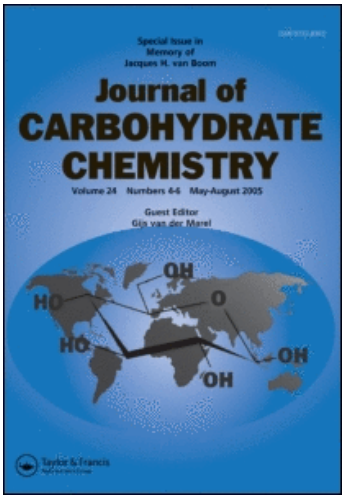

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Synthesis of 3-*S*-C (5-Acetamido-3.5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonic Acid)-3-thio-galactopyranose Derivatives

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

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ABSTRACT

3-S-α-D-Neuraminyl-(2→3)-D-galactose derivatives were synthesized. As the glycosyl acceptors, 4,6-O-ethylidene-1,2-O-isopropylidene-3-O-trifluoromethanesulfonyl-α-D-gulopyranose (6) and 1,2-di-O-acetyl-4,6-O-isopropylidene-3-O-trifluoromethanesulfonyl-β-D-gulopyranose (13) were prepared from 4,6-O-ethylidene-1,2-O-isopropylidene-α-D-galactopyranose (3) in several steps. Condensation of 6 or 13 with 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 (2) gave the corresponding 3-S-(N-acetyl-α-D-neuraminyl)-3-thio-D-galactose derivatives (14 and 15). Compound 15 was converted, via O-deisopropylidenation and subsequent acetylation, into the desired product (17).

*Studies on the thioglycosides of N-acetylneuraminic acid, Part 4. For Part 3, see ref. 1. Presented at the 13th International Carbohydrate Symposium, Ithaca, New York, U.S.A., August 10-15, 1986.

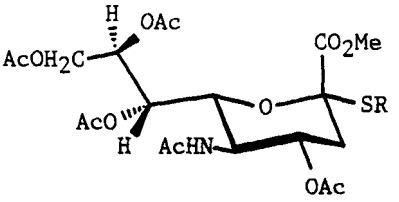
INTRODUCTION

Sialic acids[2] occur in many glycoproteins and glycolipids as the essential constituents, and participate in a variety of important biological functions; they are mainly found in α-ketosidic linkage at the C-3 or C-6 position of galactose and N-acetylgalactosamine residues in glycoconjugates. As outlined in previous papers,[3,4] we recently developed a stereoselective and high yield synthesis of a variety of α-thioglycosides of N-acetylneuraminic acid, such as alkyl N-acetyl-2-thio-D-glycero-α-D-galacto-2-nonulopyranosidoic acids and 6-S-(N-acetyl-α-D-neuraminyl)-6-thio-D-hexopyranosides. The present paper describes an application of this procedure to the synthesis of 3-S-(N-acetyl-α-D-neuraminyl)-3-thio-D-galactopyranose derivatives.

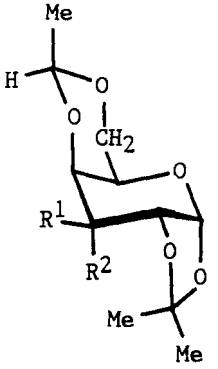
RESULTS AND DISCUSSION

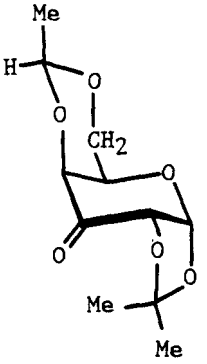
The sodium salt of methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-2-thio-D-glycero-α-D-galacto-2-nonulopyranosonate[3] (2) was used as the glycosyl donor on the α-thioglycosidation reaction, involving inversion of the configuration at the glycosyl position of the acceptor. Therefore, in order to synthesize 3-S-α-D-neuraminyl-(2→3)-D-galactose derivatives as a building unit of glycoconjugate analogs having the S-α-D-neuraminyl residue, we have chosen 4,6-O-ethylidene-1,2-O-isopropylidene-3-O-trifluoromethanesulfonyl-α-D-gulopyranose (6) and 1,2-di-O-acetyl-4,6-O-isopropylidene-3-O-trifluoromethanesulfonyl-β-D-gulopyranose (13), as the convenient glycosyl acceptors.

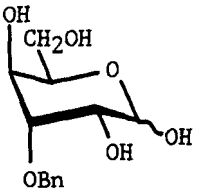
Compound 6 and 13 were prepared from 4,6-O-ethylidene-1,2-O-isopropylidene-α-D-galactopyranose[5,6] (3). Oxidation of the hydroxylgroup at C-3 in 3 with chromium trioxide-pyridine complex[7] in the presence of acetic anhydride afforded the 3-keto compound 4, which was treated with sodium borohydride in aqueous ethanol to give 4,6-O-ethylidene-1,2-O-isopropylidene-α-D-gulopyranose[6] (5; 53%) and 3 (31%), respectively. Compound 5 was converted, by treatment with trifluoromethanesulfonic anhydride in pyridine-dichloromethane, into the 3-O-triflyl derivative (6) in quantitative yield.



1. R = Ac
2. R = Na



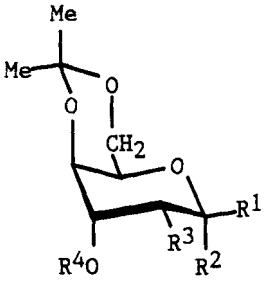


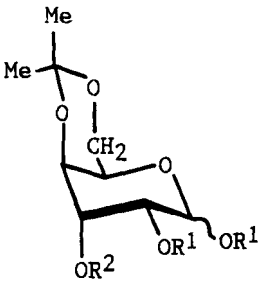


3. R^1 = OH, R^2 = H
5. R^1 = H, R^2 = OH
6. R^1 = H, R^2 = OTf
7. R^1 = H, R^2 = OBn

4

8

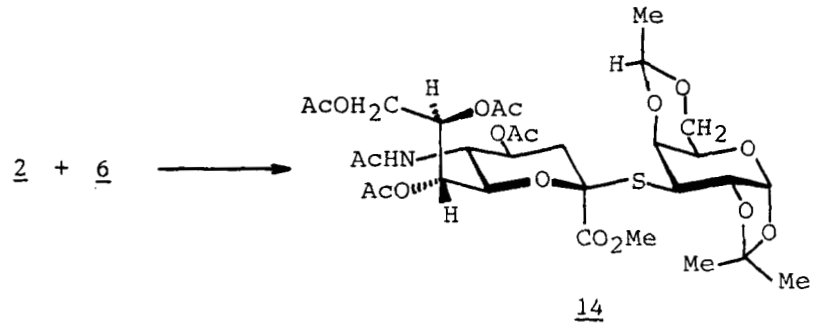




11. R^1 = H, R^2 = R^3 = OAc, R^4 = H
12. R^1 = R^3 = OAc, R^2 = R^4 = H
13. R^1 = R^3 = OAc, R^2 = H, R^4 = Tf

9. R^1 = H, R^2 = Bn
10. R^1 = Ac, R^2 = Bn

Tf = CF_3SO_2
Bn = benzyl



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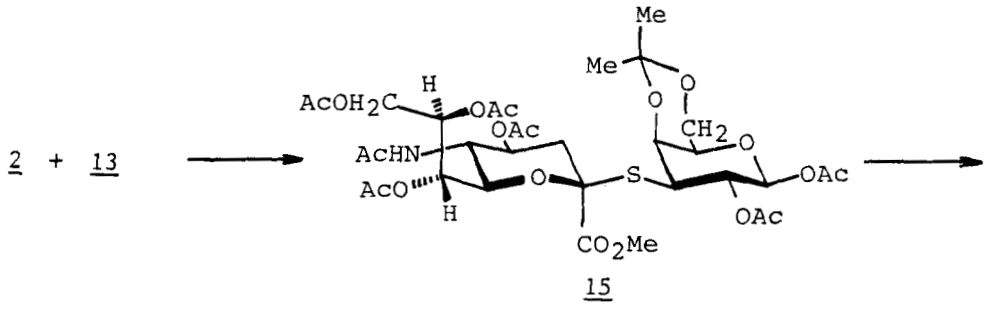

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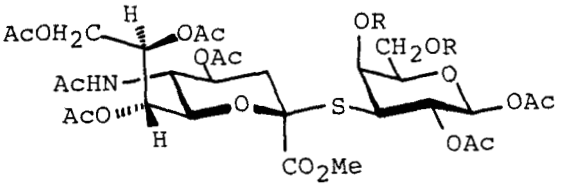

16. R = H

17. R = Ac

On the other hand, benzylation of 5 gave the 3-O-benzyl derivative (7), quantitatively, which was hydrolyzed by heating with 0.02M hydrochloric acid for 10 h at 80°C under nitrogen atmosphere to afford 3-O-benzyl-D-gulopyranose (8; 92%). Isopropylidenation of 8 with 2,2-dimethoxypropane in N,N-dimethylformamide (DMF) in the presence of p-toluenesulfonic acid gave the 4,6-O-isopropylidene derivative (9; 97%), which was then acetylated, to give 1,2-di-O-acetyl-3-O-benzyl-4,6-O-isopropylidene-D-gulopyranose (10). Hydro-

genolysis of benzyl group in 10 using Palladium black catalyst, gave 1,2-di-O-acetyl-4,6-O-isopropylidene-β-D-gulopyranose (12; 86.6%) and the corresponding α-D-gulopyranose derivative (11; 8.7%). On treatment with trifluoromethanesulfonic anhydride, compound 12 afforded the 3-O-triflyl derivative (13) in good yield.

Condensation of 6 or 13, thus obtained, with 2 was performed in dry DMF under nitrogen atmosphere to give 4,6-O-ethylidene-1,2-O-isopropylidene-3-S-(methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-3-thio-α-D-galactopyranose (14; 30%) and 1,2-di-O-acetyl-4,6-O-isopropylidene-3-S-(methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-3-thio-β-D-galactopyranose (15; 22%), on the basis of 2, respectively. In the ^{1}H-NMR spectra of 14 and 15, the resonances characteristic of both the donor and acceptor moieties were clearly observed; H-3e of Neu5Ac moiety appeared at δ 2.73 ($J_{3a,3e}$ 12.8, $J_{3e,4}$ 4.8 Hz) for 14 and at δ 2.67 ($J_{3a,3e}$ 12.5, $J_{3e,4}$ 4.8 Hz) for 15, and H-3 proton of the galactose residue also appeared at δ 3.68 ($J_{2,3}$ 8.1, $J_{3,4}$ 2.6 Hz) for 14 and at δ 3.69 ($J_{2,3}$ 11.4, $J_{3,4}$ 3.3 Hz) for 15, respectively, indicating unequivocally the structures of 3-S-(α-D-neuraminyl)-3-thio-D-galactose derivatives.[3, 4,8-10] There is a room for improvement of the coupling conditions, because of the low yields of the desired 3-S-α-D-neuraminyl-(2→3)-D-galactose derivatives.

Acetolysis of 14 with acetic anhydride-acetic acid-sulfuric acid in a usual way, gave 1,2,4,6-tetra-O-acetyl-3-S-(methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-3-thio-α-D-galactopyranose in only 18.6% yield. The major byproducts were methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-2,6-anhydro-2,3,5-trideoxy-D-glycero-D-galacto-non-2-enoate[11] and 3-S-acetyl-1,2,4,6-tetra-O-acetyl-3-thio-D-galactopyranose. Attempts to remove both the isopropylidene and ethylidene groups in 14 under other acidic conditions were unsuccessful. However, hydrolytic removal of the isopropylidene group in 15 under mild, acidic condition gave 1,2-di-O-acetyl-3-S-(methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-3-thio-β-D-galactopyranose (16), which was then acetylated with acetic anhydride in pyridine to afford 1,2,4,6-tetra-O-acetyl-3-S-(methyl 5-

acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-3-thio-β-D-galactopyranose (17) in good yield. Compound 16 and 17 might be useful as building units for a synthesis of glycoconjugate analogs carrying the S-α-D-neuraminyl residue.

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 at 25 °C, 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 JNM-GX270 (270 MHz) spectrometer, and the NMR data were confirmed by use of decoupling techniques. Preparative chromatography was performed on silica gel (Wako Co.; 200 mesh) with the solvent systems specified. Concentrations and evaporations were conducted in vacuo.

4,6-O-Ethylidene-1,2-O-isopropylidene-α-D-gulopyranose (5). Dry pyridine (55 mL) was added dropwise to a stirred suspension of chromium trioxide (16 g) in dry dichloromethane (30 mL) at 0 °C, and the stirring was continued for 15 min at room temperature. A solution of 4,6-O-ethylidene-1,2-O-isopropylidene-α-D-galactopyranose[5] (3; 9.7 g) in dry dichloromethane (15 mL) was added, with stirring, to the mixture at room temperature; the color of the mixture changed to dark-brown. Acetic anhydride (9 mL) was added, and the mixture was stirred for 0.5 h at room temperature; the reaction being monitored by TLC (ethyl acetate). The mixture was chromatographed on a column of silica gel (500 g) with ethyl acetate, to give compound 4 (7.8 g). To a solution of 4 in 70% aqueous ethanol (25 mL) was added sodium borohydride (1.2 g) at 0 °C, and the mixture was stirred for 20 min at 0 °C, and then treated with Amberlite IR-120 (H^+) resin to remove the base. The mixture was filtered and washed with methanol. The filtrate and washings were combined and concentrated to a syrup, which was chromatographed on a column of silica gel (400 g) with 1:1 ethyl acetate-hexane, to give 5 (4.1 g, 53%) as crystals and a syrup of 3 (2.9 g, 31%). Compound 5 was recrystallized from ether-hexane;

mp 134-135°, $[\alpha]_D$ -8.5° (c 0.6, chloroform) {lit.[6] $[\alpha]_D$ -19° (c 0.64, chloroform)}; IR (KBr): 3400 (OH) and 850 cm^{-1} (Me_2C); NMR at 90 MHz ($CDCl_3$): δ 5.64 (d, 1H, $J_{1,2}$ 5.0 Hz, H-1), 4.74 (q, 1H, CHMe), 4.43 (dd, 1H, $J_{2,3}$ 3.5 Hz, H-2), 4.23-3.90 (m, 4H, H-3,4,6,6'), 3.85 (m, 1H, H-5), 3.25 (broad s, 1H, OH), 1.56, 1.35 (2s, 6H, Me_2C), and 1.34 (d, 3H, CHMe).

Anal. Calcd for $C_{11}H_{18}O_6$: C, 53.65; H, 7.36. Found: C, 53.71; H, 7.32.

4,6-O-Ethylidene-1,2-O-isopropylidene-3-O-trifluoromethanesulfonyl-α-D-gulopyranose (6). A solution of 5 (500 mg) in dry pyridine (2 mL) and dry dichloromethane (2 mL) was stirred at -10°C, while a solution of trifluoromethanesulfonic anhydride (0.51 mL) in dry dichloromethane (2 mL) was added. The stirring was continued for 1 h at 0°C, the course of the reaction being monitored by TLC (10:1 dichloromethane-methanol). The mixture was extracted with dichloromethane, and the extract was successively washed with 2M hydrochloric acid, M sodium carbonate, and water, dried (sodium sulfate), and concentrated, to give 6 as crystals in almost quantitative yield; mp 106-108°, $[\alpha]_D$ +27° (c 0.52, chloroform); IR (KBr): 1400 (Tf), and 865 cm^{-1} (Me_2C); NMR at 90 MHz ($CDCl_3$): δ 5.67 (d, 1H, $J_{1,2}$ 5.4 Hz, H-1), 5.02 (dd, 1H, $J_{2,3}$ 3.8, $J_{3,4}$ 5.5 Hz, H-3), 4.70 (q, 1H, CHMe), 4.55 (dd, 1H, H-2), 4.3-4.0 (m, 3H, H-4,6,6'), and 3.89 (near d, $J_{5,6}$ 2 Hz, H-5), 1.55, 1.35 (2s, 6H, Me_2C), and 1.32 (d, 3H, CHMe).

Anal. Calcd for $C_{12}H_{17}O_8F_3S$: C, 38.09; H, 4.52. Found: C, 38.16; H, 4.45.

3-O-Benzyl-4,6-O-ethylidene-1,2-O-isopropylidene-α-D-gulopyranose (7). To a solution of 5 (2.0 g) in dry DMF (5 mL) was added sodium hydride in oil suspension (58 mg; 60% of sodium hydride by weight) at room temperature, and the mixture was stirred until none of gaseous hydrogen was liberated, then cooled to 0°C. Benzyl bromide (1.9 mL) was added, and the mixture was stirred for 1.5 h at room temperature, and then concentrated to a syrup, which was taken up in dichloromethane. The solution was successively washed with 2M hydrochloric acid, M sodium carbonate, and water, dried (sodium sulfate), and concentrated to a syrup, that was chromatographed on a column of silica gel (200 g) with dichloromethane, to give 7 quantitatively, which was crystallized from ether-hexane; mp 132-

134°, $[\alpha]_D$ -43.6° (c 0.51, chloroform); IR (KBr): 870 (Me_2C), and 750 and 700 cm^{-1} (Ph); NMR at 90 MHz ($CDCl_3$): δ 7.4-7.2 (m, 5H, Ph), 5.5 (d, 1H, $J_{1,2}$ 5.0 Hz, H-1), 4.82, 4.65 (2d, 2H, benzyl methylene), 4.72 (q, 1H, CHMe), 4.32 (dd, 1H, $J_{2,3}$ 3.5 Hz, H-2), 4.20-3.98 (m, 3H, H-4,6,6'), 3.83 (d, 1H, H-5), 3.70 (t, 1H, H-3), 1.53, 1.30 (2s, 6H, Me_2C), and 1.36 (d, 3H, CHMe).

Anal. Calcd for $C_{18}H_{24}O_6$: C, 64.27; H, 7.19. Found: C, 64.33; H, 7.13.

3-O-Benzyl-D-gulopyranose (8). A suspension of 7 (2.3 g) in 0.02M hydrochloric acid (50 mL) was vigorously stirred for 10 h at 80°C under nitrogen atmosphere; the reaction being monitored by TLC (3:1 dichloromethane-methanol). The mixture was neutralized with aqueous sodium hydroxide, and concentrated to dryness. The residue was chromatographed on a column of silica gel (150 g) with 50:1 and 20:1 dichloromethane-methanol. The latter eluate gave 8 (1.7 g, 92%) as crystals; mp 131-132°, $[\alpha]_D$ -11.4° (c 0.67, methanol; equil.); IR (KBr): 3420 (OH), 750 and 700 cm^{-1} (Ph).

Anal. Calcd for $C_{13}H_{18}O_6$: C, 61.92; H, 7.14. Found: C, 61.98; H, 7.08.

1,2-Di-O-acetyl-3-O-benzyl-4,6-O-isopropylidene-D-gulopyranose (10). To a stirred suspension of 8 (3.7 g) and Drierite (1 g) in dry DMF (37 mL) were added 2,2-dimethoxypropane (8 mL) and p-toluenesulfonic acid monohydrate (20 mg), and the mixture was stirred for 3 h at 20°C. The mixture was neutralized with sodium hydrogencarbonate, and filtered. The filtrate was concentrated to a syrup, which was chromatographed on a column of silica gel (250 g) with 150:1 and 50:1 dichloromethane-methanol. The latter eluate gave 3-O-benzyl-4,6-O-isopropylidene-D-gulopyranose (9; 4.1 g, 97%), which was crystallized from ether-hexane; mp 95-97°, $[\alpha]_D$ -21° (c 0.43, chloroform; equil.). Compound 9 (3.2 g) was acetylated with acetic anhydride (6 mL) and pyridine (12 mL) overnight at room temperature, to give 10 as an anomeric mixture quantitatively; $[\alpha]_D$ -39.1° (c 1.24, chloroform), IR (film): 1740 and 1210 (ester), 850 (Me_2C), and 730 and 700 cm^{-1} (Ph); ^1H-NMR (270 MHz, $CDCl_3$); α-anomer: δ 7.39-7.28 (m, 5H, Ph), 6.34 (d, 1H, $J_{1,2}$ 3.3 Hz, H-1), 5.33 (dd, 1H, $J_{2,3}$ 3.6 Hz, H-2), 4.70, 4.63 (2d, 2H, benzyl methylene), 2.10, and 2.05 (2s, 6H, 2AcO); β-anomer: δ 7.39-7.28 (m, 5H, Ph), 6.08 (d, 1H, $J_{1,2}$ 8.8

Hz, H-1), 5.14 (dd, 1H, $J_{2,3}$ 2.2 Hz, H-2), 4.61, 4.60 (2d, 2H, benzyl methylene), 4.03-3.88 (m, 2H, H-6,6'), 3.97 (t, 1H, H-3), 3.83 (near d, 1H, H-5), 2.10 and 2.01 (2s, 6H, 2AcO).

Anal. Calcd for $C_{20}H_{26}O_8$: C, 60.90; H, 6.64. Found: C, 60.68; H, 6.47.

1,2-Di-O-acetyl-4,6-O-isopropylidene-β-D-gulopyranose (12). Compound 10 (300 mg) in methanol (5 mL) was hydrogenated with hydrogen in the presence of freshly prepared palladium black (100 mg) for 1 h at room temperature; the course of the reaction being monitored by TLC (2:1 ethyl acetate-hexane). The catalyst was filtered off, and washed with methanol; the filtrate and washings were combined, and concentrated to a syrup, which was chromatographed on a column of silica gel (30 g) with 1:1 ethyl acetate-hexane, to give 12 (200 mg, 86.6%) and 1,2-di-O-acetyl-4,6-O-isopropylidene-α-D-gulopyranose (11; 20 mg, 8.7%). Crystallization of 12 from ether-hexane gave needles; mp 145-147°, $[\alpha]_D$ -44.4° (c 0.44, chloroform); IR (KBr): 3430 (OH), 1740 and 1220 (ester), and 850 cm^{-1} (Me_2C); NMR at 270 MHz ($CDCl_3$): δ 6.04 (d, 1H, $J_{1,2}$ 8.4 Hz, H-1), 5.18 (dd, 1H, $J_{2,3}$ 3.0 Hz, H-2), 4.14 (t, 1H, $J_{3,4}$ 3.0, H-3), 4.06 (dd, 1H, $J_{5,6}$ 2.2, $J_{6,6'}$ 13.2 Hz, H-6), 4.05 (dd, 1H, $J_{4,5}$ 1.5 Hz, H-4), 3.94 (dd, 1H, $J_{5,6'}$ 1.8 Hz, H-6'), 3.86 (d, 1H, H-5), 2.58 (broad s, 1H, OH), 2.12, 2.11 (2s, 6H, 2AcO), 1.46 and 1.45 (2s, 6H, Me_2C).

Anal. Calcd for $C_{13}H_{20}O_8$: C, 51.31; H, 6.62. Found: C, 51.25; H, 6.53.

1,2-Di-O-acetyl-4,6-O-isopropylidene-3-O-trifluoromethanesulfonyl-β-D-gulopyranose (13). A solution of 12 (150 mg) in pyridine (2 mL) and dichloromethane (1 mL) was stirred at 0°C, while a solution of trifluoromethanesulfonic anhydride (0.16 mL) in dry dichloromethane (1 mL) was added; the mixture was stirred for 4.5 h at room temperature. After extractive processing, the product was purified by chromatography on a column of silica gel (20 g) with dichloromethane, to give 13 as a syrup (167 mg, 78%); $[\alpha]_D$ -36° (c 1.6, chloroform); IR (film): 1770 and 1220 (ester), 1420 (Tf), and 840 cm^{-1} (Me_2C); NMR at 270 MHz ($CDCl_3$): δ 5.97 (d, 1H, $J_{1,2}$ 8.8 Hz, H-1), 5.29 (dd, 1H, $J_{2,3}$ 2.9 Hz, H-2), 5.17 (t, 1H, $J_{3,4}$ 2.9 Hz, H-3), 4.16 (dd, 1H, H-4), 4.09 (dd, 1H, $J_{5,6}$ 2.0, $J_{6,6'}$ 13.2 Hz,

H-6), 3.97 (dd, 1H, $J_{5,6'}$ 2.0 Hz, H-6'), 3.83 (near d, 1H, H-5), 2.13, 2.12 (2s, 6H, 2AcO), and 1.47 (s, 6H, Me_2C).

Anal. Calcd for $C_{14}H_{19}O_{10}F_3S$: C, 38.53; H, 4.38. Found: C, 38.72; H, 4.65.

4,6-O-Ethylidene-1,2-O-isopropylidene-3-S-(methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-3-thio-α-D-galactopyranose (14). Compound 2 was prepared from 1[3] (162 mg) by the method[3] described previously. To a stirred solution of 2 in dry DMF (1 mL) was added at 0°C a solution of 6 (223 mg) in dry DMF (1 mL). The mixture was stirred for 24 h at 1-2°C under nitrogen atmosphere, and extracted with dichloromethane. The extract was washed with water, dried (sodium sulfate), and concentrated to a syrup, which was chromatographed on a column of silica gel (30 g) with dichloromethane, and then 100:1 dichloromethane-methanol. The latter eluate gave 14 (65 mg, 30%) as crystals; mp 97-99°, $[\alpha]_D$ +51.7° (c 0.72, chloroform); IR (KBr): 3280 (NH), 1740 and 1220 (ester), 1660 and 1540 (amide), and 860 cm^{-1} (Me_2C); NMR at 270 MHz ($CDCl_3$): Neu5Ac unit: δ 5.43 (ddd, 1H, $J_{7,8}$ 9.2, $J_{8,9}$ 5.5, $J_{8,9'}$ 2.2 Hz, H-8), 5.30 (dd, 1H, $J_{6,7}$ 1.8 Hz, H-7), 5.23 (d, 1H, $J_{NH,5}$ 9.2 Hz, NH), 4.89 (m, 1H, H-4), 4.23 (dd, 1H, $J_{9,9'}$ 12.5 Hz, H-9'), 4.07 (dd, 1H, H-9), 4.03 (q, 1H, $J_{4,5} = J_{5,6}$ = 9.2 Hz, H-5), 3.81 (s, 3H, MeO), 2.73 (dd, 1H, $J_{3a,3e}$ 12.8 Hz, $J_{3e,4}$ 4.8 Hz, H-3e), 2.14, 2.13, 2.04, and 2.02 (4s, 12H, 4AcO), and 1.89 (s, 3H, AcN); Gal unit: δ 5.80 (d, 1H, $J_{1,2}$ 4.0 Hz, H-1), 4.64 (q, 1H, CHMe), 3.99 (dd, 1H, $J_{2,3}$ 8.1 Hz, H-2), 3.95-3.86 (m, 2H, H-6,6'), 3.83-3.75 (m, 2H, H-4,5), 3.68 (dd, 1H, $J_{3,4}$ 2.6 Hz, H-3), 1.43, 1.64 (2s, 6H, Me_2C), and 1.33 (d, 3H, CHMe).

Anal. Calcd for $C_{31}H_{45}NO_{17}S$: C, 50.60; H, 6.16; N, 1.90. Found: C, 50.51; H, 5.94; N, 2.15.

1,2-Di-O-acetyl-4,6-O-isopropylidene-3-S-(methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-3-thio-β-D-galactopyranose (15). Condensation of 2, prepared from 1 (126 mg), with 13 (120 mg), according to the method described for 14, afforded 15 (40 mg, 22%) as a syrup; $[\alpha]_D$ +39.4° (c 0.94, chloroform); IR (film): 1750 and 1250 (ester), 1660 and 1540 (amide), and 850 cm^{-1} (Me_2C); NMR at 270 MHz ($CDCl_3$): Neu5Ac

unit: δ 5.68 (m, 1H, H-8), 5.26 (dd, 1H, $J_{6,7}$ 2.2, $J_{7,8}$ 10.1 Hz, H-7), 5.20 (d, 1H, $J_{NH,5}$ 10.3 Hz, NH), 4.85 (ddd, 1H, $J_{3a,4}$ 10.3, $J_{3e,4}$ 4.8, $J_{4,5}$ 10.6 Hz, H-4), 4.35 (dd, 1H, $J_{8,9}$ 2.6, $J_{9,9'}$ 12.5 Hz, H-9), 4.08 (q, 1H, $J_{5,6}$ 10.6 Hz, H-5), 3.92 (dd, 1H, $J_{8,9'}$ 6.6 Hz, H-9'), 3.78 (s, 3H, MeO), 3.71 (dd, 1H, $J_{3a,3e}$ 12.5 Hz, H-3e), and 1.88 (s, 3H, AcN); Gal unit: δ 5.98 (d, 1H, $J_{1,2}$ 8.1 Hz, H-1), 5.08 (dd, 1H, $J_{2,3}$ 11.4 Hz, H-2), 4.01 (dd, 1H, $J_{5,6'}$ 2.0, $J_{6,6'}$ 13.0 Hz, H-6'), 3.92 (dd, 1H, $J_{5,6}$ 1.7 Hz, H-6), 3.69 (dd, 1H, $J_{3,4}$ 3.3, H-3), 3.62 (near d, 1H, H-4), 1.43, and 1.38 (2s, 6H, Me_2C); other groups: δ 2.22, 2.18, 2.08 (2), 2.04, and 2.02 (5s, 18H, 6AcO).

Anal. Calcd for $C_{33}H_{47}NO_{19}S$: C, 49.93; H, 5.96; N, 1.76. Found: C, 49.85; H, 5.88; N, 1.63.

1,2,4,6-Tetra-O-acetyl-3-S-(methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-3, 5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-3-thio-β-D-galactopyranose (**17**). A solution of **15** (74 mg) in 80% aqueous acetic acid (6 mL) was heated for 5 h at 45 °C, and then concentrated. The product was purified by chromatography on a column of silica gel (6 g) with 50:1 dichloromethane-methanol, to give **16** (56 mg, 84%) as a syrup. Compound **16** thus obtained, was acetylated with acetic anhydride in pyridine. After extractive processing, the title compound was obtained as a syrup, which showed a single spot on TLC; $[\alpha]_D$ +31.2° (c 0.62, chloroform); IR (film): 3390 (NH), 1750 and 1220 (ester), and 1670 and 1540 cm^{-1} (amide); NMR at 270 MHz ($CDCl_3$); Neu5Ac unit: δ 5.66 (ddd, 1H, $J_{7,8}$ 9.9, $J_{8,9}$ 6.6, $J_{8,9'}$ 2.6 Hz, H-8), 5.28 (d, 1H, $J_{NH,5}$ 10.6 Hz, NH), 5.28 (dd, 1H, $J_{6,7}$ 2.2 Hz, H-7), 4.83 (m, 1H, H-4), 4.34 (dd, 1H, $J_{9,9'}$ 12.1 Hz, H-9'), 4.11 (q, 1H, $J_{4,5} = J_{5,6}$ = 10.6 Hz, H-5), 3.91 (dd, 1H, H-9), 3.85 (s, 3H. MeO), 3.72 (dd, 1H, H-6), 2.66 (dd, 1H, $J_{3a,3e}$ 12.6, $J_{3e,4}$ 4.8 Hz, H-3e), and 1.88 (s, 3H, AcN); Gal unit: δ 6.05 (d, 1H, $J_{1,2}$ 8.1 Hz, H-1), 4.97 (dd, 1H, $J_{2,3}$ 11.7 Hz, H-2), 4.95 (near d, 1H, $J_{3,4}$ 3.7 Hz, H-4), 4.32 (t, 1H, $J_{5,6} = J_{5,6'}$ = 6.6 Hz, H-5), 4.09 (dd, 1H, $J_{6,6'}$ 12.1 Hz, H-6), 3.98 (dd, 1H, H-6') and 3.82 (dd, 1H, H-3); other groups: δ 2.22, 2.11, 2.10, 2.09 (2), 2.05, 2.04, and 2.02 (7s, 24H, 8AcO).

Anal. Calcd for $C_{34}H_{47}NO_{21}S$: C, 48.74; H, 5.65; N, 1.67. Found: C, 48.63; H, 5.70; N, 1.82.

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