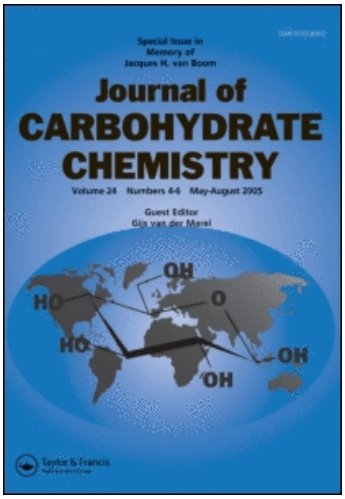

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SIMPLE CONSTRUCTION OF Neu5Ac(α2-8)Neu5Ac AND TOTAL SYNTHESIS OF GANGLIOSIDE GD_3

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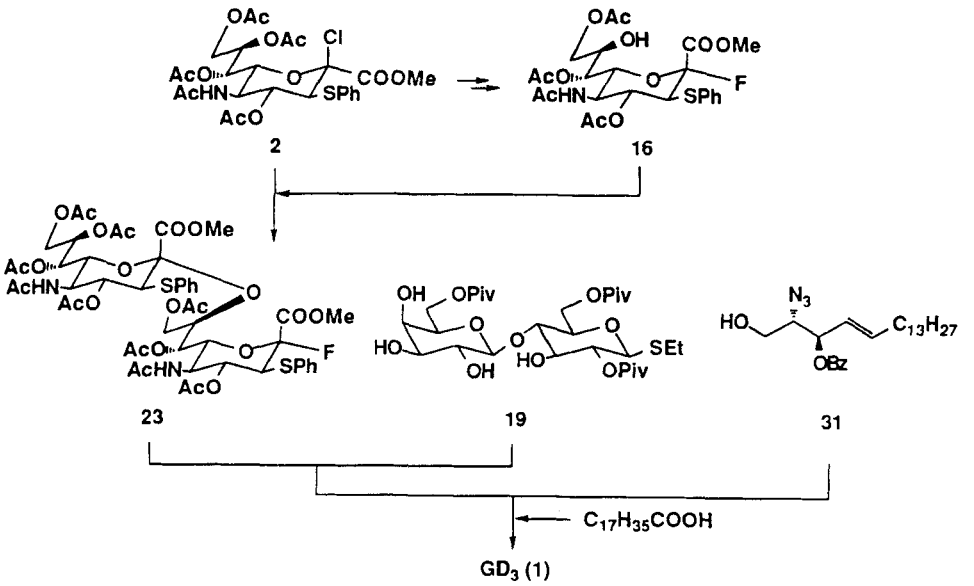
ABSTRACT

Glycosylation of an 8-unprotected sialyl fluoride **16** with 2β-chloro-3β-phenylthio-Neu5Ac **2** gave the desired α-disialate **23**. Subsequent glycosylation of a thiolactoside **19** with the disialyl fluoride **23** gave the tetrasaccharide **28**. Synthesis of GD_3 **1** was realized by condensation of the tetrasaccharide **28** with azidosphingosine **31**, following our previously reported GM_3 synthesis procedure.

INTRODUCTION

GD_3, a disialoganglioside which has been isolated from various mammalian tissues,[1] is well known as a human melanoma-associated antigen.[2] While the whole structure of GD_3 is recognized by antibodies,[2] the Neu5Ac(α2-8)Neu5Ac sequence appears to be a key structure for its biological function. The first chemical synthesis of the sialyl sialate linked by α2-8 or α2-9 glycoside bonds was performed by Goto et al. using an α-sialylation methodology based on the neighbouring group effect of the 3β-hydroxyl group.[3] This sterically promotes α-selectivity (the α:β ratio was observed to be about 3:1),[3] preventing dehydrohalogenation. As the reducing terminal acceptor 8- or 9-unprotected peracetyl 2,3-dehydro-Neu5Ac[5] were chosen because of the capacity for elongation to an oligosaccharide. Our group[4] and Ogawa et al.[5] subsequently introduced a 3β-phenylthio substituted Neu5Ac as an efficient α-glycosylation sialyl donor and Ogawa



scheme 1

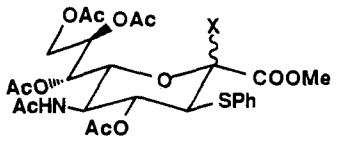
et al. prepared the benzyl protected Δ^2-disialate by condensation of perbenzyl 2β-bromo-3β-phenylthio-Neu5Ac with the 8-unprotected 2,3-dehydro-Neu5Ac acceptor, thereby completing the first synthesis of GD_3.[5] However, transformation of the 2,3-dehydro-Neu5Ac to the donor form with this process requires multiple steps. Hasegawa et al.[6] also reported a method using a colominic acid hydrolyzate,[7] sialyl-(α2-8)-sialic acid, avoiding the difficulty of chemical α2-8 linkage formation. We earlier prepared an α-sialylating donor, peracetyl 2β-chloro-3β-phenylthio-Neu5Ac[4] (**2**), and achieved total GM_3 synthesis.[8] We have documented an efficient total synthesis of GD_3 involving resio- and α-stereocontrolled production of Neu5Ac(α2-8)Neu5Ac utilizing differential reactivity between the sialyl chloride and the fluoride.

RESULTS AND DISCUSSION

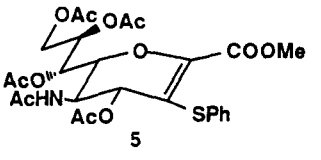
Strategy for Synthesis of GD_3. The methyl (5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-β-D-*glycero*-L-*galacto*-2-nonulopyranosyl)onate fluoride is stable under acidic and basic conditions and not labile with silver salt promotors,[9] such as silver trifluoromethanesulfonate (AgOTf), but can be activated by the Mukaiyama-Suzuki

method,[10] with AgOTf-$SnCl_2$ or AgOTf-Hf complexes, indicating its potential as a candidate sialyl donor having elongation capacity. The 3β-phenylthio substituted Neu5Ac derivative proved to be an efficient α-glycosyl donor for our GM_3 synthesis.[8] Therefore, we designed the Neu5Ac(α2-8)Neu5Ac-F (**23**) as a key intermediate in our synthetic strategy for GD_3 (scheme 1).

Synthesis of Neu5Ac(α2-8)Neu5Ac. Preparation of the methyl (5-acetamido-4,7,8,9-tetra-*O*-acetyl-5-deoxy-3-*S*-phenyl-3-thio-β-D-*erythro*-L-*gluco*-2-nonulopyranosyl)onate fluoride (**4**) from methyl (5-acetamido-4,7,8,9-tetra-*O*-acetyl-5-deoxy-3-*S*-phenyl-3-thio-α-D-*erythro*-L-*gluco*-2-nonulopyranosyl)onate chloride (**2**) was conducted as follows. Treatment of **2** with silver fluoride (AgF) in CH_3CN gave **4** in a 40% yield, accompanied by the Δ^2-product **5**. The coupling constant of H-3 ($J_{F,3}$ = 15.5 Hz) proved the anomeric configuration of the fluoride to be α. By stepwise fluorination using diethylaminosulfur trifluoride[11] (DAST), the transformation was largely improved. Treatment of the anomeric chloride of **2** with AgOTf in acetonitrile (CH_3CN) containing H_2O produced the corresponding 2-OH derivative **3**, and subsequent treatment with DAST in CH_2Cl_2 at -78 ℃ afforded the desired fluoride **4** as white crystals, stable at room temperature, in 98%.



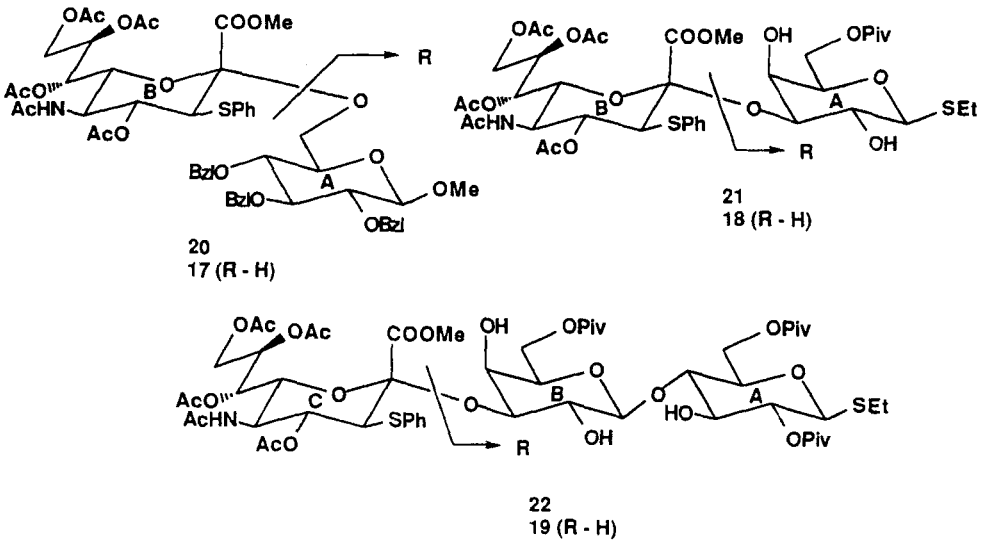
	X
2	Cl (β)
3	OH
4	F (α)



5

To evaluate the ability of glycosylation of 3β-phenylthio sialyl fluoride **4**, glycosylation was attempted with saccharides **17**, **18**, **19** using **4** as the donor. Glycosylation of the primary hydroxyl group of glucoside **17** with the fluoride **4** (the mole ratio of **17** to **4** was 1.6:1) in the presence of AgOTf and $SnCl_2$ provided the α-sialyl glucoside **20** exclusively in a 58% yield. Glycosylations using the secondary hydroxyl of galactose and lactose derivatives,[3] **18** and **19**, gave α-sialyl saccharides **21** and **22** in 37% and 65%, respectively, indicating that the anomeric configurations of the resulting sialosides **20**, **21**, and **22** were α for all according to Okamoto's rule,[3c] the |δH-9-δH-9'| and $J_{7,8}$ of sialic acid being 0.25, 0.14, and 0.25 ppm, and 8.8, 8.8, and 9.0 Hz, respectively. Therefore, this result was very promising for the possibility that the 3β-phenylthio substituted sialyl fluorides would form α-glycosyl linkages.

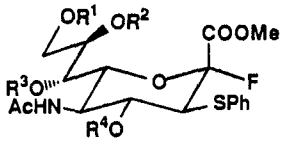
Preparation of Reducing Terminal Sialyl Acceptors. We chose the 4,9-di-*O*-acyl- and 4,7,9-tri-*O*-acyl-3β-phenylthiosialyl fluorides as candidates of sialylation acceptor, and tried sialylation with the chloride **2**.



We prepared the 4,9-di-*O*-benzoyl-3β-phenylthio derivative **8**. Deacetylation of the sialyl fluoride **4** was achieved with potassium *tert*-butoxide in methanol (MeOH) and neutralized with weak acidic ion exchange resin to give **6** in a 91% yield. Treatment with a strong acidic resin such as Dowex 50W (H^+) in MeOH led to the corresponding methyl glycoside. To the deacetylated 2α-fluoro-3β-phenylthio-Neu5Ac **6** in pyridine was added benzoyl chloride (BzCl, 2 eq) in pyridine in the presence of 4-dimethylaminopyridine (DMAP) at -40 ℃ to give a mixture of the following benzoates; 9-*O*-benzoate **7** in 36%, 8,9-di-*O*-benzoate **9** in 35%, 4,8,9-tri-*O*-benzoate **10** in 10%, and the desired 4,9-di-*O*-benzoate **8** in only 9%. From this result, the order of reactivity of the four hydroxyl groups in unprotected sialic acid derivatives was concluded to be HO-9 > HO-8 ≈ HO-4 > HO-7.[12]

To the solution of **6** in pyridine was added equimolar BzCl at -40 ℃ to afford the 9-*O*-benzoate **7** in an 81% yield, and addition of BzCl (1.1 equiv) to the solution of **7** in CH_2Cl_2 in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) and a catalytic amount of DMAP at -78 ℃ gave 4,9-di-*O*-benzoyl-2α-fluoro-3β-phenylthio-Neu5Ac **8** in a 48% yield as the major product. In the case of AcCl, the corresponding 4,9-di-*O*-acetyl-3β-phenylthio derivative **12** was prepared via 9-*O*-acetate **11**.

Acid-catalyzed selective acetonide formation of **6** was achieved with acetone in the presence of Dowex 50 (H^+) to give the 8,9-*O*-isopropylidene derivative **13** in a 76% yield and subsequent acetylation provided the diacetate **14** in 85%. Removal of the acetonide group by 80% aq acetic acid gave **15** in 76% and selective acetylation of the primary 9-hydroxyl group in **15** with equimolar acetyl chloride at -30 ℃ gave the 4,7,9-tri-*O*-acetyl-3β-phenylthiosialyl acceptor **16** in an 81% yield. The anomeric fluoride proved to be sufficiently resistant to the conditions in the course of the above transformation.



	R^1	R^2	R^3	R^4
6	H	H	H	H
7	Bz	H	H	H
8	Bz	H	H	Bz
9	Bz	Bz	H	H
10	Bz	Bz	H	Bz
11	Ac	H	H	H
12	Ac	H	H	Ac

	R^1	R^2	R^3	R^4
13	isopropyridene		H	H
14	isopropyridene		Ac	Ac
15	H	H	Ac	Ac
16	Ac	H	Ac	Ac

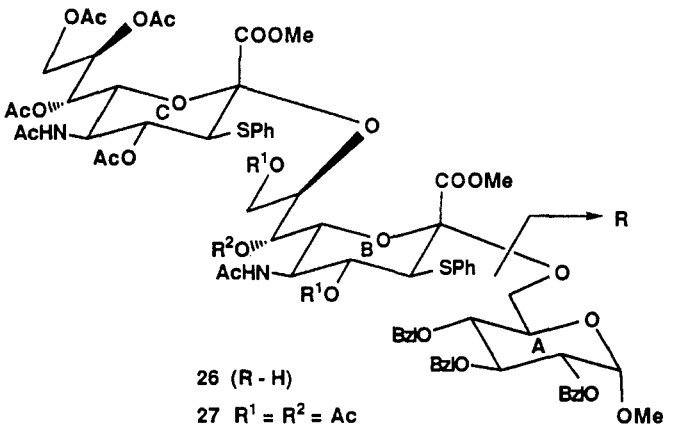
Glycosylation of Sialyl Fluorides with Sialyl Chloride. Glycosylation of sialyl acceptors **8**, **12**, **16** prepared above with the 2β-chloro-3β-phenylthio-Neu5Ac **2** (the mole ratio of **2** to **8**, **12**, **16** was 2:1) was generally conducted with AgOTf (2 eq) and 4A molecular sieves (MS-4A) in CH_2Cl_2 at room temperature.

Using 4,7,9-tri-*O*-acetyl-3β-phenylthio sialyl fluoride **16** as an acceptor, the glycosylation gave the Neu5Ac(α2-8)Neu5Ac (**23**) in a 49% yield. The anomeric configuration of the newly formed glycoside linkage in **23** was determined to be α, showing that the |δH-9-δH-9'| was 0.22 ppm.[3c]

Glycosylation of 4,9-di-*O*-benzoylated sialyl acceptor **8** with the sialyl chloride **2** at 50-65 ℃ afforded the α2-8 linked disialate **24** in less than 20%, accompanied by the 2-hydroxyl derivative **3** (38%). The anomeric configuration of the new linkage was determined to be α, since the |δH-9-δH-9'| was 0.20 ppm and $J_{7,8}$ was 8.3 Hz.[3c] In the case of the 4,9-di-*O*-acetylated sialyl acceptor **12**, the 2-hydroxyl derivative **3** predominated and a trace of disaccharide **25** was provided.

Synthesis of GD_3 Tetrasaccharide. The α-elongation ability of **23** was evaluated using methyl glucoside hydroxyl as the acceptor[13] **26**. Glycosylation of **26** with **23** (the mole ratio of **26** to **23** was 1.5:1) by the Mukaiyama method (AgOTf-$SnCl_2$) in the presence of 4A molecular sieves (MS-AW300) and Na_2HPO_4 in CH_3CN afforded a single trisaccharide, **27**, in a 47% yield. The anomeric configuration of the newly formed glycosyl linkage in **27** should be α due to strong neighbouring group participation of the 3β-phenylthio substituent.

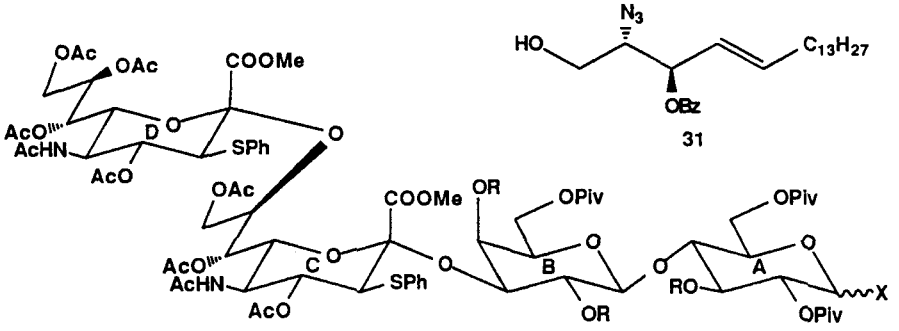
Glycosylation of the ethyl thiolactoside **19** with the α2-8 linked disialate **23** (the mole ratio of **19** to **23** was 1.2:1) in the presence of AgOTf, $SnCl_2$ and MS-AW300 in



	R	R^1	R^2
23	F	Ac	Ac
24	F	Bz	H
25	F	Ac	H

CH_3CN at room temperature gave the Neu5Ac(α2-8)Neu5Ac(α2-3)Gal(β1-4)Glc(β)-SEt **28** exclusively in a 39% yield. Acetylation of **28** for protection of the remaining hydroxyl groups gave the acetate **29** in 74%. The newly formed sialyl linkage position was determined to be at 3'-OH of the lactoside **19** since the anomer ^{13}C of the reducing terminal sialic acid correlated with the H-3 proton (B-3) of the galactose residue of the lactoside by HMBC.

Total Synthesis of GD_3. Condensation of the azidosphingosine[14] (**31**) with the thiotetrasaccharide **29** was achieved directly by activation with DMTST[15] to provide the glycosyl azidosphingosine **32** in an 84% yield. The anomeric proton appeared at δ 4.55 ppm, $J_{1,2}$ = 7.9 Hz, indicating that the glycosyl linkage was β. This direct condensation was effective for short step synthesis of gangliosides.[8] Furthermore, the glycolipid formation was realized in a total 63% yield via an imidate intermediate **30**, derived from **29** by activation with DMTST and H_2O, then treatment with trichloroacetonitrile and DBU.

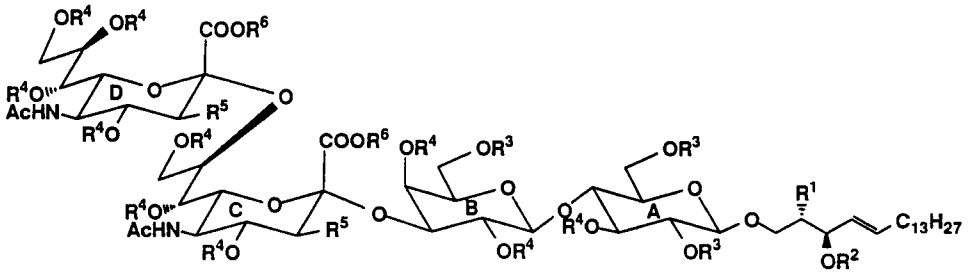


	R	X
28	H	SEt (β)
29	Ac	SEt (β)
30	Ac	OC(=NH)CCl_3 (α)

Transformation of the azide in **32** to the ceramide was accomplished according to our previously reported phosphine reduction-acylation method.[8] The reduction of the azide **32** with tri-*n*-butylphosphine (1 eq) in the presence of octadecanoic acid (2 eq) in CH_2Cl_2 followed by addition of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (WSC) for completion of the reaction afforded the corresponding ceramide **33** in a 71% yield. Removal of the two 3β-phenylthio groups in the sialyl moieties of **33** by radical reduction using tri-*n*-butyltin hydride (*n*-Bu_3SnH) in the presence of azobisisobutyronitrile (AIBN) in toluene afforded the desired compound **34** in 66% without any damage to the olefin in the ceramide moiety.

Finally, *O*-deacylation of **34** with potassium *tert*-butoxide in MeOH, with subsequent saponification of the sialate methyl ester groups, yielded the ganglioside GD_3 **1** in a quantitative yield. The ^1H NMR data of the synthetic **1** were confirmed to be completely consistent with previously reported data.[16]

The work described above showed that the 3β-phenylthio group on the Neu5Ac donor controls α-stereoselective sialylation effectively, with the differential reactivity between sialyl chloride and fluoride realizing efficient synthesis of Neu5Ac(α2-8)Neu5Ac for production of the GD_3 ganglioside. Employment of this simple methodology is a promising approach for synthesis of a series of α-polysialyl gangliosides and their analogues.



	R^1	R^2	R^3	R^4	R^5	R^6
32	N_3	Bz	Piv	Ac	SPh	Me
33	$NHCOC_{17}H_{35}$	Bz	Piv	Ac	SPh	Me
34	$NHCOC_{17}H_{35}$	Bz	Piv	Ac	H	Me
1	$NHCOC_{17}H_{35}$	H	H	H	H	H

EXPERIMENTAL

General Methods. Melting points were determined with a micro melting point apparatus (Yanaco, MP-3S) and are uncorrected. Optical rotations were determined with a JASCO

DIP-181 polarimeter at ambient temperature, and IR spectra were measured directly on a NaCl plate (film) with a JASCO FT/IR-7000S spectrophotometer. ^{1}H NMR spectra were recorded at 270 MHz with a JEOL JNM-GSX 270 and at 500 MHz with a JEOL GX-500 spectrometers. Chemical shifts (δ) from internal tetramethylsilane were expressed in parts per million unless otherwise noted, and coupling constants (J) in Hz. FABMS spectra were measured by JEOL JMS-MStation using *m*-nitrobenzyl alcohol as matrix. Preparative column chromatography was performed on silica gels (Merck, silica gel 60, or Fuji Silysia Co., BW-300), preparative-layer chromatography were performed using silica gel plates (Merck, silica gel 60 F_{254}, 0.5 mm) with the solvent systems specified. Evaporations were conducted *in vacuo*.

Methyl (5-Acetamido-4,7,8,9-tetra-*O*-acetyl-5-deoxy-3-*S*-phenyl-3-thio-β-D-*erythro*-L-*gluco*-2-nonulopyranosyl)onate fluoride (4). To a mixture of methyl (5-acetamido-4,7,8,9-tetra-*O*-acetyl-5-deoxy-3-*S*-phenyl-3-thio-α-D-*erythro*-L-*gluco*-2-nonulopyranosyl)onate chloride (**2**; 1.0 g, 1.6 mmol) and disodium hydrogenphosphate (Na_2HPO_4; 1.0 g) in acetonitrile (CH_3CN; 10 mL) a silver trifluoromethanesulfonate (AgOTf; 0.90 g, 3.5 mmol) in CH_3CN (2.5 mL) was added, and the mixture was stirred for 30 min at room temperature. Then water (0.07 mL) was added to the mixture, and the stirring was continued for 22 h at 50 ℃. After accomplishment of the reaction, the solids were filtered off and washed thoroughly with EtOAc. The filtrate and washings were combined, and the solution was successively washed with satd aq $Na_2S_2O_3$, satd aq $NaHCO_3$, water and brine, dried (Na_2SO_4), and concentrated. Then the crude product was dissolved in CH_2Cl_2 (25 mL), and cooled to -78 ℃. To the cooled solution, diethylaminosulfur trifluoride (DAST; 0.32 mL, 2.4 mmol) was added slowly and the mixture was stirred for 1 h at -78 ℃. The mixture was then warmed to room temperature, and successively washed with satd aq $NaHCO_3$, water and brine, dried with Na_2SO_4, and concentrated. The residue was chromatographed on a column of silica gel (10 g), with 3:2 hexane-acetone, to give **4** (0.94 g, 98%) as white powder; mp 120-122 ℃; $[\alpha]_D$ +26° (*c* 0.16, $CHCl_3$); IR:ν 3254 (NH), 1750 and 1220 (ester), 1654 and 1541 (amide), 1036 (CF), 772 and 693 cm^{-1} (Ph); ^{1}H NMR ($CDCl_3$): δ 1.90, 2.02, 2.06, 2.08, 2.11 (5 s, 15 H, 5Ac), 3.33 (dd, 1 H, $J_{F,3}$ = 15.5, $J_{3,4}$ = 10.5 Hz, H-3), 3.92 (s, 3H, MeO), 4.05 (dd, 1 H, $J_{8,9}$ = 5.5, $J_{9,9'}$ = 12.5 Hz, H-9), 4.22 (dd, 1 H, $J_{5,6}$ = 10.0, $J_{6,7}$ = 2.0 Hz, H-6), 4.25 (dd, 1 H, $J_{8,9'}$ = 2.5, $J_{9,9'}$ = 12.5 Hz, H-9'), 4.29 (q, 1 H, $J_{4,5}$ = $J_{5,6}$ = $J_{5,NH}$ = 10.0 Hz, H-5), 5.2 - 5.3 (m, 2 H, H-7, H-8), 5.44 (dd, 1 H, $J_{3,4}$ = 10.5, $J_{4,5}$ = 10.0 Hz, H-4), 5.46 (d, 1 H, $J_{5,NH}$ = 10.0 Hz, NH), 7.2-7.5 (m, 5 H, Ph); HRMS. Calcd for $C_{26}H_{33}FNO_{12}S$ $(M+H)^+$: 602.1708, Found: 602.1718.

Anal. Calcd for $C_{26}H_{32}FNO_{12}S$ + 1 H_2O (619.68): C, 50.39; H, 5.54; N, 2.26. Found: C, 50.40; H, 5.35; N, 2.45.

Methyl (5-Acetamido-5-deoxy-3-*S*-phenyl-3-thio-β-D-*erythro*-L-*gluco*-2-nonulopyranosyl)onate fluoride (6). A solution of **4** (1.7 g, 2.8 mmol) and potassium *tert*-butoxide (*t*-BuOK; 68 mg, 0.61 mmol) in dry methanol (MeOH; 35 mL) was stirred for 3 h at room temperature. The solution was neutralized through a Amberlite IRC-50 (H^+) column and washed thoroughly with MeOH. The solution and washings were combined and concentrated. Crystallization of the residue was achieved with acetone-diethyl ether to give **6** (1.1 g, 91%) as white powder; mp 120 °C; $[\alpha]_D$ -36° (*c* 0.09, CH_3OH); IR: ν 3600-3100 (OH, NH), 1653 and 1541 (amide), 1220 (ester), 1108 (CF), 773 cm^{-1} (Ph); ^1H NMR (D_2O): δ 2.04 (s, 3 H, Ac), 3.42 (m, 1 H, H-3), 3.53 (br. d, 1 H, $J_{7,8}$ = 9.5 Hz, H-7), 3.58 (dd, 1 H, $J_{8,9}$ = 6.0, $J_{9,9'}$ = 12.0 Hz, H-9), 3.65 (ddd, 1 H, $J_{7,8}$ = 9.5, $J_{8,9}$ = 6.0, $J_{8,9'}$ = 2.5 Hz, H-8), 3.77 (dd, 1 H, $J_{8,9'}$ = 2.5, $J_{9,9'}$ = 12.0 Hz, H-9'), 3.88 (s, 3 H, MeO), 4.1-4.2 (m, 3 H, H-4, H-5, H-6), 7.3-7.6 (m, 5 H, Ph).

Methyl (5-Acetamido-9-*O*-benzoyl-5-deoxy-3-*S*-phenyl-3-thio-β-D-*erythro*-L-*gluco*-2-nonulopyranosyl)onate fluoride (7). To a solution of **6** (2.8 g, 6.4 mmol) in pyridine (80 mL) was added benzoyl chloride (BzCl, 0.90 mL, 7.8 mmol) in pyridine (10 mL) at -40 °C, and the solution was stirred overnight at -40 °C, then to the solution EtOAc was added. The solution was washed with N aq HCl, water, satd $NaHCO_3$, and brine successively, dried with Na_2SO_4, and concentrated. The residue was crystallized with hexane-acetone to give **7** (2.8 g, 81%) as white crystals; mp 187 °C, $[\alpha]_D$ -31° (*c* 0.20, CH_3OH); ^1H NMR (CD_3OD): δ 2.01 (s, 3 H, Ac), 3.15 (dd, 1 H, $J_{F,3}$ = 15.4, $J_{3,4}$ = 10.3 Hz, H-3), 3.58 (dd, 1 H, $J_{6,7}$ = 1.0, $J_{7,8}$ = 9.0 Hz, H-7), 3.86 (s, 3 H, MeO), 3.99 (ddd, 1 H, $J_{7,8}$ = 9.0, $J_{8,9}$ = 5.8, $J_{8,9'}$ = 2.0 Hz, H-8), 4.07 (d, 1 H, $J_{5,6}$ = 8.5 Hz, H-6), 4.14 (m, 2 H, H-4, H-5), 4.33 (dd, 1 H, $J_{8,9}$ = 5.8, $J_{9,9'}$ = 11.6 Hz, H-9), 4.58 (dd, 1 H, $J_{8,9'}$ = 2.0, $J_{9,9'}$ = 11.6 Hz, H-9'), 7.2-8.1 (m, 10 H, 2 Ph).

Methyl (5-Acetamido-4,9-di-*O*-benzoyl-5-deoxy-3-*S*-phenyl-3-thio-β-D-*erythro*-L-*gluco*-2-nonulopyranosyl)onate fluoride (8). A mixture of **7** (0.86 g, 1.6 mmol) and 4-dimethylaminopyridine (DMAP; 40 mg, 0.33 mmol) in CH_2Cl_2 (70 mL) was cooled to -78 °C and added 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU; 0.26 mL, 1.7 mmol) and BzCl (0.21 mL, 1.8 mmol), and the mixture was stirred overnight at -78 °C. To the mixture EtOAc was added and the mixture was washed with 5% aq HCl, water, satd $NaHCO_3$, and brine, dried with Na_2SO_4, and concentrated. The residue was chromatographed on a column of silica gel (100 g), with 50:1 CH_2Cl_2-MeOH, to give **8** (0.49 g, 48%) as white powder; mp 214 °C, $[\alpha]_D$ -61° (*c* 0.27, $CHCl_3$); IR ν 3309 (NH), 1717 and 1270 (ester), 1647 and 1559 (amide), 1070 (CF), 753 and 710 cm^{-1} (Ph); ^1H NMR ($CDCl_3$): δ 2.17 (s, 3 H, Ac), 3.52 (dd, 1 H, $J_{F,3}$ = 14.7, $J_{3,4}$ = 10.0 Hz, H-3),

3.55 (m, 1 H, H-7), 3.93 (s, 3 H, MeO), 4.01 (dd, 1 H, $J_{5,6}$ = 11.0, $J_{6,7}$ < 1.0 Hz, H-6), 4.20 (m, 1 H, H-8), 4.27 (m, 1 H, H-5), 4.50 (dd, 1 H, $J_{8,9}$ = 6.1, $J_{9,9'}$ = 12.2 Hz, H-9), 4.74 (dd, 1 H, $J_{8,9'}$ = 2.5, $J_{9,9'}$ = 12.2 Hz, H-9'), 5.85 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 10.0 Hz, H-4), 6.23 (d, 1 H, $J_{5,NH}$ = 7.4 Hz, NH), 7.2-8.1 (m, 15 H, 3 Ph).

Methyl (5-Acetamido-9-*O*-acetyl-5-deoxy-3-*S*-phenyl-3-thio-β-D-*erythro*-L-*gluco*-2-nonulopyranosyl)onate fluoride (11). To a solution of **6** (0.20 g, 0.46 mmol) in pyridine (6.0 mL) was added acetyl chloride (AcCl, 37 mL, 0.52 mmol) at -30 °C, and the solution was stirred overnight at -30 °C. To the solution EtOAc was added and the solution was washed with 5% aq HCl, water, satd $NaHCO_3$, and brine successively, dried with Na_2SO_4, and concentrated. Column chromatography of the residue on silica gel (11 g) with 4:3 hexane-acetone gave **11** (0.10 g, 45%) as an amorphous mass; ^1H NMR ($CDCl_3$): δ 2.06, 2.08 (2 s, 6 H, 2 Ac), 2.79 (d, 1 H, $J_{8,OH}$ = 5.0 Hz, 8-OH), 3.29 (dd, 1 H, $J_{F,3}$ = 15.0, $J_{3,4}$ = 10.0 Hz, H-3), 3.47 (m, 1 H, H-7), 3.83 (s, 3 H, MeO), 3.88 (d, 1 H, $J_{5,6}$ = 10.8 Hz, H-6), 3.98 (m, 1 H, H-8), 4.04-4.28 (m, 3 H, H-4, H-5, H-9), 4.42 (dd, 1 H, $J_{8,9'}$ = 2.4, $J_{9,9'}$ = 11.5 Hz, H-9'), 4.65 (d, 1 H, $J_{7,OH}$ = 5.4 Hz, 7-OH), 6.51 (d, 1 H, $J_{5,NH}$ = 7.0 Hz, NH), 7.23-7.56 (m, 5 H, Ph).

Methyl (5-Acetamido-4,9-di-*O*-acetyl-5-deoxy-3-*S*-phenyl-3-thio-β-D-*erythro*-L-*gluco*-2-nonulopyranosyl)onate fluoride (12). A mixture of **11** (0.10 g, 0.21 mmol) and DMAP (5.0 mg, 0.041 mmol) in CH_2Cl_2 (5.0 mL) was added DBU (31 μL, 0.21 mmol) and then cooled to -78 °C, AcCl (18 mL, 0.25 mmol) was added. The mixture was stirred overnight at -78 °C. The mixture was washed with 5% aq HCl, water, satd $NaHCO_3$, and brine, dried with Na_2SO_4, and concentrated. The residue was chromatographed on a column of silica gel (10 g), with 1:1 hexane-acetone, to give **12** (60 mg, 55%) as an amorphous mass; ^1H NMR ($CDCl_3$): δ 2.01, 2.09, 2.13 (3 s, 9 H, 3 Ac), 3.35 (dd, 1 H, $J_{F,3}$ = 14.0, $J_{3,4}$ = 10.8 Hz, H-3), 3.42 (m, 1 H, H-7), 3.88 (dd, 1 H, $J_{5,6}$ = 11.3, $J_{6,7}$ < 1.0 Hz, H-6), 3.91 (s, 3 H, MeO), 4.03 (m, 1 H, H-8), 4.13 (m, 1 H, H-5), 4.18 (dd, 1 H, $J_{8,9}$ = 6.8, $J_{9,9'}$ = 11.5 Hz, H-9), 4.45 (dd, 1 H, $J_{8,9'}$ = 2.3, $J_{9,9'}$ = 11.5 Hz, H-9'), 4.61 (d, 1 H, $J_{7,OH}$ = 4.5 Hz, 7-OH), 5.57 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 10.8 Hz, H-4), 6.07 (d, 1 H, $J_{5,NH}$ = 7.9 Hz, NH), 7.25-7.55 (m, 5 H, Ph).

Methyl (5-Acetamido-5-deoxy-8,9-*O*-isopropyridene-3-*S*-phenyl-3-thio-β-D-*erythro*-L-*gluco*-2-nonulopyranosyl)onate fluoride (13). To a solution of **6** (1.2 g, 2.8 mmol) in acetone (50 mL) was added Dowex 50W × 8 (H^+, 0.5 g) resin, and the mixture was stirred for 6 h at room temperature. The mixture was then filtered and washed thoroughly with acetone. The filtrate and washings were combined and concentrated. The residue was chromatographed on a column of silica gel (55 g), with 2:1 hexane-acetone, to give **13** (1.0 g, 76%) as an amorphous mass; mp 88 °C, $[\alpha]_D$ -52° (*c* 0.23, $CHCl_3$); IR *ν* 3308 (NH), 2989 and 2956 (Me), 1742 and 1219 (ester), 1653 and

1541 (amide), 1067 (CF), 754 and 693 cm^{-1} (Ph); ^1H NMR ($CDCl_3$) δ 1.30, 1.34 (2 s, 6 H, $(CH_3)_2C$), 2.10 (s, 3 H, Ac), 3.11 (d, 1 H, $J_{4,OH}$ = 2.6 Hz, 4-OH), 3.24 (dd, 1 H, $J_{F,3}$ = 15.0, $J_{3,4}$ = 10.5 Hz, H-3), 3.41 (m, 1 H, H-7), 3.68 (d, 1 H, $J_{5,6}$ = 10.5 Hz, H-6), 3.87 (s, 3 H, MeO), 3.97 (dd, 1 H, $J_{8,9}$ = 5.0, $J_{9,9'}$ = 9.0 Hz, H-9), 4.06 (q, 1 H, $J_{5,6} = J_{5,NH}$ = 10.5 Hz, H-5), 4.09 (dd, 1 H, $J_{8,9'}$ = 6.0, $J_{9,9'}$ = 9.0 Hz, H-9'), 4.19 (ddd, 1 H, $J_{7,8}$ = 9.0, $J_{8,9}$ = 5.0, $J_{8,9'}$ = 6.0 Hz, H-8), 4.23 (t, 1 H, $J_{3,4}$ = 10.5 Hz, H-4), 4.60 (d, 1 H, $J_{7,OH}$ = 5.0 Hz, 7-OH), 5.67 (d, 1 H, $J_{5,NH}$ = 10.5 Hz, NH), 7.23-7.56 (m, 5 H, Ph).

Anal. Calcd for $C_{21}H_{28}FNO_8S$ (473.51): C, 53.26; H, 5.97; N, 2.96. Found: C, 53.14; H, 6.03; N, 2.93.

Methyl (5-Acetamido-4,7-di-*O*-acetyl-5-deoxy-8,9-*O*-isopropyridene-3-*S*-phenyl-3-thio-β-D-*erythro*-L-*gluco*-2-nonulopyranosyl)onate fluoride (14). A mixture of **13** (1.0 g, 2.1 mmol), acetic anhydride (Ac_2O; 10 mL) and pyridine (20 mL) was stirred overnight at room temperature. The mixture was concentrated to a syrup that was chromatographed on a column of silica gel (90 g), with 3:2 hexane-acetone, to give **14** (1.0 g, 85%) as an amorphous mass; mp 92 °C, $[\alpha]_D$ +30° (*c* 0.23, $CHCl_3$); IR *ν* 3370 (NH), 2989 (Me), 1749 and 1223 (ester), 1654 and 1541 (amide), 1065 (CF), 771 and 694 cm^{-1} (Ph); ^1H NMR ($CDCl_3$) δ 1.31, 1.36 (2 s, 6 H, $(CH_3)_2C$), 1.91, 2.08, 2.11 (3 s, 9 H, 3 Ac), 3.34 (dd, 1 H, $J_{F,3}$ = 15.0, $J_{3,4}$ = 10.5 Hz, H-3), 3.84 (dd, 1 H, $J_{8,9}$ = 7.5, $J_{9,9'}$ = 8.5 Hz, H-9), 3.92 (s, 3 H, MeO), 3.95 (dd, 1 H, $J_{8,9'}$ = 7.5, $J_{9,9'}$ = 8.5 Hz, H-9'), 4.11 (dd, 1 H, $J_{5,6}$ = 10.5, $J_{6,7}$ = 2.0 Hz, H-6), 4.19 (q, 1 H, $J_{7,8} = J_{8,9} = J_{8,9'}$ = 7.5 Hz, H-8), 4.31 (q, 1 H, $J_{4,5} = J_{5,6} = J_{5,NH}$ = 10.5 Hz, H-5), 5.10 (td, 1 H, $J_{6,7}$ = 2.0, $J_{7,8}$ = 7.5 Hz, H-7), 5.32 (d, 1 H, $J_{5,NH}$ = 10.5 Hz, NH), 5.53 (t, 1 H, $J_{3,4} = J_{4,5}$ = 10.5 Hz, H-4), 7.20-7.49 (m, 5 H, Ph).

Anal. Calcd for $C_{25}H_{32}FNO_{10}S$ (557.59): C, 53.85; H, 5.80; N, 2.51. Found: C, 53.55; H, 5.86; N, 2.62.

Methyl (5-Acetamido-4,7-di-*O*-acetyl-5-deoxy-3-*S*-phenyl-3-thio-β-D-*erythro*-L-*gluco*-2-nonulopyranosyl)onate fluoride (15). A solution of **14** (1.0 g, 1.8 mmol) in 80% aq acetic acid (AcOH; 20 mL) was stirred for 8 h at 50 °C. The solution was concentrated to a syrup that was chromatographed on a column of silica gel, with 1:1 hexane-acetone, to give **15** (0.70 g, 76%) as an amorphous mass; mp 98 °C, $[\alpha]_D$ +30° (*c* 0.23, $CHCl_3$); IR *ν* 3500-3100 (OH, NH), 1745 and 1226 (ester), 1670 and 1541 (amide), 1037 (CF), 753 and 693 cm^{-1} (Ph); ^1H NMR ($CDCl_3$) δ 1.92, 2.10, 2.17 (3 s, 9 H, 3 Ac), 2.85-2.92 (m, 2 H, 8-OH, 9-OH), 3.37 (dd, 1 H, $J_{F,3}$ = 15.0, $J_{3,4}$ = 10.5 Hz, H-3), 3.48 (m, 1 H, H-9), 3.65 (m, 1 H, H-9'), 3.83 (m, 1 H, H-8), 3.94 (s, 3 H, MeO), 4.37 (dd, 1 H, $J_{5,6}$ = 10.5, $J_{6,7}$ = 1.0 Hz, H-6), 4.40 (q, 1 H, $J_{4,5} = J_{5,6} = J_{5,NH}$ = 10.5

Hz, H-5), 4.87 (d, 1 H, J = 9.5 Hz, H-7), 5.54 (t, 1 H, $J_{3,4} = J_{4,5}$ = 10.5 Hz, H-4), 5.98 (d, 1 H, $J_{5,NH}$ = 10.5 Hz, NH), 7.16-7.51 (m, 5 H, Ph).

Anal. Calcd for $C_{22}H_{28}FNO_{10}S$ (517.52): C, 51.05; H, 5.46; N, 2.71. Found: C, 50.91; H, 5.46; N, 2.64.

Methyl (5-Acetamido-4,7,9-tri-*O*-acetyl-5-deoxy-3-*S*-phenyl-3-thio-β-D-*erythro*-L-*gluco*-2-nonulopyranosyl)onate fluoride (16). Acetyl chloride (AcCl; 0.12 mL, 1.7 mmol) was added to a solution of **15** (0.70 g, 1.4 mmol) in pyridine (10 mL), the mixture was stirred for 5 h at -30 °C, and then EtOAc was added. The solution was washed with 5% aq HCl, water, satd $NaHCO_3$, and brine successively, dried with Na_2SO_4, and concentrated. The residue was then chromatographed on a column of silica gel (55 g), with 3:2 hexane-acetone, to give **16** (0.61 g, 81%) as an amorphous mass; mp 83 °C, $[\alpha]_D$ +35° (c 0.30, $CHCl_3$); IR ν 3370 (OH, NH), 1745 and 1224 (ester), 1670 and 1541 (amide), 1046 (CF), 771 and 710 cm^{-1} (Ph); ^1H NMR ($CDCl_3$) δ 1.90, 2.09 (2), 2.11 (4 s, 12 H, 4 Ac), 2.62 (d, 1 H, J = 5.0 Hz, 8-OH), 3.36 (dd, 1 H, $J_{F,3}$ = 15.0, $J_{3,4}$ = 10.5 Hz, H-3), 3.94 (s, 3 H, MeO), 4.00-4.15 (m, 3 H, H-8, H-9, H-9'), 4.27 (dd, 1 H, $J_{5,6}$ = 10.0, $J_{6,7}$ = 2.0 Hz, H-6), 4.32 (q, 1 H, $J_{4,5} = J_{5,6} = J_{5,NH}$ = 10.0 Hz, H-5), 5.04 (br.d, 1 H, J = 8.3 Hz, H-7), 5.39 (d, 1 H, $J_{5,NH}$ = 10.0 Hz, NH), 5.50 (dd, 1 H, $J_{3,4}$ = 10.5, $J_{4,5}$ = 10.0 Hz, H-4), , 7.24-7.54 (m, 5 H, Ph).

Anal. Calcd for $C_{24}H_{30}FNO_{11}S$ + 0.3 H_2O (565.03): C, 51.02; H, 5.46; N, 2.48. Found: C, 51.08; H, 5.55; N, 2.52.

Methyl (Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-5-deoxy-3-*S*-phenyl-3-thio-β-D-*erythro*-L-*gluco*-2-nonulopyranosylonate)-(2→6)-2,3,4-tri-*O*-benzyl-β-D-glucopyranoside (20). To a mixture of AgOTf (47 mg, 0.18 mmol), stannous chloride ($SnCl_2$; 32 mg, 0.17 mmol), Na_2HPO_4 (100 mg), and 4A molecular sieves (MS-AW300, 100 mg) in dry CH_3CN (0.3 mL) was added methyl 2,3,4-tri-*O*-benzyl-β-D-glucopyranoside (**17**; 65 mg, 0.14 mmol) in CH_3CN (0.3 mL), and the mixture was stirred for 20 min at room temperature. To the mixture **4** (51 mg, 0.085 mmol) in CH_3CN (0.3 mL) was added and the mixture was stirred in the dark for 5 days at room temperature. The solids were filtered off and washed thoroughly with EtOAc. The filtrate and washings were combined, and the solution was successively washed with satd aq Na_2SO_4, 5% aq $Na_2S_2O_3$, 5% aq $NaHCO_3$, water and brine, dried (Na_2SO_4), and concentrated. Preparative TLC on silica gel, with 3:2 hexane-acetone, gave **20** (52 mg, 58%) as an amorphous mass, and staring material **4** (8 mg) was recovered; compd **20**: mp 85-87 °C, $[\alpha]_D$ -2.8° (c 0.18, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.89, 1.92, 1.96, 1.97, 1.98, (5 s, 15 H, 5 Ac), 3.25 (d, 1 H, $J_{3,4}$ = 11.1 Hz, B-3), 3.33 (t, 1 H, $J_{3,4} = J_{4,5}$ = 9.0 Hz, A-4), 3.36 (dd, 1 H, $J_{1,2}$ = 7.5, $J_{2,3}$ = 8.8 Hz, A-2), 3.43 (ddd, 1 H, $J_{4,5}$ = 9.0, $J_{5,6}$ = 5.0, $J_{5,6'}$ = 1.9 Hz, A-5), 3.49 (s, 3 H, MeO), 3.59 (t, 1 H, $J_{2,3} = J_{3,4}$ = 9.0 Hz, A-3),

3.78 (s, 3 H, MeO), 3.94 (dd, 1 H, $J_{8,9}$ = 5.6, $J_{9,9'}$ = 12.5 Hz, B-9), 4.04 (dd, 1 H, $J_{5,6}$ = 5.0, $J_{6,6'}$ = 10.6 Hz, A-6), 4.15 (dd, 1 H, $J_{5,6'}$ = 1.9, $J_{6,6'}$ = 10.6 Hz, A-6'), 4.19 (dd, 1 H, $J_{8,9'}$ = 2.5, $J_{9,9'}$ = 12.5 Hz, B-9'), 4.21 (d, 1 H, $J_{1,2}$ = 7.5 Hz, A-1), 4.21 (m, 1 H, B-5), 4.34 (dd, 1 H, $J_{5,6}$ = 11.3, $J_{6,7}$ = 2.3 Hz, B-6), 4.61 (d, 1 H, J = 10.0 Hz, CH_2Ph), 4.66 (d, 1 H, J = 10.0 Hz, CH_2Ph), 4.73 (d, 1 H, J = 11.3 Hz, CH_2Ph), 4.78 (d, 1 H, J = 11.3 Hz, CH_2Ph), 4.90 (d, 1 H, J = 11.3 Hz, CH_2Ph), 4.91 (d, 1 H, J = 11.3 Hz, CH_2Ph), 5.27-5.32 (m, 2 H, B-4, B-7), 5.33 (ddd, 1 H, $J_{7,8}$ = 8.8, $J_{8,9}$ = 5.6, $J_{8,9'}$ = 2.5 Hz, B-8), 5.47 (d, 1 H, $J_{5,NH}$ = 10.0 Hz, NH), 7.1-7.5 (m, 20 H, Ph); FABMS (NBA) *m/z* 1045.9 $(M+H)^+$.

Anal. Calcd for $C_{54}H_{63}O_{18}NS$ + 3 H_2O (1100.3): C, 58.94; H, 6.33; N, 1.27. Found: C, 58.54; H, 5.93; N, 1.62.

Ethyl (Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-5-deoxy-3-*S*-phenyl-3-thio-β-D-*erythro*-L-*gluco*-2-nonulopyranosylonate)-(2→3)-6-*O*-pivaloyl-1-thio-β-D-galactopyranoside (21). To a mixture of AgOTf (17 mg, 66 μmol), $SnCl_2$ (13 mg, 66 μmol), Na_2HPO_4 (40 mg), and MS-AW300 (40 mg) in dry CH_3CN (0.5 mL) was added ethyl 6-*O*-pivaloyl-1-thio-β-D-galactopyranoside (**18**; 15 mg, 50 μmol), and the mixture was stirred for 20 min at room temperature. To the mixture **4** (20 mg, 33 μmol) was added and the mixture was stirred in the dark for 42 h at room temperature. The same work-up as described for **20** gave a crude product, that was chromatographed on a column of silica gel, with 3:1 toluene-acetone, to give **21** (11 mg, 37%) as an amorphous mass, and **4** (7 mg) was recovered; compd **21**: mp 89-90 °C, $[\alpha]_D$ +30.0° (*c* 0.19, $CHCl_3$); IR (KBr), ν 3518, 3494, 3382, 2962, 1747, 1668, 1550, 1439, 1370, 1221, 1154, 1034 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.21, (s, 9 H, Piv), 1.30 (t, 3 H, J = 8.0 Hz, CH_3CH_2S), 1.92, 2.04, 2.06, 2.07, 2.14 (5 s, 15 H, Ac), 2.73 (m, 2 H, CH_3CH_2S), 2.83 (br, 1 H, A-2OH), 3.48 (d, 1 H, $J_{3,4}$ = 11.3 Hz, B-3), 3.52 (br.t, 1 H, J = 10.0 Hz, A-2), 3.66 (br.t, 1 H, J = 6.3 Hz, A-5), 3.91 (s, 3 H, MeO), 4.05 (dd, 1 H, $J_{8,9}$ = 5.6, $J_{9,9'}$ = 12.5 Hz, B-9), 4.09 (br, 1 H, A-4), 4.16 (dd, 1 H, $J_{2,3}$ = 8.8 Hz, $J_{3,4}$ = 3.1 Hz, A-3), 4.19 (dd, 1 H, $J_{8,9'}$ = 3.1, $J_{9,9'}$ = 12.5 Hz, B-9'), 4.21 (q, 1 H, $J_{4,5}$ = $J_{5,6}$ = $J_{5,NH}$ = 10.0 Hz, B-5), 4.26-4.28 (m, 2 H, A-6, A-6'), 4.35 (dd, 1 H, $J_{5,6}$ = 10.0, $J_{6,7}$ = 1.9 Hz, B-6), 4.38 (d, 1 H, $J_{1,2}$ = 10.0 Hz, A-1), 5.27 (dd, 1 H, $J_{6,7}$ = 1.9, $J_{7,8}$ = 8.8 Hz, B-7), 5.34 (ddd, 1 H, $J_{7,8}$ = 8.8, $J_{8,9}$ = 5.6, $J_{8,9'}$ = 3.1 Hz, B-8), 5.38 (dd, 1 H, $J_{3,4}$ = 11.3, $J_{4,5}$ = 10.0 Hz, B-4), 5.42 (d, 1 H, $J_{5,NH}$ = 10.0 Hz, NH), 7.2-7.6 (m, 5 H, Ph); FABMS (NBA) *m/z* 890.1 $(M+H)^+$.

Anal. Calcd for $C_{39}H_{55}O_{18}NS_2$ + 1 H_2O (908.11): C, 51.58; H, 6.34; N, 1.54. Found: C, 51.46; H, 5.99; N, 1.89.

Ethyl (Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-5-deoxy-3-*S*-phenyl-3-thio-β-D-*erythro*-L-*gluco*-2-nonulopyranosylonate)-(2→3)-6-*O*-

pivaloyl-β-D-galactopyranosyl-(1→4)-2,6-di-*O*-pivaloyl-1-thio-β-D-gluco-pyranoside (22). To a mixture of AgOTf (43 mg, 0.17 mmol), $SnCl_2$ (31 mg, 0.17 mmol), Na_2HPO_4 (100 mg), and MS-AW300 (100 mg) in dry CH_3CN (1.2 mL) was added ethyl (6-*O*-pivaloyl-β-D-galactopyranosyl)-(1→4)-2,6-di-*O*-pivaloyl-1-thio-β-D-glucopyranoside (**19**; 80 mg, 0.12 mmol), and the mixture was stirred for 20 min at room temperature. To the mixture **4** (50 mg, 83 μmol) was added and the mixture was stirred in the dark for 41 h at room temperature. Work-up procedure as described for **20** was conducted to give a crude product. Column chromatography on silica gel (25 g), with 3:1 toluene-acetone, afforded **22** (66 mg, 65%) as an amorphous mass; mp 109-110 °C, $[\alpha]_D$ +16.8° (*c* 0.40, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.14-1.27 (m, 30 H, 3 Piv, CH_3CH_2S), 1.93, 2.02, 2.06, 2.09, 2.12 (5 s, 15 H, 5 Ac), 2.57-2.77 (m, 2 H, CH_3CH_2S), 3.21 (d, 1 H, $J_{2,OH}$ = 1.0 Hz, B-2OH), 3.44 (t, 1 H, $J_{3,4} = J_{4,5}$ = 9.5 Hz, A-4), 3.47 (d, 1 H, $J_{3,4}$ = 11.0 Hz, C-3), 3.51 (dt, 1 H, $J_{1,2} = J_{2,3}$ = 7.5, $J_{2,OH}$ = 1.0 Hz, B-2), 3.60 (ddd, 1 H, $J_{5,6}$ = 2.0, $J_{5,6'}$ = 7.0, $J_{4,5}$ = 9.5 Hz, A-5), 3.70 (t, 1 H, $J_{2,3} = J_{3,4}$ = 9.5 Hz, A-3), 3.72 (ddd, 1 H, $J_{4,5}$ = 3.0, $J_{5,6}$ = 4.0, $J_{5,6'}$ = 8.0 Hz, B-5), 3.91 (s, 3 H, MeO), 4.02 (dd, 1 H, $J_{8,9}$ = 7.0, $J_{9,9'}$ = 12.5 Hz, C-9), 4.07 (br, 1 H, B-4), 4.10 (dd, 1 H, $J_{2,3}$ = 7.5, $J_{3,4}$ = 3.0 Hz, B-3), 4.11 (dd, 1 H, $J_{5,6}$ = 7.0, $J_{6,6'}$ = 12.0 Hz, A-6), 4.18 (dd, 1 H, $J_{5,6}$ = 8.6, $J_{6,6'}$ = 12.0 Hz, B-6), 4.21 (dt, 1 H, $J_{4,5}$ = 11.0, $J_{5,6} = J_{5,NH}$ = 10.0 Hz, C-5), 4.27 (dd, 1 H, $J_{9,9'}$ = 12.5 Hz, C-9'), 4.29 (s, 1 H, OH), 4.30 (d, 1 H, $J_{1,2}$ = 7.5 Hz, B-1), 4.32 (dd, 1 H, $J_{5,6'}$ = 4.0, $J_{6,6'}$ = 12.0 Hz, B-6'), 4.41 (dd, 1 H, $J_{5,6}$ = 10.0, $J_{6,7}$ = 1.5 Hz, C-6), 4.42 (d, 1 H, $J_{1,2}$ = 9.5 Hz, A-1), 4.66 (dd, 1 H, $J_{5,6'}$ = 2.0, $J_{6,6'}$ = 12.0 Hz, A-6'), 4.87 (t, 1 H, $J_{1,2} = J_{2,3}$ = 9.5 Hz, A-2), 5.23 (dd, 1 H, $J_{6,7}$ = 1.5, $J_{7,8}$ = 9.0 Hz, C-7), 5.33 (ddd, 1 H, $J_{7,8}$ = 9.0, $J_{8,9}$ = 7.0, $J_{8,9'}$ = 2.5 Hz, C-8), 5.36 (t, 1 H, $J_{3,4} = J_{4,5}$ = 11.0 Hz, C-4), 5.39 (d, 1 H, $J_{5,NH}$ = 10.0 Hz, NH), 7.13-7.25 (m, 5 H, Ph).

Anal. Calcd for $C_{55}H_{81}NO_{25}S_2$ + 1 H_2O (1238.5): C, 53.33; H, 6.77; N, 1.13. Found: C, 53.30; H, 6.68; N, 1.36.

Methyl (Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-5-deoxy-3-*S*-phenyl-3-thio-β-D-*erythro*-L-*gluco*-2-nonulopyranosylonate)-(2→8)-(5-acetamido-4,7,9-tri-*O*-acetyl-5-deoxy-3-*S*-phenyl-3-thio-β-D-*erythro*-L-*gluco*-2-nonulopyranosyl)onate fluoride (23). To a solution of **2** (440 mg, 0.71 mmol) and **16** (200 mg, 0.36 mmol) in dry CH_2Cl_2 (1.5 mL) was added 4A molecular sieves (MS-4A, 400 mg) and Na_2HPO_4 (400 mg). With stirring, AgOTf (80 mg, 0.70 mmol) in toluene (1.0 mL) was added at 0 °C, and the stirring was continued in the dark for 30 h at room temperature. An additional AgOTf (100 mg, 0.39 mmol) in toluene (0.50 mL) was added to the mixture, and the stirring was continued for 20 h at 40 °C. The solids were filtered off and washed thoroughly with EtOAc. The filtrate and washings were combined, and the solution was successively washed with satd $Na_2S_2O_3$, satd $NaHCO_3$,

water and brine, dried (Na_2SO_4), and concentrated. Column chromatography on silica gel, with 2:1 to 1:1 benzene-acetone, gave **23** (200 mg, 49%) as an amorphous mass; mp 118 °C; $[\alpha]_D$ +31° (*c* 0.11, $CHCl_3$); IR ν 3369 (NH), 1749 and 1218 (ester), 1671 and 1541 (amide), 1078 (CF), 772 and 710 cm^{-1} (Ph); ^1H NMR ($CDCl_3$): δ 1.87, 1.88, 2.00 (2), 2.03, 2.07, 2.08, 2.10, 2.12 (9 s, 27 H, 9 Ac), 3.27 (d, 1 H, $J_{3,4}$ = 11.0 Hz, B-3), 3.30 (dd, 1 H, $J_{F,3}$ = 15.0, $J_{3,4}$ = 11.0 Hz, A-3), 3.84 (br.d, 1 H, J = 11.0 Hz, B-9), 3.90, 3.97 (2 s, 6 H, 2 MeO), 3.99 (dd, 1 H, $J_{8,9}$ = 6.5, $J_{9,9'}$ = 12.0 Hz, A-9), 4.06 (m, 1 H, B-9'), 4.09 (q, 1 H, $J_{4,5}$ = $J_{5,6}$ = $J_{5,NH}$ = 10.5 Hz, B-5), 4.11 (q, 1 H, $J_{4,5}$ = $J_{5,6}$ = $J_{5,NH}$ = 10.5 Hz, A-5), 4.30 (dd, 1 H, $J_{5,6}$ = 10.5, $J_{6,7}$ = 1.5 Hz, A-6), 4.31 (m, 1 H, B-6), 4.56 (dd, 1 H, $J_{8,9'}$ = 3.0, $J_{9,9'}$ = 12.0 Hz, A-9'), 4.84 (ddd, 1 H, $J_{7,8}$ = 4.0, $J_{8,9}$ = 6.5, $J_{8,9'}$ = 3.0 Hz, A-8), 5.27-5.31 (m, 2 H, B-7, B-8), 5.32 (dd, 1 H, $J_{3,4}$ = 11.0, $J_{4,5}$ = 10.5 Hz, B-4), 5.38-5.44 (m, 2 H, A-7, B-NH), 5.53 (dd, 1 H, $J_{3,4}$ = 11.0, $J_{4,5}$ = 10.5 Hz, A-4), 5.73 (d, 1 H, $J_{5,NH}$ = 10.5 Hz, A-NH), 7.2-7.5 (m, 10 H, 2 Ph).

Anal. Calcd for $C_{50}H_{61}FN_2O_{23}S_2$ + 1 H_2O (1159.17): C, 51.81; H, 5.48; N, 2.41. Found: C, 51.77; H, 5.36; N, 2.52.

Methyl (Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-5-deoxy-3-*S*-phenyl-3-thio-β-D-*erythro*-L-*gluco*-2-nonulopyranosylonate)-(2→8)-(5-acetamido-9-*O*-benzoyl-5-deoxy-3-*S*-phenyl-3-thio-β-D-*erythro*-L-*gluco*-2-nonulopyranosyl)onate fluoride (24). A mixture of **2** (40 mg, 65 μmol), **8** (20 mg, 31 μmol), Na_2HPO_4 (40 mg) and MS-4A (40 mg) in dry CH_2Cl_2 (0.5 mL) was stirred for 2 h at room temperature. To the mixture was added, with stirring, AgOTf (20 mg, 78 μmol) in toluene (0.5 mL) and the stirring was continued in the dark for 36 h at room temperature and for 3 days at 50 °C. An additional AgOTf (20 mg, 78 μmol) in CH_3CN (0.5 mL) was added to the mixture, and the stirring was continued for 2 days at 65 °C. The same work-up procedure as described for **23** was conducted to give a crude product. Preparative TLC on silica gel, with 1:1 hexane-acetone, gave **24** (7.4 mg, 20%) as an amorphous mass, and **2** (22 mg), **8** (8.0 mg) and **3** (15 mg) were recovered; compd **24**: ^1H NMR ($CDCl_3$): δ 1.72, 1.89, 1.98 (2), 2.05, 2.10 (6 s, 18 H, 6 Ac), 3.39 (d, 1 H, $J_{3,4}$ = 10.8 Hz, B-3), 3.44 (dd, 1 H, $J_{F,3}$ = 14.0, $J_{3,4}$ = 10.8 Hz, A-3), 3.68 (m, 1 H, A-7), 3.85 (dd, 1 H, $J_{5,6}$ = 12.0, $J_{6,7}$ = 1.7 Hz, B-6), 3.92, 4.02 (2 s, 6 H, 2 MeO), 4.04 (d, 1 H, $J_{5,6}$ = 9.0 Hz, A-6), 4.11 (m, 1 H, B-5), 4.12 (dd, 1 H, $J_{8,9}$ = 2.6, $J_{9,9'}$ = 12.5 Hz, B-9), 4.32 (dd, 1 H, $J_{8,9}$ = 2.6, $J_{9,9'}$ = 12.5 Hz, B-9'), 4.37 (m, 1 H, A-5), 4.49 (dd, 1 H, $J_{8,9}$ = 2.0, $J_{9,9'}$ = 12.0 Hz, A-9), 4.88 (br.d, 1 H, J = 8.4 Hz, A-8), 5.13 (dd, 1 H, $J_{8,9}$ = 1.9, $J_{9,9'}$ = 12.0 Hz, A-9'), 5.22 (dd, 1 H, $J_{6,7}$ = 1.7, $J_{7,8}$ = 8.3 Hz, B-7), 5.28-5.46 (m, 3 H, B-4, B-8, B-NH), 5.66 (d, 1 H, $J_{5,NH}$ = 8.6 Hz, A-NH), 5.83 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 10.8 Hz, A-4), 7.1-8.0 (m, 20 H, 4 Ph).

Methyl (Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-5-deoxy-3-*S*-phenyl-3-thio-β-D-*erythro*-L-*gluco*-2-nonulopyranosylonate)-(2→8)-(methyl 5-Acetamido-4,7,9-tri-*O*-acetyl-5-deoxy-3-*S*-phenyl-3-thio-β-D-*erythro*-L-*gluco*-2-nonulopyranosylonate)-(2→6)-2,3,4-tri-*O*-benzyl-α-D-glucopy-ranoside (27). A mixture of AgOTf (23 mg, 89 μmol), $SnCl_2$ (17 mg, 90 μmol), Na_2HPO_4 (100 mg) and MS-AW300 (100 mg) in CH_3CN (0.2 mL) was stirred for 10 min at room temperature. To the mixture 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (**26**; 31 mg, 67 μmol) in CH_3CN (0.3 mL) was added and stirred for 20 min at room temperature, then **23** (50 mg, 44 μmol) was added and stirred in the dark for 24 h at room temperature. The same work-up as described for **20** gave a crude product. Column chromatography on silica gel, with 1:1 hexane-acetone, gave **27** (33 mg, 47%) as an amorphous mass; ^1H NMR ($CDCl_3$): δ 1.77, 1.87, 1.89, 1.96, 1.98, 1.99, 2.07 (2), 2.13 (9 s, 27 H, 9 Ac), 3.23 (d, 1 H, $J_{3,4}$ = 11.0 Hz, C-3), 3.27 (s, 3 H, MeO), 3.28 (d, 1 H, $J_{3,4}$ = 10.5 Hz, B-3), 3.30 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 10.0 Hz, A-4), 3.45 (dd, 1 H, $J_{1,2}$ = 3.5, $J_{2,3}$ = 10.0 Hz, A-2), 3.75 (ddd, 1 H, $J_{4,5}$ = 10.0, $J_{5,6}$ = 5.5, $J_{5,6'}$ = 1.5 Hz, A-5), 3.81 (dd, 1 H, $J_{8,9}$ = 2.0, $J_{9,9'}$ = 12.5 Hz, C-9), 3.83 (s, 3 H, MeO), 3.88 (s, 3 H, MeO), 3.89 (dd, 1 H, $J_{5,6}$ = 5.5, $J_{6,6'}$ = 10.5 Hz, A-6), 3.92 (t, 1 H, $J_{2,3}$ = $J_{3,4}$ = 10.0 Hz, A-3), 3.94 (dd, 1 H, $J_{8,9}$ = 8.5, $J_{9,9'}$ = 12.0 Hz, B-9), 4.05 (q, 1 H, $J_{4,5}$ = $J_{5,6}$ = $J_{5,NH}$ = 10.5 Hz, B-5), 4.06 (q, 1 H, $J_{4,5}$ = $J_{5,6}$ = $J_{5,NH}$ = 10.5 Hz, C-5), 4.07 (dd, 1 H, $J_{8,9}$ = 6.0, $J_{9,9'}$ = 12.5 Hz, C-9'), 4.13 (dd, 1 H, $J_{5,6'}$ = 1.5, $J_{6,6'}$ = 10.5 Hz, A-6'), 4.16 (dd, 1 H, $J_{5,6}$ = 1.5, $J_{6,6'}$ = 10.5 Hz, B-6), 4.32 (dd, 1 H, $J_{5,6}$ = 10.5, $J_{6,7}$ = 2.5 Hz, C-6), 4.51 (d, 1 H, J = 10.5 Hz, CH_2Ph), 4.60 (d, 1 H, $J_{1,2}$ = 3.5 Hz, A-1), 4.65 (d, 1 H, J = 10.5 Hz, CH_2Ph), 4.68 (d, 1 H, J = 12.0 Hz, CH_2Ph), 4.72 (dd, 1 H, $J_{8,9'}$ = 2.5, $J_{9,9'}$ = 12.5 Hz, B-9'), 4.75 (d, 1 H, J = 11.0 Hz, CH_2Ph), 4.76 (d, 1 H, J = 12.0 Hz, CH_2Ph), 4.91 (dt, 1 H, $J_{7,8}$ = $J_{8,9'}$ = 2.5, $J_{8,9}$ = 8.5 Hz, B-8), 4.93 (d, 1 H, J = 11.0 Hz, CH_2Ph), 5.2-5.4 (m, 4 H, C-4, C-7, C-8, C-NH), 5.43 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 10.5 Hz, B-4), 5.47 (dd, 1 H, $J_{6,7}$ = 1.5, $J_{7,8}$ = 2.5 Hz, B-7), 5.86 (d, 1 H, J = 10.0 Hz, B-NH), 7.1-7.5 (m, 25 H, 5 Ph).

Ethyl (Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-5-deoxy-3-*S*-phenyl-3-thio-β-D-*erythro*-L-*gluco*-2-nonulopyranosylonate)-(2→8)-(methyl 5-Acetamido-4,7,9-tri-*O*-acetyl-5-deoxy-3-*S*-phenyl-3-thio-β-D-*erythro*-L-*gluco*-2-nonulopyranosylonate)-(2→3)-6-*O*-pivaloyl-β-D-galacto-pyranosyl-(1→4)-2,6-di-*O*-pivaloyl-1-thio-β-D-glucopyranoside (28). A mixture of AgOTf (23 mg, 89 μmol), $SnCl_2$ (17 mg, 90 μmol), Na_2HPO_4 (50 mg) and MS-AW300 (100 mg) in CH_3CN (0.5 mL) was stirred for 30 min in the dark at room temperature. After addition of **19** (34 mg, 53 μmol) and stirring for 2 h at room temperature, **23** (50 mg, 44 μmol) was added and the mixture stirred for 48 h at room

temperature. The same work-up procedure as described for **20** was conducted to afford a crude product. Column chromatography on silica gel, with 3:1 toluene-acetone, gave **28** (30 mg, 39%) as an amorphous mass; mp 116 °C; $[\alpha]_D$ +23° (*c* 0.12, $CHCl_3$); IR ν 3200-3500 (OH, NH), 2970 (Me, CH_2), 1750 and 1221 (ester), 1671 and 1541 (amide), 772 and 693 cm^{-1} (Ph); ^1H NMR ($CDCl_3$): δ 1.13, 1.18, 1.19 (3 s, 27 H, 3 Piv), 1.23 (m, 3 H, SCH_2CH_3), 1.87, 1.90, 2.01, 2.02 (2), 2.07, 2.08, 2.10, 2.18 (9 s, 27 H, 9 Ac), 2.63 (m, 2 H, SCH_2CH_3), 3.29 (d, 1 H, $J_{3,4}$ = 11.0 Hz, D-3), 3.43 (dd, 1 H, $J_{3,4}$ = 10.0, $J_{4,5}$ = 8.0 Hz, A-4), 3.49 (d, 1 H, $J_{3,4}$ = 11.0 Hz, C-3), 3.50 (dd, 1 H, $J_{1,2}$ = 8.0, $J_{2,3}$ = 10.0 Hz, B-2), 3.61 (ddd, 1 H, $J_{4,5}$ = 8.0, $J_{5,6}$ = 10.0, $J_{5,6'}$ = 12.5 Hz, A-5), 3.69 (t, 1 H, $J_{2,3} = J_{3,4}$ = 10.0 Hz, A-3), 3.75 (dd, 1 H, $J_{5,6}$ = 8.0, $J_{5,6'}$ = 3.5 Hz, B-5), 3.85 (dd, 1 H, $J_{8,9}$ = 5.0, $J_{9,9'}$ = 12.5 Hz, C-9), 3.90 (s, 3 H, MeO), 3.91 (m, 1 H, C-5), 3.97 (s, 3 H, MeO), 4.00 (m, 1 H, D-5), 4.09 (dd, 1 H, $J_{8,9}$ = 4.0, $J_{9,9'}$ = 12.5 Hz, D-9), 4.12 (dd, 1 H, $J_{5,6}$ = 10.0, $J_{6,6'}$ = 12.5 Hz, A-6), 4.18 (dd, 1 H, $J_{5,6}$ = 8.0, $J_{6,6'}$ = 12.5 Hz, B-6), 4.20 (br.d, 1 H, $J_{3,4}$ = 2.5 Hz, B-4), 4.20 (m, 2 H, D-6, D-9'), 4.28 (dd, 1 H, $J_{2,3}$ = 10.0, $J_{3,4}$ = 2.5 Hz, B-3), 4.32 (dd, 1 H, $J_{5,6}$ = 3.5, $J_{6,6'}$ = 12.5 Hz, B-6'), 4.36 (d, 1 H, $J_{1,2}$ = 8.0 Hz, B-1), 4.43 (d, 1 H, $J_{1,2}$ = 10.0 Hz, A-1), 4.55 (d, 1 H, $J_{6,6'}$ = 10.5 Hz, C-6), 4.65 (dd, 1 H, $J_{5,6}$ = 2.0, $J_{6,6'}$ = 12.5 Hz, A-6'), 4.72 (dd, 1 H, $J_{8,9'}$ = 2.0, $J_{9,9'}$ = 12.5 Hz, C-9'), 4.81 (dt, 1 H, $J_{7,8} = J_{8,9}$ = 5.0, $J_{8,9'}$ = 2.5 Hz, C-8), 4.85 (t, 1 H, $J_{1,2} = J_{2,3}$ = 10.0 Hz, A-2), 5.30 (m, 2 H, D-7, D-8), 5.38 (d, 1 H, $J_{7,8}$ = 5.0 Hz, C-7), 5.41 (dd, 1 H, $J_{3,4}$ = 11.0, $J_{4,5}$ = 10.0 Hz, D-4), 5.45 (d, 1 H, $J_{5,NH}$ = 9.0 Hz, NH), 5.49 (dd, 1 H, $J_{3,4}$ = 11.0, $J_{4,5}$ = 10.0 Hz, C-4), 5.65 (d, 1 H, $J_{5,NH}$ = 10.0 Hz, NH), 7.25 - 7.45 (m, 10 H, 2 Ph); HRMS. Calcd for $C_{79}H_{110}N_2O_{36}S_3$ $(M+H)^+$ 1759.6079, Found: 1759.6005.

Ethyl (Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-5-deoxy-3-*S*-phenyl-3-thio-β-D-*erythro*-L-*gluco*-2-nonulopyranosylonate)-(2→8)-(methyl 5-Acetamido-4,7,9-tri-*O*-acetyl-5-deoxy-3-*S*-phenyl-3-thio-β-D-*erythro*-L-*gluco*-2-nonulopyranosylonate)-(2→3)-2,4-di-*O*-acetyl-6-*O*-pivaloyl-β-D-galactopyranosyl-(1→4)-3-*O*-acetyl-2,6-di-*O*-pivaloyl-1-thio-β-D-glucopyranoside (29). A solution of **28** (100 mg, 57 μmol) with Ac_2O (2.0 mL) in pyridine (4.0 mL) was stirred for 22 h at 40 °C. The solution was concentrated to a syrup that was chromatographed on a column of silica gel (10 g), with 1:1 hexane-acetone, to afford **29** (104 mg, 97%) as an amorphous mass; mp 144 °C; $[\alpha]_D$ +39° (*c* 0.18, $CHCl_3$); IR ν 3380 (NH), 1750 and 1221 (ester), 1671 and 1541 (amide), 773 and 690 cm^{-1} (Ph); ^1H NMR ($CDCl_3$): δ 1.16, 1.18, 1.24 (3 s, 27 H, 3 Piv), 1.30 (t, 3 H, SCH_2CH_3), 1.84, 1.86, 1.89 (2), 1.96, 2.01, 2.03, 2.04, 2.08, 2.12, 2.16, 2.17 (12 s, 36 H, 12 Ac), 2.69 (m, 2 H, SCH_2CH_3), 3.06 (d, 1 H, $J_{3,4}$ = 12.0 Hz, C-3), 3.33 (d, 1 H, $J_{3,4}$ = 12.0 Hz, D-3), 3.69 (br.d, 1 H, $J_{5,6}$ = 10.7 Hz, C-6), 3.70 (m, 2 H, A-4, A-5),

3.78 (dd, 1 H, J = 9.8, 12.3 Hz, B-5), 3.81-3.91 (m, 2 H, C-5, C-6), 3.84, 3.86 (2 s, 6 H, 2 MeO), 3.97-4.15 (m, 5 H, A-6, C-9, C-9', D-5, D-9), 4.26 (dd, 1 H, $J_{8,9'}$ = 2.0, $J_{9,9'}$ = 12.0 Hz, D-9'), 4.56 (d, 1 H, $J_{1,2}$ = 8.0 Hz, A-1), 4.60 (d, 1 H, $J_{6,6'}$ = 11.0 Hz, A-6'), 4.80 (d, 1 H, $J_{1,2}$ = 8.0 Hz, B-1), 4.84 (br.d, 1 H, J = 9.5 Hz, B-6), 4.93 (t, 1 H, $J_{1,2} = J_{2,3}$ = 8.0 Hz, A-2), 5.04 (dd, 1 H, $J_{2,3}$ = 10.0, $J_{3,4}$ = 4.0 Hz, B-3), 5.17 (dd, 1 H, $J_{1,2}$ = 8.0, $J_{2,3}$ = 10.0 Hz, B-2), 5.23 (dd, 1 H, $J_{5,6'}$ = 2.0, J = 11.6 Hz, B-6'), 5.26 (dd, 1 H, J = 2.0, 10.0 Hz, D-7), 5.28-5.37 (m, 6 H, A-3, B-4, C-4, D-4, D-8, D-NH), 5.91 (d, 1 H, $J_{5,NH}$ = 10.0 Hz, C-NH), 7.20-7.71 (m, 10 H, 2 Ph).

Anal. Calcd for $C_{85}H_{116}N_2O_{39}S_3$ (1886.04): C, 54.13; H, 6.20; N, 1.49. Found: C, 54.19; H, 6.19; N, 1.59.

(Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-5-deoxy-3-*S*-phenyl-3-thio-β-D-*erythro*-L-*gluco*-2-nonulopyranosylonate)-(2→8)-(methyl 5-Acetamido-4,7,9-tri-*O*-acetyl-5-deoxy-3-*S*-phenyl-3-thio-β-D-*erythro*-L-*gluco*-2-nonulopyranosylonate)-(2→3)-2,4-di-*O*-acetyl-6-*O*-pivaloyl-β-D-galactopyranosyl-(1→4)-3-*O*-acetyl-2,6-di-*O*-pivaloyl-α-D-glucopyranosyl Trichloroacetimidate (30). To a solution of **29** (10 mg, 5.3 μmol) in CH_2Cl_2 (0.25 mL) was added dimethyl(methylthio)sulfonium trifluoromethanesulfonate (DMTST; 4.1 mg, 16 μmol) in CH_2Cl_2 (0.25 mL) at -15 °C and the mixture was stirred for 20 h at the temperature. To the mixture was added 5% aq $NaHCO_3$ and the suspension was stirred for 3 h at room temperature. After removal of the aqueous layer, the organic layer was washed with brine, dried (Na_2SO_4), and concentrated to a syrup. The residue was dissolved in CH_2Cl_2 (0.5 mL) and cooled to -20 °C. To the solution was added trichloroactonitrile (CCl_3CN; 15 μL, 0.15 mmol) and DBU (0.6 μL, 4.0 μmol) at -20 °C, and the solution was stirred for 35 h at 0 °C and concentrated. Column chromatography of the residue on silica gel, with 2:1 hexane-acetone, afforded **30** (8.0 mg, 76%) as an amorphous mass; mp 160 °C, $[\alpha]_D$ + 32° (*c* 0.05, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.15 (2), 1.19 (3 s, 27 H, 3 Piv), 1.86, 1.87, 1.90 (2), 1.95, 2.01, 2.05, 2.08 (2), 2.13, 2.17, 2.18 (12 s, 36 H, 12 Ac), 3.06 (d, 1 H, $J_{3,4}$ = 11.7 Hz, C-3), 3.33 (d, 1 H, $J_{3,4}$ = 11.7 Hz, D-3), 3.85 (2) (2 s, 6 H, 2 MeO), 4.84 (d, 1 H, $J_{1,2}$ = 8.2 Hz, B-2), 5.03 (dd, 1 H, $J_{1,2}$ = 3.5, $J_{2,3}$ = 10.3 Hz, A-2), 5.65 (t, 1 H, $J_{2,3} = J_{3,4}$ = 10.3 Hz, A-3), 5.86 (d, 1 H, $J_{5,NH}$ = 9.4 Hz, NH), 6.52 (d, 1 H, $J_{1,2}$ = 3.5 Hz, A-1), 7.18-7.54 (m, 10 H, 2 Ph), 8.65 (s, 1 H, C=NH; imidate).

(Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-5-deoxy-3-*S*-phenyl-3-thio-β-D-*erythro*-L-*gluco*-2-nonulopyranosylonate)-(2→8)-(methyl 5-Acetamido-4,7,9-tri-*O*-acetyl-5-deoxy-3-*S*-phenyl-3-thio-β-D-*erythro*-L-*gluco*-2-nonulopyranosylonate)-(2→3)-2,4-di-*O*-acetyl-6-*O*-pivaloyl-β-D-galactopyranosyl-(1→4)-3-*O*-acetyl-2,6-di-*O*-pivaloyl-β-D-glucopyranosyl)-(1→

1)-(2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol (32). To a solution of **29** (3 mg, 1.6 μmol) and (2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol (**31**; 2 mg, 4.7 μmol) in dry CH_2Cl_2 (0.5 mL) was added 3A molecular sieves (MS-3A; 10 mg), and the mixture was stirred overnight at room temperature. To the suspension was added a mixture of DMTST (1.2 mg, 4.6 μmol) and MS-3A (1.2 mg), and the mixture was stirred for 3 days at room temperature. The solids were filtered off and washed thoroughly with CH_2Cl_2, and the resulting filtrate was concentrated. Column chromatography of the residue on silica gel (2 g), with 2:1 to 1:1 hexane-acetone, gave **32** (3 mg, 84%) as an amorphous solid; mp 100 °C, $[\alpha]_D$ + 32.5° (*c* 0.16, $CHCl_3$); IR *ν* 3360 (NH), 2924 and 2854 (Me, CH_2), 2114 (N_3), 1750 and 1220 (ester), 1653 and 1540 (amide), 773 cm^{-1} (Ph); ^1H NMR ($CDCl_3$): δ 0.89 (t, 3 H, J = 7.2 Hz, $(CH_2)_{12}CH_3$), 1.14, 1.20, 1.27 (3 s, 27 H, 3 Piv), 1.12-1.44 (br, 24 H, $(CH_2)_{12}CH_3$), 1.84, 1.86, 1.89, 1.90, 1.95, 2.01, 2.04, 2.05, 2.08, 2.13, 2.16, 2.18 (12 s, 36 H, 12 Ac), 3.06 (d, 1 H, $J_{3,4}$ = 11.0 Hz, C-3), 3.33 (d, 1 H, $J_{3,4}$ = 11.0 Hz, D-3), 3.59 (dd, 1 H, $J_{1,1'}$ = 10.5, $J_{1,2}$ = 5.3 Hz, H-1), 3.66-3.78 (m, 3 H, A-5, B-5, C-6), 3.80-3.91 (m, 3 H, A-4, C-5, D-6), 3.83 (dd, 1 H, $J_{1,1'}$ = 10.5, $J_{1',2}$ = 7.0 Hz, H-1'), 3.86 (2) (2 s, 6 H, 2 MeO), 3.93 (m, 1 H, H-2), 3.96-4.14 (m, 5 H, A-6, C-9, C-9', D-5, D-9), 4.26 (dd, 1 H, $J_{8,9'}$ = 2.0, $J_{9,9'}$ = 12.3 Hz, D-9'), 4.55 (d, 1 H, $J_{1,2}$ = 7.9 Hz, A-1), 4.58 (br.d, 1 H, J = 10.5 Hz, A-6'), 4.80 (d, 1 H, $J_{1,2}$ = 8.0 Hz, B-1), 4.84 (br.d, 1 H, J = 9.6 Hz, B-6), 4.93 (dd, 1 H, $J_{1,2}$ = 7.9, $J_{2,3}$ = 9.6 Hz, A-2), 5.03 (dd, 1 H, $J_{2,3}$ = 10.0 Hz, $J_{3,4}$ = 3.5 Hz, B-3), 5.16 (dd, 1 H, $J_{1,2}$ = 8.0, $J_{2,3}$ = 10.0 Hz, B-2), 5.21 (dd, 1 H, $J_{5,6'}$ = 2.0, $J_{6,6'}$ = 11.5 Hz, B-6'), 5.25 (dd, 1 H, $J_{6,7}$ = 2.0, $J_{7,8}$ = 9.0 Hz, D-7), 5.26 (t, 1 H, $J_{2,3}$ = $J_{3,4}$ = 9.6 Hz, A-3), 5.27-5.38 (m, 5 H, B-4, C-7, D-4, D-8, D-NH), 5.53 (dd, 1 H, $J_{3,4}$ = 8.8, $J_{4,5}$ = 15.0 Hz, H-4), 5.57 (dd, 1 H, $J_{2,3}$ = 3.5, $J_{3,4}$ = 8.8 Hz, H-3), 5.59 (br.s, 1 H, C-4), 5.87-5.95 (m, 2 H, H-5, C-NH), 7.18-8.08 (m, 15 H, 3 Ph); FABMS (NBA) *m/z* 2252.9 $(M+H)^+$.

Another glycosylation method using the trichloroacetimidate **30** was as follows. To a mixture of **30** (19 mg, 9.6 μmol), **31** (8.2 mg, 19 μmol) and MS-4A (300 mg) in dry CH_2Cl_2 (0.2 mL) was added boron trifluoride diethyl etherate (BF_3•OEt_2; 2.5 μL, 20 μmol) at -10 °C, and the mixture was stirred 4 h at -10 °C. An additional BF_3•OEt_2 (3.0 μL) was added to the mixture, which was stirred for a further 7 h at 0 °C. The solids were filtered off and washed with CH_2Cl_2, and the combined filtrate and washings were concentrated. Preparative TLC of the residue was conducted, with 1:1 hexane-acetone, to give **32** (18 mg, 83%) as an amorphous solid; the ^1H NMR data were in agreement with those described above.

(Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-5-deoxy-3-*S*-phenyl-3-thio-β-D-*erythro*-L-*gluco*-2-nonulopyranosylonate)-(2→8)-(methyl 5-Acet-

amido-4,7,9-tri-*O*-acetyl-5-deoxy-3-*S*-phenyl-3-thio-β-D-*erythro*-L-*gluco*-2-nonulopyranosylonate)-(2→3)-2,4-di-*O*-acetyl-6-*O*-pivaloyl-β-D-galacto-pyranosyl-(1→4)-3-*O*-acetyl-2,6-di-*O*-pivaloyl-β-D-glucopyranosyl)-(1→1)-(2*S*,3*R*,4*E*)-3-*O*-benzoyl-2-octadecanamido-4-octadecene-1,3-diol (33). To a solution of **32** (14 mg, 6.2 μmol) and octadecanoic acid (4.1 mg, 14 μmol) in CH_2Cl_2 (0.5 mL) was added tri-*n*-butylphosphine (2.0 μL, 8.0 μmol), and the solution was stirred for 20 h at room temperature. 1-Ethyl-3-(3-dimethylaminopropyl)-carbodiimide hydrochloride (WSC, 5 mg) was added to the solution, and the mixture was stirred for 16 h at room temperature. After completion of the reaction, the solution was washed with satd aq $NaHCO_3$, water and brine, dried (Na_2SO_4), and concentrated. The residue was chromatographed on silica gel by preparative TLC, with 1:1 hexane-acetone, to give **33** (11 mg, 71%) as an amorphous mass; mp 77 °C, $[\alpha]_D$ +32.0° (*c* 0.025, $CHCl_3$); IR ν 3360 (NH), 2924 and 2850 (Me, CH_2), 1750 and 1220 (ester), 1653 and 1540 (amide), 773 cm^{-1} (Ph); ^1H NMR ($CDCl_3$): δ 0.81 (t, 6 H, J = 7.2 Hz, *Me*CH_2 (2)), 1.01, 1.10, 1.12 (3 s, 27 H, 3 Piv), 1.14-1.30 (br, 52 H, 11 CH_2, 15 CH_2), 1.93-2.12 (m, 4 H, COC*H*$_2$, H-6, H-6'), 1.77, 1.80, 1.82, 1.83, 1.87, 1.95, 1.98 (2), 2.01, 2.06, 2.09 (2) (12 s, 36 H, 12 Ac), 2.98 (d, 1 H, $J_{3,4}$ = 11.4 Hz, C-3), 3.26 (d, 1 H, $J_{3,4}$ = 11.4 Hz, D-3), 3.53 (dd, 1 H, $J_{1,1'}$ = 9.9, $J_{1,2}$ = 4.1 Hz, H-1), 3.57-3.68 (m, 4 H, A-4, A-5, B-5, C-5), 3.79 (2) (2 s, 6 H, 2 MeO), 3.80 (m, 1 H, C-6), 3.89-4.07 (m, 7 H, A-6, C-9, C-9', D-6, D-9, H-1', H-2), 4.18 (dd, 1 H, $J_{8,9'}$ = 2.4, $J_{9,9'}$ = 12.3 Hz, D-9'), 4.40 (m, 1 H, D-5), 4.42 (d, 1 H, $J_{1,2}$ = 7.8 Hz, A-1), 4.46 (dd, 1 H, $J_{5,6'}$ = 1.6, $J_{6,6'}$ = 11.4 Hz, A-6'), 4.71 (d, 1 H, $J_{1,2}$ = 7.8 Hz, B-1), 4.75 (br.d, 1 H, J = 10.2 Hz, B-6), 4.81 (dd, 1 H, $J_{1,2}$ = 8.4, $J_{2,3}$ = 9.6 Hz, A-2), 4.95 (dd, 1 H, $J_{2,3}$ = 10.2, $J_{3,4}$ = 3.6 Hz, B-3), 5.08 (dd, 1 H, $J_{1,2}$ = 8.4, $J_{2,3}$ = 9.6 Hz, B-2), 5.14 (dd, 1 H, $J_{6,6'}$ = 10.2 Hz, B-6'), 5.16 - 5.30 (m, 7 H, A-3, B-4, C-4, C-7, D-4, D-7, D-8), 5.40 (dd, 1 H, $J_{3,4}$ = 7.6, $J_{4,5}$ = 15.6 Hz, H-4), 5.48 (t, 1 H, $J_{2,3}$ = $J_{3,4}$ = 7.1 Hz, H-3), 5.52 (br, 1 H, C-4), 5.68 (d, 1 H, $J_{5,NH}$ = 9.0 Hz, D-NH), 5.80 (dt, 1 H, $J_{4,5}$ = 15.3, $J_{5,6}$ = $J_{5,6'}$ = 7.1 Hz, H-5), 5.83 (d, 1 H, $J_{5,NH}$ = 10.0 Hz, C-NH), 7.12-7.97 (m, 15 H, 3 Ph); FABMS (NBA) *m/z* 2493.1 $(M+H)^+$.

(Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-β-D-*glycero*-D-*galacto*-2-nonulopyranosylonate)-(2→8)-(methyl 5-Acetamido-4,7,9-tri-*O*-acetyl-3,5-dideoxy-β-D-*glycero*-D-*galacto*-2-nonulopyranosyl-onate)-(2→3)-2,4-di-*O*-acetyl-6-*O*-pivaloyl-β-D-galactopyranosyl-(1→4)-3-*O*-acetyl-2,6-di-*O*-pivaloyl-β-D-glucopyranosyl)-(1→1)-(2*S*,3*R*,4*E*)-3-*O*-benzoyl-2-octadecanamido-4-octadecene-1,3-diol (34). To a solution of **33** (22 mg, 8.8 μmol) and α,α'-azobisisobutyronitrile (AIBN; 1.0 mg, 6.1 μmol) in toluene (5.0 mL) was added tri-*n*-butyltin hydride (*n*-Bu_3SnH; 6.0 μL, 22 μmol), and the solution was

refluxed for 2 h at 110 °C. After completion of the reaction, the solution was washed with water and brine, and concentrated. The residue was chromatographed, with 1:1 hexane-acetone, on a column of silica gel (1 g) to give **34** (13 mg, 66%) as an amorphous mass; mp 78 °C, $[\alpha]_D$ +14° (*c* 0.1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.88 (t, 6 H, *J* = 6.8 Hz, *Me*CH_2 (2)), 1.08, 1.16, 1.20 (3 s, 27 H, 3 Piv), 1.20-1.35 (br, 52 H, 11 CH_2, 15 CH_2), 1.95-2.20 (m, 4 H, COC*H*$_2$, H-6, H-6'), 1.85 (2), 1.88, 1.91, 1.97, 2.05, 2.07, 2.09, 2.17, 2.18 (2), 2.21 (12 s, 36 H, 12 Ac), 2.68 (m, 2 H, C-3eq, D-3eq), 3.59 (dd, 1 H, $J_{1,1'}$ = 9.3, $J_{1,2}$ = 3.7 Hz, H-1), 3.65 (m, 3 H, A-5, B-5, C-5), 3.72 (t, 1 H, $J_{4,5}$ = 9.3 Hz, A-4), 3.81, 3.87 (2 s, 6 H, 2 MeO), 4.23 (d, 1 H, $J_{9,9'}$ = 12.2 Hz, D-9'), 4.40-4.50 (m, 2 H, H-2, D-5), 4.47 (d, 1 H, $J_{1,2}$ = 9.3 Hz, A-1), 4.72 (br.d, 1 H, $J_{1,2}$ = 7.8 Hz, B-1), 4.83-4.93 (m, 2 H, A-2, B-3), 5.46 (dd, 1 H, $J_{3,4}$ = 7.0, $J_{4,5}$ = 15.1 Hz, H-4), 5.54 (t, 1 H, $J_{2,3}$ = $J_{3,4}$ = 7.0 Hz, H-3), 5.73 (d, 1 H, $J_{5,NH}$ = 8.8 Hz, D-NH), 5.85 (dt, 1 H, $J_{4,5}$ = 15.1, $J_{5,6}$ = $J_{5,6'}$ = 7.8 Hz, H-5), 6.07 (d, 1 H, $J_{5,NH}$ = 9.8 Hz, C-NH), 7.2-8.0 (m, 5 H, Ph); FABMS (NBA) *m/z* 2277.2 $(M+H)^+$.

Ganglioside GD_3 (1). To a solution of **34** (9 mg, 4.0 μmol) in MeOH (1.0 mL) was added *t*-BuOK (7 mg, 62 μmol), and the mixture was stirred overnight at room temperature. Water (0.1 mL) was added and the mixture was stirred for a further 24 h at room temperature. The mixture was neutralized with Dowex 50W × 8 (H^+) resin, which was then filtered off followed by thorough washing with MeOH. The filtrate and washings were combined and concentrated. The residue was chromatographed on a column of Sephadex LH-20 (1 g), with 1:1 CH_2Cl_2-MeOH, to give **1** (6 mg, quant.) as an amorphous mass; $[\alpha]_D$ -2.5° (*c* 0.1, $CHCl_3$-CH_3OH); ^1H NMR (1:1 $CDCl_3$-CD_3OD): δ 0.83 (t, 6 H, *J* = 6.5 Hz, *Me*CH_2 (2)), 1.00-1.45 (br, 52 H, 11 CH_2, 15 CH_2), 1.94, 2.03 (2 s, 6 H, 2 AcN), 2.18 (t, 2 H, *J* = 8.2 Hz, COC*H*$_2$), 2.57, 2.86 (2 m, 2 H, C-3eq, D-3eq), 4.20 (d, 1 H, $J_{1,2}$ = 7.8 Hz, A-1), 4.32 (d, 1 H, $J_{1,2}$ = 7.8 Hz, B-1), 5.42 (dd, 1 H, $J_{3,4}$ = 7.5, $J_{4,5}$ = 15.4 Hz, H-4), 5.64 (dt, 1 H, $J_{4,5}$ = 15.4, $J_{5,6}$ = $J_{5,6'}$ = 6.8 Hz, H-5); FABMS (NBA / Glycerol) *m/z* 1494.8 $(M+Na)^+$.

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