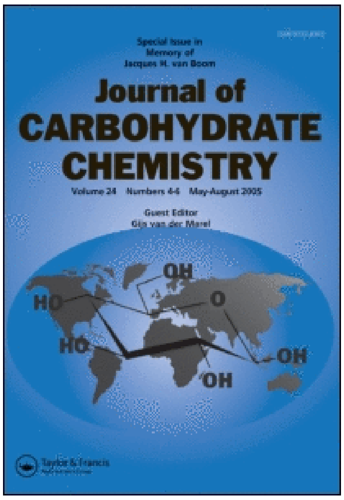

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Synthetic Studies on Sialoglycoconjugates 7: Synthesis of *N*-Acetylneuraminic Acid Derivatives and Analogs

Akira Hasegawa[a]; Minoru Morita[a]; Hideharu Ishida[a]; Makoto Kiso[a]
[a] Department of Applied Bioorganic Chemistry, Gifu University, Gifu, Japan

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SYNTHETIC STUDIES ON SIALOGLYCOCONJUGATES 7:
SYNTHESIS OF N-ACETYLNEURAMINIC ACID DERIVATIVES AND ANALOGS

Akira Hasegawa, Minoru Morita, Hideharu Ishida, and Makoto Kiso

Department of Applied Bioorganic Chemistry
Gifu University, Gifu 501-11, Japan

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ABSTRACT

Various types of the O-protected derivatives and the 9-bromo analogs of methyl [2-(trimethylsilyl)ethyl 5-acetamido-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosid]onate were synthesized from methyl [2-(trimethylsilyl)ethyl 5-acetamido-4,7-di-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosid]onate (1) or methyl [2-(trimethylsilyl)ethyl 5-acetamido-8,9-di-O-isopropylidene-D-glycero-α-D-galacto-2-nonulopyranosid]onate (3).

INTRODUCTION

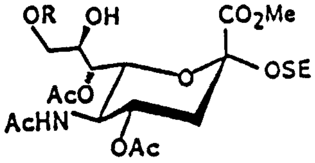
Recently, many kinds of biological functions[1-3] of sialoglycoconjugates such as gangliosides and glycoproteins have been revealed. In order to elucidate the structure-function relationship of gangliosides, synthesis of a variety of gangliosides and their various types of analogs are necessary. Naturally occuring sialo-compounds contain sialic acids in an α-glycosidic linkage[4] at the C-3 or C-6 position of galactose moiety, at C-6 of the glucose, N-acetylglucosamine or N-acetylgalactosamine moiety, and at the C-8 or C-9 position of the sialic acid skeleton.

In the previous papers, we have demonstrated the stereoselective and high yield syntheses of α-glycosides[5] and α-thioglycosides[6] of N-acetylneuraminic acid, and synthesized gangliosides GM_4[7] and its position isomer, GM_3,[8] and GM_4 thio-analog.[9] We describe here the synthesis of suitably protected sialic acid derivatives as the glycosyl acceptors, for obtaining α-Neu5Ac-(2→8)-Neu5Ac, α-Neu5Ac-(2→9)-Neu5Ac, and S-α-Neu5Ac-(2→9)-Neu5Ac.

RESULTS AND DISCUSSION

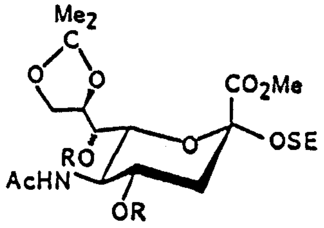
Treatment of methyl [2-(trimethylsilyl)ethyl 5-acetamido-4,7-di-*O*-acetyl-3,5-dideoxy-*D*-*glycero*-α-*D*-*galacto*-2-nonulopyranosid]onate[10] (**1**) with *tert*-butyldimethylsilyl chloride (TBDMS chloride) in pyridine at room temperature gave the 9-*O*-TBDMS derivative **2** in 97% yield as crystals. When reacted with benzyl chloromethyl ether or 2-(trimethylsilyl)ethoxymethyl chloride using *N*,*N*-diisopropylethylamine in dichloromethane at 45 °C, methyl [2-(trimethylsilyl)ethyl 5-acetamido-3,5-dideoxy-8,9-*O*-isopropylidene-*D*-*glycero*-α-*D*-*galacto*-2-nonulopyranosid]onate[10] (**3**) gave the 4,7-di-*O*-benzyloxymethyl derivative (**4**) or the 4,7-di-*O*-2-(trimethylsilyl) ethoxymethyl derivative (**5**) in high yield, respectively. *O*-Deisopropylidenation of compound **4** by mild, acid hydrolysis afforded **6** in good yield, which was converted by selective benzyloxymethylation to methyl [2-(trimethylsilyl)ethyl 5-acetamido-4,7,9-tri-*O*-benzyloxymethyl-3,5-dideoxy-*D*-*glycero*-α-*D*-*galacto*-2-nonulopyranosid]onate (**8**) in 66% yield. Compounds **6** and **8** were acetylated to **7** and **9**, respectively. The structures of compounds (**6**-**9**) were unambiguously proved by 270-MHz ^{1}H NMR spectroscopy. There were four significant signals in ^{1}H NMR spectrum of compound **7**, three three-proton singlets at δ 1.75 (*N*-acetyl), 2.05 and 2.06 (*O*-acetyl), and H-8 (ddd, $J_{7,8}$ = 7.3 Hz, $J_{8,9}$ = 5.4 Hz, $J_{8,9'}$ = 2.0 Hz) at δ 5.29. ^{1}H NMR of compounds (**6**, **8**, and **9**) are given in the Experimental Section and are consistent with structures assigned. When heated for one h at 45 °C in 90% aqueous acetic acid, compound **5** gave methyl [2-(trimethylsilyl)ethyl 5-acetamido-3,5-dideoxy-4,7-di-*O*-2-(trimethylsilyl)ethoxymethyl-*D*-*glycero*-α-*D*-*galacto*-2-nonulopyranosid]onate (**10**), which was acetylated to compound **11**. The ^{1}H NMR spectrum of **11** exhibited four sharp singlets, each integrating for three protons, at δ 1.95, 2.04, 2.09, and 3.75, which showed the presence of one *N*-acetyl, two *O*-acetyl, and one methyl ester group; H-8 appeared at δ 5.28 (ddd, $J_{7,8}$ = 7.7 Hz, $J_{8,9}$ = 4.8 Hz, $J_{8,9'}$ = 2.2 Hz).

Treatment of compound **10** with benzyl chloromethyl ether or *tert*-butyldimethylsilyl chloride gave the corresponding, desired 8-hydroxyl free derivatives (**12**,**13**) in high yields, respectively. On the other hand, when treated with *N*-bromosuccinimide in the presence of triphenylphosphine in *N*,*N*-dimethylformamide according to the procedure described by Hanessian et al.[11], compound **1** gave methyl [2-(trimethylsilyl)ethyl 5-acetamido-4,7-di-*O*-acetyl-9-bromo-3,5,9-trideoxy-*D*-*glycero*-α-*D*-*galacto*-2-nonulopyranosid]onate (**14**) as crystals in 82% yield, which was acetylated to compound **15**.

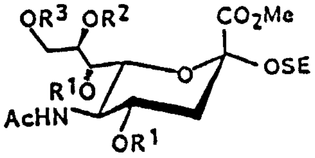


1 R = H
2 R = TBDMS

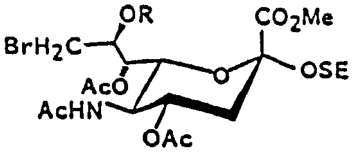
SE = $Me_3SiCH_2CH_2$-
TBDMS = $Me_3C(Me)_2Si$-



3 R = H
4 R = BOM
5 R = SEM
BOM = $C_6H_5CH_2OCH_2$-
SEM = $Me_3SiCH_2CH_2OCH_2$-



6 R^1 = BOM , R^2 = R^3 = H
7 R^1 = BOM , R^2 = R^3 = Ac
8 R^1 = R^3 = BOM , R^2 = H
9 R^1 = R^3 = BOM , R^2 = Ac
10 R^1 = SEM , R^2 = R^3 = H
11 R^1 = SEM , R^2 = R^3 = Ac
12 R^1 = SEM , R^2 = H , R^3 = BOM
13 R^1 = SEM , R^2 = H , R^3 = TBDMS



14 R = H
15 R = Ac

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 IRA-1 spectrophotometer. ^1H NMR spectra were recorded with a Jeol JNM-GX270 (270 MHz) spectrometer, and the NMR data were confirmed by use of decoupling techniques. Preparative chromatography was performed on silica gel (Waco Co.; 200 mesh) with the solvent systems specified. Concentrations and evaporations were conducted *in vacuo*.

Methyl [2-(Trimethylsilyl)ethyl 5-Acetamido-4,7-di-O-acetyl-9-O-tert-butyldimethylsilyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosid]onate (**2**). To a stirred solution of methyl [2-(trimethylsilyl)ethyl 5-acetamido-4,7-di-*O*-acetyl-3,5-dideoxy-*D*-*glycero*-α-*D*-*galacto*-2-nonulopyranosid]onate[10] (**1**; 507 mg, 1 mmol) in dry pyridine (3 mL) was added *tert*-butyldimethylsilyl chloride (302 mg, 2 mmol), and the mixture was stirred for one h at room temperature, and then methanol (1 mL) was added. The mixture was concentrated to a syrup which was extracted with dichloromethane. The extract was successively washed with 2 M hydrochloric acid, and water, dried (sodium sulfate), and concentrated to a syrup, which was chromatographed on a column of silica gel (50 g) using (a) dichloromethane, (b) 100:1, and (c) 60:1 dichloromethane-methanol as the eluants. Eluant (c) gave compound **3** (540 mg, 87%) as crystals. Recrystallization from ether-hexane gave needles: mp 117-119 °C, $[\alpha]_D$ -17° (*c* 1.0, chloroform); IR (KBr) 3550 (OH), 3200 (NH), 1750 and 1240 (ester), 1670 and 1550 (amide), and 840^{-1} (TMS); ^{1}H NMR (CDCl$_3$) δ 0.86-0.90 (m, 11H, Me$_3$Si$\underline{\text{CH}_2}$CH$_2$O), $\underline{\text{Me}_3}$CSi), 1.84 (s, 3H, AcN), 1.92 (dd, 1H, $J_{3a,3e}$ = 12.8 Hz, $J_{3a,4}$ = 11.7 Hz, H-3a), 2.01, 2.06 (2s, 6H, 2AcO), 2.63 (dd, 1H, $J_{3e,4}$ = 4.8 Hz, H-3e), 3.39, 3.82 (2q, 2H, J_{gem} = $J_{SiCH,CHO}$ = 7.7 Hz, Me$_3$CH$_2\underline{\text{CH}_2}$O), 3.52-3.61 (m, 2H, H-9,9'), 3.85 (s, 3H, MeO), 3.90 (dd, $J_{5,6}$ = 10.3 Hz, $J_{6,7}$ = 1.8 Hz, H-6), 4.07 (q, 1H, $J_{4,5}$ = $J_{5,6}$ = $J_{5,NH}$ = 10.3 Hz, H-5), 4.80 (ddd, 1H, H-4), 4.99 (dd, 1H, $J_{7,8}$ = 8.8 Hz, H-7), and 5.90 (d, 1H, NH).

Anal. Calcd for $C_{27}H_{50}NO_{11}Si_2$: C, 52.23; H, 8.11; N, 2.26. Found: C, 52.31; H, 8.06; N, 2.33.

Methyl [2-(Trimethylsilyl)ethyl 5-Acetamido-4,7-di-O-benzyloxymethyl-3,5-dideoxy-8,9-O-isopropylidene-D-glycero-α-D-galacto-2-nonulopyranosid]onate (**4**). To a stirred solution of methyl [2-(trimethylsilyl)ethyl 5-acetamido-3,5-dideoxy-8,9-O-isopropylidene-*D*-*glycero*-α-*D*-*galacto*-2-nonulopyranosid]onate[10] (**3**; 770 mg, 1.7 mmol) in dry dichloromethane (20 mL) were added benzyl chloromethyl ether (1.1 g, 7 mmol) and *N*,*N*-diisopropylethylamine (2.7 g), and the mixture was heated, with stirring, for 14 h at 45 °C (bath), and more benzyl chloromethyl ether (1.0 g) was added to the mixture. Stirring was continued for 12 h at the same temperature; the course of the reaction being monitored by TLC. Methanol (1 mL) was added to the solution, and the mixture was heated for 30 min at 45 °C, and cooled. Dichloromethane was added, and the solution successively washed with 2M hydrochloric acid, M sodium carbonate, and water, dried (sodium sulfate), and concentrated. The residue was chromatographed on a column of silica gel (70 g) with dichloromethane, and 120:1 dichloromethane-methanol. The latter eluant gave compound 4 (1.07 g, 91.5%) as a syrup: $[\alpha]_D$ -24.6° (*c* 0.75, chloroform); IR (film) 3300 (NH), 1750 and 1240 (ester), 1660 and 1550 (amide), 860 and 840 (TMS), and 740 and 700 cm^{-1} (Ph); ^1H NMR ($CDCl_3$) δ 0.87 (m, 2H, $Me_3Si\underline{CH_2}CH_2O$), 1.36, 1.39 (2s, 6H, Me_2C), 1.56 (s, 3H, AcN), 1.73 (dd, 1H, $J_{3a,3e}$ = 12.7 Hz, $J_{3a,4}$ = 12.2 Hz, H-3a), 2.82 (dd, 1H, $J_{3e,4}$ = 4.8 Hz, H-3e), 3.23 (ddd, $J_{4,5}$ = $J_{5,6}$ = 10.3 Hz, $J_{5,NH}$ = 7.1 Hz, H-5), 3.39, 3.82 (2q, 2H, J_{gem} = $J_{SiCH,CHO}$ = 8.1 Hz, $Me_3SiCH_2\underline{CH_2}O$), 4.47 (ddd, 1H, H-4), 5.70 (d, 1H, NH), and 7.14-7.40 (m, 10H, 2Ph).

Anal. Calcd for $C_{36}H_{53}NO_{11}Si$: C, 61.41; H, 7.59; N, 1.99. Found: C, 61.40; H, 7.73; N, 1.85.

Methyl [2-(Trimethylsilyl)ethyl 5-Acetamido-3,5-dideoxy-8,9-O-isopropylidene-4,7-di-O-2-(trimethylsilyl)ethoxymethyl-*D*-glycero-α-*D*-galacto-2-nonulopyranosid]onate (5). To a stirred solution of 3 (927 mg, 2 mmol) in dry dichloromethane (20 mL) were added 2-(trimethylsilyl)ethoxymethyl chloride (1.5 g, 8.8 mmol) and *N*,*N*-diisopropylethylamine (2.4 g), and the mixture was stirred for 14 h at 45 °C, and then more 2-(trimethylsilyl) ethoxymethyl chloride (500 mg) was added. The solution was heated, with stirring, for 2 h at 45 °C. After completion of the reaction, methanol (2 mL) was added to the mixture, and the mixture was heated for one h at 45 °C, and cooled. The mixture was extracted with dichloromethane (100 mL), and the extract 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 (100 g) with dichloromethane and then 120:1 dichloromethane-methanol as the eluants. The latter eluant gave compound 5 (1.12 g, 77%) as a syrup: $[\alpha]_D$ -23° (*c* 0.46, chloroform); IR (film) 3300 (NH), 1745 and 1250 (ester), 1660 and 1550 (amide), and 860 and 840 cm^{-1} (TMS, Me_2C); ^1H NMR ($CDCl_3$) δ 0.82-0.96 (m, 6H, $3Me_3Si\underline{CH_2}CH_2O$), 1.35, 1.38 (2s, 6H, Me_2C), 1.64 (dd, 1H, $J_{3a,3e}$ = 12.5 Hz, $J_{3a,4}$ = 11.4 Hz, H-3a), 1.92 (s, 3H, AcN), 2.81 (dd, 1H, $J_{3e,4}$ = 5.1 Hz, H-3e), 3.80 (s, 3H, MeO), 4.05-4.08 (m, 2H, H-9,9'), 4.48 (ddd, 1H, $J_{4,5}$ = 10.3 Hz, H-4), and 6.16 (d, 1H, $J_{NH,5}$ = 10.3 Hz, NH).

Anal. Calcd for $C_{32}H_{65}NO_{11}Si_3$: C, 53.07; H, 9.04; N, 1.93. Found: C, 53.14; H, 9.21; N, 1.95.

Methyl [2-(Trimethylsilyl)ethyl 5-Acetamido-4,7-di-O-benzyloxymethyl-*D*-glycero-α-*D*-galacto-2-nonulopyranosid]onate (6). A solution of 4 (620 mg, 0.88 mmol) in 80% aqueous acetic acid (20 mL) was heated for 1.5 h at 45 °C, and concentrated. The residue was chromatographed on a column of silica gel

(50 g) with (a) dichloromethane, (b) 100:1, and (c) 50:1 dichloromethane-methanol. Eluant (c) gave compound 6 (430 mg, 74%) as a syrup: $[\alpha]_D$ -0.9° (c 0.44, chloroform); IR (film) 3500 (OH), 3300 (NH), 1740 and 1230 (ester), 1660 and 1550 (amide), 860 and 840 (TMS), and 740 and 700 cm^{-1} (Ph); ^1H NMR ($CDCl_3$) δ 0.87 (t, 2H, $J_{gem} = J_{SiCH,CHO} = 8.1$ Hz, $Me_3SiCH_2CH_2O$), 1.73 (s, 3H, AcN), 1.83 (dd, 1H, $J_{3a,3e} = 12.9$ Hz, $J_{3a,4} = 11.7$ Hz, H-3a), 2.80 (dd, 1H, $J_{3e,4} = 4.9$ Hz, H-3e), 3.37 (q, 1H, $J_{gem} = J_{SiCH,CHO} = 8.1$ Hz, Me_3-$SiCH_2CH_2O$), 3.58 (q, 1H, $J_{4,5} = 9.8$ Hz, $J_{5,6} = 10.0$ Hz, H-5), 3.79 (s, 3H, MeO), 4.10 (near dd, 1H, $J_{6,7} = 1.7$ Hz, H-6), 4.17 (ddd, 1H, H-4), 4.51, 4.59, 4.66 (2), 4.69, 4.75, 4.83, and 4.88 (8d, 8H, $2PhCH_2OCH_2O$), 6.60 (broad d, 1H, NH), and 7.21-7.39 (m, 10H, 2Ph).

Anal. Calcd for $C_{33}H_{49}NO_{11}Si$: C, 59.71; H, 7.44; N, 2.11. Found: C, 59.55; H, 7.65; N, 2.08.

Methyl [2-(Trimethylsilyl)ethyl 5-Acetamido-8,9-di-O-acetyl-4,7-di-O-benzyloxymethyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosid]onate (7). Compound 6 (35 mg) was acetylated with acetic anhydride (0.5 mL) in pyridine (1 mL) in the usual way, to give 7 as a syrup quantitatively: $[\alpha]_D$ +2.3° (c 0.7, chloroform); IR (film) 3300 (NH), 1750 and 1240 (ester), 1660 and 1550 (amide), 860 and 840 (TMS), and 740 and 700 cm^{-1} (Ph); ^1H NMR ($CDCl_3$) δ 0.85 (m, 2H, $Me_3SiCH_2CH_2O$), 1.75 (s, 3H, AcN), 2.05, 2.06 (2s, 6H, 2AcO), 2.76 (dd, 1H, $J_{3a,3e} = 12.7$ Hz, $J_{3e,4} = 4.6$ Hz, H-3e), 3.31 (q, 1H, $J_{gem} = J_{SiCH,CHO} = 9.0$ Hz, $Me_3SiCH_2CH_2O$), 3.55 (ddd, 1H, $J_{4,5} = 10.3$ Hz, $J_{5,6} = 10.5$ Hz, $J_{5,NH} = 7.3$ Hz, H-5), 3.75 (s, 3H, MeO), 3.90 (dd, 1H, $J_{6,7} = 1.7$ Hz, $J_{7,8} = 7.3$ Hz, H-7), 4.14 (ddd, 1H, $J_{3a,4} = 11.7$ Hz, H-4), 4.22 (dd, 1H, $J_{8,9} = 5.4$ Hz, $J_{9,9'} = 12.2$ Hz, H-9), 4.24 (dd, 1H, $J_{8,9'} = 2.0$ Hz, H-8), 5.68 (d, 1H, NH), and 7.25-7.71 (m, 10H, 2Ph).

Anal. Calcd for $C_{37}H_{53}NO_{13}Si$: C, 59.42; H, 7.14; N, 1.87. Found: C, 59.31; H, 7.25; N, 1.95.

Methyl [2-(Trimethylsilyl)ethyl 5-Acetamido-4,7,9-tri-O-benzyloxymethyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosid]onate (8). To a stirred solution of 6 (663 mg, 1 mmol) in dry dichloromethane (10 mL) were added benzyl chloromethyl ether (235 mg, 1.5 mmol) and N,N-diisopropylethylamine (400 mg), and the stirring was continued for 12 h at room temperature. Benzyl chloromethyl ether (200 mg) and N,N-diisopropylethylamine (300 mg) were added to the solution, and the mixture was stirred for another 7 h at room temperature; methanol (1 mL) was added, and the solution was kept for 30 min at room temperature. Dichloromethane (100 mL) was added, and the solution successively washed with 2M hydrochloric acid, M sodium carbonate, and water, dried (sodium sulfate), and concentrated to leave a syrup, which was chromatographed on a column of silica gel (50 g) with (a) dichloromethane, (b) 150:1, and (c) 120:1 dichloromethane-methanol. Eluant (c) gave compound 8 (520 mg, 66%) as a syrup: $[\alpha]_D$ -8.5° (c 0.66, chloroform); IR (film) 3500 (OH), 3300 (NH), 1730 and 1240 (ester), 1660 and 1550 (amide), 860 and 840 (TMS), and 740 and 700 cm^{-1} (Ph); ^{1}H NMR ($CDCl_3$) δ 0.87 (t, 2H, J_{gem} = $J_{SiCH,CHO}$ = 7.8 Hz, $Me_3Si\underline{CH_2}CH_2O$), 1.73 (s, 3H, AcN), 1.85 (dd, 1H, $J_{3a,3e}$ = 12.7 Hz, $J_{3a,4}$ = 12.4 Hz, H-3a), 2.85 (dd, 1H, $J_{3e,4}$ = 4.6 Hz, H-3e), 3.38, 3.89 (2q, 2H, J_{gem} = $J_{SiCH,CHO}$ = 7.8 Hz, $Me_3SiCH_2\underline{CH_2}O$), 3.62 (ddd, 1H, $J_{4,5}$ = 10.0 Hz, $J_{5,6}$ = 10.7 Hz, $J_{5,NH}$ = 8.1 Hz, H-5), 3.80 (s, 3H, MeO), 4.00 (dd, 1H, $J_{6,7}$ = 2.7 Hz, H-6), 4.11 (ddd, 1H, $J_{7,8}$ = 7.8 Hz, $J_{8,9}$ = 2.7 Hz, $J_{8,9'}$ = 5.1 Hz, H-8), 4.16-4.28 (m, 2H, H-4,7), 4.51-4.91 (m, 12H, $3Ph\underline{CH_2}O\underline{CH_2}O$), 5.82 (d, 1H, NH), and 7.26-7.35 (m, 15H, 3Ph).

Anal. Calcd for $C_{41}H_{57}NO_{11}Si$: C, 62.81; H, 7.33; N, 1.79. Found: C, 62.63; H, 7.48; N, 1.77.

Methyl [2-(Trimethylsilyl)ethyl 5-Acetamido-8-O-acetyl-4,7,9-tri-O-benzyloxymethyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosid]onate (9). Acetylation of 8 (20 mg) with acetic anhydride (0.2 mL)-pyridine (0.5 mL), by heating for 3 h at 45 °C, gave 9 quantitatively: $[\alpha]_D$ -14.5° (c 0.5, chloroform); IR (film) 3300 (NH), 1750 and 1250 (ester), 1660 and 1550 (amide), 860 and 840 (TMS), and 740 and 700 cm^{-1} (Ph); ^{1}H NMR ($CDCl_3$) δ 0.84 (t, 2H, J_{gem} = $J_{SiCH,CHO}$ = 7.8 Hz, $Me_3Si\underline{CH_2}CH_2O$), 1.71 (s, 3H, AcN), 2.09 (s, 3H, AcO), 3.30, 3.88 (2q, 2H, J_{gem} = $J_{SiCH,CHO}$ = 7.8 Hz, Me_3SiCH_2-$\underline{CH_2}O$), 3.47 (ddd, 1H, $J_{4,5}$ = $J_{5,6}$ = 10.0 Hz, $J_{5,NH}$ = 7.8 Hz, H-5), 3.75 (s, 3H, MeO), 4.28-4.34 (m, 2H, H-4,6), 4.49-4.95 (m, 12H, $3Ph\underline{CH_2}O\underline{CH_2}O$), 5.26 (m, 1H, H-8), 5.68 (d, 1H, NH), and 7.25-7.38 (m, 15H, 3Ph).

Anal. Calcd for $C_{43}H_{59}NO_{13}Si$: C, 62.53; H, 7.20; N, 1.70. Found: C, 62.34; H, 7.35; N, 1.75.

Methyl [2-(Trimethylsilyl)ethyl 5-Acetamido-3,5-dideoxy-4,7-di-O-2-(trimethylsilyl)ethoxymethyl-D-glycero-α-D-galacto-2-nonulopyranosid]onate (10). A solution of 5 (1.15 g, 1.6 mmol) in 90% aqueous acetic acid (50 mL) was heated for one h at 45 °C, and concentrated to leave a syrup, which was chromatographed on a column of silica gel (100 g) using (a) dichloromethane, (b) 100:1, and (c) 40:1 dichloromethane-methanol as the eluants. Eluant (b) gave the starting material 5 (350 mg, 30%), and eluant (c) gave compound 10 (670 mg, 62%) as a syrup: $[\alpha]_D$ -2.0° (c 0.7, chloroform); IR (film) 3500 (OH), 3300 (NH), 1740 and 1250 (ester), 1660 and 1560 (amide), and 860 and 840 cm^{-1} (TMS); ^{1}H NMR ($CDCl_3$) δ 0.81-0.96 (m, 6H, $3Me_3Si\underline{CH_2}CH_2O$), 1.74 (dd, 1H, $J_{3a,3e}$ = 12.9 Hz, $J_{3a,4}$ = 12.5 Hz, H-3a), 1.93 (s, 3H, AcN), 2.70 (dd, 1H, $J_{3e,4}$ = 4.6 Hz, H-3e), 3.35 (q, 1H, J_{gem} = $J_{SiCH,CHO}$ = 7.8 Hz,

$Me_3SiCH_2CH_2O$), 3.82 (s, 3H, MeO), 3.47-3.97 (m, 12H, H-4-H-9', $Me_3SiCH_2CH_2O$), 4.63, 4.67 (2), 4.74 (4d, 4H, $2OCH_2O$), and 6.56 (d, 1H, $J_{NH,5}$ = 8.3 Hz, NH).

Anal. Calcd for $C_{29}H_{61}NO_{11}Si_3$: C, 50.91; H, 8.98; N, 2.05. Found: C, 51.15; H, 9.05; N, 2.13.

Methyl [2-(Trimethylsilyl)ethyl 5-Acetamido-8,9-di-O-acetyl-3,5-dideoxy-4,7-di-O-2-(trimethylsilyl)ethoxymethyl-D-glycero-α-D-galacto-2-nonulopyranosid]onate (11). Acetylation of 10 (30 mg) with acetic anhydride (0.2 mL)-pyridine (1 mL), by heating for 3 h at 45 °C, gave 11 as a syrup quantitatively: $[\alpha]_D$ -8.0° (c 0.8, chloroform); IR (film) 3280 (NH), 1750 and 1220 (ester), 1650 and 1550 (amide), and 860 and 840 cm^{-1} (TMS); ^1H NMR ($CDCl_3$) δ 0.77-0.98 (m, 6H, $3Me_3SiCH_2CH_2O$), 1.65 (t, 1H, $J_{3a,3e} = J_{3a,4}$ = 12.3 Hz, H-3a), 1.95 (s, 3H, AcN), 2.04, 2.09 (2s, 6H, 2AcO), 2.74 (dd, 1H, $J_{3e,4}$ = 4.4 Hz, H-3e), 3.75 (s, 3H, MeO), 4.16 (dd, 1H, $J_{8,9'}$ = 4.8 Hz, $J_{9,9'}$ = 12.5 Hz, H-9'), 4.25 (dd, 1H, $J_{5,6}$ = 10.6 Hz, $J_{6,7}$ = 1.5 Hz, H-6), 4.57 (dd, 1H, $J_{8,9}$ = 2.2 Hz, H-9), 4.63, 4.68 (2d, 2H, OCH_2O), 4.73 (s, 2H, OCH_2O), 5.28 (ddd, 1H, $J_{7,8}$ = 7.7 Hz, H-8), and 5.88 (d, 1H, $J_{NH,5}$ = 5.9 Hz, NH).

Anal. Calcd for $C_{33}H_{65}NO_{13}Si_3$: C, 51.60; H, 8.52; N, 1.82. Found: C, 51.65; H, 8.73; N, 1.70.

Methyl [2-(Trimethylsilyl)ethyl 5-Acetamido-9-O-benzyloxymethyl-3,5-dideoxy-4,7-di-O-2-(trimethylsilyl)ethoxymethyl-D-glycero-α-D-galacto-2-nonulopyranosid]onate (12). To a stirred solution of 10 (685 mg, 1 mmol) in dry dichloromethane (10 mL) were added benzyl chloromethyl ether (235 mg, 1.5 mmol) and N,N-diisopropylethylamine (400 mg), and the mixture was stirred for 24 h at room temperature; the course of the reaction being monitored by TLC. Methanol (1 mL) was added to the solution, and the mixture was stirred for one h to decompose the reagent. The extractive processing and column chromatography, as described for the preparation of 8, gave compound 12 (650 mg, 81%) as a syrup: $[\alpha]_D$ +0.1° (c 0.4, chloroform); IR (film) 3500 (OH), 3300 (NH), 1730 and 1240 (ester), 1660 and 1550 (amide), 860 and 840 (TMS), and 740 and 710 cm^{-1} (Ph); ^1H NMR ($CDCl_3$) δ 0.83-0.97 (m, 6H, $3Me_3SiCH_2CH_2O$), 1.74 (t, 1H, $J_{3a,3e} = J_{3a,4}$ = 12.7 Hz, H-3a), 1.95 (s, 3H, AcN), 2.77 (dd, 1H, $J_{3e,4}$ = 4.9 Hz, H-3e), 3.84 (s, 3H, MeO), 3.33-4.22 (m, 13H, H-4-H-9', $3Me_3SiCH_2CH_2O$), 4.58-4.81 (m, 8H, $2OCH_2O$, $PhCH_2OCH_2O$), 6.29 (d, 1H, $J_{NH,5}$ = 7.8 Hz, NH), and 7.24-7.35 (m, 5H, Ph).

Anal. Calcd for $C_{37}H_{69}NO_{12}Si_3$: C, 55.26; H, 8.65; N, 1.74. Found: C, 55.10; H, 8.79; N, 1.70.

Methyl [2-(Trimethylsilyl)ethyl 5-Acetamido-9-O-tert-butyldimethylsilyl-3,5-dideoxy-4,7-di-O-2-(trimethylsilyl)ethoxymethyl-D-glycero-α-D-galacto-2-nonulopyranosid]onate (13). To a solution of 10 (570 mg, 0.83

mmol) in dry pyridine (6 mL) was added tert-butyldimethylsilyl chloride (253 mg, 1.68 mmol), and the mixture was stirred for 1.5 h at room temperature; methanol (1 mL) was added, and the solution was concentrated to a syrup which was extracted with dichloromethane. The extract was successively washed with 2M hydrochloric acid, M sodium carbonate, and water, dried (sodium sulfate), and evaporated to leave a syrup, which was chromatographed on a column of silica gel (50 g) with dichloromethane and then 100:1 dichloromethane-methanol. The latter eluant gave compound 13 (640 mg, 96%) as crystals: mp 92-94 °C, $[\alpha]_D$ -23.0° (c 0.8, chloroform); IR (KBr) 3540 (OH), 3290 (NH), 1730 and 1240 (ester), 1660 and 1560 (amide), and 860 and 840 cm^{-1} (TMS, Me_2Si); ^1H NMR ($CDCl_3$) δ 0.80-0.98 (m, 15H, $3Me_3Si\underline{CH_2}CH_2O$, Me_3C), 1.69 (dd, 1H, $J_{3a,3e}$ = 12.8 Hz, $J_{3a,4}$ = 11.7 Hz, H-3a), 1.88 (s, 3H, AcN), 2.80 (dd, 1H, $J_{3e,4}$ = 4.8 Hz, H-3e), 3.22-3.90 (m, 11H, H-5, H-7-H-9', C, 45.30; H, 6.38; N, 2.21.

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