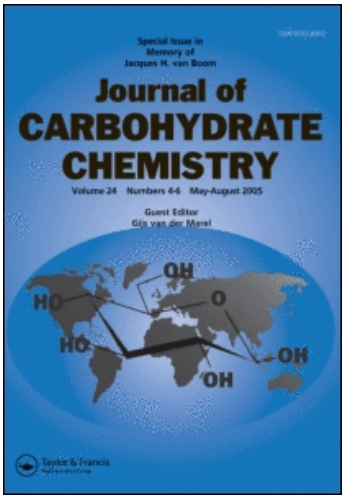

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Synthesis of 6-S-(5-Acetamido-3,5-Dideoxy-D-Glycero-α-D-Galacto-2-Nonulopyranosylonic Acid)-6-Thio-Hexopyranosides

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SYNTHESIS OF 6-S-(5-ACETAMIDO-3,5-DIDEOXY-D-GLYCERO-α-D-GALACTO-2-NONULOPYRANOSYLONIC ACID)-6-THIO-HEXOPYRANOSIDES*

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ABSTRACT

The reaction of the sodium salt of methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-2-thio-D-glycero-α-D-galacto-2-nonulopyranosonate with a variety of 6-bromo-6-deoxy-D-hexopyranosides, such as methyl 2,3,4-tri-O-acetyl-6-bromo-6-deoxy-α-D-glucopyranoside, -galactopyranoside, allyl 2,3,4-tri-O-acetyl-6-bromo-6-deoxy-β-D-glucopyranoside, and allyl 2-acetamido-3,4-di-O-acetyl-6-bromo-2,6-dideoxy-β-D-glucopyranoside, gave the corresponding (2→6)-linked disaccharides, α-glycosides of 2-thio-N-acetylneuraminic acid derivative in good yields. These disaccharides were converted, via O-deacetylation, followed by hydrolytic removal of the ester group, into the title compounds.

INTRODUCTION

Sialic acids[2] are known as constituents of glycoproteins and glycolipids and play an important role in biological processes. It is also known that naturally occurring sialocompounds contain sialic acids in α-glycosidic linkage. In previous paper[1], we de-

*Studies on the thioglycosides of N-acetylneuraminic acid, Part 2. For Part 1, see ref. 1.

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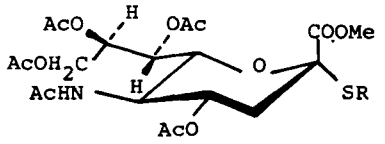
monstrated the stereoselective and high yield synthesis of a series of alkyl α-thioglycosides of N-acetylneuraminic acid, coupling of the sodium salt of methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-2-thio-D-glycero-α-D-galacto-2-nonulopyranosonate with alkyl bromides. We now report a synthesis of a variety of disaccharides, 6-S-(N-acetyl-α-D-neuraminyl)-D-hexopyranosides.

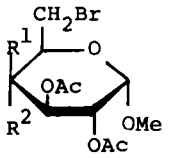
RESULTS AND DISCUSSION

For the synthesis of a variety of 6-S-(5-acetamido-3,5-dideoxy-2-thio-D-glycero-α-D-galacto-2-nonulopyranosylonic acid)-6-thio-D-hexopyranosides, several aglycons were selected, namely methyl 2,3,4-tri-O-acetyl-6-bromo-6-deoxy-α-D-glucopyranoside[3] (3), methyl 2,3,4-tri-O-acetyl-6-bromo-6-deoxy-α-D-galactopyranoside[4] (4), allyl 2,3,4-tri-O-acetyl-6-bromo-6-deoxy-β-D-glucopyranoside (7), and allyl 2-acetamido-3,4-di-O-acetyl-6-bromo-2,6-dideoxy-β-D-glucopyranoside (10). Compound 3 was prepared from methyl 6-bromo-6-deoxy-α-D-glucopyranoside[5] by acetylation. Selective bromination of methyl α-D-galactopyranoside according to the procedure of Whistler et al.[5], followed by acetylation, gave compound 4 in good yield. In a similar way, compounds (7 and 10) were respectively prepared from allyl β-D-glucopyranoside[6] (5) and allyl 2-acetamido-2-deoxy-β-D-glucopyranoside[6] (8) in good yields.

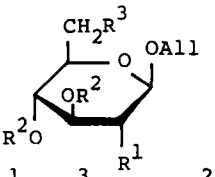
Treatment of the sodium salt of methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-2-thio-D-glycero-α-D-galacto-2-nonulopyranosonate[1] (2), freshly derived from methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-2-S-acetyl-3,5-dideoxy-2-thio-D-glycero-α-D-galacto-2-nonulopyranosonate[1] (1) by selective S-deacetylation, with 3 in dry N,N-dimethylformamide (DMF) at nitrogen atmosphere, yielded methyl 2,3,4-tri-O-6-S-(methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-6-thio-α-D-glucopyranoside (11) in 87% yield, after column chromatography. The structure of 11 was assigned by 270 MHz ^{1}H-NMR spectroscopy. The NMR spectrum of 11 exhibited ten sharp singlets, each integrating for three protons, which demonstrated the presence of one N-acetyl(δ 1.88), seven O-acetyl (δ 2.02-2.16), one O-methyl (δ 3.42), and one methyl ester groups (δ 3.83); H-3e appeared at δ 2.73 ($J_{3a,3e}$ 12.8, $J_{3e,4}$ 4.8 Hz; Neu 5Ac unit) as a doublet of doublets, and H-4 (Neu 5Ac unit) at δ 4.88 as multiplet, indicating the α-configuration[7-9] of the glycosidic linkage. Other NMR data are given in the Experimental section, and are consistent with structure 11.



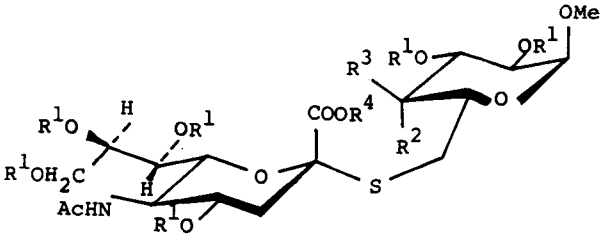
1 R = Ac
2 R = Na



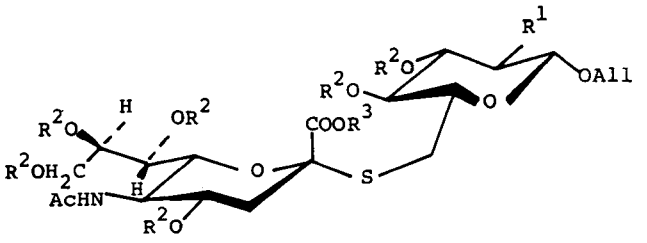
3 R^1= H, R^2 = OAc
4 R^1= OAc, R^2 = H



5 R^1 = R^3 = OH, R^2 = H
6 R^1 = OH, R^2 = H, R^3= Br
7 R^1=OAc, R^2= Ac, R^3= Br
8 R^1=NHAc, R^2=H, R^3= OH
9 R^1=NHAc, R^2=H, R^3=Br
10 R^1=NHAc, R^2=Ac, R^3=Br



11 R^1=Ac, R^2=H, R^3=OAc, R^4=Me
12 R^1=Ac, R^2=OAc, R^3=H, R^4=Me
13 R^1=R^2=H, R^3=OH, R^4=Me
14 R^1=R^3=H, R^2=OH, R^4=Me
15 R^1=R^2=R^4=H, R^3=OH
16 R^1=R^3=R^4=H, R^2=OH



17 R^1=OAc, R^2=Ac, R^3=Me
18 R^1=NHAc, R^2=Ac, R^3=Me
19 R^1=OH, R^2=H, R^3=Me
20 R^1=NHAc, R^2=H, R^3=Me
21 R^1=OH, R^2=R^3=H
22 R^1=NHAc, R^2=R^3=H

Scheme

In a same way, condensation of 2 with 4, 7, or 10 gave the corresponding α-thioglycosides (12, 17, and 18) of N-acetylneuraminic acid derivative in 67, 70, and 86% yields, respectively. NMR data of compounds (12, 17, and 18) demonstrated the occurrence of the fully blocked sialodisaccharides (see Experimental section); each H-3e signals appeared at δ 2.71, 2.73, and 2.72 as a one-proton doublet of doublets, and H-4 at δ 4.89, 4.88, and 4.87 as multiplet, indicating α-glycosidic linkage.

O-Deacetylation of 11 with sodium methoxide in methanol, afforded methyl 6-S-(methyl 5-acetamido-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-6-thio-α-D-glucopyranoside (13) in quantitative yield; significant signals in the NMR spectrum were a one-proton triplet at δ 1.81 ($J_{3a,3e} = J_{3a,4}$ = 12.4 Hz, H-3a; Neu 5Ac unit), a one-proton doublet of doublets at δ 2.75 ($J_{3a,3e}$ 12.4, $J_{3e,4}$ 4.8 Hz, H-3e; Neu 5Ac unit), and three three-proton singlets at δ 1.95 (AcN), 3.34 (MeO), and 3.68 (MeOCO); all are consistent with structure 13.

Saponification of the methyl ester group in 13 with 0.2M potassium hydroxide afforded methyl 6-S-(5-acetamido-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonic acid)-6-thio-α-D-glucopyranoside (15) in quantitative yield. The structure was unambiguously proved by NMR spectroscopy in deuterium oxide (δ 1.74 for H-3a, and δ 2.79 for H-3e).

In a similar way, O-deacetylation of compounds (12, 17, and 18), followed by saponification of the methyl ester group in 14, 19, and 20, yielded the desired 6-S-(5-acetamido-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonic acid)-6-thio-D-hexopyranosides (16, 21, and 22) in good yields.

EXPERIMENTAL

General Procedures. Melting points were determined with a Yanagimoto micro melting-point apparatus and are uncorrected. Specific rotations were determined with a Union MP-201 polarimeter, and IR spectra were recorded with a Jasco IR-1 spectrophotometer. ^{1}H-NMR spectra were recorded with a Hitachi R-22 (90 MHz) or a Jeol JMN-GX 270 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. Evaporations were conducted in vacuo.

Allyl 2,3,4-tri-O-acetyl-6-bromo-6-deoxy-β-D-glucopyranoside (7). To a solution of allyl β-D-glucopyranoside[6] (5; 920 mg) in dry pyridine

(10 mL) were added, with stirring, carbon tetrabromide (1.67 g) and triphenylphosphine (1.65 g) at 0°C, and it was stirred for 2 h at room temperature; the progress of the reaction being monitored by t.l.c.. Methanol (1 mL) was added to the mixture, and evaporated to a syrup, which was chromatographed on a column of silica gel (100 g) with chloroform and then 50:1 chloroform-methanol. The latter eluate gave the 6-bromo derivative (6), which was acetylated with acetic anhydride (3 mL)-pyridine (5 mL). Compound 7 (1.2 g, 65%) was obtained as crystals; mp 111-112°, $[\alpha]_D^{25}$ - 7.5° (c 1.0, chloroform); IR (Nujol): 1750 and 1230 (ester), and 1640 cm^{-1} (allyl); NMR data at 90 MHz ($CDCl_3$): δ 2.00 (s, 3H, AcO), 2.04 (2s, 6H, 2AcO), 3.35-3.54 (m, 2H, H-6,6'), 3.68 (m, 1H, H-2), 4.28 (m, 1H, H-5), 4.58 (d, 1H, $J_{1,2}$ 7.0 Hz, H-1), 4.88-5.38 (m, 5H, $-C=CH_2$, H-2,3,4), and 5.65-6.06 (m, 1H, =CH-).

Anal. Calcd for $C_{15}H_{21}O_8Br$: C, 44.02; H, 5.17. Found: C, 43.96; H, 5.20.

Allyl 2-acetamido-3,4-di-O-acetyl-6-bromo-2,6-dideoxy-β-D-gluco-pyranoside (10). To a solution of allyl 2-acetamido-2-deoxy-β-D-glucopyranoside[6] (8; 1.1 g) in dry pyridine (12 mL) was added, with stirring, carbon tetrabromide (1.58 g) and triphenylphosphine (1.57 g) at 0°C, and it was stirred for 5 h at room temperature, and then evaporated to a syrup, which was purified by chromatography on a column of silica gel (50 g) with 50:1 chloroform-methanol, to give allyl 2-acetamido-6-bromo-2,6-dideoxy-β-D-glucopyranoside (9). Compound (9) was acetylated with acetic anhydride (2 mL) in pyridine (3 mL) for 2 h at room temperature, to afford 10 (1.3 g, 75%) as needles; mp 174-176°, $[\alpha]_D^{25}$ - 4.5° (c 2.2, chloroform); IR (Nujol): 3270 (NH), 1750 and 1240 (ester), and 1660 and 1570 cm^{-1} (amide); NMR data at 90 MHz (in $CDCl_3$): δ 1.92 (s, 3H, AcN), 2.00, 2.02 (2s, 6H, 2AcO), 3.42 (m, 2H, H-6,6') 4.72 (d, 1H, $J_{1,2}$ 9.0 Hz, H-1), 4.89 (t, 1H, $J_{2,3} = J_{3,4}$ = 10.0 Hz, H-3), 5.06-5.36 (m, 3H, $=CH_2$, H-4), 5.63-6.02 (m, 1H, =CH-), and 6.08 (d, 1H, $J_{NH,2}$ 8.0 Hz).

Anal. Calcd for $C_{15}H_{22}NO_7Br$: C, 44.13; H, 5.43; N, 3.43. Found: C, 44.15; H, 5.40; N, 3.39.

Methyl 2,3,4-tri-O-acetyl-6-S-(methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosyl-onate)-6-thio-α-D-glucopyranoside (11). To a stirred solution of methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-2-S-acetyl-3,5-dideoxy-2-thio-D-glycero-α-D-galacto-2-nonulopyranosonate[1] (1; 200 mg) in dry methanol (6 mL), cooled to -40°C, was added a solution of sodium metal (8.3 mg) in dry methanol (2 mL), the course of the reaction

being monitored by t.l.c.; after 40 min, all of the starting material had been converted into the salt (2). The mixture was evaporated to an amorphous mass, which was dissolved in dry N,N-dimethylformamide (DMF; 2 mL). To the stirred solution was added a solution of compound 3 (208 mg) in dry DMF (2 mL), and the mixture was heated, with stirring, overnight at 60°C, and then evaporated to a syrup, which was extracted with chloroform. The extract was washed with water, dried (sodium sulfate), and evaporated to a syrup. The product was chromatographed on a column of silica gel (40 g) with chloroform, and then 150:1 chloroform-methanol. The latter eluate gave compound 11 as an amorphous mass (266.5 mg, 86.8%); mp 104-106°, $[\alpha]_D^{25}$ + 77.2° (c 1.83, chloroform); IR (Nujol): 3300 (NH), 1740 and 1220 (ester), and 1660 and 1550 cm^{-1} (amide); NMR data at 270 MHz (in $CDCl_3$): Neu 5Ac unit: δ 1.87 (s, 3H, AcN), 1.92 (near t, 1H, $J_{3a,3e} = J_{3a,4}$ = 12.8 Hz, H-3a), 2.73 (dd, $J_{3a,3e}$ 12.8, $J_{3e,4}$ 4.8 Hz, H-3e), 3.82 (s, 3H, MeO), 3.83 (dd, 1H, $J_{5,6}$ 10.2, $J_{6,7}$ 2.2 Hz, H-6), 4.02 (q, 1H, $J_{4,5} = J_{5,6} = J_{5,NH}$ = 10.2 Hz, H-5), 4.11 (dd, 1H, $J_{9,9'}$ 12.0, $J_{8,9}$ 5.1 Hz, H-9), 4.30 (dd, 1H, $J_{8,9'}$ 2.6 Hz, H-9'), 4.88 (m, 1H, H-4), 5.28-5.38 (m,2H, H-7,8), and 5.30 (d, 1H, $J_{NH,5}$ 10.2 Hz, NH); Glc unit: δ 2.92 (m, 2H, H-6,6'), 3.41 (s, 3H, MeO), 3.83 (m, 1H, H-5), 4.82-4.90 (m, 1H, H-2), 4.88 (d, 1H, $J_{1,2}$ 3.6 Hz, H-1), 4.92 (t, 1H, $J_{3,4} = J_{4,5}$ = 9.4 Hz, H-4), and 5.41 (t, 1H, $J_{2,3} = J_{3,4}$ = 9.4 Hz, H-3); other groups: δ 2.00, 2.03, 2.05, 2.06, 2.08, 2.13, 2.14 (7s, 21H, 7AcO).

Anal. Calcd for $C_{33}H_{47}NO_{20}S$: C, 50.71; H, 6.06; N, 1.79. Found: C, 50.50; H, 6.13; N, 1.75.

Other 6-S-(methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-6-thio-D-hexopyranoside derivatives (12, 17, and 18) were synthesized according to the method described for 11.

Methyl 2,3,4-tri-O-acetyl-6-S-(methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-6-thio-α-D-galactopyranoside (12). Compound 12 was obtained as an amorphous mass in 67.3% yield; mp 100-102°, $[\alpha]_D^{25}$ + 68.0° (c 1.0, chloroform); IR (Nujol): 3280 (NH), 1750 and 1230 (ester), and 1660 and 1550 cm^{-1} (amide); NMR data at 270 MHz (in $CDCl_3$): Neu 5Ac unit: δ 1.88 (s, 3H, AcN), 1.98 (near t, $J_{3a,3e} = J_{3a,4}$ = 12.3 Hz, H-3a), 2.71 (dd, 1H, $J_{3a,3e}$ 12.3, $J_{3e,4}$ 4.6 Hz, H-3e), 3.81 (dd, 1H, $J_{5,6}$ 10.2, $J_{6,7}$ 2.2 Hz, H-6), 3.82 (s, 3H, MeO), 4.05 (q, 1H, $J_{4,5} = J_{5,6} = J_{5,NH}$ = 10.2 Hz, H-5), 4.09 (dd, 1H, $J_{9,9'}$, 12.2, $J_{8,9}$ 5.2 Hz, H-9), 4.21 (dd, 1H, $J_{9,9'}$, 12.2, $J_{8,9'}$ 2.3 Hz, H-9'), 4.89 (m, 1H, H-4), 5.24 (d, 1H, $J_{5,NH}$ 10.2

Hz, NH), 5.28-5.41 (m, 2H, H-7,8); Gal unit: δ 2.67-3.00 (m, 2H, H-6,6'), 3.41 (s, 3H, MeO), 3.76-3.92 (m, 1H, H-5), 4.96 (d, 1H, $J_{1,2}$ 3.6 Hz, H-1), 5.12 (dd, $J_{1,2}$ 3.6, $J_{2,3}$ 10.6 Hz, H-2), 5.32 (dd, 1H, $J_{2,3}$ 10.6, $J_{3,4}$ 3.3 Hz, H-3), and 5.38 (dd, 1H, $J_{3,4}$ 3.3, $J_{4,5}$ 1.2 Hz, H-4); other groups: δ 1.98, 2.03 (2), 2.08, 2.13, 2.14, 2.16 (7s, 21H, 7AcO).

Anal. Calcd for $C_{33}H_{47}NO_{20}S$: C, 50.71; H, 6.06; N, 1.79. Found: C, 50.52; H, 6.21; N, 1.71.

Allyl 2,3,4-tri-O-acetyl-6-S-(methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-6-thio-β-D-glucopyranoside (17). Compound 17 was obtained as an amorphous mass in 70.2% yield; mp 89-91°, $[\alpha]_D^{25}$ + 25.5° (c 0.56, chloroform); IR (Nujol): 3300 (NH), 1750 and 1230 (ester), and 1660 and 1545 cm^{-1} (amide); NMR data at 270 MHz (in $CDCl_3$): Neu 5Ac unit: δ 1.87 (s, 3H, AcN), 1.94 (near t, 1H, $J_{3a,3e} = J_{3a,4}$ = 12.8 Hz, H-3a), 2.73 (dd, 1H, $J_{3a,3e}$ 12.8, $J_{3e,4}$ 4.8 Hz, H-3e), 3.81 (s, 3H, MeO), 3.83 (dd, 1H, $J_{5,6}$ 10.2, $J_{6,7}$ 2.2 Hz, H-6), 4.02 (q, $J_{4,5} = J_{5,6} = J_{5,NH}$ = 10.2 Hz, H-5), 4.11 (dd, 1H, $J_{8,9}$ 5.1, $J_{9,9'}$ 12.5 Hz, H-9), 4.29 (dd, 1H, $J_{8,9'}$ 2.5, $J_{9,9'}$ 12.5 Hz, H-9'), 4.88 (m, 1H, H-4), 5.25-5.36 (m, 2H, H-7,8), and 5.42 (d, 1H, $J_{NH,5}$ 10.2 Hz, NH); Glc unit: δ 2.86-3.03 (m, 2H, H-6,6'), 4.52 (d, 1H, $J_{1,2}$ 8.1 Hz, H-1), 4.93-5.38 (m, 4H,H-2,4, and $-C=CH_2$), 5.17 (t, 1H, $J_{2,3} = J_{3,4}$ = 9.2 Hz, H-3), and 5.77-5.93 (m, 1H, =CH-); other groups: δ 1.99, 2.03 (2), 2.04, 2.07, 2.10, 2.13 (7s, 21H, 7AcO).

Anal. Calcd for $C_{35}H_{49}NO_{20}S$: C, 50.30; H, 5.91; N, 1.68. Found: C, 50.19; H, 5.98; N, 1.67.

Allyl 2-acetamido-3,4-di-O-acetyl-2-deoxy-6-S-(methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-6-thio-β-D-glucopyranoside (18). Compound 18 was obtained as an amorphous mass in 86.3% yield; mp 123-125°, $[\alpha]_D^{25}$ + 28.0° (c 0.69, chloroform); IR (Nujol): 3300 (NH), 1750 and 1230 (ester), and 1670 and 1560 cm^{-1} (amide); NMR data at 270 MHz (in $CDCl_3$): Neu 5Ac unit: δ 1.87 (s, 3H, AcN), 1.97 (near t, $J_{3a,3e} = J_{3a,4}$ = 12.8 Hz, H-3a), 2.72 (dd, $J_{3a,3e}$ 12.8, $J_{3e,4}$ 4.4 Hz, H-3e), 3.81 (s, 3H, MeO), 3.89 (dd, 1H, $J_{5,6}$ 9.6, $J_{6,7}$ 1.8 Hz, H-6), 4.01 (q, 1H, $J_{4,5} = J_{5,6} = J_{5,NH}$ = 9.6 Hz, H-5), 4.33-4.40 (m, 2H, H-9,9'), 4.87 (m, 1H, H-4), 5.27 (dd, 1H, $J_{6,7}$ 1.8, $J_{7,8}$ 8.8 Hz, H-7), 5.33-5.39 (m, 1H, H-8); GlcNAc unit: δ 1.94 (s, 3H, AcN), 2.80-3.00 (m, 2H, H-6,6'), 3.80-4.14 (m, 2H, H-2,5), 4.63 (d, 1H, $J_{1,2}$ 8.1 Hz, H-1), 4.93 (t, 1H, $J_{3,4} = J_{4,5}$ = 9.6 Hz, H-4), 5.21 (t, 1H, $J_{2,3} = J_{3,4}$ = 9.6 Hz, H-3), 5.16-5.40 (m, 2H, $-C=CH_2$), and 5.80-5.95 (m, 1H, -CH=); other groups: δ

2.02, 2.03, 2.04, 2.09, 2.15 (2) (6s, 18H, 6AcO), 5.36, 5.98 (2d, 2H, 2NH).

Anal. Calcd for $C_{35}H_{50}N_2O_{19}S$: C, 50.35; H, 6.04; N, 3.36. Found: C, 50.11; H, 6.31; N, 3.27.

Methyl 6-S-(methyl 5-acetamido-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-6-thio-α-D-glucopyranoside (13). To an ice-cooled solution of 11 (235 mg) in dry methanol (5 mL) was added trace amounts of sodium methoxide, and the mixture was kept for 8 h at room temperature; at that time, all of the starting material had been converted into 13. The mixture was treated with Amberlite IR-120 (H^+) resin to remove the base, and then evaporated to a crystalline mass. Crystallization from ether gave 13 in quantitative yield; mp 127-129°, $[\alpha]_D^{25}$ + 83.5° (c 1.3, 1:1 chloroform-methanol); IR (KBr): 3500-3250 (OH, NH), 1730 and 1230 (ester), and 1640 and 1560 cm^{-1} (amide); NMR data at 270 MHz (in D_2O): Neu 5Ac unit: δ 1.81 (t, 1H, $J_{3a,3e}$ = $J_{3a,4}$ = 12.4 Hz, H-3a), 1.95 (s, 3H, AcN), 2.75 (dd, 1H, $J_{3a,3e}$ 12.4, $J_{3e,4}$ 4.8 Hz, H-3e), and 3.80 (s, 3H, MeO); Glc unit: δ 2.80-3.25 (m, 2H, H-6,6') and 3.33 (s, 3H, MeO).

Anal. Calcd for $C_{19}H_{33}NO_{13}S$: C, 44.27; H, 6.45; N, 2.72. Found: C, 44.03; H, 6.59; N, 2.70.

Other 6-S-(methyl 5-acetamido-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-6-thio-D-hexopyranosides (14, 19, and 20) were respectively prepared from 12, 17, and 18, according to the procedure described for 13.

Methyl 6-S-(methyl 5-acetamido-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-6-thio-α-D-galactopyranoside (14). Compound 14 was obtained as an amorphous mass in quantitative yield; mp 139-140°, $[\alpha]_D^{25}$ + 76.5° (c 0.7, 1:1 chloroform-methanol); IR (KBr): 3450-3300 (OH, NH), 1730 and 1230 (ester), and 1640 and 1560 cm^{-1} (amide); NMR data at 270 MHz (in D_2O): Neu 5Ac unit: δ 1.81 (dd, 1H, $J_{3a,3e}$ 12.8, $J_{3a,4}$ 11.5 Hz, H-3a), 1.96 (s, 3H, AcN), 2.77 (dd, 1H, $J_{3a,3e}$ 12,8, $J_{3e,4}$ 4.8 Hz, H-3e), and 3.82 (s, 3H, MeO); Gal unit: δ 2.82-2.93 (m, 2H, H-6,6'), and 3.35 (s, 3H, MeO).

Anal. Calcd for $C_{19}H_{33}NO_{13}S$: C, 44.27; H, 6.45; N, 2.72. Found: C, 44.25; H, 6.69; N, 2.63.

Allyl 6-S-(methyl 5-acetamido-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-6-thio-β-D-glucopyranoside (19). Compound 19 was obtained as an amorphous mass in 84% yield; mp 119-121°, $[\alpha]_D^{25}$ + 26.0° (c 0.36, methanol); IR (KBr): 3400-3300 (OH, NH), 1730 and 1230 (ester), and 1640 and 1560 cm^{-1} (amide); NMR data at 270 MHz (in

D_2O): Neu 5Ac unit: δ 1.79 (t, 1H, $J_{3a,3e} = J_{3a,4}$ = 12.6 Hz, H-3a), 1.89 (s, 3H, AcN), 2.71 (dd, 1H, $J_{3a,3e}$ 12.4, $J_{3e,4}$ 4.8 Hz, H-3e), and 3.74 (s, 3H, MeO); Glc unit: δ 2.79-3.12 (m, 2H, H-6,6'), 4.30 (d, 1H, $J_{1,2}$ 8.0 Hz, H-1), 5.13-5.28 (m. 2H, $-C=CH_2$), and 5.75-5.90 (m, 1H, =CH-).

Anal. Calcd for $C_{21}H_{35}NO_{13}S$: C, 46.57; H, 6.51; N, 2.59. Found: C, 46.38; H, 6.55; N, 2.51.

Allyl 2-acetamido-2-deoxy-6-S-(methyl 5-acetamido-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-6-thio-β-D-glycopyranoside (20). Compound 20 was obtained as an amorphous mass in quantitative yield; mp 210-212°, $[\alpha]_D^{25}$ + 22.1° (c 1.4, methanol); IR (KBr): 3400-3260 (OH, NH), 1730 and 1230 (ester), and 1650 and 1570 cm^{-1} (amide); NMR data at 270 MHz (in D_2O): Neu 5Ac unit: δ 1.79 (dd, 1H, $J_{3a,3e}$ 12.6, $J_{3a,4}$ 12.0 Hz, H-3a), 2.72 (dd, $J_{3a,3e}$ 12.6, $J_{3e,4}$ 4.3 Hz, H-3e), and 3.77 (s, 3H, MeO): GlcNAc unit: δ 2.83-3.19 (m, 2H, H-6,6'), 4.41 (d, 1H, $J_{1,2}$ 8.4 Hz, H-1), 5.13-5.24 (m, 2H, $-C=CH_2$), and 5.71-5.88 (m, 1H, =CH-); other groups: δ 1.90, 1.92 (2s, 6H, 2AcN).

Anal. Calcd for $C_{21}H_{36}N_2O_{12}S$: C, 46.66; H, 6.71; N, 5.18. Found: C, 46.63; H, 6.58; N, 5.06.

Methyl 6-S-(5-acetamido-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonic acid)-6-thio-α-D-glucopyranoside (15). To a solution of 13 (150 mg) in 1,4-dioxane (3 mL) was added, with stirring, 0.2M potassium hydroxide (2 mL), and the mixture stirred for 3.5 h at room temperature; the progress of the reaction being monitored by t.l.c.. The mixture was treated with Amberlite IR-120 (H^+) resin to remove the base, and the resin was filtered off and washed with water. The filtrate and washings were combined, and lyophilized, to afford 15 as an amorphous mass in quantitative yield, which showed a single spot in t.l.c.; mp 184-186°, $[\alpha]_D^{25}$ + 80.5° (c 0.77, 1:1 1,4-dioxane-water); IR (KBr): δ 3450-3300 (OH, NH), 1700 (C=O), and 1620 and 1550 cm^{-1} (amide); NMR data at 270 MHz (in D_2O): Neu 5Ac unit: δ 1.75 (t, 1H, $J_{3a,3e} = J_{3a,4}$ = 12.0 Hz, H-3a), 1.95 (s, 3H, AcN), and 2.73 (dd, 1H, $J_{3a,3e}$ 12.0, $J_{3e,4}$ 4.5 Hz, H-3e); Glc unit: δ 2.73-3.15 (m, 2H, H-6,6', and 3.34 (s, 3H, MeO).

Anal. Calcd for $C_{18}H_{31}NO_{13}S$: C, 43.11; H, 6.23; N, 2.79. Found: C, 42.85; H, 6.51; N, 2.63.

Other 6-S-(5-acetamido-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonic acid)-D-hexopyranosides (16, 21, and 22) were obtained from compounds (14, 19, and 20) in a similar way described for 15.

Methyl 6-S-(5-acetamido-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonic acid)-6-thio-α-D-galactopyranoside (16). Compound 16 was obtained as an amorphous mass in quantitative yield; mp 174-176°, $[\alpha]_D^{25}$ + 75.0°(c 0.38, 1:1 1,4-dioxane-water); IR (KBr): 3450-3300 (OH, NH), 1700 (C=O), and 1630 and 1550 cm^{-1} (amide); NMR data at 270 MHz (in D_2O): Neu 5Ac unit: δ 1.76 (dd, 1H, $J_{3a,3e}$ 12.8, $J_{3a,4}$ 11.4 Hz, H-3a), 1.97 (s, 3H, AcN), and 2.74 (dd, $J_{3a,3e}$ 12.8, $J_{3e,4}$ 4.4 Hz, H-3e); Gal unit: δ 2.70-2.86 (m, 2H, H-6,6'), and 3.33 (s, 3H, MeO).

Anal. Calcd for $C_{18}H_{31}NO_{13}S$: C, 43.11; H, 6.23; N, 2.79. Found: C, 43.06; H, 6.33; N, 2.75.

Allyl 6-S-(5-acetamido-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonic acid)-6-thio-β-D-glucopyranoside (21). Compound 21 was obtained as an amorphous mass in quantitative yield; mp 163-164°, $[\alpha]_D^{25}$ + 30.0° (c 0.35, water); IR (KBr): 3450 -3300 (OH, NH), 1710 (C=O), and 1640 and 1560 cm^{-1} (amide); NMR data at 270 MHz (in D_2O): Neu 5Ac unit: δ 1.83 (t, $J_{3a,3e} = J_{3a,4}$ = 11.9 Hz, H-3a), 2.01 (s,3H, AcN), and 2.75 (dd, 1H, $J_{3a,3e}$ 11.9, $J_{3e,4}$ 4.2 Hz, H-3e); Glc unit: δ 2.76-3.15 (m, 2H, H-6,6'), 4.43 (d, 1H, $J_{1,2}$ 8.1 Hz, H-1), 5.25-5.39 (m, 2H, $-C=CH_2$), and 5.88 -6.05 (m, 1H, -CH=).

Anal. Calcd for $C_{20}H_{33}NO_{13}S$: C, 45.54; H, 6.31; N, 2.66. Found: C, 45.51; H, 6.43; N, 2.69.

Allyl 2-acetamido-2-deoxy-6-S-(5-acetamido-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonic acid)-6-thio-β-D-glucopyranoside (22). Compound 22 was obtained as an amorphous mass in 95° yield; mp 208-210°, $[\alpha]_D^{25}$ + 36.0° (c 0.93, water); IR (KBr): 3450-3300 (OH, NH), 1710 (C=O), and 1630 and 1550 cm^{-1} (amide); NMR data at 270 MHz (in D_2O): Neu 5Ac unit: δ 1.81 (t, 1H, $J_{3a,3e} = J_{3a,4}$ = 12.7 Hz, H-3a), and 2.69 (dd, 1H, $J_{3a,3e}$ 12.7, $J_{3e,4}$ 4.4 Hz, H-3e); other groups: δ 1.90, 1.91 (2s, 6H, 2AcN).

Anal. Calcd for $C_{20}H_{34}N_2O_{12}S$: C, 45.62; H, 6.51; N, 5.32. Found: C, 45.46; H, 6.78; N, 5.20.

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