Synthesis of the methyl thioglycosides of deoxy-*N*-acetylneuraminic acids for use as glycosyl donors *

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ABSTRACT

Methyl 2-thioglycoside derivatives of 4-, 7-, 8-, and 9-deoxy-N-acetylneuraminic acids have been prepared as glycosyl donors for the synthesis of sialoglycoconjates. Reduction of a (phenoxy)thiocarbonyl group, selectively introduced at the 4 position of methyl [2-(trimethylsilyl)ethyl 5-acetamido-3,5-dideoxy-8,9-O-isopropylidene-D-glycero- α -D-galacto-2-nonulopyranosid]onate (1), gave the 4-deoxy compound, which was transformed via O-deisopropylidenation, acetylation, selective removal of the 2-(trimethylsilyl)ethyl group, subsequent acetylation, and displacement of the 2-acetoxy group by a methylthio group, into methyl (methyl 5-acetamido-7,8,9-tri-O-acetyl-3,4,5-trideoxy-2-thio-D-manno-2nonulopyranosid)onate (17). Methyl [2-(trimethylsilyl)ethyl 5-acetamido-8,9-di-O-acetyl-4-O-benzoyl-3,5,7-trideoxy- α -D-galacto-2-nonulopyranosid]onate, prepared from 1 in five steps, and methyl [2-(trimethylsilyl)ethyl 5-acetamido-4,7,9-tri-O-acetyl-3,5,8-trideoxy- α -D-galacto-2-nonulopyranosid]onate, prepared from 1 in six steps, were converted via selective removal of the 2-(trimethylsilyl)ethyl group, O-acetylation, and displacement of the 2-acetoxy group by a methylthio group as described for 17, into the corresponding methyl 7- and 8-deoxy-2-thioglycosides. Reductive dechlorination of methyl [2-(trimethylsilyl)ethyl 5-acetamido-4,7-di-O-benzoyl-9-chloro-3,5,9-trideoxy-D-glycero- α -D-galacto-2-nonulopyranosid]onate, prepared from methyl [2-(trimethylsilyl)ethyl 5-acetamido-3,5-dideoxy-D-glycero- α p-galacto-2-nonulopyranosid onate by selective 9-O-tert-butyldimethylsilylation, benzoylation, removal of the 9-silyl group, and selective chlorination, gave a 9-deoxy compound. This was transformed, via O-debenzoylation, O-acetylation, selective removal of the 2-(trimethylsilyl)ethyl group, 2-O-acetylation, 2-chlorination, displacement with potassium thioacetate, selective S-deacetylation, and S-methylation, into the methyl 2-thio- α -glycoside of 9-deoxy-N-acetylneuraminic acid.

INTRODUCTION

Sialic $acids^{2-4}$ are well known as constituents of glycolipids of cell membranes and play important roles in biological systems. Recently, specific biological functions^{5,6} of gangliosides have been revealed. These naturally occuring sialoglycoconjugates contain sialic acid in α -glycosidic linkage.

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^{*} Synthetic Studies on Sialoglycoconjugates, Part 29. For Part 28, see ref. 1.

We have demonstrated ⁷ that the methyl thioglycosides of sialic acid are useful glycosyl donors, affording α -glycosides when activated by dimethyl(methylthio)-sulfonium triflate⁸ (DMTST) or *N*-iodosuccinimide-trifluoromethanesulfonic acid (NIS-TfOH)^{9,10} in acetonitrile, and we have synthesized¹¹ a variety of gangliosides and their analogs. As a part of our continuing studies on the preparation and structure-function relationships of gangliosides, we describe here the synthesis of the methyl 2-thioglycosides of 4-, 7-, 8-, and 9-deoxy-*N*-acetylneuraminic acids for use as glycosyl donors in generating α -glycosides. This work is directed toward clarifying the requirements for the hydroxyl groups of *N*-acetylneuraminic acid (Neu5Ac) in the biological functions of gangliosides.

RESULTS AND DISCUSSION

For the synthesis of the methyl 2-thioglycosides of four deoxy-*N*-acetylneuraminic acids, protected suitably for use as the glycosyl donors, we set out to prepare methyl [2-(trimethylsilyl)ethyl 5-acetamido-3,5-dideoxy-8,9-*O*-isopropylidene-4-*O*-(phenoxy)thiocarbonyl-D-glycero- α -D-galacto-2-nonulopyranosid]onate (2), methyl [2-(trimethylsilyl)ethyl 5-acetamido-4-*O*-benzoyl-3,5-dideoxy-8,9-*O*-isopropylidene-7-*O*-(phenoxy)thiocarbonyl-D-glycero- α -D-galacto-2-nonulopyranosid]onate (4), methyl [2-(trimethylsilyl)ethyl 5-acetamido-4,9-di-*O*-acetyl-3,5-dideoxy-8-*O*-(phenoxy)thiocarbonyl-D-glycero- α -D-galacto-2-nonulopyranosid]onate (13), and methyl [2-(trimethylsilyl)ethyl 5-acetamido-4,8-di-*O*-benzoyl-9-chloro-3,5,9-trideoxy-D-glycero- α -D-galacto-2-nonulopyranosid]onate (13), and methyl [2-(trimethylsilyl)ethyl 5-acetamido-4,8-di-*O*-benzoyl-9-chloro-3,5,9-trideoxy-D-glycero- α -D-galacto-2-nonulopyranosid]onate (26). We then planned to undertake reductive cleavage of these (phenoxy)thiocarbonyloxy derivatives, or reductive dehalogenation of the chloro derivative, to afford the corresponding deoxy compounds, and convert the appropriately derivatized intermediates by thiomethylation into the end products 17, 19, 21, and 32.

Treatment of methyl [2-(trimethylsilyl)ethyl 5-acetamido-3,5-dideoxy-8,9-O-isopropylidene-D-glycero- α -D-galacto-2-nonulopyranosid]onate¹² (1) with phenyl chlorothionoformate¹³ in pyridine-dichloromethane gave the 4-O-(phenoxy)thiocarbonyl derivative (2) quantitatively, which was reduced with tributyltin hydride in the presence of α, α' -azobis-isobutyronitrile (AIBN) to give the 4-deoxy compound (6) in 84% yield. Hydrolysis of the 8,9-O-isopropylidene group in 6 with aqueous 80% acetic acid, and subsequent O-acetylation gave 7 in 88% yield, and this on treatment with boron trifluoride etherate in dichloromethane and subsequent O-acetylation afforded methyl 5-acetamido-2,7,8,9-tetra-O-acetyl-3,4,5trideoxy-D-manno-2-nonulopyranosonate (16) in good yield. The replacement^{7b} of the anomeric acetoxy group in 16 with methylthio by stirring for 10 h at room temperature with trimethyl(methylthio)silane in dry dichloromethane in the presence of trimethylsilyl trifluoromethanesulfonate (TMS triflate) gave the methyl 2-thioglycoside (17) of 4-deoxy-Neu5Ac in 93% yield as a ~ 1:1 anomeric mixture.

In a similar way, when treated with phenyl chlorothionoformate in pyridine for 1 h at 60°, methyl [2-(trimethylsilyl)ethyl 5-acetamido-4-O-benzoyl-3,5-dideoxy-8,9-



SE = 2-(trimethylsilyl)ethyl Ipd = isopropylidene Bz = benzoyl

O-isopropylidene-D-glycero- α -D-galacto-2-nonulopyranosid]onate (3), derived from 1 by selective O-benzoylation, afforded the 7-O-(phenoxy)thiocarbonyl derivative (4). Reductive cleavage of the 7-(phenoxy)thiocarbonyloxy group as described for **6** gave the 7-deoxy-Neu5Ac derivative (8), and this was converted via O-deisopropylidenation, O-acetylation, selective removal of the 2-(trimethylsilyl)ethyl group, 2-O-acetylation (to give 18), and finally replacement of the 2-acetoxy group with methylthio in essentially the same way described for 17, into methyl (methyl 5-acetamido-8,9-di-O-acetyl-4-O-benzoyl-3,5,7-trideoxy-2-thio-D-galacto-2-nonulopyranosid)onate (19) as a ~ 1:1 anomeric mixture.

Selective 4-O-acetylation of 1 with acetyl chloride in pyridine, removal of the isopropylidene group from the resulting 5 with aqueous 80% acetic acid overnight at room temperature, and 9-O-acetylation of the deacetalated product 11 with acetyl chloride in pyridine-dichloromethane for 30 min at -45° , gave methyl [2-(trimethylsilyl)ethyl 5-acetamido-4,9-di-O-acetyl-3,5-dideoxy-D-glycero- α -D-galacto-2-nonulopyranosid]onate (12) in good yield. Treatment of 12 with phenyl chlorothionoformate in pyridine-dichloromethane at room temperature gave the 8-O-(phenoxy)thiocarbonyl derivative 13, and this on reductive cleavage and subsequent acetylation gave methyl [2(trimethylsilyl)ethyl 5-acetamido-4,7,9-tri-O-acetyl-



SE = 2-(trimethylsilyl)ethyl Bz = benzoyl TBDMS = tert-butyldimethylsilyl

3,5,8-trideoxy- α -D-galacto-2-nonulopyranosid]onate (15) in good yield; significant signals in the ¹H-NMR spectrum of 15 were five three proton singlets at δ 2.02 (*N*-acetyl), 2.05, 2.08, 2.10 (three *O*-acetyl), and 3.81 (COOMe), two one-proton doublets of doublets at δ 2.59 and 3.78 ($J_{3ax,3cq}$ 12.6, $J_{3cq,4}$ 4.8 Hz, H-3eq; $J_{5,6}$ 10.3, $J_{6,7}$ 2.0 Hz, H-6), a two-proton multiplet at δ 1.89–2.00 (H-8,8'), and two one-proton multiplets at δ 4.85 (H-4) and 5.08 (H-7), indicating the structure assigned. Compound 15 was transformed, via selective removal of the 2-(trimethyl-silyl)ethyl group, 2-*O*-acetylation, and replacement of the anomeric acetoxy group in 20 with methylthio as described for 17, into the 8-deoxy-Neu5Ac derivative 21 in high yield.

To get the methyl 2-thioglycoside (32) of 9-deoxy-Neu5Ac, methyl [2-(trimethylsilyl)ethyl 5-acetamido-3,5-dideoxy-D-glycero- α -D-galacto-2-nonulopyranosid]onatc¹⁴ (22) was used as the starting material. Treatment of 22 with *tert*-butyldimethylsilyl chloride in pyridine for 2 h at 0° selectively gave the 9-O-tert-butyldimethylsilyl derivative 23 in 91% yield, which was further substituted to give the 4,8-di-O-benzoyl derivative 24. Hydrolysis of the 9-O-tert-butyldimethylsilyl group in 24 with aqueous 80% acetic acid afforded 25 quantitatively. When treated¹⁵ with carbon tetrachloride and triphenylphosphine in N,N-dimethylformamide (DMF), compound 25 gave the 9-chloro derivative 26 in good yield, and this was reduced¹⁶ with tributyltin hydride-AIBN in toluene to give the 9-deoxy-Neu5Ac derivative 27. O-Debenzoylation of 27 with sodium methoxide in methanol, and subsequent O-acetylation afforded methyl [2-(trimethylsilyl)ethyl 5-acetamido-4,7,8-tri-O-acetyl-3,5,9-trideoxy-D-glycero- α -D-galacto-2-nonulopyranosid]onate (28). The ¹H-NMR spectrum of 28 exhibited five sharp singlets, each integrating for three protons, at δ 1.86, 2.00, 2.08, 2.12, and 3.76, which showed the presence of one N-acetyl, three O-acetyl, and one methyl ester group; H-4 appeared at δ 4.80 (ddd), H-7 at δ 5.13 (dd, $J_{6.7}$ 1.8, $J_{7.8}$ 7.9 Hz), and H-8 at δ 5.19 (m), indicating the structure assigned. Selective removal of the 2-(trimethylsilyl)ethyl group in 28 as described for 16, followed by O-acetylation, gave 29, which was

further converted¹⁷ into the glycosyl chloride. Displacement by reaction with potassium thioacetate, selective S-deacetylation, and S-methylation gave methyl (methyl 5-acetamido-4,7,8-tri-O-acetyl-3,5,9-trideoxy-2-thio-D-glycero- α -D-galacto-2-nonulopyranosid)onate (**32**) in good yield.

The methyl 2-thioglycosides 17, 19, 21, and 32 of deoxy-Neu5Ac obtained here have been effectively used as glycosyl donors affording α -glycosides of sialic acids, as described in the immediately following paper¹⁸.

EXPERIMENTAL

General methods.—Optical rotations were determined with a Union PM-201 Polarimeter at 25° and IR spectra were recorded with a Jasco IRA-100 spectrophotometer. ¹H-NMR spectra were recorded at 270 MHz with a JEOL JNM-GX 270 spectrometer. Preparative chromatography was performed on silica gel (Wako Chemical Co., 200 mesh) with the solvent systems specified. Concentrations were conducted in vacuo.

Methyl [2-(trimethylsilyl)ethyl 5-acetamido-3,5-dideoxy-8,9-O-isopropylidene-4-O-(phenoxy)thiocarbonyl-D-glycero- α -D-galacto-2-nonulopyranosid]onate (2).—To a solution of methyl [2-(trimethylsilyl)ethyl 5-acetamido-3,5-dideoxy-8,9-O-isopropylidene-D-glycero- α -D-galacto-2-nonulopyranosid]onate¹² (1, 6.1 g, 13.2 mmol) in pyridine (50 mL) and CH₂Cl₂ (50 mL) was added, with stirring, phenyl chlorothionoformate (2 mL) at 0°, and stirring was continued for 7 h at 0°. Methanol (2 mL) was added to the mixture and it was concentrated and extracted with CH_2Cl_2 . The extract was successively washed with M HCl and water, dried (Na_2SO_4) , and concentrated. Column chromatography of the residue on silica gel (300 g) with 2:3 EtOAc-hexane gave 2 (7.7 g, 97.5%) as an amorphous mass, $[\alpha]_D = 94.6^\circ$ (c 1.4, CHCl₃); ¹H-NMR (CDCl₃): δ 0.89 (m, 2 H, Me₃SiCH₂CH₂), 1.36, 1.40 (2 s, 6 H, Me_2C), 2.00 (s, 3 H, AcN), 2.07 (t, 1 H, $J_{3ax,3eq} = J_{3ax,4} = 12.6$ Hz, H-3ax), 2.67 (dd, 1 H, J_{3eq,4} 5.1 Hz, H-3eq), 3.53 (dd, 1 H, J_{5.6} 10.4, J_{6.7} 2.4 Hz, H-6), 3.81 (s, 3 H, MeO), 4.05 (dd, 1 H, J_{8,9} 6.6, J_{9,9'} 8.4 Hz, H-9), 4.10 (q, 1 H, H-5), 4.23 (m, 1 H, $Me_3SiCH_2CH_2$, 4.33 (m, 1 H, H-8), 5.24 (ddd, 1 H, $J_{4.5}$ 10.6 Hz, H-4), 6.25 (d, 1 H, $J_{5 \text{ NH}}$ 8.1 Hz, NH), and 7.03–7.44 (m, 5 H, Ph).

Anal. Calcd for C₂₇H₄₁NO₁₀SSi (599.8): C, 54.07; H, 6.89; N, 2.34. Found: C, 53.86; H, 7.01; N, 2.36.

Methyl [2-(trimethylsilyl)ethyl 5-acetamido-4-O-benzoyl-3,5-dideoxy-8,9-O-isopropylidene-D-glycero- α -D-galacto-2-nonulopyranosid]onate (3).—To a stirred solution of 1 (5 g, 10.8 mmol) in pyridine (25 mL) and CH₂Cl₂ (100 mL), cooled to -5° , was added dropwise a cooled solution (-5°) of BzCl (2.1 mL) in CH₂Cl₂ (15 mL) during 30 min, and the mixture was stirred for 15 min at 0°. Methanol (1 mL) was added to the mixture, and the solution was evaporated to a syrup. This was dissolved in CH₂Cl₂ (100 mL), and the solution was successively washed with 2 M HCl and water, dried (Na₂SO₄), and then evaporated. The residue was chromatographed on a column of silica gel (200 g) with 1:1 EtOAc-hexane to give **3** (6.1 g, quantitative) as an amorphous mass, $[\alpha]_D - 38.0^\circ$ (*c* 0.1, CHCl₃); IR: ν 3700–3200 (OH, NH), 1730 and 1220 (ester), 1660 and 1550 (amide), 860 and 840 (Me₃Si, Me₂C), and 720 cm⁻¹ (Ph); ¹H-NMR (CDCl₃): δ 0.89 (m, 2 H, Me₃SiC- H_2 CH₂), 1.37, 1.41 (2 s, 6 H, Me₂C), 1.90 (s, 3 H, AcN), 2.10 (t, 1 H, $J_{3ax,3eq} = J_{3ax,4} = 12.6$ Hz, H-3ax), 2.76 (dd, 1 H, $J_{3eq,4}$ 5.0 Hz, H-3eq), 3.53 (dd, 1 H, $J_{5,6}$ 8.4, H-6), 3.81 (s, 3 H, MeO), 4.10 (m, 1 H, H-8), 4.10 (q, 1 H, H-5), 4.38 (m, 1 H, H-7), 5.24 (ddd, 1 H, $J_{4,5}$ 10.4 Hz, H-4), 6.13 (d, 1 H, $J_{5,NH}$ 7.9 Hz, NH), and 7.25–8.00 (m, 5 H, Ph).

Anal. Calcd for C₂₇H₄₁NO₁₀Si (567.7): C, 57.12; H, 7.28; N, 2.47. Found: C, 57.08; H, 7.41; N, 2.45.

Methyl [2-(trimethylsilyl)ethyl 5-acetamido-4-O-benzoyl-3,5-dideoxy-8,9-O-isopropylidene-7-O-(phenoxy)thiocarbonyl-D-glycero- α -D-galacto-2-nonulopyranosid/onate (4).—To a solution of 3 (3.05 g, 5.4 mmol) in pyridine (140 mL) was added phenyl chlorothionoformate (3.7 mL), and the mixture was heated for 1 h at 60°. After completion of the reaction, MeOH (1 mL) was added to the solution, and it was concentrated, then extracted with CH₂Cl₂ (200 mL). The extract was successively washed with 2 M HCl and water, dried (Na₂SO₄), and concentrated. Column chromatography (1:4 EtOAc-hexane) of the residue on silica gel (150 g) gave 4 (1.83 g, 48.5%) as an amorphous mass, $[\alpha]_{D} + 23.6^{\circ}$ (c 0.9, CHCl₃); ¹H-NMR (CDCl₃): δ 0.89 (m, 2 H, Me₃SiCH₂CH₂), 1.37, 1.43 (2 s, 6 H, Me₂C), 1.73 (s, 3 H, AcN), 2.10 (t, 1 H, $J_{3ax,3eq} = J_{3ax,4} = 12.6$ Hz, H-3ax), 2.81 (dd, 1 H, $J_{3ea,4}$ 4.8 Hz, H-3eq), 3.46 (m, 1 H, Me₃SiCH₂CH₂), 3.83 (s, 3 H, MeO), 4.08 (m, 1 H, $Me_3SiCH_2CH_2$, 4.20 (dd, 1 H, H-9), 4.24 (dd, 1 H, $J_{5,6}$ 10.6, $J_{6,7}$ 1.8 Hz, H-6), 4.28 (q, 1 H, $J_{4,5} = J_{5,\text{NH}} = 10.6$ Hz, H-5), 4.54 (m, 1 H, $J_{8,9}$ 6.6 Hz, H-8), 5.21 (m, 1 H, H-4), 5.52 (d, 1 H, NH), 6.20 (dd, 1 H, $J_{7.8}$ 2.9 Hz, H-7), and 7.18–8.00 (m, 10 H, 2 Ph).

Anal. Calcd for C₃₄H₄₅NO₁₁SSi (703.9): C, 58.01; H, 6.44; N, 1.99. Found: C, 58.05; H, 6.60; N, 1.82.

Methyl [2-(trimethylsilyl)ethyl 5-acetamido-4-O-acetyl-3,5-dideoxy-8,9-O-isopropylidene-D-glycero- α -D-galacto-2-nonulopyranosid]onate (5).—To a solution of 1 (3.5 g, 7.6 mmol) in pyridine (50 mL) and CH₂Cl₂ (30 mL), cooled to -35° , was added, with stirring, a cooled solution of acetyl chloride (1.8 mL) in CH₂Cl₂ (18 mL), and the mixture was stirred for 5 h. After completion of the reaction, MeOH (1 mL) was added to the mixture, and it was concentrated, then extracted with CH₂Cl₂ (200 mL). The extract was successively washed with 2 M HCl and water, dried (Na₂SO₄), and concentrated. Column chromatography (2:3 EtOAc-hexane) of the residue gave 5 (3.45 g, 90%) as an amorphous mass, [α]_D = -32.9° (*c* 1.8, CHCl₃); ¹H-NMR (CDCl₃): δ 0.89 (m, 2 H, Me₃SiCH₂CH₂), 1.37, 1.40 (2 s, 6 H, Me₂C), 1.95 (t, 1 H, J_{3ax,3eg} = J_{3ax,4} = 12.7 Hz, H-3ax), 1.97 (s, 3 H, AcN), 2.09 (s, 3 H, AcO), 2.63 (dd, 1 H, J_{3eq,4} 5.1 Hz, H-3eq), 3.43 (dd, 1 H, J_{5.6} 10.4 Hz, J_{6.7} 1.3 Hz, H-6), 3.51, 3.89 (2 m, 2 H, Me₃SiCH₂CH₂), 3.80 (s, 3 H, MeO), 3.92, 4.34 (2 dd, 2 H, J_{8,9} 2.4, J_{8,9}' 6.2, J_{9.9}' 12.5 Hz, H-9,9'), 3.94 (q, 1 H, J_{4.5} = J_{5.6} = J_{5.NH} = 10.4 Hz, H-5), 4.08 (m, 2 H, H-7,8), 5.00 (ddd, 1 H, H-4), and 6.02 (d, 1 H, NH). *Anal.* Calcd for C₂₂H₃₉NO₁₀Si (505.6): C, 52.25; H, 7.77; N, 2.77. Found: C, 52.10; H, 7.80; N, 2.84.

Methyl [2-(*trimethylsilyl*)*ethyl* 5-*acetamido*-8,9-O-*isopropylidene*-3,4,5-*trideoxy*- α -D-manno-2-*nonulopyranosid*]*onate* (6)—To a solution of 2 (1.0 g, 1.7 mmol) in toluene (50 mL) were added tributyltin hydride (2.0 mL) and AIBN (50 mg), and the mixture was stirred for 20 min at 100° then concentrated. Column chromatography of the residue on silica gel (50 g) with 110:1 CH₂Cl₂–MeOH gave 6 (650 mg, 84%) as an amorphous mass, $[\alpha]_D - 1.7^\circ$ (*c* 2.0, CHCl₃); IR: ν 3700–3200 (OH, NH), 1750 and 1230 (ester), 1660 and 1550 (amide), and 860 and 840 cm⁻¹ (Me₃Si, Me₂C); ¹H-NMR (CDCl₃): δ 0.87 (m, 2 H, Me₃SiCH₂CH₂), 1.38, 1.42 (2 s, 6 H, Me₂C), 1.40 (m, 1 H, H-4*ax*), 1.79 (ddd, 1 H, J_{3*ax*,3*eq*} 13.4, J_{3*ax*,4*eq*} 4.4 Hz, H-3*ax*), 2.00 (s, 3 H, AcN), 2.01 (m, 1 H, H-4*eq*), 2.36 (ddd, 1 H, H-3*eq*), 3.42 (m, 1 H, Me₃SiCH₂CH₂), 3.44 (m, 1 H, J_{5,6} 10.3, J_{6,7} 2.6 Hz, H-6), 3.80 (s, 3 H, MeO), 3.93 (m, 1 H, H-5), and 6.17 (d, 1 H, J_{5,NH} 8.4 Hz, NH).

Anal. Calcd for $C_{20}H_{37}NO_8Si$ (447.6): C, 53.66; H, 8.33; N, 3.13. Found: C, 53.62; H, 8.30; N, 3.10.

Methyl [2-(trimethylsilyl)ethyl 5-acetamido-7,8,9-tri-O-acetyl-3,4,5-trideoxy-α-D-manno-2-nonulopyranosid]onate (7).—A solution of **6** (200 mg, 0.5 mmol) in aq 80% acetic acid (6 mL) was stirred for 15 h at room temperature, and concentrated. The residue was acetylated with acetic anhydride (7 mL)–pyridine (10 mL) overnight at room temperature. The product was purified by chromatography on a column of silica gel (50 g) with 2:3 EtOAc–hexane to give **7** (210 mg, 88%) as an amorphous mass, $[\alpha]_D + 26.7^\circ$ (*c* 0.6, CHCl₃); ¹H-NMR (CDCl₃): δ 0.86 (m, 2 H, Me₃SiCH₂CH₂), 1.28 (m, 1 H, H-4ax), 1.76 (m, 1 H, H-3ax), 1.89-2.12 (4 s, 12 H, 3 AcO, AcN), 2.27 (m, 1 H, $J_{3ax,3eq}$ 13.7, $J_{3eq,4ax}$ 3.5 Hz, H-3eq), 3.25 (m, 1 H, Me₃SiCH₂CH₂), 3.74 (s, 3 H, MeO), 3.81–3.94 (m, 2 H, H-5, Me₃SiCH₂CH₂), 4.02 (dd, 1 H, $J_{5,6}$ 10.4 Hz, H-6), 4.11 (dd, 1 H, $J_{8,9}$ 5.3, $J_{9,9'}$ 12.5 Hz, H-9), 4.30 (dd, 1 H, $J_{8,9'}$ 2.6 Hz, H-9'), 5.27 (d, 1 H, $J_{5,NH}$ 9.3 Hz, NH), 5.33 (dd, 1 H, $J_{6,7}$ 2.2, $J_{7,8}$ 10.8 Hz, H-7), and 5.40 (m, 1 H, H-8).

Anal. Calcd for C₂₃H₃₉NO₁₁Si (533.7): C, 51.76; H, 7.37; N, 2.62. Found: C, 51.79; H, 7.40; N, 2.61.

Methyl [2-(trimethylsilyl)ethyl 5-acetamido-4-O-benzoyl-8,9-O-isopropylidene-3,5,7-trideoxy- α -D-galacto-2-nonulopyranosid]onate (8).—To a solution of 4 (1.83 g, 2.6 mmol) in toluene (92 mL) were added tributyltin hydride (3.6 mL) and AIBN (110 mg), and the mixture was heated for 1 h at 100°. After completion of the reaction, the mixture was concentrated to a syrup that was chromatographed on a column of silica gel (200 g), with 1:3 EtOAc-hexane, to give 8 (1.36 g, 92.5%) as an amorphous mass, $[\alpha]_D - 25.6^\circ$ (c 1.4, CHCl₃); ¹H-NMR (CDCl₃): δ 0.89 (m, 2 H, Me₃SiCH₂CH₂), 1.37, 1.43 (2 s, 6 H, Me₂C), 1.82 (s, 3 H, AcN), 1.74–1.85 (m, 2 H, H-7,7'), 2.03 (t, 1 H, $J_{3ax,3eg} = J_{3ax,4} = 12.6$ Hz, H-3ax), 2.77 (dd, 1 H, $J_{3eq,4}$ 4.8 Hz, H-3eq), 3.46 (m, 1 H, Me₃SiCH₂CH₂), 3.64 (m, 1 H, $J_{5,6}$ 10.3 Hz, H-6), 3.82 (s, 3 H, MeO), 3.84 (m, 1 H, Mc₃SiCH₂CH₂), 4.05 (q, 1 H, $J_{4,5} = J_{5,6} = J_{5,NH} = 10.6$ Hz, H-5), 4.13, 4.14 (2 dd, 2 H, H-9,9'), 4.22 (m, 1 H, H-8), 5.62 (d, 1 H, N*H*), and 7.38–7.98 (m, 5 H, Ph).

Anal. Calcd for C₂₇H₄₁NO₉Si (551.7): C, 58.78; H, 7.49; N, 2.54. Found: C, 58.60; H, 7.58; N, 2.55.

Methyl [2-(*trimethylsilyl*)*ethyl* 5-*acetamido*-4-O-*benzoyl*-3,5,7-*trideoxy*-α-pgalacto-2-*nonulopyranosid*]*onate* (9).—A solution of **8** (1.9 g, 3.4 mmol) in aq 80% acetic acid (25 mL) was stirred overnight at room temperature and concentrated. Column chromatography (4:1 EtOAc-hexane) of the residue on silica gel (100 g) gave **9** (1.47 g, 84%) as an amorphous mass, $[\alpha]_D - 36.6^\circ$ (*c* 1.1, CHCl₃); IR: ν 3700–3200 (OH, NH), 1730 and 1230 (ester), 1660 and 1550 (amide), 860 and 840 (Me₃Si), and 710 cm⁻¹ (Ph); ¹H-NMR (CDCl₃): δ 0.87 (m, 2 H, Me₃SiCH₂CH₂), 1.64–1.84 (m, 2 H, H-7,7'), 1.88 (s, 3 H, AcN), 2.06 (t, 1 H, $J_{3ax,3eq} = J_{3ax,4} = 12.6$ Hz, H-3*ax*), 2.81 (dd, 1 H, $J_{3eq,4}$ 4.9 Hz, H-3*eq*), 3.46, 3.87 (2 m, 2 H, Me₃SiCH₂-CH₂), 3.75 (s, 3 H, MeO), 4.17 (q, 1 H, $J_{4,5} = J_{5,6} = J_{5,NH} = 10.2$ Hz, H-5), 5.05 (ddd, 1 H, H-4), 6.40 (d, 1 H, NH), and 7.27–8.05 (m, 5 H, Ph).

Anal. Calcd for C₂₄H₃₇NO₉Si (511.7): C, 56.34; H, 7.29; N, 2.74. Found: C, 56.29; H, 7.41; N, 2.68.

Methyl [2-(*trimethylsilyl*)*ethyl* 5-acetamido-8,9-di-O-acetyl-4-O-benzoyl-3,5,7-trideoxy-α-D-galacto-2-nonulopyranosid]onate (10).—Compound 9 (1.43 g, 2.8 mmol) was acetylated with acetic anhydride (10 mL)–pyridine (20 mL) overnight at room temperature. The product was purified by chromatography (2:3 EtOAc–hexane) on a column of silica gel (60 g) to give 10 (1.63 g, 98%) as an amorphous mass, $[\alpha]_D$ – 27.8° (*c* 1.4, CHCl₃); ¹H-NMR (CDCl₃): δ 0.86 (m, 2 H, Me₃SiCH₂CH₂), 1.78–2.02 (m, 2 H, H-7,7'), 1.83 (s, 3 H, AcN), 2.02 (t, 1 H, $J_{3ax,3eq} = J_{3ax,4} = 12.6$ Hz, H-3ax), 2.03, 2.10 (2 s, 6 H, 2 AcO), 2.73 (dd, 1 H, $J_{3eq,4}$ 4.8 Hz, H-3eq), 3.37, 3.90 (2 m, 2 H, Me₃SiCH₂CH₂), 3.71 (ddd, 1 H, $J_{5,6}$ 10.3, $J_{6,7}$ 2.4 Hz, H-6), 3.78 (s, 3 H, MeO), 4.01, 4.32 (2 dd, 2 H, $J_{8,9}$ 5.9, $J_{8,9'}$ 3.7, $J_{9,9'}$ 11.9 Hz, H-9,9'), 4.06 (q, 1 H, $J_{4,5} = J_{5,NH} = 10.3$ Hz, H-5), 5.01 (ddd, 1 H, H-4), 5.35 (ddd, 1 H, H-8), 5.60 (d, 1 H, NH), and 7.38–7.98 (m, 5 H, Ph).

Anal. Calcd for C₂₈H₄₁NO₁₁Si (595.7): C, 56.45; H, 6.94; N, 2.35. Found: C, 56.31; H, 6.99; N, 2.33.

Methyl [2-(trimethylsilyl)ethyl 5-acetamido-4-O-acetyl-3,5-dideoxy-D-glycero- α -D-galacto-2-nonulopyronosid/onate (11). — A solution of 5 (3.35 g, 6.6 mmol) in aq 80% acetic acid (25 mL) was stirred overnight at room temperature, and concentrated. The product was purified by column chromatography (EtOAc) on silica gel (200 g) to give 11 (2.95 g, 95.5%) as an amorphous mass, $[\alpha]_D - 28.6^\circ$ (c 1.0, CHCl₃); ¹H-NMR (CDCl₃): δ 0.89 (m, 2 H, Me₃SiCH₂CH₂), 1.99 (t, 1 H, $J_{3ax,3eq} = J_{3ax,4} = 13.0$ Hz, H-3ax), 2.00 (s, 3 H, AcN), 2.10 (s, 3 H, AcO), 2.69 (dd, 1 H, $J_{3eq,4}$ 5.1 Hz, H-3eq), 3.42, 3.89 (2 m, 2 H, Me₃SiCH₂CH₂), 3.87 (s, 3 H, MeO), 3.96 (q, 1 H, $J_{4,5} = J_{5,6} = J_{5,NH} = 10.4$ Hz, H-5), 4.94 (ddd, 1 H, H-4), and 6.45 (d, 1 H, NH).

Anal. Calcd for C₁₉H₃₅NO₁₀Si (465.6): C, 49.01; H, 7.58; N, 3.01. Found: C, 48.73; H, 7.68; N, 3.05.

Methyl [2-(*trimethylsilyl*)*ethyl* 5-acetamido-4,9-di-O-acetyl-3,5-dideoxy-D-glyceroα-D-galacto-2-nonulopyranosid]onate (12).—To a solution of 11 (2.91 g, 6.3 mmol) in pyridine (25 mL) and CH₂Cl₂ (30 mL), cooled to -45° , was added a solution of acetyl chloride (1.5 mL) in CH₂Cl₂ (16 mL), the mixture was stirred for 30 min at -45° , and then MeOH (1 mL) was added. The solution was concentrated to a syrup that was chromatographed on a column of silica gel (150 g) with 50:1 CH₂Cl₂-MeOH, to give 12 (2.1 g, 63%) as an amorphous mass, $[\alpha]_D - 30.6^{\circ}$ (*c* 1.0, CHCl₃); ¹H-NMR (CDCl₃): δ 0.88 (m, 2 H, Me₃SiCH₂CH₂), 1.99 (s, 3 H, AcN), 2.02 (t, 1 H, $J_{3ax,3eq} = J_{3ax,4} = 13.0$ Hz, H-3ax), 2.06, 2.11 (2 s, 6 H, 2 AcO), 2.68 (dd, 1 H, $J_{3eq,4}$ 4.9 Hz, H-3eq), 3.39, 3.91 (2 m, 2 H, Me₃SiCH₂CH₂), 3.47 (dd, 1 H, $J_{5,6}$ 10.3, $J_{6,7}$ 2.6 Hz, H-6), 3.85 (s, 3 H, MeO), 4.10 (m, 1 H, H-8), 4.20, 4.47 (2 dd, 2 H, $J_{8,9}$ 6.6, $J_{8,9'}$ 2.0, $J_{9,9'}$ 11.4 Hz, H-9,9'), 4.90 (ddd, 1 H, H-4), and 6.04 (d, 1 H, NH).

Anal. Calcd for C₂₁H₃₇NO₁₁Si (507.6): C, 49.69; H, 7.35; N, 2.76. Found: C, 49.58; H, 7.39; N, 2.68.

Methyl [2-(*trimethylsilyl*)*ethyl* 5-*acetamido*-4,9-*di*-O-*acetyl*-3,5-*dideoxy*-8-O-(*phenoxy*)*thiocarbonyl*-D-glycero- α -D-galacto-2-*nonulopyranosid*]*onate* (13).—To a solution of 12 (1.99 g, 3.9 mmol) in pyridine (35 mL) and CH₂Cl₂ (35 mL) was added phenyl chlorothionoformate (1.4 mL), and the mixture was stirred for 3.5 h at room temperature. A workup similar to that described for 2 gave 13 (1.76 g, 70%) as an amorphous mass, $[\alpha]_D + 7.2^\circ$ (*c* 1.1, CHCl₃); IR: ν 3700–3300 (OH, NH), 1750 and 1230 (ester), 1660 and 1550 (amide), 860 and 840 (Me₃Si, Me₂C), and 700 cm⁻¹ (Ph); ¹H-NMR (CDCl₃): δ 0.88 (m, 2 H, Me₃SiCH₂CH₂), 1.96 (s, 3 H, AcN), 2.03 (t, 1 H, $J_{3ax,3eq} = J_{3ax,4} = 12.8$ Hz, H-3*ax*), 2.10, 2.15 (2 s, 6 H, 2 AcO), 2.67 (dd, 1 H, $J_{3eq,4}$ 4.8 Hz, H-3*eq*), 3.32, 4.16 (2 m, 2 H, Me₃SiCH₂CH₂), 3.86 (dd, 1 H, $J_{5,6}$ 10.4, $J_{6,7}$ 1.7 Hz, H-6), 3.88 (s, 3 H, MeO), 4.04 (q, 1 H, $J_{4,5} = J_{5,6} = J_{5,NH} = 10.4$ Hz, H-5), 4.16 (d, 1 H, $J_{7,OH}$ 7.1 Hz, OH-7), 4.49, 4.91 (2 dd, 2 H, $J_{8,9}$ 3.5, $J_{8,9'}$ 2.4, $J_{9,9'}$ 12.6 Hz, H-9,9'), 4.99 (ddd, 1 H, H-4), 5.81 (m, 1 H, H-8), 6.08 (d, 1 H, NH), and 7.28–7.48 (m, 5 H, Ph).

Anal. Calcd for $C_{28}H_{41}NO_{12}SSi$ (643.8): C, 52.24; H, 6.42; N, 2.18. Found: C, 52.31; H, 6.58; N, 2.15.

Methyl [2-(trimethylsilyl)ethyl 5-acetamido-4,9-di-O-acetyl-3,5,8-trideoxy-α-D-galacto-2-nonulopyranosid]onate (14).—To a solution of 13 (1.76 g, 2.7 mmol) in toluene (80 mL) were added tributyltin hydride (5.8 mL) and AIBN (155 mg), and the mixture was stirred for 2.5 h at 100°. A workup similar to that described for 6 gave 14 (1.2 g, 87%) as an amorphous mass, $[\alpha]_D - 31.5^\circ$ (c 1.35, CHCl₃); ¹H-NMR (CDCl₃): δ 0.89 (m, 2 H, Me₃SiCH₂CH₂), 1.85–2.00 (m, 2 H, H-8,8'), 1.99 (s, 3 H, AcN), 2.01 (t, 1 H, J_{3ax,3eq} = J_{3ax,4} = 12.6 Hz, H-3ax), 2.03, 2.09 (2 s, 6 H, 2 AcO), 2.62 (dd, 1 H, J_{3eq,4} 4.8 Hz, H-3eq), 3.44, 4.19 (2 m, 2 H, Me₃SiCH₂CH₂), 3.67 (m, 1 H, H-7), 3.81 (s, 3 H, MeO), 3.93 (m, 1 H, J_{4,5} 10.4, J_{5,6} 10.3, J_{5,NH} 8.1 Hz, H-5), 4.18–4.35 (m, 2 H, H-9,9'), 4.40 (d, 1 H, J_{7,OH} 4.6 Hz, OH-7), 4.93 (ddd, 1 H, H-4), and 6.03 (d, 1 H, NH).

Anal. Calcd for C₂₁H₃₇NO₁₀Si (491.6): C, 51.30; H, 7.59; N, 2.85. Found: C, 51.13; H, 7.64; N, 2.80.

Methyl [2-(*trimethylsilyl*)*ethyl* 5-acetamido-4,7,9-tri-O-acetyl-3,5,8-trideoxy-α-D-galacto-2-nonulopyranosid]onate (**15**).—Acetylation of **14** (1.88 g, 3.9 mmol) with acetic anhydride (10 mL)–pyridine (15 mL) overnight at room temperature, and purification by column chromatography (1:1 EtOAc–hexane) on silica gel (100 g) gave **15** (1.78 g, 91%) as an amorphous mass, $[\alpha]_D - 24.0^\circ$ (*c* 0.9, CHCl₃); ¹H-NMR (CDCl₃): δ 0.88 (m, 2 H, Me₃SiCH₂CH₂), 1.89–2.00 (m, 2 H, H-8,8'), 1.94 (t, 1 H, J_{3ax,3eq} = J_{3ax,4} = 12.6 Hz, H-3ax), 2.02 (s, 3 H, AcN), 2.05, 2.08, 2.10 (3 s, 9 H, 3 AcO), 2.59 (dd, 1 H, J_{3eq,4} 4.8 Hz, H-3eq), 3.45, 3.88 (2 m, 2 H, Me₃SiCH₂CH₂), 3.78 (dd, 1 H, J_{5,6} 10.3, J_{6,7} 2.0 Hz, H-6), 3.81 (s, 3 H, MeO), 4.11 (q, J_{4,5} = J_{5,6} = J_{5,NH} = 10.3 Hz, H-5), 4.03–4.27 (m, 2 H, H-9,9'), 4.85 (ddd, 1 H, H-4), 5.08 (m, 1 H, H-7), and 5.32 (d, 1 H, NH).

Anal. Calcd for C₂₃H₃₉NO₁₁Si (533.7): C, 51.76; H, 7.37; N, 2.62. Found: C, 51.69; H, 7.30; N, 2.61.

Methyl 5-acetamido-2,7,8,9-tetra-O-acetyl-3,4,5-trideoxy-D-manno-2-nonulopyranosonate (16).—To a stirred solution of 7 (200 mg, 0.4 mmol) in CH₂Cl₂ (5 mL), cooled to 0°, was added dropwise BF₃ · OEt₂ (0.15 mL). The mixture was stirred for 2 h at 0°, CH₂Cl₂ (50 mL) was added, and the solution was successively washed with M Na₂CO₃ and water, dried (Na₂SO₄), and concentrated. The residue was acetylated with acetic anhydride (5 mL)–pyridine (8 mL) overnight at room temperature. Column chromatography of the product on silica gel (50 g) with 3:2 EtOAc–hexane gave 16 (120 mg, 67.5%) as an amorphous mass, $[\alpha]_D - 40^\circ$ (c 0.5, CHCl₃); IR: ν 3500 (NH), 1750 and 1220 (ester), and 1660 and 1550 cm⁻¹ (amide).

Anal. Calcd for $C_{20}H_{29}NO_{12}$ (475.5): C, 50.52; H, 6.15; N, 2.95. Found: C, 50.31; H, 6.24; N, 2.90.

Methyl (methyl 5-acetamido-7,8,9-tri-O-acetyl-3,4,5-trideoxy-2-thio-D-manno-2nonulopyranosid)onate (17).—To a stirred solution of 16 (500 mg, 1.0 mmol) in dry CH₂Cl₂ (20 mL), cooled to 0°, were added trimethyl(methylthio)silane (Me₃Si · SMe, 400 mg, 3.33 mmol) and TMS triflate (120 mg, 0.05 mmol), and the mixture was stirred for 10 h at room temperature, the course of the reaction being monitored by TLC. Aqueous M Na₂CO₃ (10 mL) was added to the mixture, the organic layer was separated, washed with water, dried (Na₂SO₄), and concentrated to a syrup that was chromatographed on a column of silica gel (60 g), with 2:1 EtOAc-hexane, to give 17 (450 mg, 92.5%) as an amorphous mass, $[\alpha]_D - 45^\circ$ (*c* 0.8, CHCl₃); IR: ν 3450 (NH), 1760 and 1230 (ester), and 1680 and 1560 cm⁻¹ (amide); ¹H-NMR (CDCl₃): δ 3.79, 3.80 (2 s, MeO), 4.35 (dd, J_{5.6} 11.5, J_{6.7} 2.3 Hz, H-6), 4.85 (dd, J_{8.9} 2.2, J_{9.9'} 12.4 Hz, H-9 β), 5.16 (dt, H-8 β), 5.36 (dd, J_{7.8} 8.5 Hz, H-7 α), 5.40 (m, H-8 α), 5.46 (m, H-7 β), 5.82, and 6.06 (2 d, NH); the anomeric ratio (α : β) was estimated as ~ 1:1 from the ratio of the intensities of the ester-methyl signals.

Anal. Calcd for $C_{19}H_{29}NO_{10}S$ (463.5): C, 49.23; H, 6.31; N, 3.02. Found: C, 49.00; H, 6.48; N, 2.94.

Methyl 5-acetamido-2,8,9-tri-Oacetyl-4-O-benzoyl-3,5,7-trideoxy-D-galacto-2nonulopyranosylonate (18).—To a solution of 10 (1.63 g, 2.7 mmol) in CH₂Cl₂ (25 mL), cooled to 0°, was added BF₃ · OEt₂ (2.8 mL), and the mixture was stirred for 9 h at 0°, and then extracted with CH₂Cl₂ (100 mL). The extract was successively washed with M Na₂CO₃ and water, dried (Na₂SO₄), and concentrated. The residue was acetylated with acetic anhydride (10 mL)–pyridine (8 mL) overnight at room temperature. Column chromatography (1:1 EtOAc–hexane) of the product on silica gel (100 g) gave 18 (1.29 g, 88%) as an amorphous mass, $[\alpha]_D - 44.5^\circ$ (*c* 1.0, CHCl₃); ν 3400 (NH), 1740 and 1220 (ester), 1660 and 1540 (amide), and 710 cm⁻¹ (Ph).

Anal. Calcd for C₂₅H₃₁NO₁₂ (537.5): C, 55.86; H, 5.81; N, 2.61. Found: C, 55.63; H, 5.99; N, 2.60.

Methyl (methyl 5-acetamido-8,9-di-O-acetyl-4-O-benzoyl-3,5,7-tride oxy-2-thio-Dgalacto-2-nonulopyranosid)onate (19).—To a solution of 18 (1.29 g, 2.4 mmol) in CH₂Cl₂ (25 mL), cooled to 0°, were added Me₃Si · SMe (1.4 mL) and TMS triflate (0.7 mL), and the mixture was stirred for 5.5 h at room temperature. Processing as described for the preparation of 17 gave 19 (960 mg, 72%) as an amorphous mass, $[\alpha]_D - 70.4^\circ$ (c 1.0, CHCl₃): IR: ν 3500 (NH), 1740 and 1230 (ester), 1660 and 1550 (amide), and 710 cm⁻¹ (Ph); ¹H-NMR (CDCl₃): δ 2.29 (dd, $J_{3ax,3eq}$ 12.4 Hz, $J_{3ax,4}$ 11.7 Hz, H-3ax- β), 2.67 (dd, $J_{3eq,4}$ 4.7 Hz, H-3eq- β), 2.90 (dd, H-3eq- α), 3.80 (s, MeO β), 3.82 (s, MeO α), 5.06 (ddd, $J_{4,5}$ 10.3 Hz, H-4 β), 5.24 (m, H-8 β), 5.38 (m, H-8 α), 5.48 (ddd, H-4 α), 5.57 (d, NH α), and 5.75 (d, NH β); the anomeric ratio ($\alpha: \beta$) was estimated as ~1:1 from the ratio of intensities of the ester-methyl signals.

Anal. Calcd for $C_{24}H_{31}NO_{10}S$ (525.6): C, 54.84; H, 5.95; N, 2.67. Found: C, 54.60; H, 6.15; N, 2.64.

Methyl 5-acetamido-2,4,7,9-tetra-O-acetyl-3,5,8-trideoxy-D-galacto-2-nonulopyranosonate (20).—To a solution of 15 (1.78 g, 3.3 mmol) in CH₂Cl₂ (25 mL), cooled to 0°, was added BF₃ · OEt₂ (5.3 mL), the mixture was stirred for 12.5 h at 0°, and then CH₂Cl₂ (100 mL) was added. The solution was successively washed with M Na₂CO₃ and water, dried (Na₂SO₄), and evaporated. The residue was acetylated with acetic anhydride (18 mL)–pyridine (16 mL) overnight at room temperature. Workup as described for 16 gave 20 (1.4 g, 85%) as an amorphous mass, $[\alpha]_D - 41^\circ$ (c 0.9, CHCl₃); IR: ν 3500 (NH), 1740 and 1220 (ester), and 1660 and 1540 cm⁻¹ (amide); the anomeric ratio (α : β) was estimated as ~ 1:5 from the ratio of intensities of the ester-methyl signals.

Anal. Calcd for $C_{20}H_{29}NO_{12}$ (475.5): C, 50.52; H, 6.15; N, 2.95. Found: C, 50.53; H, 6.25; N, 2.81.

Methyl (methyl 5-acetamido-4,7,9-tri-O-acetyl-3,5,8-trideoxy-2-thio-D-galacto-2nonulopyranosid)onate (21).—To a solution of 20 (1.29 g, 2.7 mmol) in CH₂Cl₂ (25 mL), cooled to 0°, were added Me₃Si · SMe (2.3 mL) and TMS triflate (0.8 mL), and the mixture was stirred for 2 h at 40°. Workup as described for 17 gave 21 (1.25 g, quantitative) as an amorphous mass, $[\alpha]_D - 56.7^\circ$ (c 0.8, CHCl₃): IR: ν 3500 (NH), 1740 and 1230 (ester), and 1660 and 1540 cm⁻¹ (amide); ¹H-NMR (CDCl₃): δ 2.52 (dd, $J_{3ax,3eq}$ 13.5, $J_{3eq,4}$ 5.0 Hz, H-3eq- β), 2.76 (dd, H-3eq- α), 3.82 (s, MeO β) 3.84 (s, MeO α), 4.92 (ddd, H-4 α), 5.12 (dt, $J_{6.7}$ 2.2, $J_{7.8} = J_{7.8'} = 7.0$ Hz, H-7), 5.19–5.37 (m, H-4 β ,7), 5.37, and 5.54 (2 d, NH); the anomeric ratio (α : β) was estimated as ~ 1 : 1 from the ratio of intensities of the ester-methyl signals.

Anal. Calcd for C₁₉H₂₉NO₁₀S (463.5): C, 49.23; H, 6.31; N, 3.02. Found: C, 49.19; H, 6.38; N, 2.91.

Methyl [2-(trimethylsilyl)ethyl 5-acetamido-9-O-tert-butyldimethylsilyl-3,5-dideoxy-D-glycero- α -D-galacto-2-nonulopyranosid/onate (23).—To a solution of methyl [2-(trimethylsilyl)ethyl 5-acetamido-3,5-dideoxy-D-glycero- α -D-galacto-2-nonulopyranosid]onate¹⁴ (22, 8.2 g, 19.4 mmol) in pyridine (40 mL), cooled to 0°, was added, with stirring, tert-butyldimethylsilyl chloride (7.0 g), and the mixture was stirred for 2 h at 0°. Methanol (2 mL) was added to the mixture, and it was stirred for 1 h and concentrated to a syrup that was chromatographed on a column of silica gel (200 g), with 4:1 EtOAc-hexane, to give 23 (9.45 g, 91%) as an amorphous mass, [α]_D -10.6° (c 1.4, CHCl₃); ¹H-NMR (CDCl₃): δ 0.33 (s, 6 H, Me₂Si), 0.85 (m, 11 H, Me₃SiCH₂CH₂, Me₃C), 2.01 (s, 3 H, AcN), 2.73 (dd, 1 H, J_{3ax,3eq} 13.0, J_{3eq,4} 4.3 Hz, H-3eq), and 3.82 (s, 3 H, MeO).

Anal. Calcd for C₂₃H₄₇NO₇Si₂ (537.8): C, 51.36; H, 8.81; N, 2.60. Found: C, 51.29; H, 8.85; N, 2.52.

Methyl [2-(trimethylsilyl)ethyl 5-acetamido-4,8-di-O-benzoyl-9-O-tert-butyldimethylsilyl-3,5-dideoxy-D-glycero- α -D-galacto-2-nonulopyranosid]onate (24).—To a solution of 23 (9.0 g, 1.67 mmol) in pyridine (25 mL) and CH₂Cl₂ (100 mL), cooled to -5° , was added, with stirring, a solution of BzCl (10 mL) in CH₂Cl₂ (20 mL), and the solution was stirred for 1 h at -5° . Methanol (2 mL) was added and the mixture was concentrated to a syrup, which was extracted with CH₂Cl₂ (200 mL). The solution was successively washed with 2 M HCl and water, dried (Na₂SO₄), and concentrated. Column chromatography (2:3 EtOAc-hexane) of the residue on silica gel (200 g) gave 24 (10.0 g, 80%) as an amorphous mass, $[\alpha]_D - 33.0^{\circ}$ (*c* 0.8, CHCl₃); ¹H-NMR (CDCl₃): δ 0.33 (s, 6 H, Me₂Si), 0.84 (m, 11 H, Me₃SiCH₂CH₂, Me₃C), 1.92 (s, 3 H, AcN), 2.09 (t, 1 H, J_{3ax,3eq} = J_{3ax,4} = 12.5 Hz, H-3ax), 2.73 (dd, 1 H, J_{3ca,4} 4.3 Hz, H-3eq), and 3.82 (s, 3 H, MeO).

Anal. Calcd for C₃₇H₅₅NO₁₁Si₂ (730.0); C, 51.36; H, 8.81; N, 2.60. Found: C, 51.29; H, 8.85; N, 2.52.

Methyl [2-(trimethylsilyl)ethyl 5-acetamido-4,8-di-O-benzoyl-3,5-dideoxy-D-glycero- α -D-galacto-2-nonulopyranosid]onate (25).—A solution of 24 (9.5 g, 12.7 mmol) in aq 80% acetic acid (120 mL) was heated, with stirring, for 4 h at 40°, and concentrated. Column chromatography (3:2 EtOAc-hexane) of the residue on silica gel (200 g) gave 25 (8.0 g, 99%) as an amorphous mass, $[\alpha]_D - 42.0^\circ$ (*c* 0.6, CHCl₃); IR: ν 3700–3200 (OH, NH), 1730 and 1230 (ester), 1660 and 1550 (amide), 860 and 840 (Me₃Si), and 710 cm⁻¹ (Ph); ¹H-NMR (1:1 CDCl₃-CD₃OD): δ 0.85 (m, 2 H, Me₃SiCH₂CH₂), 1.90 (s, 3 H, AcN), 2.00 (t, 1 H, J_{3ax,3eq} = J_{3ax,4} = 12.6 Hz, H-3ax), 2.69 (dd, 1 H, J_{3eq,4} 4.8 Hz, H-3eq), 3.27 (s, 3 H, MeO), 3.36 (m, 1 H, $Me_3SiCH_2CH_2$), 3.73 (dd, 1 H, $J_{5,6}$ 10.4, $J_{6,7}$ 1.6 Hz, H-6), 4.15 (t, 1 H, H-5), 5.15 (ddd, 1 H, H-4), 5.38 (m, 1 H, H-8), and 7.25-8.06 (m, 10 H, 2 Ph).

Anal. Calcd for C₃₁H₄₁NO₁₁Si (631.8): C, 58.93; H, 6.54; N, 2.22. Found: C, 58.69; H, 6.77; N, 2.18.

Methyl [2-(trimethylsilyl)ethyl 5-acetamido-4,8-di-O-benzoyl-9-chloro-3,5,9-trideoxy-D-glycero- α -D-galacto-2-nonulopyranosid/onate (26).—To a solution of 25 (5.05 g, 8.0 mmol) in N,N-dimethylformamide (50 mL), cooled to 0°, were added, with stirring, CCl₄ (10 mL) and triphenylphosphine (6.0 g), and the mixture was stirred for 3 h at room temperature. Methanol (2 mL) was added and the solution was concentrated. Column chromatography (1:4 EtOAc-hexane) of the residue on silica gel (150 g) gave 26 (4.12 g, 81%) as an amorphous mass, $[\alpha]_D - 68.5^\circ$ (c 0.8, CHCl₃); ¹H-NMR (CDCl₃): δ 0.84 (m, 2 H, Me₃SiCH₂CH₂), 1.91 (s, 3 H, AcN), 2.05 (t, 1 H, J_{3ax,3eq} = J_{3ax,4} = 12.6 Hz, H-3ax), 2.67 (dd, 1 H, J_{3eq,4} 4.8 Hz, H-3eq), 3.25 (s, 3 H, MeO), 3.38 (m, 1 H, Me₃SiCH₂CH₂), 3.70 (dd, 1 H, J_{5,6} 10.4, J_{6,7} 1.7 Hz, H-6), 5.17 (ddd, 1 H, H-4), 5.58 (m, 1 H, H-8), 6.18 (d, 1 H, NH), and 7.22–8.04 (m, 10 H, 2 Ph).

Anal. Calcd for C₃₀H₃₈ClNO₁₀Si (636.2): C, 56.64; H, 6.02; N, 2.20. Found: C, 56.51; H, 6.24; N, 2.15.

Methyl [2-(*trimethylsily*)*ethyl* 5-acetamido-4,8-di-O-benzoyl-3,5,9-trideoxy-D-glycero- α -D-galacto-2-nonulopyranosid]onate (27).—To a solution of 26 (760 mg, 1.2 mmol) in toluene (20 mL), were added tributyltin hydride (1.0 mL) and AIBN (20 mg), and the mixture was heated for 1 h at 100°, and then concentrated. Column chromatography (1:4 EtOAc-hexane) of the residue on silica gel (100 g) gave 27 (480 mg, 65%) as an amorphous mass, $[\alpha]_D + 7.7^\circ$ (*c* 0.6, CHCl₃); ¹H-NMR (1:1 CDCl₃-CD₃OD): δ 0.88 (m, 2 H, Me₃SiCH₂CH₂), 1.47 (d, 3 H, $J_{8,9}$ 6.0 Hz, CH₃CH), 1.91 (s, 3 H, AcN), 1.98 (t, 1 H, $J_{3ax,3eq} = J_{3ax,4} = 12.6$ Hz, H-3ax), 2.71 (dd, 1 H, $J_{3eq,4}$ 4.8 Hz, H-3eq), 3.30 (s, 3 H, MeO), 3.39, 3.95 (2 m, 2 H, Me₃SiCH₂CH₂), 3.65 (dd, 1 H, $J_{6,7}$ 1.7, $J_{7,8}$ 8.1 Hz, H-7), 3.75 (dd, 1 H, $J_{5,6}$ 10.4 Hz, H-6), 4.17 (t, 1 H, $J_{4,5}$ 10.4 Hz, H-5), 5.15 (ddd, 1 H, H-4), 5.38 (m, 1 H, $J_{8,9}$ 6.2 Hz, H-8), and 7.28–8.02 (m, 10 H, 2 Ph).

Anal. Calcd for $C_{31}H_{41}NO_{10}Si$ (615.8): C, 60.46; H, 6.71; N, 2.27. Found: C, 6.41; H, 6.84; N, 2.20.

Methyl [2-(trimethylsilyl)ethyl 5-acetamido-4,7,8-tri-O-acetyl-3,5,9-trideoxy-D-glycero- α -D-galacto-2-nonulopyranosid]onate (28).—To a solution of 27 (2.1 g, 3.4 mmol) in MeOH (20 mL) was added 3 mL of 28% NaOMe in MeOH, and the mixture was stirred for 30 min at room temperature. After completion of the reaction, the solution was neutralized with Amberlite IR-120 (H⁺) resin and filtered. The resin was washed with MeOH, and the combined filtrate and washings were concentrated. Acetylation of the residue with acetic anhydride (10 mL)–pyridine (15 mL) overnight at room temperature gave 28 (1.55 g, 85%) as an amorphous mass after column chromatography (2:3 EtOAc-hexane) on silica gel (140 g), [α]_D – 13.5° (*c* 0.81, CHCl₃); IR: ν 3500 (NH), 1740 and 1230 (ester), 1670 and 1550 (amide), 860 and 840 cm⁻¹ (Me₃Si); ¹H-NMR (CDCl₃): δ 0.87 (m, 2 H, $\begin{aligned} \text{Me}_{3}\text{SiC}H_{2}\text{CH}_{2}\text{), 1.18 (d, 3 H, }J_{8.9} \text{ 6.0 Hz, }\text{C}H_{3}\text{CH}\text{), 1.86 (s, 3 H, AcN), 1.96 (t, 1 H, }J_{3ax,3eg} = J_{3ax,4} = 12.6 \text{ Hz, H-}3ax\text{), 2.00, 2.08, 2.12 (3 s, 9 H, 3 AcO), 2.56 (dd, 1 H, }J_{3eq,4} \text{ 4.6 Hz, H-}3eq\text{), 3.32, 3.86 (2 m, 2 H, Me}_{3}\text{SiCH}_{2}\text{C}H_{2}\text{), 3.76 (s, 3 H, MeO), } 4.02 (dd, 1 H, }J_{5.6} \text{ 10.6, }J_{6.7} \text{ 1.8 Hz, H-}6\text{), 4.08 (q, 1 H, }J_{4.5} = J_{5.6} = J_{5.NH} = 10.6 \text{ Hz, } \text{H-}5\text{), 4.80 (ddd, 1 H, H-}4\text{), 5.13 (dd, 1 H, }J_{7.8} \text{ 7.9 Hz, H-}7\text{), 5.19 (m, 1 H, H-}8\text{), and } 5.31 (d, 1 H, NH). \end{aligned}$

Anal. Calcd for C₂₃H₃₉NO₁₁Si (533.7): C, 51.76; H, 7.37; N, 2.62. Found: C, 51.51; H, 7.40; N, 2.65.

Methyl 5-acetamido-2,4,7,8-tetra-O-acetyl-3,5,9-trideoxy-D-glycero-D-galacto-2nonulopyranosonate (29).—To a solution of 28 (1.51 g, 2.8 mmol) in CH₂Cl₂ (30 mL), cooled to 0°, was added BF₃ · OEt₂ (0.62 mL), and the mixture was stirred for 3 h at 0°, then extracted with CH₂Cl₂ (200 mL). The extract was successively washed with M Na₂CO₃ and water, dried (Na₂SO₄), and concentrated. The residue was acetylated with acetic anhydride (7 mL)–pyridine (10 mL) overnight at room temperature. Workup as described for 16 gave 29 (1.22 g, 91%) as an amorphous mass, $[\alpha]_D - 41.5^\circ$ (c 1.1, CHCl₃); IR: ν 3500 (NH), 1740 and 1220 (ester), and 1660 and 1550 cm⁻¹ (amide); the anomeric ratio (α : β) was estimated as ~ 1:5 from the ratio of intensities of the ester-methyl signals.

Anal. Calcd for $C_{20}H_{29}NO_{12}$ (475.5): C, 50.52; H, 6.15; N, 2.95. Found: C, 50.58; H, 6.20; N, 2.71.

Methyl 5-acetamido-4,7,8-tri-O-acetyl-2-S-acetyl-3,5,9-trideoxy-2-thio-D-glycero- α -D-galacto-nonulopyranosonate (31).-Hydrogen chloride was bubbled through a solution of 29 (1.51 g, 3.2 mmol) in CH₂Cl₂ (30 mL) for 10 min while the solution was cooled to -20° . The mixture was kept for 24 h at room temperature and concentrated. Drierite (2 g) was added to a solution of the residue in acetone (10 mL) and CH₂Cl₂ (15 mL), and the mixture was stirred for 1 h at room temperature. Potassium thioacetate (1.36 g, 11.9 mmol) was added, and stirring was continued for 3 h at room temperature. The mixture was filtered, the insoluble material was washed with CH_2Cl_2 , and the combined filtrate and washings was concentrated. Column chromatography (1:1 EtOAc-hexane) of the residue on silica gel (60 g) gave **31** (1.22 g, 78%) as an amorphous mass, $[\alpha]_{\rm D}$ +35.0° (c 1.0, CHCl₃); ¹H-NMR (CDCl₃): δ 1.25 (d, 3 H, $J_{8,9}$ 6.4 Hz, CH₃CH), 1.89 (s, 3 H, AcN), 1.94 (t, 1 H, $J_{3ax,3eg} = J_{3ax,4} = 12.8$ Hz, H-3ax), 2.02, 2.04, 2.14, 2.16 (4 s, 12 H, 3 AcO, AcS), 2.68 (dd, 1 H, J_{3eg,4} 4.8 Hz, H-3eq), 3.79 (s, 3 H, MeO), 4.12 (q, 1 H, $J_{4.5} = J_{5.6} = J_{5.NH} = 10.4$ Hz, H-5), 4.53 (dd, 1 H, $J_{6.7}$ 2.2 Hz, H-6), 4.93 (ddd, 1 H, H-4), 5.07 (m, 1 H, H-8), 5.19 (dd, 1 H, J₇₈ 7.0 Hz, H-7), and 5.54 (d, 1 H, NH).

Anal. Calcd for $C_{20}H_{29}NO_{11}S$ (491.5): C, 48.87; H, 5.95; N, 2.85. Found: C, 48.85; H, 6.20; N, 2.83.

Methyl (methyl 5-acetamido-4,7,8-tri-O-acetyl-3,5,9-trideoxy-2-thio-D-glycero- α -D-galacto-2-nonulopyranosid)onate (32).—To a stirred solution of 31 (980 mg, 2.0 mmol) in dry MeOH (4 mL), cooled to -40° , was added a solution of Na metal (47 mg) in MeOH (2 mL). The mixture was stirred for 5 min at -40° , and concentrated at 0° to an amorphous mass, which was dissolved in dry N,N-dimethylform-

amide (12 mL). Methyl iodide (1 mL) was added to the stirred solution, stirring was continued for 3 h at room temperature, and the mixture was concentrated. Column chromatography (1:1 EtOAc-hexane) of the residue on silica gel (60 g) gave **32** (820 mg, 89%) as an amorphous mass, $[\alpha]_D - 23.5^\circ$ (*c* 1.1, CHCl₃); ¹H-NMR (CDCl₃): δ 1.25 (d, 3 H, $J_{8,9}$ 6.4 Hz, CH_3 CH), 1.88 (s, 3 H, AcN), 1.99 (t, 1 H, $J_{3ax,3eq} = J_{3ax,4} = 12.6$ Hz, H-3*ax*), 2.04, 2.12, 2.13, 2.16 (4 s, 12 H, 3 AcO, MeS), 2.72 (dd, 1 H, $J_{3eq,4}$ 4.8 Hz, H-3*eq*), 3.79 (dd, 1 H, $J_{5.6}$ 10.4, $J_{6.7}$ 2.2 Hz, H-6), 3.80 (s, 3 H, MeO), 4.12 (q, 1 H, $J_{4.5} = J_{5.6} = J_{5.NH} = 10.4$ Hz, H-5), 4.86 (ddd, 1 H, H-4), 5.15 (dd, 1 H, $J_{7.8}$ 8.4 Hz, H-7), 5.23 (m, 1 H, H-8), and 5.38 (d, 1 H, NH).

Anal. Calcd for $C_{19}H_{29}NO_{10}S$ (463.5): C, 49.23; H, 6.31; N, 3.02. Found: C, 49.19; H, 6.35; N, 2.95.

ACKNOWLEDGMENT

This work was supported in part by a Grant-in-Aid (No. 03255207) for Scientific Research on Priority Areas from the Ministry of Education, Science and Culture of Japan.

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