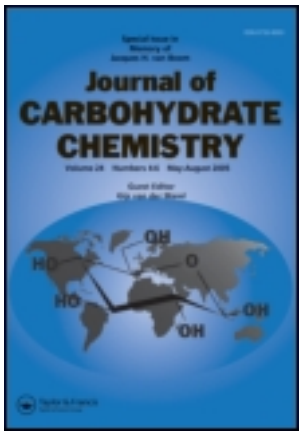

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BROMOHYDROXYLATION OF GLYCALS—AN INVESTIGATION INTO THE REACTION OF SOME 4-N-ACYLATED DERIVATIVES OF METHYL 5-ACETAMIDO-7,8,9-TRI-O-ACETYL-2,6-ANHYDRO-3,4,5-TRIDEOXY-D-GLYCERO-D-GALACTO-NON-2-ENONATE AND ITS 4-EPIMER

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BROMOHYDROXYLATION OF GLYCALS—AN INVESTIGATION INTO THE REACTION OF SOME 4-*N*-ACYLATED DERIVATIVES OF METHYL 5-ACETAMIDO-7,8,9-TRI-*O*-ACETYL-2,6-ANHYDRO-3,4,5-TRIDEOXY-D-*GLYCERO*-D-*GALACTO*-NON-2-ENONATE AND ITS 4-EPIMER

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ABSTRACT

Bromohydroxylation of some 4-*N*-acylated derivatives of the glycals of *N*-acetylneuraminic acid, methyl 5-acetamido-7,8,9-tri-*O*-acetyl-2,6-anhydro-3,4,5-trideoxy-D-*glycero*-D-*galacto*-non-2-enonate (**4**) and methyl 5-acetamido-7,8,9-tri-*O*-acetyl-2,6-anhydro-3,4,5-trideoxy-D-*glycero*-D-*talo*-non-2-enonate (the 4-epimer of **4**), with *N*-bromosuccinimide (NBS) and water in the presence of a co-solvent has provided a range of new glycosyl donors. The stereoselectivity of the halohydroxylation reaction was found to be governed by solvent composition, reaction temperature and the stereoelectronic nature of the substituent at C-4.

Key Words: *N*-acetylneuraminic acid; Sialosyl donor; Ulosonic acids; Glycal; Halohydroxylation

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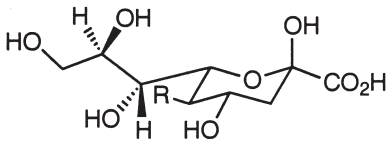
INTRODUCTION

Ulosonic acids, in particular, *N*-acetylneuraminic acid (Neu5Ac, **1**) are widespread in nature. As constituents of glycoconjugates such as glycoproteins, glycolipids and oligosaccharides, these carbohydrate structures are involved in many biological processes including molecular recognition, cell adhesion and inflammation.[1] There has been therefore considerable interest over the years both in the glycobiology and chemistry of this class of carbohydrates. As part of our continuing research interest in ulosonic acid-recognising proteins and their role in carbohydrate metabolism, we required a series of 4-*N*-acylated and 4-*epi*-*N*-acylated derivatives of Neu5Ac as sialosyl donors in *O*-glycosylation reactions.

We envisaged that the most direct entry into a range of such compounds would be via successive acylation and halohydroxylation of the well-known amine, methyl 5-acetamido-7,8,9-tri-*O*-acetyl-4-amino-2,6-anhydro-3,4,5-trideoxy-D-*glycero*-D-*galacto*-non-2-enonate (**2**)[2] or its 4-epimer **3**. Indeed, it has been previously demonstrated[3] by Okamoto and coworkers that glycals such as the methyl ester of peracetylated Neu5Ac2en **4** can be converted into the corresponding glycosyl donors such as 2,3-dibromo- and 2-halo-3-hydroxyl-*N*-acetylneuraminic acid derivatives by the electrophilic addition of bromine or halohydroxylation. In the latter case, in the absence of any neighbouring group participation and serious steric constraints, halohydroxylation reactions on **4** appear to proceed with high regiocontrol according to Markovnikov's rule.[4] Herein we report our findings when we extend this methodology to some C-4 *N*-acylated derivatives of **4**.

RESULTS AND DISCUSSION

The amines **2** and its 4-epimer **3** used in this study were prepared by reduction of the corresponding azides **5**[2] and **6**,[5] respectively under catalytic hydrogenolysis conditions as previously described. Acylation of these amines with either acetic or benzoic anhydride and DMAP in pyridine afforded the corresponding 4-*N*-acylated glycals **7–9**. The 4-*epi*-*N*-(9′-fluorenylmethoxycarbonyl) (Fmoc)-protected amine **10** and its C-4 epimer **11** were prepared by respectively treating **3** and **2** with Fmoc-ONSu under standard conditions. Coupling of the amine **2** with 4-hydroxyphenylacetic acid in the presence of dicyclohexylcarbodi-



1 R = NHAc

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Table 1. Reaction of Glycals **7–11** and **13** with NBS and Water in the Presence of a Co-solvent

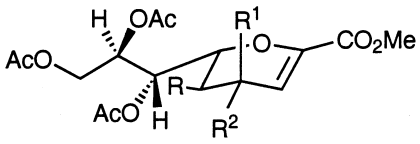
		Reaction Conditions			
Entry	Substrate	Solvent System	Temp. (°C)	Time (h)	Product (% Yield)
1	**7**	H_2O/CH_3CH (1:9)	20	2	**14a:14b** = 1:1 (85)
2	**8**	H_2O/CH_3CN (1:9)	20	2	**15a:15b** = 7:1 (72)
3	**9**	H_2O/CH_3CN (1:9)	20	2	**16a:16b** = 2:1 (34) **16d** (33)
4	**9**	H_2O/CH_3CN (1:1)	20	2	**16a:16b** = 1:2 (35) **16d** (39)
5	**9**	H_2O/CH_3CN (1:9)	80	0.5	**16d** (84)
6	**9**	H_2O/DMSO (1:1)	−20	6	**16a:16b** = 1:5 (56)
7	**7**	H_2O/CH_3CN (1:9)	60	0.5	**14b** (83)
8	**10**	H_2O/CH_3CN (1:4)	20	2	**17a:17b** = 3:1 (17) **17c** (79)
9	**10**	H_2O/CH_3CN (1:1)	60	0.5	**17a:17b** = 4:1 (37) **17c** (55)
10	**11**	H_2O/CH_3CN (1:4)	0	72	**18a:18b** = 3:1 (72)
11	**11**	H_2O/CH_3CN (1:4)	20	2	**18a:18b** = 3:1 (72)
12	**11**	H_2O/CH_3CN (1:4)	60	0.5	**18a:18b** = 3:1 (70)
13	**13**	H_2O/CH_3CN (1:9)	20	2	**19a:19b** = 1:1 (60)

imide (DCC) and 1-hydroxybenzotriazole (HOBT) hydrate gave, after conventional workup, the 4-(4′-hydroxyphenyl)acetamido compound **12** in 96% yield. Subsequent acetylation of **12** under standard conditions gave, after column chromatography, the 4-(4′-acetoxyphenyl)acetamido-4-deoxy glycal **13** in 83% yield.

This series of 4-*N*-acylated amines were then used in halohydroxylation reactions employing varying reaction conditions such as temperature and solvent composition. These results are summarised in Table 1.

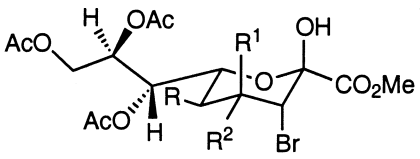
Halohydroxylation of glycal **7** with NBS and aqueous acetonirile at rt for 2 h proceeded uneventfully to provide the two bromohydrins **14a** and **14b** in a 1:1 ratio (by ^{1}H NMR spectroscopy) (Table 1, entry 1). The two adducts were chromatographically inseparable on silica gel for all of the different solvent combinations investigated and, as a consequence, the spectral data of the product composition were not easy to interpret due to overlapping signals. Notwithstanding these difficulties, bromohydroxylation, in mechanistic terms, should yield either a mixture of the bromohydrins, or if there is stereocontrol in the addition process a preferred bromohydrin. Clearly the possibilities are either the *trans*-2,3-diaxial isomer **14a** and/or the 2,3-diequatorial isomer. In this system, however, it is to be expected that the initially formed 2,3-diequatorial adduct, given time, would equilibrate or mutarotate to the thermodynamically more stable 2-axial-3-equatorial isomer **14b** due to the anomeric effect.[6]

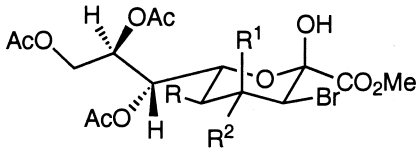
In some systems (*vide infra*), the 2,3-diequatorial adduct can be observed (by TLC analysis or ^{1}H NMR spectroscopy) in the crude reaction product mixture. As can be expected, mutarotation to the more stable β-anomer then occurs with pro-



R = NHAc

2	$R^1 = H, R^2 = NH_2$
3	$R^1 = NH_2, R^2 = H$
4	$R^1 = H, R^2 = OAc$
5	$R^1 = H, R^2 = N_3$
6	$R^1 = N_3, R^2 = H$
7	$R^1 = H, R^2 = NHAc$
8	$R^1 = NHAc, R^2 = H$
9	$R^1 = H, R^2 = NHBz$
10	$R^1 = NHFmoc, R^2 = H$
11	$R^1 = H, R^2 = NHFmoc$
12	$R^1 = H, R^2 = NHCOBnpOH$
13	$R^1 = H, R^2 = NHCOBnpOAc$





R = NHAc

14a	$R^1 = H, R^2 = NHAc$	**14b**
15a	$R^1 = NHAc, R^2 = H$	**15b**
16a	$R^1 = H, R^2 = NHBz$	**16b**
17a	$R^1 = NHFmoc, R^2 = H$	**17b**
18a	$R^1 = H, R^2 = NHFmoc$	**18b**
19a	$R^1 = H, R^2 = NHCOBnpOAc$	**19b**

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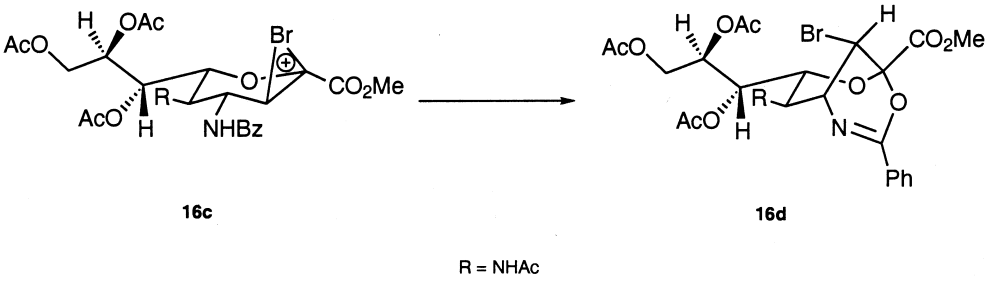
longed handling of the reaction product such as column purification, a process that complicates the physical analysis and spectral interpretation even further. It may be speculated therefore that where both diaxial and diequatorial adducts are formed in a reaction, the adducts obtained after chromatographic purification are the thermodynamically more stable β-anomers. In the case of products from the D-*glycero*-D-*galacto* system (e.g. **7**), the smaller coupling constant for $^3J_{3,4}$ (ca. 3 Hz) is more characteristic of the diaxial adduct (e.g. **14a**) while a larger $^3J_{3,4}$ coupling constant (ca. 10 Hz) is more characteristic of the adduct with an equatorial Br at C-3. For products derived from the D-*glycero*-D-*talo* system (e.g. **8**), the two adducts (eg **15a** and **b**) are not discernible on the basis of the $^3J_{3,4}$ coupling constant with both being about 3 Hz in magnitude. For either system however, the long range coupling $^4J_{3,OH\text{-}C(2)}$ (ca. 1 Hz) can sometimes be observed in the ^{1}H NMR spectrum. In conformational terms this can only be fulfilled by an axially-oriented OH at C-2 and an equatorial Br at C-3.

While an approximate 1:1 stereochemical outcome of the halohydroxylation reaction can be expected for glycals with no serious steric influences at C-4 such as **7** (Table 1, entry 1), stereoselectivity in favour of the diaxial adduct (**15a**) was obtained for its epimer **8**[7] (Table 1, entry 2). In the latter situation, an inherent conformational bias due to the substituent at C-4 residing in an axial orientation, forces mainly *anti* addition to the double bond.

While halohydroxylation of the glycals **7** and **8** with NBS in aqueous CH_3CN at rt appears straightforward, this is not the case for the other 4-*N*-acylated glycals such as **9–11**. Thus, treatment of the 4-benzamido-4-deoxy glycal **9** with NBS in 10% aqueous CH_3CN at rt for 2 h gave the desired bromohydrins **16a** and **16b** as a mixture [R_f (EtOAc) = 0.55] in only 34% yield (Table 1, entry 3). A slower migrating component [by TLC analysis; R_f (EtOAc) = 0.38] was also isolated after column chromatography and was determined (by both ^{1}H NMR and mass spectroscopy) to be the oxazine **16d** (33%), formed by competitive intramolecular nucleophilic attack on the intermediate bromonium ion intermediate **16c** (Scheme 1). The absence of the second N*H* resonance in the ^{1}H NMR spectrum and a $(M + H)^+$ peak *m/z* at 615/613 in the mass spectrum are in accord with the assigned structure of **16d**. Furthermore, aqueous acid hydrolysis (HOAc:H_2O:EtOAc = 1:2:2, 50°C, 40 h) of **16d** at 50°C afforded only the bromohydrin **16b** (41% isolated yield after chromatography on silica). A coupling constant of 10.5 Hz for $^3J_{3,4}$ in the ^{1}H NMR spectrum of this compound (**16b**) is consistent for H-3 being axial. From this result, an analysis of the spectral information for the earlier mixture of bromohydrins revealed that the diaxial bromohydrin **16a** was the major product formed from the intermolecular reaction (**16a**:**16b** = 2:1).

As shown by previous studies,[4] and as our subsequent experiments demonstrate, besides the polar and steric requirements of the substituent, the nature of the solvent composition and the reaction temperature can also influence the course of the reaction. Hence, in the halohydroxylation reaction of **9** with NBS and aqueous CH_3CN, when the proportion of H_2O was increased from 10% to 50%, the major bromohydrin formed was **16b** rather than **16a** (**16a**:**16b** = 1:2; combined yield of 35%) (Table 1, entry 4). The oxazine **16d** was also formed in the reaction (39%).



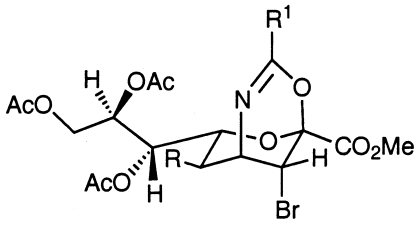
Scheme 1.

With an increase in temperature (Table 1, entry 5), halohydroxylation of **9** with NBS in 10% aqueous CH_3CN at 80°C for 30 min, gave the oxazine **16d** exclusively (84% isolated yield after chromatography on silica). On the other hand, the reaction when conducted at −20°C in a 1:1 mixture of DMSO/H_2O (Table 1, entry 6) gave no detectable amount of oxazine **16d**; rather a 1:5 mixture of **16a** and **16b** being formed in 56% yield. It is worth noting that the ^1H NMR spectrum taken of the *crude* product of this reaction showed no resonances that correspond to the bromohydrin **16b** suggesting that mutarotation of the initially formed 2,3-diequatorial adduct may have occurred during the purification process.

These results suggested that it would be of value to investigate halohydroxylation of the 4-acetamido-4-deoxy glycal **7** with NBS in aqueous CH_3CN at a higher temperature. As Table 1, entry 7 shows, only the 2-axial-3-equatorial adduct **14b** was obtained when the temperature was increased to 60°C, implying that at a higher temperature, the thermodynamically more stable reaction intermediate was the 2,3-diequatorial bromonium ion adduct.

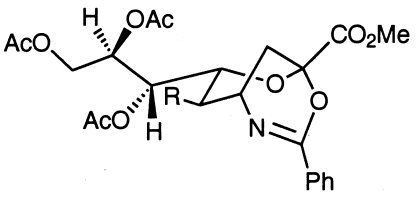
Next, we investigated halohydroxylation of the 4-*epi*-Fmoc-amino-4-deoxy glycal **10** with NBS/aqueous CH_3CN. When **10** was treated with NBS in 20% aqueous CH_3CN at rt for 2 h (Table 1, entry 8), the desired bromohydrins **17a** and **17b** were formed as an inseparable mixture in very low yield (17%). A faster migrating component (by TLC analysis), isolated after chromatography on silica, was found to be the oxazine **17c** (79%). Aqueous acid hydrolysis of the oxazine **17c** gave the diaxial bromohydrin **17a** in approximately 50% yield, contaminated with approximately 20% of the glycal starting material **10** (by ^1H NMR spectroscopy). In the light of this result, the major bromohydrin formed in the intermolecular version of the reaction was the diaxial adduct **17a**. The yield of the desired bromohydrins **17a** and **17b** improved to 37% (**17a**:**17b** = 4:1) when the reaction was conducted at 60°C for 30 min, with a concomitant increase in the amount of water in the reaction (Table 1, entry 9). The oxazine **17c** was formed as the major product of this reaction (55%).

In contrast to its 4-epimer, the reaction of the glycal **11** with NBS in aqueous CH_3CN over a range of temperatures (0°C, rt and 60°C) (Table 1 entries 10–12) did not result in any formation of the corresponding oxazine analogue. Only the desired bromohydrins **18a** and **18b** were produced. In this situation, with the more



17c, R^1 = Fluorenylmethoxy

R = NHAc



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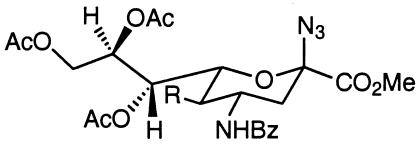

21

sterically-demanding Fmoc group at C-4, the course of the reaction was biased in favour of the diaxial adduct **18a** in all three cases.

When the 4-(4′-acetoxyphenyl)acetamido)-4-deoxy glycal **13** was treated with NBS in aqueous CH_3CN at rt for 2 h (Table 1, entry 13), a 1:1 mixture of the bromohydrins **19a** and **19b** was obtained, with no oxazine being formed. Thus, compared to the 4-benzamido-4-deoxy glycal **9**, the intramolecular version of the addition reaction is, in this case, not observed for a weaker nucleophile.

Finally, in a reaction reminiscent of that involving the introduction[8] of nucleophiles such as azide and sulfur at the C-4 position of Neu5Ac2en via the oxazoline analogue, 7,8,9-tri-*O*-acetyl-2,6-anhydro-3,4,5-trideoxy-2′-methyl(methyl D-*glycero*-D-*talo*-non-2-enonate)[5,4-*d*]oxazole, the 1,3-oxazine analogue **16d** was also found to be amenable to attack by nucleophiles at the activated C-2 position. Thus, treatment of the oxazine **16d** with *n*-Bu_3SnH/AIBN furnished the corresponding debrominated oxazine **20**. Subsequent treatment of **20** with $TMSN_3$ gave, after column chromatography, the 2-β-azide **21** in 52% yield. The glycal **9** was also obtained as a by-product (16%).

In conclusion, several novel 4-*N*-acylated sialosyl donors have been prepared via halohydroxylation of the corresponding glycal with NBS and aqueous CH_3CN. Depending upon the nature of the substituent at C-4 a competing intramolecular version of the process leading to oxazine analogues was also observed with the

amount formed being temperature and solvent-composition dependent. These oxazine analogues can, however, be readily hydrolysed into the desired bromohydrins. Further study employing these bromohydrins in glycosylation reactions is presently underway.

EXPERIMENTAL

General Methods. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra (in δppm) were obtained using a Bruker AMX-300 spectrometer. All NMR spectra were recorded in $CDCl_3$ (unless otherwise stated) and referenced using solvent residues. J-Values are given in hertz (Hz). Low resolution (LR) electrospray ionization (ESI) mass spectra were recorded on a Micromass Platform II mass spectrometer and high resolution (HR) mass spectra were recorded on a Bruker BIOAPEX II Fourier Transform Ion Cyclotron Resonance mass spectrometer with "Analytica" ESI source. Reactions were monitored by TLC on Kieselgel 60 F_{254} plate (Merck 5554) and detection of the spots was carried out by spraying with a 95% aqueous solution containing 5% H_2SO_4 and charring of the plates at 180°C. Hexane refers to the fraction of petroleum ether that boils in the range 60–80°C. All solvents and reagents were distilled and NBS (purchased from Aldrich) was recrystallised from H_2O, before use.

Preparation of the 4-*N*-acylated-4-deoxy glycals 7–13. The amine **2** was prepared from the azide **5** according to literature methods.[2] Acylation of the amine **2** under standard conditions (Ac_2O, py, DMAP, rt, 24 h) provided compound **7** in 54% yield. The ^{1}H NMR spectral data for **7** were consistent with the literature.[7] Acylation of the amine **2** with benzoic anhydride in pyridine gave, after chromatography on silica gel (EtOAc/hexane, 1.3–1:1), the 4-benzamido-4-deoxy compound **9** in 89% yield. The azide **6** was prepared from Neu5Ac **1** following published procedures,[5] and following catalytic hydrogenolysis (10% Pd/C, atmospheric H_2, rt, 50 min) in MeOH, the amine **3** was obtained in 92% yield. Acetylation of **3** under standard conditions (Ac_2O, py) provided the 4-acetamido-4-deoxy glycal **8** in 35% yield. The Fmoc-protected amines **10** and **11** were prepared by treating the amines **3** and **2** respectively with Fmoc-ONSu at 0°C until TLC analysis indicated complete consumption of starting material. In each case, the product was isolated after chromatography on silica gel (EtOAc/hexane, 2:1), **10** (72%), **11** (97%). For the preparation of **13**, the amine **2** was added to a mixture containing a molar equivalent each of DCC, HOBT-hydrate and 4-hydroxyphenylacetic acid. Conventional workup followed by chromatography on silica (EtOAc) furnished the corresponding 4-(4′-hydroxyphenyl)acetamido-4-deoxy glycal **12** in 96% yield. This compound was then treated with Ac_2O/DMAP/py under standard conditions affording, after chromatography on silica (EtOAc), the desired glycal **13** in 83% isolated yield.

Methyl 4,5-diacetamido-7,8,9-tri-O-acetyl-2,6-anhydro-3,4,5-trideoxy-D-*glycero*-D-*talo*-non-2-enonate (8). R_f 0.29 (EtOAc/MeOH, 9:1); ^{1}H NMR δ

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6.03 (1 H, d, $J_{3,4}$ 4.8, H-3), 5.63 (2 H, m, NH_a and NH_b), 5.46 (1 H, dd, $J_{7,6}$ 3.9, $J_{7,8}$ 3.9, H-7), 5.29 (1 H, m, H-8), 4.77 (1 H, ddd, $J_{4,5}$ 4.8, $J_{4,NH}$ 7.8, H-4), 4.68 (1 H, dd, $J_{9,8}$ 3.0, $J_{9,9'}$ 12.6, H-9), 4.42 (1 H, ddd, $J_{5,6}$ 9.0, $J_{5,NH}$ 9.0, H-5), 4.20 (1 H, dd, $J_{9',8}$ 5.4, H-9′), 4.18 (1 H, dd, H-6), 3.80 (3 H, s, $COOCH_3$), 2.12, 2.09, 2.06, 2.04, 1.95 (each 3 H, s, $OCOCH_3 \times 3$, $NHCOCH_3 \times 2$); ^{13}C NMR δ 171.1, 170.8, 170.7, 169.9, 162.0 (carbonyls), 144.4 (C-2), 108.8 (C-3), 74.1, 71.5, 68.4 (C-6, C-7, C-8), 62.1 (C-9), 52.4, 45.8, 42.8 (C-4, C-5, $COOCH_3$), 22.9 ($NHCOCH_3 \times 2$), 20.7, 20.6, 20.5 ($OCOCH_{3\times 3}$); LRMS (cone voltage 30V): 472 (MH^+, 100%); HRMS: Calcd for $C_{20}H_{29}N_2O_{11}$:[$M^+ + 1$], 473.1760. Found: *m/z*, 473.1756.

Methyl 5-Acetamido-7,8,9-tri-*O*-acetyl-2,6-anhydro-4-benzamido-3,4,5-trideoxy-D-*glycero*-D-*galacto*-non-2-enonate (9). R_f 0.60 (EtOAc); $[\alpha]_D$ +98° (*c* 1.00, $CHCl_3$); ^{1}H NMR δ 7.74–7.40 (5 H, m, aromatic protons), 6.54 (1 H, d, $J_{NHa,5}$ 8.4, NH_a), 6.05 (1 H, d, $J_{3,4}$ 2.4, H-3), 5.93 (1 H, d, $J_{NHb,4}$ 9.9, NH_b), 5.55 (1 H, dd, $J_{7,6}$1.0, $J_{7,8}$ 5.1, H-7), 5.35 (1 H, ddd, $J_{8,9}$ 2.7, $J_{8,9'}$ 7.2, H-8), 4.99 (1 H, m, H-4), 4.71 (1 H, dd, $J_{9,9'}$ 12.3, H-9), 4.41–4.36 (2 H, m, H-5, H-6), 4.20 (1 H, dd, H-9′), 3.79 (3 H, s, $COOCH_3$), 2.11, 2.09, 2.07, 1.85 (each 3 H, s, $NHCOCH_3$, $OCOCH_3 \times 3$); ^{13}C NMR δ 171.6, 170.6, 170.3, 169.8, 168.4, 161.7 (carbonyls), 144.4 (C-3), 133.3, 131.9, 128.7, 126.9 (aromatic carbons), 110.7 (C-2), 77.1, 71.5, 68.1 (C-6, C-7, C-8), 62.3 (C-9), 52.3, 49.7, 46.5 (C-4, C-5, $COOCH_3$), 22.6 ($NHCOCH_3$), 20.8, 20.7, 20.5 ($OCOCH_{3\times 3}$); LRMS (cone voltage 30V): 535 (MH^+, 100%), 338 (8), 60 (5); HRMS: Calcd for $C_{25}H_{31}N_2O_{11}$:[$M^+ + 1$], 535.1928. Found: *m/z*, 535.1902.

Methyl 5-Acetamido-7,8,9-tri-*O*-acetyl-2,6-anhydro-4-*N*-(9′-fluorenylmethoxycarbonyl)amino-3,4,5-trideoxy-D-*glycero*-D-*talo*-non-2-enonate (10). R_f 0.50 (EtOAc/hexane, 3:1); $[\alpha]_D$ −92° (*c* 1.40, $CHCl_3$); ^{1}H NMR δ 7.80–7.26 (8 H, m, aromatic protons, 6.00 (1 H, d, $J_{3,4}$ 5.1, H-3), 5.55 (1 H, br s, NH_a), 5.45 (1 H, dd, $J_{7,6}$3.3, $J_{7,8}$ 4.2, H-7), 5.26 (1 H, ddd, $J_{8,9}$ 3.0, $J_{8,9'}$ 7.5, H-8), 4.75 (1 H, d, $J_{NHb,4}$ 7.8, NH_b), 4.69 (1 H, dd, $J_{9,9'}$ 12.6, H-9), 4.50–4.40 (4 H, m, H-4, H-5, -C*H*-CH_2O-), 4.18 (1 H, dd, H-9′), 4.03 (1 H, dd, $J_{6,5}$ 9.6, H-6), 3.80 (3 H, s, $COOCH_3$), 2.10, 2.09, 2.06, 1.89 (each 3 H, s, $NHCOCH_3$, $OCOCH_3 \times 3$); ^{13}C NMR δ 170.6, 170.0, 161.9, 156.1 (carbonyls), 144.5, 143.6, 143.4, 141.2, 127.8, 127.1, 127.0, 124.8, 120.0 (C-2 and aromatic carbons), 108.3 (C-3), 73.7, 71.4, 68.4 (C-6, C-7, C-8), 66.9, 62.1 (C-9, -*C*H_2OC(O)-), 52.4, 47.0, 45.7, 44.8 (C-4, C-5, $COOCH_3$, -*C*H-CH_2O-), 23.0 ($NHCOCH_3$), 20.8, 20.7, 20.5 ($OCOCH_{3\times 3}$); LRMS (cone voltage 30V): 653 (MH^+, 50%), 431 (10), 414 (100); HRMS: Calcd for $C_{33}H_{37}N_2O_{12}$:[$M^+ + 1$], 653.2347. Found: *m/z*, 653.2344.

Methyl 5-Acetamido-7,8,9-tri-*O*-acetyl-2,6-anhydro-4-*N*-(9′-fluorenylmethoxycarbonyl)amino-3,4,5-trideoxy-D-*glycero*-D-*galacto*-non-2-enonate (11). R_f 0.50 (EtOAc/hexane, 3:1); $[\alpha]_D$ +46° (*c* 1.00, $CHCl_3$); ^{1}H NMR δ 7.76–7.27 (8 H, m, aromatic protons), 6.00 (1 H, d, $J_{NHb,4}$ 9.3, NH_a), 5.94 (1 H, br s, H-3), 5.52 (1 H, m, H-7), 5.31 (2 H, m, H-8, NH_b), 4.72 (1 H, dd, $J_{9,8}$ 2.4, $J_{9,9'}$12.3, H-9), 4.53 (1 H, m, H-4), 4.15–4.40 (6 H, m, H-5, H-6, H-9′, -C*H*CH_2O-), 3.78 (3

H, s, $COOCH_3$), 2.12, 2.06, 2.05, 2.02 (each 3 H, s, $NHCOCH_3$, $OCOCH_3 \times 3$); LRMS (cone voltage 30V): 653 (MH^+, 100%), 414 (10), 338 (20), 60 (8); HRMS: Calcd for $C_{33}H_{37}N_2O_{12}$:[$M^+ + 1$], 653.2347. Found: *m/z*, 653.2308.

Methyl 5-Acetamido-7,8,9-tri-*O*-acetyl-2,6-anhydro-4-(4′-hydroxyphenyl)acetamido-3,4,5-trideoxy-D-*glycero*-D-*galacto*-non-2-enonate (12). R_f 0.22 (EtOAc/hexane, 3:1); $[\alpha]_D$ −14° (*c* 0.98, $CHCl_3$); ^1H NMR δ 7.04–6.73 (4 H, m, aromatic protons), 6.11 (1 H, d, $J_{NHa,5}$ 9.9, NH_a), 5.90 (1 H, d, $J_{NHb,4}$ 9.0, NH_b), 5.82 (1 H, d, $J_{3,4}$ 2.4, H-3), 5.47 (1 H, dd, $J_{7,6}$1.9, $J_{7,8}$ 4.8, H-7), 4.69 (1 H, ddd, $J_{8,9}$ 2.8, $J_{8,9'}$ 7.5, H-8), 4.85 (1 H, ddd, $J_{4,5}$ 9.6, H-4) 4.69 (1 H, dd, $J_{9,9'}$12.5, H-9), 4.27 (1 H, dd, $J_{6,5}$ 9.6, H-6), 4.18 (1 H, ddd, H-5), 4.16 (1 H, dd, H-9′), 3.79 (3 H, s, $COOCH_3$), 3.44 (1 H, d, $J_{10,10'}$15.3, CH_{10}-Ph), 3.37 (1 H, d, C$H_{10'}$-Ph), 2.08, 2.07, 2.06, 1.63 (each 3 H, m, $NHCOCH_3$, $OCOCH_3 \times 3$); ^{13}C NMR δ 173.3, 172.0, 170.7, 170.3, 170.0, 161.8 (carbonyls), 155.8, 144.6, 130.3, 125.6, 115.9 (C-2, aromatic carbons), 110.6 (C-3), 77.2, 71.4, 68.0 (C-6, C-7, C-8), 62.2 (C-9), 52.4, 48.3, 46.5 (C-4, C-5, $COOCH_3$), 33.8 (-CH_2-C_6H_4-), 22.4 ($NHCOCH_3$), 20.8, 20.7, 20.5 ($OCOCH_3 \times 3$); LRMS (cone voltage 30V): 565 (MH^+, 100%), 225 (20).

Methyl 5-Acetamido-4-(4′-acetoxyphenyl)acetamido-7,8,9-tri-*O*-acetyl-2,6-anhydro-3,4,5-trideoxy-D-*glycero*-D-*galacto*-non-2-enonate (13). R_f 0.31 (EtOAc); ^1H NMR δ 7.27–7.04 (4 H, m, aromatic protons), 5.98 (1 H, d, $J_{NHa,5}$ 8.1, NH_a), 5.96 (1 H, d, $J_{NHb,4}$ 9.3, NH_b), 5.84 (1 H, d, $J_{3,4}$ 2.4, H-3), 5.48 (1 H, dd, $J_{7,6}$ 2.1, $J_{7,8}$ 4.8, H-7), 5.30 (1 H, ddd, $J_{8,9}$ 2.7, $J_{8,9'}$ 7.2, H-8), 4.83 (1 H, ddd, $J_{4,5}$ 9.6, H-4), 4.70 (1 H, dd, $J_{9,9'}$ 12.3, H-9), 4.29 (1 H, dd, $J_{6,5}$ 10.2, H-6), 4.15 (1 H, ddd, H-5), 4.16 (1 H, dd, H-9′), 3.78 (3 H, s, $COOCH_3$), 3.52 (1 H, d, $J_{10,10'}$ 15.0, CH_{10}-Ph) 3.46 (1 H, d, C$H_{10'}$-Ph), 2.29, 2.09, 2.07, 2.06, 1.69 (each 3 H, s, $NHCOCH_3$, $OCOCH_3 \times 4$); ^{13}C NMR δ 172.0, 171.3, 170.6, 170.3, 169.8, 169.4, 161.7 (carbonyls), 144.6 (C-2), 149.8, 132.0, 130.3 (aromatic carbons), 110.4 (C-3), 77.4, 71.5, 67.9 (C-6, C-7, C-8), 62.2 (C-9), 52.3, 48.6, 46.4 (C-4, C-5, $COOCH_3$), 42.6 (-CH_2-C_6H_4-), 22.6 ($NHCOCH_3$), 21.0, 20.8, 20.7, 20.5 ($OCOCH_3 \times 4$); LRMS (cone voltage 30V): 642 (MNa^+, 55%), 607 (MH^+, 100), 327 (10), 60 (12); HRMS: Calcd for $C_{28}H_{38}N_3O_{13}$:[$M + NH_4^+$], 624.2404. Found: *m/z*, 624.2404.

Representative Procedure for the Reaction of the 4-*N*-Acylated-4-deoxy Glycals 7–11 and 13 with NBS and H_2O in a Co-solvent. To a stirring solution of the glycal (0.2 mmol) in H_2O and a co-solvent (see Table 1) was added NBS (1.1 molar equivalents). After stirring at the temperature and time as specified in Table 1, the reaction mixture was concentrated to dryness under diminished pressure. The resulting residue was purified by flash chromatography on silica gel affording the adducts as specified in Table 1.

Methyl 4,5-Diacetamido-7,8,9-tri-*O*-acetyl-3-bromo-3,4,5-trideoxy-D-*erythro*-β-L-*manno*-2-nonulopyranosonate (14a) and Methyl 4,5-diacetamido-7,8,9-tri-*O*-acetyl-3-bromo-3,4,5-trideoxy-D-*erythro*-β-L-*gluco*-2-nonulopyranosonate (14b).

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14a: R_f 0.72 (EtOAc/MeOH, 4:1); ^{1}H NMR δ 7.03 (1 H, d, $J_{NHa,5}$ 9.3, NH_a), 6.32 (1 H, d, $J_{NHb,4}$ 8.4, NH_b), 5.44 (1 H, m, H-7), 5.33 (1 H, ddd, $J_{8,7}$ 6.6, $J_{8,9}$ 2.1, $J_{8,9'}$ 6.6, H-8), 4.85 (1 H, dd, $J_{9,9'}$ 12.3, H-9), 4.63 (1 H, m, H-4), 4.60 (1 H, d, $J_{3,4}$ 3.0, H-3), 4.40 (1 H, m, ddd, $J_{5,4}$ 9.0, $J_{5,6}$ 9.0, H-5), 4.36 (1 H, m, H-6), 4.19 (1 H, dd, H-9′), 3.81 (3 H, s, $COOCH_3$), 2.14, 2.11, 2.06, 2.05, 1.93 (each 3 H, s, $NHCOCH_3 \times 2$, $OCOCH_3 \times 3$).

14b: R_f 0.72 (EtOAc/MeOH, 4:1); ^{1}H NMR δ 8.79 (1 H, br, OH), 6.77 (1 H, d, $J_{NHa,5}$ 9.9, NH_a), 6.38 (1 H, d, $J_{NHb,4}$ 9.9, NH_b), 5.34 (1 H, dd, $J_{7,6}$ 2.4, $J_{7,8}$ 6.6, H-7), 5.21 (1 H, ddd, $J_{8,9}$ 2.4, $J_{8,9'}$ 6.6, H-8), 4.57 (1 H, ddd, $J_{4,5}$ 10.8, H-4), 4.37 (1 H, dd, $J_{6,5}$ 10.5, H-6), 4.32 (1 H, dd, $J_{9,9'}$ 12.6, H-9), 4.23 (1 H, d, $J_{3,4}$ 11.4, H-3), 4.11 (1 H, ddd, H-5), 4.01 (1 H, dd, H-9′), 3.92 (3 H, s, $COOCH_3$), 2.12, 2.10, 2.02, 1.97, 1.91 (each 3 H, s, $NHCOCH_3 \times 2$, $OCOCH_3 \times 3$); ^{13}C NMR δ 178.5, 171.7, 171.4, 170.7, 170.3, 169.8, 167.8 (carbonyls), 95.4 (C-2), 70.6, 69.8, 67.7 (C-6, C-7, C-8), 62.4 (C-9), 53.9, 52.9, 50.5, 50.3 (C-3, C-4, C-5, $COOCH_3$), 22.9, 22.8 ($NHCOCH_3 \times 2$), 20.8, 20.6, 20.5 ($OCOCH_3 \times 3$); LRMS (cone voltage 30V): 571, 569 (MH^+, 5%), 490 (15), 419 (25), 374 (60), 83 (100); HRMS: Calcd for $C_{20}H_{33}N_3O_{12}{}^{79}Br$:[M + NH_4^+], 586.1247. Found: *m/z*, 586.1247.

Methyl 4,5-Diacetamido-7,8,9-tri-*O*-acetyl-3-bromo-3,4,5-trideoxy-D-*erythro*-β-L-*altro*-2-nonulopyranosonate (15a) and Methyl 4,5-Diacetamido-7,8,9-tri-*O*-acetyl-3-bromo-3,4,5-trideoxy-D-*erythro*-β-L-*allo*-2-nonulopyranosonate (15b).

15a: R_f 0.36 (CH_2Cl_2/MeOH, 9:1); ^{1}H NMR δ 7.45 (1 H, br, NH_a), 6.80 (1 H, br, NH_b), 5.37 (1 H, m, H-7), 5.29 (1 H, m, H-8), 5.02 (1 H, m, H-4), 4.75–4.55 (4 H, m, H-5, H-6, H-9, OH), 4.39 (1 H, m, H-3), 4.07 (1 H, dd, $J_{9',8}$ 8.1, $J_{9',9}$ 13.2, H-9′), 3.78 (3 H, s, $COOCH_3$), 2.16, 2.09, 2.04, 2.03, 1.97 (each 3 H, s, $OCOCH_3 \times 3$, $NHCOCH_3 \times 2$); ^{13}C NMR ($CDCl_3$/CD_3OD, 20:1): δ 171.2, 171.0, 170.7, 170.2, 168.9, 167.4 (carbonyls), 95.8 (C-2), 72.6, 69.0, 68.2 (C-6, C-7, C-8), 62.9 (C-9), 52.7, 51.2, 47.1, 41.0 (C-3, C-4, C-5, $COOCH_3$), 23.1, 22.6 ($NHCOCH_3 \times 2$), 20.8, 20.7, 20.6 ($OCOCH_3 \times 3$); LRMS (cone voltage 30V): 593, 591 (MNa^+, 30%), 571, 569 (MH^+, 100), 490 (10); HRMS: Calcd for $C_{20}H_{30}N_2O_{12}{}^{79}Br$:[$M^+$ + 1], 568. 8982. Found: *m/z*, 569.0997.

15b: R_f 0.42 (CH_2Cl_2/MeOH, 9:1); ^{1}H NMR δ 6.13 (1 H, d, $J_{NHa,5}$ 9.9, NH_a), 5.94 (1 H, br s, NH_b), 5.36 (1 H, dd, $J_{7,6}$ 4.8, $J_{7,8}$ 6.3, H-7), 5.18 (1 H, m, H-8), 4.88 (1 H, m, H-4), 4.50 (1 H, m, H-5), 4.42 (1 H, dd, $J_{9,8}$ 3.6, $J_{9,9'}$ 12.3, H-9), 4.19 (1 H, dd, $J_{9',8}$ 6.3, H-9′), 4.06 (1 H, dd, $J_{6,5}$ 6.3, H-6), 3.96 (1 H, d, $J_{3,4}$ 2.7, H-3), 3.93 (1 H, br s, OH), 3.81 (3 H, s, $COOCH_3$), 2.12, 2.08, 2.05, 2.03, 1.99 (each 3 H, s, $OCOCH_3 \times 3$, $NHCOCH_3 \times 2$); ^{13}C NMR ($CDCl_3$/CD_3OD, 20:1): δ 170.9, 170.6, 170.8 (carbonyls), 96.0 (C-2), 73.2, 71.0, 68.6 (C-6, C-7, C-8), 61.7 (C-9), 57.8, 53.2, 44.8, 42.9 (C-3, C-4, C-5, $COOCH_3$), 22.7, 22.6 ($NHCOCH_3 \times 2$), 20.6, 20.5, 20.4 ($OCOCH_3 \times 3$); LRMS (cone voltage 30V): 490 (MH^+ - Br, 100%).

Methyl 5-Acetamido-7,8,9-tri-*O*-acetyl-4-benzamido-3-bromo-3,4,5-trideoxy-D-*erythro*-β-L-*manno*-2-nonulopyranosonate (16a), Methyl 5-acetamido-7,8,9-tri-*O*-acetyl-4-benzamido-3-bromo-3,4,5-trideoxy-D-*erythro*-β-L-*gluco*-2-nonulopyranosonate (16b) and 2-Phenyl(Methyl 5-acetamido-7,8,9-tri-*O*-acetyl-3-bromo-3,4,5-trideoxy-D-*erythro*-β-L-*gluco*-2-nonulopyranosonate)4*H*-1,3-oxazine (16d).

16a: R_f 0.55 (EtOAc); selected ^{1}H NMR δ 5.52 (1 H, dd, $J_{7,6}$ 1.5 $J_{7,8}$ 4.2, H-7), 5.38 (1 H, ddd, $J_{8,9}$ 2.4, $J_{8,9'}$ 6.9, H-8), 4.87 (1 H, dd, $J_{9,9'}$ 12.3, H-9), 4.79 (1 H, d, $J_{3,4}$ 3.3, H-3), 4.22 (1 H, dd, H-9′), 3.81 (3 H, s, $COOCH_3$); selected ^{13}C NMR δ 172.4, 172.1, 170.3, 169.2, 168.0, 167.9, 167.7 (carbonyls), 73.0, 71.8, 68.6 (C-6, C-7, C-8), 62.9 (C-9), 54.6, 52.9, 50.8, 44.8 (C-3, C-4, C-5, $COOCH_3$).

16b: R_f 0.55 (EtOAc); ^{1}H NMR δ 7.66–7.31 (5 H, m, aromatic protons), 6.64 (1 H, d, $J_{NHa,5}$ 10.2, NH_a), 6.44 (1 H, d, $J_{NHb,4}$ 9.9, NH_b), 5.34 (1 H, dd, $J_{7,6}$ 2.4, $J_{7,8}$ 7.5, H-7), 5.19 (1 H, ddd, $J_{8,9}$ 2.4, $J_{8,9'}$ 6.3, H-8), 4.92 (1 H, d, $J_{OH,3}$ 0.9, OH), 4.85 (1 H, ddd, $J_{4,3}$ 10.5, $J_{4,5}$ 10.5, H-4), 4.44 (1 H, dd, $J_{6,5}$ 10.5, H-6), 4.33 (1 H, dd, H-3), 4.24 (1 H, ddd, H-5), 4.26 (1 H, dd, $J_{9,9'}$ 12.6, H-9), 3.96 (1 H, dd, H-9′), 3.87 (1 H, s, $COOCH_3$), 2.04, 2.03, 2.02 (each 3 H, s, $OCOCH_3 \times 3$), 1.70 (3 H, s, $NHCOCH_3$); ^{13}C NMR ($CDCl_3$): δ 171.6, 170.6, 170.0, 169.8, 168.5, 167.7 (carbonyls), 133.7, 131.9, 128.7, 127.0 (aromatic carbons), 95.4 (C-2), 70.8, 69.6, 67.7 (C-6, C-7, C-8), 62.4 (C-9), 54.0, 53.7, 50.7, 50.6 (C-3, C-4, C-5, $COOCH_3$), 22.7 ($NHCOCH_3$), 20.8, 20.6 ($OCOCH_3 \times 3$); LRMS for (cone voltage 30V): 655, 653 (MNa^+, 12%), 633, 631 (MH^+, 30), 551 (100); HRMS: Calcd for $C_{25}H_{32}N_2O_{12}{}^{79}Br$:[$M^+ + 1$], 631.1139. Found: *m/z*, 631.1140.

16d: R_f 0.38 (EtOAc); ^{1}H NMR δ 7.92–7.35 (5 H, m, aromatic protons), 5.84 (1 H, br, NH), 5.32 (1 H, ddd, $J_{8,7}$ 6.9, $J_{8,9}$ 2.4, $J_{8,9'}$ 5.7, H-8), 5.25 (1 H, dd, $J_{7,6}$ 1.5, H-7), 4.68 (1 H, d, $J_{3,4}$ 3.9, H-3), 4.49 (1 H, dd, $J_{9,9'}$ 12.3, H-9), 4.47–4.44 (2 H, m, H-5, H-6), 4.12–4.07 (2 H, m, H-4, H-9′), 3.93 (3 H, s, $COOCH_3$), 2.11, 2.07, 2.04 (each 3 H, s, $OCOCH_3$), 1.79 ($NHCOCH_3$); ^{13}C NMR δ 170.6, 169.7, 169.4, 169.1, 164.6 (carbonyls), 152.3 (C=N), 131.5, 130.9, 128.1, 127.6 (aromatic carbons), 94.7 (C-2), 70.1, 69.6, 68.5 (C-6, C-7, C-8), 62.0 (C-9), 55.4, 53.4, 47.9, 42.0 (C-3, C-4, C-5, $COOCH_3$), 23.3 ($NHCOCH_3$), 20.8, 20.7, 20.0 ($OCOCH_3 \times 3$); LRMS (cone voltage 30V): 615, 613 (MH^+, 100%), 537 (20); HRMS: Calcd for $C_{25}H_{30}N_2O_{11}{}^{79}Br$:[$M^+ + 1$], 613.1033. Found: *m/z*, 613.1005.

Methyl 5-Acetamido-7,8,9-tri-*O*-acetyl-3-bromo-3,4,5-trideoxy-4-*N*-(9′-Fluorenylmethoxycarbonyl)amino-D-*erythro*-β-L-*altro*-2-nonulopyranosonate (17a), Methyl 5-Acetamido-7,8,9-tri-*O*-acetyl-3-bromo-3,4,5-trideoxy-4-*N*-(9′-Fluorenylmethoxycarbonyl)amino-D-*erythro*-β-L-*allo*-2-nonulopyranosonate (17b) and 2-Fluorenylmethoxy(Methyl 5-Acetamido-7,8,9-tri-*O*-acetyl-3-bromo-3,4,5-trideoxy-D-*erythro*-β-L-*altro*-2-nonulopyranosonate)4*H*-1,3-oxazine (17c).

17a: R_f 0.46 (CH_2Cl_2/MeOH, 19:1); ^{1}H NMR δ 7.85–7.30 (8 H, m, aromatic protons), 5.50 (1 H, br, NH_a), 5.32–5.25 (2 H, m, H-7, H-8), 5.20 (1 H, d, $J_{NHb,5}$ 10.2, NH_b), 4.95 (1 H, ddd, $J_{5,4}$ 3.0, $J_{5,6}$ 10.5, H-5), 4.64 (1 H, dd, $J_{9,8}$ 2.1, $J_{9,9'}$ 12.3, H-9), 4.56–4.24 (4 H, m, OH and -C*H*CH_2O-), 4.20 (1 H, m, H-9′), 3.89 (3 H, s, $COOCH_3$), 3.87 (1 H, dd, $J_{6,7}$ 1.5, H-6), 3.75 (1 H, m, H-4), 2.16, 2.08, 2.06 (each 3 H, s, $OCOCH_3$ × 3), 1.86 (3 H, s, NHCOC*H*$_3$); ^{13}C NMR δ 172.0, 171.8, 171.4, 170.2, 167.6, 156.3 (carbonyls), 143.4, 141.2, 127.8, 127.0, 124.9, 124.8, 120.0 (aromatic carbons), 95.6 (C-2), 72.6, 72.2, 68.8 (C-6, C-7, C-8), 67.6, 62.8 (C-9, -*C*H$_2$OC(O)-), 54.5, 52.9, 51.4, 46.8, 45.0 (C-3, C-4, C-5, COO*C*H$_3$, -*C*HCH$_2$O-), 23.0 (NHCO*C*H$_3$), 21.0, 20.8, 20.7 (OCO*C*H$_3$ × 3); LRMS (cone voltage 30V): 733, 731 (MH^+, 100%), 555, 553 (15). HRMS: Calcd for $C_{33}H_{38}N_2O_{13}{}^{79}$Br:[$M^+$ + 1], 749.1557. Found: *m/z*, 749.1559.

17b: R_f 0.46 (CH_2Cl_2/MeOH, 19:1); ^{1}H NMR δ 7.79–7.30 (8 H, m, aromatic protons), 6.02 (1 H, d, $J_{NHa,5}$ 9.3, NH_a), 5.40 (1 H, br, NH_b), 5.33 (1 H, dd, $J_{7,6}$ 1.8, $J_{7,8}$ 4.5, H-7), 5.25 (1 H, m, H-8), 5.03 (1 H, m, H-9), 4.74 (1 H, m, H-5), 4.55–4.20 (7 H, m, H-3, H-4, H-6, -C*H*-CH_2-, OH), 4.04 (1 H, dd, $J_{9',8}$ 7.8, $J_{9',9}$ 12.6, H-9′), 3.85 (3 H, s, $COOCH_3$), 2.18, 2.10, 2.04 (each 3 H, s, $OCOCH_3$ × 3), 1.87 (3 H, s, NHCOC*H*$_3$).

17c: R_f 0.56 (CH_2Cl_2/MeOH, 19:1); ^{1}H NMR δ 7.85–7.30 (8 H, m, aromatic protons), 5.35–5.25 (2 H, m, H-7, H-8), 5.20 (1 H, d, $J_{NHb,5}$ 10.2, NH_b), 4.95 (1 H, ddd, $J_{5,4}$ 3.0, $J_{5,6}$ 10.5, H-5), 4.64 (1 H, dd, $J_{9,8}$ 2.1, $J_{9,9'}$ 12.3, H-9), 4.56–4.30 (4 H, m, H-3, -C*H*CH_2O-), 4.12 (1 H, dd, $J_{9',8}$ 7.5, H-9′), 3.90 (3 H, s, $COOCH_3$), 3.86 (1 H, dd, $J_{6,7}$ 1.5, H-6), 3.76 (1 H, dd, $J_{4,3}$ 3.3, H-4), 2.16, 2.08, 2.06 (each 3 H, s, $OCOCH_3$ × 3), 1.86 (3 H, s, NHCOC*H*$_3$); ^{13}C NMR δ 171.1, 170.6, 169.9, 167.6, 156.8 (carbonyls), 143.7, 143.5, 141.2, 127.7, 127.1, 125.1, 125.0, 120.0 (C=N, aromatic carbons), 95.4 (C-2), 71.0, 70.2, 67.7 (C-6, C-7, C-8), 67.4, 62.4 (-CH*C*H$_2$O-, C-9), 55.2, 54.0, 51.0, 50.3, 46.9 (C-3, C-4, C-5, COO*C*H$_3$, -*C*HCH$_2$O-), 22.9 (NHCO*C*H$_3$), 20.8, 20.7, 20.6 (OCO*C*H$_3$ × 3); LRMS (cone voltage 30V): 733, 731 (MH^+, 100%), 555, 553 (18); HRMS: Calcd for $C_{33}H_{36}N_2O_{12}{}^{79}$Br:[$M^+$ + 1], 731.1452. Found: *m/z*, 731.1443.

Methyl 5-Acetamido-7,8,9-tri-*O*-acetyl-4-*N*-(9′-Fluorenylmethoxycarbonyl)amino-3-bromo-3,4,5-trideoxy-D-*erythro*-β-L-*manno*-2-nonulopyranosonate (18a) and Methyl 5-Acetamido-7,8,9-tri-*O*-acetyl-4-*N*-(9′-Fluorenylmethoxycarbonyl)amino-3-bromo-3,4,5-trideoxy-D-*erythro*-β-L-*gluco*-2-nonulopyranosonate (18b).

18a: R_f 0.50 (EtOAc/hexane, 2:1); ^{1}H NMR δ 7.76–7.28 (8 H, m, aromatic protons), 6.23 (1 H, d, $J_{NHa,5}$ 8.4, NH_a), 5.86 (1 H, br, NH_b), 5.44–5.42 (2 H, m, H-7, OH), 5.31 (1 H, m, H-8), 4.93 (1 H, dd, $J_{9,8}$ 2.1, $J_{9,9'}$ 12.6, H-9), 4.58 (1 H, br, H-3), 4.40–4.15 (6 H, m, H-5, H-6, H-9′, -C*H*CH_2O-), 3.82 (3 H, s, $COOCH_3$), 2.17, 2.06, 2.01 (each 3 H, s, $OCOCH_3$ × 3), 1.82 (3 H, s, NHCOC*H*$_3$); ^{13}C NMR δ 172.0, 171.8, 171.6, 170.2, 167.6, 156.3 (carbonyls),

143.4, 141.1, 127.8, 127.1, 125.4, 119.9 (aromatic carbons), 95.6 (C-2), 72.6, 72.2, 68.8 (C-6, C-7, C-8), 67.6, 62.8 (C-9, -*C*H_2OC(O)-), 54.5, 52.9, 51.4, 46.8, 45.0 (C-3, C-4, C-5, -*C*HCH$_2$O-, COO*C*H_3), 22.9 (NHCO*C*H_3), 21.0, 20.9, 20.7 (OCO*C*H_3 × 3); LRMS (cone voltage 30V): 751, 749 (MNa^+, 80%), 609 (35), 491 (15), 338 (40), 181 (100).

18b: R_f 0.60 (EtOAc/hexane, 2:1); ^{1}H NMR δ 7.75–7.29 (8 H, m, aromatic protons), 5.95 (1 H, d, $J_{NHa,5}$ 9.3, NH_a), 5.34 (1 H, dd, $J_{7,6}$ 1.8, $J_{7,8}$ 6.9, H-7), 5.21 (1 H, m, H-8), 5.02 (1 H, br, NH_b), 4.90 (1 H, br, OH), 4.40–4.15 (8 H, m, H-3, H-4, H-5, H-6, H-9, -C*H*C*H*$_2$-), 3.99 (1 H, dd, $J_{9',8}$ 6.3, $J_{9',9}$ 12.3, H-9′), 3.94 (3 H, s, COOCH_3), 2.17, 2.08, 2.02 (each 3 H, s, OCOCH_3 × 3), 1.82 (3 H, s, NHCOC*H*$_3$); ^{13}C NMR δ 171.2, 170.7, 170.3, 170.0, 167.7, 156.9 (carbonyls), 143.7, 143.6, 141.2, 127.8, 127.3, 125.2, 125.0, 120 (aromatic carbons), 95.4 (C-2), 71.0, 70.3, 67.8 (C-6, C-7, C-8), 67.5, 62.5 (C-9, -*C*H_2OC(O)-), 54.1, 51.0, 50.4, 46.9, 45.8 (C-3, C-4, C-5, -*C*HCH$_2$O-, COO*C*H_3), 29.6 (C-3), 23.0 (NHCO*C*H_3), 20.9, 20.7, 20.6 (OCO*C*H_3 × 3); LRMS (cone voltage 30V): 773, 771 (MNa^+, 100%), 751, 749 (55), 669 (80); HRMS: Calcd for $C_{33}H_{38}N_2O_{13}{}^{79}$Br:[$M^+$ +1], 749.1557. Found: *m/z*, 749.1526

Methyl 5-Acetamido-7,8,9-tri-*O*-acetyl-4-(4′-Acetoxyphenyl)acetamido-3-bromo-3,4,5-trideoxy-D-*erythro*-β-L-*manno*-2-nonulopyranosonate (19a) and Methyl 5-Acetamido-7,8,9-tri-*O*-acetyl-4-(4′-Acetoxyphenyl)acetamido-3-bromo-3,4,5-trideoxy-D-*erythro*-β-L-*gluco*-2-nonulopyranosonate (19b).

19a/19b: R_f 0.40 (EtOAc); ^{1}H NMR δ 7.22–7.03 (4 H, m, aromatic protons), 6.32, 6.29, 5.99 (2 H, d, *J* 7.8, 9.9, 9.6 respectively, NH_a, NH_b), 5.40–5.17 (2 H, m, H-7, H-8), 4.90–3.95 (6 H, m, H-3, H-4, H-5, H-6, H-9, H-9′), 3.92, 3.83 (3 H, s, COOCH_3), 3.47 (2 H, m, -C*H*$_2$-C$_6$H$_4$-), 2.29, 2.81, 2.12, 2.09, 2.06, 2.03, 2.02, 1.72, 1.70 (15 H, s, NHCOC*H*$_3$, OCOCH_3 × 4); ^{13}C NMR δ 170.6, 170.0, 169.9, 169.7, 169.6, 169.5, 168.1, 167.9, 167.5 (carbonyls), 149.8, 148.7, 132.0, 131.9, 130.4, 130.1 121.9 (aromatic carbons), 95.4, 95.3 (C-2), 71.8, 71.2, 70.8, 69.8, 68.5, 67.6 (C-6, C-7, C-8), 62.9, 62.4 (C-9), 54.2, 54.0, 53.0, 52.9, 50.5, 50.3, 50.1, 44.5 (C-3, C-4, C-5, COO*C*H_3), 42.8, 42.5 (-*C*H_2-C$_6$H$_4$-), 22.6, 21.0, 21.9, 20.8, 20.7, 20.6 (NHCO*C*H_3, OCO*C*H_3 × 4); LRMS (cone voltage 30V): 705, 703 (MH^+, 100%), 641 (55), 623 (20); HRMS: Calcd for $C_{28}H_{36}N_2O_{14}{}^{79}$Br:[$M^+$ + 1], 703.1350. Found: *m/z*, 703.1315.

2-Phenyl(Methyl 5-Acetamido-7,8,9-tri-*O*-acetyl-3,4,5-trideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosonate)4*H*-1,3-oxazine (20). A stirring solution of the oxazine **16d** (180 mg, 0.294 mmol), *n*-Bu_3SnH (257 mg, 0.882 mmol) and AIBN (5 mg) in anhydrous THF (5 mL) was heated under reflux for 2 h, and cooled. The volatiles were removed *in vacuo* and the resulting residue gave, after column chromatography on silica (EtOAc), the title compound **20** as a colourless amorphous mass, 150 mg (96%); R_f 0.13 (EtOAc); ^{1}H NMR δ 7.95–7.35 (5 H, m, Ph), 6.09 (1 H, d, $J_{NH,5}$ 6.9, NH), 5.40 (1 H, m, H-8), 5.23 (1 H, d, *J* 8.1, H-7), 4.37

(1 H, dd, $J_{9,8}$ 1.0, $J_{9,9'}$ 12.6, H-9), 4.22 (1 H, dd, $J_{9',8}$ 4.5, H-9′), 4.20–4.17 (3 H, m, H-4, H-5, H-6), 3.87 (3 H, s, $COOCH_3$), 3.23 (1 H, m, H-3), 2.94 (1 H, dd, $J_{3',3}$ 10.8, $J_{3',4}$ 7.2, H-3′), 2.07, 2.05, 2.04, 1.99 (each 3 H, s, $NHCOCH_3$, $OCOCH_3$ × 3); ^{13}C NMR δ 171.0, 170.5, 170.4, 169.5, 167.0, 152.9 (carbonyls, C=N), 132.4, 131.0, 128.0, 127.3 (aromatic carbons), 95.7 (C-2), 68.9, 67.8, 65.2 (C-6, C-7, C-8), 62.0 (C-9), 54.5, 53.0, 49.0 (C-4, C-5, $COOCH_3$), 25.1 (C-3), 23.5 ($NHCOCH_3$), 20.8, 20.5, 20.4 ($OCOCH_3$ × 3); LRMS (cone voltage 30V): 535 (MH^+, 100%), 338 (8), 60 (5); HRMS: Calcd for $C_{25}H_{31}N_2O_{11}$:[M^+ + 1], 535.1928. Found: *m/z*, 535.1927.

Methyl 5-Acetamido-7,8,9-tri-*O*-acetyl-2-azido-4-benzamido-2,3,4,5-tetradeoxy-D-*glycero*-β-D-*galacto*-2-nonulopyranosonate (21). A stirring solution of the oxazine **20** (50 mg, 0.094 mmol) and azidotrimethylsilane (0.037 mL, 0.279 mmol) in anhydrous THF (5 mL) was heated under reflux for 16 h, and cooled. The volatiles were removed under diminished pressure and the resulting residue purified by column chromatography on silica gel (EtOAc/hexane, 2:1) affording the 2-β-azide **21** as a colourless syrup, 28 mg (52%). Further elution of the column gave the glycal **9**, 8 mg (16%); R_f (EtOAc/hexane, 2:1): R_f (**21**) = 0.20; R_f (**9**) = 0.15.

21: $[\alpha]_D$ −40° (*c* 2.02, $CHCl_3$); ^{1}H NMR δ 7.70–7.39 (5 H, m, Ph), 6.63 (1 H, d, *J* 8.1, NH_a), 6.20 (1 H, d, *J* 9.6, NH_b), 5.56 (1 H, dd, $J_{7,6}$ 1.8, $J_{7,8}$ 6.0, H-7), 5.26 (1 H, ddd, $J_{8,9}$ 2.4, $J_{8,9'}$ 6.0, H-8), 4.57 (1 H, dd, $J_{9,9'}$ 12.6, H-9), 4.54 (1 H, m, H-4), 4.35 (1 H, dd, $J_{6,5}$ 10.2, H-6), 4.13 (1 H, dd, H-9′), 4.08 (1 H, m, H-5), 3.88 (3 H, s, $COOCH_3$), 2.45 (1 H, dd, $J_{3eq,3ax}$ 4.2, $J_{3eq,4}$ 13.5, H-3_{eq}), 2.13, 2.09, 2.06, 1.80 (each 3 H, s, $NHCOCH_3$, $OCOCH_3$ × 3), 1.99 (1 H, m, H-3_{ax}); ^{13}C NMR δ 172.1, 170.5, 170.1, 169.6, 168.0, 166.4 (carbonyls), 133.4, 131.9, 128.7, 126.9 (aromatic carbons), 90.2 (C-2), 73.1, 70.8, 67.8 (C-6, C-7, C-8), 62.0 (C-9), 53.3, 49.0, 48.5 (C-4, C-5, $COOCH_3$), 36.4 (C-3), 22.7 ($NHCOCH_3$), 20.9, 20.6, 20.5 ($OCOCH_3$ × 3); IR (υ_{max}, KBr): 2106 cm^{-1} (N_3); LRMS (cone voltage 30V): 578 (MH^+, 80%), 73 (28), 60 (100); HRMS: Calcd for $C_{25}H_{32}N_5O_{11}$:[M^+ + 1], 578.2098. Found: *m/z*, 578.2096.

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