A facile synthesis of Neu5Ac2en derivatives from the glycosides of *N*-acetylneuraminic acid

Gaik B. Kok, Darrin Groves and Mark von Itzstein *

Department of Medicinal Chemistry, Monash University (Parkville Campus), 381 Royal Parade, Parkville 3052, Victoria, Australia

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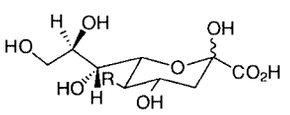
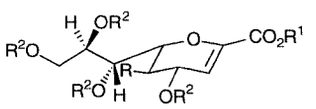
In a one-pot reaction, acetolysis of some functionalised methyl glycosides of *N*-acetylneuraminic acid (Neu5Ac) methyl ester provides a direct and efficient entry into the corresponding 2,3-unsaturated (Neu5Ac2en) derivatives. Other glycosides of Neu5Ac, such as benzyl and 2-(trimethylsilyl)ethyl glycosides, like their methyl counterpart, are also transformed into the 2,3-unsaturated analogues. This reaction has also been applied to the synthesis of some novel 4-bis-substituted-Neu5Ac2en derivatives, which in turn has led to the synthesis of the C-4 homologue of the per-acetylated methyl ester of Neu5Ac2en, compound **10**.

Introduction

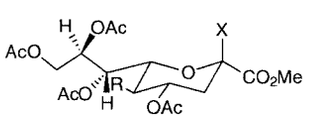
The 2,3-unsaturated derivatives of *N*-acetylneuraminic acid (Neu5Ac, **1**) constitute an important class of ulosonic acids. Some of these carbohydrates have biological activity as inhibitors of sialidases. For example, 5-acetamido-2,6-anhydro-3,5-dideoxy-D-*glycero*-D-*galacto*-non-2-enonic acid (Neu5Ac2en, **2**) itself, first reported nearly thirty years ago by Meindl and Tuppy,[1] still remains one of the most potent inhibitors of the sialidase (EC 3.2.1.18) from *Vibrio cholerae*. Several years ago, we reported[2] that some C-4 nitrogen-substituted 2,3-unsaturated Neu5Ac derivatives have potent activity against the influenza virus sialidase. In addition, Neu5Ac2en **2** itself and its *N*-glycolyl analogue **3** have been found[3] as metabolic products in body fluids and secretions. Moreover, these 2,3-unsaturated or glycal ulosonic acid derivatives have also been employed[4] as reactive building blocks for the construction of oligosaccharides and other higher carbohydrates. Thus, this class of ulosonic acids and various derivatives are an intensely investigated area of organic synthesis.



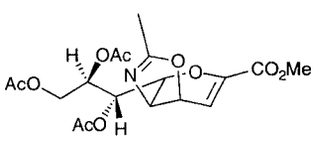
1, R = NHAc



2, $R^1 = R^2 = H$, R = NHAc
3, $R^1 = R^2 = H$, R = $NHCOCH_2OH$
4, R^1 = Me, R^2 = Ac, R = NHAc



5a, X = Cl, R = NHAc
5b, X = Br, R = NHAc



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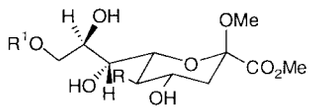
Two different strategies have been reported for the preparation of the per-acetylated methyl ester of Neu5Ac2en (Neu4,5,7,8,9$Ac_5$2en1Me, **4**), and hence of Neu5Ac2en **2** itself, from Neu5Ac. One strategy has involved conversion of Neu5Ac into unstable acetohalogenoses (**5a** and **5b**) and subsequent elimination of HX (X = Br or Cl) with bases such as DBU and Et_3N.[5] More recently, a well known and efficient method for this transformation from easily accessible starting materials was introduced by Claesson and Luthman.[6] Thus, the oxazoline **6** was prepared in three steps from **1** following sequential methanolysis, per-acetylation and elimination of acetic acid with trimethylsilyl triflate (TMSOTf). While these strategies are quite straightforward when applied to the synthesis of **4** itself, they cannot readily be applied to the synthesis of functionalised Neu5Ac2en systems in general.

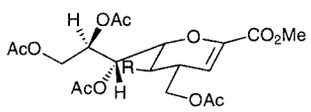
Over the years, many transformations have been carried out on the saturated Neu5Ac system in efforts to provide a systematic understanding of structure–activity relationships of sialic acids at the molecular level. During these transformations, it is generally necessary for the anomeric hydroxy group to be suitably protected. In this regard, the β-methyl glycoside of Neu5Ac1Me, compound **7**, readily accessible[7] *via* methanolysis of Neu5Ac, is often chosen as a starting material. The methyl glycosidic bond is usually compatible with the various conditions employed for the subsequent chemical manipulation of the remaining hydroxy groups. However, cleavage of the glycosidic linkage to give the reducing sugar, or the conversion of the Neu5Ac system into its corresponding Neu5Ac2en system, is a challenge. Whilst deglycosidation of some α-methyl ketosides of Neu5Ac may be achieved enzymically, for example with fowl plague sialidase,[8] in most cases, the removal of the methyl glycoside usually requires harsh aqueous acid hydrolysis at elevated temperatures. Direct conversion of the methyl glycoside into the corresponding unstable 2-halogeno derivative also employs drastic conditions with reagents such as hydrogen chloride (or bromide). In the case of the synthesis of Neu5Ac2en systems, these intermediates will then have to be subsequently suitably manipulated to install the 2,3-olefinic double bond into the systems. It is therefore not surprising that most, if not all, of the previously reported[1] structurally varied Neu5Ac2en derivatives have been prepared using Neu5Ac2en **2** itself as starting material. This latter approach also has its limitations however; the existing 2,3-olefinic double bond in the Neu5Ac2en system necessarily limits functional group manipulations of the remaining hydroxy groups to mild conditions. Ideally, a protocol to accomplish the direct conversion of glycosides into glycals would be highly desirable.

In a recent paper, we briefly reported[9] our findings on direct entry into some functionalised Neu5Ac2en systems from the corresponding Neu5Ac1Me β-methyl glycosides using acetic

anhydride in the presence of acetic and sulfuric acids. The first reaction studied was the acetolysis of the β-methyl glycoside of Neu5Ac1Me itself, compound **7**, and this process was subsequently extended to more elaborated derivatives of **7**. This present work is concerned with the evaluation of the scope and efficacy of this reaction and, in particular, with the extension of this method to the synthesis of some novel 4-bis-substituted-Neu5Ac2en derivatives. This has provided an avenue into the synthesis of the C-4 homologue of per-acetylated Neu5Ac2en1Me, compound **10**.



7, R^1 = H, R = NHAc
8, R^1 = Ts, R = NHAc
9, R^1 = TBDPS, R = NHAc



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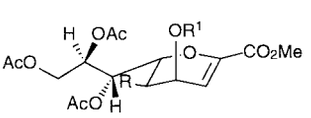
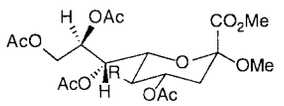
Results and discussion

In our earlier work,[9] we established that when a mixture of the β-methyl glycoside of Neu5Ac1Me, compound **7**[7] in glacial acetic acid was treated with acetic anhydride in the presence of sulfuric acid [acetic acid–acetic anhydride–sulfuric acid = 10 : 10 : 1 (v/v)], an 82% yield of the Neu5Ac2en oxazoline analogue **6** was isolated following work-up with aqueous sodium hydrogen carbonate and chromatographic separation from about 5–8% (by ^{1}H NMR spectroscopy) of 4-*epi*-Neu5Ac2en derivative, the allyl acetate **11**. Systematic studies were then performed to determine a more direct synthesis of the allyl acetate **11** or the corresponding allyl alcohol **12** from **7** by varying the work-up procedure. Thus, we have found that upon increasing the pH of the reaction mixture during work-up to 5 with sodium acetate, the intermediate oxazoline **6** was acetylated *in situ* to afford the allyl acetate **11** in 91% yield. Upon work-up at pH 2 the corresponding allyl alcohol **12** [R_f (ethyl acetate) = 0.23] was obtained in 64% yield after chromatographic separation from unidentified reaction by-products [R_f (ethyl acetate) = 0.28]. Interestingly, when the allyl alcohol **12** was left for a prolonged period of time at room temperature, some decomposition (by TLC) to the higher-R_f impurities was observed. Moreover, when the crude reaction mixture was acetylated under standard conditions (acetic anhydride and pyridine) or under the present acetolysis conditions following work-up with sodium acetate, only 4-*epi*-Neu5Ac2en derivative **11** was obtained. This has led us to postulate that the higher-R_f impurities may be products due to scrambling of the acetate groups.



11, R^1 = Ac, R = NHAc
12, R^1 = H, R = NHAc

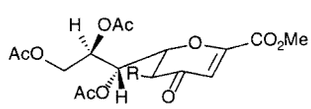
The acetolysis process appears to be independent of the anomeric configuration (C-2) on the starting material. Thus, the α-methyl glycoside **13**[10] reacted in an analogous manner to afford 4-*epi*-Neu5Ac2en derivative **11** following work-up with sodium acetate. Furthermore, acetolysis of either per-acetylated Neu5Ac2en1Me, compound **4**, or 4-*epi*-Neu5Ac2en derivative **11** gave the oxazoline **6** after work-up with aqueous sodium hydrogen carbonate, suggesting that the process is also independent of the relative stereochemistry about C-4 on the substrate.



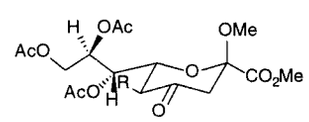
13, R = NHAc

Acetolysis of a series of variously substituted derivatives of **7** was performed to demonstrate the versatility of this reaction. It was found[9] that while the 9-*O*-tosyl group in the substrate **8** was compatible with the acetolysis conditions, the 9-*O*-*tert*-butyldiphenylsilyl group in compound **9** was not retained in the process. In the latter case, 4-*epi*-Neu5Ac2en derivative **11** was obtained after work-up with sodium acetate. Not surprisingly, an *O*-isopropylidene protecting group was also replaced by acetates under the reaction conditions. Hence, the *O*-isopropylidene and the *O*-silyl ether protecting groups can be used to facilitate regioselective manipulations on the poly-hydroxylated Neu5Ac system prior to the installation of 2,3-unsaturation, and can then be readily removed upon acetolysis.

The synthesis of the 4-oxo-Neu5Ac2en derivative, enone **14**, using the acetolysis reaction was also explored. Thus, we selected the 4-oxo-Neu5Ac derivative **15** as a suitable substrate. This compound was readily synthesised following previously published[7,11] procedures from the β-methyl glycoside of Neu-5Ac1Me **7** *via* sequential acetonide protection across the 8- and 9-hydroxy groups and PDC oxidation of the C-4 hydroxy group. Acetolysis of **15** proceeded to give the enone **14** in good yield (71%). This is in contrast to our previous attempts[9] at synthesising the enone **14** by oxidation of the allyl alcohol **12** with manganese dioxide using the procedure reported by Kumar and co-workers[12] which met with limited success.

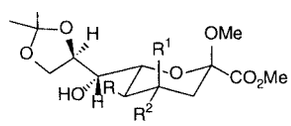


14, R = NHAc

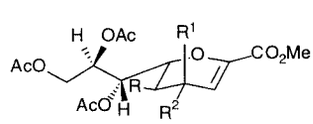


15, R = NHAc

In the absence of an electrophilic centre at C-4, exemplified by compounds **16** and **17**[13] with a methyl group at this position, acetolysis proceeded smoothly to give the glycals **18** and **19**, respectively. It should be noted that while most of the acetolysis reactions took approximately 48 h to complete, compound **17** required a prolonged reaction time to be converted into the glycal **19**. This is presumably due to the quasi-axial orientation of the methyl group at C-4 imposing some degree of steric congestion at C-2.

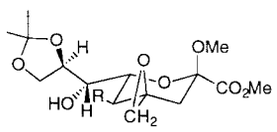
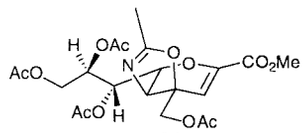
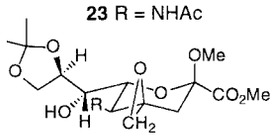
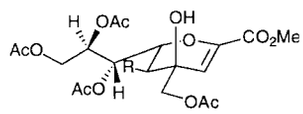
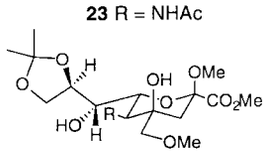
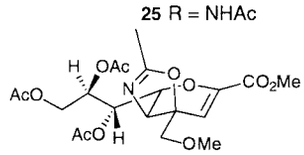
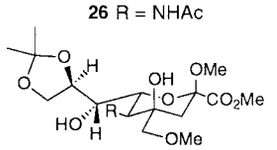
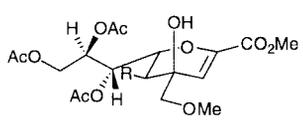
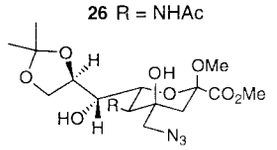
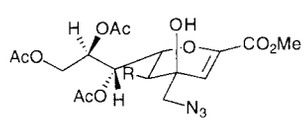
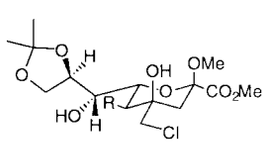
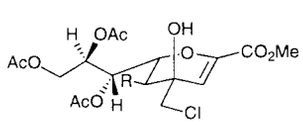


16, R^1 = H, R^2 = Me, R = NHAc
17, R^1 = Me, R^2 = H, R = NHAc



18, R^1 = H, R^2 = Me, R = NHAc
19, R^1 = Me, R^2 = H, R = NHAc

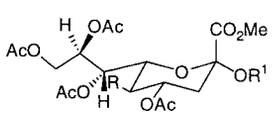
Table 1 Acetolysis[a] of some 4-bis-substituted Neu5Ac derivatives

Entry	Substrate[b]	Work-up procedure[c]	Product	Isolated yield (%)
1[d]	 **23** R = NHAc	A	 **24**	56
2[e]	 **23** R = NHAc	B	 **25** R = NHAc	53
3	 **26** R = NHAc	A	 **27**	60
4	 **26** R = NHAc	B	 **28** R = NHAc	67
5	 **29** R = NHAc	B	 **30** R = NHAc	68
6	 **31** R = NHAc	B	 **32** R = NHAc	72

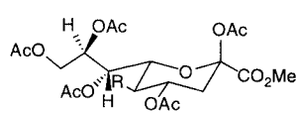
[a] See Experimental section for typical procedure. [b] Compounds were prepared according to ref. 11. [c] See Experimental section for work-up procedure. [d] This reaction also gave approximately 10% of the 1,3-oxazine derivative **33** (see body of text). [e] Approximately 13% of the (4*S*)-configured regioisomer **34** was also isolated.

Acetolysis of other glycosides of Neu5Ac was also explored. The α-benzyl and α-[2-(trimethylsilyl)ethyl] (TMSE) glycosides (**20** and **21**) were prepared using known[14] methods and subsequently subjected to the above-mentioned acetolysis conditions. Like the β-methyl glycoside **7**, deglycosidation of compounds **20** and **21** readily occurred to afford, in each case, the 4-*epi*-Neu5Ac2en derivative **11** after work-up with sodium acetate.

We thought it of value to examine acetolysis of the β-methyl glycoside of Neu5Ac1Me, compound **7**, by acetic anhydride using Lewis acid catalysts such as TMSOTf and $BF_3{\cdot}Et_2O$. Thus, in the presence of TMSOTf (2 mol equiv.) and acetic anhydride, compound **7** was readily converted to, after sodium hydrogen carbonate-based work-up, the oxazoline **6**. Interestingly, elimination was not promoted by $BF_3{\cdot}Et_2O$ and only the peracetate **22** was obtained after the usual work-up procedure.[9]



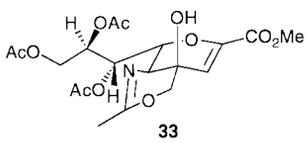
20, R^1 = Bn, R = NHAc
21, R^1 = TMSE, R = NHAc



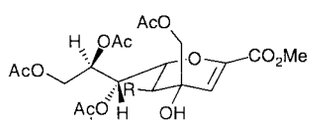
22, R = NHAc

Our interest in modified sialic acids led us to explore logical extensions of this methodology to the reaction of more complex templates such as 4-bis-substituted-Neu5Ac derivatives.[11] Representative examples of a series of these derivatives are presented in Table 1. These reactions demonstrate that in the presence of an electrophilic centre at C-4, the acetamido moiety at C-5 acts as an internal nucleophile. Accordingly, when the epoxide **23** was acetolysed and subsequently treated with base during work-up, the 1,3-oxazole derivative **24** was isolated in 56% yield after chromatography. Examination of the ^{1}H NMR spectrum of the crude product of this reaction indicated the presence of a singlet at δ 6.08 ppm which led us to suggest that the 1,3-oxazine derivative **33** may also be formed as a minor product (*ca.* 10%, by ^{1}H NMR spectroscopy). This by-product was, however, not isolated in the purification process. The NMR and mass spectral data for compound **24** are consistent with the assigned structure. Most notably, a doublet characteristic of an NH resonance is absent in the ^{1}H NMR spectrum. In the ^{13}C NMR spectrum of **24**, the resonance at δ_C ~14 ppm is characteristic of the methyl group attached to the sp carbon of an oxazoline ring. The structure of **24** was also unambiguously established by subsequent hydrogenolysis experiments (*vide infra*).

As expected, a work-up procedure involving addition of water to the reaction mixture following acetolysis (pH 2) of the epoxide **23** resulted in the hydrolysis of the oxazoline moiety. Accordingly, the allyl alcohol **25** was obtained, albeit in low yield (isolated yield after chromatography, 25–30%). Concomitant formation of side products that were not characterised was also observed (by TLC analysis). Modest yield of the desired product was, however, obtained when the reaction mixture was treated with sodium acetate during work-up (pH 5) and the resulting mixture stirred for an extended period of time (approximately 6 h) at room temperature (Table 1, entry 2). As is to be expected, this reaction also gave the (4*R*)-configured regioisomer **25** as the major product of the reaction (53% isolated yield after flash chromatography) with the (4*S*)-configured bis-substituted derivative **34** being obtained as a minor product (13% isolated yield).



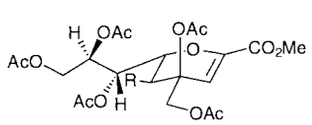
33



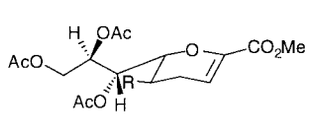
34, R = NHAc

Acetolysis of various other 4-bis-substituted derivatives such as **26**, **29** and **31** proceeded smoothly to afford the corresponding glycals in modest yields (Table 1, entries 3–6). Interestingly, unlike a previous example involving the intermediate oxazoline **6** which was acetylated with acetic anhydride at pH 5 during work-up (Method B; NaOAc), the intermediate oxazolines in the 4-bis-substituted systems were not acetylated under these conditions (Table 1, entries 2, 4, 5 and 6). The tertiary hydroxy group at C-4 in these systems can, however, be subsequently acetylated under standard conditions (Ac_2O, pyridine, DMAP) at an elevated temperature (50 °C) for 24 h. For example, the alcohol **25** could be acetylated to give the peracetate **35** in 85% yield.

Finally, as previously alluded to, we have been interested in C-4-modified Neu5Ac2en derivatives due to their inhibitory activity against various sialidases. Very recently, our attention has focussed on the synthesis of the *hitherto* unknown C-4 homologue of Neu5Ac2en, compound **10**. Single-carbon elongation can usually be achieved with organometallic reagents, olefination (*e.g.*, Wittig or Peterson), and a variety of other protocols, on the appropriate carbonyl derivatives. In this regard, the well known 4-oxo-Neu5Ac derivative **15** may be used as starting material. However, besides having to address the issue of stereochemistry when using these more conventional methods of chain extension, the 4-oxo compound **15** has also been reported [12] to be highly prone to enolisation and is therefore not amenable to these processes.

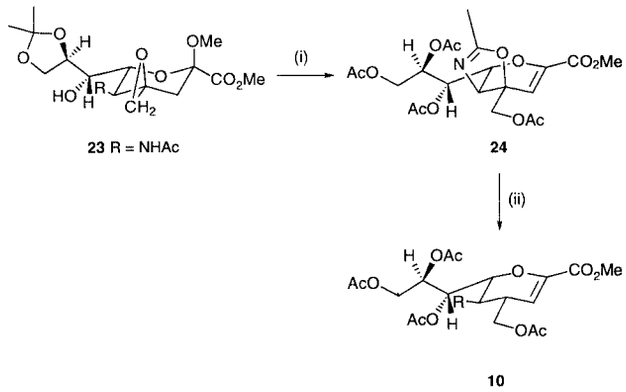


35, R = NHAc



36, R = NHAc

Several years ago, Schreiner and co-workers [15] demonstrated that the oxazoline **6** could be converted into the 4-deoxy-Neu5Ac2en derivative **36** under catalytic hydrogenolysis conditions. We felt that a reasonable strategy (Scheme 1) for the synthesis of the C-4 homologue of Neu5Ac2en **10** could involve



23 R = NHAc **24** **10**

Scheme 1 *Reagents and conditions*: (i) Ac_2O–HOAc–*c*.H_2SO_4 (10 : 10 : 1, v/v), rt, 48 h, $NaHCO_3$; (ii) H_2, 10% Pd/C, dioxane, rt, 24 h.

the initial preparation of a suitably 4-substituted oxazoline derivative such as **24**. Subsequent deoxygenation of **24** under hydrogenolysis conditions [15] could then provide the derivative with a hydroxymethyl substituent at C-4. Thus, exposure of the bis-substituted Neu5Ac2en derivative **24** to hydrogenolysis has provided the target compound **10**. The ^{1}H NMR spectrum of the product shows a coupling constant between H-3 and H-4 ($^3J_{3,4}$) of 2.5 Hz, indicative of the (4*S*)-configuration for **10** and hence is a confirmation of the (4*R*)-configuration for its bis-substituted precursor **24**. C-4 Epimers of Neu5Ac2en are usually readily distinguished on the basis of the coupling constants of the H-3 resonances in their respective ^{1}H NMR spectra. Generally, smaller $^3J_{3,4}$ couplings (typically 2–3 Hz) are associated with a C-4 substituent in an equatorial position, while larger $^3J_{3,4}$ couplings (4.5–6 Hz) are characteristic of 4-*epi*-Neu5Ac2en derivatives.[16] In view of the successful synthesis of **10**, it is conceivable that hydrogenolysis of C-4-bis-substituted oxazoline derivatives prepared from compounds such as **26**, **29**, and **31** will lead to further interesting functionalised Neu5Ac2en analogues.

In summary, a concise one-step conversion of glycosides of Neu5Ac into their 2,3-unsaturated (Neu5Ac2en) derivatives has been described. This conversion of modified Neu5Ac glycosides into their corresponding glycal analogues provides ready access to a wide range of novel biological probes of sialic-acid-recognising proteins. These may prove to be useful in understanding aspects of the biochemistry of these proteins and in the discovery of potent inhibitors. The acetolysis process is compatible with the wide variety of functionalities and the inherent stereochemical features present in the system. In particular, this process has provided access to a number of 4-bis-substituted-Neu5Ac2en derivatives that would otherwise be difficult to obtain.

Experimental

General

Commercial analytical-grade acetic anhydride was distilled from sodium acetate, and glacial acetic acid from P_2O_5 before use. Concentrated sulfuric acid (analytical grade) was purchased from Ajax Chemicals Australia and used without further purification. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded on a Bruker AMX300 spectrometer operating at 303 K and were referenced to solvent residues; *J*-values are in hertz (Hz). Low-resolution (LR) and high-resolution (HR) fast-atom bombardment (FAB) and electrospray ionisation (ESI) mass spectra were obtained using a JEOL JMS-DX300 spectrometer and a Micromass Platform II spectrometer, respectively. Optical rotations were measured using a JASCO DIP-370 polarimeter; $[\alpha]_D$-values are in units of 10^{-1} deg cm^2 g^{-1}. Column chromatography was performed on Merck silica gel 60 (0.040–0.063 mm). Reactions were moni-

tored by TLC on Kieselgel 60 F_{254} plate (Merck 5554) and detection of the spots was carried out by spraying with a 95% aq. ethanol solution containing 5% H_2SO_4 and charring at *ca.* 180 °C.

Starting materials

The β-methyl ketoside of Neu5Ac1Me, compound **7**, was prepared following published [7,11] procedures. The α-methyl ketoside **13** was synthesised by the reaction of peracetylated β-chloro-Neu5Ac1Me **5a** with methanol following the procedure reported [10] by Kononov and Magnusson. The 9-*O*-tosylate **8** was obtained in 76% yield from the reaction of **7** with 2 mol equiv. of toluene-*p*-sulfonyl chloride in pyridine. Reaction of **7** with 1.1 mol equiv. of *tert*-butyldiphenylsilyl chloride and 2 mol equiv. of imidazole in pyridine–dichloromethane afforded a 74% yield of the 9-*O*-*tert*-butyldiphenylsilyl derivative **9** after flash chromatography. The 4-oxo compound **15** was prepared from Neu5Ac following literature [7,11] procedures. Compounds **23**, **26**, **29** and **31** were prepared from the 4-oxo compound **15** using the methods reported [11] by Groves and von Itzstein. The 4-deoxy-4-*C*-methyl and the 4-deoxy-4-*epi*-*C*-methyl compounds **16** and **17** were obtained using the method of Hartmann and co-workers.[13] The α-benzyl and α-trimethylsilylethyl glycosides **20** and **21**, respectively, were prepared according to literature procedures.[14]

The ^{1}H NMR spectral data for compounds **7**, **13**, **15**, **16**, **17**, **20**, **21**, **23**, **26**, **29** and **31** were found to be indistinguishable from those previously [7,11,13,14] reported. However, the literature [13] ^{1}H NMR assignments for compounds **16** and **17** have been interchanged. Also, there was inconsistency in the assignment of some of the coupling constants in the ^{1}H NMR spectrum ($CDCl_3$) of compound **17**—$J_{3a,4}$ 3.7, $J_{5,4}$ 5.0 Hz (lit.,[13] $J_{3a,4}$ 12.1, $J_{5,4}$ 10.5 Hz).

Methyl (methyl 5-acetamido-3,5-dideoxy-9-*O*-tosyl-D-*glycero*-β-D-*galacto*-non-2-ulopyranosid)onate 8

$[a]_D$ −37 (*c* 1.00, $CHCl_3$); selected δ_H($CDCl_3$) 1.73 (1 H, pseudo-t, $J_{3a,3e}$ 11.6, $J_{3a,4}$ 11.6, H-3a), 2.09 (3 H, s, NHCOCH_3), 2.46 (3 H, s, $C_6H_4CH_3$), 2.49 (1 H, dd, $J_{3e,4}$ 4.4, H-3e), 3.26 (3 H, s, OCH_3), 3.83 (3 H, s, CO_2CH_3), 7.81–7.36 (4 H, m, aromatic protons); δ_C($CDCl_3$) 21.5, 22.9 (NHCOCH_3, $C_6H_4CH_3$), 40.2 (C-3), 51.1, 52.8 (C-5, CO_2CH_3, OCH_3), 60.3 (C-9), 66.4, 68.3, 68.7, 70.7 (C-4, C-6, C-7, C-8), 73.1 (C-9), 99.1 (C-2), 127.9, 129.9, 132.3, 144.9 (aromatic carbons), 169.2, 173.7 (carbonyls); LRMS (FAB): 476 (M^+ + 1, 6%), 460 (50), 442 (100), 320 (11).

Methyl (methyl 5-acetamido-3,5-dideoxy-9-*O*-*tert*-butyldiphenylsilyl-D-*glycero*-β-D-*galacto*-non-2-ulopyranosid)onate 9

$[a]_D$ −40 (*c* 0.93, $CHCl_3$); selected δ_H($CDCl_3$) 1.06 [9 H, s, C(CH_3)$_3$], 1.75 (1 H, pseudo-t, $J_{3a,3e}$ 12.8, $J_{3a,4}$ 12.8, H-3a), 2.00 (3 H, s, NHCOCH_3), 2.44 (1 H, dd, $J_{3e,4}$ 4.4, H-3e), 3.28 (3 H, s, OCH_3), 3.80 (3 H, s, CO_2CH_3), 7.39–7.66 (10 H, m, aromatic protons); δ_C($CDCl_3$) 22.9, 26.8 [NHCOCH_3, C(CH_3)$_3$], 40.9 (C-3), 51.1, 52.7, 52.9, 66.6, 68.6, 69.9, 71.3 (C-4, C-5, C-6, C-7, C-8, CO_2CH_3, OCH_3), 60.4 (C-9), 65.3 [C(CH_3)$_3$], 99.1 (C-2), 127.5, 127.8, 129.6, 129.8, 132.8, 133.1, 134.7, 135.1, 135.4, 135.5 (aromatic carbons), 169.2, 173.3 (carbonyls); LRMS (FAB): 560 (M^+ + 1, 5%), 544 (24), 526 (29), 466 (29), 448 (52), 135 (100).

Acetolysis reaction

General procedure. Conc. sulfuric acid (0.1 ml) was added during 1 min to a stirred solution of the substrate (100 mg) in glacial acetic acid (1.0 ml) and acetic anhydride (1.0 ml) at rt under nitrogen. The resulting solution was stirred for 48 h (unless otherwise stated) at rt. In the work-up, the reaction mixture was treated using any of the following three procedures. Procedure A: saturated aq. sodium bicarbonate was added (pH 9) and the mixture stirred for 2 h before extraction with ethyl acetate. Procedure B: solid sodium acetate was added (pH 5) and the mixture stirred for 2–6 h before extraction with ethyl acetate. Procedure C: water was added and the mixture extracted with ethyl acetate after 4 h.

2-Methyl-4,5-dihydro(methyl 7,8,9-tri-*O*-acetyl-2,6-anhydro-3,4,5-trideoxy-D-*glycero*-D-*talo*-non-2-enonato)[5,4-*d*][1,3]-oxazole [9] 6

Spectral data of **6** are consistent with the literature.[17]

Methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-2,6-anhydro-3,5-dideoxy-D-*glycero*-D-*talo*-non-2-enonate [9] 11

$[a]_D$ −112 (*c* 0.82, $CHCl_3$); ^{1}H and ^{13}C NMR spectral data are consistent with those previously reported;[17] LRMS (FAB): 474 (M^+ + 1, 22%), 414 (100).

Methyl 5-acetamido-7,8,9-tri-*O*-acetyl-2,6-anhydro-3,5-dideoxy-D-*glycero*-D-*talo*-non-2-enonate [9] 12

$[a]_D$ +64 (*c* 1.41, $CHCl_3$); δ_H($CDCl_3$) 1.94 (3 H, s, NHCOCH_3), 2.04, 2.06, 2.09 (each 3 H, s, $OCOCH_3$ × 3), 3.79 (3 H, s, CO_2CH_3), 4.16 (1 H, dd, $J_{9,8}$ 7.7, $J_{9,9'}$ 12.4, H-9), 4.23 (1 H, m, H-4), 4.24 (1 H, m, H-6), 4.34 (1 H, ddd, $J_{5,4}$ 3.7, $J_{5,6}$ 8.7, $J_{5,NH}$ 8.7, H-5), 4.78 (1 H, dd, $J_{9',8}$ 2.6, H′-9), 5.28 (1 H, ddd, $J_{8,7}$ 4.1, H-8), 5.44 (1 H, dd, $J_{7,6}$ 2.0, H-7), 6.13 (1 H, d, NH), 6.14 (1 H, d, $J_{3,4}$ 5.5, H-3); δ_C[$CDCl_3$–CD_3OD (9:1)] 20.4, 20.5, 22.5 (NHCOCH_3, OCOCH_3), 46.6 (C-5), 52.1 (CO_2CH_3), 60.6 (C-4), 62.1 (C-9), 67.9, 71.4, 72.4 (C-6, C-7, C-8), 110.0 (C-3), 144.0 (C-2), 162.2, 170.2, 170.4, 170.7, 170.8 (carbonyls); LRMS (FAB): 432 (M^+ + 1, 28%), 414 (100); HRMS (FAB): Calc. for $C_{18}H_{26}NO_{11}$: [M^+ + 1], 432.1506. Found: *m*/*z*, 432.1496.

Methyl 5-acetamido-7,8,9-tri-*O*-acetyl-2,6-anhydro-3,5-dideoxy-D-*manno*-non-2-en-4-ulosonate [9] 14

$[a]_D$ −37 (*c* 1.09, $CHCl_3$); δ_H($CDCl_3$) 2.03, 2.05, 2.06, 2.15 (each 3 H, s, NHCOCH_3, $OCOCH_3$ × 3), 3.88 (3 H, s, CO_2CH_3), 4.18 (1 H, dd, $J_{9,8}$ 5.9, $J_{9,9'}$ 12.7, H-9), 4.59 (1 H, dd, $J_{9',8}$ 2.1, H′-9), 4.69 (1 H, br d, H-6), 4.71 (1 H, pseudo-t, $J_{5,4}$ 8.0, $J_{5,NH}$ 8.0, H-5), 5.37 (1 H, ddd, $J_{8,7}$ 5.8, H-8), 5.40 (1 H, dd, $J_{7,6}$ 1.2, H-7), 5.78 (1 H, d, NH), 6.29 (1 H, s, H-3); δ_C($CDCl_3$) 20.6, 20.7, 22.7 (NHCOCH_3, OCOCH_3), 51.7, 53.2 (C-5, CO_2CH_3), 61.9 (C-9), 67.8, 70.3, 79.9 (C-6, C-7, C-8), 108.0 (C-3), 158.1 (C-2), 160.9, 169.9, 170.5, 171.0 (carbonyls), 190.9 (C-4); LRMS (FAB): 430 (M^+ + 1, 100%), 388 (40), 370 (57), 328 (41); HRMS (FAB): Calc. for $C_{18}H_{24}NO_{11}$: [M^+ + 1], 430.1350. Found: *m*/*z*, 430.1364.

Methyl 5-acetamido-7,8,9-tri-*O*-acetyl-2,6-anhydro-3,4,5-trideoxy-4-*C*-methyl-D-*glycero*-D-*galacto*-non-2-enonate [9] 18

$[a]_D$ +6 (*c* 1.54, $CHCl_3$); δ_H($CDCl_3$) 1.10 (3 H, d, $J_{10,4}$ 7.2, $CHCH_3$), 1.97 (3 H, s, NHCOCH_3), 2.06, 2.07, 2.12 (each 3 H, s, $OCOCH_3$ × 3), 2.40 (1 H, ddd, $J_{4,3}$ 2.7, $J_{4,5}$ 9.8, H-4), 3.78 (3 H, s, CO_2CH_3), 3.84 (1 H, pseudo-q, $J_{5,6}$ 9.9, $J_{5,NH}$ 9.9, H-5), 4.09 (1 H, dd, $J_{6,7}$ 2.0, H-6), 4.20 (1 H, dd, $J_{9,8}$ 7.4, $J_{9,9'}$ 12.4, H-9), 4.75 (1 H, dd, $J_{9',8}$ 2.6, H′-9), 5.26 (1 H, d, NH), 5.31 (1 H, ddd, $J_{8,7}$ 4.6, H-8), 5.50 (1 H, dd, H-7), 5.94 (1 H, d, H-3); δ_C($CDCl_3$) 17.6 (C-10), 20.7, 20.9, 23.3 (NHCOCH_3, OCOCH_3), 35.0 (C-4), 48.9, 52.1 (C-5, CO_2CH_3), 62.3 (C-9), 68.1, 71.9, 77.1 (C-6, C-7, C-8), 115.5 (C-3), 142.5 (C-2), 170.1, 170.4, 170.5 (carbonyls); LRMS (FAB): 430 (M^+ + 1, 100%); HRMS (FAB): Calc. for $C_{19}H_{28}NO_{10}$: [M^+ + 1], 430.1713. Found: *m*/*z*, 430.1710.

Methyl 5-acetamido-7,8,9-tri-*O*-acetyl-2,6-anhydro-3,4,5-trideoxy-4-*C*-methyl-D-*glycero*-D-*talo*-non-2-enonate [9] 19

$[a]_D$ −13 (*c* 1.05, $CHCl_3$); δ_H($CDCl_3$) 1.06 (3 H, d, $J_{10,4}$ 7.2,

CHCH_3), 1.95 (3 H, s, NHCOCH_3), 2.03, 2.04, 2.08 (each 3 H, s, OCOCH_3 × 3), 2.79 (1 H, ddd, $J_{4,3}$ 5.6, $J_{4,5}$ 3.4, H-4), 3.76 (3 H, s, CO_2CH_3), 4.18 (1 H, dd, $J_{6,7}$ 2.0, H-6), 4.18 (1 H, pseudo-q, $J_{5,6}$ 9.9, $J_{5,NH}$ 9.9, H-5), 4.20 (1 H, dd, $J_{9,8}$ 7.4, $J_{9,9'}$ 12.4, H-9), 4.75 (1 H, dd, $J_{9',8}$ 2.6, H′-9), 5.26 (1 H, d, NH), 5.31 (1 H, ddd, $J_{8,7}$ 4.6, H-8), 5.50 (1 H, dd, H-7), 5.94 (1 H, d, H-3); δ_C($CDCl_3$) 17.6 (C-10), 20.7, 20.9, 23.3 (NHCO*C*H_3, OCO*C*H_3), 35.0 (C-4), 48.9, 52.1 (C-5, CO_2CH_3), 62.3 (C-9), 68.1, 71.9, 77.1 (C-6, C-7, C-8), 115.5 (C-3), 142.5 (C-2), 170.1, 170.4, 170.5 (carbonyls); LRMS (FAB): 430 (M^+ + 1, 100%); HRMS (FAB): Calc. for $C_{19}H_{28}NO_{10}$: [M^+ + 1], 430.1713. Found: *m*/*z*, 430.1710.

2-Methyl-4,5-dihydro(methyl 4-*C*-acetoxymethyl-7,8,9-tri-*O*-acetyl-2,6-anhydro-3,4,5-trideoxy-D-*glycero*-D-*talo*-non-2-enonato)[5,4-*d*][1,3]oxazole 24

According to the acetolysis conditions as described above, reaction of **23** gave **24** (work-up procedure A) after column chromatography (CH_2Cl_2–MeOH, 9:1) (Table 1, entry 1); [α]$_D$ +21 (*c* 1.48, $CHCl_3$); δ_H($CDCl_3$) 2.00, 2.03, 2.04, 2.06, 2.15 (each 3 H, s, OCOCH_3 × 4, oxazoline CH_3), 3.46 (1 H, dd, $J_{6,7}$ 2.8, $J_{6,5}$ 10.3, H-6), 3.80–3.83 (4 H, m, H-5, CO_2CH_3), 3.98 (1 H, d, $J_{10,10'}$ 11.7, H-10), 4.13 (1 H, d, H′-10), 4.21 (1 H, dd, $J_{9,8}$ 6.4, $J_{9,9'}$ 12.4, H-9), 4.58 (1 H, dd, $J_{9',8}$ 2.7, H′-9), 5.42 (1 H, ddd, $J_{8,7}$ 5.8, H-8), 5.62 (1 H, dd, H-7), 6.30 (1 H, s, H-3); δ_C($CDCl_3$) 14.0 (N=C*C*H_3), 20.4, 20.5, 20.6, 20.7 (OCO*C*H_3), 52.5 ($CO_2C$$H_3$), 61.9 (C-9), 64.8 (C-5), 66.5 (*C*H_2OAc), 68.7, 70.2, 78.1 (C-6, C-7, C-8), 80.1 (C-4), 108.2 (C-3), 147.8 (C-2), 161.5, 169.5, 169.7, 170.2, 170.5 (carbonyls), 166.3 (N=*C*CH_3); LRMS (FAB): 486 (M^+ + 1, 100%), 444 (21), 426 (22), 384 (25), 366 (31); HRMS (FAB): Calc. for $C_{21}H_{28}NO_{12}$: [M^+ + 1], 486.1612. Found: *m*/*z*, 486.1597.

Methyl 5-acetamido-4-*C*-acetoxymethyl-7,8,9-tri-*O*-acetyl-2,6-anhydro-3,5-dideoxy-D-*glycero*-D-*talo*-non-2-enonate 25 and methyl 5-acetamido-4-*C*-acetoxymethyl-7,8,9-tri-*O*-acetyl-2,6-anhydro-3,5-dideoxy-D-*glycero*-D-*galacto*-non-2-enonate 34

Acetolysis of the epoxide **23** according to the general conditions as previously described (work-up procedure B) afforded **25** and **34** after column chromatography [2 columns: ethyl acetate then CH_2Cl_2–MeOH (19:1)] (Table 1, entry 2); **25**: [α]$_D$ +2 (*c* 1.08, $CHCl_3$); δ_H($CDCl_3$) 1.95 (3 H, s, NHCOCH_3), 2.05, 2.06, 2.09, 2.11 (each 3 H, s, OCOCH_3 × 4), 3.81 (3 H, s, CO_2CH_3), 3.93 (1 H, d, $J_{10,10'}$ 11.6, H-10), 4.17 (1 H, dd, $J_{9,8}$ 6.5, $J_{9,9'}$ 12.1, H-9), 4.18 (1 H, d, H′-10), 4.30 (1 H, dd, $J_{6,5}$ 11.0, $J_{6,7}$ 1.2, H-6), 4.34 (1 H, pseudo-t, $J_{5,6}$ 11.0, $J_{5,NH}$ 11.1, H-5), 4.78 (1 H, dd, $J_{9',8}$ 2.6, H′-9), 5.32 (1 H, ddd, $J_{8,7}$ 4.4, H-8), 5.48 (1 H, dd, H-7), 5.88 (1 H, d, NH), 6.11 (1 H, s, H-3); δ_C($CDCl_3$) 20.7, 20.9, 23.0 (NHCO*C*H_3, OCO*C*H_3), 47.2 (C-5), 52.5 ($CO_2C$$H_3$), 62.3 (C-9), 67.2, 68.3 (C-4, *C*H_2OAc), 68.0, 72.3, 74.1 (C-6, C-7, C-8), 109.8 (C-3), 145.4 (C-2), 162.1, 170.2, 170.4, 170.6, 170.8, 171.0 (carbonyls); LRMS (FAB): 504 (M^+ + 1, 63%), 486 (100), 444 (28); HRMS (FAB): Calc. for $C_{21}H_{30}NO_{13}$: [M^+ + 1], 504.1717. Found: *m*/*z*, 504.1724.

34: δ_H($CDCl_3$) 1.98 (3 H, s, NHCOCH_3), 2.04, 2.07, 2.09, 2.12 (each 3 H, s, OCOCH_3 × 4), 3.84 (3 H, s, CO_2CH_3), 4.06 (1 H, dd, $J_{9,8}$ 6.1, $J_{9,9'}$ 12.5, H-9), 4.21 (1 H, dd, $J_{6,5}$ 10.3, $J_{6,7}$ 1.8, H-6), 4.45–4.55 (2 H, m, H′-9 and H-10), 4.65 (1 H, d, $J_{10',10}$ 12.8, H′-10), 4.76 (1 H, pseudo-t, $J_{5,NH}$ 10.3, H-5), 5.33 (1 H, m, H-8), 5.37 (1 H, dd, $J_{7,8}$ 6.9, H-7), 5.48 (1 H, d, NH), 5.85 (1 H, s, H-3).

2-Methyl-4,5-dihydro(methyl-7,8,9-tri-*O*-acetyl-2,6-anhydro-3,4,5-trideoxy-4-*C*-methoxymethyl-D-*glycero*-D-*talo*-non-2-enonato)[5,4-*d*][1,3]oxazole 27

According to the general acetolysis procedure as described above, reaction of **26** gave **27** (work-up procedure A) after column chromatography (ethyl acetate) (Table 1, entry 3); [α]$_D$ +178 (*c* 0.66, $CHCl_3$); δ_H($CDCl_3$) 2.04, 2.05, 2.07, 2.16 (each 3 H, s, OCOCH_3 × 3, oxazoline CH_3), 3.37–3.44 (4 H, m, H-6, CH_2OCH_3), 3.58 (1 H, d, $J_{10,10'}$ 9.7, H-10), 3.80–3.83 (4 H, m, H-5, CO_2CH_3), 3.90 (1 H, d, H′-10), 4.23 (1 H, dd, $J_{9,8}$ 6.6, $J_{9,9'}$ 12.4, H-9), 4.59 (1 H, dd, $J_{9',8}$ 2.8, H′-9), 5.44 (1 H, ddd, $J_{8,7}$ 4.9, H-8), 5.64 (1 H, dd, $J_{7,6}$ 3.2, H-7), 6.34 (1 H, s, H-3); δ_C($CDCl_3$) 14.1 (N=C*C*H_3), 20.5, 20.7, 20.8 (OCO*C*H_3), 52.4 ($CO_2C$$H_3$), 59.7 ($CH_2OC$$H_3$), 61.9 (C-4), 64.6 (C-5), 68.8, 70.3, 78.0 (C-6, C-7, C-8), 75.9 (*C*H_2OCH$_3$), 81.1 (C-4), 109.6 (C-3), 147.1 (C-2), 161.7, 169.6, 169.7, 170.5 (carbonyls), 166.3 (N=*C*CH_3); LRMS (FAB): 458 (M^+ + 1, 100%), 264 (22), 237 (74); HRMS (FAB): Calc. for $C_{20}H_{28}NO_{11}$: [M^+ + 1], 458.1662. Found: *m*/*z*, 458.1685.

Methyl 5-acetamido-7,8,9-tri-*O*-acetyl-2,6-anhydro-3,5-dideoxy-4-*C*-methoxymethyl-D-*glycero*-D-*talo*-non-2-enonate 28

According to the general acetolysis procedure as described above, reaction of **26** gave **28** (work-up procedure B) after column chromatography (ethyl acetate) (Table 1, entry 4); [α]$_D$ −26 (*c* 1.24, $CHCl_3$); δ_H($CDCl_3$) 1.97 (3 H, s, NHCOCH_3), 2.06, 2.07, 2.11, 2.13 (each 3 H, s, OCOCH_3 × 4), 3.26 (1 H, d, $J_{10,10'}$ 9.2, H-10), 3.33 (1 H, d, H′-10), 3.81 (3 H, s, CO_2CH_3), 4.17 (1 H, dd, $J_{9,8}$ 5.1, $J_{9,9'}$ 12.4, H-9), 4.20 (1 H, pseudo-t, $J_{5,6}$ 10.9, $J_{5,NH}$ 10.9, H-5), 4.30 (1 H, dd, $J_{6,7}$ 1.8, H-6), 4.74 (1 H, dd, $J_{9',8}$ 2.6, H′-9), 5.34 (1 H, ddd, $J_{8,7}$ 4.9, H-8), 5.48 (1 H, dd, H-7), 5.77 (1 H, d, NH), 6.22 (1 H, s, H-3); δ_C($CDCl_3$) 20.7, 20.8, 23.1 (NHCO*C*H_3, OCO*C*H_3), 47.3 (C-5), 52.4 ($CO_2C$$H_3$), 59.4 ($CH_2OC$$H_3$), 62.3 (C-9), 68.0, 71.8, 73.9 (C-6, C-7, C-8), 68.5, 75.5 (C-4, *C*H_2OCH$_3$), 111.0 (C-3), 144.8 (C-2), 162.3, 170.2, 170.4, 170.6 (carbonyls); LRMS (FAB): 476 (M^+ + 1, 37%), 458 (100), 416 (18); HRMS (FAB): Calc. for $C_{20}H_{30}NO_{12}$: [M^+ + 1], 476.1768. Found: *m*/*z*, 476.1789.

Methyl 5-acetamido-7,8,9-tri-*O*-acetyl-2,6-anhydro-4-*C*-azidomethyl-3,5-dideoxy-D-*glycero*-D-*talo*-non-2-enonate 30

Acetolysis of **29** according to the general conditions as previously described (work-up procedure B) afforded **30** after column chromatography (ethyl acetate) (Table 1, entry 5); [α]$_D$ −5 (*c* 1.70, $CHCl_3$); δ_H($CDCl_3$) 1.97 (3 H, s, NHCOCH_3), 2.05, 2.07, 2.09 (each 3 H, s, OCOCH_3 × 3), 3.21 (1 H, d, $J_{10,10'}$ 12.5, H-10), 3.46 (1 H, d, H′-10), 3.80 (3 H, s, CO_2CH_3), 4.15 (1 H, dd, $J_{9,8}$ 7.8, $J_{9,9'}$ 12.4, H-9), 4.22 (1 H, pseudo-t, $J_{5,6}$ 9.8, $J_{5,NH}$ 9.8, H-5), 4.30 (1 H, dd, $J_{6,7}$ 1.6, H-6), 4.80 (1 H, dd, $J_{9',8}$ 2.5, H′-9), 5.28 (1 H, ddd, $J_{8,7}$ 4.0, H-8), 5.47 (1 H, dd, H-7), 6.10 (1 H, d, NH), 6.17 (1 H, s, H-3); δ_C($CDCl_3$) 20.6, 20.7, 20.9, 23.0 (NHCO*C*H_3, OCO*C*H_3), 47.7, 52.6 (C-5, $CO_2C$$H_3$), 56.9 ($CH_2N_3$), 62.2 (C-9), 69.2 (C-4), 67.9, 72.6, 74.1 (C-6, C-7, C-8), 109.6 (C-3), 145.1 (C-2), 162.0, 170.2, 170.7, 171.2 (carbonyls); LRMS (ESI; cone voltage 30 V): 509 (M^+ + Na, 100%), 487 (30), 469 (90); HRMS (ESI): Calc. for $C_{19}H_{27}N_4O_{11}$: [M^+ + 1], 487.1676. Found: *m*/*z* 487.1669.

Methyl 5-acetamido-7,8,9-tri-*O*-acetyl-2,6-anhydro-4-*C*-chloromethyl-3,5-dideoxy-D-*glycero*-D-*talo*-non-2-enonate 32

Acetolysis of **31** according to the general conditions as previously described (work-up procedure B) afforded **32** after column chromatography (ethyl acetate) (Table 1, entry 6); [α]$_D$ −16 (*c* 1.04, $CHCl_3$); δ_H($CDCl_3$) 1.97 (3 H, s, NHCOCH_3), 2.05, 2.07, 2.09 (each 3 H, s, OCOCH_3 × 3), 3.48 (1 H, d, $J_{10,10'}$ 11.5, H-10), 3.59 (1 H, d, H′-10), 3.81 (3 H, s, CO_2CH_3), 4.16 (1 H, dd, $J_{9,8}$ 7.5, $J_{9,9'}$ 12.4, H-9), 4.27–4.38 (2 H, m, H-5 and H-6), 4.77 (1 H, dd, $J_{9',8}$ 2.6, H′-9), 5.31 (1 H, ddd, $J_{8,7}$ 4.3, H-8), 5.47 (1 H, dd, $J_{7,6}$ 1.5, H-7), 6.02 (1 H, d, $J_{NH,5}$ 8.2, NH), 6.26 (1 H, s, H-3); δ_C($CDCl_3$) 20.7, 20.9, 23.0 (OCO*C*H_3, NHCO*C*H_3), 48.0 (C-5), 50.1 (CH_2Cl), 52.7 ($CO_2C$$H_3$), 62.3 (C-9), 68.8 (C-4), 68.0, 72.2, 74.4 (C-6, C-7, C-8), 109.4 (C-3), 145.4 (C-2), 162.1, 170.2, 170.4, 170.6, 170.8, 171.0 (carbonyls); LRMS (ESI; cone

voltage 30 V): 482 [$M^+(^{37}Cl)$ + 1, 22%], 480 [$M^+(^{35}Cl)$ + 1, 57], 462 (100), 464 (25); HRMS (ESI): Calc. for $C_{19}H_{26}{}^{35}ClNNaO_{11}$ [M^+ + Na], 502.1092. Found: *m*/*z*, 502.1097.

Methyl 5-acetamido-4-*C*-acetoxymethyl-4,7,8,9-tetra-*O*-acetyl-2,6-anhydro-3,5-dideoxy-D-*glycero*-D-*talo*-non-2-enonate 35

Acetylation of the alcohol **25** (120 mg, 0.238 mmol) with Ac_2O (1.0 ml) and DMAP (5 mg) in pyridine (2 ml) at 50 °C for 24 h gave the title compound **35** (110 mg, 85%) after flash chromatography on silica (ethyl acetate); $\delta_H(CDCl_3)$ 1.92 (3 H, s, NHCOCH_3), 2.02, 2.04, 2.05, 2.06, 2.10 (each 3 H, s, $OCOCH_3$ × 5), 3.79 (3 H, s, CO_2CH_3), 4.16 (1 H, dd, $J_{9,8}$ 7.7, $J_{9,9'}$ 12.4, H-9), 4.25 (1 H, d, $J_{10,10'}$ 11.1, H-10), 4.33 (1 H, d, $J_{6,5}$ 11.1, $J_{6,7}$ 1.8, H-6), 4.46 (1 H, d, H′-10), 4.57 (1 H, pseudo-t, $J_{5,NH}$ 10.8, H-5), 4.80 (1 H, dd, $J_{9',8}$ 2.4, H′-9), 5.30 (1 H, ddd, $J_{8,7}$ 3.6, H-8), 5.47 (1 H, dd, H-7), 5.65 (1 H, d, NH), 6.51 (1 H, s, H-3); $\delta_C(CDCl_3)$ 20.7, 20.9, 21.5, 23.1 ($OCOCH_3$, $NHCOCH_3$), 46.2, 52.6 (C-5, CO_2CH_3), 62.2, 62.7 (C-9, C-10), 68.0, 72.1, 74.1 (C-6, C-7, C-8), 76.3 (C-4), 107.3 (C-3), 146.0 (C-2), 161.6, 167.9, 168.7, 169.9, 170.0, 170.2, 170.5 (carbonyls); LRMS (ESI; cone voltage 30 V): 568 (M^+ + Na, 45%), 486 (100), 426 (28), 413 (15).

Methyl 5-acetamido-4-*C*-acetoxymethyl-7,8,9-tri-*O*-acetyl-2,6-anhydro-3,4,5-trideoxy-D-*glycero*-D-*galacto*-non-2-enonate 10

A mixture of the oxazoline **24** (249 mg, 0.505 mmol) in 1,4-dioxane (25 ml) and 10% Pd/C (50 mg) was hydrogenated for 24 h at atmospheric pressure H_2.[15] The catalyst was filtered off, and the filtrate was concentrated under diminished pressure. The resulting residue was purified by flash chromatography [two columns: ethyl acetate then toluene–acetone (2:1)] which gave compound **10** as a colourless amorphous solid (133 mg, 54%); $[\alpha]_D$ +57 (*c* 1.49, $CHCl_3$); $\delta_H(CDCl_3)$ 1.97 (3 H, s, NHCOCH_3), 2.05, 2.06, 2.07, 2.12 (each 3 H, s, $OCOCH_3$ × 4), 2.83 (1 H, m, H-4), 3.79 (3 H, s, CO_2CH_3), 3.82–3.92 (2 H, m, H_2-10, 4.15–4.25 (3 H, m, H-5, H-6, H-9), 4.72 (1 H, dd, $J_{9',8}$ 2.6, $J_{9',9}$ 12.5, H′-9), 5.30 (1 H, ddd, $J_{8,7}$ 4.8, $J_{8,9}$ 7.3, H-8), 5.42 (1 H, d, $J_{NH,5}$ 9.0, NH), 5.49 (1 H, m, H-7), 6.51 (1 H, d, $J_{3,4}$ 2.5, H-3); $\delta_C(CDCl_3)$ 20.7, 23.1 ($OCOCH_3$, $NHCOCH_3$), 39.3 (C-4), 44.4 (C-5), 52.2 (CO_2CH_3), 62.3, 64.1 (C-9, C-10), 67.9, 71.7, 76.6 (C-6, C-7, C-8), 110.6 (C-3), 144.3 (C-2), 162.1, 170.3, 170.6, 170.9 (carbonyls); LRMS (ESI; cone voltage 30 V): 488 (M^+ + 1, 100%), 428 (40); HRMS (FAB): Calc. for $C_{21}H_{30}NO_{12}$: [M^+ + 1], 488.1768. Found: *m*/*z*, 488.1745.

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