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Syntheses of sialic acid analogues with acylamino groups at C-4 (*N*-acyl regioisomers of sialic acids)

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Abstract

Methyl 5,7,8,9-tetra-*O*-acetyl-4-acylamino-2,6-anhydro-3,4-dideoxy-D-*glycero*-D-*galacto*- and D-*talo*-non-2-enonates were synthesized from the reaction of the peracetate of Kdn methyl ester with several nitriles in the presence of a Lewis acid. Treatment of these 2,4-dideoxy-4-acylamino-Kdn methyl esters with *N*-bromosuccinimide in methanol gave methyl (methyl 5,7,8,9-tetra-*O*-acetyl-4-acylamino-3-bromo-3,4-dideoxy-D-*erythro*-α-L-*manno*-non-2-ulopyranosid)onates (**16**, **18**, and **20**) and oxazine-type derivatives, 2-alkyl-(methyl 5,7,8,9-tetra-*O*-acetyl-3-bromo-3,4-dideoxy-D-*erythro*-α-L-*manno*-non-2-ulopyranosonate)-5,6-dihydro-4*H*-1.3-oxazine (**29**, **30**, and **31**). Debromination of **16**, **18**, and **20** with Bu_3SnH/AIBN in toluene gave methyl (methyl 5,7,8,9-tetra-*O*-acetyl-4-acylamino-3,4-dideoxy-β-D-glycero-D-*galacto*-nonulopyranosid)onate (**23**, **24**, and **25**), whereas hydrolysis with HOAc and subsequent debromination with Bu_3SnH/AIBN in toluene of **32** and **33** gave methyl 5,7,8,9-tetra-*O*-acetyl-4-acylamino-3,4-dideoxy-β-D-*glycero*-D-*talo*-2-nonulopyranosonate (**35** and **36**) in the final step of the synthesis.

Keywords: Sialic acid; Kdn; 4-Acylamino-4-deoxy-; 5,6-Dihydro-4*H*-1.3-oxazine; Iso-sialic acids

1. Introduction

Sialic acids, *N*-acetylneuraminic acid (**1**, Neu5Ac); *N*-glycocylneuraminic acid (**2**, Neu5Gc); 3-deoxy-β-D-*glycero*-D-*galacto*-non-2-ulosonic acid (**3**, Kdn), and their conjugates, play an important role in molecular recognition, cell adhesion and differentiation phenomena [1–4]. During the last ten years, the chemical and enzymatic synthesis of sialic acids [5] and various analogues [6,7] have received much attention due to their biological functions, which include potential inhibitory activity against sialidase [8] and sialyltransferase [9]. In particular, 4-amino- and 4-guanidino-substituted Neu5Ac2en were found to be high-affinity inhibitors for influenza virus sialidase [10].

We have established a chemical method for the preparation of Kdn (**3**) on a large scale [11] and have synthesized several derivatives of Kdn [12,13]. As a part of our work on the synthesis and biological activity of structurally modified sialic acids, we herein report a straightforward chemical methodology for the introduction of nitrogen at the C-4 position on

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Kdn, namely the syntheses of methyl 5,7,8,9-tetra-*O*-acetyl-4-acylamino-2,6-anhydro-3,4-dideoxy-D-*glycero*-D-*galacto*- and D-*talo*-non-2-enonates, which we term protected 'iso-sialic acids' [6].

2. Results and discussion

Crystalline Kdn (**3**) was prepared in high purity and high yield by the aldol condensation of D-mannose with oxalacetic acid without formation of 4-*epi*-Kdn, and per-*O*-acetyl Kdn methyl ester (**7**) was prepared from Kdn by the reported method [11]. Methyl 5,7,8,9-tetra-*O*-acetyl-4-acetylamino-2,6-anhydro-3,4-dideoxy-D-*glycero*-D-*galacto*- and D-*talo*-non-2-enonates (**8** and **9**) were prepared from the peracetate of Kdn methyl ester (**7**) with acetonitrile catalyzed by trimethylsilyl triflate (TMSOTf) at room temperature as previously described [13]. Here, we performed similar reactions by using the peracetate of Kdn methyl ester (**7**) with methoxyacetonitrile or benzonitrile catalyzed by trimethylsilyl triflate (TMSOTf) at room temperature to yield two epimers of methyl 5,7,8,9-tetra-*O*-acetyl-4-acylamino-2,6-anhydro-3,4-dideoxy-D-*glycero*-D-*galacto*- and D-*talo*-2-enonates (**10**, **11**, **12**, and **13**) in high yield, respectively. It was presumed that these reactions occur via an S_N1 process [13], and the formation of (4*R*)-configured amides **9**, **11**, and **13** was predominant over (4*S*)-configured amides **8**, **10**, and **12**. The structures of these products were elucidated mainly on the basis of the proton nuclear magnetic resonance (^{1}H NMR) and IR spectral data [13]. The orientations of the 4-acylamino groups were easily deduced from the values of the coupling constants between H-3 and H-4, and H-4 and H-5. For instance, the coupling constants $J_{3,4} = 2.3–2.7$ Hz and $J_{4,5} = 8.4–9.3$ Hz indicated the (4*S*)-configuration for **8**, **10**, and **12**, whereas the coupling constants $J_{3,4} = 5.1–5.7$ Hz and $J_{4,5} = 4.8–5.1$ Hz indicated (4*R*)-configuration for **9**, **11**, and **13** (Scheme 1).

For the preparation of desired 'iso-sialic acids', at first, treatment of (4*S*)-per-*O*-acetyl-4-acylamino-2,4-dideoxy-Kdn methyl ester **8**, **10**, and **12** with *N*-bromosuccinimide (NBS) in methanol at room temperature under argon atmosphere [7,14] afforded the mixture of corresponding diaxial (**16**, **18**, and **20**) and diequatorial isomers (**17**, **19**, and **21**), which were readily separated by silica gel column chromatography (2:1 *n*-hexane–acetone) and gave an excellent overall isolated yield. Interestingly, as the diequatorial adducts, oxazine-type derivatives **17**, **19**, and **21** were obtained in these bromomethoxylation, which may be formed by intramolecular nucleophilic substitution reaction via a bromonium ion intermediate **15** in company with the conversion of the ring form to boat conformation. In addition, per-*O*-acetyl-4-benzoylamino-2,4-dideoxy-Kdn methyl ester (**12**) gave a diequatorial intramolecular, nucleophilically substituted product **22**, also. This result could be explained by the fact that the intramolecular nucleophilic substitution reaction took place competitively via the bromonium ion intermediate **15** derived from **12**, in which the nucleophilic activity of the carbonyl group decreased due to conjugation of the carbonyl with the phenyl group (Scheme 2).

The structural assignments by ^{1}H NMR spectroscopy for the diaxial and diequatorial isomers are in accord with the spin–spin coupling constants between H-3 and H-4; i.e., the coupling constants between H-3 and H-4 are each 3.6 Hz for the diaxial isomer **16**, **18**, and **20**, and 7.2 Hz for the diequatorial isomer **22**. The oxazine structures were determined

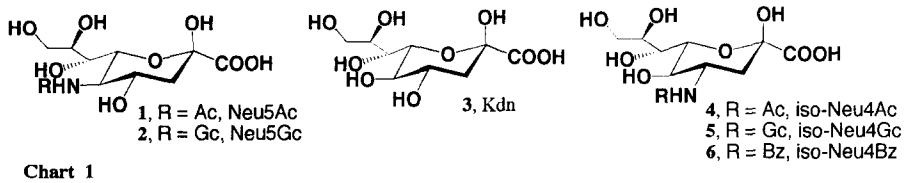
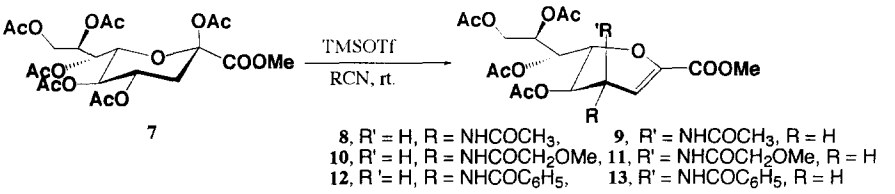
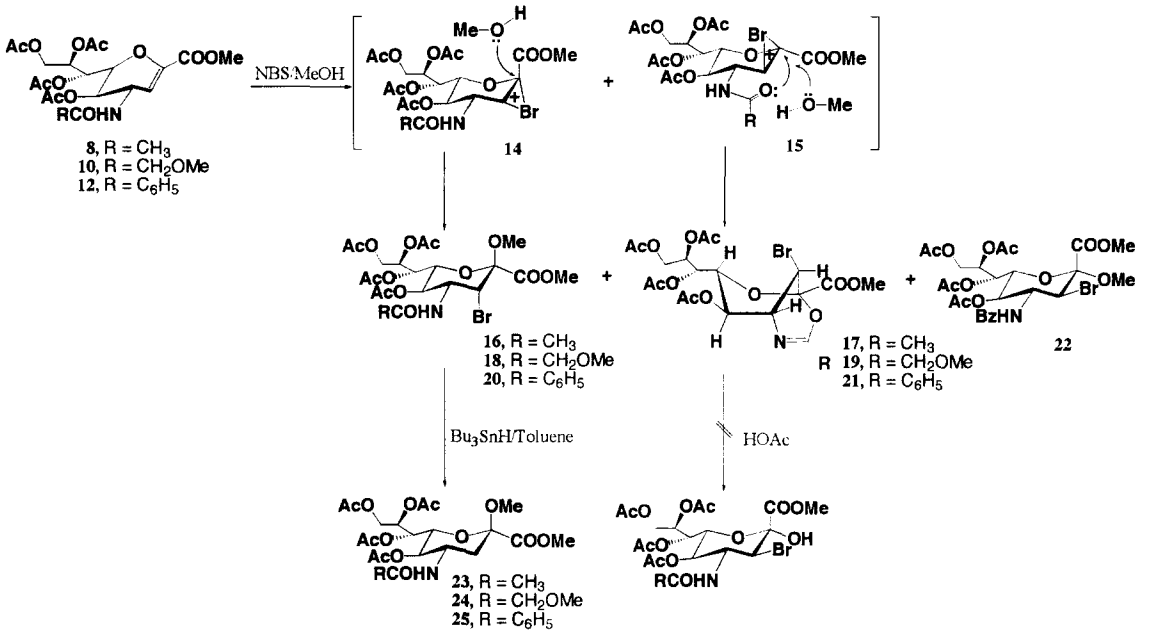


Chart 1

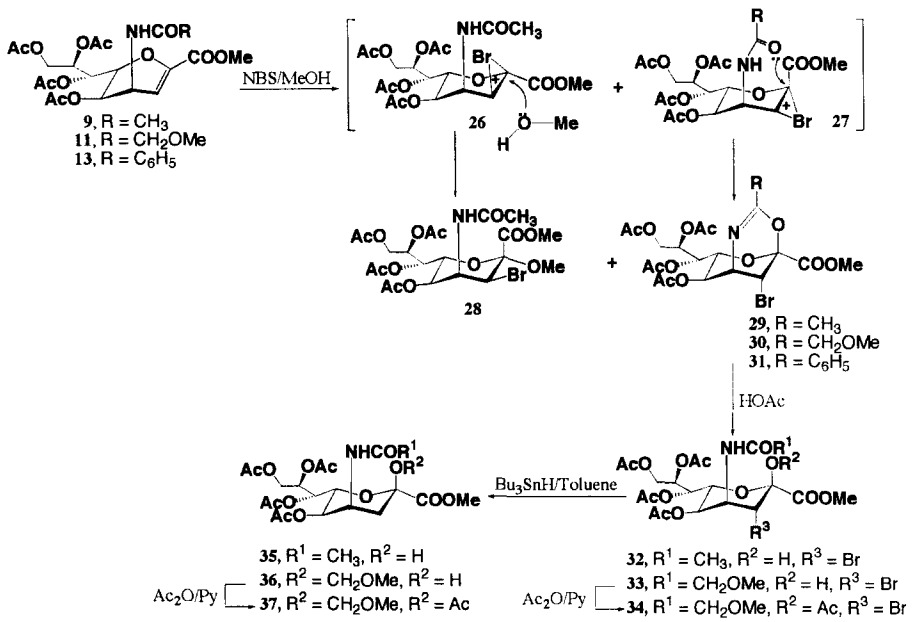


Scheme 1.



Scheme 2.

from both ^{1}H NMR and ^{13}C NMR spectroscopy where there were no NH and OMe peaks found. Furthermore, these were checked by MS spectroscopy. The assertion that the pyranoid ring of the Kdn moiety was in the boat conformation was supported by the spin–spin coupling constants between H-3 and H-4 (3.6–3.9 Hz), H-4 and H-5 (0.9–1.2 Hz), H-5 and H-6 (8.4–8.7 Hz), all of which differ from those of the chair form derivatives. In particular, long-range coupling between H-3 and H-5 was observed in all these compounds, in which $^{4}J_{3,5}$ are 0.6 Hz for **17**, 0.9 Hz for **19**, and 1.2 Hz for **21**.



Scheme 3.

However, hydrolysis of these oxazines with HOAc has not yet been successful.

On the other hand, the bromomethoxylation of per-*O*-acetyl-4-acylamino-2,4-dideoxy-4-*epi*-Kdn methyl ester (**9**, **11**, and **13**) afforded the oxazine derivatives **29**, **30**, and **31** exclusively as the diaxial isomers, except per-*O*-acetyl-4-acetylamino-2,4-dideoxy-4-*epi*-Kdn methyl ester **9**, from which diequatorial isomer **28** was also obtained as shown in Scheme 3. The formation of these oxazine derivatives was thought to be by way of intermolecular nucleophilic substitutions via the bromonium-ion intermediate **27**, and without the formation of intramolecular nucleophilic substitutions of methoxyl anion from axial orientation via the bromonium-ion intermediate **27** because of the steric hindrance from the 4-*epi*-acylamino groups. For the same reason, a bromonium-ion intermediate like **26** did not form from **11** and **13**, which have larger groups (methoxyacetylamino, benzoylamino) than **9** (acetylamino); thus, there were no diequatorial adducts formed from **11** and **13**.

The structures of the oxazine derivatives were determined by ^{1}H NMR and ^{13}C NMR spectroscopy. No NH and OMe peaks were found, and the conformation of Kdn moieties of **29**, **30**, and **31** were of the chair form, which was supported by the spin–spin coupling constants between H-3 and H-4 (4.2–4.5 Hz), H-4 and H-5 (3.6–4.5 Hz), H-5 and H-6 (each 3.6 Hz). Furthermore, the hydrolysis with HOAc of these oxazine derivatives gave methyl 5,7,8,9-tetra-*O*-acetyl-4-acylamino-3-bromo-3,4-dideoxy-D-*erythro*-α-L-*altro*-non-2-ulopyranosonate (**32** and **33**), and subsequent acetylation gave methyl 2,5,7,8,9-penta-*O*-acetyl-3-bromo-3,4-dideoxy-4-methoxyacetylamino-D-*erythro*-α-L-*altro*-non-2-ulopyranosonate (**34**). However, the 2′-phenyl-oxazine (**31**) could not be hydrolyzed with HOAc, even when stirred for 48 h at room temperature.

Clean debromination and reduction of these 3-bromo-3-deoxy-Kdn derivatives **16**, **18**, **20**, **32**, and **33** were accomplished by treatment with Bu_3SnH/AIBN in toluene at 70–90 °C to give the corresponding target compounds **23**, **24**, **25**, **35**, and **36**. The stereochemistry of the anomeric position was determined according to the determined precursors **16**, **18**, **20**, **32**, and **33**, above, and ^{1}H NMR spectroscopy showed the coupling constants between H-3 and H-4, $J_{3eq,4} = 3.9–4.5$ Hz and $J_{3ax,4} = 9.9–11.7$ Hz for the β anomers **23**, **24**, and **25**, whereas $J_{3eq,4}$ = each 4.5 Hz and $J_{3ax,4} = 2.4$ and 2.7 Hz for the β anomers **35** and **36**. Surprisingly, there was an unusual spin–spin long-range coupling (^4J) between 3-H_{eq} and 2-OH ($J = 2.1$ Hz) in **36** as observed in $CDCl_3$ solution. In order to verify this, we determined the ^{1}H NMR spectrum in $CDCl_3$ with added D_2O, and the coupling between H-3_{eq} and 2-OH disappeared in this spectrum. Furthermore, acetylation of **36** with Ac_2O–Py afforded a 2-*O*-acetyl derivative **40**, and the coupling of H-3_{eq} above was not observed with certainty. On the contrary, the similar coupling between H-3_{eq} and 2-OH could not be observed in compound **35**, which has a 2-OH and 4-*epi*-*N*-acetyl group. The model analysis of **36** indicated that H-3_{eq} and 2-OH were in 1,3-diaxial conformation due to the intramolecular hydrogen bond between 4-NH and 2-OH. This could be explained by the spectroscopic difference between **35** and **36**, in the ^{1}H NMR spectrum, where the chemical shift of NH in **36** is shifted downfield (7.83 ppm) relative to that in **35** (6.76 ppm). In the IR spectrum, the absorption of NH and N–C=O are also at lower frequency in **36** (3530 and 1694 cm^{-1}) than in **35** (3600 and 1708 cm^{-1}).

In conclusion, we have developed a facile synthetic method for the preparation of 4-acylamino-4-deoxy-Kdn derivatives, which have a sialic acid-like structures. The biological activities are under investigation. In addition, intramolecular nucleophilic substitution reactions occurred to form oxazine-type derivatives in these methoxybromination, and these products may be useful for other reactions, an example of which is glycosylation, which will be the subject of future investigations.

3. Experimental

General procedures.—Melting points were measured on a Yamato melting point apparatus without correction. Fast-atom-bombardment mass spectra (FABMS) were taken on a JEOL JMS-DX 300 instrument. Optical rotations were measured with a JASCOJIP-4 digital polarimeter at 21 °C. IR spectra were obtained on a Perkin–Elmer 983G infrared spectrometer. The ^{1}H NMR (300 MHz) spectra were determined with Varian VXR-300 spectrometers in $CDCl_3$ solution with tetramethylsilane (TMS) as an internal reference. Thin-layer chromatography (TLC) was performed on Kieselgel 60 F_{254} (E. Merck) plates, and zones were detected under ultraviolet (UV) irradiation or by spraying with 5% sulfuric acid solution.

Column chromatography was conducted on E. Merck Silica Gel 60 (70–230 mesh).

Methyl 5,7,8,9-tetra-O-acetyl-4-acetylamino-2,6-anhydro-3,4-dideoxy-D-glycero-D-galacto-non-2-enonate (**8**) *and methyl 5,7,8,9-tetra-O-acetyl-4-acetylamino-2,6-anhydro-3,4-dideoxy-D-glycero-D-talo-non-2-enonate* (**9**).—These compounds were prepared as described [13].

Methyl 5,7,8,9-tetra-O-acetyl-2,6-anhydro-3,4-dideoxy-4-methoxyacetylamino-D-glycero-D-galacto-non-2-enonate (**10**) *and methyl 5,7,8,9-tetra-O-acetyl-2,6-anhydro-3,4-dideoxy-4-methoxyacetylamino-D-glycero-D-talo-non-2-enonate* (**11**).—A solution of trimethylsilyl triflate (TMSOTf) (490 mg, 1.88 mmol) in methoxyacetonitrile (1 mL) was added to a solution of **7** (500 mg, 0.94 mmol) in methoxyacetonitrile (20 mL) at 0 °C. The mixture was stirred at room temperature for 5 h until the starting material was no longer detectable by TLC (10:1 $CHCl_3$–MeOH). Potassium carbonate (259 mg, 2 equiv) was then added, and the mixture was stirred for a further 15 min. Solids were removed by filtration, and concentration of the filtrate under reduced pressure gave a residue, which was purified by silica gel chromatography with 3:1 *n*-hexane–acetone to yield **10** (35 mg, 7.6%), and **11** (320 mg, 69%). Data for **10**: colorless syrup. $[\alpha]_D$ −11° (*c* 0.35, MeOH); IR (ν_{max}, CCl_4): 1745 (COO), 1685 (CON) cm^{-1}; ^1H NMR δ: 5.90 (d, 1 H, $J_{3,4}$ 2.7 Hz, H-3), 4.94 (ddd, 1 H, $J_{4,4NH}$ 8.4, $J_{4,5}$ 9.3 Hz, H-4), 5.00 (dd, 1 H, $J_{5,6}$ 9.6 Hz, H-5), 4.31 (dd, 1 H, $J_{6,7}$ 2.4 Hz, H-6), 5.51 (dd, 1 H, $J_{7,8}$ 6.6 Hz, H-7), 5.38 (ddd, 1 H, $J_{8,9a}$ 6.0, $J_{8,9b}$ 2.4 Hz, H-8), 4.19 (dd, 1 H, $J_{9a,9b}$ 12.3 Hz, H-9a), 4.57 (dd, 1 H, H-9b), 6.69 (d, 1 H, NH), 3.79 (s, 3 H, $COOCH_3$), 3.39 (s, 3 H, $COCH_2OCH_3$), 3.90 (d, 1 H, *J* 15.6 Hz, $COCH_2OCH_3$), 3.81 (d, 1 H, $COCH_2OCH_3$), 2.04, 2.05, 2.06, 2.06 (each s, 3 H, OAc × 4). FABMS *m/z*: 504 ($M^+ + 1$) (*m*-NBA as matrix); Anal. Calcd for $C_{21}H_{29}NO_{13}$: C, 50.01; H, 5.77; N, 2.78. Found: C, 49.96; H, 5.84; N 2.78.

Data for **11**: colorless prisms. mp 143–145 °C; $[\alpha]_D$ −129° (*c* 0.63, MeOH); IR (ν_{max}, CCl_4): 1749 (COO), 1690 (CON) cm^{-1}; ^1H NMR δ: 5.96 (d, 1 H, $J_{3,4}$ 5.7 Hz, H-3), 4.89 (ddd, 1 H, $J_{4,4NH}$ 8.4, $J_{4,5}$ 5.1 Hz, H-4), 4.97 (dd, 1 H, $J_{5,6}$ 9.6 Hz, H-5), 4.14 (dd, 1 H, $J_{6,7}$ 2.7 Hz, H-6), 5.48 (dd, 1 H, $J_{7,8}$ 5.5 Hz, H-7), 5.34 (ddd, 1 H, $J_{8,9a}$ 6.9, $J_{8,9b}$ 2.7 Hz, H-8), 4.16 (dd, 1 H, $J_{9a,9b}$ 12.6 Hz, H-9a), 4.64 (dd, 1 H, H-9b), 6.46 (d, 1 H, NH), 3.76 (s, 3 H, $COOCH_3$), 3.39 (s, 3 H, $COCH_2OCH_3$), 3.89 (d, 1 H, *J* 15.6 Hz, $COCH_2OCH_3$), 3.83 (d, 1 H, *J* 15.6 Hz, $COCH_2OCH_3$), 1.95, 2.02, 2.04, 2.06 (each s, 3 H, OAc × 4). FABMS *m/z*: 504 ($M^+ + 1$) (*m*-NBA as matrix); Anal. Calcd for $C_{21}H_{29}NO_{13}$: C, 50.01; H, 5.77; N, 2.78. Found: C, 50.03; H, 5.86; N 2.76.

Methyl 5,7,8,9-tetra-O-acetyl-2,6-anhydro-4-benzoylamino-3,4-dideoxy-D-glycero-D-galacto-non-2-enonate (**12**) *and methyl 5,7,8,9-tetra-O-acetyl-2,6-anhydro-4-benzoylamino-3,4-dideoxy-D-glycero-D-talo-non-2-enonate* (**13**).—A solution of TMSOTf (490 mg, 1.88 mmol) in benzonitrile (2 mL) was added to a solution of **7** (800 mg, 1.50 mmol) in benzonitrile (20 mL) at 0 °C. The mixture was processed as described for **10** and **11** to yield **12** (64 mg, 8%) and **13** (381 mg, 48%). Data for **12**: colorless prisms. mp 125–127 °C; $[\alpha]_D$ +62° (*c* 0.63, MeOH); IR (ν_{max}, CCl_4): 1742 (COO), 1660 (CON) cm^{-1}; ^1H NMR δ: 6.06 (d, 1 H, $J_{3,4}$ 2.3 Hz, H-3), 5.05 (m, 1 H, H-4), 5.08 (m, 1 H, H-5), 4.38 (dd, 1 H, $J_{5,6}$ 10.2, $J_{6,7}$ 2.1 Hz, H-6), 5.55 (dd, 1 H, $J_{7,8}$ 6.9 Hz, H-7), 5.39 (ddd, 1 H, $J_{8,9a}$ 6.3, $J_{8,9b}$ 2.7 Hz, H-8), 4.21 (dd, 1 H, $J_{9a,9b}$ 12.3 Hz, H-9a), 4.57 (dd, 1 H, H-9b), 6.54 (d, 1 H, $J_{4,4NH}$ 5.7 Hz, NH), 3.77 (s, 3 H, $COOCH_3$), 7.45–7.72 (m, 5 H, C_6H_5), 2.05, 2.06, 2.09, 2.10 (each s, 3 H, OAc × 4). FABMS *m/z*: 536 ($M^+ + 1$) (*m*-NBA as matrix); Anal. Calcd for $C_{25}H_{29}NO_{12}$: C, 56.07; H, 5.42; N, 2.62. Found: C, 56.15; H, 5.52; N, 2.75.

Data for **13**: $[\alpha]_D$ −157° (*c* 0.54, MeOH); IR (ν_{max}, CCl_4): 1746 (COO), 1670 (CON) cm^{-1}; ^1H NMR δ: 6.06 (d, 1 H, $J_{3,4}$ 5.1 Hz, H-3), 5.51 (dd, 1 H, $J_{7,8}$ 5.4, $J_{6,7}$ 2.7 Hz, H-7), 5.38 (ddd, 1 H, $J_{8,9a}$ 2.4, $J_{8,9b}$ 6.9 Hz, H-8), 5.13 (ddd, 1 H, $J_{4,4NH}$ 8.4, $J_{4,5}$ 4.8 Hz, H-4), 5.08 (dd, 1 H, $J_{5,6}$ 9.3 Hz, H-5), 4.66 (dd, 1 H, $J_{9a,9b}$ 12.6 Hz, H-9a), 4.25 (dd, 1 H, H-6), 4.17 (dd, 1 H, H-9b), 6.28 (d, 1 H, NH), 3.78 (s, 3 H, $COOCH_3$), 7.40–7.87 (m, 5 H, C_6H_5), 1.98, 2.03, 2.05, 2.06 (each s, 3 H, OAc × 4). FABMS *m/z*: 536 ($M^+ + 1$) (*m*-NBA as matrix); Anal. Calcd for $C_{25}H_{29}NO_{12}$: C, 56.07; H, 5.42; N, 2.62. Found: C, 56.21; H, 5.32; N, 2.76.

Methyl (methyl 5,7,8,9-tetra-O-acetyl-4-acetylamino-3-bromo-3,4-dideoxy-β-D-erythro-α-L-manno-non-2-ulopyranosid)onate (**16**) *and 2-methyl-(methyl 5,7,8,9-tetra-O-acetyl-3-bromo-3,4-dideoxy-β-D-erythro-α-L-manno-non-2-ulopyranosonate)-5,6-dihydro-4H-1,3-oxazine* (**17**).—To a solution of **8** (57 mg, 0.12 mmol) in methanol (20 mL), was added NBS (27 mg, 0.15 mmol). The mixture was stirred at room temperature for 2 h, then evaporated in vacuo to give a residue. The residue was dissolved into ethyl acetate, and the solution was washed with water and brine, dried over anhydrous Na_2SO_4, and concentrated to a syrup in vacuo. The syrup was purified by

silica gel column chromatography with 4:1 *n*-hexane–acetone to yield **16** (38 mg, 55%) and **17** (26 mg, 36%). Data for **16**: $[\alpha]_D$ +39° (*c* 0.17, MeOH); ^{1}H NMR δ: 5.39 (dd, 1 H, $J_{6,7}$ 1.8, $J_{7,8}$ 5.1 Hz, H-7), 5.38 (ddd, 1 H, $J_{8,9a}$ 2.4, $J_{8,9b}$ 6.0 Hz, H-8), 4.95 (t, 1 H, $J_{5,6}$ 9.9, $J_{6,7}$ 9.9 Hz, H-5), 4.73 (dd, 1 H, $J_{9a,9b}$ 12.6 Hz, H-9a), 4.69 (ddd, 1 H, $J_{3,4}$ 3.6, $J_{4,4NH}$ 8.4 Hz, H-4), 4.58 (d, 1 H, H-3), 4.20 (dd, 1 H, H-9b), 4.12 (dd, 1 H, H-6), 5.93 (d, 1 H, NH), 3.82 (s, 3 H, $COOCH_3$), 3.27 (s, 3 H, OCH_3), 2.02, 2.06, 2.07, 2.11 (each s, 3 H, OAc × 4), 1.94 (s, 3H, NHAc). FABMS *m/z*: 584, 586 (M^+ + 1) (*m*-NBA as matrix).

Data for **17**: $[\alpha]_D$ +30° (*c* 0.41, MeOH); ^{1}H NMR δ: 5.36 (ddd, 1 H, $J_{7,8}$ 7.8, $J_{8,9b}$ 5.1, $J_{8,9a}$ 2.4 Hz, H-8), 5.31 (dt, 1 H, $J_{6,7}$ 1.2 Hz, H-7), 4.72 (br s, 2 H, 5, H-6), 4.48 (dd, 1 H, $J_{3,4}$ 3.9, $J_{4,5}$ 0.9 Hz, H-4), 4.46 (dd, 1 H, $J_{9a,9b}$ 12.6 Hz, H-9a), 4.20 (dd, 1 H, H-9b), 3.95 (dd, 1 H, $J_{3,5}$ 0.6 Hz, H-3), 3.87 (s, 3 H, $COOCH_3$), 2.77 (s, 3 H, =C–CH_3), 2.05, 2.09, 2.11, 2.14 (each s, 3 H, OAc × 4). FABMS *m/z*: 552, 554 (M^+ + 1) (*m*-NBA as matrix).

*Methyl (methyl 5,7,8,9-tetra-*O*-acetyl-3-bromo-3,4-dideoxy-4-methoxyacetylamino-β-*D*-*erythro*-α-*L*-manno-non-2-ulopyranosid)onate* (**18**) *and 2-methoxy methyl (methyl 5,7,8,9-tetra-*O*-acetyl-3-bromo-3,4-dideoxy-*D*-erythro-β-*L*-gluco-2-nonulopyranosonate)-5,6-dihydro-4*H*-1.3-oxazine* (**19**).—To a solution of **10** (30 mg, 0.06 mmol) in methanol (10 mL), was added NBS (13 mg, 0.072 mmol). The mixture was processed as described for **16** and **17** to yield **18** (18 mg, 49%) and **19** (14 mg, 40%). Data for 18: $[\alpha]_D$ +8° (*c* 0.29, MeOH); ^{1}H NMR δ: 5.42 (dd, 1 H, $J_{6,7}$ 1.8, $J_{7,8}$ 5.7 Hz, H-7), 5.38 (ddd, 1 H, $J_{8,9a}$ 2.4, $J_{8,9b}$ 6.6 Hz, H-8), 5.07 (t, 1 H, $J_{5,6}$ 10.2, $J_{4,5}$ 10.2 Hz, H-5), 4.77 (dd, 1 H, $J_{9a,9b}$ 12.6 Hz, H-9a), 4.74 (ddd, 1 H, $J_{3,4}$ 3.6, $J_{4,4NH}$ 8.7 Hz, H-4), 4.60 (d, 1 H, H-3), 4.20 (dd, 1 H, H-9b), 4.14 (dd, 1 H, H-6), 6.97 (d, 1 H, NH), 3.83 (s, 3 H, $COOCH_3$), 3.40 (s, 3 H, CH_2OCH_3), 3.30 (s, 3 H, 2-OCH_3), 3.89 (d, 1 H, *J* 15.6 Hz, $COCH_2OCH_3$), 3.82 (d, 1 H, $COCH_2OCH_3$), 2.03, 2.04, 2.08, 2.13 (each s, 3 H, OAc × 4). FABMS *m/z*: 614, 616 (M^+ + 1) (*m*-NBA as matrix).

Data for **19**: $[\alpha]_D$ +4° (*c* 0.19, MeOH); ^{1}H NMR δ: 5.36 (ddd, 1 H, $J_{7,8}$ 7.5, $J_{8,9a}$ 2.7, $J_{8,9b}$ 4.8 Hz, H-8), 5.33 (dd, 1 H, $J_{6,7}$ 2.4 Hz, H-7), 4.81 (ddd, 1 H, $J_{5,6}$ 8.7, $J_{4,5}$ 1.2, $J_{3,5}$ 0.9 Hz, H-5), 4.74 (dd, 1 H, H-6), 4.49 (dd, 1 H, $J_{3,4}$ 3.6 Hz, H-4), 4.46 (dd, 1 H, $J_{9a,9b}$ 12.6 Hz, H-9a), 4.18 (dd, 1 H, H-9b), 4.06 (dd, 1 H, H-3), 3.94 (d, 1 H, *J* 13.8 Hz, $COCH_2OCH_3$), 3.87 (d, 1 H, $COCH_2OCH_3$), 3.87 (s, 3 H, $COOCH_3$), 3.41 (s, 3 H, CH_2OCH_3), 2.05, 2.07, 2.12, 2.15 (each s, 3 H, OAc × 4). FABMS *m/z*: 582, 584 (M^+ + 1) (*m*-NBA as matrix).

*Methyl (methyl 5,7,8,9-tetra-*O*-acetyl-4-benzoylamino-3-bromo-3,4-dideoxy-β-*D*-erythro-α-*L*-manno-non-2-ulopyranosid)onate* (**20**) and 2-phenyl (methyl 5,7,8,9-tetra-O-acetyl-3-bromo-3,4-dideoxy-D-erythro-β-L-gluco-*2-non-2-ulopyranosonate)-5,6-dihydro-4*H*-1.3-oxazine* (**21**).—To a solution of **12** (40 mg, 0.074 mmol) in methanol (10 mL), was added NBS (18 mg, 0. 10 mmol). The mixture was processed as described for **16** and **17** to yield **20** (18 mg, 40%) and **21** (14 mg, 29%) and *methyl (methyl 5,7,8,9-tetra-*O*-acetyl-4-benzoylamino-3-bromo-3,4-dideoxy-*D*-erythro-β-*L*-gluco-non-2-ulopyrano-sid)onate* (**22**) (14 mg, 29%). Data for **20**: $[\alpha]_D$ +20° (*c* 0.22, MeOH); ^{1}H NMR δ: 5.47 (dd, 1 H, $J_{7,8}$ 5.7, $J_{6,7}$ 1.8 Hz, H-7), 5.42 (ddd, 1 H, $J_{8,9a}$ 2.1, $J_{8,9b}$ 6.0 Hz, H-8), 5.11 (t, 1 H, $J_{4,5}$ 9.9, $J_{5,6}$ 9.9 Hz, H-5), 4.89 (ddd, 1 H, $J_{4,4NH}$ 8.1, $J_{3,4}$ 3.6 Hz, H-4), 4.79 (d, 1 H, H-3), 4.77 (dd, 1 H, $J_{9a,9b}$ 12.3 Hz, H-9a), 4.24 (dd, 1 H, H-9b), 4.20 (dd, 1 H, H-6), 6.65 (d, 1 H, NH), 3.83 (s, 3 H, $COOCH_3$), 3.33 (s, 3 H, 2-OCH_3), 7.74–7.40 (m, 5 H, C_6H_5), 2.04, 2.05, 2.10, 2.15 (each s, 3 H, OAc × 4). FABMS *m/z*: 646, 648 (M^+ + 1) (*m*-NBA as matrix).

Data for **21**: $[\alpha]_D$ +0.81° (*c* 1.35, MeOH); ^{1}H NMR δ: 5.36 (ddd, 1 H, $J_{7,8}$ 7.5, $J_{8,9b}$ 5.1, $J_{8,9a}$ 2.7 Hz, H-8), 5.31 (dd, 1 H, $J_{6,7}$ 2.1 Hz, H-7), 4.86 (dt, 1 H, $J_{5,6}$ 8.4, $J_{3,5}$ 1.2, $J_{4,5}$ 1.2 Hz, H-5), 4.74 (dd, 1 H, H-6), 4.61 (dd, 1 H, $J_{3,4}$ 3.6 Hz, H-4), 4.47 (dd, 1 H, $J_{9a,9b}$ 12.6 Hz H-9a), 4.20 (dd, 1 H, H-3), 4.14 (dd, 1 H, H-9b), 3.92 (s, 3 H, $COOCH_3$), 7.94–7.35 (m, 5 H, C_6H_5), 1.76, 2.04, 2.12, 2.17 (each s, 3 H, OAc × 4). FABMS *m/z*: 614, 616 (M^+ + 1) (*m*-NBA as matrix).

Data for **22**: $[\alpha]_D$ −20° (*c* 0.25, MeOH); ^{1}H NMR δ: 5.43 (ddd, 1 H, $J_{7,8}$ 4.5, $J_{8,9a}$ 3.9, $J_{8,9b}$ 2.4 Hz, H-8), 5.42 (dd, 1 H, $J_{6,7}$ 1.5 Hz, H-7), 5.08 (dd, 1 H, $J_{5,6}$ 10.8, $J_{4,5}$ 9.0 Hz, H-5), 4.97 (ddd, 1 H, $J_{3,4}$ 7.2, $J_{4,4NH}$ 9.0 Hz, H-4), 4.91 (dd, 1 H, H-6), 4.32 (dd, 1 H, $J_{9a,9b}$ 12.6 Hz, H-9a), 4.16 (dd, 1 H, H-9b), 4.12 (d, 1 H, H-3), 6.29 (d, 1 H, NH), 3.85 (s, 3 H, $COOCH_3$), 3.49 (s, 3 H, 2-OCH_3), 7.74–7.40 (m, 5 H, C_6H_5), 2.02, 2.06, 2.10, 2.12 (each s, 3 H, OAc × 4). FABMS *m/z*: 646, 648 (M^+ + 1) (*m*-NBA as matrix).

*Methyl (methyl 5,7,8,9-tetra-*O*-acetyl-4-acetylamino-3,4-dideoxy-*D*-glycero-β-*D*-galacto-non-2-ulopyranosid)onate* (**23**).—An anhydrous toluene solution of 16 (30 mg, 0.05 mmol) was treated with tri-*n*-butyltin hydride (82 mg, 0.2 mmol, 4 equiv) in the presence of a catalytic amount of AIBN under a

nitrogen atmosphere. After stirring at 80 °C for 2 h, the solution was evaporated in vacuo to give a residue. The residue was partitioned between acetonitrile and *n*-hexane, and the acetonitrile extract was washed with several portions of *n*-hexane and concentrated to a syrup in vacuo. The syrup was purified by silica gel column chromatography with 4:1 *n*-hexane–acetone to yield **23** (23 mg, 87%): $[\alpha]_D$ −17° (*c* 0.19, MeOH); IR (ν_{max}, CCl_4): 1735 (COO), 1644 (CON) cm^{-1}; ^1H NMR δ: 5.45 (dd, 1 H, $J_{7,8}$ 6.3, $J_{6,7}$ 2.4 Hz, H-7), 5.32 (ddd, 1 H, $J_{8,9a}$ 2.7, $J_{8,9b}$ 6.0 Hz, H-8), 4.65 (dd, 1 H, $J_{9a,9b}$ 12.6 Hz, H-9a), 4.59 (t, 1 H, $J_{4,5}$ 9.9, $J_{5,6}$ 9.9 Hz, H-5), 4.48 (dddd, 1 H, $J_{4,4NH}$ 8.4, $J_{3eq,4}$ 4.2, $J_{3ax,4}$ 9.9 Hz, H-4), 4.18 (dd, 1 H, H-9b), 4.09 (dd, 1 H, H-6), 5.58 (d, 1 H, NH), 3.79 (s, 3 H, $COOCH_3$), 3.25 (s, 3 H, OCH_3), 2.55 (dd, 1 H, $J_{3ax,3eq}$ 13.2 Hz, H-3_{eq}), 1.62 (dd, 1 H, H-3_{ax}), 2.03,2.07, 2.08, 2.11 (each s, 3 H, OAc × 4), 1.89 (s, 3 H, NHAc). FABMS *m/z*: 506 (M^+ + 1) (*m*-NBA as matrix); Anal. Calcd for $C_{21}H_{31}NO_{13}$: C, 49.90; H, 6.18; N, 2.77. Found: C, 50.00; H, 6.44; N 2.61.

*Methyl (methyl 5,7,8,9-tetra-O-acetyl-3,4-dideoxy-4-methoxyacetylamino-*D-glycero-*β*-D-galacto-*non-2-ulopyranosid)onate* (**24**).—An anhydrous toluene solution of **18** (16 mg, 0.026 mmol) was treated with tri-*n*-butyltin hydride (41 mg, 0.1 mmol, 4 equiv) in the presence of a catalytic amount of AIBN under a nitrogen atmosphere. The mixture was processed as described for **23** to yield **24** (12 mg, 86%): mp 82–84 °C; $[\alpha]_D$ +117° (*c* 1.04, MeOH); IR (ν_{max}, CCl_4): 1740 (COO), 1680 (CON) cm^{-1}; ^1H NMR δ: 5.45 (dd, 1 H, $J_{6,7}$ 1.8, $J_{7,8}$ 6.0 Hz, H-7), 5.32 (ddd, 1 H, $J_{8,9a}$ 2.4, $J_{8,9b}$ 6.3 Hz, H-8), 4.69 (t, 1 H, $J_{4,5}$ 10.2, $J_{5,6}$ 10.2 Hz, H-5), 4.66 (dd, 1 H, $J_{9a,9b}$ 12.3 Hz, H-9a), 4.53 (dddd, 1 H, $J_{4,4NH}$ 9.0, $J_{3eq,4}$ 4.5, $J_{3ax,4}$ 11.7 Hz, H-4), 4.17 (dd, 1 H, H-9b), 4.10 (dd, 1 H, H-6), 6.60 (d, 1 H, NH), 3.79 (s, 3 H, $COOCH_3$), 3.36 (s, 3 H, CH_2OCH_3), 3.25 (s, 3 H, 2-OCH_3), 3.86 (d, 1 H, *J* 11.1 Hz, $COCH_2OCH_3$), 3.80 (d, 1 H, $COCH_2OCH_3$), 2.52 (dd, 1 H, $J_{3ax,3eq}$ 13.2 Hz, H-3_{eq}), 1.71 (dd, 1 H, H-3_{ax}), 2.02, 2.04, 2.08, 2.11 (each s, 3 H, OAc × 4). FABMS *m/z*: 536 (M^+ + 1) (*m*-NBA as matrix); Anal. Calcd for $Q_2H_{33}No_{14}$: C, 49.34; H, 6.21; N, 2.62. Found: C, 50.25; H, 6.47; N 2.47.

*Methyl (methyl 5,7,8,9-tetra-*O*-acetyl-4-benzoylamino-3,4-dideoxy-*D-glycero-*β*-D-galacto-*nonulopyranosid)onate* (**25**).—An anhydrous toluene solution of **20** (30 mg, 0.046 mmol) was treated with tri-*n*-butyltin hydride (82 mg, 0.2 mmol, 4 equiv) in the presence of a catalytic amount of AIBN under a nitrogen atmosphere. The mixture was processed as described for **23** to yield **25** (23 mg, 88%): $[\alpha]_D$ +6° (*c* 0.30, MeOH); IR (ν_{max}, CCl_4): 1739 (COO), 1639 (CON) cm^{-1}; ^1H NMR δ: 5.50 (dd, 1 H, $J_{7,8}$ 6.3, $J_{6,7}$ 2.1 Hz, H-7), 5.35 (ddd, 1 H, $J_{8,9a}$ 2.4, $J_{8,9b}$ 6.3 Hz, H-8), 4.74 (t, 1 H, $J_{4,5}$ 9.6, $J_{5,6}$ 9.6 Hz, H-5), 4.69 (dddd, 1 H, $J_{4,4NH}$ 7.2, $J_{3ax,4}$ 11.4, $J_{3eq,4}$ 3.9 Hz, H-4), 4.67 (dd, 1 H, $J_{9a,9b}$ 12.6 Hz, H-9a), 4.20 (dd, 1 H, H-9b), 4.17 (dd, 1 H, H-6), 6.45 (d, 1 H, NH), 3.79 (s, 3 H, $COOCH_3$), 3.28 (s, 3 H, 2-OCH_3), 7.70–7.37 (m, 5 H, C_6H_5), 2.74 (dd, 1 H, $J_{3ax,3eq}$ 13.5 Hz, H-3_{eq}) 1.70 (dd, 1 H, H-3_{ax}), 2.04, 2.05, 2.09, 2.13 (each s, 3 H, OAc × 4). FABMS *m/z*: 568 (M^+ + 1) (*m*-NBA as matrix); Anal. Calcd for $C_{26}H_{33}NO_{13}$: C, 55.02; H, 5.86; N, 2.47. Found: C, 54.65; H, 5.83; N 2.57.

*2-Methyl (methyl 5,7,8,9-tetra-*O*-acetyl-3-bromo-3,4-dideoxy-*D-erythro-*α*-L-altro-*non-2-ulopyranosonate) - 5, 6 - dihydro - 4*H *- 1.3 - oxazine* (**29**).—To a solution of **9** (100 mg, 0.21 mmol) in methanol (20 mL) was added NBS (54 mg, 0.30 mmol). The mixture was processed as described for **16** and **17** to yield **29** (74 mg, 60%) and *methyl (methyl 5,7,8,9-tetra-*O*-acetyl-4-acetylamino-3-bromo-3,4-dideoxy-*D-erythro-*α*-L-allo-*non-2-ulopyranosid)onate* (**28**) (20 mg, 17%). Data for **28**: $[\alpha]_D$ +162° (*c* 0.30, MeOH); ^1H NMR δ: 5.43 (dd, 1H, $J_{6,7}$ 2.4, $J_{7,8}$ 5.4 Hz, H-7), 5.41 (dd, 1 H, $J_{5,6}$ 10.8, $J_{4,5}$ 3.9 Hz, H-5), 5.36 (ddd, 1 H, $J_{8,9a}$ 2.1, $J_{8,9b}$ 6.3 Hz, H-8), 4.67 (dd, 1 H, $J_{9a,9b}$ 12.6 Hz, H-9a), 4.53 (dd, 1 H, H-6), 4.33 (d, 1 H; $J_{3,4}$ 3.6 Hz, H-3), 4.29 (dd, 1 H, H-4), 4.25 (dd, 1 H, H-9b), 8.88 (s, 1 H, NH), 3.80 (s, 3 H, $COOCH_3$), 3.69 (s, 3 H, OCH_3), 2.00, 2.03, 2.05, 2.12 (each s, 3 H, OAc × 4), 1.85 (s, 3 H, NHAc). FABMS *m/z*: 584, 586 (M^+ + 1) (*m*-NBA as matrix).

Data for **29**: $[\alpha]_D$ −9° (*c* 0.40, MeOH); ^1H NMR δ: 5.38 (dd, 1 H, $J_{4,5}$ 3.6, $J_{5,6}$ 11.1 Hz, H-5), 5.35 (dt, 1 H, $J_{7,8}$ 5.1, $J_{6,7}$ 1.8 Hz, H-7), 5.32 (ddd, 1 H, $J_{8,9a}$ 2.4, $J_{8,9b}$ 6.0 Hz, H-8), 4.57 (dd, 1 H, $J_{9a,9b}$ 12.6 Hz, H-9a), 4.50 (d, 1 H, $J_{3,4}$ 4.5 Hz, H-3), 4.17 (dd, 1 H, H-9b), 4.12 (dd, 1 H, H-4), 4.02 (dd, 1 H, H-6), 3.82 (s, 3 H, $COOCH_3$), 2.71 (s, 3 H, =C-CH_3), 2.04, 2.04, 2.05, 2.09 (each s, 3 H, OAc × 4). FABMS *m/z*: 552, 554 (M^+ + 1) (*m*-NBA as matrix).

*2-Methoxymetyl (methyl 5,7,8,9-tetra-*O*-acetyl-3-bromo - 3, 4 - dideoxy -* D *- erythro - α - L - altro - non - 2 - ulopyranosonate) - 5, 6 - dihydro - 4*H *- 1.3 - oxazine* (**30**).—To a solution of **11** (207 mg, 0.41 mmol) in methanol (20 mL), was added NBS (80 mg, 0.44 mmol). The mixture was processed as described for **16** and **17** to yield **30** (223 mg, 93%): $[\alpha]_D$ +14° (*c* 0.91, MeOH); ^1H NMR δ: 5.42 (dd, 1 H, $J_{5,6}$ 10.5, $J_{4,5}$ 3.6 Hz, H-5), 5.37 (dd, 1 H, $J_{7,8}$ 6.6, $J_{6,7}$ 1.8 Hz,

H-7), 5.35 (ddd, 1 H, $J_{8,9a}$ 2.4 Hz, $J_{8,9b}$ 5.4 Hz, H-8), 4.54 (dd, 1 H, $J_{9a,9b}$ 12.6 Hz, H-9a), 4.52 (d, 1 H, $J_{3,4}$ 4.2 Hz, H-3), 4.27 (dd, 1 H, H-4), 4.19 (dd, 1 H, H-9b), 4.05 (dd, 1 H, H-6), 4.03 (d, 1 H, *J* 13.8 Hz, $COCH_2OCH_3$), 3.87 (d, 1 H, $COCH_2OCH_3$), 3.84 (s, 3 H, $COOCH_3$), 3.43 (s, 3 H, CH_2OCH_3), 2.03, 2.06, 2.11, 2.14 (each s, 3 H, OAc × 4). FABMS *m/z*: 582, 584 ($M^+ + 1$) (*m*-NBA as matrix).

2-Phenyl (methyl 5,7,8,9-tetra-O-*acetyl-3-bromo-3,4-dideoxy*-D-erythro-*α*-L-altro-*non-2-ulopyranosonate)-5,6-dihydro-4*H-*1,3-oxazine* (**31**).—To a solution of **13** (180 mg, 0.34 mmol) in methanol (20 mL), was added NBS (70 mg, 0.40 mmol). The mixture was processed as described for **16** and **17** to yield **31** (170 mg, 82%): $[\alpha]_D$ −36° (*c* 1.07, MeOH); ^{1}H NMR *δ*: 5.50 (dd, 1 H, $J_{5,6}$ 10.8, $J_{4,5}$ 3.6 Hz, H-5), 5.39 (ddd, 1 H, $J_{7,8}$ 4.8, $J_{8,9a}$ 2.1, $J_{8,9b}$ 5.4 Hz, H-8), 5.38 (dd, 1 H, $J_{6,7}$ 1.2 Hz, H-7), 4.64 (d, 1 H, $J_{3,4}$ 4.5 Hz, H-3), 4.57 (dd, 1 H, $J_{9a,9b}$ 12.6 Hz, H-9a), 4.43 (dd, 1 H, H-4), 4.20 (dd, 1 H, H-9b), 4.10 (dd, 1 H, H-6), 3.90 (s, 3 H, $COOCH_3$), 7.93–7.38 (m, 5 H, C_6H_5), 1.94, 2.00, 2.10, 2.13 (each s, 3 H, OAc × 4). FABMS *m/z*: 614, 616 ($M^+ + 1$) (*m*-NBA as matrix).

Methyl 5,7,8,9-tetra-O-*acetyl-4-acetylamino-3-bromo-3,4-dideoxy*-D-erythro-*α*-L-altro-*non-2-ulopyranosonate* (**32**).—To a solution of **29** (80 mg, 0.145 mmol) in EtOAc (4 mL), 3 drops of H_2O and 2 drops of HOAc were added. The mixture was stirred at room temperature for 12 h, then evaporated in vacuo to give a residue. The residue was purified by silica gel column chromatography with 3:1 *n*-hexane–acetone to yield **32** (76 mg, 92%): $[\alpha]_D$ +20° (*c* 0.21, MeOH); ^{1}H NMR *δ*: 5.40 (dd, 1 H, $J_{7,8}$ 4.5, $J_{6,7}$ 1.8 Hz, H-7), 5.31 (dt, 1 H, $J_{4,5}$ 4.2, $J_{5,6}$ 11.1 Hz, H-5), 5.30 (ddd, 1 H, $J_{8,9a}$ 2.4, $J_{8,9b}$ 7.2 Hz, H-8), 4.93 (dd, 1 H, $J_{9a,9b}$ 13.2 Hz, H-9a), 4.92 (ddd, 1 H, $J_{3,4}$ 3.0, $J_{4,4NH}$ 9.3 Hz, H-4), 4.38 (dd, 1 H, H-6), 4.25 (d, 1 H, H-3), 4.11 (dd, 1 H, H-9b), 6.93 (d, 1 H, NH), 6.24 (br, 1 H, OH), 3.80 (s, 3 H, $COOCH_3$), 2.03, 2.08, 2.11, 2.16 (each s, 3 H, OAc × 4), 1.94 (s, 3 H, NHAc). FABMS *m/z*: 570, 572 ($M^+ + 1$) (*m*-NBA as matrix).

Methyl 5,7,8,9-tetra-O-*acetyl-3-bromo-3,4-dideoxy-4-methoxyacetylamino*-D-erythro-*α*-L-altro-*non-2-ulopyranosonate* (**33**).—To a solution of **30** (96 mg, 0.164 mmol) in EtOAc (4 mL), 3 drops of H_2O and 2 drops of HOAc were added. The mixture was processed as described for **32** to yield **33** (85 mg, 87%): $[\alpha]_D$ +13° (*c* 0.45, MeOH). ^{1}H NMR *δ*: 5.40 (dd, 1 H, $J_{6,7}$ 1.5, $J_{7,8}$ 4.8 Hz, H-7), 5.36 (ddd, 1 H, $J_{8,9a}$ 1.8, $J_{8,9b}$ 7.2 Hz, H-8), 5.33 (dd, 1 H, $J_{4,5}$ 4.5, $J_{5,6}$ 10.2 Hz, H-5), 4.95 (dd, 1 H, $J_{9a,9b}$ 11.7 Hz, H-9a), 4.94 (ddd, 1 H, $J_{4,4NH}$ 9.6, $J_{3,4}$ 3.0 Hz, H-4), 4.36 (dd, 1 H, H-6), 4.24 (d, 1 H, H-3), 4.10 (dd, 1 H, H-9b), 7.87 (d, 1 H, NH), 5.76 (s, 1 H, OH), 3.93 (d, 1 H, *J* 15.0 Hz, $COCH_2OCH_3$), 3.87 (d, 1 H, $COCH_2OCH_3$), 3.82 (s, 3 H, $COOCH_3$), 3.44 (s, 3 H, CH_2OCH_3), 1.95, 2.04, 2.09, 2.12 (each s, 3 H, OAc × 4). FABMS *m/z*: 600, 602 ($M^+ + 1$) (*m*-NBA as matrix).

Methyl 2,5,7,8,9-penta-O-*acetyl-3-bromo-3,4-dideoxy-4-methoxyacetylamino*-D-erythro-*α*-L-altro-*non-2-ulopyranosonate* (**34**).—To a solution of **33** (40 mg, 0.067 mmol) in pyridine (10 mL), acetic anhydride (10 mL) and a little 4-dimethylaminopyridine were added. This was stirred for 12 h at room temperature, then poured into 0.5 N HCl (40 mL) and extracted with ethyl acetate (180 mL × 3). The extract was washed with sodium hydrogencarbonate solution and brine, dried, and concentrated. The residue was purified on a column of silica gel with 6:4 *n*-hexane–ether to yield **34** (37 mg, 87%): $[\alpha]_D$ −1° (*c* 0.36, MeOH); ^{1}H NMR *δ*: 5.43 (dd, 1 H, $J_{6,7}$ 2.4, $J_{7,8}$ 5.1 Hz, H-7), 5.41 (dd, 1 H, $J_{5,6}$ 10.8, $J_{4,5}$ 4.2 Hz, H-5), 5.17 (ddd 1 H, $J_{3,4}$ 3.0, $J_{4,4NH}$ 9.6 Hz, H-4), 4.98 (ddd, 1 H, $J_{8,9a}$ 2.4, $J_{8,9b}$ 6.0 Hz, H-8), 4.63 (dd, 1 H, $J_{9a,9b}$ 12.3 Hz, H-9a), 4.23 (d, 1 H, H-3), 4.20 (dd, 1 H, H-9b), 4.116 (dd, 1 H, H-6), 7.67 (d, 1 H, NH), 3.98 (d, 1 H, *J* 15.0 Hz, $COCH_2OCH_3$), 3.91 (d, 1 H, $COCH_2OCH_3$), 3.83 (s, 3 H, $COOCH_3$), 3.47 (s, 3 H, CH_2OCH_3), 1.95, 2.03, 2.05, 2.13, 2.22 (each s, 3 H, OAc × 5). FABMS *m/z*: 642, 644 ($M^+ + 1$) (*m*-NBA as matrix).

Methyl 5,7,8,9-tetra-O-*acetyl-4-acetylamino-3,4-dideoxy*-D-glycero-*β*-D-talo-*2-nonulopyranosonate* (**35**).—An anhydrous toluene solution of **32** (40 mg, 0.07 mmol) was treated with tri-*n*-butyltin hydride (100 mg, 0.35 mmol, 5 equiv) in the presence of a catalytic amount of AIBN under a nitrogen atmosphere. The mixture was processed as described for **23** to yield **35** (29 mg, 85%): $[\alpha]_D$ −2° (*c* 0.32, MeOH). IR (ν_{max}, CCl_4): 1740 (COO), 1708 (CON) cm^{-1}; ^{1}H NMR *δ*: 5.39 (dd, 1 H, $J_{7,8}$ 6.3, $J_{6,7}$ 2.1 Hz, H-7), 5.29 (ddd, 1 H, $J_{8,9a}$ 2.4, $J_{8,9b}$ 6.6 Hz, H-8), 4.75 (dddd, 1 H, $J_{3eq,4}$ 4.5, $J_{4,5}$ 3.9, $J_{4,4NH}$ 8.4, $J_{3ax,4}$ 2.4 Hz, H-4), 4.73 (dd, 1 H, $J_{5,6}$ 10.5 Hz, H-5), 4.49 (dd, 1 H, $J_{9a,9b}$ 12.6 Hz, H-9a), 4.29 (dd, 1 H, H-6), 4.04 (dd, 1 H, H-9b), 2.47 (dd, 1 H, $J_{3ax,3eq}$ 15.0 Hz, H-3_{eq}) 1.87 (dd, 1 H, H-3_{ax}), 6.76 (d, 1 H, NH), 4.58 (br, 1 H, OH), 3.87 (s, 3 H, $COOCH_3$), 2.01, 2.04, 2.08, 2.12 (each s, 3 H, OAc × 4), 1.97 (s, 3 H, NHAc). FABMS *m/z*: 492 ($M^+ + 1$) (*m*-NBA as matrix); Anal. Calcd for $C_{20}H_{28}NO_{13}$: C, 48.88; H, 5.95; N, 2.85. Found: C, 48.97; H, 6.82; N 2.76.

Methyl 5,7,8,9-tetra-O-acetyl-3,4-dideoxy-4-methoxyacetylamino-D-glycero-β-D-talo-non-2-ulopyranosonate (**36**).—An anhydrous toluene solution of **33** (30 mg, 0.05 mmol) was treated with tri-*n*-butyltin hydride (73 mg, 0.25 mmol) in the presence of a catalytic amount of AIBN under nitrogen atmosphere. The mixture was processed as described for **23** to yield **36** (22 mg, 85%): $[\alpha]_D$ −7° (*c* 0.29, MeOH); IR (ν_{max}, CCl_4): 1746 (COO), 1694 (CON) cm^{-1}; ^1H NMR δ: 5.39 (dd, 1 H, $J_{6,7}$ 1.8, $J_{7,8}$ 7.2 Hz, H-7), 5.32 (ddd, 1 H, $J_{8,9a}$ 2.4, $J_{8,9b}$ 6.3 Hz, H-8), 4.78 (dddd, 1 H, $J_{3eq,4}$ 4.5, $J_{3ax,4}$ 2.7, $J_{4,5}$ 3.9, $J_{4,4NH}$ 9.0 Hz, H-4), 4.75 (dd, 1 H, $J_{5,6}$ 10.2 Hz, H-5), 4.43 (dd, 1 H, $J_{9a,9b}$ 12.9 Hz, H-9a), 4.39 (d, 1 H, $J_{2OH,3eq}$ 2.1 Hz, 2-OH), 4.30 (dd, 1 H, H-6), 4.08 (dd, 1 H, H-9b), 7.83 (d, 1 H, NH), 2.51 (ddd, 1 H, $J_{3ax,3eq}$ 14.4 Hz, H-3_{eq}), 1.90 (dd, 1 H, H-3_{ax}), 3.95 (d, 1H, *J* 12.0 Hz, $COCH_2OCH_3$), 3.82 (d, 1 H, $COCH_2OCH_3$), 3.87 (s, 3 H, $COOCH_3$), 3.44 (s, 3 H, CH_2OCH_3), 1.98, 2.04, 2.09, 2.12 (each s, 3 H, OAc × 4). FABMS *m/z*: 524 (M^+ + 1) (*m*-NBA as matrix); Anal. Calcd for $C_{21}H_{31}NO_{14}$: C, 48.37; H, 5.99; N, 2.69. Found: C, 47.98; H, 6.07; N 2.67.

Methyl 2,5,7,8,9-penta-O-acetyl-3,4-dideoxy-4-methoxyacetylamino-D-glycero-β-D-talo-non-2-ulopyranosonate (**37**).—To a solution of **36** (15 mg, 0.029 mmol) in pyridine (10 mL), acetic anhydride (10 mL) and a little of 4-dimethylaminopyridine were added. The mixture was processed as described for **34** to yield **37** (14 mg, 87%): $[\alpha]_D$ +3° (*c* 0.16, MeOH). IR (ν_{max}, CCl_4): 1742 (COO), 1695 (CON) cm^{-1}; ^1H NMR δ: 5.45 (dd, 1 H, $J_{6,7}$ 2.1 Hz, $J_{7,8}$ 5.4 Hz, H-7), 5.17 (ddd, 1 H, $J_{8,9a}$ 2.7, $J_{8,9b}$ 6.6 Hz, H-8), 4.81 (dd, 1 H, $J_{4,5}$ 4.2, $J_{5,6}$ 10.0 Hz, H-5), 4.76 (dd, 1 H, $J_{4,4NH}$ 9.0 Hz, H-4), 4.54 (dd, 1 H, $J_{9a,9b}$ 12.6 Hz, H-9a), 4.19 (dd, 1 H, H-6), 4.17 (dd, 1 H, H-9b), 7.57 (d, 1 H, NH), 2.24 (m, 2 H, 3-H_{eq}, H-3_{ax}), 3.97 (d, 1 H, *J* 15.0 Hz, $COCH_2OCH_3$), 3.88 (d, 1 H, $COCH_2OCH_3$), 3.80 (s, 3 H, $COOCH_3$), 3.48 (s, 3 H, CH_2OCH_3), 1.96, 2.03, 2.06, 2.10, 2.20 (each s, 3 H, OAc × 5). FABMS *m/z*: 566 (M^+ + 1) (*m*-NBA as matrix); Anal. Calcd for $C_{21}H_{31}NO_{14}$: C, 49.02; H, 5.90; N, 2.49. Found: C, 48.90; H, 5.98; N 2.50.

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