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A new approach to the synthesis of legionaminic acid analogues†

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Legionaminic acid is a member of the nonulosonic acids, which are a class of sugars considered to be a virulence factor within a wide variety of pathogenic bacteria. We have developed a synthetic pathway towards C-7 analogues of legionaminic acid starting from Neu5Ac, resulting in the complete synthesis of both legionaminic acid, and its C-7 epimer, from a common precursor. Our approach involves the late-stage introduction of the requisite C-7 nitrogen functionality, thus making our strategy amenable to the introduction of a range of different amide groups at C-7 of legionaminic acid.

Introduction

The nonulosonic acid class of sugars consists of 9-carbon α-keto acid carbohydrate monomers. Unique to bacterial species are the recently identified 5,7-diamino-3,5,7,9-tetradeoxy-nonulosonate derivatives, which are an important sub-class of nonulosonic acids.[1] There appear to be two predominant parent compounds: legionaminic acid (Leg, **1**) and pseudaminic acid (Pse, **2**) (Fig. 1).[1] Both Pse and Leg occur naturally as several derivatives, notably with changes in the nature of the amide groups attached to carbon-5 and carbon-7, or in the case of Leg, also as epimers at C-4 and C-8. Legionaminic acid was first reported in 1994, where it was discovered as an α-(2,4)-linked homopolymer component of the *Legionella pneumophila* serotype 1, O-chain LPS.[2] *L. pneumophila* is the causative agent of Legionnaires' disease, and as it is understood that the LPS of serotype 1 is the key determinant for the development of the disease, studies have shown that Leg is important to the virulence capabilities of *L. pneumophila*.[3] Other pathogenic species from which legionaminic acid and its derivatives have been isolated include *Acinetobacter*,[4–7] *Pseudomonas*,[4,8,9] *Salmonella*,[10] *Campylobacter*,[11,12] *Escherichia*,[13–15] and *Vibrio*.[4,16–19]

Given the importance of these nonulosonic acids within a range of human pathogenic bacteria, there is much interest in better understanding their role in pathogenesis and recognition events. However, the structural complexity of these sugars that makes them such attractive biological probes, also makes the synthesis of these sugars quite difficult. Towards this end, a pivotal piece of work by Tsvetkov and colleagues in 2001, describes the synthesis of nine of the possible fifteen stereo-isomers of pseudaminic acid.[20] This work resulted in the absolute stereochemistry of Pse and Leg being confirmed, as

well as the confirmation of the natural stereoisomers 4-*epi*-Leg and 8-*epi*-Leg. The key step in the Tsvetkov synthesis to gain access to the nine-carbon sugars was an aldol condensation between a series of previously prepared hexose sugars and oxaloacetic acid, although the chemical yield for this aldol condensation was below 5% in all cases.[20] In 2015, Matthies *et al.* published a synthesis of five legionaminic acid analogues, *via* a strategy that commenced with D-threonine, and involved a series of chelation-controlled organometallic additions and a Petasis multicomponent reaction.[21] Importantly this work provided a route to legionaminic acid derivatives that could be effectively attached to solid surfaces, thus facilitating serological studies into human pathogens that contain legionaminic acid.[21] In 2017, a complete synthesis of disaccharides of legionaminic acid was published by the Crich group, and involved converting commercially available *N*-acetylneuraminic acid (Neu5Ac, **3**) into a legionaminic acid glycosyl donor *via* a fifteen-step synthetic route with an overall yield of 17%.[22] A chemo-enzymatic approach to legionaminic acid synthesis has recently been reported, by Santra *et al.*,[23] wherein D-fucose was converted through 9 synthetic steps (44% overall yield) into a trideoxy mannose derivative that was subsequently condensed with sodium pyruvate in the presence of the sialic acid aldolase from *Pasteurella multocida* to give **1**.[23]
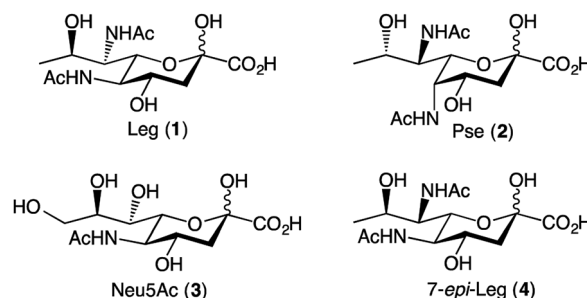
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Fig. 1 Structures of important nonulosonic acids.

Despite the important contribution of all these nonulosonic acid syntheses, to date there does not exist a synthetic pathway towards C-7 analogues of Leg. The C-7 functionality of Leg is vital to its role in the bacteria, which can be seen from the fact that there are multiple naturally occurring C-7 analogues of legionaminic acid,[4,5,12,13,18] as well as the fact that there are multiple steps in the biosynthetic pathway dedicated to introducing the amide functionality at this position.[24] Our approach towards legionaminic acid synthesis was therefore designed to synthesise a range of C-7 analogues of Leg, including the C-7 epimer (4) and a variety of nitrogenous C-7 functionalities; generating all of these analogues from a common, commercially accessible precursor; and keeping the C-7 functionalisation step as late in the synthesis as possible to avoid different functionalities interfering in later reactions.

Results and discussion

We based our approach towards legionaminic acid synthesis on our earlier efforts in synthesising 8-epi-Pse.[25] Our approach towards 8-epi-Pse was achieved in 8 steps and 35% yield from KDN, and involved a halogenation–hydrogenation approach to deoxygenate C-9, and an activation-azide displacement approach to achieve the introduction of the nitrogen functionalities at C-5 and C-7.[25] Based on the experience we gained during our synthesis of 8-epi-Pse, our proposed approach towards C-7 modified legionaminic acids is shown in retrosynthetic terms in Fig. 2. Commencing with Neu5Ac (3), after esterification and methyl glycoside introduction, our plan was to deoxygenate at C-9, and then selectively protect the C-4 and C-8 hydroxyls to give 5, such that the C-7 hydroxyl is available for either activation and displacement with azide thereby leading to 7-epi-legionaminic acids (e.g. 4). Alternatively, the C-7 stereochemistry in 5 could be inverted to give 6, which would then afford legionaminic acids via activation of the inverted C-7 hydroxyl and subsequent displacement with azide and elaboration into C-7 amides.

During some preliminary investigations into legionaminic acid synthesis we found that C-9 deoxygenation late in the synthesis gave a complex mixture of products, and so we opted to perform this step as early in the synthesis as possible. Accordingly, C-9 of the methyl ester methyl glycoside derivative 7 of Neu5Ac was iodinated under Garegg–Samuelsson conditions,[26] which involved refluxing 7 in THF with imidazole,

triphenylphosphine, and iodine chips, to furnish 8 in 77% yield after chromatography (Scheme 1). The presence of the iodine at carbon nine was clearly observed by examination of the ^{13}C NMR spectra, notably by the change in chemical shift of the C-9 peak from δ 60 ppm in 7 to δ 17 ppm in 8. It should be noted that triphenylphosphine oxide salts were particularly difficult to separate from the product 8 and required extensive column chromatography using different solvent systems to obtain 8 pure. Reductive removal of the iodo group in 8 was first attempted using the same conditions as we had developed for the 8-epi-Pse synthesis,[25] which involved exposure of a methanolic solution of 8 to Pd(OH)$_2$/C catalyst, N,N-diisopropylethylamine, under hydrogen gas at atmospheric pressure. Unfortunately, while the reaction gave us good yields of the 9-deoxy derivative 9, it proceeded very slowly, returning ∼60% unreacted 8 after 3 days. However, changing from a hydrogen atmosphere at atmospheric pressure to 300 kPa on the Parr hydrogenator meant the reaction proceeded more quickly, and afforded the desired 9-deoxy derivative 9 in 70% yield (Scheme 1), with only limited amounts of unreacted 8 being recovered. The 9-deoxy product 9 was identified by examination of the ^{1}H NMR spectrum which showed a characteristic doublet at δ 1.3 ppm integrating to 3H indicating the C-9 methyl group, as well as the change in multiplicity of H-8 from a doublet of doublets in 8 to a quartet of doublets in 9.

The final step before we could begin work on modification of the C-7 was the selective protection of the hydroxyl groups attached to C-4 and C-8. As the silyl ether protecting group had served us well at carbon four in our 8-epi-Pse synthesis,[25] we elected to attempt to use this protecting group again. Exposure of the triol 9 to 2.4 molar equivalents of TBSCl and 5 molar equivalents of imidazole overnight at room temperature gave the 4,8-bis-silyl derivative 5 in reasonable yield (75%). The lack of any product with a silyl group at C-7 was expected, based on the pattern of selective protection of sialic acids.[27]

In order to synthesise legionaminic acid with the natural stereochemistry at C-7, an inversion of stereochemistry at C-7 in 5 would be required prior to introduction of the nitrogen-based functionality. We initially explored two approaches towards this: the displacement of a leaving group with a nitrite nucleophile based on the work of Dong et al.,[28] and the displacement with an acetate nucleophile based on the work of Battistini et al.[29] While the former did successfully produce the 7-epi-Neu5Ac derivative 6, the yield over the two reactions was poor
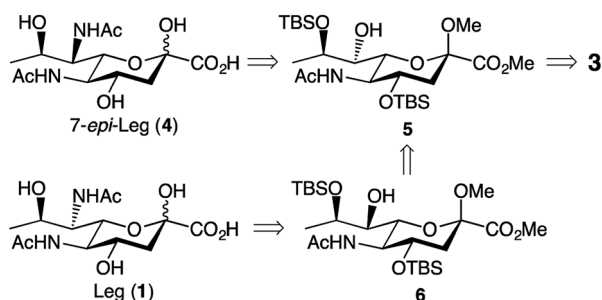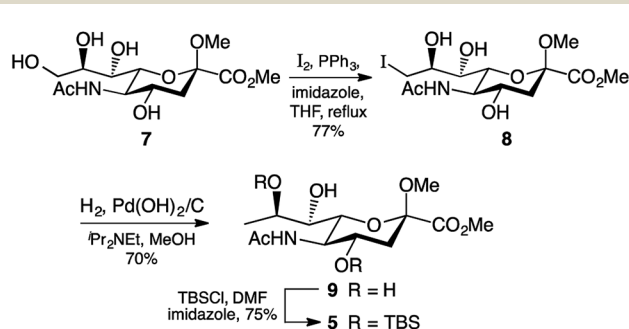

Fig. 2 Our retrosynthetic approach towards legionaminic acids (e.g. 1) and 7-epi-legionaminic acids (e.g. 4).


Scheme 1 Synthesis of the pivotal C-7 hydroxyl derivative 5.

(18%). The latter method gave even poorer results, with none of the desired 7-*epi*-acetoxy derivative formed at all.

Another approach towards inversion of C-7 stereochemistry is the oxidation-reduction approach. This is the approach used by the Crich group for the inversion of C-7 stereochemistry in their legionaminic acid synthesis.[22] The approach uses Dess–Martin periodinane[30] to oxidise the C-7 hydroxyl to a ketone, followed by reduction to regenerate the hydroxyl functionality. Accordingly, treatment of **5** with 1.5 molar equivalents of Dess–Martin periodinane in dichloromethane afforded the 7-keto derivative **10** in an 83% yield after two hours at 0 °C (Scheme 2). Extensive purification through column chromatography was required to remove the iodinane by-product produced during the reaction. The presence of the ketone in **10** was evident by the shift of the C-7 signal in the ^{13}C NMR spectrum, changing from δ 74 ppm in **5** to δ 207 ppm in **10**. Following the successful C-7 oxidation, the next step was to reduce the ketone to the hydroxyl. Following the conditions reported by the Crich group[22] cerium(III) chloride in methanol was added to a solution of the 7-keto derivative **10** in dichloromethane at −78 °C. After one hour, sodium borohydride was added to form Luche's reagent,[31] and after another hour visualisation on TLC showed that the starting material had been completely consumed. To our delight, this reduction gave the desired 7-*epi*-hydroxy derivative **6** in 88% yield, with no formation of **5** detectable. Obtaining a single stereoisomer from reduction of the keto group in **10** was particularly pleasing, since in the work reported by the Crich group[22] gave a 6 : 1 preference of the inverted stereoisomer over the original C-7 stereochemistry.

Due to our prior success in the introduction of nitrogen functionality *via* the azide displacement of a triflate group,[25] we believed that the most viable approach towards our target legionaminic acid derivatives would be to once again explore this avenue. After considerable experimentation, it was found that the conditions that gave the greatest yield of the triflate derivatives **11** and **12** was using *N,N*-dimethylaminopyridine as base, and leaving the reaction overnight at 4 °C. In this way the triflates **11** and **12** could be obtained from **5** and **6** in 74% and 68% yield, respectively (Scheme 3). The presence of the triflate groups in both **11** and **12** could be determined by a quartet peak centred at δ 120 ppm in the respective ^{13}C NMR spectra, due to the fluorine atoms of the triflate group splitting the methyl carbon. To introduce the desired nitrogen functionality at C-7, the triflates **11** and **12** were exposed to an excess of sodium azide in *N,N*-DMF overnight at 4 °C, and gave the azide

Scheme 2 Synthesis of the C-7 epimeric derivative **6**.
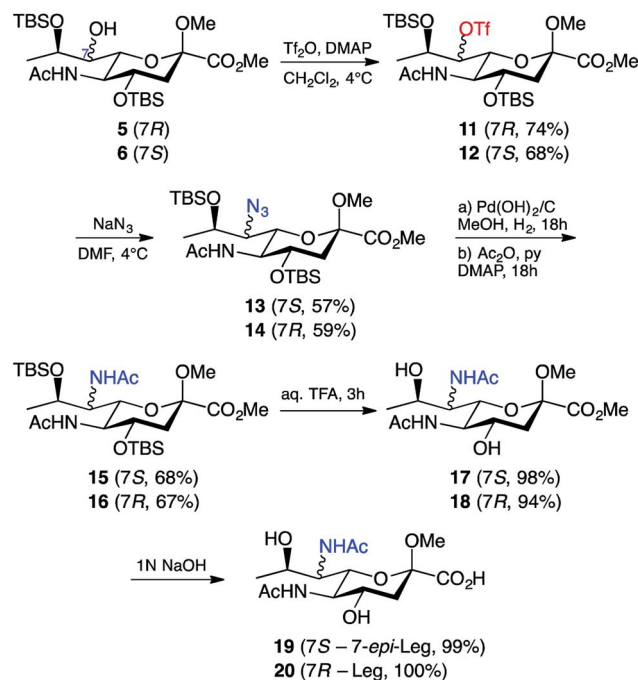
Scheme 3 Synthesis of legionaminic acid derivative **20** and the 7-*epi*-legionaminic acid derivative **19**.

derivatives **13** and **14** in 57% and 59% yields, respectively. The use of alternative sources of azide, *e.g.* trimethylsilyl azide, or altering the reaction conditions, failed to improve the yield of the desired C-7 azide derivatives. The presence of the azide group in **13** and **14** was confirmed by IR spectroscopy, with a sharp peak around 2100 cm^{-1}.

With the nitrogen functionality in place at C-7, it was decided that the reduction and acylation should take place before the deprotection, as the acylation in the presence of free hydroxyl groups would acetylate them and consequently require a second deprotection. The first attempt at reduction of the azide in **13** involved treating **13** with zinc and ammonium chloride in aqueous methanol for half an hour,[32] followed by filtration, evaporation of the solvent *in vacuo*, and acylation (Ac$_2$O/Py) of the crude reaction mixture. This method was successful in giving the 7-acetamido derivative **15**, however only in a disappointing 38% yield. Alternative conditions for the reduction of the azide are hydrogenation conditions, so **13** was exposed to a hydrogen atmosphere in the presence of palladium hydroxide on carbon. The crude product was acetylated (Ac$_2$O/Py) to give a 68% yield of 7-*epi*-Leg derivative **15**. These hydrogenation conditions were also applied to **14**, which gave the protected Leg derivative **16** in a 67% yield. The presence of the second acetamide group in both **15** and **16** was confirmed using both ^{1}H and ^{13}C NMR spectroscopy. By ^{1}H NMR, for compound **15** the presence of a second acetamido group could be seen by a second NH resonance at δ 5.75 ppm (the C-5 NH peak is at δ 6.53 ppm) and a second acetyl peak at δ 1.98 ppm (with the first at δ 1.99 ppm). By ^{13}C NMR, two acetyl peaks could now be seen at δ 170 ppm and δ 23 ppm (carbonyl and methyl carbons, respectively), and the change in chemical shift of the C-7 peak from δ 70 ppm in **13** to δ 54 ppm in **15**. Similar peaks for the
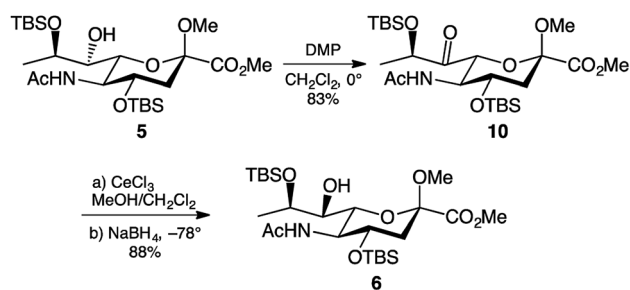
additional acetamido group were also observed in the ^{1}H & ^{13}C spectra of compound **16**. With the key modifications of the 7-acetamido and 9-deoxy functionality in place, the only remaining steps towards our target compounds was removal of the protecting groups: the two silyl ethers, the methyl ester and the methyl glycoside. We began with the silyl ethers and exposed **15** and **16** to 20% aqueous trifluoroacetic acid at room temperature for 2 hours, followed by removal of the solvent *in vacuo*. In this way the de-silylated derivatives **17** and **18** were obtained in high yield (Scheme 3). Compounds **17** and **18** had ^{1}H & ^{13}C NMR spectra consistent with their structures as shown, together with a parent ion in their mass spectra at *m/z* 385 [M + Na]$^+$. The only remaining step was to remove the methyl ester and methyl glycoside; however, this was a step that proved challenging in our synthesis of pseudaminic acid,[33] a very similar substrate. The method eventually successfully utilised in that approach involved the removal of the ester with 1 M NaOH, followed by the removal of the glycoside using acidic resin.[33] Using this published strategy, **17** was stirred in 1 M NaOH overnight at room temperature, then acidified to pH 1 with Dowex-WX50(H$^+$) resin and stirred overnight at 80 °C. Unfortunately, the major product of this reaction could no longer be identified as a non-ulosonic acid. An alternative strategy was to remove just the methyl ester and leave the glycoside intact. To this end, **17** was stirred overnight at room temperature in 1 M NaOH, and after purification, the carboxylic acid **19** was isolated in quantitative yield. The same conditions were then used to quantitatively generate **20** from **18**. This was confirmed by a mass spectrum *m/z* peak of 371.2 [M + Na]$^+$, with the ^{1}H and ^{13}C NMR spectra of **19** and **20** being consistent with the structures shown. Significantly, this research marks the first reported chemical synthesis of 7-*epi*-legionaminic acid, also known as 8-*epi*-acinetaminic acid, a compound that has been reported as being found in *Acinetobacter baumannii*.[34]

Conclusions

Through our synthetic approach towards legionaminic acid analogues, we were able to synthesise the methyl glycosides of both 7-*epi*-legionaminic acid and legionaminic acid from a common precursor in 5 steps with an 18% yield and in 7 steps with an 8% yield, respectively. To date, this represents the first chemical synthesis of 7-*epi*-legionaminic acid, which can also be referred to as 8-*epi*-acinetaminic acid, a compound which has been isolated from *Acinetobacter baumannii*.[34] We were also able to leave the functionalisation of the C-7 nitrogen to the very last step (excepting deprotection reactions), making this a very attractive approach for the synthesis of any other C-7 amide analogues of legionaminic acid.

Experimental

General information

All the reactions were carried out under a nitrogen or an argon atmosphere and monitored by thin layer chromatography (TLC) using Merck precoated aluminium silica plates with detection by charring with 5% (v/v) H$_2$SO$_4$ in ethanol or by ultraviolet (UV)

detection. All the chemicals were purchased from Sigma-Aldrich Chemicals Company. Solvents used in the reactions were either distilled prior to use, following protocols described in Armarego & Chai,[35] or were purchased as anhydrous solvents of 99% purity or greater. 'Flash' chromatography using silica gel was performed routinely in order to purify all products. ^{1}H and ^{13}C NMR spectra were obtained using a Bruker 400 MHz spectrometer at 400 and 100 MHz, respectively. Signals are reported in terms of their chemical shift (δ in ppm) relative to CDCl$_3$ (^{1}H, δ 7.26 ppm and ^{13}C, δ 77.0 ppm), CD$_3$OD (^{1}H, δ 3.30 ppm and ^{13}C, δ 49.0 ppm), CD$_3$CN (^{1}H, δ 1.96 ppm and ^{13}C, δ 1.39 ppm) and D$_2$O (^{1}H, δ 4.78 ppm and ^{13}C external reference used). For ^{1}H spectra, multiplicity, integration intensity, coupling constants and assignment values are reported, two-dimensional COSY, HSQC and HMBC spectra were used to aid assignment. ^{1}H coupling constants are reported in their entirety for each peak seen within a spectrum. Mass spectral analysis was performed using a Bruker esquire 3000 electrospray ionisation mass spectrometer. IR spectral analysis was performed using a Bruker Alpha-P diamond ATR FT-IR spectrometer.

Methyl(methyl 5-acetamido-3,5,9-trideoxy-9-iodo-D-*glycero*-D-galacto-non-2-ulopyranosid)onate (8)

To a solution of **7** (4.71 g, 14.0 mmol) in anhydrous tetrahydrofuran (140 mL), triphenylphosphine (5.49 g, 20.9 mmol), iodine chips (5.32 g, 20.9 mmol), and imidazole (1.90 g, 27.9 mmol) were added. After stirring for 2 h at reflux under a nitrogen atmosphere, Na$_2$S$_2$O$_5$ (2.65 g, 14.0 mmol) in MeOH (140 mL) was added, the mixture absorbed onto non-flash silica, and evaporated *in vacuo*. The desired product (4.73 g, 10.8 mmol, 77%) was obtained using column chromatography on silica gel in CHCl$_3$/MeOH (10 : 1), then EtOAc/MeOH (15 : 1), and obtained as a yellow solid.

^{1}H NMR (400 MHz, CD$_3$CN) δ 7.19 (1H, d, N*H*), 4.09 (1H, ddd, $J_{4,3e}$ = 5.0 Hz, $J_{4,3a}$ = 12 Hz, $J_{4,5}$ = 8.5 Hz, H4), 3.76 (3H, s, CO$_2$C*H$_3$*), 3.70–3.75 (2H, m, H5, undetermined), 3.55–3.63 (2H, m, H9, undetermined), 3.43–3.48 (2H, m, H9′, undetermined), 3.20 (3H, s, COC*H$_3$*), 2.28 (1H, dd, $J_{3e,3a}$ = 13.2 Hz, $J_{3e,4}$ = 5.0 Hz, H3e), 1.98 (3H, s, AcN), 1.65 (1H, dd, $J_{3a,3e}$ = 13.2 Hz, $J_{3a,4}$ = 12 Hz, H3a).

^{13}C NMR (100 MHz CD$_3$CN) δ 175.0 (C1), 169.1 (NC*O*CH$_3$), 100.6 (C2), 72.7, 72.2, 70.4 (C6, C7, C8), 66.7 (C4), 53.9 (C5), 54.5 (C*O*$_2$CH$_3$), 52.2 (COC*H$_3$*), 41.4 (C3), 23.7 (NCO*C*H$_3$), 16.6 (C9).

m/z 470.1 [M + Na]$^+$.

IR = 1737 cm^{-1} (CO$_2$Me), 620 cm^{-1} (C–I).

Methyl(methyl 5-acetamido-3,5,9-trideoxy-D-*glycero*-D-galacto-non-2-ulopyranosid)onate (9)

To a solution of **8** (1.6 g, 3.7 mmol) in methanol (35 mL), Pd(OH)$_2$/C (330 mg) and *N,N*-diisopropylethylamine (64 μL, 0.37 mmol) were added, and the reaction mixture fixed to a Parr hydrogenator under 300 kPa H$_2$. After shaking for 18 h at room temperature additional DIPEA (64 μL, 0.37 mmol) was added, and the reaction allowed to continue. After a further 18 h, the reaction was filtered through a Celite pad and the solvent evaporated *in vacuo*. The desired product (492 mg, 1.53 mmol,

70%), as well as unreacted starting material (923 mg, 2.11 mmol) were obtained using column chromatography on silica gel in $CHCl_3$/MeOH (7 : 1) and obtained as a white solid.

^{1}H NMR (400 MHz, CD_3CN) δ 4.01 (1H, ddd, $J_{4,3e}$ = 5.0 Hz, $J_{4,3a}$ = 18.0 Hz, $J_{4,5}$ = 13.3 Hz, H4), 3.87 (1H, dq, H8), 3.78 (3H, s, CO_2CH_3), 3.71 (1H, dd, $J_{5,4}$ = 13.3 Hz, $J_{5,6}$ = 6.6 Hz, H5), 3.28 (1H, dd, $J_{6,5}$ = 6.6 Hz, $J_{6,7}$ = 7.2 Hz, H6), 3.21 (3H, s, $COCH_3$), 3.17 (1H, dd, H7), 2.28 (1H, dd, $J_{3e,3a}$ = 13.8 Hz, $J_{3e,4}$ = 5.0 Hz, H3e), 1.95 (3H, s, AcN), 1.64 (1H, dd, $J_{3a,3e}$ = 13.8 Hz, $J_{3a,4}$ = 18.0 Hz, H3a), 1.22 (3H, d, $J_{9,8}$ = 6.28 Hz, H9).

^{13}C NMR (100 MHz CD_3OD) δ 174.8 (C1), 171.6 (NCOCH_3), 100.6 (C2), 74.5 (C7), 72.1 (C8), 67.8 (C4), 53.7 (C5), 53.8 (CO_2CH_3), 51.9 ($COCH_3$), 50.0 (C6), 41.6 (C3), 23.0 (NCOCH_3), 21.5 (C9).

m/z 344.2 [M + Na]$^+$.

IR = 1736 cm^{-1} (CO_2Me).

Methyl(methyl 5-acetamido-4,8-O-bis-*tert*-butyldimethylsilyl-3,-5,9-trideoxy-D-*glycero*-D-galacto-non-2-ulopyranosid)onate (5)

To a solution of **9** (662 mg, 2.06 mmol) in anhydrous dimethylformamide (10 mL), *tert*-butyldimethylsilyl chloride (869 mg, 5.77 mmol) and imidazole (825 mg, 12.1 mmol) were added. After stirring for 18 h at room temperature under a nitrogen atmosphere, the reaction was evaporated *in vacuo*. The desired product (847 mg, 1.54 mmol, 75%) was obtained using column chromatography on silica gel in EtOAc/Hex (2 : 3) and obtained as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.18 (1H, d, NH), 4.02–4.09 (2H, m, H4, H8), 3.78–3.82 (2H, m, H6, H7), 3.78 (3H, s, CO_2CH_3), 3.28 (1H, d, $J_{5,6}$ = 14.9 Hz, $J_{5,4}$ = 7.4 Hz, H5), 3.24 (3H, s, $COCH_3$), 2.29 (1H, dd, $J_{3e,3a}$ = 13.1 Hz, $J_{3e,4}$ = 5.0 Hz, H3e), 2.00 (3H, s, AcN), 1.73 (1H, dd, $J_{3a,3e}$ = 13.1 Hz, $J_{3a,4}$ = 10.8 Hz, H3a), 1.30 (3H, s, H9), 0.87 (3×3H, s, $(CH_3)_3CSi$), 0.85 (3×3H, s, $(CH_3)_3CSi$), 0.07 (2×3H, s, CH_3Si), 0.06 (3H, s, CH_3Si), 0.05 (3H, s, CH_3Si).

^{13}C NMR (100 MHz $CDCl_3$) δ 171.2 (C1), 168.6 (NCOCH_3), 99.1 (C2), 73.6 (C7), 70.9 (C6), 69.1 (C8), 67.4 (C4), 53.8 (C5), 52.6 (CO_2CH_3), 51.3 ($COCH_3$), 41.0 (C3), 26.0 ((CH_3)CSi), 25.5 ((CH_3)CSi), 23.4 (NCOCH_3), 18.2 ((CH_3)CSi), 17.8 ((CH_3)CSi), −3.0 (CH_3Si), −4.0 (CH_3Si), −4.2 (CH_3Si), −4.7 (CH_3Si).

IR = 1749 cm^{-1} (CO_2Me), 1047 cm^{-1} (Si–OC).

m/z 572.4 [M + Na]$^+$.

Methyl(methyl 5-acetamido-4,8-O-bis-*tert*-butyldimethylsilyl-3,5,9-trideoxy-7-keto-D-*glycero*-L-altro-non-2-ulopyranosid)onate (10)

To a solution of **5** (254 mg, 0.46 mmol) in anhydrous dichloromethane (5 mL), Dess–Martin periodinane (294 mg, 0.69 mmol) was added. After stirring for 2 h at 0 °C under a nitrogen atmosphere, the reaction was diluted with diethyl ether, washed with 20% aq. $Na_2S_2O_3$ and sat. aq. NaCl, dried (Na_2SO_4), and evaporated *in vacuo*. The desired product (209 mg, 0.38 mmol, 83%) was obtained using column chromatography on silica gel in Hex/EtOAc (3 : 1) and obtained as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.45 (1H, d, $J_{NH,5}$ = 8.7 Hz, NH), 4.74 (1H, q, $J_{8,9}$ = 6.8 Hz, H8), 4.37 (1H, d, $J_{6,7}$ = 10.7 Hz, H6), 4.10 (1H, ddd, $J_{4,3e}$ = 5.0 Hz, $J_{4,3a}$ = 10.7 Hz, $J_{4,5}$ = 9.4 Hz, H4),

3.87 (1H, q, $J_{5,4}$ = 9.4 Hz, $J_{5,6}$ = 10.7 Hz, $J_{5,NH}$ = 8.7 Hz, H5), 3.81 (3H, s, CO_2CH_3), 3.22 (3H, s, $COCH_3$), 2.30 (1H, dd, $J_{3e,3a}$ = 13.2 Hz, $J_{3e,4}$ = 5.0 Hz, H3e), 1.92 (3H, s, AcN), 1.80 (1H, dd, $J_{3a,3e}$ = 13.2 Hz, $J_{3a,4}$ = 10.7 Hz, H3a), 1.42 (3H, d, $J_{9,8}$ = 6.8 Hz, H9), 0.90 (3×3H, s, $(CH_3)_3CSi$), 0.84 (3×3H, s, $(CH_3)_3CSi$), 0.09 (3H, s, CH_3Si), 0.06 (3H, s, CH_3Si), 0.05 (3H, s, CH_3Si), 0.03 (3H, s, CH_3Si).

^{13}C NMR (100 MHz $CDCl_3$) δ 206.7 (C7), 169.7 (C1), 167.9 (NCOCH_3), 99.5 (C2), 73.6 (C6), 72.3 (C8), 67.7 (C4), 54.3 (C5), 52.7 (CO_2CH_3), 51.1 ($COCH_3$), 41.4 (C3), 25.8 ((CH_3)CSi), 25.5 ((CH_3)CSi), 23.5 (NCOCH_3), 20.3 (C9), 18.3 ((CH_3)CSi), 17.8 ((CH_3)CSi), −4.5 (CH_3Si), −4.9 (CH_3Si), −4.9 (CH_3Si), −4.9 (CH_3Si).

IR = 1756 cm^{-1} (CO_2Me), 1733 cm^{-1} (C=O), 1047 cm^{-1} (Si–OC).

m/z 570.5 [M + Na]$^+$.

Methyl(methyl 5-acetamido-4,8-O-bis-*tert*-butyldimethylsilyl-3,5,9-trideoxy-D-*glycero*-L-altro-non-2-ulopyranosid)onate (6)

To a solution of **10** (170 mg, 0.31 mmol) in anhydrous dichloromethane (3 mL) at −78 °C, a solution of cerium(III) chloride (347 mg, 0.93 mmol) in methanol (6 mL) was added. After stirring for 1 h under a nitrogen atmosphere, sodium borohydride (18 mg, 0.47 mmol) was added, and the reaction stirred for a further hour. After completion, the reaction was quenched with sat. aq. NH_4Cl, evaporated *in vacuo*, dissolved in EtOAc, washed with H_2O and sat. aq. NaCl, dried (Na_2SO_4), and evaporated *in vacuo*. The desired product (150 mg, 0.27 mmol, 88%) was obtained using column chromatography on silica gel in EtOAc/Hex (2 : 3) and obtained as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.45 (1H, d, $J_{NH,5}$ = 9.0 Hz, NH), 4.07 (1H, q, $J_{8,7}$ = 5.8 Hz, $J_{8,9}$ = 6.2 Hz, H8), 3.99–4.06 (1H, m, H4), 3.74–3.82 (1H, m, H5), 3.77 (3H, s, CO_2CH_3), 3.67 (1H, dd, $J_{6,7}$ = 3.3 Hz, $J_{6,5}$ = 10.6 Hz, H6), 3.49 (1H, dd, $J_{7,6}$ = 3.3 Hz, $J_{7,8}$ = 5.8 Hz, H7), 3.24 (3H, s, $COCH_3$), 2.23 (1H, dd, $J_{3e,3a}$ = 13.1 Hz, $J_{3e,4}$ = 5.0 Hz, H3e), 1.96 (3H, s, AcN), 1.74 (1H, dd, $J_{3a,3e}$ = 13.1 Hz, $J_{3a,4}$ = 10.6 Hz, H3a), 1.25 (3H, d, $J_{9,8}$ = 6.2 Hz, H9), 0.88 (3×3H, s, $(CH_3)_3CSi$), 0.84 (3×3H, s, $(CH_3)_3CSi$), 0.10 (3H, s, CH_3Si), 0.08 (3H, s, CH_3Si), 0.04 (3H, s, CH_3Si), 0.03 (3H, s, CH_3Si).

^{13}C NMR (100 MHz $CDCl_3$) δ 170.1 (C1), 168.6 (NCOCH_3), 98.9 (C2), 75.8 (C7), 73.6 (C6), 68.1 (C4), 68.0 (C8), 54.4 (C5), 52.5 (CO_2CH_3), 50.8 ($COCH_3$), 41.1 (C3), 25.9 ((CH_3)CSi), 25.6 ((CH_3)CSi), 23.6 (NCOCH_3), 18.1 ((CH_3)CSi), 17.8 ((CH_3)CSi), −4.0 (CH_3Si), −4.4 (CH_3Si), −4.8 (CH_3Si), −4.8 (CH_3Si).

IR = 1755 cm^{-1} (CO_2Me), 1050 cm^{-1} (Si–OC).

m/z 572.5 [M + Na]$^+$.

Methyl(methyl 5-acetamido-4,8-O-bis-*tert*-butyldimethylsilyl-3,5,9-trideoxy-7-trifluoromethanesulfonyl-D-*glycero*-D-galacto-non-2-ulopyranosid)onate (11)

To a solution of **5** (971 mg, 1.77 mmol) in anhydrous dichloromethane (20 mL) at −78 °C, trifluoromethanesulphonic anhydride (415 µL, 2.47 mmol) and N,N-dimethylaminopyridine (634 mg, 5.19 mmol) were added. After stirring for 18 h at 4 °C under an argon atmosphere, the reaction was

washed with cold 1 M HCl, followed by cold H_2O, dried (Na_2SO_4), and evaporated *in vacuo*. The desired product (645 mg, 0.85 mmol, 74%), along with unreacted starting material (269 mg, 0.49 mmol) was obtained using column chromatography on silica gel in EtOAc/Hex (1 : 4) and obtained as a white solid.

^{1}H NMR (400 MHz, CDCl$_3$) δ 5.60 (1H, d, $J_{NH,5}$ = 7.0 Hz, NH), 5.09 (1H, dd, $J_{7,6}$ = 2.6 Hz, $J_{7,8}$ = 2.2, H7), 4.75 (1H, dd, $J_{6,5}$ = 10.3 Hz, $J_{6,7}$ = 2.6 Hz, H6), 4.56 (1H, ddd, $J_{4,3e}$ = 5.0 Hz, $J_{4,3a}$ = 10.7 Hz, $J_{4,5}$ = 5.9 Hz, H4), 4.11 (1H, dq, $J_{8,7}$ = 2.2 Hz, $J_{8,9}$ = 6.3 Hz, H8), 3.78 (3H, s, CO$_2$CH_3), 3.23 (3H, s, COCH_3), 3.02 (1H, ddd, $J_{5,4}$ = 5.9 Hz, $J_{5,NH}$ = 7.0 Hz, $J_{5,6}$ = 2.6 Hz, H5), 2.30 (1H, dd, $J_{3e,3a}$ = 13.2 Hz, $J_{3e,4}$ = 5.0 Hz, H3e), 1.96 (3H, s, AcN), 1.64 (1H, dd, $J_{3a,3e}$ = 13.2 Hz, $J_{3a,4}$ = 10.7 Hz, H3a), 1.35 (3H, d, $J_{9,8}$ = 6.3 Hz, H9), 0.87 (3×3H, s, (CH$_3$)$_3$CSi), 0.85 (3×3H, s, (CH$_3$)$_3$CSi), 0.06 (3H, s, CH$_3$Si), 0.06 (3H, s, CH$_3$Si), 0.05 (3H, s, CH$_3$Si), 0.03 (3H, s, CH$_3$Si).

^{13}C NMR (100 MHz CDl$_3$) δ 170.6 (C1), 167.9 (NCOCH$_3$), 120.1 (CF_3SO$_2$) 99.2 (C2), 90.9 (C7), 69.1 (C8), 68.8 (C6), 65.3 (C4), 57.0 (C5), 52.6 (CO$_2$CH$_3$), 51.2 (COCH$_3$), 41.5 (C3), 25.6 ((CH$_3$)CSi), 25.6 ((CH$_3$)CSi), 23.7 (NCOCH$_3$), 18.5 (C9), 18.0 ((CH$_3$)CSi), 17.8 ((CH$_3$)CSi), −4.6 (CH$_3$Si), −4.9 (CH$_3$Si), −4.9 (CH$_3$Si), −5.2 (CH$_3$Si).

Methyl(methyl 5-acetamido-4,8-*O*-bis-*tert*-butyldimethylsilyl-3,5,9-trideoxy-7-trifluoromethanesulfonyl-D-*glycero*-L-*altro*-non-2-ulo-pyranosid)onate (12)

To a solution of **6** (238 mg, 0.43 mmol) in anhydrous dichloromethane (5 mL) at −78 °C, trifluoromethane-sulphonic anhydride (102 μL, 0.61 mmol) and *N,N*-dimethylaminopyridine (265 mg, 2.17 mmol) were added. After stirring for 18 h at 4 °C under an argon atmosphere, the reaction was washed with cold 1 M HCl, followed by cold H_2O, dried (Na_2SO_4), and evaporated *in vacuo*. The desired product (200 mg, 0.29 mmol, 68%), was obtained using column chromatography on silica gel in EtOAc/Hex (1 : 4) and obtained as a white solid.

^{1}H NMR (400 MHz, CDCl$_3$) δ 5.60 (1H, d, $J_{NH,5}$ = 7.5 Hz, NH), 5.10 (1H, dd, $J_{7,6}$ = 1.1 Hz, $J_{7,8}$ = 4.7, H7), 4.76 (1H, dd, $J_{6,5}$ = 10.4 Hz, $J_{6,7}$ = 1.1 Hz, H6), 4.56 (1H, ddd, $J_{4,3e}$ = 4.9 Hz, $J_{4,3a}$ = 11.0 Hz, $J_{4,5}$ = 5.9 Hz, H4), 4.17 (1H, dq, $J_{8,7}$ = 2.2 Hz, $J_{8,9}$ = 6.3 Hz, H8), 3.78 (3H, s, CO$_2$CH_3), 3.23 (3H, s, COCH_3), 2.99–3.07 (1H, m, H5), 2.31 (1H, dd, $J_{3e,3a}$ = 12.9 Hz, $J_{3e,4}$ = 4.9 Hz, H3e), 2.19 (3H, s, AcN), 1.64 (1H, dd, $J_{3a,3e}$ = 12.9 Hz, $J_{3a,4}$ = 11.0 Hz, H3a), 1.31 (3H, d, $J_{9,8}$ = 6.3 Hz, H9), 0.88 (3×3H, s, (CH$_3$)$_3$CSi), 0.87 (3×3H, s, (CH$_3$)$_3$CSi), 0.14 (3H, s, CH$_3$Si), 0.10 (3H, s, CH$_3$Si), 0.09 (3H, s, CH$_3$Si), 0.07 (3H, s, CH$_3$Si).

^{13}C NMR (100 MHz CDl$_3$) δ 171.4 (C1), 168.2 (NCOCH$_3$), 121.3 (CF_3SO$_2$) 99.1 (C2), 90.9 (C7), 69.2 (C8), 68.8 (C6), 65.0 (C4), 54.9 (C5), 52.5 (CO$_2$CH$_3$), 51.2 (COCH$_3$), 40.2 (C3), 25.8 ((CH$_3$)CSi), 25.7 ((CH$_3$)CSi), 21.1 (NCOCH$_3$), 19.7 (C9), 18.1 ((CH$_3$)CSi), 17.9 ((CH$_3$)CSi), −4.1 (2×CH$_3$Si), −4.3 (CH$_3$Si), −4.7 (CH$_3$Si).

Methyl(methyl 5-acetamido-4,8-*O*-bis-*tert*-butyldimethylsilyl-3,5,7,9-tetradeoxy-7-azido-D-*glycero*-L-*altro*-non-2-ulopyranosid)onate (13)

To a solution of **11** (205 mg, 0.30 mmol) in anhydrous dimethylformamide (2.5 mL) at 0 °C, sodium azide (190 mg, 2.94 mmol) was added. After stirring for 18 h at 4 °C under an argon atmosphere, the reaction was evaporated *in vacuo*. The desired product (96 mg, 0.17 mmol, 57%) was obtained using column chromatography on silica gel in EtOAc/Hex (1 : 4) and obtained as a white solid.

^{1}H NMR (400 MHz, CDCl$_3$) δ 5.33 (1H, d, $J_{NH,5}$ = 8.6 Hz, NH), 4.22 (1H, ddd, $J_{4,3e}$ = 5.0 Hz, $J_{4,3a}$ = 10.4, $J_{4,5}$ = 9.6 Hz, H4), 4.03 (1H, dq, $J_{8,7}$ = 7.3 Hz, $J_{8,9}$ = 6.2 Hz, H8), 3.97 (1H, dd, $J_{6,5}$ = 10.4 Hz, $J_{6,7}$ = 2.7 Hz, H6), 3.78 (3H, s, CO$_2$CH_3), 3.67 (1H, q, $J_{5,4}$ = 9.6 Hz, $J_{5,NH}$ = 8.6 Hz, $J_{5,6}$ = 10.4 Hz, H5), 3.31 (1H, dd, $J_{7,6}$ = 2.7 Hz, $J_{7,8}$ = 7.3 Hz, H7), 3.23 (3H, s, COCH_3), 2.25 (1H, dd, $J_{3e,3a}$ = 13.1 Hz, $J_{3e,4}$ = 5.0 Hz, H3e), 1.97 (3H, s, AcN), 1.69 (1H, dd, $J_{3a,3e}$ = 13.1 Hz, $J_{3a,4}$ = 10.4 Hz, H3a), 1.29 (3H, d, $J_{9,8}$ = 6.16 Hz, H9), 0.90 (3×3H, s, (CH$_3$)$_3$CSi), 0.84 (3×3H, s, (CH$_3$)$_3$CSi), 0.12 (3H, s, CH$_3$Si), 0.09 (3H, s, CH$_3$Si), 0.05 (3H, s, CH$_3$Si), 0.04 (3H, s, CH$_3$Si).

IR = 2106 cm^{-1} (N$_3$), 1752 cm^{-1} (CO$_2$Me), 1100 cm^{-1} (Si–OC).

m/*z* 597.5 [M + Na]$^+$.

Methyl(methyl 5-acetamido-4,8-*O*-bis-*tert*-butyldimethylsilyl-3,5,7,9-tetradeoxy-7-azido-D-*glycero*-D-*galacto*-non-2-ulopyranosid)onate (14)

To a solution of **12** (163 mg, 0.24 mmol) in anhydrous dimethylformamide (2 mL) at 0 °C, sodium azide (155 mg, 2.39 mmol) was added. After stirring for 18 h at 4 °C under an argon atmosphere, the reaction was evaporated *in vacuo*. The desired product (81 mg, 11.9 mmol, 59%) was obtained using column chromatography on silica gel in EtOAc/Hex (1 : 4) and obtained as a white solid.

IR = 2103 cm^{-1} (N$_3$), 1753 cm^{-1} (CO$_2$Me), 1098 cm^{-1} (Si–OC).

m/*z* 597.5 [M + Na]$^+$.

Methyl(methyl 5,7-diacetamido-4,8-*O*-bis-*tert*-butyldimethylsilyl-3,5,7,9-tetradeoxy-D-*glycero*-L-*altro*-non-2-ulopyranosid)onate (15)

To a solution of **13** (91 mg, 0.16 mmol) in methanol (1.5 mL), Pd(OH)$_2$/C (18 mg) was added. After stirring under a hydrogen atmosphere for 18 h at 25 °C, the reaction was filtered through a Celite pad, evaporated *in vacuo*, and redissolved in pyridine/acetic anhydride (2 : 1, 3 mL). 4-Dimethylaminopyridine (10 mg, 0.08 mmol) was added, and the reaction stirred for 18 h at 25 °C under a nitrogen atmosphere. The reaction was then evaporated *in vacuo*, dissolved in ethyl acetate, washed with 1 M HCl followed by H_2O, dried (Na_2SO_4), and evaporated *in vacuo*. The desired product (64 mg, 0.70 mmol, 68%) was obtained using column chromatography on silica gel in EtOAc/Hex (10 : 1).

^{1}H NMR (400 MHz, CDCl$_3$) δ 6.53 (1H, d, $J_{NH,5}$ = 8.4 Hz, C5NH), 5.75 (1H, d, $J_{NH,5}$ = 7.9 Hz, C7NH), 4.38 (1H, dq, $J_{8,7}$ = 2.2 Hz, $J_{8,9}$ = 6.2, H8), 3.84–3.98 (3H, m, H4, H5, H7), 3.74 (3H, s, CO$_2$CH_3), 3.71–3.78 (1H, m, H6), 3.17 (3H, s, COCH_3), 2.21 (1H, dd, $J_{3e,3a}$ = 13.2 Hz, $J_{3e,4}$ = 4.4 Hz, H3e), 1.99 (3H, s, AcN), 1.98 (3H, s, AcN), 1.77 (1H, dd, $J_{3a,3e}$ = 13.2 Hz, $J_{3a,4}$ = 10.4 Hz, H3a), 1.13 (3H, d, $J_{9,8}$ = 6.2 Hz, H9), 0.88 (3×3H, s, (CH$_3$)$_3$CSi), 0.84

(3×3H, s, (CH$_3$)$_3$CSi), 0.10 (3H, s, CH$_3$Si), 0.09 (3H, s, CH$_3$Si), 0.03 (3H, s, CH$_3$Si), 0.03 (3H, s, CH$_3$Si).

^{13}C NMR (100 MHz CDCl$_3$) δ 169.9 (NCOCH$_3$), 169.9 (NCOCH$_3$), 168.0 (C1), 98.8 (C2), 73.2 (C6), 68.8 (C4), 64.7 (C8), 53.9 (C7), 53.3 (C5), 52.3 (CO$_2$CH$_3$), 50.3 (COCH$_3$), 41.1 (C3), 25.9 ((CH$_3$)CSi), 25.5 ((CH$_3$)CSi), 23.6 (NCOCH$_3$), 23.5 (C9), 23.3 (NCOCH$_3$), 17.9 ((CH$_3$)CSi), 17.8 ((CH$_3$)CSi), −4.1 (CH$_3$Si), −4.4 (CH$_3$Si), −4.8 (CH$_3$Si), −4.9 (CH$_3$Si).

IR = 1756 cm^{-1} (CO$_2$Me), 1042 cm^{-1} (Si–OC).

m/z 613.5 [M + Na]$^+$.

Methyl(methyl 5,7-diacetamido-4,8-O-bis-tert-butyldimethylsilyl-3,5,7,9-tetradeoxy-D-glycero-D-galacto-non-2-ulopyranosid)onate (16)

To a solution of **14** (76 mg, 0.13 mmol) in methanol (1 mL), Pd(OH)$_2$/C (15 mg) was added. After stirring under a hydrogen atmosphere for 18 h at 25 °C, the reaction was filtered through a Celite pad, evaporated *in vacuo*, and redissolved in pyridine/acetic anhydride (2 : 1, 1.5 mL). 4-Dimethylaminopyridine (5 mg, 0.04 mmol) was added, and the reaction stirred for 18 h at 25 °C under a nitrogen atmosphere. The reaction was then evaporated *in vacuo*, dissolved in ethyl acetate, washed with 1 M HCl followed by H$_2$O, dried (Na$_2$SO$_4$), and evaporated *in vacuo*. The desired product (52 mg, 0.09 mmol, 67%) was obtained using column chromatography on silica gel in EtOAc/Hex (7 : 1).

^{1}H NMR (400 MHz, CDCl$_3$) δ 6.53 (1H, d, $J_{NH,7}$ = 6.8 Hz, C7N*H*), 5.94 (1H, d, C5N*H*), 4.36 (1H, ddd, $J_{8,7}$ = 5.4 Hz, $J_{8,9}$ = 6.0, H8), 3.85–3.89 (3H, m, H4, H5, H7), 3.72–3.78 (1H, m, H6), 3.72 (3H, s, CO$_2$C*H*$_3$), 3.14 (3H, s, COC*H*$_3$), 2.19 (1H, dd, $J_{3e,3a}$ = 12.6 Hz, $J_{3e,4}$ = 3.3 Hz, H3e), 1.97 (3H, s, AcN), 1.95 (3H, s, AcN), 1.75 (1H, dd, $J_{3a,3e}$ = 12.6 Hz, $J_{3a,4}$ = 10.3 Hz, H3a), 1.10 (3H, d, $J_{9,8}$ = 6.0 Hz, H9), 0.86 (3×3H, s, (CH$_3$)$_3$CSi), 0.81 (3×3H, s, (CH$_3$)$_3$CSi), 0.08 (3H, s, CH$_3$Si), 0.06 (3H, s, CH$_3$Si), 0.01 (3H, s, CH$_3$Si), 0.01 (3H, s, CH$_3$Si).

^{13}C NMR (100 MHz CDCl$_3$) δ 169.9 (NCOCH$_3$), 169.9 (C1), 168.0 (NCOCH$_3$), 98.7 (C2), 73.1 (C6), 68.8 (C4), 64.6 (C8), 53.9 (C7), 53.2 (C5), 52.3 (CO$_2$CH$_3$), 50.3 (COCH$_3$), 41.1 (C3), 25.9 ((CH$_3$)CSi), 25.5 ((CH$_3$)CSi), 23.6 (NCOCH$_3$), 23.5 (NCOCH$_3$), 23.3 (C9), 17.9 ((CH$_3$)CSi), 17.7 ((CH$_3$)CSi), −4.2 (CH$_3$Si), −4.4 (CH$_3$Si), −4.8 (CH$_3$Si), −4.9 (CH$_3$Si).

IR = 1754 cm^{-1} (CO$_2$Me), 1043 cm^{-1} (Si–OC).

m/z 613.5 [M + Na]$^+$.

Methyl(methyl 5,7-diacetamido-3,5,7,9-tetradeoxy-D-glycero-L-altro-non-2-ulopyranosid)onate (17)

A solution of **15** (65 mg, 0.11 mmol) in trifluoroacetic acid/water (4 : 1, 1 mL) was stirred for 2 h at 25 °C, then evaporated *in vacuo*. The desired product (39 mg, 0.11 mmol, 98%) was obtained using column chromatography on silica gel in EtOAc/MeOH (4 : 1) and obtained as a white solid.

^{1}H NMR (400 MHz, CD$_3$OD) δ 8.09 (1H, d, $J_{NH,7}$ = 9.1 Hz, C7N*H*), 4.53 (1H, dq, $J_{8,7}$ = 6.4 Hz, $J_{8,9}$ = 6.4 Hz, H8), 3.83 (3H, s, CO$_2$C*H*$_3$), 3.82–3.97 (3H, m, H4, H5, H7), 3.62 (1H, dd, $J_{6,5}$ = 10.4 Hz, $J_{6,7}$ = 1.6 Hz, H6), 3.21 (3H, s, COC*H*$_3$), 2.35 (1H, dd, $J_{3e,3a}$ = 13.0 Hz, $J_{3e,4}$ = 4.5 Hz, H3e), 2.35 (3H, s, AcN), 2.03

(3H, s, AcN), 1.69 (1H, dd, $J_{3a,3e}$ = 13.0 Hz, $J_{3a,4}$ = 10.8 Hz, H3a), 1.11 (3H, d, $J_{9,8}$ = 6.4 Hz, H9).

^{13}C NMR (100 MHz CD$_3$OD) δ 174.3 (NCOCH$_3$), 173.5 (C1), 170.4 (NCOCH$_3$), 100.3 (C2), 78.2 (C6), 67.3 (C4), 66.4 (C8), 54.4 (C5), 53.6 (CO$_2$CH$_3$), 53.3 (C7), 51.6 (COCH$_3$), 41.4 (C3), 22.9 (NCOCH$_3$), 22.6 (NCOCH$_3$), 20.5 (C9).

IR = 1739 cm^{-1} (CO$_2$Me).

m/z 385.3 [M + Na]$^+$.

Methyl(methyl 5,7-diacetamido-3,5,7,9-tetradeoxy-D-glycero-D-galacto-non-2-ulopyranosid)onate (18)

A solution of **16** (43 mg, 0.07 mmol) in trifluoroacetic acid/water (4 : 1, 1 mL) was stirred for 3 h at 25 °C, then evaporated *in vacuo*. The desired product (25 mg, 0.07 mmol, 94%) was obtained using column chromatography on silica gel in EtOAc/MeOH (4 : 1) and obtained as a white solid.

^{1}H NMR (400 MHz, CD$_3$OD) δ 4.52 (1H, ddd, $J_{8,7}$ = 12.7 Hz, $J_{8,9}$ = 6.4 Hz, H8), 3.93 (1H, dd, H7), 3.89 (1H, ddd, H4), 3.82 (3H, s, CO$_2$C*H*$_3$), 3.80–3.86 (1H, m, H5), 3.60 (1H, dd, H6), 3.19 (3H, s, COC*H*$_3$), 2.34 (1H, dd, $J_{3e,3a}$ = 13.0 Hz, $J_{3e,4}$ = 4.5 Hz, H3e), 2.34 (3H, s, AcN), 2.02 (3H, s, AcN), 1.68 (1H, dd, $J_{3a,3e}$ = 13.0 Hz, $J_{3a,4}$ = 10.9 Hz, H3a), 1.10 (3H, d, $J_{9,8}$ = 6.36 Hz, H9).

^{13}C NMR (100 MHz CD$_3$OD) δ 174.29 (NCOCH$_3$), 173.47 (C1), 170.42 (NCOCH$_3$), 100.27 (C2), 78.19 (C6), 67.28 (C4), 66.40 (C8), 54.37 (C5), 53.60 (CO$_2$CH$_3$), 53.31 (C7), 51.60 (COCH$_3$), 41.40 (C3), 22.94 (NCOCH$_3$), 22.56 (NCOCH$_3$), 20.49 (C9).

IR = 1737 cm^{-1} (CO$_2$Me).

m/z 385.3 [M + Na]$^+$.

Methyl 5,7-diacetamido-3,5,7,9-tetradeoxy-D-glycero-L-altro-non-2-ulopyranosidonic acid (19)

A solution of **17** (39 mg, 0.11 mmol) in 1 M sodium hydroxide (1 mL) was stirred for 18 h at 25 °C and evaporated *in vacuo*. The desired product (37 mg, 0.11 mmol, 99%) was obtained using column chromatography on reversed phase silica gel in H$_2$O and obtained as a white solid.

^{1}H NMR (400 MHz, D$_2$O) δ 4.53 (1H, m, H8), 3.61–4.00 (3H, m, H4, H6, H7), 3.16–3.22 (1H, m, H5), 3.16 (3H, s, COC*H*$_3$), 2.37 (1H, dd, $J_{3e,3a}$ = 13.2 Hz, $J_{3e,4}$ = 4.7 Hz, H3e), 2.08 (3H, s, AcN), 2.07 (3H, s, AcN), 1.70 (1H, t, $J_{3a,3e}$ = 13.2 Hz, $J_{3a,4}$ = 12.0 Hz, H3a), 1.10 (3H, d, $J_{9,8}$ = 6.3 Hz, H9).

m/z 371.2 [M + Na]$^+$.

Methyl 5,7-diacetamido-3,5,7,9-tetradeoxy-D-glycero-D-galacto-non-2-ulopyranosidonic acid (20)

A solution of **18** (26 mg, 0.07 mmol) in 1 M sodium hydroxide (1 mL) was stirred for 18 h at 25 °C and evaporated *in vacuo*. The desired product (25 mg, 0.07 mmol, 100%) was obtained using column chromatography on reversed phase silica gel in H$_2$O and obtained as a white solid.

^{1}H NMR (400 MHz, D$_2$O) δ 4.51 (1H, m, H8), 3.58–4.04 (4H, m, H4, H5, H6, H7), 3.17 (3H, s, COC*H*$_3$), 2.32 (1H, dd, $J_{3e,3a}$ = 13.0 Hz, $J_{3e,4}$ = 4.5 Hz, H3e), 2.32 (3H, s, AcN), 2.03 (3H, s, AcN), 1.69 (1H, t, $J_{3a,3e}$ = 13.0 Hz, $J_{3a,4}$ = 10.9 Hz, H3a), 1.08 (3H, d, $J_{9,8}$ = 6.4 Hz, H9).

m/z 371.2 [M + Na]$^+$.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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