1} (Ph); ^1H NMR ($CDCl_3$) δ 0.89 (m, 11H, $Me_3Si\underline{CH_2}CH_2$, Me_3CSi), 1.37, 1.45 (2s, 6H, Me_2C), 1.84 (dd, 1H, $J_{3a,3e}$ = 12.8 Hz, $J_{3a,4}$ = 11.3 Hz, H-3a), 2.04 (s, 3H, AcN), 2.67 (dd, 1H, $J_{3e,4}$ = 4.5 Hz, H-3e), 4.13 (m, 2H, H-5,9), 4.28 (q, 1H, H-8), 5.22 (d, 1H, $J_{NH,5}$ = 8.4 Hz, NH), 5.18, 5.36 (2d, 2H, J_{gem} = 11.9 Hz, $Ph\underline{CH_2}$), and 7.39-7.45 (m, 5H, Ph).

Anal. Calcd for $C_{32}H_{55}NO_9Si_2$ (654.0): C, 58.77; H, 8.48; N, 2.14. Found: C, 58.76; H, 8.62; N, 2.08.

Benzyl [2-(Trimethylsilyl)ethyl 5-Acetamido-7-O-acetyl-4-O-t-butyldimethylsilyl-3,5-dideoxy-8,9-O-isopropylidene-D-glycero-α-D-galacto-2-nonulopyranosid]onate (4). Acetylation of 3 (360 mg, 0.55 mmol) with acetic anhydride (2 mL) in pyridine (6 mL) overnight at 40 °C, gave 4 (380 mg, quantitative) as a syrup: $[\alpha]_D$ +15.2° (c 2.0, chloroform); ^1H NMR ($CDCl_3$) δ 0.83 (m, 11H, $Me_3Si\underline{CH_2}CH_2$, Me_3CSi), 1.30, 1.33 (2s, 6H, Me_2C), 1.69 (t, 1H, $J_{3a,3e} = J_{3a,4}$ = 12.8 Hz, H-3a), 1.93 (s, 3H, AcN), 2.16 (s, 3H, AcO), 2.63 (dd, 1H, $J_{3e,4}$ = 4.8 Hz, H-3e), 3.18 (q, 1H, $J_{4,5} = J_{5,6} = J_{5,NH}$ = 9.3 Hz, H-5), 3.40, 3.79 (2m, 2H, $Me_3SiCH_2\underline{CH_2}$), 4.21 (td, 1H, $J_{7,8} = J_{8,9}$ = 7.4 Hz, $J_{8,9'}$ = 2.6 Hz, H-8), 5.23, 5.27 (2d, 2H, J_{gem} = 11.8 Hz, $Ph\underline{CH_2}$), 5.38 (d, 1H, NH), 5.45 (m, 1H, H-7), and 7.36-7.42 (m, 5H, Ph).

Anal. Calcd for $C_{34}H_{57}NO_{10}Si_2$ (696.0): C, 58.67; H, 8.26; N, 2.01. Found: C, 58.66; H, 8.40; N, 1.94.

Benzyl [2-(Trimethylsilyl)ethyl 5-Acetamido-4-O-chloroacetyl-3,5-dideoxy-8,9-O-isopropylidene-D-glycero-α-D-galacto-2-nonulopyranosid]onate (5). To a solution of 1 (400 mg, 0.74 mmol) in pyridine (1 mL) and dichloromethane (10 mL) was added molecular sieves 4A (MS-4A; 1.0 g), and the mixture was stirred for 3 h, and then cooled to -40 °C. A solution of chloroacetic anhydride (300 mg) in dry dichloromethane (3 mL) was added, with stirring, to the mixture at -40 °C; after 1 h, no starting material was detectable on TLC. The mixture was extracted with dichloromethane, and the extract was successively washed with 2M hydrochloric acid, water, dried (sodium sulfate), and concentrated to a syrup, which was chromatographed on a column of silica gel (60 g) with 2:3 ethyl acetate-hexane to

give 5 (410 mg, 89.7%) as a syrup: $[\alpha]_D$ -31.5° (c 0.6, chloroform); IR (film) 3600-3300 (OH, NH), 1760, 1740, and 1230 (ester), 1640 and 1560 (amide), 860 (Me_2C), 840 (TMS), and 700 cm^{-1} (Ph); ^1H NMR ($CDCl_3$) δ 0.87 (m, 2H, $Me_3SiCH_2CH_2$), 1.38, 1.47 (2s, 6H, Me_2C), 2.06 (s, 3H, AcN), 2.80 (dd, 1H, $J_{3a,3e}$ = 12.6 Hz, $J_{3e,4}$ = 5.1 Hz, H-3e), 3.51, 3.90 (2m, 2H, $Me_3SiCH_2CH_2$), 3.57 (dd, $J_{5,6}$ = 10.6 Hz, $J_{6,7}$ = 1.5 Hz, H-6), 4.01-4.32 (m, 6H, H-5,8,9,9', $ClCH_2CO$), 5.17 (td, 1H, $J_{3a,4}$ = $J_{4,5}$ = 10.6 Hz, H-4), 5.27, 5.37 (2d, 2H, J_{gem} = 11.9 Hz, $PhCH_2$), 6.15 (d, 1H, $J_{NH,5}$ = 8.1 Hz, NH), and 7.42-7.48 (m, 5H, Ph).

Anal. Calcd for $C_{28}H_{42}NO_{10}ClSi$ (616.2): C, 54.58; H, 6.87; N, 2.27. Found: C, 54.39; H, 6.99; N, 2.25.

Benzyl [2-(Trimethylsilyl)ethyl 5-Acetamido-7-O-acetyl-4-O-chloroacetyl-3,5-dideoxy-8,9-O-isopropylidene-D-glycero-α-D-galacto-2-nonulopyranosid]onate (6). Acetylation of 5 (200 mg, 0.32 mmol) with acetic anhydride-pyridine as described for 4, gave 6 (200 mg, 94%) as a syrup: $[\alpha]_D$ -22.7° (c 0.44, chloroform); ^1H NMR ($CDCl_3$) δ 0.86 (m, 2H, $Me_3SiCH_2CH_2$), 1.32, 1.34 (2s, 6H, Me_2C), 1.91 (s, 3H, AcN), 2.15 (s, 3H, AcO), 2.76 (dd, 1H, $J_{3a,3e}$ = 12.7 Hz, $J_{3e,4}$ = 4.9 Hz, H-3e), 3.41, 3.80 (2m, 2H, $Me_3SiCH_2CH_2$), 3.90 (dd, 1H, $J_{8,9}$ = 1.9 Hz, $J_{9,9'}$ = 10.7 Hz, H-9), 4.05 (s, 2H, $ClCH_2CO$), 4.26 (m, 1H, H-8), 5.07 (ddd, 1H, H-4), 5.24, 5.31 (2d, 2H, J_{gem} = 11.9 Hz, $PhCH_2$), 5.31 (d, 1H, $J_{NH,5}$ = 9.9 Hz, NH), 5.43 (near t, $J_{6,7}$ = $J_{7,8}$ = 2.9 Hz, H-7), and 7.41 (s, 5H, Ph).

Anal. Calcd for $C_{30}H_{44}NO_{11}ClSi$ (658.2): C, 54.74; H, 6.74; N, 2.13. Found: C, 54.73; H, 6.80; N, 2.12.

Benzyl [2-(trimethylsilyl)ethyl 5-Acetamido-3,5-dideoxy-8,9-O-isopropylidene-4-O-2-(trimethylsilyl)ethoxymethyl-D-glycero-α-D-galacto-2-nonulopyranosid]onate (7). To a stirred solution of 1 (330 mg, 0.61 mmol) in dry dichloromethane (5 mL), cooled to 0 °C, were added 2-(trimethylsilyl)ethoxymethyl chloride (263 mg, 1.6 mmol) and N,N-diisopropylethylamine (0.32 mL), and the mixture was stirred overnight at room temperature. After completion of the reaction, methanol (1 mL) was added to the mixture, and the mixture was stirred for 4 h at room temperature, and concentrated. The residue was dissolved in dichloromethane (50 mL) and the solution was successively washed with 2M hydrochloric acid, M sodium carbonate, and water, dried (sodium sulfate), and concentrated to a syrup, which was chromatographed on a column of silica gel (50 g) with 150:1 dichloromethane-methanol to give 7 (350 mg, 87%) as a syrup: $[\alpha]_D$ -39.0° (c 0.84, chloroform); ^1H NMR ($CDCl_3$) δ 0.94 (m, 4H, $2Me_3SiCH_2CH_2$), 1.36, 1.43 (2s, 6H,

Me_2C), 1.70 (t, 1H, $J_{3a,3e} = J_{3a,4} = 12.2$ Hz, H-3a), 2.00 (s, 3H, AcN), 2.92 (dd, 1H, $J_{3e,4} = 4.8$ Hz, H-3e), 4.58 (td, 1H, $J_{4,5} = 12.2$ Hz, H-4), 5.30 (2d, 2H, $J_{gem} = 12.3$ Hz, $PhCH_2$), 6.22 (d, 1H, $J_{NH,5} = 7.2$ Hz, NH), and 7.33-7.44 (m, 5H, Ph).

Anal. Calcd for $C_{32}H_{55}NO_{10}Si_2$ (658.0): C, 58.41; H, 8.43; N, 2.13. Found: C, 58.29; H, 8.44; N, 2.09.

Benzyl [2-(trimethylsilyl)ethyl 5-Acetamido-7-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosid]onate (8). A solution of 4 (380 mg, 0.55 mmol) in 80% aqueous acetic acid (15 mL) was heated overnight at 45 °C, and concentrated to a syrup, which was chromatographed on a column of silica gel (60 g) with 30:1 dichloromethane-methanol to give 8 (190 mg, 64.2%) as a syrup: $[\alpha]_D$ -11.0° (c 2.1, chloroform); ^1H NMR ($CDCl_3$) δ 0.86 (m, 2H, $Me_3SiCH_2CH_2$), 1.90 (t, 1H, $J_{3a,3e} = J_{3a,4} = 12.6$ Hz, H-3a), 2.07 (s, 3H, AcN), 2.16 (s, 3H, AcO), 2.84 (dd, 1H, $J_{3e,4} = 4.7$ Hz, H-3e), 3.33 (m, 1H, one proton in $Me_3SiCH_2CH_2$), 5.10 (dd, 1H, $J_{6,7} = 1.0$ Hz, $J_{7,8} = 9.2$ Hz, H-7), 5.27, 5.36 (2d, 2H, $J_{gem} = 12.1$ Hz, $PhCH_2$), and 7.42 (s, 5H, Ph).

Anal. Calcd for $C_{25}H_{39}NO_{10}Si$ (541.7): C, 55.44; H, 7.26; N, 2.59. Found: C, 55.39; H, 7.40; N, 2.58.

Benzyl [2-(Trimethylsilyl)ethyl 5-Acetamido-4-O-chloroacetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosid]onate (9). A solution of 5 (190 mg, 0.31 mmol) in 80% aqueous acetic acid (10 mL) was stirred overnight at room temperature, and concentrated to a syrup, which was chromatographed on a column of silica gel (30 g) with 30:1 chloroform-methanol to afford 9 (176 mg, quantitative) as an amorphous mass: $[\alpha]_D$ -34.2° (c 0.5, methanol); ^1H NMR (1:1 $CDCl_3$-CD_3OD) δ 0.85 (m, 2H, Me_3Si-CH_2CH_2), 2.00 (s, 3H, AcN), 2.90 (dd, 1H, $J_{3a,3e} = 12.8$ Hz, $J_{3e,4} = 4.9$ Hz, H-3e), 3.60 (dd, 1H, $J_{5,6} = 8.7$ Hz, $J_{6,7} = 1.6$ Hz, H-6), 3.73 (dd, 1H, $J_{8,9} = 6.1$ Hz, $J_{9,9'} = 12.2$ Hz, H-9), 4.17 (t, 1H, $J_{4,5} = J_{5,6} = 10.4$ Hz, H-5), 4.23 (s, 2H, $ClCH_2CO$), 5.09 (ddd, 1H, H-4), 5.36 (s, 2H, $PhCH_2$), and 7.40-7.86 (m, 5H, Ph).

Anal. Calcd for $C_{25}H_{38}NO_{10}ClSi$ (576.1): C, 52.12; H, 6.65; N, 2.43. Found: C, 52.00; H, 6.73; N, 2.28.

Benzyl [2-(Trimethylsilyl)ethyl 5-Acetamido-7,8,9-tri-O-acetyl-4-O-chloroacetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosid]onate (10). Acetylation of 9 (400 mg, 0.69 mmol) with acetic anhydride (3 mL)-

pyridine (5 mL) gave 10 (420 mg, 86%) as an amorphous mass: $[\alpha]_D$ -17.0° (c 0.7, chloroform); ^{1}H NMR ($CDCl_3$) δ 0.84 (m, 2H, $Me_3SiCH_2CH_2$), 1.91 (s, 3H, AcN), 2.06, 2.15, 2.16 (3s, 9H, 3AcO), 2.71 (dd, 1H, $J_{3a,3e}$ = 12.7 Hz, $J_{3e,4}$ = 4.6 Hz, H-3e), 3.26 , 3.86 (m, 2H, $Me_3SiCH_2CH_2$), 4.05 (s, 2H, $ClCH_2CO$), 4.33 (dd, 1H, $J_{8,9}$ = 2.2 Hz, $J_{9,9'}$ = 12.5 Hz, H-9), 4.92 (m, 1H, H-4), 5.25 (d, 1H, $J_{NH,5}$ = 10.4 Hz, NH), 5.26, 5.30 (2d, 2H, J_{gem} = 12.1 Hz, $PhCH_2$), 5.33-5.43 (m, 2H, H-7,8), and 7.40 (s, 5H, Ph).

Anal. Calcd for $C_{31}H_{44}NO_{11}ClSi$ (702.2): C, 53.02; H, 6.32; N, 1.99. Found: C, 53.11; H, 6.48; N, 2.03.

Benzyl [2-(Trimethylsilyl)ethyl 5-Acetamido-7-O-acetyl-4-O-chloroacetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosid]onate (11). A solution of 6 (130 mg, 0.2 mmol) in 80% aqueous acetic acid (5 mL) was stirred for 15 h at room temperature. The product was purified by chromatography on a column of silica gel (20 g) with 40:1 dichloromethane-methanol. Compound 11 (103 mg, 82%) had $[\alpha]_D$ -28.2° (c 2.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 0.86 (m, 2H, $Me_3SiCH_2CH_2$), 1.94 (s, 3H, AcN), 2.05 (t, 1H, $J_{3a,3e} = J_{3a,4}$ = 12.5 Hz, H-3a), 2.20 (s, 3H, AcO), 2.88 (dd, $J_{3e,4}$ = 4.9 Hz, H-3e), 3.34, 3.85 (2m, 2H, $Me_3SiCH_2CH_2$), 4.10 (s, 2H, $ClCH_2CO$), 4.33 (q, 1H, $J_{4,5} = J_{5,6} = J_{5,NH}$ = 10.3 Hz, H-5), 5.04 (ddd, 1H, H-4), 5.13 (dd, 1H, $J_{6,7}$ = 1.0 Hz, $J_{7,8}$ = 7.0 Hz, H-7), 5.27, 5.43 (2d, 2H, J_{gem} = 12.1 Hz, $PhCH_2$), 6.27 (d, 1H, NH), and 7.42-7.43 (m, 5H, Ph).

Anal. Calcd for $C_{27}H_{40}NO_{11}ClSi$ (618.2): C, 52.46; H, 6.52; N, 2.27. Found: C, 52.41; H, 6.79; N, 2.25.

Benzyl [2-(Trimethylsilyl)ethyl 5-Acetamido-7,9-di-O-acetyl-4-O-chloroacetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosid]onate (12). To a solution of 11 (97 mg, 0.16 mmol) in pyridine (1 mL) and dichloromethane (2 mL), cooled to -40 °C, was added dropwise, with stirring, a solution of acetyl chloride (0.012 mL) in dichloromethane (1 mL), and the mixture was stirred for 20 min at -40 °C; the progress of the reaction was monitored by TLC. Methanol (0.1 mL) was added to the mixture, the mixture was concentrated to a syrup, and then chromatographed on a column of silica gel (10 g) with 70:1 dichloromethane-methanol to give 12 (88 mg, 84%) as a syrup: $[\alpha]_D$ -26.5° (c 2.8, chloroform); ^{1}H NMR ($CDCl_3$) δ 0.85 (m, 2H, $Me_3SiCH_2CH_2$), 1.91 (s, 3H, AcN), 2.13, 2.15 (2s, 6H, 2AcO), 2.85 (dd, 1H, $J_{3a,3e}$ = 13.0 Hz, $J_{3e,4}$ = 4.9 Hz, H-3e), 3.34, 3.84 (2m, 2H, $Me_3SiCH_2CH_2$), 3.95 (dd, 1H, $J_{5,6}$ = 10.7 Hz, $J_{6,7}$ = 2.3 Hz, H-6), 4.24 (q, 1H,

$J_{4,5} = J_{5,6} = J_{5,NH} = 10.3$ Hz, H-5), 4.94 (ddd, 1H, H-4), 5.16 (dd, 1H, $J_{6,7} = 1.6$ Hz, $J_{7,8} = 6.4$ Hz, H-7), 5.27, 5.38 (2d, 2H, $J_{gem} = 11.9$ Hz, $PhCH_2$), 5.62 (d, 1H, NH), and 7.42 (s, 5H, Ph).

Anal. Calcd for $C_{29}H_{42}NO_{11}ClSi$ (660.2): C, 52.76; H, 6.41; N, 2.12. Found: C, 52.66; H, 6.35; N, 2.21.

Benzyl [2-(Trimethylsilyl)ethyl 5-Acetamido-3,5-dideoxy-4-O-2-(trimethylsilyl)ethoxymethyl-D-glycero-α-D-galacto-2-nonulopyranosid]onate (13). A solution of 7 (300 mg, 0.46 mmol) in 80% aqueous acetic acid (10 mL) was stirred for 24 h at room temperature, and concentrated to a syrup which was chromatographed on a column of silica gel (40 g) with 50:1 dichloromethane-methanol, to give 13 (210 mg, 73.2%) as a syrup: $[\alpha]_D$ +10.3° (c 0.4, chloroform); ^{1}H NMR (1:1 $CDCl_3$-CD_3OD) δ 0.93 (m, 4H, $2Me_3SiCH_2CH_2$), 1.89 (t, 1H, $J_{3a,3e} = J_{3a,4} = 12.4$ Hz, H-3a), 2.06 (s, 3H, AcN), 2.88 (dd, 1H, $J_{3e,4} = 4.8$ Hz, H-3e), 4.68, 4.73 (2d, 2H, $J_{gem} = 7.0$ Hz, OCH_2O), 5.31, 5.39 (2d, 2H, $J_{gem} = 12.0$ Hz, $PhCH_2$), and 7.38-7.45 (m, 5H, Ph).

Anal. Calcd for $C_{29}H_{51}NO_{10}Si_2$ (629.9): C, 55.30; H, 8.16; N, 2.22. Found: C, 55.18; H, 8.33; N, 2.14.

Benzyl [2-(Trimethylsilyl)ethyl 5-Acetamido-7,8,9-tri-O-acetyl-3,5-dideoxy-4-O-2-(trimethylsilyl)ethoxymethyl-D-glycero-α-D-galacto-2-nonulopyranosid]onate (14). Acetylation of 13 (160 mg, 0.25 mmol) with acetic anhydride (2 mL) in pyridine (4 mL) for 8 h at 40 °C gave 14 (180 mg, 94%) as a syrup: $[\alpha]_D$ +3.6° (c 0.67, chloroform); ^{1}H NMR (1:1 $CDCl_3$-CD_3OD) δ 0.84 (m, 4H, $2Me_3SiCH_2CH_2$), 1.90 (s, 3H, AcN), 2.02, 2.12, 2.13 (3s, 9H, 3AcO), 2.73 (dd, 1H, $J_{3a,3e} = 12.8$ Hz, $J_{3e,4} = 4.4$ Hz, H-3e), 3.27, 3.54, 3.66, 3.84 (4m, 4H, $2Me_3SiCH_2CH_2$), 4.12 (dd, 1H, $J_{8,9} = 5.6$ Hz, $J_{9,9'} = 12.5$ Hz, H-9), 4.18 (dd, 1H, $J_{5,6} = 9.6$ Hz, $J_{6,7} = 2.0$ Hz, H-6), 4.33 (dd, 1H, $J_{8,9'} = 2.6$ Hz, H-9'), 4.59, 4.66 (2d, 2H, $J_{gem} = 7.1$ Hz, OCH_2O), 5.21 (s, 2H, $PhCH_2$), 5.35 (m, 1H, H-8), 5.43 (dd, 1H, $J_{7,8} = 8.1$ Hz, H-7), and 7.39 (s, 5H, Ph).

Anal. Calcd for $C_{35}H_{57}NO_{13}Si_2$ (756.0): C, 55.60; H, 7.60; N, 1.85. Found: C, 55.48; H, 7.79; N, 1.89.

Benzyl 5-Acetamido-7,8,9-tri-O-acetyl-3,5-dideoxy-D-glycero-β-D-galacto-2-nonulopyranosonate (15). To a solution of 14 (170 mg, 0.22 mmol) in dry dichloromethane (8 mL) was added, with stirring, boron trifluoride etherate (200 mg) at 0 °C, and the mixture was stirred at 0 °C; after 8 h,

the starting material was not detectable on TLC. The mixture was treated with Amberlite IR-410 (OH^-) resin, and the solution was concentrated to a syrup, which was chromatographed on a column of silica gel (15 g) with 25:1 dichloromethane-methanol to give 15 (77 mg, 65.3%) as an amorphous mass: $[\alpha]_D$ +14.5° (c 1.5, chloroform); IR (KBr) 3700-3300 (OH, NH), 1750, 1250, and 1220 (ester), 1660 and 1550 (amide), and 730 and 690 cm^{-1} (Ph); ^1H NMR (1:1 $CDCl_3$-CD_3OD) δ 1.94 (s, 3H, AcN), 1.99, 2.05, 2.11 (3s, 9H, 3AcO), 2.29 (dd, 1H, $J_{3a,3e}$ = 12.9 Hz, $J_{3e,4}$ = 4.6 Hz, H-3e), 3.48 (t, 1H, $J_{4,5} = J_{5,6}$ = 10.3 Hz, H-5), 3.85 (td, 1H, $J_{3a,4}$ = 10.3 Hz, H-4), 3.99 (dd, 1H, $J_{8,9}$ = 8.2 Hz, $J_{9,9'}$ = 12.4 Hz, H-9), 4.12 (dd, 1H, $J_{6,7}$ = 2.0 Hz, H-6), 4.60 (dd, 1H, $J_{8,9'}$ = 2.3 Hz, H-9'), 5.17 (m, 1H, H-8), 5.24 (s, 2H, $PhCH_2$), 5.35 (dd, 1H, $J_{7,8}$ = 4.2 Hz, H-7), and 7.36 (s, 5H, Ph).

Anal. Calcd for $C_{24}H_{31}NO_{12}$ (525.5): C, 54.85; H, 5.94; N, 2.67. Found: C, 54.73; H, 5.98; N, 2.61.

5-Acetamido-7,8,9-tri-O-acetyl-3,5-dideoxy-D-glycero-β-D-galacto-2-nonulopyranosonic acid (16). Compound 15 (75 mg, 0.14 mmol) was dissolved in ethanol (6 mL), 10% Pd-C catalyst (60 mg) was added, and hydrogen was bubbled through the mixture as it was being stirred for 2 h at room temperature. The catalyst was filtered off, and the filtrate was concentrated below 25 °C, to give 16 (60 mg, 97%) as an amorphous mass: $[\alpha]_D$ +14.6° (c 0.56, 1:1 chloroform-methanol); IR (KBr) 3500-3250 (OH, NH), 1730 and 1220 (ester), 1700 (C=O), and 1650 and 1540 cm^{-1} (amide); ^1H NMR (CD_3OD) δ 1.91 (s, 3H, AcN), 2.00, 2.03, 2.09 (3s, 9H, 3AcO), 2.15 (dd, 1H, $J_{3a,3e}$ = 13.0 Hz, $J_{3e,4}$ = 4.6 Hz, H-3e), 4.12 (dd, 1H, $J_{8,9}$ = 7.0 Hz, $J_{9,9'}$ = 12.3 Hz, H-9), 4.49 (dd, 1H, $J_{8,9'}$ = 2.5 Hz, H-9'), 5.21 (m, 1H, H-8), and 5.38 (dd, 1H, $J_{6,7}$ = 2.3 Hz, $J_{7,8}$ = 5.4 Hz, H-7).

Anal. Calcd for $C_{17}H_{25}NO_{12}$ (435.4): C, 46.90; H, 5.79; N, 3.22. Found: C, 46.82; H, 5.93; N, 3.08.

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