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N,N-Diacetylsialyl chloride—a novel readily accessible sialyl donor in reactions with neutral and charged nucleophiles in the absence of a promoter

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ABSTRACT

N,N-Diacetylneuraminic acid glycosyl chloride was prepared for the first time and made to react with various nucleophiles to give the corresponding α-glycosyl phosphate, β-glycosyl dibenzyl phosphate, α-glycosyl azide, α-phenyl thioglycoside and α-glycosyl xanthate in 65–82% yields and high stereoselectivity while its reactions with simple alcohols were not stereoselective. The new sialyl donor made possible the first stereoselective synthesis of sialic acid glycosyl phosphate with α-configuration and highly efficient synthesis of β-configured sialic acid glycosyl dibenzyl phosphate.

1. Introduction

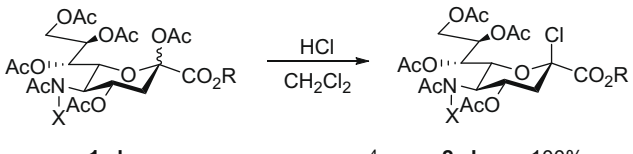
Sialic acid-containing glycoconjugates are involved in a wide range of cell-surface recognition phenomena in living systems.[1] For this reason, tremendous efforts have been made in order to develop efficient methods for the synthesis of sialo-oligosaccharides.[2] Thioglycoside derivatives of neuraminic acid with modified substituents at the nitrogen atom N(5), *N,N*-diacetyl-derivative being the first of them,[2a] have recently been demonstrated to be superior as sialyl donors in comparison with more traditional *N*-acetylneuraminic acid (Neu5Ac) glycosyl donors in terms of reactivity and stereoselectivity.[2c,d] However, the reasons for success of these modified sialyl donors still remain obscure. According to the concept of supramer-mediated reactivity, which has recently been introduced by us,[3] different behaviour of *N*-acetyl- and *N,N*-diacetyl-sialic acid derivatives in glycosylation reactions is related to the differences in structures of supramers formed in the solutions of the respective sialyl donors.[3a,b]

In order to gain deeper understanding of the influence of the *remote* substituent at N(5) on the reactivity of sialyl donors we set out to prepare previously unknown *N,N*-diacetylneuraminic acid ($Neu5Ac_2$) glycosyl chloride **2b** (Scheme 1) and study its reactivity in glycosylation reactions with various nucleophiles using the known Neu5Ac glycosyl chloride **2a**[4] as a reference. Unlike sialic acid thioglycosides, which are widely used in oligosaccharide synthesis, sialyl chloride **2a** has found application only in reactions with simple alcohols and negatively charged nucleophiles, a *niche* where it surpasses other types of sialyl donors.[2a]

2. Results and discussion

The title compound **2b** was easily prepared (Scheme 1) in quantitative yield by treatment of the known peracetylated $Neu5Ac_2$ glycosyl acetate **1b**[5] with HCl in CH_2Cl_2 (HCl was generated in situ from AcCl and MeOH[4b] as described in the most convenient procedure[4d] for the preparation of **2a**). The chloride **2b** was found to be fairly stable at ambient temperature (it can be stored for several months at −18 °C) and can be prepared on a multigram scale without any problem.

As the first step, we studied reactions of **2b** with simple alcohols in the *absence* of any added promoter (see Table 1 and Scheme 2) since it has earlier been shown[4c] that Neu5Ac glycosyl chloride **2a** does react with neat MeOH within 1 h to give Neu5Ac α-methyl



1a,b,c **a** : X = H, R = Me[4] **b** : X = Ac, R = Me **c** : X = H, R = H[4c] **2a,b,c** : ~100%

Scheme 1. Synthesis of sialyl chlorides **2**.

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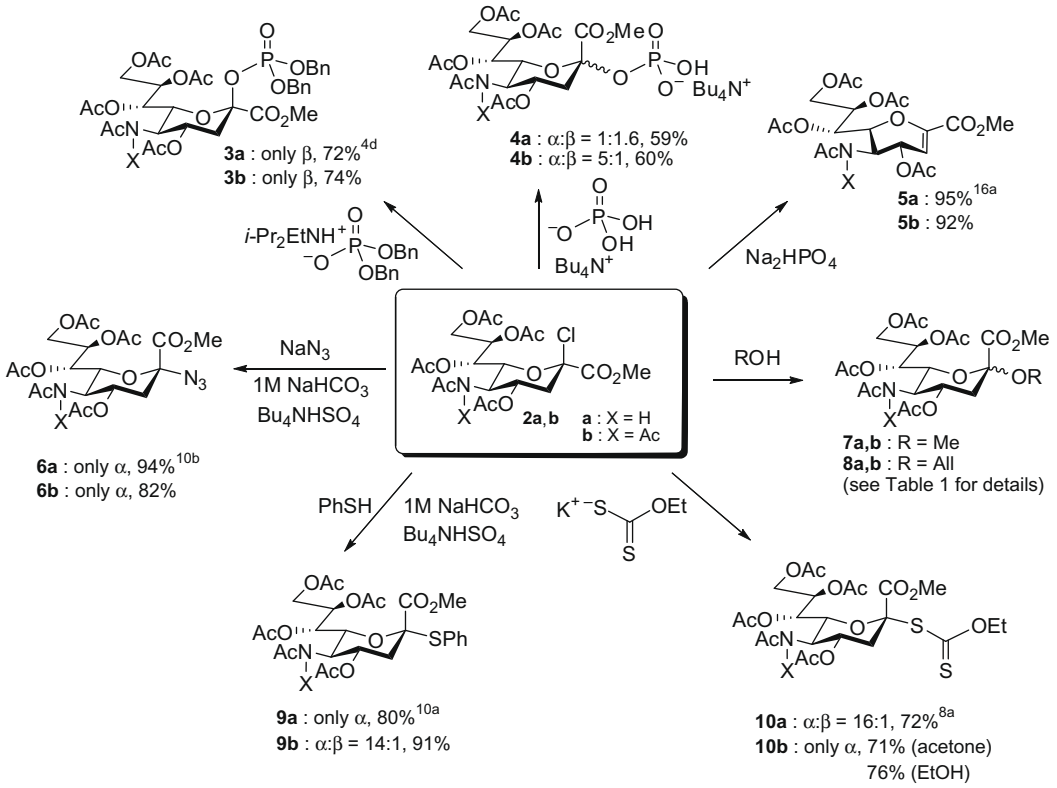
Table 1
Results of reactions of glycosyl chlorides **2a** and **2b** with alcohols ROH

Entry	ROH	Glycosyl donor	Reaction time (h)	Yield of glycoside	Anomeric ratio (α:β)	Products
1	MeOH[a]	**2a**	1	96%[c,d]	~30:1[d]	Only **7a**
2	MeOH[b]	**2a**	3	100%[c]	12:1	Only **7a**
3	MeOH[a]	**2b**	0.5	96%[c]	11:1	Only **7b**
4	MeOH[b]	**2b**	3	100%[c]	3:1	Only **7b**
5	AllOH[a]	**2a**	24	77%[e]	6:1	**8a** + **5a** (2%[e])
6	AllOH[b]	**2a**	24	89%[e]	3:1	**8a** + **5a** (4%[e])
7	AllOH[a]	**2b**	24	47%[c] (**8a**) + 29%[c] (**8b**)	1.3:1 (**8a**) + 1.9:1 (**8b**)	**8a** + **8b**
8	AllOH[b]	**2b**	24	19%[c] (**8a**) + 58%[c] (**8b**)	1.4:1 (**8a**) + 1.4:1 (**8b**)	**8a** + **8b**

[a] Reaction was performed in neat alcohol.
[b] Reactions were performed in MeCN as the solvent.
[c] Isolated yields.
[d] See Ref. 4c.
[e] Yields were calculated by taking into account signals integrals in ^{1}H NMR spectra and the masses of the worked-up reaction mixtures.



Scheme 2. Reactions of sialyl chlorides **2a,b** with nucleophiles.

glycoside **7a**[4c] in high yield and stereoselectivity (entry 1 in Table 1). Based on the known higher reactivity of Neu5Ac$_2$ *thioglycosides*[2d] we expected that Neu5Ac$_2$ glycosyl *chloride* **2b** would be more reactive than Neu5Ac glycosyl chloride **2a**. Indeed, the reaction of the chloride **2b** with neat MeOH was complete within 0.5 h, methyl glycoside **7b**[2e] being the only product. However, considerable amounts of β-anomer were formed in addition to α-methyl glycoside **7b** (entry 3 in Table 1). The stereoselectivity decreased even further and to a greater extent for **2b** than for **2a** when the reactions with MeOH were performed in MeCN as the solvent (entries 2, 4 in Table 1).

The parent *N*-acetylchloroneuraminic acid **2c** corresponding to the methyl ester **2a** is known[4c] to react with neat allyl alcohol (AllOH) in the absence of added promoter to give the respective allyl glycoside in high yield and stereoselectivity (α:β ~ 30:1). Chloride **2a** also reacted with neat AllOH to give after 24 h the respective allyl glycoside **8a**[6] obtained as the mixture of anomers (α:β = 6:1), which was isolated in 77% yield after additional O-acetylation (treatment with Ac_2O/Py was required since de-O-acetylation is known to take place under the reaction conditions[4c]). Again, stereoselectivity decreased when reaction was performed in MeCN as the solvent (entries 5 and 6 in Table 1). It is interesting to note that similar reactions of Neu5Ac$_2$ glycosyl chloride **2b** with AllOH were almost not stereoselective (entries 7 and 8 in Table 1) and resulted in substantial de-N-acetylation leading to formation of *N*-acetylsialoside **8a** along with the expected *N*,*N*-diacetyl-sialoside **8b**. This additional instability of *N*-acetyl group in **2b**/**8b** under reaction conditions makes the use of glycosyl chloride **2b** in reaction with AllOH less practical than the use of more traditional glycosyl chloride **2a**.

Thus, although the yields of glycosides were higher than 76% in all cases (Table 1) the stereoselectivities of the glycosylations of simple alcohols with Neu5Ac$_2$ glycosyl chloride **2b** was lower than those observed in glycosylations with Neu5Ac glycosyl chloride **2a**

in all cases studied. This is especially clear for the reactions of **2a** and **2b** with MeOH (entries 1–4 in Table 1) when the reaction times were small. Reactions of **2a** and **2b** with AllOH (entries 5–8 in Table 1) were considerably slower and accompanied by the HCl-catalyzed anomerization, which is known[4c] to contribute greatly to the stereochemical outcome of unpromoted sialylation at prolonged reaction times. This lower stereoselectivity of sialylation of simple alcohols by $Neu5Ac_2$ glycosyl *chloride* **2b** is especially striking considering much higher stereoselectivities obtained in glycosylations of carbohydrate glycosyl acceptors with $Neu5Ac_2$ *thioglycosides*.[2a,d,e,7] Thus the use of $Neu5Ac_2$ glycosyl chloride **2b** in reactions with simple alcohols offers no practical advantages over more common Neu5Ac glycosyl chloride **2a**.

The next stage was to study the reactions of $Neu5Ac_2$ glycosyl chloride **2b** with negatively charged nucleophiles (Scheme 2) which are known[2a] to react with the parent Neu5Ac glycosyl chloride **2a** smoothly to give the corresponding substitution products stereoselectively.

The reaction of Neu5Ac glycosyl chloride **2a** with *O*-ethyl-*S*-potassium dithiocarbonate (KSCSOEt) has been reported to give the mixture of anomers of sialyl xanthate **10a** (72%, α:β = 16:1)[8a] contaminated with inseparable glycal **5a** (24%) in acetone and pure α-xanthate **10a** in anhydrous EtOH (71%)[8b] or under phase transfer catalysis (PTC[9]) conditions (72% after crystallization[8c]). When $Neu5Ac_2$ glycosyl chloride **2b** was treated with KSCSOEt in acetone or in 95% EtOH α-sialyl xanthate **10b** was formed in 71% and 76% yields, respectively. It is worth mentioning that the yield of xanthate **10b** was slightly lower in acetone, incapable of reacting with sialyl chloride **2b**, than in ethanol, which might be able to react with sialyl chloride **2b** to give the corresponding ethyl glycoside. We have never performed such a reaction since the use of ethyl sialoside offers no advantages over the use of methyl sialoside while lacking valuable features of allyl sialosides. By analyzing Table 1 one can surmise that within 1 h a noticeable amount of ethyl sialoside would be formed. However, no competition between S- and O-nucleophiles has ever been observed in these reactions. Similar to the published reaction of sialyl chloride **2a** with KSCSOEt in ethanol[8b] no formation of ethyl sialoside could be detected in the case of **2b** under similar conditions although a mixture of glycosyl chloride **2b** and KSCSOEt in ethanol was allowed to react for 1 h at ambient temperature.

The reactions of Neu5Ac glycosyl chloride **2a** with PhSH and NaN_3 under PTC conditions have been reported to give phenyl α-thiosialoside **9a**[10a] and α-glycosyl azide **6a**[10b] in 80% and 94% yields, respectively. Application of PTC conditions (Bu_4NHSO_4, AcOEt, 1 M $NaHCO_3$)[8c,10] for reactions of **2b** with PhSH or NaN_3 resulted in clean formation of phenyl thiosialoside **9b** (91%, α:β = 14:1) and α-glycosyl azide **6b** (82%).

Complete inversion of anomeric configuration during these reactions suggests S_N2-like mechanism of chlorine substitution in both sialyl chlorides **2a** and **2b** (see the discussion of the mechanism below). The products of these reactions (glycosyl azides **6a**,**b**, thioglycosides **9a**,**b** and glycosyl xanthates **10a**,**b**) are configurationally stable under the reaction conditions. The preparation of glycosyl phosphates is a more demanding task due to possibility of product anomerization.[11]

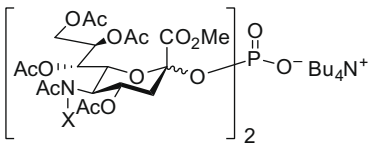
The reaction of Neu5Ac glycosyl chloride **2a** with ethyldi(isopropyl)ammonium dibenzyl phosphate ($[Pr^i_2NHEt][(BnO)_2PO_2]$) in MeCN has recently been reported[4d] to give the corresponding β-phosphate **3a** in 72% yield albeit contaminated with inseparable *N*-acetyl-glycal **5a**. A similar reaction of $Neu5Ac_2$ glycosyl chloride **2b** with $[Pr^i_2NHEt][(BnO)_2PO_2]$ in MeCN smoothly gave β-configured $Neu5Ac_2$ dibenzyl phosphate **3b** in 74% yield along with the corresponding glycal **5b** (19%), which could easily be separated by silica gel chromatography. This is the highest yield of sialic acid glycosyl dibenzyl phosphate with β-configuration ever obtained by glycosylation. Glycosylation of dibenzyl phosphoric acid ($(BnO)_2P(O)OH$) with Neu5Ac glycosyl phosphite gave compound **3a** in 53% yield[12a] while the attempted[12b] glycosylation of $(BnO)_2P(O)OH$ with Neu5Ac glycosyl chloride **2a** in the presence of AgOTf failed.

Stereoselective formation of β-phosphate **3b**, that is, overall *retention* of anomeric configuration, was apparently caused by the in situ anomerization of the α-phosphate, which was formed initially in the reaction medium in an S_N2-like process proceeding with inversion of anomeric configuration. This is not surprising as the β-isomers of Neu5Ac are known to be thermodynamically more stable[2a] and dibenzyl phosphoric acid residue is a fairly good leaving group (good nucleofuge). Anomerization of equatorial glycosyl phosphates to the more thermodynamically stable isomers with axial phosphate moiety is well known.[11] Moreover, the α-configured Neu5Ac and $Neu5Ac_2$ dibenzyl phosphates (α-**3a,b**), prepared by a different route, were found to gradually isomerize upon storage to the corresponding β-anomers.[13] The ease of such anomerization is related to the nucleofugality of phosphate anion (which is proportional to the acidity of the conjugate phosphoric acid). For this reason one can expect that the use of a phosphate nucleophile with lower nucleofugality, hence lower tendency to anomerization of glycosyl phosphate, may result in more α-selective reaction.

Indeed, a reaction of Neu5Ac glycosyl chloride **2a** with $[Bu_4N]H_2PO_4$,[14] which is a source of nucleophile ($H_2PO_4^-$) with lower nucleofugality than $(BnO)_2P(O)O^-$, in MeCN was reported[15] to give Neu5Ac glycosyl phosphate **4a** in 39% yield as a mixture of *both* anomers (α:β = 2.3:1). Further research revealed that the amount of β-isomer was in fact higher than had been reported initially and the phosphate **4a** could be obtained in 59% yield (α:β = 1:1.6). A similar reaction of $Neu5Ac_2$ glycosyl chloride **2b** with $[Bu_4N]H_2PO_4$, resulted in formation of $Neu5Ac_2$ glycosyl phosphate **4b** in 60% yield and much higher α-stereoselectivity (α:β = 5:1). This is the first example of *stereoselective* synthesis of a sialic acid glycosyl phosphate with α-configuration. A related Neu5Ac phenyl phosphate with α-configuration has been isolated as the *minor* product (α:β ≈ 1:6) upon reaction of Neu5Ac glycosyl phosphite with phenyl phosphoric acid ($PhOP(O)(OH)_2$) at −40 °C,[12a] which is not surprising considering higher acidity of $PhOP(O)(OH)_2$ than that of H_3PO_4. Hence sialyl phenyl phosphate is more prone to anomerization (α→β) than sialyl phosphates **4a,b**, resulting in lower α/β ratio of anomeric phosphorylation.

Reactions of both chlorides **2a,b** with $[Bu_4N]H_2PO_4$ in MeCN were also found to give phosphodiesters **11a,b** as by-products (yields 11% and 4%, respectively), which could be formed in the reaction of glycosyl chlorides **2a,b** with phosphomonoesters **4a,b** (Scheme 3).

Neu5Ac glycosyl chloride **2a** is known[16a] to react with much more basic Na_2HPO_4 (a disubstituted salt of phosphoric acid) in refluxing MeCN (no reaction occurs at ambient temperature) to give exclusively an elimination product, Neu5Ac glycal **5a**,[16] in quantitative yield. No product of nucleophilic substitution could be detected. When $Neu5Ac_2$ glycosyl chloride **2b** was involved in the reaction with Na_2HPO_4 under identical conditions, only Neu5Ac glycal **5a**, lacking one of the two *N*-acetyl groups present



11a : X = H, 11%
11b : X = Ac, 4%

Scheme 3. Structures of bis(sialyl) phosphates **11a,b**.

in **2b**, was formed in quantitative yield after 3 h rather than the expected Neu5Ac$_2$ glycal **5b**. We found that the rate of de-N-acetylation is temperature dependent. Decreasing temperature resulted in the formation of mixtures of **5a** with the increasing amounts of Neu5Ac$_2$ glycal **5b**,[17] which could be prepared in pure form (92% yield) when reaction was performed at ambient temperature although the overall reaction rate considerably decreased (full conversion of **2b** was achieved only after 1 month). Further experiments demonstrated that the *N*-acetyl group of Neu5Ac$_2$ residue could be removed *only* from N(5) of glycosyl chloride **2b**. Glycal **5b** was stable under the reaction conditions. Other sialic acid derivatives with two *N*-acetyl groups (e.g., **1b** or **9b**) did not react with Na_2HPO_4 either.

As can be seen from the results obtained, stereoselectivities achieved in glycosylation reactions with Neu5Ac glycosyl chloride **2a** or Neu5Ac$_2$ glycosyl chloride **2b** are dramatically dependent on the nature of nucleophile used and therefore need commenting. First of all, we have to stress that glycosylation with both sialyl chlorides **2a** and **2b** leading to products, which are configurationally stable under the reaction conditions (i.e., glycosyl azides **6a**,**b**, thioglycosides **9a**,**b** and glycosyl xanthates **10a**,**b**), always proceeded with inversion of configuration of anomeric centre and resulted in the products with α-configuration independent of the number of acetyl groups at N(5). This observation is very important and suggests that initially reactions of sialyl chlorides **2a** and **2b** with nucleophiles proceed as S_N2-like processes leading to α-configured products, which may further experience an in situ anomerization leading to β-configured products. The possibility of this anomerization greatly depends on the nucleofugality of aglycon moiety and reaction conditions. Currently there is no generally accepted rationale how the second acetyl group at N(5) in glycosyl chloride **2b** can influence the outcome of the reactions at anomeric position at (C(2)) including glycosylation and anomerization steps (cf. Refs.[3a,3b]). At the moment it is only clear that the acid-catalyzed anomerization (HCl is formed during these promoter-free glycosylations) of alkyl sialosides **7a,b** and **8a,b** is favored in the case of Neu5Ac$_2$ glycosyl derivatives, especially in more polar MeCN. On the contrary, the presence of an additional *N*-acetyl group in sialyl phosphate **4b** makes this compound less prone to anomerization than the 5-acetamido counterpart **4a** under the reaction conditions. It is important to note that the anomeric phosphorylation leading to glycosyl phosphates **4a,b** proceeds with no visible change in the acidity of reaction medium probably due to the buffering effect of the excess of phosphate salt used as a source of nucleophile. For this reason one can not exclude that different pathways for anomerization[18] may be operative in these two cases.

The most amazing feature of sialyl chlorides **2a,b** is their profound ability to give substitution products with *inverted* anomeric configuration (see the discussion above). Inversion of configuration is usually anticipated for an S_N2-like reaction, an associative mechanism, featuring concomitant attack of a nucleophile and loss of the aglycon (A_ND_N in IUPAC notation[19]). However, considering the tertiary structure of the anomeric centre in sialyl chlorides, this is generally assumed to be a very unlikely scenario. Although the anomeric carbon of NeuAc has three non-hydrogen substituents and is believed to be somewhat hindered, it is very important that A_ND_N-like chemistry has been identified for NeuAc in the case of the *trans*-sialidase enzyme, which can utilize this pathway, despite the bulky environment at the anomeric centre.[18b]

An alternative S_N1-like mechanism ($D_N + A_N$ according to IUPAC[19]) would lead to dissociative loss of the aglycon (chloride in our case), first producing a solvent-equilibrated glycosyl oxocarbenium ion, followed by nucleophilic capture. This mechanism is considered to be quite common in nucleophilic substitution reactions at tertiary centres (like in *tert*-butyl chloride) especially when the respective carbenium ion is stabilized like in the case of oxacarbenium ions generated from glycosyl donors.[18] Remarkably, nucleophilic substitution at anomeric position involving S_N1-like mechanism would inevitably lead to a considerable loss of stereoselectivity. This situation indeed occurs during sialylation with sialic acid *thioglycosides* where it is very difficult to achieve substantial level of stereocontrol (moderate stereoselectivities of α:β ~ 7:1 are quite common even in participating nitrile solvents).[2] An important feature of these reactions is that stereoselectivity of sialylation with *thioglycosides* usually does not depend on the anomeric configuration of the starting thioglycoside.[2]

Consideration of intermediate preassociation mechanism ($D_N * A_{Nint}$),[19] which involves formation of intimate ion-pair intermediate,[20] could allow interpretation of the observed stereoselectivities (including inversion) during sialylation with sialyl chlorides **2a,b**. However, high α-stereoselectivities in nucleophilic substitution in sialyl chlorides **2a,b** are observed even in polar solvents such as acetonitrile or alcohols, where the dominant reaction of ion-pairs is their separation to free ions.[20]

These considerations suggest the involvement of S_N1-like mechanism ($D_N + A_N$ or $D_N * A_{Nint}$) to be highly unlikely in *unpromoted* reactions of sialyl chlorides **2a,b** and make S_N2-like mechanism (A_ND_N) of substitution fairly feasible. It would be very interesting to study the mechanistic details of nucleophilic substitution in sialyl chlorides **2a,b** both theoretically and experimentally.

3. Conclusions

In conclusion, a novel sialyl donor *N*,*N*-diacetylneuraminic acid glycosyl chloride **2b** was prepared for the first time and its reactions with nucleophiles were studied. Neu5Ac$_2$ glycosyl chloride **2b** showed its best in reactions with charged nucleophiles and made possible the first stereoselective synthesis of sialic acid glycosyl phosphate with α-configuration and highly efficient synthesis of β-configured sialic acid glycosyl dibenzyl phosphate. The compounds prepared from **2b** have potential for wide applications and some of them have already been used. Thioglycoside **9b**, xanthate **10b** and dibenzyl phosphate **3b** are sialyl donors themselves while azide **6b** may be useful for the preparation of glycosyl amines and in 'click chemistry'-based approaches[21] for the construction of simple glycoside and oligosaccharide mimetics, glyco-macrocycles, glycopeptides, glyco-clusters and carbohydrate arrays. The novel α-configured glycosyl phosphate **α-4a** has already been used in the first synthesis of sialic acid polyprenyl glycosyl phosphate, a probable biosynthetic intermediate of bacterial polysialic acid.[22]

4. Experimental

4.1. General methods

The reactions were performed with the use of commercial reagents (Aldrich, Fluka, Acros Organics) and distilled solvents purified according to standard procedures. Thin-layer chromatography was carried out on Silica Gel 60 F_{254} plates on aluminium foil (Merck), spots were visualized under UV light and by heating the plates after immersion in a 1:10 (v/v) mixture of 85% aqueous H_3PO_4 and 95% EtOH. The ^1H and ^{13}C NMR spectra of solutions in $CDCl_3$ were recorded on a Bruker AC-200 instrument (200.13, and 50.32 MHz, respectively) and a Bruker AVANCE 600 instrument (600.13 and 150.9 MHz, respectively) while ^{31}P NMR spectra were recorded on a Bruker AC-200 instrument (81.02 MHz). The ^1H chemical shifts are referred to the signal of the residual $CHCl_3$ (δ_H 7.27 ppm), and the ^{13}C of the ^{13}C NMR—to the signal of $CDCl_3$ (δ_C 77.0 ppm) while ^{31}P chemical shifts of ^{31}P NMR—to the signal of 75% H_3PO_4 in D_2O (δ_P 0.0 ppm, external standard). The assignment

of the signals in the ^{1}H and ^{13}C NMR spectra was made using ^{1}H,^{1}H-COSY 2D NMR and APT (JMODXH) experiments, respectively. Mass spectra (electrospray ionization, ESI) were recorded on a Finnigan LCQ mass spectrometer for 2×10^{-5} M solutions. The optical rotation ($[\alpha]_D$) was measured on a JASCO DIP-360 polarimeter at 20–27 °C. Reactions of glycosyl chlorides **2a,b** with nucleophiles were carried out with the use of glycosyl chlorides **2a,b**, which were freshly prepared as described below from the fully acetylated neuraminic acid methyl esters **1a** or **1b** and dried for 3 h in vacuum of an oil pump. The yields are quoted with respect to the amount of starting glycosyl acetates **1a,b** used for the preparation of glycosyl chlorides **2a**,**b** since the prepared chlorides **2a,b** may contain coordinated HCl.[4b–d]

4.2. Tetrabutylammonium dihydrogen phosphate

The title compound was prepared essentially as described in Ref. 14. Phosphoric acid (96% aqueous solution of H_3PO_4, 4 mL) was added to deionized H_2O (20 mL) followed by Bu_4NOH (75 mL of 20% aqueous solution, Merck) and the resulting mixture was stirred for 18 h at room temperature (~20 °C). Then more 96% H_3PO_4 was added portion-wise (3×20 μl) with pH monitoring. For the determination of pH, aliquots (1 mL) of the obtained opalescent solution were diluted with deionized H_2O (9 mL) and then pH of the resulting clear solution was measured with a Metrohm 744 pH-meter. After pH reached 5.19 the reaction mixture was concentrated on a rotary evaporator (at +35 °C) and anhydrous MeCN (310 mL, Merck, c(H_2O) <0.3%) was added to the residue and the mixture was magnetically stirred for 3 days and then the white fine crystalline precipitate was filtered off. The filtrate was concentrated on a rotary evaporator (at +40 °C) and the residue was dried in vacuo (oil pump) for 1.5 h to give $[Bu_4N][H_2PO_4]$ (20.72 g), which was stored in a desiccator over NaOH. This salt was used in reactions without additional drying. ^{1}H NMR (200.13 MHz, $CDCl_3$): δ_H 0.90 (t, J = 7.0 Hz, 12H, CH_3CH$_2$CH$_2$CH$_2$N), 1.40 (sextet, J = 7.0 Hz, 8H, CH$_3$CH_2CH$_2$CH$_2$N), 1.51–1.70 (m, 8H, CH$_3$CH$_2$CH_2CH$_2$N), 3.10–3.40 (m, 8H, CH$_3$CH$_2$CH$_2$CH_2N); ^{1}H NMR (200.13 MHz, D_2O) δ_H 0.80 (t, J = 7.5 Hz, 12 H, CH_3CH$_2$CH$_2$CH$_2$N), 1.31 (sextet, J = 7.5 Hz, 8H, CH$_3$CH$_2$CH$_2$CH$_2$N), 1.50–1.70 (m, 8H, CH$_3$CH$_2$CH_2CH$_2$N), 3.09–3.22 (m, 8H, CH$_3$CH$_2$CH$_2$CH_2N); ^{13}C NMR (54.24 MHz, $CDCl_3$): δ_C 13.6 (CH_3), 19.4 (CH_2), 23.8 (CH_2), 58.3 (NCH_2); ^{13}C NMR (54.24 MHz, D_2O) δ_C 13.7 (CH_3), 20.0 (CH_2), 30.0 (CH_2), 58.9 (NCH_2); ^{31}P NMR (81.02 MHz, D_2O): δ_P +0.6.

4.3. Methyl 4,7,8,9-tetra-*O*-acetyl-2-chloro-5-(*N*,*N*-diacetylamino)-2,3,5-trideoxy-β-D-*glycero*-D-*galacto*-non-2-ulopyranosonate (2b)

4.3.1. Small scale procedure

Anhydrous MeOH (0.9 mL, 0.02 mol) was slowly added dropwise to AcCl (2.5 mL, 0.035 mol) with cooling in an ice-water bath. The resulting solution was added to a cold solution of glycosyl acetate **1b** (51.2 mg, 0.088 mmol) in a mixture of anhydrous CH_2Cl_2 (2.5 mL) and AcCl (2.5 mL, 0.035 mol) and the reaction mixture was kept at +4 °C for 12 h (TLC control: R_f = 0.26 (**2b**), R_f = 0.23 (**1b**), AcOEt–petroleum ether, 1:1). Volatile components were evaporated, CCl_4 (5 mL) was added, volatile components were again evaporated and the addition of CCl_4 and evaporation was repeated five times. The residue was dried in vacuo (oil pump) to give glycosyl chloride **2b** as a white foam (53 mg, ~100%), which was used without additional purification.

4.3.2. Large scale procedure

Anhydrous MeOH (14 mL, 0.346 mol) was slowly added dropwise to AcCl (25 mL, 0.351 mol) with cooling in an ice-water bath. The resulting solution was added to a cold solution of glycosyl acetate **1b** (18.6 g, 32.1 mmol) in a mixture of anhydrous CH_2Cl_2 (200 mL) and AcCl (25 mL, 0.351 mmol) and the reaction mixture was kept at +4 °C for 12 h (TLC control: R_f = 0.26 (**2b**), R_f = 0.23 (**1b**), AcOEt–petroleum ether, 1:1). Volatile components were evaporated, CCl_4 (~100 mL) was added, and volatile components were again evaporated, the addition of CCl_4 and evaporation was repeated (3–5 times) until no smell of HCl could be detected. The residue was dried in vacuo (oil pump) to give glycosyl chloride **2b** as the slightly yellow solid (17.66 g, ~100%; R_f = 0.62 AcOEt; R_f = 0.26, AcOEt–petroleum ether, 1:1), identical to that obtained by the small scale procedure, which was used without additional purification.

4.3.3. Data for methyl 4,7,8,9-tetra-*O*-acetyl-2-chloro-5-(*N*,*N*-diacetylamino)-2,3,5-trideoxy-β-D-*glycero*-D-*galacto*-non-2-ulopyranosonate (2b)

$[\alpha]_D^{20}$ −37.8 (*c* 1.7, $CHCl_3$); ^{1}H NMR (200.13 MHz, $CDCl_3$): δ_H 1.97, 2.01, 2.05, 2.08 (4 s, 3H each, 4 × AcO), 2.19 (dd, $J_{3ax,4}$ = 10.4 Hz, 1H, H-3ax), 2.30, 2.41 (2 s, 3H each, Ac_2N), 2.89 (dd, $J_{3eq,4}$ = 5.1 Hz, $J_{3eq,3ax}$ = 13.8 Hz, 1H, H-3eq), 3.85 (s, 3H, OMe), 4.07 (dd, $J_{8,9b}$ = 5.2 Hz, $J_{9a,9b}$ = 12.7 Hz, 1H, H-9b), 4.30 (dd, $J_{8,9a}$ = 2.6 Hz, 1H, H-9a), 4.31 (t, 1H, H-5), 5.18 (ddd, 1H, H-8), 5.25 (dd, $J_{6,7}$ = 2.1 Hz, $J_{7,8}$ = 7.5 Hz, 1H, H-7), 5.41 (dd, $J_{5,6}$ = 10.2 Hz, 1H, H-6), 5.89 (ddd, $J_{4,5}$ = 10.3 Hz, 1H, H-4); ^{13}C NMR (54.24 MHz, $CDCl_3$): δ_C 20.6, 20.8 (OC(O)CH_3), 26.1, 27.9 (2 × NC(O)CH_3), 41.8 (C-3), 53.6 (OMe), 56.1 (C-5), 61.6 (C-9), 66.4, 66.7, 69.1, 71.3 (C-4, C-6, C-7, C-8), 95.9 (C-2), 165.8 (C-1), 169.5, 169.9, 170.5, 173.3, 174.3 (C═O).

4.4. Methyl 4,7,8,9-tetra-*O*-acetyl-5-(*N*,*N*-diacetylamino)-2-*O*-di(benzyloxy)phosphoryl-3,5-dideoxy-β-D-*glycero*-D-*galacto*-non-2-ulo-pyranosonate (3b)

Ethyldi(isopropyl)amine (0.066 mL, 0.37 mmol) was added to a solution of $(BnO)_2P(O)OH$ (117 mg, 0.42 mmol) in MeCN (1 mL). The solution of salt thus prepared was added dropwise to a solution of glycosyl chloride **2b** (prepared from **1b** (52.1 mg, 0.091 mmol)) in MeCN (2 mL). The flask, in which salt was prepared, was additionally rinsed with MeCN (2 mL). The course of the reaction was monitored by TLC (R_f = 0.59 (**3b**), R_f = 0.62 (**2b**), AcOEt). After completion of the reaction (24 h), the reaction mixture was cooled in an ice-water bath, and cold saturated $NaHCO_3$ solution (10 mL) and $CHCl_3$ (10 mL) were added. The aqueous phase was extracted with $CHCl_3$ (3×5 mL). The organic phase was concentrated at ambient temperature. The residue was dissolved in CH_2Cl_2 and applied onto a silica gel HPLC column (Silasorb 600, 7.5 μm, 15 × 250 mm). The products were eluted with gradient of AcOEt in petroleum ether (0→100%) to give **3b** as a colourless syrup (53.7 mg, 74%; R_f = 0.59, AcOEt) and glycal **5b** (8.7 mg, 19%, R_f = 0.62, AcOEt). $[\alpha]_D^{27}$ −4.0 (*c* 1, $CHCl_3$); ^{1}H NMR (600.13 MHz, $CDCl_3$): δ_H 1.986, 1.989, 2.00, 2.14 (4 s, 3H each, 4 × AcO), 2.14 (from COSY) (dd, 1H, H-3ax), 2.32, 2.40 (2 s, 3H each, Ac_2N), 2.896 (dd, $J_{3eq,4}$ = 5.3 Hz, $J_{3eq,3ax}$ = 13.7 Hz, 1H, H-3eq), 3.75 (s, 3H, OMe), 4.22 (dd, $J_{8,9b}$ = 6.5 Hz, $J_{9a,9b}$ = 12.4 Hz, 1H, H-9b), 4.31 (dd, $J_{4,5}$ = 10.3 Hz, $J_{5,6}$ = 10.3 Hz, 1H, H-5), 4.47 (dd, $J_{8,9a}$ = 2.7 Hz, 1H, H-9a), 5.10–5.20 (m, 4H, 2 × OCH_2Ph), 5.242 (ddd, 1H, H-8), 5.27 (dd, $J_{6,7}$ = 1.9 Hz, $J_{7,8}$ = 5.4 Hz, 1H, H-7), 5.42 (dd, 1H, H-6), 5.93 (ddd, $J_{3ax,4}$ = 11.0 Hz, 1H, H-4); ^{13}C NMR (150.9 MHz, $CDCl_3$): δ_C 20.67, 20.73, 20.9 (OC(O)CH_3), 26.0, 28.0 (2 × NC(O)CH_3), 38.0 (d, $^3J_{C,P}$ = 4.2 Hz, C-3), 53.3 (OMe), 56.5 (C-5), 62.0 (C-9), 66.2, 67.7, 70.2, 70.7 (C-4, C-6, C-7, C-8), 69.9 (d, $J_{C,P}$ = 4.0 Hz, OCH_2Ph), 99.9 (d, $^2J_{C,P}$ = 5.3 Hz, C-2), 128.1, 128.2, 128.5 (Ph), 135.54 (d, $^3J_{C,P}$ = 8.0 Hz, C-quat. Ph), 135.60 (d, $^3J_{C,P}$ = 7.7 Hz, C-quat. Ph), 165.9 (C-1), 169.4, 170.0, 170.2, 170.6,

173.5, 174.3 (C=O); ^{31}P NMR (81.02 MHz, $CDCl_3$): δ_P −6.9; ESIMS: found *m/z* 815.9 [M+Na], calcd for $C_{36}H_{44}NNaO_{17}P$: 816.2.

4.5. Methyl 4,7,8,9-tetra-*O*-acetyl-5-acetamido-2-*O*-dihydroxyphosphoryl-3,5-dideoxy-α-D-*glycero*-D-*galacto*-non-2-ulo-pyranosonate, tetrabutylammonium salt (α-4a); methyl 4,7,8,9-tetra-*O*-acetyl-5-acetamido-2-*O*-dihydroxyphosphoryl-3,5-dideoxy-β-D-*glycero*-D-*galacto*-non-2-ulo-pyranosonate, tetrabutylammonium salt (β-4a); bis[methyl (4,7,8,9-tetra-*O*-acetyl-5-acetamido-3,5-dideoxy-D-*glycero*-D-*galacto*-non-2-ulo-pyranosyl)onate]phosphate, tetrabutylammonium salt (11a)

Glycosyl chloride **2a** (prepared from **1a** (100 mg, 0.19 mmol)) was dissolved in MeCN (2 mL) and solid $[Bu_4N]H_2PO_4$ (284 mg, 0.84 mmol) was added. The reaction mixture was stirred for 4 h (TLC control: R_f = 0.00 (**4a, 11a**), R_f = 0.48 (**5a**), R_f = 0.50 (**2a**), AcOEt; R_f = 0.30 (α-**4a**), R_f = 0.40 (β-**4a**), R_f = 0.60 (**11a**), R_f = 0.81 (**5a**), $CHCl_3$–MeOH–H_2O, 65:25:4). The reaction mixture was evaporated at ambient temperature and suspended in deionized H_2O (0.5 mL) and the suspension was applied on a C18 cartridge (16 × 20 mm, Mega Bond Elut C18 (Varian)). The cartridge was washed with H_2O (20 mL) and MeCN (40 mL). The acetonitrile phase was evaporated to give a mixture (133.4 mg) of glycosyl phosphate **4a**, glycal **5a** and anomeric mixture of phosphodiesters **11a** as a dark yellow syrup (**4a**:**5a**:**11a** = 5.4:1.5:1). The yields of **4a** (91.0 mg, α:β = 1:1.6, 59%; R_f = 0.30 (α-**4a**) and 0.40 (β-**4a**), $CHCl_3$–MeOH–H_2O, 65:25:4), **5a** (14.7 mg, 16%), and **11a** (27.7 mg, 11%; R_f = 0.60, $CHCl_3$–MeOH–H_2O, 65:25:4) were calculated by integration of the respective signals in the ^{1}H NMR spectrum and taking into account the molecular masses of **4a**, **5a** and **11a** (812.88 and 473.42, 1286.31, respectively). Analytical samples of pure glycosyl phosphates α-**4a** and β-**4a** were obtained from this mixture by reversed phase chromatography on a C18 cartridge (16 × 20 mm, Mega Bond Elut C18 (Varian); gradient elution (0→100%) with MeCN in deionized H_2O).

4.5.1. Data for methyl 4,7,8,9-tetra-*O*-acetyl-5-acetamido-2-*O*-dihydroxyphosphoryl-3,5-dideoxy-α-D-*glycero*-D-*galacto*-non-2-ulo-pyranosonate, tetrabutylammonium salt (α-4a)

^{1}H NMR (200.13 MHz, $CDCl_3$): δ_H 0.96 (t, J = 7.2 Hz, 12H, C*H*$_3$CH$_2$CH$_2$CH$_2$N), 1.30–1.51 (m, 8H, CH$_3$C*H*$_2$CH$_2$CH$_2$N), 1.53–1.74 (m, 8H, CH$_3$CH$_2$C*H*$_2$CH$_2$N), 1.82 (s, 3H, AcN), 1.97, 1.98 (2 s, 6H, 2 × AcO), 2.04, 2.06 (2 s, 6H, 2 × AcO), 2.01–2.25 (m ∼ 't', 1H, H-3ax), 3.01 (dd, $J_{3eq,4}$ = 4.9 Hz, $J_{3eq,3ax}$ = 13.3 Hz, 1 H, H-3eq), 3.23–3.37 (m, 8 H, CH$_3$CH$_2$CH$_2$C*H*$_2$N), 3.73 (s, 3 H, OMe), 3.68–3.77 (m, 1H, H-6), 3.90–4.14 (m, 2 H, H-5, H-9a), 4.27–4.37 (m ∼ 'dd', $J_{9a,9b}$ ≈ 12.4 Hz, $J_{8,9b}$ ≈ 2.4 Hz, 1H, H-9b), 5.03–5.20 (m ∼ 'ddd', $J_{3eq,4}$ = 4.9, $J_{4,5}$ = 10.3, 1H, H-4), 5.15–5.30 (m, 2 H, H-7, H-8), 5.42 (d, $J_{5,NH}$ = 9.7 Hz, 1 H, NH); ^{13}C NMR (54.24 MHz, $CDCl_3$): δ_C 13.7 (CH_3), 19.7 (CH_2), 20.8, 21.1 (C(O)*C*H$_3$), 23.2 (NC(O)*C*H$_3$), 24.0 (CH_2), 38.0 (br s, C-3), 49.7 (C-5), 52.6 (OCH_3), 59.0 (NCH_2), 62.2 (C-9), 67.6, 69.4, 69.9, 72.2 (C-4, C-8, C-7, C-6), 97.67 (d, $J_{C,P}$ = 3.2 Hz, C-2), 169.2 (C-1), 170.1, 170.2, 170.4, 170.8, 171.1 (C=O); ^{31}P NMR (81.02 MHz, D_2O): δ_P −4.9; ESIMS: found *m/z* 538.1 [M−Bu$_4$N–OMe–H]$^-$. Calcd for $C_{19}H_{25}NO_{15}P$: 538.10. Found *m/z* 1382.1 [M$_2$−Bu$_4$N]$^-$. Calcd for $C_{56}H_{94}NO_{16}P$: 1382.53.

4.5.2. Data for methyl 4,7,8,9-tetra-*O*-acetyl-5-acetamido-2-*O*-dihydroxyphosphoryl-3,5-dideoxy-β-D-*glycero*-D-*galacto*-non-2-ulo-pyranosonate, tetrabutylammonium salt (β-4a)

^{1}H NMR (200.13 MHz, $CDCl_3$): δ_H 0.99 (t, J = 7.1 Hz, 12H, C*H*$_3$CH$_2$CH$_2$CH$_2$N,), 1.33–1.53 (m, 8H, CH$_3$C*H*$_2$CH$_2$CH$_2$N), 1.55–1.78 (m, 8H, CH$_3$CH$_2$C*H*$_2$CH$_2$N), 1.75–1.90 (m, 1 H, H-3ax), 1.85 (s, 3 H, AcN), 2.00, 2.01, 2.04, 2.13 (4 s, 3H each, 4 × AcO), 2.68 (dd, $J_{3eq,4}$ = 4.9 Hz, $J_{3eq,3ax}$ = 12.9 Hz, 1H, H-3eq), 3.22–3.35 (m, 8 H, CH$_3$CH$_2$CH$_2$C*H*$_2$N), 3.74 (s, 3H, OCH_3), 4.14 (ddd ∼ q, J ≈ 10.2 Hz, 1 H, H-5), 4.39 (dd, $J_{8,9a}$ = 7.1 Hz, $J_{9a,9b}$ = 12.3 Hz, 1H, H-9a), 4.64 (dd, $J_{5,6}$ = 10.9, $J_{6,7}$ = 2.1 Hz, 1 H, H-6), 4.77 (dd, $J_{8,9b}$ = 7.1 Hz, $J_{9a,9b}$ = 12.3 Hz, 1H, H-9b), 4.90 (br d, $J_{NH,5}$ ≈ 10 Hz, 1H, NH), 5.24–5.54 (m, 3H, H-4, H-7, H-8); ^{13}C NMR (54.24 MHz, $CDCl_3$): δ_C 13.7 (CH_3), 19.6 (CH_2), 20.92, 20.95, 21.02, 21.06 (OC(O)*C*H$_3$), 23.0 (NC(O)*C*H$_3$), 24.0 (CH_2), 37.8 (C-3), 48.6 (C-5), 52.3 (OCH_3), 58.7 (NCH_2), 61.8 (C-9), 69.7, 70.7, 71.4, 72.0 (C-4, C-8, C-7, C-6), 95.8 (d, J = 5.7 Hz, C-2), 169.6 (C-1), 170.35, 170.42, 170.52, 170.61, 172.3 (C=O); ^{31}P NMR (81.02 MHz, $CDCl_3$): δ_P −3.8; ESIMS: found *m/z* 569.9 [M−Bu$_4$N]$^-$. Calcd for $C_{20}H_{29}NO_{16}P$: 570.12. Found *m/z* 1382.1 [M$_2$−Bu$_4$N]$^-$. Calcd for $C_{56}H_{94}NO_{16}P$: 1382.53.

4.5.3. Data for bis[methyl (4,7,8,9-tetra-*O*-acetyl-5-acetamido-3,5-dideoxy-D-*glycero*-D-*galacto*-non-2-ulo-pyranosyl)onate] phosphate, tetrabutylammonium salt (11a)

^{1}H NMR (200.13 MHz, $CDCl_3$, selected signals): δ_H 1.02 (t, J = 6.9 Hz, 12H, C*H*$_3$CH$_2$CH$_2$CH$_2$N), 1.35–1.53 (m, 8H, CH$_3$C*H*$_2$CH$_2$CH$_2$N), 1.54–1.76 (m, 8H, CH$_3$CH$_2$C*H*$_2$CH$_2$N), 1.86, 1.89 (2 s, 3H each, 2 × AcN), 2.03, 2.08, 2.11, 2.13 (4 s, 24H, 8 × AcO), 3.20–3.36 (m, 8H, CH$_3$CH$_2$CH$_2$C*H*$_2$N), 3.75, 3.81 (2 s, 3 H each, 2 × OMe); ^{31}P NMR (81.02 MHz, $CDCl_3$): δ_P −11.0, −12.5; ESIMS: found *m/z* 1043.2 [M]$^-$. Calcd for $C_{40}H_{56}N_2O_{28}P$: 1043.28.

4.6. Methyl 4,7,8,9-tetra-*O*-acetyl-5-(*N,N*-diacetylamino)-2-*O*-dihydroxyphosphoryl-3,5-dideoxy-α-D-*glycero*-D-*galacto*-non-2-ulo-pyranosonate, tetrabutylammonium salt (α-4b); methyl 4,7,8,9-tetra-*O*-acetyl-5-(*N,N*-diacetylamino)-2-*O*-dihydroxyphosphoryl-3,5-dideoxy-β-D-*glycero*-D-*galacto*-non-2-ulo-pyranosonate, tetrabutylammonium salt (β-4b); bis[methyl (4,7,8,9-tetra-*O*-acetyl-5-(*N,N*-diacetylamino)-3,5-dideoxy-D-*glycero*-D-*galacto*-non-2-ulo-pyranosyl)onate]phosphate, tetrabutylammonium salt (11b)

Glycosyl chloride **2b** (prepared from **1b** (56.5 mg, 0.098 mmol)) was dissolved in MeCN (1 mL) and solid $Bu_4H_2PO_4$ (150 mg, 0.442 mmol) was added. The reaction mixture was stirred for 2 h at ambient temperature (20 °C) (TLC control: R_f = 0.00 (**4b, 11b**), R_f = 0.62 (**2b**), AcOEt; 65:25:4, R_f = 0.24 (β-**4b**), R_f = 0.32 (α-**4b**), R_f = 0.68 (**5b**), R_f = 0.73 (**11b**), $CHCl_3$–MeOH–H_2O). The reaction mixture was diluted with deionized H_2O (500 mL). The obtained milky solution was filtered through a C18 cartridge (16 × 20 mm, Mega Bond Elut C18 (Varian)). The cartridge was washed with deionized H_2O (30 mL) and the combined filtrate was filtered again through the same cartridge. The cartridge was washed with MeCN (100 mL) and the acetonitrile phase was evaporated to give a mixture (71 mg) of glycosyl phosphate **4b**, glycal **5b** and **11b** as a dark yellow syrup (**α,β-4b**:**5b**:**11b** = 13.8:2.3:1). The yields of **4b** (50.5 mg, α:β = 4.9:1, 60%) and **5b** (14.9 mg, 30%), **11b** (5.6 mg, 4%) were calculated by integration of the respective signals in the ^{1}H NMR (for **5b** and **α,β-4b**) and ^{31}P NMR (for **α,β-4b** and **11b**) spectra and taking into account the molecular masses of **4b**, **5b** and **11b** (854.92, 515.46 and 1370.88, respectively). ^{1}H NMR (**5b**:α-**4b**:β-**4b** = 2.9:4.9:1), ^{31}P NMR (α-**4b**:β-**4b**:**11b** = 4.8:1:0.43). Analytical sample of pure glycosyl phosphate α-**4b** contaminated with a trace amount of glycal (α-**4b**:**5b** = 24:1) was obtained from this mixture by reversed phase chromatography on a C18 cartridge (16 × 20 mm, Mega Bond Elut C18 (Varian); gradient elution (0→100%) with MeCN in deionized H_2O).

4.6.1. Data for methyl 4,7,8,9-tetra-*O*-acetyl-5-(*N,N*-diacetylamino)-2-*O*-dihydroxyphosphoryl-3,5-dideoxy-α-D-*glycero*-D-*galacto*-non-2-ulo-pyranosonate, tetrabutylammonium salt (α-4b)

^{1}H NMR (600.13 MHz, $CDCl_3$): δ_H 1.01 (t, J = 7.3 Hz, 12H, C*H*$_3$CH$_2$CH$_2$CH$_2$N), 1.45 (tq, J = 7.3 Hz, 8H, CH$_3$C*H*$_2$CH$_2$CH$_2$N), 1.63–1.71 (m, 8H, CH$_3$CH$_2$C*H*$_2$CH$_2$N), 1.957, 2.00, 2.07, 2.12 (4 s, 3H each,

4 × AcO), 2.34–2.40 (from COSY—signal at 2.37) (m, 1H, H-3ax), 2.28, 2.36 (2 s, 3H each, Ac_2N), 3.14 (dd, $J_{3eq,4}$ = 5.4 Hz, $J_{3eq,3ax}$ = 13.3 Hz, 1H, H-3eq), 3.27–3.34 (m, 8 H, $CH_3CH_2CH_2CH_2N$), 3.80 (s, 3H, OMe), 4.07 (t, J = 10.0 Hz, 1H, H-5), 4.15 (dd, $J_{9a,9b}$ = 12.5 Hz, $J_{8,9a}$ = 4.9 Hz, 1H, H-9a), 4.36 (dd, $J_{9a,9b}$ = 12.5 Hz, $J_{8,9b}$ = 2.9 Hz, 1H, H-9b), 4.72 (dd, $J_{5,6}$ = 9.8 Hz, $J_{6,7}$ = 1.5 Hz, 1H, H-6), 5.13 (dd, $J_{6,7}$ = 1.5 Hz, $J_{7,8}$ = 8.0 Hz, 1H, H-7), 5.20–5.24 (m, 1H, H-8), 5.71 (ddd, $J_{4,5}$ = 10.4 Hz, $J_{3ax,4}$ = 10.4 Hz, $J_{3eq,4}$ = 5.4 Hz, 1H, H-4); ^{13}C NMR (150.9 MHz, $CDCl_3$): δ_C 13.7 (CH_3), 19.7 (CH_2), 20.76, 20.85, 20.98 (OC(O)*C*H$_3$), 24.0 (CH_2), 25.5, 27.9 (NC(O)*C*H$_3$), 38.2 (C-3), 52.4 (OCH_3), 57.9 (C-5), 58.9 (CH_2N), 61.5 (C-9), 67.2, 67.8, 69.2, 69.4 (C-4, C-6, C-7, C-8), 98.0 (d, $J_{C,P}$ = 2.1 Hz, C-2), 168.9 (C-1), 169.5, 170.0, 170.6 (CO), 173.9, 174.7 (NCO); ^{31}P NMR (81.02 MHz, $CDCl_3$): δ_P −5.1; ESIMS: found *m/z* 580.1 [M−Bu$_4$N−OMe−H]$^-$. Calcd for $C_{21}H_{27}NO_{16}P$: 580.11.

4.6.2. Data for methyl 4,7,8,9-tetra-*O*-acetyl-5-(*N*,*N*-diacetylamino)-2-*O*-dihydroxyphosphoryl-3,5-dideoxy-β-D-*glycero*-D-*galacto*-non-2-ulo-pyranosonate, tetrabutylammonium salt (β-4b)

^{1}H NMR (600.13 MHz, $CDCl_3$): δ_H 1.01 (t, J = 7.3 Hz, 12H, C*H*$_3$CH$_2$CH$_2$CH$_2$N), 1.45 (tq, J = 7.3 Hz, 8H, CH$_3$*C*H$_2$CH$_2$CH$_2$N), 1.63–1.71 (m, 8H, CH$_3$CH$_2$*C*H$_2$CH$_2$N), 1.962, 1.99, 2.08, 2.12 (4 s, 3 H each, 4 × AcO), 2.34–2.40 (from COSY—signal at 2.13) (m, 1H, H-3ax), 2.24, 2.41 (2 s, 3H each, Ac_2N), 2.93 (dd, $J_{3eq,4}$ = 5.5 Hz, $J_{3eq,3ax}$ = 13.2 Hz, 1H, H-3eq), 3.27–3.34 (m, 8 H, CH$_3$CH$_2$CH$_2$C*H*$_2$N), 3.80 (s, 3H, OMe), 4.30 (t, J = 10.0 Hz, 1H, H-5), 4.37–4.39 (m, 1H, H-9a), 4.61–4.64 (m, 1H, H-9b), 5.15–5.17 (m, 1H, H-6), 5.20–5.24 (m, 1H, H-7), 5.25–5.27 (m, 1H, H-8), 5.75 (ddd, $J_{4,5}$ = 10.0 Hz, $J_{4,3ax}$ = 10.0 Hz, $J_{4,3eq}$ = 5.5 Hz, 1H, H-4); ^{13}C NMR (150.9 MHz, $CDCl_3$): δ_C 13.7 (CH_3), 19.7 (CH_2), 20.71, 20.78, 20.81, 20.90 (OC(O)*C*H$_3$), 24.0 (CH_2), 25.4, 27.7 (NC(O)*C*H$_3$), 39.1 (d, $J_{C,P}$ = 6.4 Hz, C-3), 52.4 (OCH_3), 57.2 (C-5), 58.9 (CH_2N), 61.6 (C-9), 67.6, 68.1, 68.5, 71.6 (C-4, C-6, C-7, C-8), 99.1 (d, $J_{C,P}$ = 6.4 Hz, C-2), 168.9 (C-1), 169.6, 170.0, 170.1, 170.7 (CO), 174.1, 174.6 (NCO); ^{31}P NMR (81.02 MHz, $CDCl_3$): δ_P −4.2.

4.6.3. Data for bis[methyl (4,7,8,9-tetra-*O*-acetyl-5-(*N*,*N*-diacetylamino)-3,5-dideoxy-D-*glycero*-D-*galacto*-non-2-ulo-pyranosyl)onate]phosphate, tetrabutylammonium salt (11b)

^{1}H NMR (200.13 MHz, $CDCl_3$, selected signals): δ_H 1.01 (t, J = 7.0 Hz, 12 H, C*H*$_3$CH$_2$CH$_2$CH$_2$N), 1.34–1.55 (m, 8H, CH$_3$*C*H$_2$CH$_2$CH$_2$N), 1.56–1.79 (m, 8H, CH$_3$CH$_2$*C*H$_2$CH$_2$N), 2.59 (dd, $J_{3eq,4}$ = 5.3 Hz, $J_{3eq,3ax}$ = 13.0 Hz, 1H, H-3eq-A), 3.13 (dd, $J_{3eq,4}$ = 5.4 Hz, $J_{3eq,3ax}$ = 13.0 Hz, 1H, H-3eq-B), 3.21–3.39 (m, 8H, CH$_3$CH$_2$CH$_2$C*H*$_2$N), 3.79, 3.85 (2 s, 6H, 2 × OMe); ^{31}P NMR (81.02 MHz, $CDCl_3$): δ_P −11.9, −13.6.

4.7. Methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-2,6-anhydro-D-*glycero*-D-*galacto*-non-2-enonate (5a)

Glycosyl chloride **2b** (prepared from **1b** (21.2 mg, 0.037 mmol)) was dissolved in MeCN (0.6 mL), then Na_2HPO_4 (6 mg, 0.042 mmol) was added and the suspension refluxed (TLC control: R_f = 0.48 (**5a**), R_f = 0.62 (**2b**), AcOEt). After 3 h the mixture was cooled to ambient temperature, filtered through a silica gel pad and the volatiles were evaporated. The residue was dried under vacuum (oil pump) to give crude glycal **5a** (17.5 mg, 100%; R_f = 0.48, AcOEt), which was almost pure according to NMR spectroscopy and has the ^{1}H and ^{13}C NMR spectra identical to those described in the literature.[16] ^{1}H NMR (200.13 MHz, $CDCl_3$): δ_H 1.92 (s, 3H, AcN), 2.04, 2.05, 2.07, 2.11 (4 s, 3H each, 4 × AcO), 3.79 (s, 3H, OMe), 4.18 (dd, J = 12.4 Hz, J = 7.1, 1H, H-9b), 4.34–4.45 (m, 2H, H-5 and H-6), 4.63 (dd, J = 12.4 Hz, J = 3.0 Hz, 1H, H-9a), 5.28–5.39 (m, 1H, H-8), 5.45–5.54 (m, 2H, H-4 and H-7), 5.92 (d, J = 8.7 Hz, 1H, NH), 5.98 (d, J = 2.9 Hz, 1H, H-3); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ_C 20.7, 20.8 (OC(O)*C*H$_3$), 23.1 (NC(O)*C*H$_3$), 46.4 (C-5), 52.5 (OMe), 61.9 (C-9), 67.6 (C-4), 67.9 (C-7), 70.7 (C-8), 76.4 (C-6), 107.9 (C-3), 145.0 (C-2), 161.6 (C-1), 170.2, 170.6, 170.8 (C=O); ESIMS: found *m/z* 496.0 [M+Na]; calcd for $C_{20}H_{27}NNaO_{12}$: 496.1.

4.8. Methyl 4,7,8,9-tetra-*O*-acetyl-5-(*N*,*N*-diacetylamino)-3,5-dideoxy-2,6-anhydro-D-*glycero*-D-*galacto*-non-2-enonate (5b)

Glycosyl chloride **2b** (R_f = 0.62, AcOEt; prepared from **1b** (20.1 mg, 0.035 mmol)) was dissolved in MeCN (0.6 mL), then Na_2HPO_4 (6 mg, 0.042 mmol) was added and the reaction mixture was stirred for 30 days at ambient temperature (25–30 °C). The reaction mixture was filtered through silica gel pad, volatiles were evaporated and the residue was dried in vacuum of the oil pump and applied onto a silica gel column which was eluted with gradient of AcOEt in petroleum ether (0→100%) to give pure **5b** as a white foam (16.6 mg, 92%; R_f = 0.62, AcOEt). $[\alpha]_D^{20}$ +42.2 (*c* 0.6, $CHCl_3$) (lit.[17] $[\alpha]_D$ +51 (*c* 0.6, $CHCl_3$)). The ^{1}H and ^{13}C NMR spectra of the product **5b** were identical to those described in the literature.[17] Signals of NAc_2 methyl groups are broadened in ^{1}H NMR spectrum and not present in ^{13}C NMR spectrum at all (probably due to exchange); ^{1}H NMR (600.13 MHz, $CDCl_3$): δ_H 2.03, 2.04, 2.06, 2.10 (4 s, 3H each, 4 × AcO), 2.39 (br s, 6H, Ac_2N), 3.81 (s, s, 3H, OMe), 4.17 (dd, $J_{8,9b}$ = 6.3 Hz, $J_{9a,9b}$, = 12.5 Hz, 1H, H-9b), 4.52 (dd, $J_{8,9a}$ = 2.8Hz, 1H, H-9a), 4.56 (dd, $J_{4,5}$ = 9.3 Hz, $J_{5,6}$ = 10.1Hz, 1H, H-5), 5.16 (dd, $J_{6,7}$, = 1.6 Hz, 1H, H-6), 5.22 (dd, $J_{7,8}$ = 6.1 Hz, 1H, H-7), 5.34 (ddd, 1H, H-8), 5.93 (d, $J_{3,4}$ = 2.7 Hz, 1H, H-3), 6.08 (dd, 1H, H-4); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ_C 20.69, 20.72, 20.75, 20.77 (OC(O)*C*H$_3$), 52.5 (OMe), 55.1 (C-5), 61.9 (C-9), 67.3, 67.8, 70.2, 76.3 (C-4, C-6, C-7, C-8), 108.9 (C-3), 146.4 (C-2), 161.6 (C-1), 169.7, 170.0, 170.3, 170.5 (C=O); ESIMS: found *m/z* 538.0 [M+Na]. Calcd for $C_{22}H_{29}NNaO_{13}$: 538.5.

4.9. Methyl 4,7,8,9-tetra-*O*-acetyl-2-azido-5-(*N*,*N*-diacetylamino)-2,3,5-trideoxy-α-D-*glycero*-D-*galacto*-non-2-ulopyranosonate (6b)

A solution of chloride **2b** (prepared from **1b** (45.1 mg, 0.078 mmol)) in CH_2Cl_2 (1 mL) was added to a stirred solution of Bu_4NHSO_4 (26.4 mg, 0.078 mmol) and NaN_3 (25.4 mg, 0.39 mmol) in saturated aqueous $NaHCO_3$ (1 mL). The mixture was stirred for 0.5 h (TLC control: 7:3; R_f = 0.56 (**6b**), R_f = 0.53 (**2b**), AcOEt–petroleum ether). Organic layer was washed successively with 2 M H_2SO_4 (20 mL), saturated aqueous $NaHCO_3$ (20 mL), and brine (30 mL). The combined extracts were filtered through a cotton wool plug and concentrated to give the residue, which was purified by silica gel column chromatography using AcOEt as the eluent to give azide **6b** (35.8 mg, 82%; R_f = 0.56, AcOEt–petroleum ether). $[\alpha]_D^{20}$ +74.8 (*c* 0.8, $CHCl_3$).

^{1}H NMR (200.13 MHz, $CDCl_3$): δ_H 1.76 (dd, $J_{3ax,4}$ = 10.9 Hz, $J_{3eq,3ax}$ = 13.1 Hz, 1H, H-3ax), 2.00, 2.03, 2.12, 2.14 (4 s, 3H each, 4 × AcO), 2.32, 2.38 (2 s, 3H each, Ac_2N), 2.71 (dd, $J_{3eq,4}$ = 5.3 Hz, 1H, H-3eq), 3.93 (s, 3H, OMe), 4.16 (dd, $J_{8,9b}$ = 5.3 Hz, $J_{9a,9b}$ = 12.4 Hz, 1H, H-9b), 4.23 (dd, $J_{4,5}$ = 9.7 Hz, $J_{5,6}$ = 10.0 Hz, 1H, H-5), 4.34 (dd, $J_{8,9a}$ = 2.8 Hz, 1H, H-9a), 4.79 (dd, $J_{6,7}$ = 1.4 Hz, 1H, H-6), 5.15 (dd, $J_{7,8}$ = 7.3 Hz, 1H, H-7), 5.24–5.37 (m, 1H, H-8), 5.63 (ddd, 1H, H-4); ^{13}C NMR (54.24 MHz, $CDCl_3$): δ_C 20.7, 20.9 (OC(O)*C*H$_3$), 26.1, 28.0 (2 × NC(O)*C*H$_3$), 37.2 (C-3), 53.5 (OCH_3), 56.7 (C-5), 61.7 (C-9), 66.6, 67.1, 69.2, 71.3 (C-4, C-6, C-8, C-7), 89.1 (C-2); the carbonyl signals are not present in ^{13}C NMR spectrum due to exchange or too short relaxation delay during spectrum acquisition; ESIMS: found *m/z* 581.0 [M+Na]. Calcd for $C_{22}H_{30}N_4NaO_{13}$: 581.2.

4.10. Methyl [methyl 4,7,8,9-tetra-*O*-acetyl-5-acetamido-3,5-dideoxy-D-*glycero*-D-*galacto*-non-2-ulopyranoside]onate (7a) (entry 2 in Table 1)

Methanol (0.6 mL, 14.8 mmol) was added to a solution of chloride **2a** (prepared from **1a** (19.7 mg, 0.037 mmol) in MeCN (0.6 mL) and the mixture was stirred for 3 h at ambient temperature (20 °C). Then the reaction mixture was concentrated to give methyl glycoside **7a** (18.7 mg, 100%, α:β = 12:1) as a colourless syrup.

4.10.1. Data for methyl [methyl 4,7,8,9-tetra-*O*-acetyl-5-acetamido-3,5-dideoxy-α-D-*glycero*-D-*galacto*-non-2-ulopyranoside]onate (α-7a)

The ^{1}H NMR spectrum of the product α-**7a** was identical to that described in the literature.[4c] ^{1}H NMR (200.13 MHz, $CDCl_3$): δ_H 1.89 (s, 3 H, AcN), 1.99–2.10 (m, 1H, H-3ax), 2.03, 2.05, 2.14, 2.16 (4 s, 3H each, 4 × AcO), 2.57 (dd, $J_{3eq,4}$ = 4.5 Hz, $J_{3eq,3ax}$ = 12.8 Hz, 1H, H-3eq), 3.32, 3.82 (2 s, 3H each, OMe), 4.07–4.17 (m, 2H, H-5, H-9a, H-6), 4.32 (dd, $J_{8,9b}$ = 2.8 Hz, $J_{H\text{-}9a,H\text{-}9b}$ = 12.5 Hz, 1H, H-9b), 4.85 (ddd, $J_{4,5}$ = 10.1 Hz, $J_{3ax,4}$ = 10.1 Hz, 1H, H-4), 5.21 (d, $J_{NH,5}$ = 9.7 Hz, 1H, NH), 5.33 (dd, $J_{6,7}$ = 1.7 Hz, $J_{7,8}$ = 8.7 Hz, 1H, H-7), 5.43 (ddd, $J_{8,9a}$ = 5.6 Hz, 1 H, H-8).

4.10.2. Data for methyl [methyl 4,7,8,9-tetra-*O*-acetyl-5-acetamido-3,5-dideoxy-β-D-glycero-D-galacto-non-2-ulopyranoside]onate (β-7a)

^{1}H NMR (200.13 MHz, $CDCl_3$, selected signals not overlapping with those of α-**7a**): δ_H 3.27 (OMe).

4.11. Methyl [methyl 4,7,8,9-tetra-*O*-acetyl-5-(*N*,*N*-diacetylamino)-3,5-dideoxy-D-*glycero*-D-*galacto*-non-2-ulopyranoside]onate (7b)

4.11.1. Method A, entry 3 in Table 1

A solution of chloride **2b** (prepared from **1b** (29.9 mg, 0.054 mmol)) in MeOH (2 mL, 49.4 mmol) was stirred for 30 min at ambient temperature (20 °C). Then the mixture was concentrated to give methyl glycoside **7b** (28.4 mg, 96%, α:β = 11:1) as a colourless syrup.

4.11.2. Method B, entry 4 in Table 1

Methanol (0.597 mL, 14.88 mmol) was added to a solution of chloride **2b** (prepared from **1b** (19.7 mg, 0.034 mmol)) in MeCN (0.6 mL) and the mixture was stirred for 3 h at ambient temperature (20 °C). Then the reaction mixture was concentrated to give methyl glycoside **7b** (18.7 mg, 100%, α:β = 3:1) as a colourless syrup.

4.11.3. Data for methyl [methyl 4,7,8,9-tetra-*O*-acetyl-5-(*N*,*N*-diacetylamino)-3,5-dideoxy-α-D-*glycero*-D-*galacto*-non-2-ulopyranoside]onate (α-7b)

The ^{1}H and ^{13}C NMR spectra of the product α-**7b** were identical to those described in the literature.[2e] ^{1}H NMR (200.13 MHz, $CDCl_3$): δ_H 1.84 (dd, $J_{3ax,4}$ = 10.9 Hz, $J_{3eq,3ax}$ = 12.8 Hz, 1H, H-3ax), 1.98, 2.02, 2.13, 2.15 (4 s, 3 H each, 4 × AcO), 2.29, 2.38 (2 s, 3H each, Ac_2N), 2.76 (dd, $J_{3eq,4}$ = 5.2 Hz, 1H, H-3eq), 3.35, 3.85 (2 s, 3H each, OMe), 4.08–4.25 (m, 2 H, H-5, H-9a), 4.33 (dd, $J_{8,9b}$ = 2.8 Hz, $J_{H\text{-}9a,H\text{-}9b}$ = 12.5 Hz, 1H, H-9b), 4.99 (dd, $J_{5,6}$ = 10.1 Hz, $J_{6,7}$ = 1.7 Hz, 1H, H-6), 5.16 (dd, $J_{7,8}$ = 8.0 Hz, 1H, H-7), 5.32–5.44 (m, 1 H, H-8), 5.50 (ddd, $J_{4,5}$ = 10.4 Hz, 1H, H-4); ^{13}C NMR (54.24 MHz, $CDCl_3$): δ_C 20.8 ($OC(O)CH_3$), 26.0, 28.0 ($NC(O)CH_3$), 38.9 (C-3), 52.3, 52.8 (OMe), 57.1 (C-5), 62.0 (C-9), 66.8, 67.3, 68.6, 69.6 (C-4, C-6, C-7, C-8), 98.9 (C-2), 167.4 (C-1), 169.7, 170.2, 170.7, 173.6 (C=O).

4.11.4. Data for methyl [methyl 4,7,8,9-tetra-*O*-acetyl-5-(*N*,*N*-diacetylamino)-3,5-dideoxy-β-D-*glycero*-D-*galacto*-non-2-ulopyranoside]onate (β-7b)

^{1}H NMR (200.13 MHz, $CDCl_3$, selected signals not overlapping with those of α-**7b**): δ_H 1.96, 2.06, 2.08, 2.14 (4 s, 3H each, 4 × AcO), 2.58 (dd, $J_{3eq,4}$ = 5.5 Hz, $J_{3eq,3ax}$ = 12.8 Hz, 1H, H-3eq), 3.28, 3.81 (2 s, 3H each, OMe), 4.64 (dd, $J_{8,9b}$ = 2.1 Hz, $J_{9a,9b}$ = 11.4 Hz, 1H, H-9b), 5.79 (ddd, $J_{3ax,4}$ = 10.4 Hz, $J_{4,5}$ = 10.4 Hz, 1H, H-4).

4.12. Methyl [allyl 4,7,8,9-tetra-*O*-acetyl-5-*N*-acetyl-3,5-dideoxy-D-*glycero*-D-*galacto*-non-2-ulopyranoside]onate (8a)

4.12.1. Method A, entry 5 in Table 1

A solution of chloride **2a** (prepared from **1a** (71.7 mg, 0.134 mmol)) in allyl alcohol (2.3 mL, 33.8 mmol) was stirred for 24 h at ambient temperature (20 °C). Then the mixture was concentrated and treated with Ac_2O (0.5 mL, 5.3 mmol) and pyridine (0.5 mL, 6.2 mmol) for 24 h. The volatiles were evaporated and coevaporated with toluene (5 × 1 mL) give the residue, which was purified by silica gel column chromatography using AcOEt as the eluent to give a mixture (56.1 mg) of allyl glycoside **8a** with a trace amount of glycal **5a** as a colourless syrup. The yields of allyl glycoside **8a** (54.6 mg, 77%, α:β = 6:1) and glycal **5a** (1.5 mg, 2%) were calculated by integration of the respective signals in the ^{1}H NMR spectrum and taking into account the molecular masses of **8a** and **5a** (531.54 and 473.43, respectively).

4.12.2. Method B, entry 6 in Table 1

Allyl alcohol (0.6 mL, 8.8 mmol) was added to a solution of chloride **2a** (prepared from **1a** (30.2 mg, 0.057 mmol)) in MeCN (0.6 mL) and the mixture was stirred for 24 h at ambient temperature (20 °C). Then the mixture was concentrated and treated with Ac_2O (0.5 mL, 5.3 mmol) and pyridine (0.5 mL, 6.2 mmol) for 24 h. The volatiles were evaporated and coevaporated with toluene (5 × 1 mL) to give the residue, which was purified by silica gel column chromatography using AcOEt as the eluent to give a mixture (28.1 mg) of allyl glycoside **8a** with a trace amount of glycal **5a** as a colourless syrup. The yields of allyl glycoside **8a** (26.9 mg, 89%, α:β = 3:1) and glycal **5a** (1.2 mg, 4%) were calculated by integration of the respective signals in the ^{1}H NMR spectrum and taking into account the molecular masses of **8a** and **5a** (531.54 and 473.43, respectively).

4.12.3. Data for methyl [allyl 4,7,8,9-tetra-*O*-acetyl-5-*N*-acetyl-3,5-dideoxy-α-D-*glycero*-D-*galacto*-non-2-ulopyranoside]onate (α-8a)

The ^{1}H and ^{13}C NMR spectra of α-anomer α-**8a** were identical to those described in the literature.[6a] ^{1}H NMR (600.13 MHz, $CDCl_3$): δ_H 1.86 (s, 3H, AcN), 1.97 (dd, $J_{3eq,3ax}$ = 12.8 Hz, $J_{3ax,4}$ = 12.3 Hz, 1H, H-3ax), 2.01, 2.03, 2.12, 2.13 (4 s, 3H each, 4 × AcO), 2.60 (dd, $J_{3eq,3ax}$ = 12.8 Hz, $J_{3eq,4}$ = 4.7 Hz, 2H, H-3eq), 3.77 (s, 3H, OMe), 3.86 (dddd, J = 12.8 Hz, J = 5.9 Hz, J = 1.3 Hz, J = 1.3 Hz, 1H, OCH_{2a}), 4.05–4.12 (m, 3H, H-5, H-6, H-9a), 4.26 (dddd, J = 12.8 Hz, J = 5.3 Hz, J = 1.4 Hz, J = 1.4 Hz, 1H, OCH_{2b}), 4.31 (dd, $J_{9a,9b}$ = 12.4 Hz, $J_{8,9b}$ = 2.7 Hz, 1H, H-9b), 4.85 (ddd, $J_{3ax,4}$ = 12.3 Hz, $J_{4,5}$ = 9.8 Hz, $J_{3eq,4}$ = 4.7 Hz, 1H, H-4), 5.13–5.17 (m ('dq', J = 10.4 Hz, J = 1.4 Hz), 1H, CH_{2a}=CH), 5.24–5.29 (m ('dq', J = 17.2 Hz, J = 1.5 Hz), 1H, CH_{2b}=CH), 5.31 (dd, $J_{7,8}$ = 8.3 Hz, $J_{6,7}$ = 2.1 Hz, 1H, H-7), 5.34 (d, $J_{5,NH}$ = 9.6 Hz, 1H, NH), 5.40 (ddd, $J_{7,8}$ = 8.3 Hz, $J_{8,9a}$ = 5.8 Hz, $J_{8,9b}$ = 2.7 Hz, 1H, H-8), 5.80–5.88 (m, 1H, CH_2=CH); ^{13}C NMR (54.24 MHz, $CDCl_3$): δ_C 20.8 ($OC(O)CH_3$), 23.2 ($NC(O)CH_3$), 38.1 (C-3), 49.5 (C-5), 52.7 (OMe), 62.4 (C-9), 65.9 (OCH_2), 67.4, 68.7, 69.1, 72.5 (C-4, C-6, C-7, C-8), 98.5 (C-2), 117.2 (CH_2), 133.6 (CH), 168.4 (C-1), 170.1, 170.2, 170.6, 171.0 (C=O).

4.12.4. Data for methyl [allyl 4,7,8,9-tetra-*O*-acetyl-5-*N*-acetyl-3,5-dideoxy-β-D-*glycero*-D-*galacto*-non-2-ulopyranoside]onate (β-8a)

The β-anomer β-**8a** was described in the literature, however no NMR data were reported for it.[6b] ^{1}H NMR (600.13 MHz, $CDCl_3$, selected signals not overlapping with those of α-**8a**): δ_H 2.49 (dd, $J_{3eq,4}$ = 4.9 Hz, $J_{3eq,3ax}$ = 12.9 Hz, 1H, H-3eq), 3.79 (s, 3H, OMe), 3.95 (dd, $J_{5,6}$ = 10.5 Hz, $J_{6,7}$ = 2.3 Hz, 1H, H-6), 3.98–4.00 (m ∼ 'dt', J = 5.2 Hz, J = 1.4 Hz, 1H, OCH_{2a}), 4.02–4.04 (m ∼ 'dt', J = 5.4 Hz, J = 1.4 Hz, 1H, OCH_{2b}), 4.79 (dd, $J_{9a,9b}$ = 12.3 Hz, $J_{8,9b}$ = 2.5 Hz, 1H, H-9b), 5.82–5.89 (m, 1H, CH_2=C*H*); ^{13}C NMR (54.24 MHz, $CDCl_3$): δ_C 21.1 (OC(O)*C*H$_3$), 23.2 (NC(O)*C*H$_3$), 37.4 (C-3), 49.4 (C-5), 52.7 (O*C*H$_3$), 62.4 (C-9), 64.7 (OCH_2), 68.4, 68.9, 71.2, 72.0 (C-4, C-6, C-7, C-8), 98.3 (C-2), 117.3 (CH_2), 133.2 (CH), 167.4 (C-1), 170.1, 170.3, 170.6, 170.7 (C=O).

4.13. Methyl [allyl 4,7,8,9-tetra-*O*-acetyl-5-(*N*,*N*-diacetylamino)-3,5-dideoxy-D-*glycero*-D-*galacto*-non-2-ulopyranoside]onate (8b)

4.13.1. Method A, entry 7 in Table 1

A solution of chloride **2b** (prepared from **1b** (55 mg, 0.095 mmol)) in AllOH (1.6 mL, 23.5 mmol) was stirred for 48 h at ambient temperature (20 °C). Then the mixture was concentrated and treated with Ac_2O (0.5 mL, 5.3 mmol) and pyridine (0.5 mL, 6.2 mmol) for 24 h. The volatiles were evaporated and coevaporated with toluene (5 × 1 mL) give the residue, which was purified by silica gel column chromatography using gradient of AcOEt in petroleum ether (0→100%) as the eluent to give allyl glycoside **8b** as a colourless syrup (15.6 mg, 29%, α:β = 1.9:1) and allyl glycoside **8a** as a white foam (23.8 mg, 47%, α:β = 1.3:1).

4.13.2. Method B, entry 8 in Table 1

Allyl alcohol (2.3 mL, 33.8 mmol) was added to a solution of chloride **2b** (prepared from **1b** (75.4 mg, 0.131 mmol)) in MeCN (2.3 mL) and the mixture was stirred for 48 h at ambient temperature (20 °C). Then the mixture was concentrated and treated with Ac_2O (0.5 mL, 5.3 mmol) and pyridine (0.5 mL, 6.2 mmol) for 24 h. The volatiles were evaporated and coevaporated with toluene (5 × 1 mL) give the residue, which was purified by silica gel column chromatography using gradient of AcOEt in petroleum ether (0→100%) as the eluent to give allyl glycoside **8b** as a colourless syrup (43.6 mg, 58%, α:β = 1.4:1) and allyl glycoside **8a** as a white foam (13.1 mg, 19%, α:β = 1.4:1).

4.13.3. Data for methyl [allyl 4,7,8,9-tetra-*O*-acetyl-5-(*N*,*N*-diacetylamino)-3,5-dideoxy-α-D-*glycero*-D-*galacto*-non-2-ulopyranoside]onate (α-8b)

^{1}H NMR (600.13 MHz, $CDCl_3$): δ_H 1.90 (dd, $J_{3eq,3ax}$ = 13.0 Hz, $J_{3ax,4}$ = 11.0 Hz, 1H, H-3ax), 1.99, 2.03, 2.13, 2.15 (4 s, 3H each, 4 × AcO), 2.29, 2.38 (2 s, 3H each, Ac_2N), 2.81 (dd, $J_{3eq,4}$ = 5.2 Hz, $J_{3eq,3ax}$ = 13.0 Hz, 1H, H-3eq), 3.83 (s, 3H, OMe), 3.93–3.99 (m, 2H, H-9a, OCH_{2a}), 4.203 (t, J = 10.1Hz, 1H, H-5), 4.31 (dt, J = 5.2 Hz, J = 1.5 Hz, 1H, OCH_{2b}), 4.34 (dd, $J_{9a,9b}$ = 12.4 Hz, $J_{8,9b}$ = 2.7 Hz, 1H, H-9b), 4.98 (dd, $J_{5,6}$ = 10.1 Hz, $J_{6,7}$ = 1.8 Hz, 1H, H-6), 5.15 (dd, $J_{7,8}$ = 8.0 Hz, $J_{6,7}$ = 1.8 Hz, 1H, H-7), 5.15–5.18 (m, 1H, C*H*$_{2a}$=CH), 5.29 (dq, J = 17.2 Hz, J = 1.7 Hz, 1H, C*H*$_{2b}$=CH), 5.37 (ddd, $J_{7,8}$ = 8.0 Hz, $J_{8,9a}$ = 5.3 Hz, $J_{8,9b}$ = 2.7 Hz, 1H, H-8), 5.51 (ddd, $J_{3eq,4}$ = 5.2 Hz, $J_{3ax,4}$ = 11.0 Hz, $J_{4,5}$ = 10.1 Hz, 1H, H-4), 5.82–5.90 (m, 1H, CH); ^{13}C NMR (54.24 MHz, $CDCl_3$): δ_C 20.70, 20.73, 20.93, 21.06 (OC(O)*C*H$_3$), 25.9, 28.0 (NC(O)*C*H$_3$), 39.0 (C-3), 52.7 (OMe), 57.1 (C-5), 61.95 (C-9), 65.6 (OCH_2), 66.9, 67.3, 68.8, 69.7 (C-4, C-6, C-7, C-8), 98.5 (C-2), 117.0 (CH_2), 133.7 (CH), 167.7 (C-1), 169.6, 170.10, 170.15, 170.6 (OCO), 173.6, 174.5 (NCO).

4.13.4. Data for methyl [allyl 4,7,8,9-tetra-*O*-acetyl-5-(*N*,*N*-diacetylamino)-3,5-dideoxy-β-D-*glycero*-D-*galacto*-non-2-ulopyranoside]onate (β-8b)

^{1}H NMR (600.13 MHz, $CDCl_3$): δ_H 1.83 (dd, $J_{3eq,3ax}$ = 13.0, $J_{3ax,4}$ = 10.9 Hz, 1H, H-3ax), 1.97, 2.02, 2.05, 2.14 (4 s, 3H each, 4 × AcO), 2.31, 2.39 (2 s, 3H each, Ac_2N), 2.65 (dd, $J_{3eq,4}$ = 5.3 Hz, $J_{3eq,3ax}$ = 13.0 Hz, 1H, H-3eq), 3.79 (s, 3H, OMe), 3.93–3.99 (m, 1H, OCH_{2a}), 4.06–4.10 (m, 1H, OCH_{2b}), 4.16 (dd, $J_{9a,9b}$ = 12.5 Hz, $J_{8,9a}$ = 5.4 Hz, 1H, H-9a), 4.200 (t, J = 10.0 Hz, 1H, H-5), 4.61 (dd, $J_{9a,9b}$ = 12.5 Hz, $J_{8,9a}$ = 2.5 Hz, 1H, H-9b), 5.05 (dd, $J_{5,6}$ = 10.0 Hz, $J_{6,7}$ = 1.8 Hz, 1H, H-6), 5.21 (dd, $J_{7,8}$ = 5.4 Hz, $J_{6,7}$ = 1.8 Hz, 1H, H-7), 5.20–5.25 (m, 1H, CH_{2a}=CH), 5.31–5.35 (m, 1H, H-8), 5.41 (dq, J = 17.2 Hz, J = 1.7 Hz, 1H, C*H*$_{2b}$=CH), 5.82–5.94 (m, 2H, H-4, CH); ^{13}C NMR (54.24 MHz, $CDCl_3$): δ_C 20.70, 20.73, 20.88, 20.96 (OC(O)*C*H$_3$), 25.9, 28.0 (NC(O)*C*H$_3$), 38.7 (C-3), 52.6 (OMe), 57.2 (C-5), 62.00 (C-9), 64.5 (OCH_2), 66.8, 68.2, 68.5, 70.9 (C-4, C-6, C-7, C-8), 98.3 (C-2), 116.9 (CH_2), 133.1 (CH), 167.6 (C-1), 169.5, 170.18, 170.20, 170.5 (OCO), 173.7, 174.3 (NCO).

4.14. Methyl [phenyl 4,7,8,9-tetra-*O*-acetyl-5-(*N*,*N*-diacetylamino)-3,5-dideoxy-2-thio-α-D-*glycero*-D-*galacto*-non-2-ulopyranoside]onate (9b)

A solution of chloride **2b** (prepared from **1b** (64.9 mg, 0.113 mmol)) in AcOEt (1 mL) was added to a stirred solution of Bu_4NHSO_4 (38.1 mg, 0.112 mmol) in saturated aqueous $NaHCO_3$ (1 mL). Then PhSH (0.046 mL, 0.45 mmol) was added and the mixture was stirred for 1.5 h at ambient temperature (20 °C) (TLC control: R_f = 0.53 (**9b**), R_f = 0.62 (**2b**), AcOEt). Organic layer was washed with saturated aqueous $NaHCO_3$ (50 mL), and brine (70 mL). The combined extracts were filtered through a cotton wool plug and concentrated to give the residue, which was purified by silica gel HPLC (Silasorb 600, 7.5 μm, 15 × 250 mm) using gradient of AcOEt in petroleum ether (0→100%) as the eluent to give thioglycoside **9b** as a colourless syrup (57.4 mg, 91%; α:β = 14:1; R_f = 0.53, AcOEt) and small amount of glycal **5b** (5.3 mg, 9%). $[\alpha]_D^{25}$ +32.5 (*c* 0.36, $CHCl_3$). ESIMS: found *m/z* 648.0 [M+Na]. Calcd for $C_{28}H_{35}NNaO_{13}S$: 648.2.

4.14.1. Data for methyl [phenyl 4,7,8,9-tetra-*O*-acetyl-5-(*N*,*N*-diacetylamino)-3,5-dideoxy-2-thio-α-D-*glycero*-D-*galacto*-non-2-ulopyranoside]onate (α-9b)

^{1}H NMR (600.13 MHz, $CDCl_3$): δ_H 1.93 (dd, $J_{3ax,3eq}$ = 12.9 Hz, $J_{3ax,4}$ = 11.2 Hz, 1H, H-3ax), 1.99, 2.029, 2.031, 2.17 (4 s, 3H each, 4 × AcO), 2.30, 2.35 (2 s, 3H each, Ac_2N), 3.01 (dd, $J_{3ax,3eq}$ = 12.9 Hz, $J_{3eq,4}$ = 5.2 Hz, 1H, H-3eq), 3.59 (s, 3H, OMe), 4.08 (dd, $J_{4,5}$ = 10.3 Hz, $J_{5,6}$ = 10.2 Hz, 1H, H-5), 4.24 (dd, $J_{9a,9b}$ = 12.5 Hz, $J_{8,9a}$ = 5.4 Hz, 1H, H-9a), 4.34 (dd, $J_{9a,9b}$ = 12.5 Hz, $J_{8,9b}$ = 2.7 Hz, 1H, H-9b), 4.82 (dd, $J_{5,6}$ = 10.2 Hz, $J_{6,7}$ = 1.6 Hz, 1H, H-6), 5.12 (dd, $J_{7,8}$ = 7.1Hz, $J_{6,7}$ = 1.6 Hz, 1H, H-7), 5.19 (ddd, $J_{7,8}$ = 7.1 Hz, $J_{8,9a}$ = 5.4 Hz, $J_{8,9b}$ = 2.7 Hz, 1H, H-8), 5.50 (ddd, $J_{3ax,4}$ = 11.2 Hz, $J_{4,5}$ = 10.3 Hz, $J_{3eq,4}$ = 5.2 Hz, 1H, H-4), 7.33–7.37 (m, 2H, Ph), 7.39–7.43 (m, 1H, Ph), 7.52–7.55 (m, 2H, Ph); ^{13}C NMR (54.24 MHz, $CDCl_3$): δ_C 20.8, 20.9 (OC(O)*C*H$_3$), 25.9, 28.0 (2 × NC(O)*C*H$_3$), 39.2 (C-3), 52.7 (OMe), 57.2 (C-5), 61.6 (C-9), 67.2, 67.5, 69.8, 72.1 (C-4, C-6, C-7, C-8), 87.4 (C-2), 128.8, 129.9, 136.4 (Ph), 167.6 (C-1), 169.5, 169.9, 170.2, 170.6 (OCO), 173.7, 174.4 (NCO).

4.14.2. Data for methyl [phenyl 4,7,8,9-tetra-*O*-acetyl-5-(*N*,*N*-diacetylamino)-3,5-dideoxy-2-thio-β-D-*glycero*-D-*galacto*-non-2-ulopyranoside]onate (β-9b)

^{1}H NMR (600.13 MHz, $CDCl_3$, selected signals not overlapping with those of α-**9b**): δ_H 2.78 (dd, $J_{3ax,3eq}$ = 12.9 Hz, $J_{3eq,4}$ = 5.2 Hz, 1H, H-3eq).

4.15. Methyl 4,7,8,9-tetra-*O*-acetyl-5-(*N*,*N*-diacetylamino)-3,5-dideoxy-2-ethoxythiocarbonyl-2-thio-α-D-*glycero*-D-*galacto*-non-2-ulo-pyranosonate (10b)

4.15.1. Method A

Glycosyl chloride **2b** (prepared from **1b** (100 mg, 0.174 mmol)) was dissolved in dry acetone (7 mL) and solid *O*-ethyl *S*-potassium dithiocarbonate (63.9 mg, 0.40 mmol) was added. The mixture was stirred for 2 h at ambient temperature (20 °C) (TLC control: R_f = 0.50 (**10b**), R_f = 0.53 (**2b**), AcOEt–petroleum ether, 7:3) and then the volatiles were evaporated to give the residue, which was purified by silica gel column chromatography using gradient of AcOEt in petroleum ether (0→100%) as the eluent to give a mixture (81.2 mg, 25:1) of α-xanthate **10b** with a small amount of glycal **5b** as a yellow syrup. The yields of **10b** (78.7 mg, 71%) and **5b** (2.5 mg, 3%) were calculated by integration of the respective signals in the ^{1}H NMR spectrum and taking into account the molecular masses of **10b** and **5b** (637.67 and 515.46, respectively).

4.15.2. Method B

Glycosyl chloride **2b** (prepared from **1b** (24.8 mg, 0.043 mmol)) was dissolved in 95% EtOH (1 mL) and solid *O*-ethyl *S*-potassium dithiocarbonate (10.2 mg, 0.064 mmol) was added. The mixture was stirred for 1 h at ambient temperature (20 °C) (TLC control: R_f = 0.50 (**10b**), R_f = 0.53 (**2b**), AcOEt–petroleum ether, 7:3) and then the volatiles were evaporated to give the residue, which was purified by silica gel column chromatography using gradient of AcOEt in petroleum ether (0→100%) as the eluent to give a mixture (22 mg, 15:1) of α-xanthate **10b** with a small amount of glycal **5b** as a yellow syrup. The yields of **10b** (20.9 mg, 76%) and **5b** (1.1 mg, 5%) were calculated by integration of the respective signals in the ^{1}H NMR spectrum and taking into account the molecular masses of **10b** and **5b** (637.67 and 515.46, respectively). ^{1}H NMR (600.13 MHz, $CDCl_3$): δ_H 1.36 (t, J = 7.1 Hz, 3H, CH_2CH_3), 1.94 (dd, $J_{3ax,4}$ = 10.3 Hz, $J_{3eq,3ax}$ = 13.2 Hz, 1H, H-3ax), 1.98, 2.00, 2.10, 2.11 (4 s, 3H each, 4 × AcO), 2.28, 2.37 (2 br s, 3H each, Ac_2N), 2.85 (dd, $J_{3eq,4}$ = 5.0 Hz, $J_{3eq,3ax}$ = 13.2 Hz, 1H, H-3eq), 3.82 (s, 3H, OMe), 4.15 (dd, $J_{4,5}$ = 10.0 Hz, $J_{5,6}$ = 10.2 Hz, 1H, H-5), 4.20 (dd, $J_{8,9a}$ = 5.3 Hz, $J_{9a,9b}$ = 12.5 Hz, 1H, H-9a), 4.32 (dd, $J_{8,9a}$ = 2.7 Hz, $J_{9a,9b}$ = 12.5 Hz, 1H, H-9a), 4.54–4.61 (m, 1H, $SCH_{2a}CH_3$), 4.75–4.81 (m, 1H, $SCH_{2b}CH_3$), 5.11 (dd, $J_{6,7}$ = 1.5 Hz, $J_{7,8}$, = 7.3 Hz, 1H, H-7), 5.25 (ddd, $J_{7,8}$ = 7.3 Hz, $J_{8,9a}$ = 2.7 Hz, $J_{8,9a}$ = 5.3 Hz, 1H, H-8), 5.31 (dd, $J_{5,6}$ = 10.2 Hz, $J_{6,7}$ = 1.5 Hz, 1H, H-6), 5.49 (ddd, $J_{3ax,4}$ = 10.3 Hz, $J_{3eq,4}$ = 5.0 Hz, $J_{4,5}$ 10.0 Hz, 1H, H-4; ^{13}C NMR (54.24 MHz, $CDCl_3$): δ_C 13.3 (OCH_2CH_3), 20.6, 20.7, 20.8, 20.9 ($OC(O)CH_3$), 25.8, 27.8 (2 × $NC(O)CH_3$), 38.2 (C-3), 53.2 (OMe), 56.9 (C-5), 61.5 (C-9), 67.0, 67.3, 69.6, 72.1 (C-4, C-6, C-7, C-8), 70.4 (OCH_2CH_3), 86.8 (C-2), 168.1 (C-1), 169.4, 170.0, 170.1, 170.5 (OCO), 173.4, 174.4 (NCO), 207.5 (C=S); ESIMS: found *m/z* 659.9 [M+Na]. Calcd for $C_{25}H_{35}NNaO_{14}S_2$: 660.2.

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