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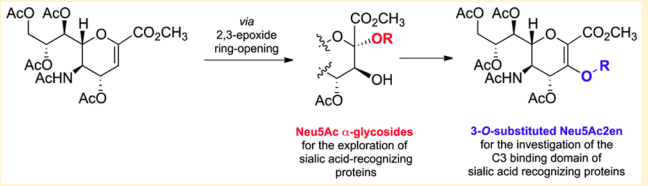
Access to 3-*O*-Functionalized *N*-Acetylneuraminic Acid Scaffolds

Mauro Pascolutti, Paul D. Madge, Robin J. Thomson, and Mark von Itzstein*

Institute for Glycomics, Griffith University – Gold Coast Campus, Queensland 4222, Australia

Supporting Information

ABSTRACT: Direct access to 3-*O*-functionalized 2-α-*N*-acetylneuraminides and their corresponding 2,3-dehydro-2-deoxy-*N*-acetylneuraminic acid derivatives is described. Initially, a stereoselective ring-opening of the key intermediate *N*-acetylneuraminic acid (Neu5Ac) 2,3-β-epoxide with an alcohol provided the 3-hydroxy α-glycoside. *O*-Alkylation of the C3 hydroxyl group generated novel 3-*O*-functionalized Neu5Ac derivatives that provided the corresponding unsaturated derivatives upon elimination.



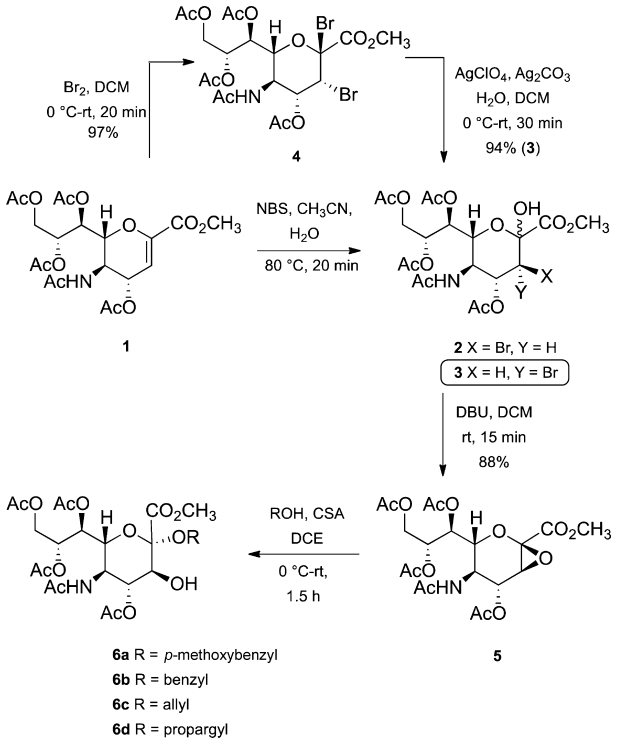
Sialic acids, including *N*-acetylneuraminic acid (Neu5Ac), are essential to a range of biological, pathological, and immunological processes.[1] In nature, α-glycosidically linked sialic acids are found as a part of glycoconjugates, often as the terminating carbohydrate residue.[1] Sialyl-*O*-glycosides are often utilized to investigate and understand the recognition and functional characteristics of sialic acid-recognizing proteins.[2]

Sialic acids are naturally unsubstituted at C3, and little exploration has been undertaken to date to incorporate, and biologically assess, extensive functionalization at this position. Some glycosides of 3-hydroxy-Neu5Ac are known to be refractory to sialidase activity,[3,4] and some inhibit Siglecs,[5] while 3-fluoro-neuraminyl fluorides[6,7] are known to inhibit sialidase action. In addition, C3 *C*-linked alkyl derivatives of the general sialidase inhibitor 2,3-dehydro-2-deoxy-*N*-acetylneuraminic acid (Neu5Ac2en) have provided novel probes of influenza virus sialidase.[8]

The synthesis of C3-modified Neu5Ac and Neu5Ac2en derivatives as biological probes remains a relatively unexplored area. To expand the repertoire of C3 functionality on Neu5Ac and Neu5Ac2en derivatives we sought to introduce C3-oxygen linked functionalities on the Neu5Ac template. Our synthetic strategy toward C3 oxygen-functionalized derivatives requires initial introduction of a hydroxyl group in an equatorial configuration at C3 of the Neu5Ac template. Alkylation of the C3 hydroxyl group, followed by elimination of the C3 proton and an "activating" substituent at the anomeric (C2) position would provide a C3 *O*-functionalized Neu5Ac2en derivative.

Introduction of the desired equatorially substituted hydroxyl group at C3 of the Neu5Ac template can be achieved via opening of the 2,3-β-epoxide **5** (Scheme 1). The epoxide itself is ultimately derived from protected Neu5Ac2en derivative **1**. Direct epoxidation of the 2,3-double bond of **1** was reportedly unsuccessful;[9,10] therefore, we (data not shown) and others[9] have generated epoxide **5** via reaction of *trans*-diaxial bromohydrin **3** with DBU.[9] Bromohydroxylation of **1** (NBS, CH_3CN/H_2O, 80 °C, 20 min) provides a mixture of *trans*-2,3-diequatorial (**2**) and *trans*-2,3-diaxial (**3**) bromohydrins in a reported[9] maximum ratio of 1:3 (Scheme 1). In our hands,

Scheme 1. Synthesis of C3-Hydroxy Neu5Ac α-Glycosides



despite the use of different solvent combinations, **2** and **3** were found to be difficult to separate on silica gel and required several chromatographic purifications for reasonable separation.

The need for a high-yielding synthesis of epoxide **5** led us to investigate the stereoselective formation of the precursor *trans*-2,3-diaxial bromohydrin **3**. Bromohydroxylation of Neu5Ac2en derivative **1** using KBr and H_2O_2 catalyzed by chloroperoxidase provided exclusively *trans*-2,3-diaxial bromohydrin **3**; however,

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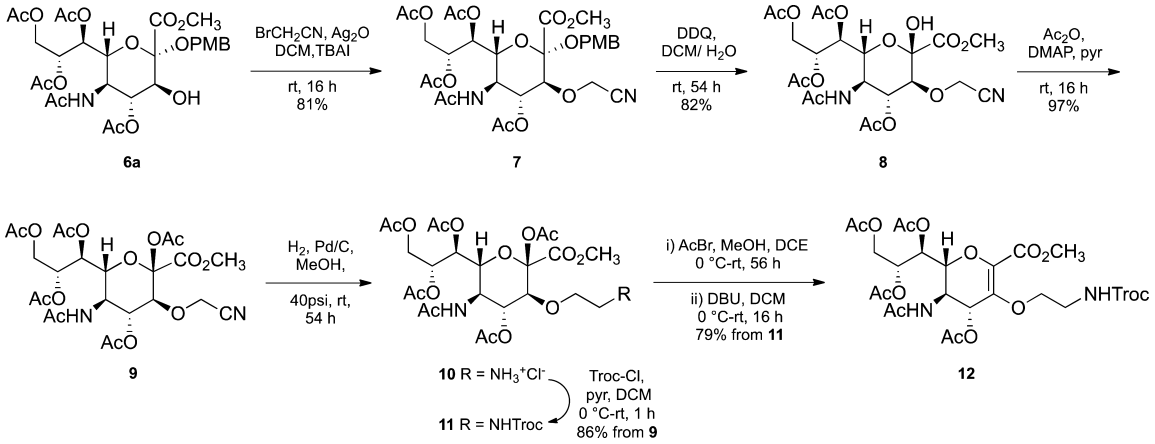
Scheme 2. Synthetic Approach to C3-*O*-Functionalized Neu5Ac2en Derivatives



the reaction yield was only moderate (65%).[11] We examined preparation of **3** through a quick, two-step reaction sequence (Scheme 1), involving initial 2,3-dibromination of Neu5Ac2en derivative **1** followed by hydrolysis of the anomeric bromide to give the *trans*-2,3-diaxial bromohydrin **3** as a single isomer. This pathway takes advantage of the high-yielding formation of 2,3-diaxial dibromide **4**[9] achieved in reaction of Neu5Ac2en **1** with Br_2 in DCM.

Investigations were undertaken to find an efficient method to hydrolyze the anomeric bromide of **4** to produce **3** (a full list of methods examined is given in the Supporting Information, Table S1). Gratifyingly, reaction of **4** under commonly used glycosylation conditions employing AgOTf and Na_2HPO_4,[12] with water as the glycosyl acceptor, proved successful in generating the *trans*-2,3-diaxial bromohydrin **3** in high yield (87% yield; Table S1, entry 7). Under optimized conditions, hydrolysis of the glycosyl bromide was reproducible and scale-independent (Table S1, entry 8). Alternative glycosylation conditions using a combination of $AgClO_4$ and Ag_2CO_3,[13,14] in an optimal 1:1 ratio, resulted in an even higher yield (94% yield; Table S1, entry 11). To the best of our knowledge, this is the first report that describes the synthesis of a single bromohydrin isomer in such high yield. The yield of the target *trans*-2,3-diaxial bromohydrin **3** over two steps from **1** was 91%. Epoxide **5** was subsequently obtained by reaction of **3** with DBU in acetonitrile according to the reported procedure,[9] in good isolated yield (Scheme 1).

Previous publications have reported ring opening of epoxide **5** leading to 2β-halo 3-eq-hydroxy-Neu5Ac derivatives,[9] or to the 3-eq-hydroxy Neu5Ac α-methyl glycoside derivative.[15] While a halide at the anomeric position would make for an easier introduction of the 2,3-double bond in the subsequent synthetic pathway to C3-substituted Neu5Ac2en derivatives, it would undoubtedly prove to be a liability during alkylation reactions on the 3-hydroxy-Neu5Ac template. Therefore, we chose to introduce the *p*-methoxybenzyl group (PMB) for the protection of the anomeric center because it would be stable to *O*-alkylation reaction conditions and could be readily and selectively removed for the introduction of an activating species at C2.

Accordingly, reaction of epoxide **5** was carried-out with *p*-methoxybenzyl alcohol in 1,2-dichloroethane (DCE) in the presence of a catalytic amount of camphorsulfonic acid (CSA),[15] successfully producing the *p*-methoxybenzyl α-glycoside **6a**. When a large excess (20 mol equiv) of the alcohol was used, this reaction was found not only to be rapid and high-yielding (89% yield), but also showed an excellent stereoselectivity (>95:5 α:β). The α-anomeric configuration of the glycoside was confirmed by ^{1}H NMR spectroscopy, which showed a vicinal coupling constant between H-7 and H-8 of 8.4 Hz and a $\Delta\delta$ |H-9a;H-9b| of 0.2 ppm, which is in accordance with the reported data for α-glycosides of Neu5Ac derivatives.[3,10,15] To confirm this, NOE spectroscopy was employed and showed a long-range coupling between H-3 and the benzylic methylene protons indicating the α-configuration of the *p*-methoxybenzyl group at C2.

Given the successful stereoselective formation of the *p*-methoxybenzyl α-glycoside **6a**, we were interested to see if other alcohols would give a similar result. It has been reported that reactions of epoxide **5** with a carbohydrate primary hydroxyl group was unsuccessful under CSA catalysis,[15] whereas primary or secondary carbohydrate hydroxyl groups under Lewis acid catalysis produced only the β-glycosides.[15] Benzyl alcohol, allyl alcohol, and propargyl alcohol were reacted with **5** in the presence of CSA, and in each case the corresponding α-glycoside (**6b**−**6d**) was provided in good yield with excellent stereoselectivity (Scheme 1). While the PMB and benzyl glycosides offer temporary, readily removed protection of the anomeric position, the allyl and propargyl glycosides provide opportunities for further functionalization.[16] The efficient formation of the allyl and propargyl 3-hydroxy-Neu5Ac α-glycosides described herein offers entry into potentially sialidase-resistant compounds with a range of functionality at the anomeric position to explore interactions with biologically important sialic acid-recognizing proteins.[3,5] Moreover, the presence of the C3 hydroxyl group on Neu5Ac α-glycosides **6a**−**d** provides opportunity for further manipulation to investigate the C3 binding domain of *N*-acetylneuraminic acid-recognizing proteins.

To advance the design of 3-*O*-substituted Neu5Ac2en derivatives, we considered the introduction of a functionalized C3 side-chain with the potential for further manipulation. We decided to introduce a nitrogen-terminated alkyl side-chain because of its versatility in chemical derivatization. Many attempts to obtain C3-*O*-alkylated species using electrophiles such as $TsOCH_2CH_2N_3$, $BrCH_2CH_2OTHP$, or $BrCH_2CH_2Br$-(N_3) either under neutral conditions (Ag_2O in DCM or DMF) or in the presence of a strong base such as sodium hydride, at room temperature, failed. This may have been due to either insufficient reactivity of these electrophiles or the tendency for

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these halides to undergo elimination rather than substitution. We therefore thought to introduce at C3 a nitrogen-terminated alkyl side-chain masked as a cyanomethyl ether. Thus, alkylation of the C3 hydroxyl group in **6a** using bromoacetonitrile and freshly prepared silver(I) oxide in DCM successfully produced the C3 cyanomethyl ether derivative **7** in 81% yield (Scheme 2).

Transformation at the anomeric center to introduce an appropriate leaving group for subsequent β-elimination commenced with cleavage of the PMB ether. Reaction of **7** with DDQ in a solution of DCM/H_2O (9:1) for 54 h generated C2 β-hydroxy derivative **8** as a single isomer in 82% yield. Acetylation of **8** using standard conditions (Ac_2O, DMAP, pyridine) provided the corresponding C2 acetoxy derivative **9** in almost quantitative yield. Conversion of the cyano moiety into its corresponding protected amine was accomplished by reducing derivative **9** under a hydrogen atmosphere (40 psi) in the presence of a stoichiometric amount of aq HCl giving the amino salt derivative **10**, which was subsequently Troc-protected to give derivative **11** in 89% yield over two steps.

The insertion of the 2,3-double bond in derivative **11** was initially explored by following our previous reports for the synthesis of C3-*C*-substituted Neu5Ac2en derivatives,[8] through the formation of a glycosyl chloride and subsequent DBU promoted elimination (i. AcCl, MeOH/DCM, 5 °C-rt, 48h; ii. DBU, DCM, rt, 16 h). Unfortunately, this method did not produce the desired eliminated species. Further investigation using different bases (NaH, LiHMDS, *t*BuOK) or silver salts to activate the anomeric chloride proved also to be unsuccessful. Lewis acids were also employed as a promoter of the anomeric acetoxy group of **11** (TMSOTf,[17] BF_3Et_2O[18]) without any encouraging results. In our opinion, the presence of an ether substituent at C3 in the first instance reduces the acidity of H3 and also potentially deactivates the anomeric center for the subsequent elimination. To our delight, introduction of the glycosyl bromide (found to be highly unstable) led to the successful generation of the 2,3-unsaturated species **12**. This was accomplished through a two step sequence: conversion of 2-*O*-acetyl derivative **11** to the 2β-bromo derivative by reaction with in situ generated HBr (AcBr/MeOH at 0 °C in DCE)[19] followed by treatment with DBU in DCM which afforded the desired 3-*O*-[2′-(*N*-Troc)aminoethyl]-Neu5Ac2en derivative **12** in 79% yield.

In summary, we have developed a synthetic approach to provide the first examples of C3-alkoxy-substituted *N*-acetylneuraminic acid derivatives. The high-yielding synthesis of Neu5Ac *trans*-2,3-diaxial bromohydrin **3** improves access to the 2,3-β-epoxide **5**, which can be used to introduce functionality at C2 and C3. The highly stereoselective ring-opening of epoxide **5**, to give the 2-α-*O*-*p*-methoxybenzyl glycoside and other glycosides, provides not only useful transient protection of the anomeric center but also the possibility of creating a range of 3-*O*-functionalized Neu5Ac α-glycosides as a starting point for further investigation of the C3 binding domain. Finally, we have also developed the synthesis to allow introduction of the 2,3-double bond in the presence of C3-*O*-substituents. This provides a novel scaffold to explore the C3 binding of unsaturated *N*-acetylneuraminic acid derivatives, as shown, for example, with C3-*C*-substituted Neu5Ac2en in influenza virus sialidase.[8]

EXPERIMENTAL SECTION

For ^1H and ^{13}C spectra, chemical shifts are expressed as parts per million (ppm, δ) and are relative to the solvent used [$CDCl_3$: 7.26 (s) for ^1H; 77.0 (t) for ^{13}C]. $^1H-^1H$ correlation spectroscopy (COSY) and $^1H-^{13}C$ heteronuclear single quantum coherence (HSQC) was used to confirm ^1H and ^{13}C assignments. High-resolution mass spectra (HRMS) were recorded using a Fourier transform MS (FTMS) instrument fitted with an ESI source.

General Procedure A for the Synthesis of Neu5Ac α-Glycosides 6a–6d. To a solution of epoxide **5** (0.204 mmol) in anhydrous 1,2-dichloroethane (2 mL) at 0 °C under argon was added alcohol (4.08 mmol) followed by a catalytic amount of CSA. After the reaction mixture was stirred for 15 min at 0 °C, the reaction was allowed to warm to room temperature for 1 h. The chlorinated solvent was removed under vacuum, and the residual oily solution was diluted with EtOAc and washed successively with water and brine. The organic phase was dried over Na_2SO_4 and then concentrated. The residue was purified by chromatography on silica gel.

Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-2,6-anhydro-3,5-dideoxy-D-*glycero*-D-*galacto*-non-2-enonate (1). Preparation was completed according to the reported procedure.[20]

Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-2,3-dibromo-2,3,5-trideoxy-β-D-*erythro*-L-*manno*-non-2-ulopyranosonate (4). According to the procedure of Okamoto et al.,[9] bromine (5.17 mL, 100.42 mmol) was added slowly to a solution of glycal **1** (36.0 g, 76.08 mmol) in anhydrous DCM (300 mL) at 0 °C under argon. The solution was stirred for 10 min at 0 °C and for a further 10 min at room temperature. At the completion of the reaction, the mixture was concentrated to dryness under reduced pressure to afford dibromo derivative **4** (46.7 g, yield 97%). The crude product was purified by crystallization from EtOAc/hexane. R_f 0.59 (EtOAc). ^1H NMR (300 MHz, $CDCl_3$): δ 1.94, 2.04, 2.07, 2.10, 2.14 (15H, 5 × s, NHCOCH_3, OCOCH_3 × 4), 2.31 (OH), 3.89 (3H, s, COOCH_3), 4.11 (1H, dd, $J_{9a,8}$ 5.4 Hz, $J_{9a,9b}$ 12.6 Hz, H-9a), 4.39–4.54 (3H, m, H-5, H-6, H-9b), 5.02 (1H, d, $J_{3,4}$ 3.3 Hz, H-3), 5.23 (1H, m, H-8), 5.39–5.42 (2H, m, H-7, NHCOCH$_3$), 5.74 (1H, dd, $J_{4,3}$ 3.3 Hz, $J_{4,5}$ 10.2 Hz, H-4). LRMS (ESI): *m*/*z* 654.0 [($C_{20}H_{27}{}^{79}Br_2NO_{12}$+Na)$^+$, 50%], 656.0 [($C_{20}H_{27}{}^{79,81}Br_2NO_{12}$+Na)$^+$, 100%], 657.9 [($C_{20}H_{27}{}^{81}Br_2NO_{12}$+Na)$^+$, 50%]. The ^1H NMR data was in accordance with that previously reported.[9]

Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3-bromo-3,5-dideoxy-β-D-*erythro*-L-*manno*-non-2-ulopyranosonate (3; Table S1, Entry 11). To a solution of dibromide **4** (1.10 g, 1.74 mmol) and H_2O (38 μL, 2.09 mmol) in DCM (40 mL) at 0 °C was added $AgClO_4$ (542 mg, 2.61 mmol), and the reaction was stirred in the dark for 2–3 min. Ag_2CO_3 (720 mg, 2.61 mmol) was then added, and the solution was stirred vigorously for 10 min at 0 °C and for a further 15 min at room temperature. At the completion of the reaction, the reaction mixture was filtered through Celite; the solid precipitate was washed thoroughly with EtOAc to remove product from the agglomeration of silver salts, and the combined filtrate was concentrated under reduced pressure. The residue was dissolved in EtOAc, and the solution was washed successively with satd aq $NaHCO_3$, water, and brine; dried (Na_2SO_4); filtered; and evaporated under reduced pressure. The crude product was purified by chromatography on silica (hexane/acetone 6:4) to afford the title compound **3** (934 mg, 94%) as a white foam. Note: this reaction was not reproducible on a larger scale (>5 g of **4**) potentially because of the large amount of agglomerated silver salts produced. R_f 0.5 (EtOAc). ^1H NMR (300 MHz, $CDCl_3$): δ 1.90, 2.02, 2.05, 2.07, 2.16 (15H, 5 × s, NHCOCH_3, OCOCH_3 × 4), 3.78 (3H, s, COOCH_3), 4.12 (1H, dd, $J_{9a,8}$ 8.7 Hz, $J_{9a,9b}$ 12.3 Hz, H-9a), 4.36 (2H, m, H-5, H-6), 4.59 (1H, d, $J_{3,4}$ 3.9 Hz, H-3), 4.92 (dd, $J_{9b,8}$ 2.4 Hz, $J_{9a,9b}$ 12.3 Hz, H-9b). 5.25 (1H, m, H-8), 5.34–5.40 (2H, m, H4, H-7), 6.26 (1H, br d, $J_{NH,5}$ 9.3 Hz, NHCOCH$_3$), 6.35 (1H, br s, OH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 20.8, 20.9, 21.0, 21.2 (OCOCH_3 × 4), 23.2 (NHCOCH_3), 45.8 (C-3), 51.4 (C-5), 53.2 (COOCH_3), 63.0 (C-9), 68.7 (C-7), 68.9 (C-4), 71.8 (C-8), 73.2 (C-6), 96.3 (C-2), 167.5 (C-1), 170.6, 170.7, 171.5, 172.4 (NHCOCH$_3$, OCOCH$_3$ × 4). LRMS (ESI): *m*/*z* 592.0 [($C_{20}H_{28}{}^{79}BrNO_{13}$+Na)$^+$, 95%], 594.0

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[$(C_{20}H_{28}{}^{81}BrNO_{12}+Na)^+$, 100%]. The ^{1}H NMR data was in accordance with that previously reported.[9]

*Reaction of **4** with AgOTf and Na_2HPO_4 in Toluene (Table S1, Entry 6).* To a solution of dibromide **4** (100 mg, 0.16 mmol), Na_2HPO_4 (80 mg, 0.62 mmol), and H_2O (3.4 μL, 0.19 mmol) in toluene at 0 °C was added slowly a solution of AgOTf (56 mg, 0.22 mmol) in anhydrous toluene (2 mL). The reaction was stirred vigorously for 15 min at 0 °C and for a further 45 min at room temperature. The progress of the reaction was monitored by TLC. The reaction mixture was filtered through Celite; the solid precipitate was washed thoroughly with EtOAc (2 × 5 mL), and the combined filtrate was concentrated under reduced pressure. The residue was dissolved in EtOAc, and the solution was washed successively with satd aq $NaHCO_3$, water, and brine; dried (Na_2SO_4); filtered; and evaporated under reduced pressure. The crude product was purified by chromatography on silica (hexane/acetone 6:4) to afford the title compound **3** (72.9 mg, yield 81%) as a white foam.

*Reaction of **4** with AgOTf and Na_2HPO_4 in Toluene-DCM (Table S1, Entry 8).* To a solution of dibromide **4** (5.00 g, 8.07 mmol), Na_2HPO_4 (4.47 g, 31.5 mmol), and H_2O (173 μL, 9.68 mmol) in DCM (50 mL) at 0 °C was added slowly a solution of AgOTf (2.90 g, 11.3 mmol) in anhydrous toluene (30 mL). The reaction was stirred vigorously for 30 min at 0 °C and for a further 1.5 h at room temperature. Workup of the reaction as described above for reaction in toluene (Table S1 in the Supporting Information, entry 6) afforded the title compound **3** (3.99 g, yield 87%) as a white foam.

Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-2,3-anhydro-5-deoxy-β-D-*erythro*-L-*gluco*-non-2-ulopyranosonate (5). According to the method of Okamoto et al.,[9] a solution of **3** (2.45 g, 4.30 mmol) in anhydrous acetonitrile (15 mL) under argon at room temperature was treated with DBU (0.81 mL, 5.27 mmol). The mixture was stirred for 15 min at room temperature; then, the reaction mixture was evaporated to a one-third of the initial volume. The solution was loaded onto a silica gel column and chromatographed (toluene/acetone 3:2) to give the title compound **5** (1.85 g, 88% yield) as a white foam. R_f 0.53 (EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.89, 2.03, 2.05, 2.09, 2.10 (15H, 5 × s, NHCOCH_3, OCOCH_3 × 4), 3.59 (1H, s, H-3), 3.83 (3H, s, COOCH_3), 4.05 (1H, dd, $J_{6,7}$ 4.5 Hz, $J_{6,5}$ 8.4 Hz, H-6), 4.15 (1H, dd, $J_{9a,8}$ 6.9 Hz, $J_{9a,9b}$ 12.6 Hz, H-9a), 4.24 (1H, m, H-5), 4.51 (1H, dd, $J_{9b,8}$ 3.0 Hz, $J_{9b,9a}$ 12.6 Hz, H-9b), 5.18 (1H, d, $J_{4,5}$ 7.5 Hz, H-4), 5.25 (1H, m, H-8), 5.40 (1H, dd, $J_{7,6}$ 4.5 Hz, $J_{7,8}$ 5.1 Hz, H-7), 5.51 (1H, d, $J_{NH,5}$ 10.2 Hz, N*H*COCH$_3$). LRMS (ESI): *m*/*z* 512.1 [(M+Na)$^+$, 100%]. The ^{1}H NMR data was in accordance with that previously reported.[9]

Methyl (*p*-Methoxybenzyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-5-deoxy-α-D-*erythro*-L-*gluco*-non-2-ulopyranosid)onate (6a). According to the general procedure A, epoxide **5** (1.11 g, 2.28 mmol) was treated with *p*-methoxybenzyl alcohol (6.3 mL, 45.6 mmol) to yield **6a** (>95:5 α/β, 1.27 g, 89%) as a white solid. α anomer (**6a**): purification by chromatography on silica (EtOAc/DCM gradient 1:1 to 8:2; R_f 0.39 EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.88, 2.01, 2.04, 2.08, 2.12 (15H, 5 × s, NHCOCH_3, OCOCH_3 × 4), 2.80 (1H, d, $J_{OH,3}$ 5.2 Hz, OH), 3.79 (3H, s, ArOCH_3), 3.80 (3H, s, COOCH_3), 3.85 (1H, dd, $J_{3,4}$ 9.6 Hz, $J_{3,OH}$ 5.2 Hz, H-3), 4.04 (1H, dd, $J_{9a,8}$ 6.0 Hz, $J_{9a,9b}$ 12.4 Hz, H-9a), 4.20−4.28 (2H, m, H-5, H-9b), 4.58 (1H, dd, $J_{6,7}$ 2.0 Hz, $J_{6,5}$ 10.8 Hz, H-6), 4.64 (2H, AB q, *J* 11.6 Hz, CH_2Ar), 5.13 (1H, app t, $J_{4,3} \approx J_{4,5}$ 10.0 Hz, H-4), 5.26 (1H, dd, $J_{7,6}$ 2.0 Hz, $J_{7,8}$ 8.4 Hz, H-7), 5.37 (1H, m, H-8), 5.43 (1H, d, $J_{NH,5}$ 10.0 Hz, N*H*COCH$_3$), 6.86 (2H, d, *J* 8.7 Hz, Ar*H*-*m*-OCH$_3$), 7.31 (2H, d, *J* 8.7 Hz, Ar*H*-*o*-OCH$_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 20.7, 20.8, 20.9, 21.0 (OCOCH_3 × 4), 23.1 (NHCOCH_3), 48.4 (C-5), 52.7, 55.3 (ArOCH_3, COOCH_3), 62.4 (C-9), 67.0 (*C*H$_2$Ar), 67.3 (C-7), 68.7 (C-8), 72.6 (C-6), 73.2 (C-4), 74.45 (C-3), 100.2 (C-2), 113.7, 129.5, 129.6, 159.3 (Ar*C* × 6), 169.2, 169.8. 170.1, 170.2 170.6, 171.6 (C-1, NH*C*OCH$_3$, O*C*OCH$_3$ × 4). LRMS (ESI): *m*/*z* 649.9 [(M+Na)$^+$, 100%]. HRMS *m*/*z* calcd for [$C_{28}H_{37}NNaO_{15}$]$^+$: 650.2055. Found: 650.2073.

Methyl (Benzyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-5-deoxy-α-D-*erythro*-L-*gluco*-non-2-ulopyranosid)onate (6b). According to the general procedure A, epoxide **5** (100 mg, 0.204 mmol) was treated with benzyl alcohol (420 μL, 4.08 mmol) to yield **6b** (>95:5 α/β, 103 mg, 84%) as a white solid. α anomer (**6b**): purification by chromatography on silica (EtOAc/hexane 9:1; R_f 0.33 EtOAc/hexane 9:1). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.86, 2.00, 2.04, 2.06, 2.09 (15H, 5 × s, NHCOCH_3, OCOCH_3 × 4), 3.76 (3H, s, COOCH_3), 3.87 (1H, d, $J_{3,4}$ 9.2 Hz, H-3), 4.03 (1H, dd, $J_{9a,8}$ 6.0, $J_{9a,9b}$ 12.4 H-9a), 4.21−4.29 (2H, m, H-5, H-9b), 4.56 (1H, dd, $J_{6,7}$ 2.0, $J_{6,5}$ 10.8 Hz, H-6), 4.72 (2H, AB q, *J* 12.0 Hz, CH_2Ar), 5.18 (1H, app t $J_{4,3} \approx J_{4,5}$ 10.0 Hz, H-4), 5.26 (1H, dd, $J_{7,6}$ 2.0 Hz, $J_{7,8}$ 8.0 Hz, H-7), 5.31−5.36 (1H, m, H-8), 5.84 (1H, d, $J_{NH,5}$ 10.0 Hz, N*H*COCH$_3$), 7.23−7.40 (5H, m, Ar*H*). ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 20.72, 20.75, 20.8, 20.9 (OCH_3 × 4), 23.0 (NHCOCH_3), 48.3 (C-5), 52.7 (COOCH_3), 62.4 (C-9), 67.1 (*C*H$_2$Ar), 67.3 (C-7), 68.9 (C-8), 72.5 (C-6), 73.6 (C-4), 74.4 (C-3), 100.3 (C-2), 127.7, 127.8, 128.3, 137.7 (Ar*C* × 5), 169.3, 169.8, 170.1, 170.3, 170.6, 171.7 (C-1, NH*C*OCH$_3$, O*C*OCH$_3$ × 4). LRMS (ESI): *m*/*z* 620.3 [(M+Na)$^+$, 100%]. HRMS *m*/*z* calcd for [$C_{27}H_{35}NO_{14}$+H]$^+$: 598.2136: Found: 598.2152.

Methyl (Allyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-5-deoxy-α-D-*erythro*-L-*gluco*-non-2-ulopyranosid)onate (6c). According to the general procedure A, epoxide **5** (100 mg, 0.204 mmol) was treated with allyl alcohol (250 μL, 4.08 mmol) to yield **6c** (>95:5 α/β, 94 mg, 85%) as a white solid. α anomer (**6c**): purification by chromatography on silica (EtOAc/hexane 9:1; R_f 0.30 EtOAc/hexane 9:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.88, 22.03, 2.07, 2.08, 2.13 (15H, 5 × s, NHCOCH_3, OCOCH_3 × 4), 3.81 (3H, s, COOCH_3), 3.85 (1H, d, $J_{3,4}$ 9.6 Hz), 4.04−4.11 (2H, m, H-9a, OCH_2), 4.22 (1H, app q, $J_{5,4} \approx J_{5,NH} \approx J_{5,6}$ 10.4 Hz, H-5), 4.26−4.34 (2H, m, H-9b, OCH_2), 4.54 (1H, dd, $J_{6,7}$ 2.0, $J_{6,5}$ 10.8 Hz, H-6), 5.14 (1H, app t $J_{4,3} \approx J_{4,5}$ 10.4 Hz, H-4), 5.19 (1H, m, CH═CH_2), 5.26 (1H, dd, $J_{7,6}$ 2.0 Hz, $J_{7,8}$ 8.0 Hz, H-7), 5.28−5.37 (2H, m, CH═CH_2, H-8), 5.52 (1H, d, $J_{NH,5}$ 10.4 Hz, N*H*COCH$_3$), 5.88−5.98 (1H, m, C*H*═CH$_2$). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 20.82, 20.84, 21.0, 21.1 (OCH_3 × 4), 23.1 (NHCOCH_3), 48.4 (C-5), 52.7 (COOCH_3), 62.5 (C-9), 66.3 (OCH_2), 67.3 (C-7), 68.8 (C-8), 72.6 (C-6), 73.4 (C-4), 74.3 (C-3), 100.1 (C-2), 117.3 (CH═*C*H$_2$), 133.9 (*C*H═CH$_2$), 169.1, 169.8, 170.2, 170.6, 170.6, 171.7 (C-1, NH*C*OCH$_3$, O*C*OCH$_3$ × 4). LRMS (ESI): *m*/*z* 570.3 [(M+Na)$^+$, 100%]. HRMS *m*/*z* calcd for [$C_{23}H_{33}NO_{14}$+H]$^+$: 548.1974. Found: 548.1986.

Methyl (Prop-2′-ynyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-5-deoxy-α-D-*erythro*-L-*gluco*-non-2-ulopyranosid)onate (6d). According to the general procedure A, epoxide **5** (100 mg, 0.204 mmol) was treated with propargyl alcohol (240 μL, 4.08 mmol) to yield **6d** (>95:5 α/β, 92 mg, 83%) as a white solid. α anomer (**6d**): purification by chromatography on silica (EtOAc/hexane 9:1; R_f 0.28 EtOAc/hexane 9:1). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.89, 2.03, 2.07, 2.08, 2.13 (15H, 5 × s, NHCOCH_3, OCOCH_3 × 4), 2.49 (1H, t, *J* 2.4 Hz, C≡CH), 3.83 (3H, s, COOCH_3), 3.88 (1H, d, $J_{3,4}$ 9.6 Hz, H-3), 4.06 (1H, dd, $J_{9a,8}$ 6.4, $J_{9a,9b}$ 12.4 Hz, H-9a), 4.18−4.29 (2H, m, H-5, H-9b), 4.32 (1H, dd, *J* 2.4, *J* 15.6 Hz, OCH_2), 4.48 (1H, dd, *J* 2.4, *J* 15.6 Hz, CH_2), 4.53 (1H, dd, $J_{6,7}$ 2.0, $J_{6,5}$ 10.8 Hz, H-6), 5.17 (1H, app. t, $J_{4,3} \approx J_{4,5}$ 10.0 Hz, H-4), 5.24 (1H, dd, $J_{7,6}$ 2.0 Hz, $J_{7,8}$ 8.4 Hz, H-7), 5.36 (1H, m, H-8), 5.52 (1H, d, $J_{NH,5}$ 10.0 Hz, N*H*COCH$_3$). ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 20.81, 20.82, 20.9, 21.1 (OCH_3 × 4), 23.1 (NHCOCH_3), 48.3 (C-5), 52.8 (COOCH_3), 53.3 (OCH_2), 62.5 (C-9), 67.2 (C-7), 68.6 (C-8), 72.7 (C-6), 73.1 (C-4), 74.1 (C-3), 74.6 (C≡*C*H), 77.2 (*C*≡CH), 99.9 (C-2) 168.6, 169.8, 170.17, 170.20, 170.6, 171.7 (C-1, NH*C*OCH$_3$, O*C*OCH$_3$ × 4). LRMS (ESI): *m*/*z* 568.2 [(M+Na)$^+$, 100%]. HRMS *m*/*z* calcd for [$C_{23}H_{31}NO_{14}$+H]$^+$: 546.1817. Found: 546.1835.

Methyl (*p*-Methoxybenzyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3-*O*-cyanomethyl-5-deoxy-α-D-*erythro*-L-*gluco*-non-2-ulopyranosid)onate (7). Compound **6a** (2.89 g, 4.61 mmol) was dissolved in anhydrous DCM (85 mL) under argon at room temperature and activated MS 4 Å (4.6 g) were added followed by bromoacetonitrile (1.23 mL, 18.41 mmol). After the mixture was stirred for 1 h, freshly prepared Ag_2O (4.27 g, 18.41 mmol) and TBAI (1.70 g, 4.61 mmol) were added. After completion of addition, the reaction mixture was stirred, protected from light, for 16 h at room temperature. The solution was filtered through Celite, and the filtrate was concentrated under reduced pressure. The residue was purified by chromatography on silica (Hexane/acetone 6:4) to yield **7** (2.47 g,

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81%) as a white solid foam. R_f 0.68 (EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.88, 2.01, 2.07, 2.13 (15H, 4 × s, NHCOCH_3, OCOCH_3 × 4), 3.71 (1H, d, $J_{3,4}$ 10.6 Hz, H-3), 3.80 (3H, s, ArOCH_3), 3.82 (3H, s, COOCH_3), 4.03 (1H, dd, $J_{9a,8}$ 6.0 Hz, $J_{9a,9b}$ 12.3 Hz, H-9a), 4.21 (1H, dd, $J_{9b,8}$ 2.4 Hz, $J_{9b,9a}$ 12.3 Hz, H-9b), 4.29 (1H, app q, H-5), 4.43 (2H, app d, J 2.7 Hz, CH_2CN), 4.61 (2H, AB q, J 11.4 Hz, CH_2Ar), 4.71 (1H, m, H-6), 5.13 (1H, dd, $J_{4,5}$ 9.6 Hz, $J_{4,3}$ 10.6 Hz, H-4), 5.26 (1H, dd, $J_{7,6}$ 2.1 Hz, $J_{7,8}$ 9.0 Hz, H-7), 5.29 (1H, m, NHCOCH$_3$), 5.35 (1H, m, H-8,), 6.86 (2H, d, J 11.4 Hz, ArH-m-OCH$_3$), 7.29 (2H, d, J 11.4 Hz, ArH-o-OCH$_3$). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 20.7−20.9 (OCOCH_3 × 4), 23.1 (NHCOCH_3), 48.3 (C-5), 52.8 (ArOCH_3), 55.3 (COOCH_3), 56.9 (CH_2CN), 62.5 (C-9), 66.9 (C-7), 67.6 (CH_2Ar), 68.2 (C-8), 71.7 (C-4), 72.6 (C-6), 82.1 (C-3), 100.3 (C-2), 115.5 (CH$_2$CN), 113.8, 128.9 129.4, 159.4 (ArC × 6), 168.9, 169.6, 170.1, 170.2, 170.6, 171.3 (C-1, NHCOCH$_3$, OCOCH$_3$ × 4). LRMS (ESI): m/z 688.9 [(M+Na)$^+$, 100%]. HRMS m/z calcd for [$C_{30}H_{38}N_2NaO_{15}$]$^+$: 689.2164. Found: 689.2164.

Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3-*O*-cyanomethyl-5-deoxy-*β*-D-*erythro*-L-*gluco*-non-2-ulopyranosonate (8). To a solution of **7** (2.43 g, 3.65 mmol) in a mixture of DCM (150 mL) and H_2O (15 mL) was added DDQ (2.48 g, 10.95 mmol). The reaction was stirred for 54 h at room temperature. The reaction mixture was then washed with satd aq $NaHCO_3$ and brine, dried (Na_2SO_4), and filtered. The organic phase was concentrated under reduced pressure, and the crude residue was purified by chromatography on silica (hexane/acetone 6:4) to yield **8** (1.63 mg, 82%). R_f 0.52 (EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.86, 2.00, 2.08, 2.09, 2.12, (15H, 5 × s, NHCOCH_3, OCOCH_3 × 4), 3.89 (1H, m, H-9a), 3.93 (3H, s, COOCH_3), 4.11 (1H, d, $J_{3,4}$ 9.6 Hz, H-3), 4.21−4.33 (2H, m, H-5, H-6), 4.36 (2H, app d, J 2.1 Hz, CH_2CN), 4.46 (1H, dd, $J_{9b,8}$ 2.4 Hz, $J_{9b,9a}$ 12.3 Hz, H-9b), 5.17 (2H, m, H-4, H-8), 5.31 (1H, dd, $J_{7,6}$ 1.5 Hz, $J_{7,8}$ 5.1 Hz, H-7), 6.01 (1H, br d, $J_{NH,5}$ 12.6 Hz NHCOCH$_3$). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 20.7, 20.9, 21.0 (OCOCH_3 × 4), 23.0 (NHCOCH_3), 49.0 (C-5), 54.0 (COOCH_3), 57.5 (CH_2CN), 62.4 (C-9), 67.8 (C-7), 70.7 (C-6), 71.6 (C-8), 72.6 (C-4), 79.5 (C-3), 94.9 (C-2), 115.6 (CH$_2$CN), 167.9 (C-1), 170.1, 170.3, 171.0, 171.1, 171.3 (NHCOCH$_3$, OCOCH$_3$ × 4). LRMS (ESI): m/z 569.1 [(M+Na)$^+$, 100%]. HRMS m/z calcd for [$C_{22}H_{30}N_2NaO_{14}$]$^+$: 569.1589. Found: 569.1611.

Methyl 5-Acetamido-2,4,7,8,9-penta-*O*-acetyl-3-*O*-cyanomethyl-5-deoxy-*β*-D-*erythro*-L-*gluco*-non-2-ulopyranosonate (9). Compound **8** (1.45 g, 2.66 mmol) was dissolved in anhydrous pyridine (15 mL), and acetic anhydride (10 mL) and DMAP (catalytic amount) were added to the reaction mixture. After the reaction mixture was stirred for 16 h, the reaction mixture was concentrated and the residue was diluted with EtOAc (100 mL) and washed with 1 M aq sol HCl. The aqueous phase was extracted with EtOAc (3 × 100 mL). The organic phases were combined and washed with satd aq $NaHCO_3$ and brine, dried (Na_2SO_4), filtered, and evaporated under reduced pressure, and the residue was purified by chromatography on silica (hexane/acetone 6:4) yielding **9** (1.52 g, 97%). R_f 0.48 (EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.86, 2.02, 2.04, 2.11, 2.13, 2.14 (18H, 6 × s, NHCOCH_3, OCOCH_3 × 5), 3.81 (3H, s, COOCH_3), 4.02 (1H, dd, $J_{9a,8}$ 6.6 Hz, $J_{9a,9b}$ 12.3 Hz, H-9a), 4.12 (1H, d, $J_{3,4}$ 9.6 Hz, H-3), 4.12−4.23 (2H, m, H-5, H-6), 4.39 (2H, AB q, J 16.8 Hz, CH_2CN), 4.42 (1H, dd, $J_{9b,8}$ 2.7 Hz, $J_{9b,9a}$ 12.3 Hz, H-9b), 5.06 (1H, m, H-8), 5.14 (1H, dd, $J_{4,3}$ 9.6 Hz, $J_{4,5}$ 10.2 Hz, H-4), 5.32 (1H, dd, $J_{7,6}$ 1.8 Hz, $J_{7,8}$ 6.0 Hz, H-7), 5.35 (1H, m, NHCOCH$_3$). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 20.7−20.8 (OCOCH_3 × 5), 23.1 (NHCOCH_3), 48.7 (C-5), 53.5 (COOCH_3), 57.5 (CH_2CN), 62.0 (C-9), 67.1 (C-7), 70.8 (C-8), 71.7 (C-4), 72.2 (C-6), 78.7 (C-3), 97.2 (C-2), 115.8 (CH$_2$CN), 165.8 (C-1), 167.8, 169.9, 170.1, 170.2, 170.6, 171.4 (NHCOCH$_3$, OCOCH$_3$ × 5). LRMS (ESI): m/z 611.2 [(M+Na)$^+$, 100%]. HRMS m/z calcd for [$C_{24}H_{32}N_2NaO_{15}$]$^+$: 611.1695. Found: 611.1712.

Methyl 5-Acetamido-2,4,7,8,9-penta-*O*-acetyl-5-deoxy-3-*O*-[2′-(2″,2″,2″-trichlorethoxycarbamido)-ethyl]-*β*-D-*erythro*-L-*gluco*-non-2-ulopyranosonate (11). To a mixture of **9** (950 mg, 1.62 mmol) and Pd/C (10%, 920 mg) in methanol (20 mL) was added 1 M aq sol of HCl (1.8 mL, 1.8 mmol). The mixture was stirred and shaken for 16 h at room temperature in a Parr hydrogenation apparatus at a hydrogen pressure of 40 psi. The reaction mixture was then filtered through Celite, and the filtrate was concentrated to dryness under vacuum. The crude product **10** was ninhydrin positive on TLC and was employed without purification for the following amine protection reaction. R_f 0.42 (EtOAc/MeOH/H_2O 7:2:1).

To an ice-cold solution of **10** (603 mg, 0.95 mmol) in anhydrous DCM (10 mL) and anhydrous pyridine (7.5 mL) under argon was added dropwise trichloroethyl chloroformate (260 μL, 1.90 mmol). The reaction was stirred at room temperature until the disappearance of the starting material by TLC. After 4 h, the reaction mixture was concentrated to dryness and the crude residue was purified by chromatography on silica (hexane/acetone 6:4) to give derivative **11** (626 mg, 86% over two steps from **9**). R_f 0.48 (EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.85, 2.01, 2.03, 2.06, 2.10, 2.17, (18H, 6 × s, NHCOCH_3, OCOCH_3 × 5), 3.28 (2H, m, CH_2b), 3.69 (2H, m, CH_2a), 3.80 (3H, s, COOCH_3), 3.85 (1H, d, $J_{3,4}$ 10.2 Hz, H-3), 4.01−4.10 (2H, m, H-6, H-9a), 4.22 (1H, app q, H-5), 4.45 (1H, dd, $J_{9b,8}$ 2.4 Hz, $J_{9b,9a}$ 12.3 Hz, H-9b), 4.69 (2H, app s, CH_2c), 5.01 (1H, m, H-8), 5.18 (1H, app t, $J_{4,3} \approx J_{4,5}$ 10.2 Hz, H-4), 5.32 (1H, dd, $J_{7,6}$ 2.4 Hz, $J_{7,8}$ 5.1 Hz, H-7), 5.42 (1H, br d, $J_{NH,5}$ 9.9 Hz, NHCOCH$_3$), 5.56 (1H, br t, $J_{NH,CH2}$ 5.4 Hz, NHTroc). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 20.7, 20.8, 20.9, 21.0 (OCOCH_3 × 5), 23.0 (NHCOCH_3), 41.2 (Cb), 48.0 (C-5), 53.4 (COOCH_3), 62.0 (C-9), 67.4 (C-7), 71.3 (C-8), 72.2 (C-6), 72.3 (Ca), 73.0 (C-4), 74.5 (Cc), 78.8 (C-3), 95.6 (CCl$_3$), 97.3 (C-2), 154.7 (COOCH$_2$CCl$_3$), 165.6 (C-1), 168.1, 170.1, 170.2, 170.4, 170.6, 171.2 (NHCOCH$_3$, OCOCH$_3$ × 5). LRMS (ESI): m/z 789.1 (95%), 790.0 (30%), 791.1 (100%), 792.1 (30%), 793.1 (35%) [$C_{27}H_{37}Cl_3N_2O_{17}$+Na$^+$]. HRMS m/z calcd for [$C_{27}H_{37}{}^{35}Cl_3N_2NaO_{17}$]$^+$: 789.1050. Found: 789.1043. [$C_{27}H_{37}{}^{35}Cl_2{}^{37}ClN_2NaO_{17}$]$^+$: 791.1021. Found: 791.1020.

Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-2,6-anhydro-3-*O*-[2′-(2″,2″,2″-trichlorethoxycarbamido)-ethyl]-5-deoxy-D-*glycero*-D-*galacto*-non-2-enonate (12). Compound **11** (796 mg 1.03 mmol) was dissolved in anhydrous 1,2-dichloroethane (15 mL) and acetyl bromide (2.3 mL, 30.9 mmol) under argon, and the solution was cooled to 0 °C, when anhydrous methanol (0.63 mL,15.5 mmol) was added dropwise. The reaction mixture was stirred at room temperature in a sealed vessel for 56 h. The reaction mixture was concentrated under reduced pressure and azeotroped with toluene (2 × 10 mL), giving the corresponding β-glycosyl bromide derivative as a yellow solid, which was used without purification for the subsequent elimination reaction. The crude β-glycosyl bromide was taken up in anhydrous DCM (4 mL) under argon; the solution was cooled to 0 °C; DBU (632 mL, 4.16 mmol) was added, and the reaction was left to stir at room temperature for 16 h. The reaction mixture was diluted with DCM and washed with satd aq NH_4Cl, water, and brine; dried (Na_2SO_4); filtered; and concentrated under reduced pressure. The residue was purified by chromatography on silica (hexane/acetone 6:4) to give compound **12** (580 mg, 79% over two steps from **11**) as a white foam. R_f 0.50 (EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.92, 2.03, 2.05, 2.11 (15H, 4 × s, NHCOCH_3, OCOCH_3 × 4), 3.46 (2H, m, CH_2b), 3.76−3.83 (1H, m, CHa), 3.80 (3H, s, COOCH_3), 4.00−4.05 (1H, m, CHa), 4.15 (1H, dd, $J_{9a,8}$ 6.6 Hz, $J_{9a,9b}$ 12.3 Hz, H-9a), 4.26 (1H, dd, $J_{6,7}$ 3.9 Hz, $J_{6,5}$ 8.7 Hz, H-6), 4.33 (1H, m, H-5), 4.55 (1H, dd, $J_{9b,8}$ 3.0 Hz, $J_{9b,9a}$ 12.3 Hz, H-9b), 4.72 (2H, AB q, J 12.0 Hz, CH_2c), 5.28 (1H, m, H-8), 5.46 (1H, dd, $J_{7,6}$ 3.9 Hz, $J_{7,8}$ 5.1 Hz, H-7), 5.55 (1H, br d, $J_{NH,5}$ 8.7 Hz, NHCOCH$_3$), 5.78 (1H, dd, $J_{4,5}$ 6.6 Hz, H-4), 6.17 (1H, br t, $J_{NH,CH2}$ 5.4 Hz, NHTroc). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 20.7−20.9 (OCOCH_3 × 4), 23.2 (NHCOCH_3), 41.0 (Cb), 48.3 (C-5), 52.5 (COOCH_3), 61.9 (C-9), 67.2 (C-7), 67.7 (C-4), 70.4 (C-8), 72.2 (Ca), 74.5 (Cc), 76.2 (C-6), 95.7 (CCl$_3$), 136.7 (C-3), 142.3 (C-2), 154.8 (COOCH$_2$CCl$_3$), 161.2 (C-1), 170.0, 170.1, 170.6, 170.8 (NHCOCH$_3$, OCOCH$_3$ × 4). LRMS (ESI): m/z 729.6 (85%), 730.4 (30%), 731.1 (100%), 732.1 (30%), 733.1 (35%) [$C_{25}H_{33}Cl_3N_2O_{15}$+Na$^+$]. HRMS m/z calcd for [$C_{25}H_{33}{}^{35}Cl_3N_2NaO_{15}$]$^+$: 729.0839. Found 729.0842. [$C_{25}H_{33}{}^{35}Cl_2{}^{37}ClN_2NaO_{15}$]$^+$: 731.0809. Found: 739.0814.

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■ ASSOCIATED CONTENT

Supporting Information

Copies of NMR spectra for all novel compounds and table of optimization reactions for hydrolysis of **4** to give **3**. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00992.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: m.vonitzstein@griffith.edu.au. Tel: +61755527025. Fax: +61755529040.

Notes

The authors declare no competing financial interest.

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