Tetrahedron Vol. 43, No. 24, pp. 5909 to 5918, 1987
Printed in Great Britain.

0040-4020/87 $3.00+.00

A STEREOSPECIFIC β-GLYCOSYLATION OF 2β,3α-DIBROMO-N-ACETYLNEURAMINIC ACID[1]

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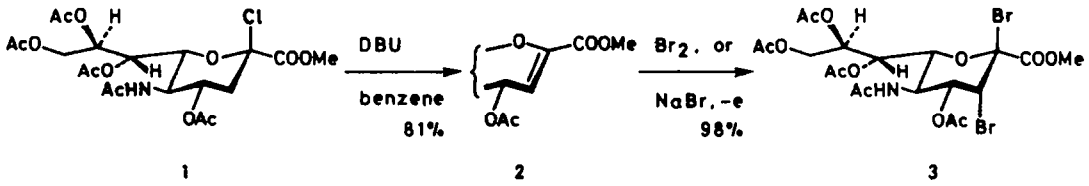
(*Received in UK 7 September* 1987)

Abstract - Condensation of a new glycosyl donor, methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-2,3-dibromo-2,3,5-trideoxy-β-D-*erythro*-L-*manno*-2-nonulopyranosonate with various acceptors such as methyl 2,3,4-tri-O-benzyl-α-D-glucopyranoside, cholesterol, methyl 2,4,6-tri-O-benzyl-β-D-galactopyranoside, and methyl 5-acetamido-4,7,9-tri-O-acetyl-2,6-anhydro-3,5-dideoxy-D-*glycero*-D-*galacto*-non-2-enopyranosonate gave only the corresponding β-glycosides. The 3α-bromo group of the glycosides obtained above was reduced with tributylstannane to the corresponding glycosides, which were deprotected to give the free glycosides in high yields.

One of the most important problems for the synthesis of gangliosides is the glycosylation of N-acetylneuraminic acid (NeuAc), which is the most common one of the sialic acids and plays an important role in a large number of biological processes as constituents of glycoproteins and glycolipids.[2] The preparation of alkyl glycosides of NeuAc is usually performed with methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-2-chloro-2,3,5-trideoxy-β-D-*glycero*-D-*galacto*-2-nonulopyranosonate (1)[3] and the appropriate glycosyl acceptor under the Koenigs-Knorr-like conditions in the presence of silver carbonate or mercury(II) salts.[4] When the reactivity of the glycosyl acceptor is low, methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-2,6-anhydro-3,5-dideoxy-D-*glycero*-D-*galacto*-non-2-enopyranosonate (2)[5,6] was produced as the major product without the desired glycosides by intramolecular dehydrochlorination reaction. We already reported[6] the preparation of new glycosyl donors such as 2,3-dibromo-, 2,3-epoxy-, and 2-halo-3-hydroxy-NeuAc derivatives which were blocked at 3-position to prevent the elimination reaction. We report here a new glycosylation method by using methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-2,3-dibromo-2,3,5-trideoxy-β-D-*erythro*-L-manno-2-nonulopyranosonate (3) to produce only β-glycosides in high yield.[7]

Scheme 1



1 2 3

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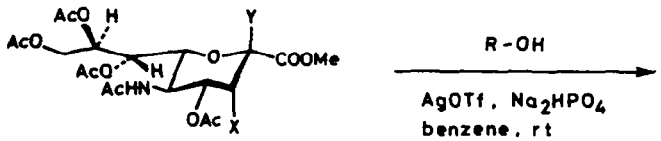
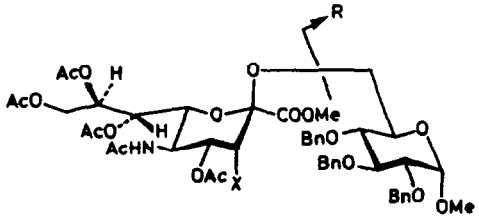
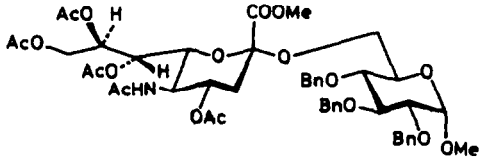
Scheme 2



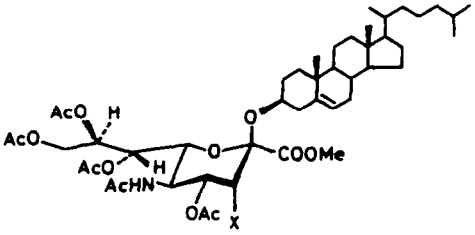
1 X = H, Y = Cl
2 X = Br, Y = Br



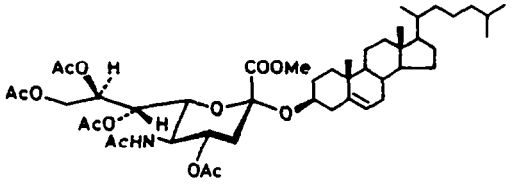
4 R-OH
5 X = Br (70%)
6 X = H (97%)



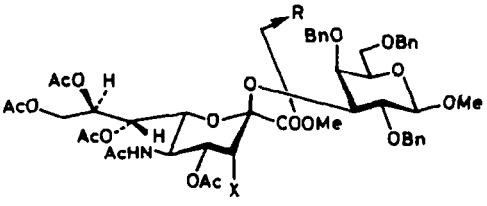
7



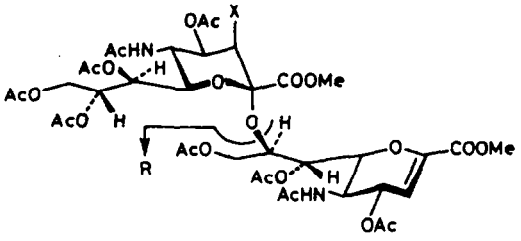
8 X = Br (88%)
9 X = H (96%)
10 deprotected 9 (96%)



11
12 deprotected 11 (92%)



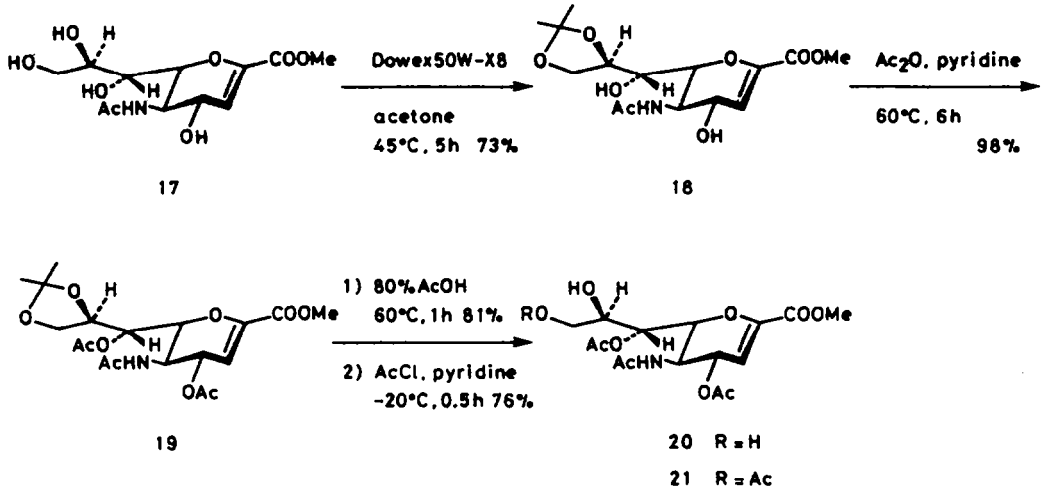
13 R-OH
14 X = Br (50%)
15 X = H (96%)
16 deprotected 15 (90%)



21 R-OH
22 X = Br (58%)
23 X = H (95%)
24 deprotected 23 (93%)

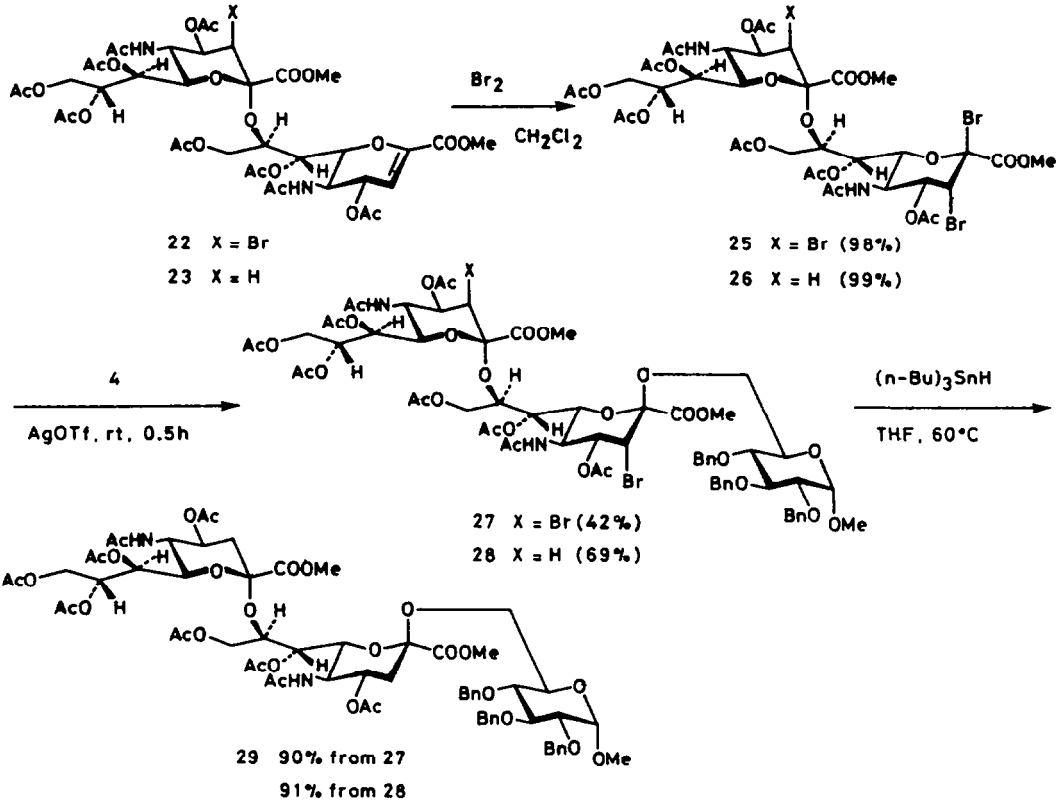
Condensation of the dibromide **3**, prepared[6] by the bromination of the 2,3-dehydro compound **2** (Scheme 1), with methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (**4**)[8] (1.06 equiv.) in benzene at room temperature for 0.5 h in the presence of silver triflate (AgOTf) (1.06 equiv.) and disodium hydrogenphosphate (Na_2HPO_4) as a buffer gave only the glycoside **5** in 70% yield (Scheme 2). Anomeric configuration was determined by our empirical rule[9] in ^{1}H-NMR spectrum. Thus, from the data that the coupling constant $J_{7,8}$ and $\Delta\delta|H\text{-}9'\text{-}H\text{-}9|$ values were 2.0 Hz and 1.03 ppm, respectively, the structure of the anomeric position was estimated as β configuration. Debromination of **5** with tributylstannane gave in 97% yield the corresponding glycoside **6**,[10] which was identical with the β-glycoside obtained by glycosylation of **4** with the chloride **1** in the presence of AgOTf followed by

Scheme 3



17 18 19 20 R = H 21 R = Ac

Scheme 4



22 X = Br 23 X = H 25 X = Br (98%) 26 X = H (99%) 27 X = Br (42%) 28 X = H (69%) 29 90% from 27 91% from 28

separation of the mixture to α- and β-glycosides, **7** (33% yield) and **6** (37% yield). The β-glycoside **6** showed 2.2 Hz and 0.94 ppm as the $J_{7,8}$ and $\Delta\delta|$H-9'-H-9$|$ values, respectively, in ^{1}H-NMR spectrum. And the fact that H-3eq and H-4 of NeuAc unit appeared at 2.47 and 5.16 ppm, respectively, confirmed the structure of **6** as β configuration.[11] Since the $J_{7,8}$ and $\Delta\delta|$H-9'-H-9$|$ values remained unaltered even if the 3-position was substituted by the bromo group, these values were applicable to the determination of the anomeric configuration of 3-substituted NeuAc derivatives.[9]

Glycosylation of cholesterol (1.06 equiv.) with **3** was carried out in benzene in the presence of

AgOTf (1.06 equiv.) and disodium hydrogenphosphate as a buffer to give the protected 3-O-(3α-bromo-2β-neuraminyl)cholesterol **8** in 88% yield. The $J_{7,8}$ and $\Delta\delta|H\text{-}9'\text{-}H\text{-}9|$ values of NeuAc unit of **8** suggested that the anomeric position of **8** was β configuration. Indeed, reduction of the 3-bromo group of **8** with tributylstannane gave in 96% yield the glycoside **9**, which was identical with the β-glycoside obtained by condensation of the chloride **1** with cholesterol in the same manner as described above. In ^{1}H-NMR spectrum of **9**, the H-3eq and H-4 appeared at 2.52 and 5.25 ppm, respectively. These data agreed with those deduced from the empirical rule.[11] The similar condensation of the dibromide **3** with methyl 2,4,6-tri-O-benzyl-β-D-galactopyranoside (**13**)[12] gave in 50% yield the 3-O-(3α-bromo-2β-neuraminyl)galactopyranoside **14**, whose bromo group was removed with tributylstannane to give the glycoside **15** in 96% yield. Since no glycoside was obtained by treatment of the galactopyranoside **13** with the chloride **1**, the anomeric configuration of the glycoside **15** was deduced as β by analysis of its ^{1}H-NMR spectrum; the H-4 of NeuAc unit appeared at 4.98 ppm and the $J_{7,8}$ and $\Delta\delta|H\text{-}9'\text{-}H\text{-}9|$ values were 2.1 Hz and 0.99 ppm, respectively.

In order to investigate the condensation of the dibromide **3** with methyl 5-acetamido-4,7,9-tri-O-acetyl-2,6-anhydro-3,5-dideoxy-D-glycero-D-galacto-non-2-enopyranosonate (**21**), we prepared the acceptor **21** from the 2,3-dehydro-NeuAc methyl ester **17**[5] by the following four steps (Scheme 3): The 2,3-dehydro-NeuAc derivative **17** was treated with acetone in the presence of Dowex 50W-X8 [H^+] at 40 °C for 5 h to give the 8,9-O-isopropyridene compound **18** (73% yield), whose hydroxyl groups were acetylated with acetic anhydride in pyridine at 60 °C for 6 h to afford the diacetate **19** as white crystals in 98% yield. The treatment of **19** with 80% acetic acid at 60 °C for 1 h gave the diol **20** as crystals in 81% yield. Finally, selective acetylation of the diol **20** was carried out with acetyl chloride in pyridine at -20 °C for 0.5 h to give the 8-free 2,3-dehydro-NeuAc derivative **21** in 76% yield. Glycosylation of the neuraminyl acceptor **21** with the dibromide **3** in the same manner as above gave in 58% yield the 3α-bromo β-glycoside **22**, which was debrominated with tributylstannane to afford the (β2-8) linked dineuraminyl saccharide **23** in 95% yield (Scheme 2). The anomeric configuration of **23** was determined as β from the ^{1}H-NMR data without comparison with an authentic sample.

The glycosides, **9**, **11**, **15**, and **23**, were deprotected quantitatively by hydrogenolysis (10% Pd-C in methanol) and/or deacetylation (potassium t-butoxide in methanol at room temperature), saponification (1N sodium hydroxide in methanol at room temperature), and neutralization (Dowex 50W-X8 [H^+] at 0 °C) to give the free glycosides, **10**, **12**, **16**, and **24**, respectively.

The feature of our synthetic strategy is that further elongation of the sugar chain is possible by repetition of the same procedure. The dineuraminyl saccharides, **22** and **23**, had also a 2,3-double bond in the second NeuAc unit, which could be converted to the corresponding tribromide **25** and dibromide **26** quantitatively. Condensation of the tribromide **25** with the glucose derivative **4** in the presence of AgOTf afforded the trisaccharide **27** in 42% yield. Similarly, the dibromide **26** with **4** gave the trisaccharide **28** in 69% yield. The bromo group(s) of **27** and **28** were reduced with tributylstannane to give the corresponding NeuAc(β2-8)NeuAc(β2-6)Glc derivative **29** in 91 and 90% yield, respectively. The H-3eq and H-4 of the central NeuAc unit appeared at 2.46 and 5.26 ppm, respectively, indicating that the anomeric position of the central NeuAc unit of **29** was β configuration.

In conclusion we found that the 2,3-dibromo-NeuAc derivative **3** is a useful donor for the stereospecific β-glycosylation since the bromo group at 3 position prevents the dehydrobromination reaction and has steric hindrance on α side.[13] In this procedure we could first synthesize the NeuAc-(β2-8)NeuAc linkage. The 2,3-double bond of the dineuraminyl saccharides was available for the second glycosylation reaction in the synthesis of the trisaccharide.

This method can be applied to the stereospecific synthesis of unnatural type gangliosides.

EXPERIMENTAL

General. Melting points were taken on a Mitamura Riken flat-bulb thermometer with a heating metal block and uncorrected. Elemental analyses were done on a Perkin-Elmer 240C elemental analyzer. Nuclear magnetic resonance spectra (NMR) were obtained with a JEOL GX-500 instrument in the FT mode. Chemical shifts were expressed in parts per milion from internal tetramethylsilane (δ) unless otherwise noted. Coupling constants are in hertz (Hz) and splitting pattern abbreviations are: s, singlet; d, doublet; dd, doublet of doublets; ddd, doublet of double doublets; m, mutiplet; br, broad. Mass spectra (MS) were obtained on a JEOL DX-300 spectrometer. Infrared spectra (IR) were recorded on a JASCO A-3 spectrophotometer. Optical rotations $[\alpha]_D$ were recorded on a JASCO DIP-181 digital polarimeter.

Analytical thin layer chromatography (TLC) was conducted on precoated TLC glass sheets (silica gel 60F-254, layer thickness 0.25 mm) manufactured by E. Merck. Detection was effected by dipping into 2% concentrated sulfuric acid ethanol solution followed by heating on a hot plate (ca 120 °C).

Column chromatography was performed with Merck silica gel 60 (70-230 mesh) or aluminum oxide 90 (70-230 mesh) deactivated by addition of 4.4 wt% water.

^{1}H-NMR data were summarized in Table 1 - 4 and MS, elemental analyses, Mp, Rf, $[\alpha]_D$, and IR data were in Table 5.

Table 1. ^{1}H-NMR data for **18** - **21** in chloroform-d

Compound	Chemical shifts, δ (multiplicities)										
	H-3 (d)	H-4 (dd)	H-5 (ddd)	H-6 (dd)	H-7 (dd)	H-8 (ddd)	H-9 (dd)	H-9' (dd)	Me ester (s)	NH (d)	O-Ac, N-Ac (s)
18[a]	5.91	4.52[b]	3.93	3.96	3.58[b]	4.27	3.98	4.09	3.75	7.52	1.27,[c]1.30,[c]2.03
19[d]	5.94	5.67	4.23	4.41	5.39	4.38	3.97	4.14	3.81	5.54	1.36,[c]1.37,[c]1.94, 2.07, 2.13
20[e]	5.92	5.58	4.48	4.56	5.03	4.05	3.53	3.70	3.81	6.18	1.92, 2.08, 2.16
21	5.95	5.59	4.39	4.56	5.20	4.25	4.14	4.19	3.81	5.74	1.93, 2.08, 2.10, 2.12

Compound	First-order coupling constants, Hz								
	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,NH}$	$J_{6,7}$	$J_{7,8}$	$J_{8,9}$	$J_{8,9'}$	$J_{9,9'}$
18[f]	2.4	10.2	4.6		0	7.4	5.5	6.1	- 8.6
19	2.7	8.6	10.1	9.2	2.4	5.5	6.5	6.3	- 9.0
20	2.4	8.5	10.0	9.5	2.0	9.2	3.8	2.5	-12.5
21	2.8	8.2	10.1	9.5	2.7	7.9	6.1	3.4	-11.9

[a] 4-OH (4.59, d) and 7-OH (4.93, d) were also observed. [b] Multiplicity: ddd. [c] These values are signals of 8,9-O-isopropylidene groups. [d] 8-OH (3.31, br. s) was also observed. [e] Measured in acetone-d_6. [f] $J_{OH,4}$=6.4 Hz, $J_{OH,7}$=4.3 Hz.

Table 2. ^{1}H-NMR data for reducing unit (Glc, Gal) in chloroform-d

Compound	Chemical shifts, δ (multiplicities)							First-order coupling constants, Hz						
	H-1 (d)	H-2 (dd)	H-3 (dd)	H-4 (dd)	H-5 (ddd)	H-6 (dd)	H-6' (dd)	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$
5	4.88	3.67	3.98	3.70	3.75	3.77	3.90	3.4	9.5	8.5	7.8	2.5	2.0	-10.0
6	4.89	3.61	3.97	3.70	3.74	3.80	3.81	3.7	9.5	9.2	10.1	2.5	2.0	-10.8
7	4.60	3.51	3.94	3.59	3.76	3.42	4.21	3.4	9.6	9.2	10.1	2.0	4.0	-10.7
14	4.33	3.77	3.87	4.02[a]	3.83	3.72	3.74	7.3	8.5	2.5	0	6.3	7.5	-17.0
15	4.34	3.75	4.09	3.94[a]	3.77	3.69	3.71	7.3	9.8	2.8	0	6.1	6.1	- 9.8
16[b]	4.37	3.65	3.74	4.28[a]	d	d	d	7.9	10.4	3.1	0	d	d	d
27[c]	4.71	3.59	3.98	3.63	3.78	3.72	3.88	3.4	9.2	9.0	7.0	3.3	1.8	-10.9
28[c]	4.72	3.62	3.98	3.67	3.78	3.82	3.99[a]	3.4	9.5	9.2	10.2	2.5	0	-12.9
29[c]	4.69	3.55	3.97	3.62	3.77	3.81	3.90	3.5	9.2	9.5	8.8	4.2	2.1	-10.4

Aglycon (cholesterol)

Compound	Chemical shifts, δ (multiplicities)								First-order coupling constants, Hz		
	H-3 (m)	H-6 (m)	H-18 (s)	H-19 (s)	H-21 (d)	H-26 (d)	H-27 (d)	others	$J_{20,21}$	$J_{25,26}$	$J_{25,27}$
8	3.50-3.58	5.24-5.28	0.67	0.99	0.91	0.86[e]	0.87[e]	d	6.4	6.7	6.7
9	3.53-3.62	5.22-5.29	0.67	1.00	0.91	0.86[e]	0.87[e]	d	6.4	6.7	6.7
10[h]	d	5.24-5.28	0.71	1.00	0.93	0.87[e]	0.88[e]	d	6.4	6.4	6.4
11	3.62-3.68	5.35-5.38	0.67	0.98	0.91	0.86[e]	0.87[e]	d	6.4	6.6	6.6
12[g]	d	5.25-5.29	0.65	0.95	0.90	0.84[e]	0.85[e]	d	6.4	6.3	6.3

Table 2. (continued) ^{1}H-NMR data for reducing or central unit (NeuAc) in chloroform-d

Compound	Chemical shifts, δ (multiplicities)											
	H-3eq (dd)	H-3ax (dd)	H-4 (ddd)	H-5 (ddd)	H-6 (dd)	H-7 (dd)	H-8 (ddd)	H-9 (dd)	H-9' (dd)	Me ester (s)	NH (d)	O-Ac, N-Ac (s)
22	5.97[a]		5.55[f]	4.50	4.56	5.53	4.35	4.17	4.63	3.81[e]	6.32	1.91, 2.06, 2.07, 2.18[e]
23	5.99[a]		5.52[f]	4.52	4.55	5.51	4.53	4.15	4.61	3.82[e]	6.24	1.89, 2.04, 2.07, 2.16[e]
24	6.03[a]		4.52[f]	4.06	4.29	3.85	4.51	4.66	4.89			2.06[e]
25	5.05[a]		5.52[f]	4.83	4.62	5.53	4.35	4.17	4.60	3.89[e]	6.52	1.93, 2.06, 2.11, 2.21[e]
26	5.07[a]		5.51[f]	4.82	4.59	5.52	4.02	4.18	4.57	3.92[e]	6.52	1.89, 2.03, 2.12, 2.18[e]
27[c]	4.66[a]		5.42[f]	4.43	4.60	5.34	4.27	4.18	4.70	3.76[e]	5.99	1.91, 2.02, 2.06, 2.18[e]
28[c]	4.66[a]		5.43[f]	4.38	4.58	5.24	4.49	4.03	4.57	3.77[e]	5.78	1.89, 1.96, 2.03, 2.14[e]
29[c]	2.46	1.88	5.26	4.12	4.36	5.27	4.51	4.06	4.71	3.74[e]	5.93	1.87, 1.97, 2.01, 2.14[e]

Compound	First-order coupling constants, Hz									
	$J_{3eq,3ax}$	$J_{3eq,4}$	$J_{3ax,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,NH}$	$J_{6,7}$	$J_{7,8}$	$J_{8,9}$	$J_{8,9'}$	$J_{9,9'}$
22		2.4		11.5	10.5	9.8	2.2	3.8	4.9	3.1	-12.8
23		2.5		9.7	10.8	9.5	2.0	2.5	6.1	2.5	-12.8
24[b]		2.4		8.5	9.5		0.5	7.0	7.9	3.5	-11.9
25		3.4		10.7	10.4	10.1	1.5	1.8	4.7	3.1	-12.6
26		3.4		10.3	10.5	10.4	2.1	2.0	6.9	3.4	-12.3
27[c]		3.6		10.6	d	d	d	1.5	5.0	5.5	-12.5
28[c]		3.4		10.5	10.1	10.9	1.4	2.0	5.4	5.0	-11.1
29[c]	-13.5	5.2	11.2	10.5	10.4	10.8	2.1	1.8	5.3	5.6	-11.2

[a]Multiplicity: d. [b]Measured in D_2O (t-BuOH=1.23 ppm). [c]Measured at 50 °C. [d]Not assigned owing to the complexity of the spectrum. [e]Assignments may be interchanged with non-reducing unit. [f]Multiplicity: dd. [g]Measured in dimethylsulfoxide-d_6. [h]Measured in methanol-d_4.

Methyl 2,3,4-tri-O-benzyl-6-O-[methyl (5-acetamido-4,7,8,9-tetra-O-acetyl-3-bromo-3,5-dideoxy-β-D-erythro-L-manno-2-nonulopyranosyl)onate]-α-D-glucopyranoside (5). To a stirred solution of the dibromide 3[b] (400 mg, 0.63 mmol), 4 (310 mg, 0.67 mmol), and anhydrous Na_2HPO_4 (340 mg) in benzene (6 ml) was added a solution of AgOTf (170 mg, 0.66 mmol) in benzene (6 ml) at room temp under nitrogen. The mixture was stirred for 30 min and filtered through Celite 545 bed and the solid was washed with ethyl acetate. The combined filtrates and washings were evaporated in vacuo to a residue. A solution of the residue in ethyl acetate was washed with 5% $Na_2S_2O_3$, 5% $NaHCO_3$, and brine, dried over anhydrous Na_2SO_4, and evaporated in vacuo to give a syrup, which was chromatographed on a silica gel column (benzene-acetone, gradient elution from 5:1 to 3:1) to give 5 (450 mg, 70%) as a syrup.

3-O-[Methyl (5-acetamido-4,7,8,9-tetra-O-acetyl-3-bromo-3,5-dideoxy-β-D-erythro-L-manno-2-nonulopyranosyl)onate]cholesterol (8). A mixture of 3 (310 mg, 0.49 mmol), cholesterol (200 mg, 0.52 mmol), AgOTf (135 mg, 0.52 mmol), and anhydrous Na_2HPO_4 (250 mg) in benzene (10 ml) was treated in the same manner as described above to give a crude material, which was chromatographed on a silica gel column (benzene-acetone, gradient elution from 5:1 to 3:1) and crystallized from hexane-ethyl acetate to give 8 (405 mg, 88%) as white crystals.

Methyl 2,4,6-tri-O-benzyl-3-O-[methyl (5-acetamido-4,7,8,9-tetra-O-acetyl-3-bromo-3,5-dideoxy-β-D-erythro-L-manno-2-nonulopyranosyl)onate]-β-D-galactopyranoside (14). A mixture of 3 (350 mg, 0.55 mmol), 13 (270 mg, 0.58 mmol), AgOTf (150 mg, 0.58 mmol), and anhydrous Na_2HPO_4 (300 mg) in benzene (11 ml) was treated in the same manner as described above. The crude syrup was chromatographed on a silica gel column (benzene-acetone, 5:1) to give 14 (280 mg, 50%) as a syrup.

Methyl 5-acetamido-2,6-anhydro-3,5-dideoxy-8,9-O-isopropylidene-D-glycero-D-galacto-non-2-enopyranosonate (18). A mixture of 17[b] (470 mg, 1.54 mmol) and Dowex 50W-X8 [H^+] (250 mg) was stirred at 40 °C for 5 h under nitrogen. The resin was removed by filtration and washed well with acetone and the combined filtrates and washings were condensed to a solid, which was recrystallized from chloroform-hexane to give 18 (390 mg, 73%) as white crystals.

Methyl 5-acetamido-4,7-di-O-acetyl-2,6-anhydro-3,5-dideoxy-8,9-O-isopropylidene-D-glycero-D-galacto-non-2-enopyranosonate (19). A solution of 18 (360 mg, 1.04 mmol) in acetic anhydride (2.0 ml) and pyridine (4.0 ml) was heated at 60 °C for 6 h under nitrogen. The reaction mixture was condensed to a syrup which was chromatographed on a silica gel column (ethyl acetate-acetone, 6:1) and recrystallized from carbon tetrachloride to give 19 (440 mg, 98%) as white crystals.

Methyl 5-acetamido-4,7-di-O-acetyl-2,6-anhydro-3,5-dideoxy-D-glycero-D-galacto-non-2-enopyranosonate (20). A solution of 19 (840 mg, 1.96 mmol) in 80% acetic acid was heated at 60 °C for 1 h and evaporated in vacuo to give an oil, which was chromatographed on a silica gel column (ethyl acetate-acetone, gradient elution from 4:1 to 2:1) and recrystallized from hexane-ethyl acetate to give 20 (620 mg, 81%) as white crystals.

Methyl 5-acetamido-4,7,9-tri-O-acetyl-2,6-anhydro-3,5-dideoxy-D-glycero-D-galacto-non-2-enopyranosonate (21). To a stirred solution of 20 (620 mg, 1.59 mmol) in pyridine (6 ml) was added dropwise acetyl chloride (0.12 ml, 1.68 mmol) at -20 °C under nitrogen. The mixture was stirred for 30 min at the same temp and condensed to a syrup, which was chromatographed on a silica gel

Table 3. ^{1}H-NMR data for non-reducing unit (NeuAc) in chloroform-d

Compound	Chemical shifts, δ (multiplicities)											
	H-3eq (dd)	H-3ax (dd)	H-4 (ddd)	H-5 (ddd)	H-6 (dd)	H-7 (dd)	H-8 (ddd)	H-9 (dd)	H-9' (dd)	Me ester (s)	NH (d)	O-Ac, N-Ac (s)
5	4.64[a]		5.35[b]	4.35	4.49	5.34	5.27	4.16	5.19	3.75	5.53	1.87,1.97,2.06,2.07,2.17
6	2.47	1.88	5.16	4.11	4.27	5.38	5.27	4.13	5.07	3.72	5.49	1.86,1.97,2.01,2.05,2.13
7	2.65	1.97	4.85	3.99	4.09	5.25	5.33	3.78	4.05	3.73	5.12	1.82,1.85,2.00,2.01,2.12
8	4.64[a]		5.52[b]	4.26–4.33		5.32	5.17	4.22	4.84	3.82	5.38	1.91,2.02,2.07,2.08,2.16
9	2.52	c	5.25	4.09	4.11	5.38	5.06	4.15	4.88	3.80	5.52	1.87,2.02,2.02,2.08,2.13
10[d]	2.45	1.57	4.02	c	c	c	c	c	c			2.00
11	2.59	1.96	4.86	4.0–4.8		5.30	5.34	4.17	4.35	3.79	5.21	1.88,2.02,2.02,2.12,2.14
12[e]	2.54	1.52	c	c	c	c	c	c	c			1.90
14	4.73[a]		5.05[b]	4.51	3.87	5.09	5.19	4.03	5.23	3.53	3.51	1.59,1.97,2.02,2.05,2.08
15	2.70	1.80	4.98	3.99	3.91	5.15	5.15	4.00	4.99	3.54	3.86	1.64,1.98,2.00,2.03,2.06
16[f]	2.50	1.73	4.20	c	c	c	c	c	c			2.09
22	4.58[a]		5.22[b]	4.62	4.56	5.29	5.33	4.07	5.05	3.80[g]	6.08	1.86,2.05,2.06,2.13,2.20[g]
23	2.49	1.84	5.09	4.08	4.62	5.37	5.31	4.01	4.92	3.78[g]	6.06	1.87,1.99,2.05,2.11,2.17[g]
24[f]	2.31	2.15	4.05	3.90[b]	4.02	3.59	3.69	3.61	3.79			2.03[g]
25	4.60[a]		5.24[b]	4.61	4.46	5.25	5.39	4.03	5.20	3.81[g]	5.96	1.88,2.05,2.11,2.15,2.24[g]
26	2.52	1.84	5.17	4.11	4.47	5.34	5.33	3.97	5.06	3.79[g]	6.14	1.88,2.00,2.04,2.16,2.24[g]
27[h]	4.60[a]		5.21[b]	4.65	4.61	5.34	5.34	4.10	5.08	3.60[g]	6.20	1.83,1.94,2.02,2.07,2.26[g]
28[h]	2.42	1.81	5.15	4.12	4.68	5.46	5.33	4.07	5.02	3.64[g]	6.29	1.84,1.95,2.02,2.07,2.26[g]
29[h]	2.43	1.80	5.11	4.11	4.63	5.41	5.33	4.07	4.96	3.61[g]	6.12	1.82,1.94,2.00,2.05,2.22[g]

Compound	First-order coupling constants, Hz										
	$J_{3eq,3ax}$	$J_{3eq,4}$	$J_{3ax,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,NH}$	$J_{6,7}$	$J_{7,8}$	$J_{8,9}$	$J_{8,9'}$	$J_{9,9'}$
5		3.7		9.8	10.2	9.5	1.8	2.0	9.2	2.1	-12.5
6	-12.9	5.1	10.8	11.2	10.4	10.4	2.3	2.2	9.3	2.2	-12.5
7	-12.8	4.9	12.3	10.4	10.7	10.1	2.1	9.2	4.9	2.6	-12.5
8		3.7		10.3	c	8.9	0	2.4	7.3	2.1	-12.5
9	-13.1	4.9	c	10.1	10.0	9.5	2.0	2.0	7.9	1.8	-12.5
10[d]	-12.5	5.0	11.3	10.1	c		c	c	c	c	c
11	-12.5	4.6	12.8	c	c	9.8	1.8	7.0	5.9	2.5	-12.5
12[e]	-12.5	4.5	11.3	c	c		c	c	c	c	c
14		3.7		10.7	8.5	10.3	2.5	2.5	9.2	2.0	-11.9
15	-13.4	4.6	11.6	11.2	10.7	10.4	1.8	2.1	8.5	2.1	-12.5
16[f]	-13.1	4.6	11.7	10.5	c		c	c	c	c	c
22		3.4		10.1	10.5	9.8	2.2	2.3	9.2	2.5	-12.2
23	-13.3	4.7	10.5	11.3	10.6	10.1	2.5	2.7	8.9	2.4	-12.2
24[f]	-13.1	4.9	11.9	10.4	10.1		1.1	9.2	5.5	2.4	-11.9
25		3.4		9.9	10.1	9.2	2.1	1.9	9.8	2.1	-12.2
26	-13.2	4.7	11.8	9.8	10.4	10.1	2.1	2.0	9.9	2.1	-12.2
27[h]		3.7		10.7	10.3	10.4	1.8	0	9.5	2.4	-12.2
28[h]	-13.3	5.0	11.0	10.9	11.0	10.7	2.7	1.9	9.4	2.3	-12.2
29[h]	-13.5	4.9	11.3	10.3	10.4	10.7	2.4	2.4	9.2	2.4	-11.8

[a]Multiplicity: d. [b]Multiplicity: dd. [c]Not assigned owing to the complexity of the spectrum. [d]Measured in methanol-d_4. [e]Measured in dimethylsulfoxide-d_6. [f]Measured in D_2O (t-BuOH=1.23 ppm). [g]Assignments may be interchanged with reducing unit. [h]Measured at 50 °C.

Table 4. ^{1}H-NMR data for other groups in chloroform-d

Compound	Chemical shifts, δ (multiplicities)		First-order coupling constants, Hz
	O-CH_3 (s)	$PhCH_2$ (AB quartet)	Ph (m)	J_{gem}
5	3.38	4.69 and 4.78, 4.74 and 4.87, 4.79 and 4.92	7.2-7.5	-11.9, -10.7, -11.0
6	3.35	4.70 and 4.87, 4.75 and 4.82, 4.84 and 4.97	7.2-7.4	-10.8, -12.0, -11.0
7	3.36	4.65 and 4.79, 4.75 and 4.90, 4.78 and 4.84	7.2-7.5	-13.1, -11.0, -11.0
14	3.50	4.57 and 4.58, 4.75 and 4.86, 4.83 and 4.91	7.2-7.5	-12.0, -11.6, -13.7
15	3.46	4.56[a], 4.68 and 4.88, 4.79 and 4.80	7.2-7.5	-11.0, -12.5
16	3.60			
27[b]	3.41	4.67 and 4.77, 4.71 and 4.89, 4.79 and 4.93	7.2-7.4	-11.3, -11.3, -11.0
28[b]	3.38	4.69 and 4.78, 4.74 and 4.87, 4.79 and 4.92	7.2-7.5	-11.9, -10.7, -11.0
29[b]	3.39	4.68 and 4.78, 4.72 and 4.86, 4.79 and 4.93	7.2-7.4	-11.9, -11.0, -11.3

[a]Mutiplicity: s. [b]Measured at 50 °C.

Table 5. Ms, elemental analyses, Mp, Rf, $[\alpha]_D$, and IR data for 5 - 29

com-pound	Formula	MS (M+H)	Anal.	% C	% H	% N	Mp (°C)	Rf	$[\alpha]_D$ (c)[a] (Temp)	ν_{max}^{KBr} NH,OH	ester	amideI	II
5	$C_{48}H_{58}NO_{18}Br$	1017[b]	Calcd.	56.69	5.75	1.38		0.57[c]	+49.6°(1.1)	3400	1750	1660	1542
			Found	56.98	5.54	1.04			(27°C)				
6	$C_{48}H_{59}NO_{18}$	938[d]	Calcd.	61.46	6.34	1.49		0.52[c]	+23.3°(1.0)	3400	1748	1665	1540
			Found	61.59	6.34	1.31			(29°C)				
7	$C_{48}H_{59}NO_{18}$	938[d]	Calcd.	61.46	6.34	1.49	103-105[e]	0.42[c]	+ 1.0°(1.0)	3300	1742	1660	1540
			Found	61.23	6.27	1.08			(27°C)				
8	$C_{47}H_{72}NO_{13}Br$	938[d]	Calcd.	60.12	7.73	1.49	224-225[e]	0.58[c]	-15.0°(1.1)	3400	1745	1660	1533
		940	Found	60.46	7.46	1.32			(29°C)				
9	$C_{47}H_{73}NO_{13}$	860[d]	Calcd.	65.63	8.56	1.63	119-120[f]	0.54[c]	-40.0°(1.1)	3400	1755	1665	1550
			Found	65.52	8.28	1.37			(29°C)				
10	$C_{38}H_{63}NO_{9}$	678[d]	Calcd.	67.32	9.37	2.07	156-157[g]	0.62[h]	-41.5°(1.1)[i]	3430	1740[j]	1630	1580
			Found	67.30	9.78	2.00			(26°C)				
11	$C_{47}H_{73}NO_{13}$	860[d]	Calcd.	65.63	8.56	1.63	105-106[e]	0.49[c]	-24.1°(1.1)	3400	1753	1667	1545
			Found	65.43	8.74	1.39			(26°C)				
12	$C_{38}H_{63}NO_{9}$	678[d]	Calcd.	67.32	9.37	2.07	170-171[g]	0.58[h]	-11.3°(0.6)[k]	3400	1723[j]	1640	1570
			Found	67.15	9.26	1.98			(26°C)				
14	$C_{48}H_{58}NO_{18}Br$	1017[b]	Calcd.	56.69	5.75	1.38		0.65[c]	+34.4°(1.0)	3405	1750	1685	1530
			Found	55.98	5.62	1.17			(28°C)				
15	$C_{48}H_{59}NO_{18}$	938[d]	Calcd.	61.46	6.34	1.49		0.58[c]	+ 5.3°(1.0)	3400	1743	1685	1540
			Found	61.23	6.27	1.08			(29°C)				
16	$C_{18}H_{31}NO_{14}$	486[d]	Calcd.	44.54	6.44	2.88	215-217[l]	0.17[h]	-18.3°(1.2)[i]	3500	1730[j]	1660	1570
			Found	44.55	6.62	2.92			(23°C)				
18	$C_{15}H_{23}NO_{8}$	346[d]	Calcd.	52.17	6.71	4.06	166-167[m]	0.34[n]	+50.8°(1.1)	3350	1715	1660	1536
			Found	52.38	6.73	3.88			(27°C)				
19	$C_{19}H_{27}NO_{10}$	430[d]	Calcd.	53.14	6.34	3.26	77-78[o]	0.59[p]	+46.7°(1.0)	3310	1747	1658	1552
			Found	53.31	6.74	3.33			(27°C)				
20	$C_{16}H_{23}NO_{10}$	390[d]	Calcd.	49.36	5.95	3.60	190-192[e]	0.24[n]	+44.5°(1.1)	3320	1738	1660	1545
			Found	49.31	5.98	3.85			(26°C)				
21	$C_{18}H_{25}NO_{11}$	432[d]	Calcd.	50.11	5.84	3.25		0.34[n]	+48.1°(1.1)	3380	1740	1660	1543
			Found	50.32	5.57	3.35			(26°C)				
22	$C_{38}H_{51}N_2O_{23}Br$	983[d]	Calcd.	46.40	5.22	2.85		0.31[q]	+57.1°(1.2)	3400	1752	1665	1540
			Found	46.33	5.12	2.42			(25°C)				
23	$C_{38}H_{52}N_2O_{23}$	905[d]	Calcd.	50.44	5.79	3.10		0.25[q]	+31.2°(1.2)	3400	1745	1662	1538
			Found	50.64	5.66	3.49			(25°C)				
24	$C_{22}H_{34}N_2O_{16}$	583[d]	Calcd.	45.36	5.83	4.81	232-235[r]	0.51[s]	+42.6°(1.1)[t]	3400	1720[j]	1630	1570
			Found	45.22	5.98	4.48			(25°C)				
25	$C_{38}H_{51}N_2O_{23}Br_3$		Calcd.	39.91	4.50	2.45		0.34[q]	+ 6.0°(1.1)	3400	1752	1670	1548
			Found	39.89	4.10	2.18			(25°C)				
26	$C_{38}H_{52}N_2O_{23}Br_2$	1065[d]	Calcd.	42.87	4.92	2.63		0.28[q]	-15.6°(0.6)	3400	1748	1650	1538
			Found	42.19	5.30	2.46			(25°C)				
27	$C_{66}H_{82}N_2O_{29}Br_2$	1526[b]	Calcd.	51.91	5.41	1.83		0.46[q]	+31.7°(0.2)	3420	1752	1685	1535
		1528	Found	51.85	5.13	1.67			(23°C)				
28	$C_{66}H_{83}N_2O_{29}Br$		Calcd.	54.73	5.78	1.93		0.42[q]	+ 8.6°(0.8)	3420	1750	1685	1530
			Found	54.55	5.44	1.87			(25°C)				
29	$C_{66}H_{84}N_2O_{29}$	1368[b]	Calcd.	57.89	6.18	2.05		0.33[q]	- 2.0°(0.3)	3410	1750	1685	1535
		1369	Found	57.64	6.09	1.52			(24°C)				

[a]Measured in chloroform. [b]Field disorption method. [c]Solvent system is benzene-acetone (2:1). [d]Fast atom bombardment method. [e]Recrystallized from hexane-ethyl acetate. [f]Recrystallized from 1-pentane. [g]Recrystallized from methanol-water. [h]Solvent system is 1-butanol-acetic acid-water (3:1:1). [i]Measured in methanol. [j]Absorption of carboxylic acid. [k]Measured in chloroform-methanol (1:1). [l]Triturated with ether-methanol. [m]Recrystallized from hexane-chloroform. [n]Solvent system is chloroform-methanol (10:1). [o]Recrystallized from carbon tetrachloride. [p]Solvent system is ethyl acetate-acetone (6:1). [q]Solvent system is benzene-acetone-methanol (30:20:1). [r]Triturated with chloroform-methanol. [s]Solvent system is 1-propanol-water (7:3). [t]Measured in water.

column (ethyl acetate-acetone, gradient elution from 8:1 to 5:1) to give **21** (525 mg, 76%) as a colorless viscous syrup.

Methyl 5-acetamido-4,7,9-tri-O-acetyl-2,6-anhydro-3,5-dideoxy-8-O-[methyl (5-acetamido-4,7,8,9-tetra-O-acetyl-3-bromo-3,5-dideoxy-β-D-erythro-L-manno-2-nonulopyranosyl)onate]-D-glycero-D-galacto-non-2-enopyranosonate (22). A mixture of **3** (720 mg, 1.14 mmol), **21** (490 mg, 1.14 mmol), AgOTf (300 mg, 1.17 mmol), and anhydrous Na_2HPO_4 (600 mg) in benzene (20 ml) was treated in the same manner as described above to give a crude material, which was chromatographed on a silica gel column (ethyl acetate-acetone, gradient elution from 5:1 to 3:1) to give **22** (650 mg, 58%) as a viscous syrup.

Condensation of the chloride **1** with **4**. To a mixture of **1**[3] (200 mg, 0.39 mmol), **4** (400 mg, 0.86 mmol), and anhydrous Na_2HPO_4 (385 mg) in benzene (3 ml) was added a solution of AgOTf (220 mg, 0.86 mmol) in benzene (3 ml) at room temp under nitrogen. After stirring for 12 h, the mixture was filtered and the solid was washed with ethyl acetate. The combined filtrates and washings were condensed to a residue, which was dissolved in ethyl acetate, washed with 5% $Na_2S_2O_3$, 5% $NaHCO_3$, and brine, dried over anhydrous Na_2SO_4, and evaporated *in vacuo* to give a crude syrup. This syrup was

chromatographed on a silica gel column (benzene-acetone, gradient elution from 6:1 to 2:1). The fast migrating zone was methyl 2,3,4-tri-O-benzyl-6-O-[methyl (5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-β-D-glycero-D-galacto-2-nonulopyranosyl)onate]-α-D-glucopyranoside (6) (130 mg, 35%) as a syrup and the slow one was the α-isomer, which was crystallized from hexane-ethyl acetate to give 7 (95 mg, 26%).

Methyl 2,3,4-tri-O-benzyl-6-O-[methyl (5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-β-D-glycero-D-galacto-2-nonulopyranosyl)onate]-α-D-glucopyranoside (6). To a solution of 5 (380 mg,0.37 mmol) in tetrahydrofuran (5 ml) was added tributylstannane (0.2 ml, 0.74 mmol) under nitrogen. The mixture was heated at 60 °C for 30 min and condensed to a residue, which was chromatographed on an aluminum oxide 90 column (benzene-ethyl acetate, 1:1) to give 6 (340 mg, 97%) as a syrup.

Condensation of the chloride 1 with cholesterol. To a stirred mixture of 1 (350 mg, 0.69 mmol) cholesterol (530 mg, 1.37 mmol), and anhydrous Na_2HPO_4 (400 mg) in benzene (10 ml) was added a solution of AgOTf (200 mg, 0.78 mmol) in benzene (4 ml) at room temp under nitrogen. The mixture was stirred for 12 h and filtered. The insoluble solid was washed well with ethyl acetate and the combined filtrates and washings were condensed in vacuo to a syrup. A solution of the residue in ethyl acetate was washed with 5% $Na_2S_2O_3$, 5% $NaHCO_3$, and brine, dried over Na_2SO_4, and evaporated in vacuo to give a crude syrup, which was chromatographed on a silica gel column (ethyl acetate-hexane, 3:4). The fast eluted isomer was a β-isomer and the slow one was an α-isomer, which were recrystallized from hexane-ethyl acetate to give the 3-O-[methyl (5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-α-D-glycero-D-galacto-2-nonulopyranosyl)onate]cholesterol (11) (200 mg, 33%) and the corresponding β-glycoside 9 (220 mg, 37%).

3-O-[Methyl (5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-β-D-glycero-D-galacto-2-nonulopyranosyl)onate]cholesterol (9). A solution of 8 (300 mg, 0.32 mmol) and tributylstannane (0.21 ml, 0.78 mmol) in tetrahydrofuran (5 ml) was heated at 60 °C for 30 minn with stirring under nitrogen. After condensation, the residue was chromatographed on an aluminum oxide 90 column (benzene-ethyl acetate, 1:1) and crystallized from pentane to give 9 (265 mg, 96%) as white crystals.

Methyl 2,4,6-tri-O-benzyl-3-O-[methyl (5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-β-D-glycero-D-galacto-2-nonulopyranosyl)onate]-β-D-galactopyranoside (15). A solution of 14 (145 mg, 0.14 mmol) and tributylstannane (0.08 ml, 0.30 mmol) in tetrahydrofuran (3 ml) was stirred at 60 °C for 30 min under nitrogen. The mixture was condensed to a residue, which was chromatographed on an aluminum oxide 90 column (benzene-ethyl acetate, 1:1) to give 15 (128 mg, 96%) as a syrup.

Methyl 5-acetamido-4,7,9-tri-O-acetyl-2,6-anhydro-3,5-dideoxy-8-O-[methyl (5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-β-D-glycero-D-galacto-2-nonulopyranosyl)onate]-D-glycero-D-galacto-non-2-enopyranosonate (23). A mixture of 22 (120 mg, 0.12 mmol) and tributylstannane (0.07 ml, 0.26 mmol) in tetrahydrofurn (3 ml) was stirred at 60 °C for 2 h under nitrogen. The mixture was condensed in vacuo to a residue, which was chromatographed on a silica gel column (ethyl acetate-acetone, 1:1), triturated with hexane-ethyl acetate, and washed with hexane to give 23 (105 mg, 95%) as a white powder.

3-O-(5-Acetamido-3,5-dideoxy-β-D-glycero-D-galacto-2-nonulopyranosyl)cholesterol (10). A mixture of 9 (330 mg, 0.38 mmol) and potassium t-butoxide (cat. amount) in absolute methanol (25 ml) was stirred for 1 h at room temp under nitrogen. To the above mixture was added 1N NaOH (3.0 ml) and after stirring for 2 h the mixture was cooled (0 °C), acidified with Dowex 50W-X8 [H^+], and filtered. The resin was washed well with methanol and the combined filtrates and washings were condensed to give a crystal, which was recrystallized from methanol-water to give 10 (250 mg, 96%) as white crystals.

3-O-(5-Acetamido-3,5-dideoxy-α-D-glycero-D-galacto-2-nonulopyranosyl)cholesterol (12). To a solution of 11 (110 mg, 0.13 mmol) in absolute methanol (10 ml) was added potassium t-butoxide (cat. amount) at room temp under nitrogen. The mixture was stirred for 1 h and 1N NaOH (1.5 ml) was added to it. After stirring for further 2 h at room temp, the reaction mixture was cooled (0 °C), acidified with Dowex 50W-X8 [H^+], and filtered. The resin was washed with methanol and the combined filtrates and washings were condensed to a residue, which was recrystallized from methanol-water to give 12 (80 mg, 92%) as white crystals.

Mehtyl 3-O-(5-acetamido-3,5-dideoxy-β-D-glycero-D-galacto-2-nonulopyranosyl)-β-D-galactopyranoside (16). A mixture of 15 (110 mg, 0.12 mmol) and 10% palladium on carbon (200 mg) in methanol (15 ml) was stirred vigorously for 2 days under hydrogen. The catalyst was removed by filtration and washed well with methanol. The combined filtrates and washings were condensed to a residue. To a solution of the residue in absolute methanol (8 ml) was added potassium t-butoxide (cat. amount) and the mixture was stirred for 30 min at room temp under nitrogen. After addition of 1N NaOH (0.8 ml), the mixture was stirred for additional 1 h, cooled (0 °C), acidified with Dowex 50W-X8 [H^+], and filtered. The resin was washed with methanol and the combined filtrates and washings were evaporated in vacuo to give a viscous syrup, which was triturated with ether-methanol to give the white powder 16 (51 mg, 90%).

5-Acetamido-2,6-anhydro-3,5-dideoxy-8-O-(5-acetamido-3,5-dideoxy-β-D-glycero-D-galacto-2-nonulopyranosyl)-D-glycero-D-galacto-non-2-enpyranose (24). To a solution of 23 (70 mg, 0.077 mmol) in absolute methanol (7 ml) was added potassium t-butoxide (cat. amount) under nitrogen. The mixture was stirred for 30 min at room temp, and to this was added 1N NaOH (1.0 ml). After stirring for additional 1 h, the resulting mixture was cooled (-10 °C), acidified with Dowex 50W-X8 [H^+], and filtered. The resin was washed with methanol-water (1:1) and the combined filtrates and washings were condensed to a residue, which was triturated with chloroform-methanol to give 24 (42 mg, 93%) as white powder.

Methyl 5-acetamido-4,7,9-tri-O-acetyl-2,3-dibromo-2,3,5-trideoxy-8-O-[methyl (5-acetamido-4,7,8,9-tetra-O-acetyl-3-bromo-3,5-dideoxy-β-D-erythro-L-manno-2-nonulopyranosyl)onate]-β-D-erythro-L-manno-2-nonulopyranosonate (25). To a solution of **22** (35 mg, 0.036 mmol) in dichloromethane (2 ml) was added bromine (2 drops) at 0 °C under nitrogen. The mixture was stirred for 10 min and the solvent was removed in vacuo to give a crude material, which was chromatographed on a silica gel column (ethyl acetate-acetone-mathanol, 5:5:1) to give the tribromide **25** (40 mg, 98%) as a syrup.

Methyl 5-acetamido-4,7,9-tri-O-acetyl-2,3-dibromo-2,3,5-trideoxy-8-O-[methyl (5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-β-D-glycero-D-galacto-2-nonulopyranosyl)onate]-β-D-erythro-L-manno-2-nonulopyranosonate (26). A mixture of **23** (30 mg, 0.033 mmol) and bromine (2 drops) in dichloromethane (2 ml) was treated in the same manner as described above to give a crude material, which was chromatographed on a silica gel column (ethyl acetate-acetone-methanol, 5:5:1) to give the dibromide **26** (35 mg, 99%) as a viscous syrup.

Condensation of the tribromide 25 with 4. To a stirred mixture of **25** (15 mg, 0.014 mmol), **4** (7 mg, 0.015 mmol), and anhydrous Na_2HPO_4 (10 mg) in benzene (0.3 ml) was added a solution of AgOTf (4 mg, 0.016 mmol) in benzene (0.5 ml) under nitrogen. The heterogeneous mixture was stirred for 30 min at room temp. The solid was removed by filtration and washed well with ethyl acetate. The combined filtrates and washings were condensed in vacuo to a residue. The residue was dissolved in ethyl acetate, washed with 5% $Na_2S_2O_3$, 5% $NaHCO_3$, and brine, dried over anhydrous Na_2SO_4, and evaporated in vacuo to give a syrup. This was chromatographed on a silica gel column (ethyl acetate-acetone-methanol, 24:4:1) to give the methyl 2,3,4-tri-O-benzyl-6-O-[methyl (5-acetamido-4,7,9-tri-O-acetyl-3-bromo-3,5-dideoxy-8-O-[methyl (5-acetamido-4,7,8,9-tetra-O-acetyl-3-bromo-3,5-dideoxy-β-D-erythro-L-manno-2-nonulopyranosyl)onate]-β-D-erythro-L-manno-2-nonulopyranosyl)onate]-α-D-glucopyranoside (27) (9 mg, 42%) as a syrup.

Condensation of the dibromide 26 with 4. A mixture of **26** (35 mg, 0.033 mmol), **4** (17 mg, 0.039 mmol), anhydrous Na_2HPO_4 (20 mg), and AgOTf (10 mg, 0.039 mmol) in benzene (1 ml) was treated in the same manner as described above to give a syrup, which was chromatographed on a silica gel column (benzene-acetone-methanol, 30:20:1) to give the methyl 2,3,4-tri-O-benzyl-6-O-[methyl (5-acetamido-4,7,9-tri-O-acetyl-3-bromo-3,5-dideoxy-8-O-[methyl (5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-β-D-erythro-L-manno-2-nonulopyranosyl)onate]-β-D-glycero-D-galacto-2-nonulopyranosyl)-onate]-α-D-glucopyranoside (28) (33 mg, 69%) as a syrup.

Methyl 2,3,4-tri-O-benzyl-6-O-[methyl (5-acetamido-4,7,9-tri-O-acetyl-3,5-dideoxy-8-O-[methyl (5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-β-D-glycero-D-galacto-2-nonulopyranosyl)onate]-β-D-glycero-D-galacto-2-nonulopyranosyl)onate]-α-D-glucopyranoside (29). **From 27.** To a solution of **27** (9 mg, 0.0058 mmol) in tetrahydrofuran (0.5 ml) was added tributylstannane (30 µl, 0.11 mmol) under nitrogen. The mixture was stirred at 60 °C for 3 h and the solvent was removed in vacuo to a residue, which was chromatographed on a silica gel column (benzene-acetone-methanol, 15:10:1), triturated with hexane-ethyl acetate, and washed with hexane to give **29** (7.3 mg, 90%) as a powder.

From 28. A mixture of **28** (11 mg, 0.0076 mmol) and tributylstannane (25 µl, 0.093 mmol) in tetrahydrofuran (0.5 ml) was treated in the same manner as described above to give **29** (9.5 mg, 91%) as a powder.

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