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Article

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Use of Phenols as Nucleophiles in the Zbiral Oxidative Deamination of *N*-Acetyl Neuraminic Acid. Isolation and Characterization of Tricyclic 3-Keto-2-Deoxy-nonulosonic Acid (KDN) Derivatives via an Intermediate Vinyl Diazonium Ion

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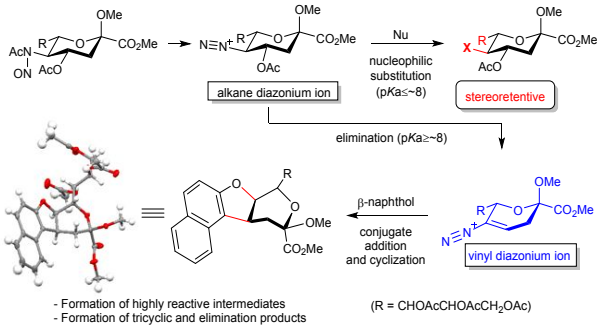
Graphical abstract



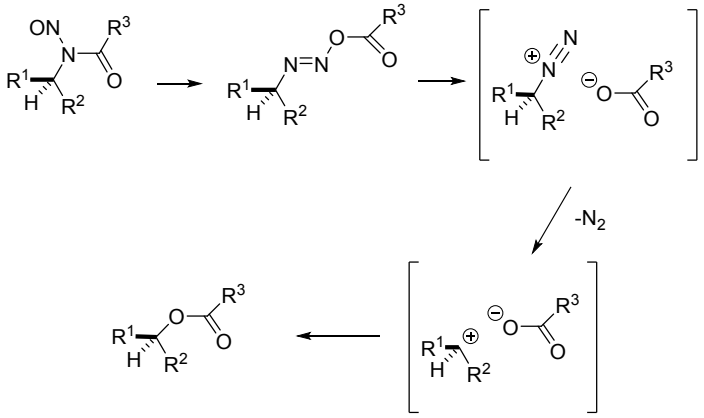
Abstract

It is well established that the *N*-nitrososamide derived from peracetylated derivatives of *N*-acetylneuraminic acid on treatment with a mixture of sodium isopropoxide and trifluoroethanol, followed by addition of acetic acid gives an oxidative deamination product in which the AcN(NO)-C5 bond is replaced a AcO-C5 with retention of configuration, affording a practical synthesis of 2-keto-3-deoxy-D-glycero-D-galactononulosonic acid (KDN) derivatives. Application of other strong acids, including hydrogen fluoride, thioacetic acid, trifluoromethanesulfonic acid and hydrogen azide, functions similarly to afford KDN derivatives functionalized at the 5-position. We describe our attempts to extend the range of useful nucleophiles employed in this oxidative deamination process to include phenols and thiophenols, resulting in the discovery of a new branch of the general reaction and the formation of a series of products resulting from substitution of the 5-acetamido group and of the 4-acetoxy group from neuraminic acid. A mechanistic rationale for the formation of these products is advanced according to which, in the absence of acids of pKa ≤8, the intermediate diazonium ion resulting from elimination of acetic acid nitrogen from the nitrosoacetamide undergoes elimination of acetic acid from the 4-position to afford a highly

electrophilic alkenediazonium ion. Reversible conjugate addition of the nucleophile to the 4-position then initiates the reaction cascade leading to the ultimate products.

Introduction

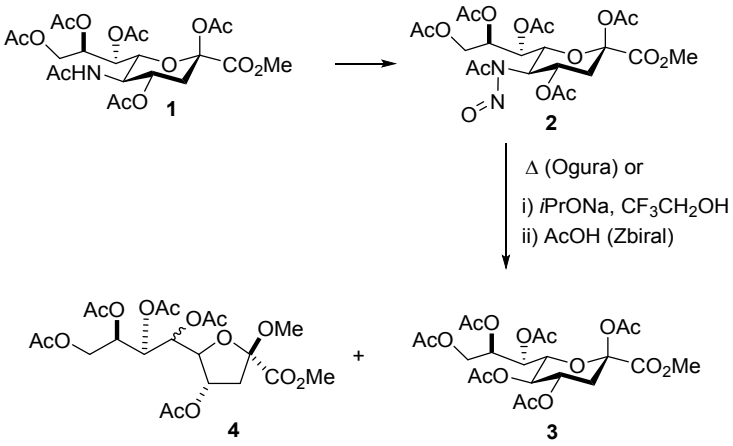
The oxidative degradation of aliphatic amides by thermolysis of their *N*-nitroso derivatives in the presence and absence of external carboxylic acids giving rise to the corresponding esters with loss of nitrogen was first described by White.[1-4] An extensive series of studies employing ^{18}O-labelling experiments, and variation of solvent, substrate, and external acid demonstrated that under thermal conditions the reaction proceeds with a preponderance of with retention of configuration when applied to chiral secondary and tertiary amides leading to the suggestion of a mechanism involving the formation and collapse of a series of two tight ion pairs, following initial N→O migration of the acyl moiety (Scheme 1).[1-4]



Scheme 1. White Mechanism for Oxidative Deamination of *N*-Nitroso Amides

Among the numerous applications of this reaction some of the more important are in the field of carbohydrate chemistry[5] and in particular in the conversion of the widely available *N*-acetyl neuraminic acid (NeuAc, **1**) and its derivatives to the less widely available but increasingly

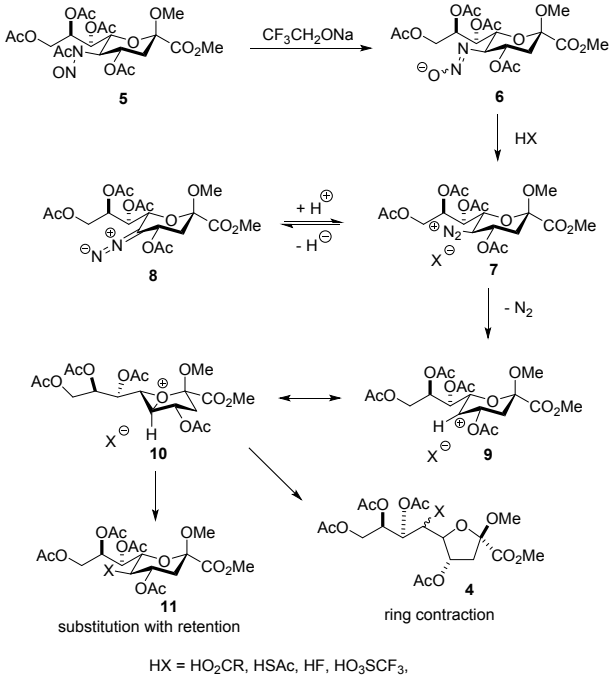
biologically relevant 3-keto-2-deoxy-nonulsonic acid (KDN, **3**) derivatives (Scheme 2).[6-8] Indeed, this has proven to be a pivotal transformation in the synthesis of the pseudaminic acid, glycosides such as found in the lipopolysaccharides from *Pseudomonas aeruginosa* and other pathogens.[9-11]



Scheme 2. Ogura and Zbiral's NeuAc to KDN Conversion.

The oxidative deamination protocol was first applied to NeuAc by Ogura and coworkers who relied on simple White-type thermal degradation of the *N*-nitroso amide **2**, obtaining a KDN derivative **3** and, albeit without supporting spectral data, the product of a ring contraction **4** with inversion of configuration at the site of reaction (Scheme 2).[12] It was Zbiral and Schreiner, however, who developed practical conditions for the NeuAc to KDN conversion involving the stepwise treatment of the *N*-nitroso amide with sodium isopropoxide and trifluoroethanol followed rapidly by acetic acid.[6] The Zbiral laboratory also observed the formation of and characterized the ring contraction product (Scheme 2).[6] In our laboratory we modified the Zbiral conditions to render them compatible with NeuAc thioglycosides, leading to a ready preparation of a KDN donor and ultimately to the highly stereocontrolled synthesis of KDN-*a*-glycosides.[7] We further modified the Zbiral conditions to permit replacement of the previously ubiquitous acetic acid nucleophile by thioacetic acid, hydrogen fluoride, triflic acid, and levulinic acid derivatives, leading to the

formation of the corresponding desacetamido acetylthio, trifloxy, fluoro, and levulinoxyl derivatives, each with retention of configuration.[8, 13] We also demonstrated the compatibility of the reaction with NeuAc di- and trisaccharides and its potential for application in the development of improved aminoglycoside antibiotics.[13, 14] The very high levels of retention of configuration in these reactions prompted us to probe the reaction mechanism, leading to the exclusion of participation by the neighboring esters and the invocation of participation by the pyranoside ring oxygen via a 1-oxabicyclo[3.1.0]hexanium-type intermediate **10**,[15] which also satisfactorily accounts for the formation of the ring contraction product observed by the early workers in the field (Scheme 3). Although unusual, such 1-oxabicyclo[3.1.0]hexane-type intermediates have been invoked by Corey and coworkers in the course of a total synthesis of glabrescol,[16] and by Stevens,[17] Hanessian,[18] Horton,[19] and Cassinelli[20] in a variety of pyranoside to furanoside ring contractions. Equivalent 1-thiabicyclo[3.1.0]hexanium[21] and 1-azabicyclo[3.1.0]hexanium[22] are also widely postulated in the literature.



Scheme 3. Proposed Mechanism of Zbiral Reaction and Ring Contraction

Continuing our earlier studies on the use of alternative nucleophiles to the original acetic acid with the goal of preparing novel NeuAc derivatives with which to probe and exploit structural differences between sialic acid binding proteins of different origins, we turned to the use of phenols as nucleophiles. As we report, a series of structurally interesting derivatives were formed albeit not the simple 5-*O*-aryl KDN ones initially envisaged. Rather, *cine*-substitution occurs leading to the formation of a series of vinyl ethers and, in the case of ambient nucleophiles such as β-naphthol, the formation of structurally unusual tricyclic systems. These products shed further light on the mechanism of the Zbiral reaction in the presence of weakly acidic nucleophiles and invoke the formation of a little studied class of electrophile, the vinyl diaozonium ions,[23-30] as intermediates.

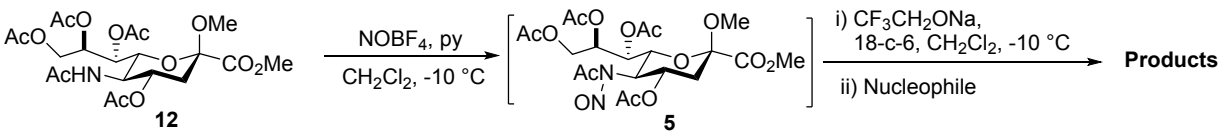
Results

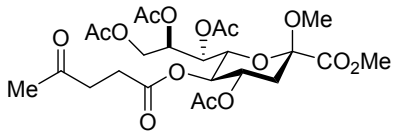
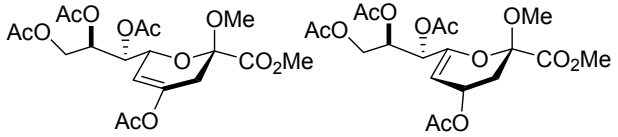
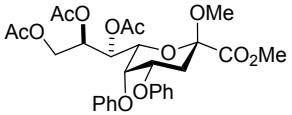
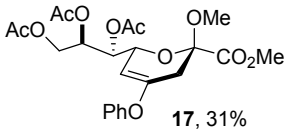
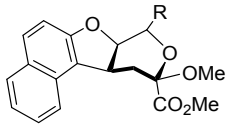
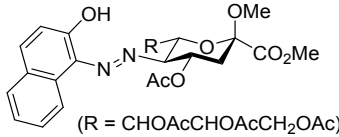
Methyl (methyl 4,7,8,9-tetra-O-acetyl-3,5-dideoxy-5-(*N*-nitrosoacetamido)-D-glycero-β-D-galacto-non-2-ulopyranosid)onate **5** was prepared according to a procedure reported in the literature[7, 15] from commercially available *N*-acetylneuraminic (NeuAc) by nitrosylation of the corresponding amide **12** with nitrosyl tetrafluoroborate ($NOBF_4$) and pyridine in dichloromethane at – 10 °C; it was used immediately for the oxidative deamination without further purification. The deamination reactions were typically affected by treatment of the nitrosoamide **5** with sodium trifluoroethoxide in the presence of 18-crown-6 in anhydrous dichloromethane at – 10 °C, as described previously,[15] followed after 10 mins (sufficient time for the consumption of **5**) by addition of an excess of the putative nucleophile. After stirring for a further 5 mins the reactions were quenched by addition of aqueous sodium bicarbonate, washed with aqueous sodium hydroxide to remove the excess nucleophile, and then subjected to chromatographic purification

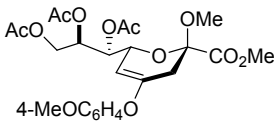
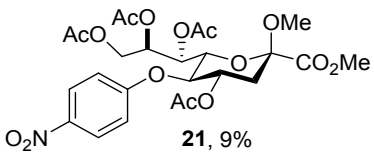
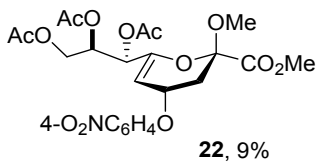
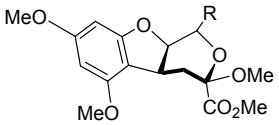
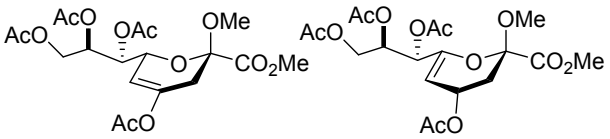
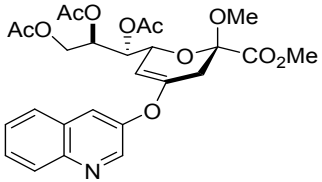
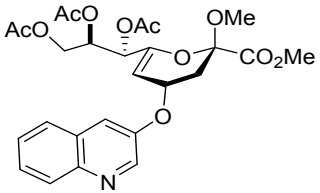
to afford the products (Table 1). Under these conditions the use of levulinic acid as nucleophile afforded the typical substitution product **13** with retention of configuration in 31% isolated yield, accompanied by the regioisomeric elimination products **14** and **15** in 34% combined yield (Table 1, entry 1). Replacement of the carboxylic acid nucleophile by phenol resulted in the isolation of the disubstitution product **16**, in which the acetoxy group at the 4-position was substituted by phenol with retention of configuration in addition to replacement of the nitrosoamide at the 5-position with inversion of configuration (Table 1, entry 2). Additionally, enol ether **17** was isolated from this reaction in 31% yield. The use of β-naphthol as nucleophile on the other hand afforded the tricyclic product **18** in 57% yield along with the azo dye **19** in 13% yield (Table 1, entry 3). Returning to simple monocyclic phenols, the use of *p*-methoxyphenol afforded 36% of the enol ether **20** (Table 1, entry 4), whereas that of *p*-nitrophenol gave 9% of the typical substitution product **21** and 9% of the elimination product **22** (Table 1, entry 5). The use of 3,5-dimethoxyphenol on the other hand resulted in the isolation of the tricyclic adduct **23** in 34% yield (Table 1, entry 6). Turning to the use of heteroaromatic phenols as nucleophiles, attempted use of 2-quinolinol gave only the elimination products **14** and **15** in 86% combined yield (Table 1, entry 7), whereas 3-quinolinol afforded **24** and **25** in 21 and 12% yield, respectively (Table 1, entry 8). With the use of 6-quinolinol on the other hand the pattern of reactivity seen with β-naphthol and 3,5-dimethoxyphenol was again observed with the isolation of the tricyclic product **26** in 53% yield (Table 1, entry 9). This latter reaction was conducted in the poorly nucleophilic hexafluoroisopropanol[31, 32] as solvent owing to the limited solubility of the nucleophile in the more typical dichloromethane. The same pattern was reverted to with 5-hydroxyindole resulting in the isolation of the tricyclic product **27** in 3% yield when the reaction was conducted at -10 °C (Table 1, entry 10), and in 27% yield when the reaction temperature was lowered to -40 °C (Table 1, entry

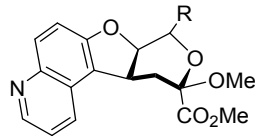
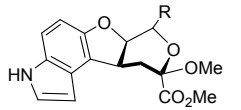
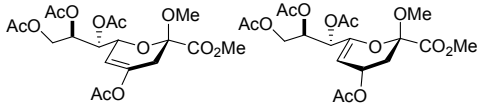
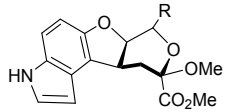
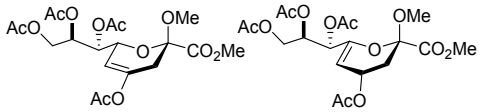
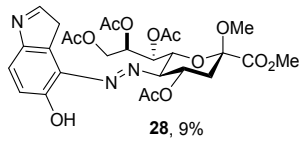
11). The formation of **27** was accompanied by that of the elimination products **14** and **15** in 35% and 7% combined yield at -10 and -40 °C, respectively (Table 1, entries 10 and 11), while 9% of the azo dye **28** was also isolated from the reaction at the lower temperature (Table 1, entry 11).

Table 1. Application of Levulinic Acid and of Phenols as Nucleophiles in the Zbiral Reaction[a]



Entry	Nucleophile[b]	p*K*a	Products (% yield)[c]
1	Levulinic Acid	4.60[33]	 **13**, 31%, eq only  **14** + **15**, 34%; **14**:**15** = 1:2.5
2	Phenol	9.98[34]	 **16**, 33%  **17**, 31%
3	β-Naphthol	9.5[35]	 (R = CHOAcCHOAcCH2OAc) **18**, 57%  (R = CHOAcCHOAcCH2OAc) **19**, 13%

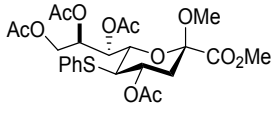
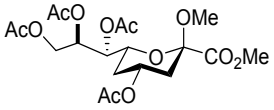
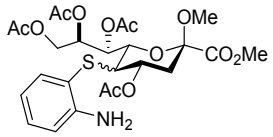
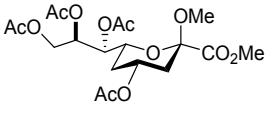
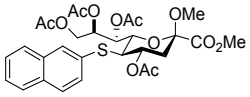
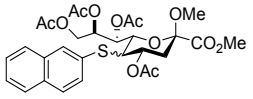
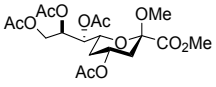
4	4-Methoxyphenol	10.21[34]	 **20**, 36%
5	4-Nitrophenol	7.15[34]	 **21**, 9%  **22**, 9%
6	3,5-Dimethoxyphenol	9.5	 (R = $CHOAcCHOAcCH_2OAc$) **23**, 34%
7	2-Hydroxyquinoline	7.86[36]	 **14** + **15**, 86%; **14**:**15** = 2.5:1
8	3-Hydroxyquinoline	8.03[36]	 **24**, 21%  **25**, 12%

9[d]	6-Hydroxyquinoline	8.87[36]	 (R = $CHOAcCHOAcCH_2OAc$) **26**, 53%
10	5-Hydroxyindole	-	 (R = $CHOAcCHOAcCH_2OAc$) **27,** 3%  **14** + **15**, 35%; **14**:**15** = 1:1.3
11[e]	5-Hydroxyindole	-	 (R = $CHOAcCHOAcCH_2OAc$) **27,** 27%  **14** + **15**, 7%; **14**:**15** = 1:1.3  **28**, 9%

a) Unless otherwise stated all reactions were conducted at -10 °C in dichloromethane. b) Nucleophiles were employed in 10-20 fold excess as detailed in the Supporting Information. c) The elimination products **14** and **15** are the major side products in all reactions as determined by inspection of the crude reaction mixtures by mass spectrometry and NMR spectroscopy, albeit they were not isolated and quantified in every case. d) 6-Hydroxyquinoline was added as a solution in hexafluoroisopropanol. e) This reaction was performed at – 40 °C.

Attention was next turned to the use of thiophenols as nucleophiles. With the parent, the direct substitution product **29** was isolated in 23% yield and retention of configuration (Table 2, entry 1), accompanied by the reduction product **30** in 19% yield. The use of 2-aminothiophenol on the other hand gave 58% of the substitution product **31**, but in the form of a 3:1 axial:equatorial mixture of isomers (Table 2, entry 2), together with the reduction product **30** in 20% yield. Finally, the use of 2-mercaptonaphthalene as nucleophile gave the substitution with retention product **32a** in 30% yield, contaminated with a minor amount of the stereoisomer **32b** (25%), and the reduction product **30** (13%) (Table 2, entry 3).

Table 2. Application of Thiophenols in the Zbiral Reaction[a]

Entry	Nucleophile[b]	p*K*a	**Products (% yield)[c]**
1	Thiophenol	6.6[35]	 **29**, 23%  **30**, 19%
2	2-Aminothiophenol	6.59[37]	 **31**, 58%; ax:eq = 1:3  **30**, 20%
3	2-Mercaptonaphthalene	5.9[35]	 **32a**, 30%  **32a + 32b**, 25%; ax:eq = 1:4  **30**, 13%

a) All reactions were conducted at -10 °C in dichloromethane. b) Nucleophiles were employed in 10-20 fold excess as detailed in the Supporting Information. c) The elimination products **14** and **15** are the major side products in all reactions as determined by inspection of the crude reaction mixtures by mass spectrometry and NMR spectroscopy, albeit they were not isolated and quantified in this series of reactions.

Structural Elucidation

While the structures of the direct substitution products **13**, **21**, **29**, **23**, **31** and **32**, the elimination products **14** and **15**, and the reduction product **30** follow directly from the ^{1}H-NMR spectra and require no further discussion, the elucidation of some of the unexpected products deserves comment. The structure of the disubstitution product **16** follows directly from analysis of the $^{3}J_{H,H}$ coupling constants and nOe contacts around the pyranose ring. Thus, the $^{3}J_{H4,H5}$ and $^{3}J_{H5,H6}$ coupling constants of 4.5 and 2.0 Hz, respectively, for a spectrum recorded in $CDCl_3$ owing to the co-incidence of H's 5 and 6 in $CDCl_3$, are indicative of the all *cis*-nature of the substituents at C's 4, 5, and 6, and are supported by the nOe correlation between H's 4 and 6. The structure of the tricyclic product **18** was determined by X-ray crystallography (Fig 1) of a crystal obtained from diethyl ether. In the crystal the pyranose ring adopts a conformation best described as approximating to the $^{3,6}B$ boat. This $^{3,6}B$ conformation also predominates in solution as indicated by the observed pattern of ^{3}J scalar couplings in the $H_{3a,b}$, H_4, H_5, H_6 spin system (Table 3) as well as by nOe interactions measured between one of the H3 protons and the aromatic proton peri to the ring junction.

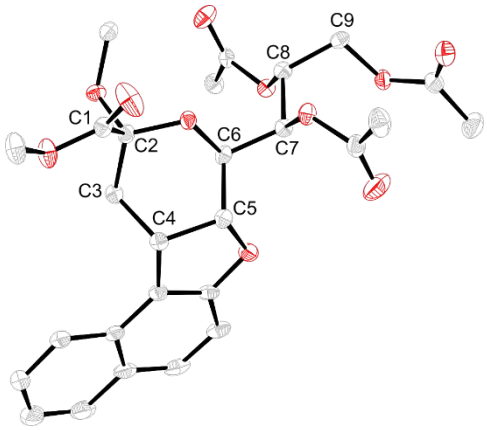


Figure 1: X-ray crystallographic structure of product **18** (CCDC 1941624)

It is noteworthy in view of the current interest in the influence of side chain conformation on the reactivity of glycosyl donors,[11, 38, 39] that the side chain of **18** adopts what is effectively the *gauche,gauche*-conformation (*gg*)[40, 41] similar to that found in NeuAc itself.[42-48] In this regard, it is also of interest to note

that the side chain of **16**, with the axial substituent at C5 and $^{3}J_{6,7}$ of 5.6 Hz, does not take up the *gg*-conformation, which is characterized by $^{3}J_{6,7}$ of ~ 2 Hz in the standard $^{2}C_{5}$ chair conformation.[42-48] This is presumably due to the strong dipolar and steric (syn-pentane-type) interactions that would exist between the C5-O5 and C7-O7 bonds in such a conformation.[8]

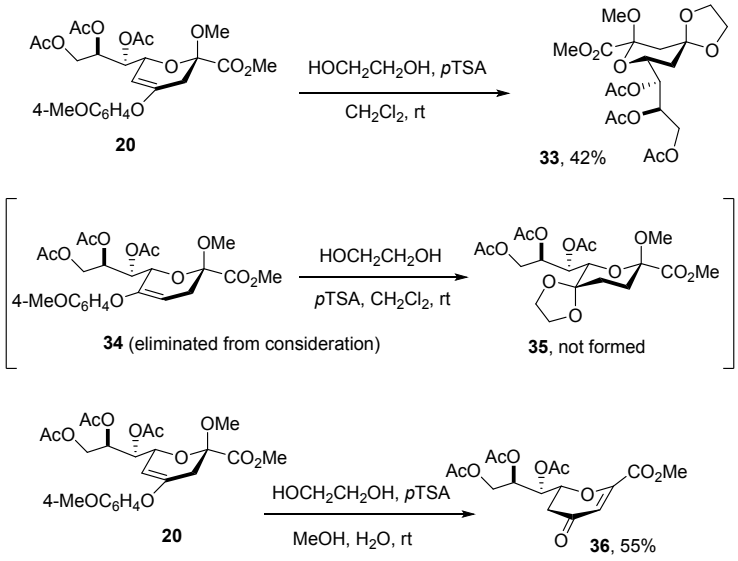
The structures and solution conformations of the bicyclic products **23**, **26**, and **27** are assigned by analogy to that of **18** and the close homology of the coupling constants in the $H_{3a,b}$, H_4, H_5, H_6 spin system (Table 3). In each of the tricyclic products **18**, **23**, **26**, and **27** the ^{3}J coupling constant between the pseudo-axial bowsprit H3 and H4 is at the upper limit (12.9-13.5 Hz) of the usual range seen for a pair of coupled trans-diaxial spins in a saturated aliphatic systems lacking direct electronegative substituents.[49]

Table 3. Diagnostic Chemical shifts and Coupling Constants for **16**, **18**, **23**, **26**, and **27**.[a]

	Chemical Shifts (δ, ppm)[b]						Coupling Constants (Hz)					
Product	H3pa	H3pe	H4	H5	H6	H7	$^3J_{3pa,4}$	$^3J_{3pe,4}$	$^3J_{4,5}$	$^3J_{5,6}$	$^3J_{6,7}$	$^2J_{3pa,pe}$
16	2.55	2.47	4.52	3.14	3.13	4.99	8.9	3.2	3.7	-	5.3	14.9
16[c]	2.77	2.57	4.61	3.01	3.18	5.16	8.8	3.4	4.5	2.0	5.7	14.8
18	1.90	2.86	3.87	4.94	4.21	5.69	13.5	5.0	9.2	9.4	5.1	14.9
23	1.79	2.63	3.47	4.70	4.03	5.59	12.9	5.4	9.1	9.4	4.6	14.9
26	1.92	2.78	3.88	4.99	4.21	5.68	13.4	5.1	8.9	9.3	5.0	14.9
27	2.02	2.72	3.77	4.82	4.12	5.67	12.8	5.5	8.8	9.4	5.0	14.9

a) All spectra were recorded in $CDCl_3$ unless otherwise stated. b) H3pa and H3pe refer to the pseudo-axial and pseudo-equatorial protons at C3, respectively. c) Recorded in C_6D_6.

The usual ^{1}H and ^{13}C spectroscopic methods did not allow unambiguous distinction between two possible regioisomers for the enol ethers **17**, **20**, and **24** owing to the multiplicity of long range coupling constants spanning the alkene. Ultimately, taking **20** as a representative example, the structure was assigned following treatment with ethylene glycol in dichloromethane in the presence of *p*-toluenesulfonic acid at room temperature when the cyclic ketal **33** was isolated in 42% yield (Scheme 4). The isolated nature of the two methylene spin systems in this ketal clearly points to **33** as the structure and not the alternative **35**, and thus to **20** as the structure of the enol ether as opposed to **34**. Further confirmation of the structure of **20** was obtained on treatment with ethylene glycol and *p*-toluenesulfonic acid in wet methanol at room temperature when the enone **36** was isolated in 55% yield (Scheme 4). The structures of **17**, and **24** follow from the close homologies of their NMR spectra with those of **20**. The structures of the azo dyes **19** and **28** follow directly from their mass and NMR spectra, and their intense yellow colors with λ_{max} 380 nm (acetonitrile, ε = 8699 M^{-1} cm^{-1}) and 365 nm (dichloromethane, ε = 2391 $M^{-1}cm^{-1}$), respectively, in the UV/visible spectra recorded.

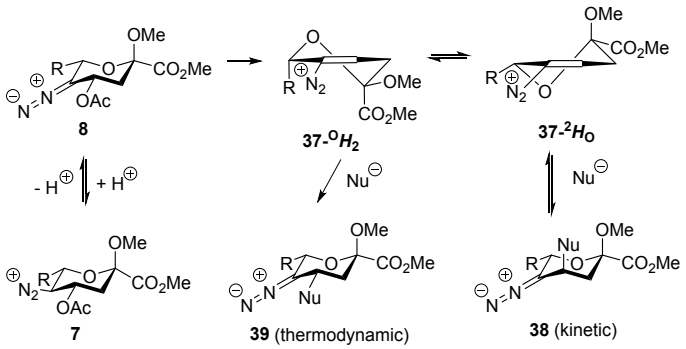


Scheme 4. Structural Elucidation of **20**.

Discussion

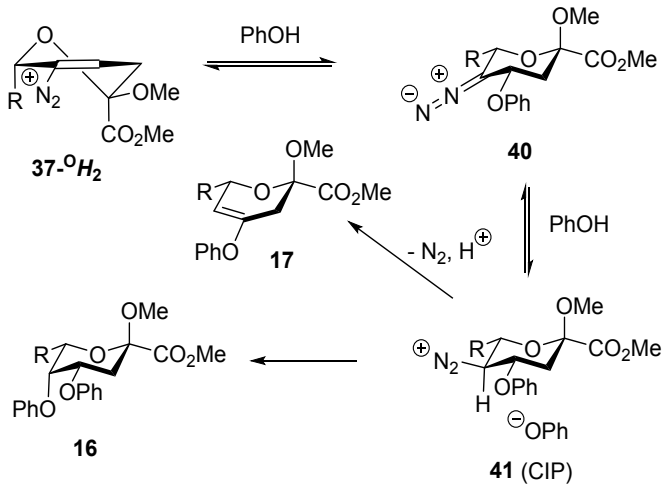
The results are best interpreted in terms of a new branch of the mechanism we advanced previously for the Zbiral reaction. Thus, reaction of the *N*-nitrosoacetamide **5** with trifluoroethoxide leads to the formation of a diazonium ion **7**, which undergoes reversible deprotonation to the diazoalkane **8**. Evidence for the formation of the diazonium ion as a discrete intermediate in this process is now provided in the form of the azo dyes **19** and **28**, which are the typical products of the reaction of diazonium ions with β-naphthols and related phenols. The reversibility of the deprotonation was previously established through the use of deuterioacetic acid as nucleophile, which resulted in the formation of monodeuterio-KDN with selective introduction of a deuterium atom in the 5-position.[15]

The p*K*a of the methyldiazonium ion[50] (p*K*a~10) and, by extrapolation, that of the diazonium ion **7**, with its electron-withdrawing and acidity-enhancing β-C-O bonds, is such that with carboxylic acids and more acidic species as reaction partner the diazonium ion – diazoalkane equilibrium strongly favors the diazonium ion and, following loss of nitrogen, the heretofore standard substitution and elimination products (Scheme 2). With less acidic reaction partners such as the phenols employed here we postulate that the diazoalkane **8** undergoes β-elimination of the acetoxy group from the 4-position to give the α,β-unsaturated diazonium ion **37**, a member of the little-studied class of alkenediazonium ions (Scheme 5). This strongly electrophilic species can be considered to populate at least the two half-chair conformers **37-$^{O}H_2$** and **37-$^{2}H_O$**, and related boat conformers, with **37-$^{2}H_O$** undergoing kinetic Michael addition from the β-face past the minimally sterically demanding methoxy group to afford the new diazoalkane **38** directly in a chair conformation. Under thermodynamic conditions a process of reversible additions and eliminations leads to the eventual introduction of the nucleophile in the equatorial position, presumably by bottom face attack on **37-$^{O}H_2$** leading directly to the observed chair conformation, but possibly by bottom face attack on **37-$^{2}H_O$** and subsequent conformational equilibration.



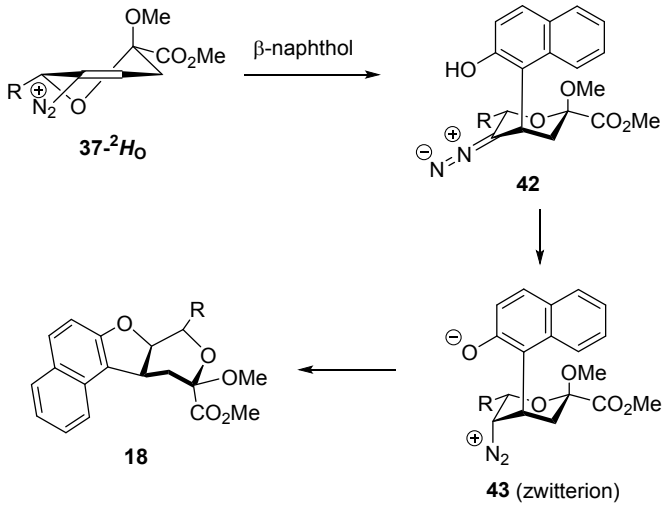
Scheme 5. Mechanism of Substitution at C4

With phenol as nucleophile, the thermodynamic mode of addition is observed and is followed by protonation of the diazoalkane from the α-face by a second molecule of phenol giving a contact ion pair (CIP) **41**, which collapses with loss of nitrogen and inversion of configuration to give the observed product **16** (Scheme 6). α-Face protonation of **40** to give **41** is consistent with the protonation of diazoalkane **8**, returning diazonium ion **7** (Scheme 3), established in our earlier studies by deuterium labelling experiements.[15] In the case of the more acidic nucleophiles classically employed in the Zbiral reaction, invertive collapse of the analogous CIP is retarded by the reduced nucleophilicity of the anion, leading to participation by the ring oxygen and overall substitution with retention of configuration at the 5-position (Scheme 3). Finally, loss of nitrogen from **41** followed by, or in concert with, deprotonation affords the enol ether **17** (Table 1, entry 2). *p*-Methoxyphenol and 3-quinolinol follow a similar path to phenol itself with the enol ethers **20**, **24** and **25** as major isolated products (Table 1, entries 4 and 8). *p*-Nitrophenol on the other hand is considerably more acidic than phenol such that reprotonation of the diazonium ion **37** is competitive with elimination and the standard substitution product **21** is formed at least in a minor amount (Table 1, entry 5).



Scheme 6. Formation of Disubstitution Product **16**.

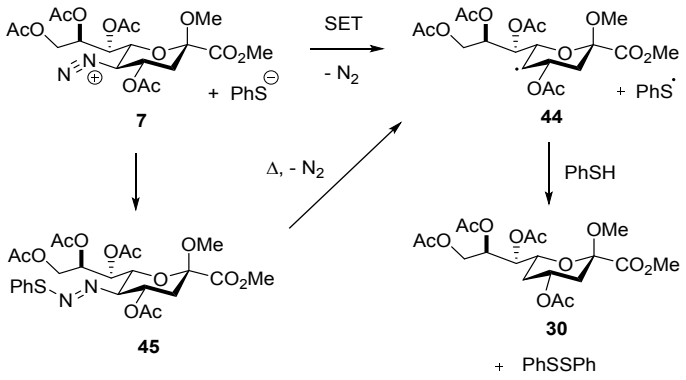
With the less aromatic ambident nucleophile β-naphthol, and analogously the other electrophilic aromatic substitution prone phenols, the kinetic Michael addition product **42** is trapped by intramolecular proton transfer, possibly from the rearomatized phenol as shown or possibly as a part of the rearomatization process, leading a zwitterion **43** that undergoes ring closure with loss of nitrogen and inversion of configuration leading to the tricyclic product **18** (Scheme 7). 2-Quinolinol, which exists predominantly in the quinolinone form, is both more acidic and only very weakly nucleophilic resulting in predominant formation of the elimination products **14** and **15** (Table 1, entry 7).



Scheme 7. Formation of Tricyclic Product **18**.

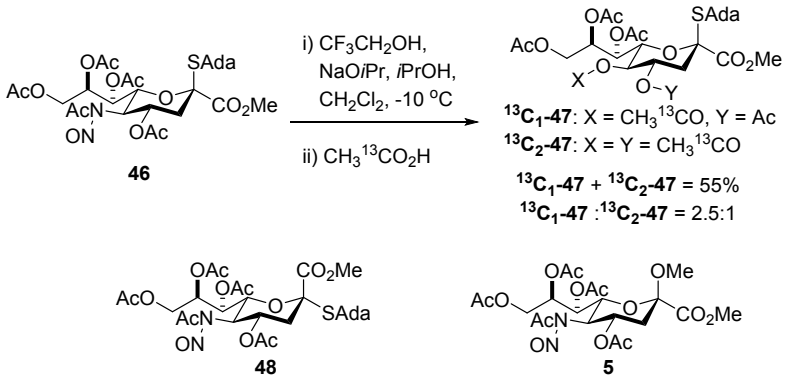
With the more acidic thiophenols as reaction partners, the acidity of the reaction medium is sufficient that the initial diazonium ion – diazoalkane equilibrium strongly favors the former such that the prototypical simple substitution with retention of configuration (Scheme 3) is the predominant reaction pathway. The observation of minor amounts of the substitution with inversion in this series suggests, however, that direct displacement of nitrogen from the diazonium ion by the sulfur-based nucleophile is in competition with participation by the ring oxygen. The formation of the reduction product **30** in the presence of thiophenol most likely arises either from single electron transfer from the thiophenate to the diazonium ion **7**, followed by loss of molecular nitrogen and hydrogen atom transfer to the ensuing alkyl radical **44** from the thiophenol (Scheme 8), consistent with the established mechanism of reduction of arenediazonium ions by thiophenols.[51] Alternatively, diazonium ion **7** and thiophenate may combine to give the arylthiodiazene **45**, that undergoes homolytic scission to afford radical **44**, followed by trapping with thiophenol (Scheme 8). Either way, the isolation of the reduction product **30** constitutes

further evidence in support of the existence of the diazonium ion **7** as a discrete intermediate in the Zbiral chemistry.



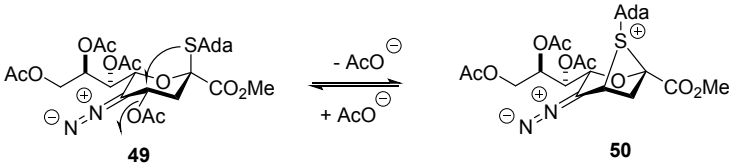
Scheme 8. Mechanism for the formation of the Reduction Product **30**.

Finally we return to the substitution of the ester at the 4-position with retention of configuration observed during our earlier studies on the mechanism of the classical Zbiral reaction with carboxylic acids as nucleophiles.[15] Thus it was found through the use of ^{13}C-enriched acetic acid as nucleophile, and confirmed with the use of levulinic acid, that in addition to the substitution of the acetamido group with retention of configuration in the β-thioglycoside **46** up to 30% of the ester at the 4-position also underwent substitution with retention of configuration as in **$^{13}C_2$-47** (Scheme 9).



Scheme 9. Substitution at the 4- and 5-Positions in the Axial Thioglycoside **46** as Revealed by Isotopic Labelling.

This previously unobserved substitution of the ester at the 4-position only occurred with the β-thioglycoside **46**, and not with its α-anomer **48** or the simple methyl glycoside **5** prompting us to write a mechanism involving reversible ring closure by the thioether onto C5 at the level of the diazoalkane followed by a reversible series of acyl migrations and cleavages.[15] In the light of the results described in this Article, it is clear that a more likely mechanism involves reversible displacement of the acetoxy group from the 4-position of the diazoalkane **49** by the thioether (Scheme 10) resulting in overall substitution with retention of configuration. Displacement of the acetoxy group from the 4-position by the thioether is facilitated by the presence of the neighboring diazoalkane resulting in what is effectively an allylic displacement.



Scheme 10. Likely Mechanism for Acetoxy Substitution at the 4-Position

Conclusion

Attempted use of phenols as nucleophiles in the Zbiral oxidative deamination of *N*-nitroso-*N*-acetylneuraminic acid has resulted in the discovery of a new branch of this valuable reaction. In effect, with nucleophiles of p*K*a≥8 the intermediate diazoalkane is favored over its protonated form, the diazonium ion, and instead suffers elimination of the acetoxy group from the 4-position to give an alkenediazonium ion. This highly electrophilic species undergoes reversible conjugate addition of the phenolic nucleophiles resulting ultimately in the 4,5-disubstituted products. When

the nucleophile is β-naphthol or other highly electron-rich phenols nucleophilic attack takes place on carbon rather than oxygen ultimately affording a series of structurally unusual tricyclic ulosonic acid derivatives. When the more acidic thiophenols, capable of protonating the intermediate diazoalkane, are employed as nucleophiles, the reaction follows the classical Zbiral-like path with the introduction of the nucleophile at the 5-position largely with retention of configuration. Although we have restricted ourselves in this Article to the use of phenols and thiophenols as nucleophiles, we anticipate that this new class of substitution reactions, which complements existing methods for substitution and inversion at the 4-position of *N*-acetylneuraminic acid,[52-56] will afford entry into a broad spectrum of unusual ulosonic acid derivatives with potential for exploitation in medicinal chemistry.

Experimental Section

General. All reactions were performed using oven-dried glassware under an atmosphere of argon. All reagents and solvents were purchased from commercial suppliers and were used without further purification unless otherwise specified. Chromatographic purifications were performed on silica gel (230-400 mesh) columns (20-50 g) of silica gel per gram of crude compound). Reactions were monitored by analytical thin-layer chromatography on pre-coated glass backed plates (w/UV 254) and visualized by UV irradiation (254 nm) or by staining with 25% H_2SO_4 in EtOH or ceric ammonium molybdate (CAM) solution. Specific rotations were measured on an automatic polarimeter with a path length of 100 mm in the solvent specified. Concentrations are given in g/100 mL. High resolution mass spectra (HRMS) were recorded with an electrospray ionization (ESI) source coupled to a time-of-flight (TOF) mass analyzer or with an electron impact (EI) source coupled to a TOF mass analyzer. ^{1}H, ^{13}C, ^{19}F, spectra were recorded on a 400, 500 or 600 MHz spectrometer. NMR solvents were used without purification. Chemical

shifts are given in ppm (δ) and coupling constants (*J*) are given in Hz. Multiplicities are given as singlet (s), broad singlet (br s), doublet (d), triplet (t), doublet of doublets (dd), triplet of doublets (td), multiplet (m), apparent quartet (app q), apparent pentet (app p), etc. Spectral assignments were made by a combination of COSY, HSQC and HMBC spectra.

General Procedure of oxidative deamination. Using the quantities described in the individual experiments, sodium 2,2,2-trifluoroethoxide and 18-crown-6 were dissolved in anhydrous CH_2Cl_2 under Ar and cooled to -10 °C. The solution was added to the nitrosyl sialoside (0.1 M solution in anhydrous CH_2Cl_2) at -10 °C under Ar. The mixture was stirred for 5 min at -10 °C. The nucleophile (10-20 equiv) dissolved in the solvent described under Ar at -10 °C was added to the reaction mixture in one portion. After stirring for 5 min, the reaction was quenched by addition of saturated $NaHCO_3$ solution and diluted with DCM. The reaction mixture was washed with NaOH (1M) to remove excess phenolic nucleophile. The organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to afford the crude product which was purified by column chromatography over silica gel.[57]

Methyl (methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-glycero-β-D-galacto-non 2-ulopyranosid)onate (12). Compound **12** (6 g, 95%) was obtained by a literature procedure[15] over two steps as a white solid from *N*-acetylneuraminic acid (20 g, 64.7 mmol).

Methyl (methyl 4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-5-(*anti*/*syn*-*N*-nitrosoacetamido)-D-glycero-β-D-galacto-non-2-ulopyranosid)onate (5). A solution of compound **12** (330 mg, 0.7 mmol) in dry dichloromethane (7 mL) was treated with dry pyridine (0.5 mL, 6.5 mmol, 10 equiv) and cooled to -10 °C. After stirring for 15 min, crushed nitrosyl tetrafluoroborate (382 mg, 3.0 mmol, 5 equiv) was added in one portion. The reaction mixture was stirred at -10 °C until TLC

showed complete conversion (4-5 h). The mixture was diluted with cold dichloromethane (3 mL) and washed with cold 1N HCl, saturated $NaHCO_3$ and brine. The organic layer was dried over anhydrous Na_2SO_4 and concentrated under 10 °C to obtain **5** as a yellowish foam which was carried forward for next reaction without further purification.[15]

Methyl (methyl 4,7,8,9-tetra-*O*-acetyl-3-deoxy-5-*O*-levulinyl-D-glycero-β-D-galacto-non-2-ulopyranosid)onate (13) and a mixture of Methyl (methyl 4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-β-D-arabino-non-4-en-2-ulopyranosid)onate (14) and Methyl (methyl 4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-β-D-ribo-non-5-en-2-ulopyranosid)onate (15). The nitrosyl sialoside **5** (267 mg, 0.5 mmol) in CH_2Cl_2 (5 mL) was deaminated using the general procedure for oxidative deamination with sodium 2,2,2-trifluoroethoxide (122 mg, 1 mmol), 18-crown-6 (291 mg, 1.1 mmol) in CH_2Cl_2 (2.5 mL) and levulinic acid (1.16 g, 10 mmol, 20 eq) in CH_2Cl_2 (5 mL) to afford **13** after column chromatography over silica gel eluting with (hexane/ethyl acetate 3:1), as colorless crystals from methanol/CH_2Cl_2 (88 mg, 31%) and an inseparable mixture of **14** and **15** as a colorless oil (1:2.5 ratio, 75 mg, 34%).

Compound **13**; colorless crystals, m.p. = 132-134 °C; $[\alpha]_D^{20}$ – 5.7° (*c* 0.4, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.34 – 5.19 (m, 3H, H8, H7 and H4), 4.87 (t, *J* = 9.9 Hz, 1H, H5), 4.65 (dd, *J* = 12.6, 2.4 Hz, 1H, H9), 4.09 (dd, *J* = 12.5, 6.7 Hz, 1H, H9'), 4.00 (dd, *J* = 10.1, 2.2 Hz, 1H, H6), 3.75 (s, 3H, CH_3), 3.21 (s, 3H, CH_3), 2.79 – 2.69 (m, 1H, H3e), 2.61 – 2.35 (m, 4H, CH_2CH_2), 2.11 (s, 3H, CH_3), 2.05 (s, 3H, CH_3), 2.02 (s, 3H, CH_3), 1.98 (s, 3H, CH_3), 1.97 (s, 3H, CH_3), 1.77 (dd, *J* = 13.0, 11.5 Hz, 1H, H3a). ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 205.9, 171.7, 170.6, 170.2, 170.0, 167.2, 98.9, 70.9, 70.1, 68.7, 67.8, 67.6, 62.1, 52.7, 51.4, 37.9, 37.8, 37.0, 29.7, 28.0, 21.0, 20.9, 20.8, 20.7. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{24}H_{34}NaO_{15}$ 585.1795; Found: 585.1792.

14 and **15** (1:2.5 mixture); colorless oil; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{26}NaO_{12}$ 469.1322; Found: 469.1322.

Compound **15**; ^1H NMR (400 MHz, $CDCl_3$) δ 5.51 (m, 1H, H8), 5.46 (m, 1H, H7), 5.25 (m, 1H, H4), 5.07 (dq, *J* = 4.4, 1.1 Hz, 1H, H5), 4.36 (dd, *J* = 12.1, 3.0 Hz, 1H, H9), 4.30 (dd, *J* = 12.1, 7.1 Hz, 1H, H9'), 3.75 (s, 3H, CH_3), 3.36 (s, 3H, CH_3), 2.31 (dd, *J* = 14.1, 3.6 Hz, 1H, H3), 2.16 (dd, *J* = 14.2, 5.3 Hz, 1H, H3'), 2.11 (s, 3H, CH_3), 2.04 (s, 3H, CH_3), 2.03 (s, 3H, CH_3), 1.96 (s, 3H, CH_3). ^{13}C {^1H} NMR (101 MHz, $CDCl_3$) δ 170.8, 170.1, 170.0, 169.3, 167.7, 149.8, 99.2, 98.0, 70.4, 70.3, 63.0, 61.9, 52.7, 52.2, 34.6, 21.1, 20.9, 20.9.

Compound **14** was identified in the mixture by the following diagnostic signals; ^1H NMR (400 MHz, $CDCl_3$) δ 5.43 (dd, *J* = 6.1, 2.5 Hz, 1H, H8), 5.33 – 5.29 (m, 2H, H7 and H5), 4.58 (ddd, *J* = 12.6, 2.4, 1.3 Hz, 1H, H9), 4.51 (dq, *J* = 4.7, 2.5 Hz, 1H, H6), 4.19 (ddd, *J* = 12.5, 5.9, 1.3 Hz, 1H, H9'), 3.78 (s, 3H, CH_3), 3.24 (s, 3H, CH_3), 2.68 (ddd, *J* = 17.0, 3.9, 2.4 Hz, 1H, H3. ^{13}C {^1H} NMR (101 MHz, $CDCl_3$) δ 170.7, 170.4, 169.9, 168.5, 168.0, 144.5, 110.0, 98.1, 70.7, 70.1, 69.2, 62.4, 52.7, 51.5, 34.8, 21.0, 20.9, 20.7.

Methyl (methyl 7,8,9-tri-*O*-acetyl-3-deoxy-4,5-di-*O*-phenyl-D-glycero-β-D-gulo-non-2-ulopyranosid)onate (16) and Methyl (methyl 7,8,9-tri-*O*-acetyl-3,5-dideoxy-4-*O*-phenyl-β-D-arabino-non-4-en-2-ulopyranosid)onate (17). The nitrosyl sialoside **5** (200 mg, 0.4 mmol) in CH_2Cl_2 (4 mL) was deaminated using the general procedure for oxidative deamination with sodium 2,2,2-trifluoroethoxide (90 mg, 0.7 mmol), 18-crown-6 (195 mg, 0.7 mmol) in CH_2Cl_2 (2 mL) and phenol (188 mg, 2 mmol, 5 eq) in CH_2Cl_2 (1 mL) followed by column chromatography over silica gel eluting with (hexane/ethyl acetate 1:1) to afford **16** (71 mg, 33%) and **17** (56 mg, 31%).

Compound **16**: colorless oil, $[\alpha]_D^{20}$ – 32.4° (*c* 0.25, $CHCl_3$). ^1H NMR (600 MHz, C_6D_6) δ 7.29 – 7.23 (m, 4H, ArH), 7.09 (dt, *J* = 7.7, 1.1 Hz, 2H, ArH), 7.04 (t, *J* = 7.3 Hz, 1H, ArH), 6.96 (t, *J* = 7.3 Hz, 1H, ArH), 6.87 (d, *J* = 8.5 Hz, 2H, ArH), 5.19 (td, *J* = 5.8, 3.7 Hz, 1H, H8), 4.99 (t, *J* = 5.3 Hz, 1H, H7), 4.52 (dt, *J* = 8.9, 3.7 Hz, 1H), 4.20 (dd, *J* = 12.3, 3.6 Hz, 1H, H9), 4.14 (dd, *J* = 12.2, 6.3 Hz, 1H, H9'), 3.56 (s, 3H, CH_3), 3.48 (s, 3H, CH_3), 3.17 – 3.12 (m, 2H, H6 and H5), 2.55 (dd, *J* = 14.9, 8.9 Hz, 1H, H3a), 2.47 (dd, *J* = 14.9, 3.2 Hz, 1H, H3e), 2.07 (s, 3H, CH_3), 2.04 (s, 3H, CH_3), 2.02 (s, 3H, CH_3). ^1H NMR (600 MHz, C_6D_6) δ 7.28 – 7.26 (m, 2H, ArH), 7.08 (dt, *J* = 8.6, 7.3 Hz, 4H, ArH), 6.99 – 6.96 (m, 2H, ArH), 6.84 (tt, *J* = 7.3, 1.2 Hz, 1H, ArH), 6.78 (tt, *J* = 7.4, 1.2 Hz, 1H, ArH), 5.36 (ddd, *J* = 6.2, 5.7, 3.6 Hz, 1H, H8), 5.16 (t, *J* = 5.7 Hz, 1H, H7), 4.61 (ddd, *J* = 8.8, 4.6, 3.4 Hz, 1H, H4), 4.20 (dd, *J* = 12.3, 3.6 Hz, 1H, H9), 4.15 (dd, *J* = 12.2, 6.3 Hz, 1H, H9'), 3.26 (s, 3H, CH_3), 3.24 (s, 3H, CH_3), 3.18 (dd, *J* = 5.7, 2.1 Hz, 1H, H6), 3.01 (dd, *J* = 4.5, 2.0 Hz, 1H, H5), 2.77 (dd, *J* = 14.8, 8.8 Hz, 1H, H3a), 2.57 (dd, *J* = 14.8, 3.4 Hz, 1H, H3e), 1.65 (s, 3H, CH_3), 1.63 (s, 3H, CH_3), 1.57 (s, 3H, CH_3). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 170.6, 170.1, 169.7, 168.3, 157.4, 154.4, 129.8, 129.7, 123.3, 122.1, 118.8, 116.0, 101.3, 71.6, 70.6, 70.5, 61.6, 57.4, 54.1, 52.8, 50.4, 37.1, 20.9, 20.8, 20.8. $^{13}C\{^1H\}$ NMR (151 MHz, C_6D_6) δ 169.8, 169.6, 169.3, 168.1, 158.1, 155.1, 129.9, 129.9, 128.2, 128.1, 127.9, 123.3, 122.1, 119.3, 116.6, 101.8, 72.6, 71.2, 71.0, 61.7, 57.6, 54.4, 52.1, 50.2, 37.4, 20.4, 20.2, 20.1. ESI-HRMS Calcd. for ($C_{29}H_{34}NaO_{12}$) :([M+Na]$^+$) m/z: 597.1948; found: 597.1943.

Compound **17**: colorless oil, $[\alpha]_D^{20}$ – 32.1° (*c* 0.26, $CHCl_3$).^1H NMR (600 MHz, $CDCl_3$) δ 7.32 (t, *J* = 7.9 Hz, 2H, ArH), 7.12 (t, *J* = 7.4 Hz, 1H, ArH), 6.98 (d, *J* = 7.7 Hz, 2H, ArH), 5.44 (dd, *J* = 6.2, 2.3 Hz, 1H, H8), 5.26 (dd, *J* = 6.4, 2.7 Hz, 1H, H7), 4.69 (t, *J* = 1.9 Hz, 1H, H5), 4.57 (dd, *J* = 12.5, 2.4 Hz, 1H, H9), 4.48 (p, *J* = 2.6 Hz, 1H, H6), 4.21 (dd, *J* = 12.5, 6.1 Hz, 1H, H9'), 3.83 (s, 3H, CH_3), 3.31 (s, 3H, CH_3), 2.65 (ddd, *J* = 17.2, 3.7, 2.2 Hz, 1H, H3), 2.54 (dd, *J* = 17.2, 2.6

Hz, 1H, H3'), 2.08 (s, 3H, CH_3), 2.04 (s, 3H, CH_3), 2.03 (s, 3H, CH_3).^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$) δ 170.8, 170.0, 169.9, 168.4, 154.6, 151.0, 129.8 (2 carbons), 124.4, 120.2 (2 carbons), 99.4, 98.5, 71.3, 70.2, 69.4, 62.5, 52.8, 51.6, 34.5, 21.0, 20.9, 20.9. ESI-HRMS Calcd. for ($C_{23}H_{28}NaO_{11}$) :([M+Na]$^+$) m/z: 503.1529; found: 503.1529.

Methyl (methyl 7,8,9-tri-*O*-acetyl-3,4-dideoxy-4-*C*,5-*O*-(naphthalen-1,2-diyl)-D-glycero-β-D-talo-non-2-ulopyranosid)onate (18) and Methyl (methyl 4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-5-(2-hydroxynaphthalen-1-diazenyl)-D-glycero-β-D-galacto-non-2-ulopyranosid)onate (19). The nitrosyl sialoside **5** (534 mg, 1 mmol) in CH_2Cl_2 (10 mL) was deaminated using the general procedure for oxidative deamination with sodium 2,2,2-trifluoroethoxide (244 mg, 2 mmol), 18-crown-6 (582 mg, 2 mmol) in CH_2Cl_2 (5 mL) and 2-naphthol (2.88 g, 20 mmol, 20 eq) in Et_2O (10 mL) to afford, after flash chromatography over silica gel eluting with (hexane/ethyl acetate 1:1), **18** as white crystals (282 mg, 57%) from diethyl ether, and **19** as deep yellow crystals (81 mg, 13%) from methanol/CH_2Cl_2.

Compound **18**: white crystals, m.p. = 107-109 °C; $[\alpha]_D^{20}$ – 116.0^o (*c* 1.0, $CHCl_3$).^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.2 Hz, 1H, ArH), 7.69 (d, *J* = 8.8 Hz, 1H, ArH), 7.53 (dd, *J* = 8.0, 1.2 Hz, 1H, ArH), 7.46 (ddd, *J* = 8.3, 6.7, 1.2 Hz, 1H, ArH), 7.32 (ddd, *J* = 8.1, 6.7, 1.3 Hz, 1H, ArH), 7.10 (d, *J* = 8.8 Hz, 1H, ArH), 5.69 (dd, *J* = 6.0, 5.1 Hz, 1H, H7), 5.47 (td, *J* = 6.0, 2.7 Hz, 1H, H8), 4.94 (t, *J* = 9.2 Hz, 1H, H5), 4.48 (dd, *J* = 12.3, 2.7 Hz, 1H, H9), 4.35 (dd, *J* = 12.3, 6.0 Hz, 1H, H9'), 4.21 (dd, *J* = 9.4, 5.1 Hz, 1H, H6), 3.92 (s, 3H, CH_3), 3.87 (ddd, *J* = 13.5, 9.2, 5.0 Hz, 1H, H4), 3.31 (s, 3H, CH_3), 2.86 (dd, *J* = 14.9, 5.0 Hz, 1H, H3pe), 2.18 (s, 3H, CH_3), 2.10 (s, 3H, CH_3), 2.09 (s, 3H, CH_3), 1.90 (dd, *J* = 14.9, 13.5 Hz, 1H, H3pa).^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 170.8, 170.2, 169.9, 169.3, 157.1, 130.4, 130.0, 129.8, 129.1, 127.2, 123.4, 122.1, 119.8,

112.5, 99.4, 80.0, 70.6, 69.8, 69.6, 61.8, 53.0, 51.7, 37.1, 34.1, 21.0, 20.9. ESI-HRMS Calcd. for ($C_{27}H_{30}O_{11}Na$) :([M+Na]$^+$) m/z: 553.1686; found: 553.1686.

Compound **19**: deep yellow crystals; m.p. = 163-165 °C; $[\alpha]_D^{20}$ – 21.6^o (*c* 0.7, $CHCl_3$).^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (d, *J* = 8.3 Hz, 1H, ArH), 7.75 (d, *J* = 9.2 Hz, 1H, ArH), 7.65 (d, *J* = 7.9 Hz, 1H, ArH), 7.53 (ddd, *J* = 8.3, 7.0, 1.4 Hz, 1H, ArH), 7.38 (ddd, *J* = 8.1, 7.1, 1.3 Hz, 1H, ArH), 6.98 (d, *J* = 9.3 Hz, 1H, ArH), 5.86 (ddd, *J* = 11.2, 10.0, 5.1 Hz, 1H, H4), 5.42 (td, *J* = 6.1, 2.4 Hz, 1H, H8), 5.35 (dd, *J* = 6.5, 1.9 Hz, 1H, H7), 4.60 (dd, *J* = 12.5, 2.5 Hz, 1H, H9), 4.44 (dd, *J* = 10.4, 1.9 Hz, 1H, H6), 4.18 – 4.07 (m, 1H, H9), 4.00 (t, *J* = 10.2 Hz, 1H, H5), 3.83 (s, 3H, CH_3), 3.32 (s, 3H, CH_3), 2.66 (dd, *J* = 12.9, 5.1 Hz, 1H, H3), 2.13 (s, 3H, CH_3), 2.02 (s, 3H, CH_3), 1.94 (s, 3H, CH_3), 1.83 (s, 3H, CH_3), 1.26 – 1.22 (m, 1H, H3'). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 170.7, 170.1, 169.7, 169.5, 167.4, 161.9, 138.1, 133.3, 129.7, 128.5, 128.4, 128.0, 125.1, 122.5, 121.3, 99.0, 70.4, 70.2, 69.5, 68.9, 67.5, 62.1, 52.8, 51.5, 36.7, 21.0, 20.8, 20.7, 20.7. UV/vis λ_{max} = 380 nm (acetonitrile, ε = 8699 M^{-1} cm^{-1}). ESI-HRMS Calcd. for ($C_{29}H_{34}N_2O_{13}Na$) :([M+Na]$^+$) m/z: 641.1959; found: 641.1964.

Methyl (methyl 7,8,9-tri-*O*-acetyl-3,5-dideoxy-4-*O*-(4-methoxyphenyl)-β-D-arabino-non-4-en-2-ulopyranosid)onate (20) The nitrosyl sialoside **5** (267 mg, 0.5 mmol) in CH_2Cl_2 (5 mL) was deaminated using the general procedure for oxidative deamination with sodium 2,2,2-trifluoroethoxide (122 mg, 1 mmol), 18-crown-6 (291 mg, 1.1 mmol) in CH_2Cl_2 (2.5 mL) and 4-methoxyphenol (1.24 g, 10 mmol, 20 eq) in CH_2Cl_2 (5 mL) to afford, after flash column chromatography over silica gel eluting with (toluene/ethyl acetate 3:1), **20** as a colorless oil (92 mg, 36%); $[\alpha]_D^{20}$ – 10.9^o (*c* 0.7, CH_2Cl_2). ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.93 – 6.87 (m, 2H, ArH), 6.87 – 6.80 (m, 2H, ArH), 5.42 (td, *J* = 6.2, 2.3 Hz, 1H, H8), 5.23 (dd, *J* = 6.3, 2.7 Hz, 1H, H7), 4.56 (dd, *J* = 12.5, 2.4 Hz, 1H, H9), 4.51 (t, *J* = 1.9 Hz, 1H, H5), 4.45 (dt, *J* = 5.3, 2.6 Hz, 1H, H6),

4.19 (dd, *J* = 12.5, 6.1 Hz, 1H, H9'), 3.83 (s, 3H, CH_3), 3.78 (s, 3H, CH_3), 3.30 (s, 3H, CH_3), 2.64 (ddd, *J* = 17.1, 3.5, 2.0 Hz, 1H, H3), 2.53 (dd, *J* = 17.1, 2.5 Hz, 1H, H3'), 2.07 (s, 3H, CH_3), 2.03 (s, 3H, CH_3), 2.02 (s, 3H, CH_3). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 170.8, 170.0, 169.8, 168.5, 156.6, 152.0, 147.6, 121.8, 114.8, 98.4, 96.9, 71.4, 70.2, 69.4, 62.5, 55.7, 52.8, 51.6, 34.6, 21.0, 20.9, 20.9. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{24}H_{30}NaO_{12}$ 533.1635; Found: 533.1636.

Methyl (methyl 4,7,8,9-tetra-*O*-acetyl-3-deoxy-5-*O*-(4-nitrophenyl)-D-glycero-β-D-galacto-non-2-ulopyranosid)onate (21) and Methyl (methyl 7,8,9-tri-*O*-acetyl-3,5-dideoxy-4-*O*-(4-nitrophenyl)-β-D-arabino-non-4-en-2-ulopyranosid)onate (22). The nitrosyl sialoside **5** (267 mg, 0.5 mmol) in CH_2Cl_2 (5 mL) was deaminated using the general procedure for oxidative deamination with sodium 2,2,2-trifluoroethoxide (122 mg, 1 mmol), 18-Crown-6 (291 mg, 1.1 mmol) in CH_2Cl_2 (2.5 mL) and 4-nitrophenol (1.39 g, 10 mmol, 20 eq) in THF (5 mL) to afford **21** (27 mg, 9%), **22** (25 mg, 9%) and an inseparable mixture of **14** and **15** (52 mg, 23%) after flash column chromatography over silica gel eluting with (toluene/ethyl acetate 3:1).

Compound **21**: colorless oil, $[\alpha]_D^{20}$ – 3.7° (*c* 0.8, $CHCl_3$).^1H NMR (600 MHz, $CDCl_3$) δ 8.17 (d, *J* = 9.3 Hz, 2H, ArH), 6.97 (d, *J* = 9.2 Hz, 2H, ArH), 5.42 (dd, *J* = 4.8, 2.2 Hz, 1H, H7), 5.30 (ddd, *J* = 7.2, 4.9, 2.5 Hz, 1H, H8), 5.14 (dd, *J* = 10.1, 9.3 Hz, 1H, H5), 4.88 (ddd, *J* = 11.3, 9.2, 4.9 Hz, 1H, H4), 4.77 (dd, *J* = 12.5, 2.5 Hz, 1H, H9), 4.14 (dd, *J* = 12.5, 7.1 Hz, 1H, H9'), 4.11 (dd, *J* = 10.1, 2.2 Hz, 1H, H6), 3.82 (s, 3H, CH_3), 3.31 (s, 3H, CH_3), 2.66 (dd, *J* = 13.3, 4.9 Hz, 1H, H3e), 2.14 (s, 3H, CH_3), 2.08 (s, 3H, CH_3), 2.03 (s, 3H, CH_3), 1.95 (dd, *J* = 13.3, 11.3 Hz, 1H, H3a), 1.87 (s, 3H, CH_3). ^{13}C $\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 170.6, 170.5, 170.2, 169.6, 167.1, 162.6, 142.2, 126.1, 115.6, 99.1, 74.3, 71.3, 70.6, 68.4, 67.6, 62.3, 53.1, 51.6, 37.3, 21.1, 20.9, 20.8, 20.8. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{25}H_{31}NNaO_{15}$ 608.1591; Found: 608.1595.

Compound **22**: colorless oil, $[\alpha]_D^{20}$ – 46.8° (*c* 0.6, $CHCl_3$).^{1}H NMR (600 MHz, $CDCl_3$) δ 8.20 (d, *J* = 9.2 Hz, 2H, ArH), 6.90 (d, *J* = 9.2 Hz, 2H, ArH), 5.56 – 5.51 (m, 2H, H8 and H7), 5.18 (d, *J* = 3.6 Hz, 1H, H5), 5.04 (tdd, *J* = 5.5, 3.8, 1.2 Hz, 1H, H4), 4.41 (dd, *J* = 12.2, 2.7 Hz, 1H, H9), 4.33 (dd, *J* = 12.1, 7.1 Hz, 1H, H9'), 3.79 (s, 3H, CH_3), 3.41 (s, 3H, CH_3), 2.43 (dd, *J* = 13.8, 5.6 Hz, 1H, H3), 2.37 (dd, *J* = 13.8, 5.3 Hz, 1H, H3'), 2.14 (s, 3H, CH_3), 2.07 (s, 3H, CH_3), 2.065 (s, 3H, CH_3). ^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$) δ 170.8, 170.1, 169.4, 167.4, 162.0, 149.9, 142.0, 126.2, 126.1, 118.2, 115.6, 115.5, 99.4, 97.9, 70.5, 70.4, 66.9, 61.9, 53.0, 52.4, 34.5, 21.0, 20.94, 20.92. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{23}H_{27}NNaO_{13}$ 548.1380; Found: 548.1389.

Methyl (methyl 7,8,9-tri-*O*-acetyl-3,4-dideoxy-4-*C*,5-*O*-(3,5-dimethoxyphenyl-2,1-diyl)-D-glycero-β-D-talo-non-2-ulopyranosid)onate (23). The nitrosyl sialoside **5** (267 mg, 0.5 mmol) in CH_2Cl_2 (5 mL) was deaminated using the general procedure for oxidative deamination with sodium 2,2,2-trifluoroethoxide (122 mg, 1 mmol), 18-crown-6 (291 mg, 1.1 mmol) in CH_2Cl_2 (2.5 mL) and 3,5-dimethoxyphenol (1.54 g, 10 mmol, 20 eq) in CH_2Cl_2 (5 mL) to afford **23**, after flash column chromatography over silica gel eluting with (hexane/ethyl acetate 1:1) as a colorless oil in (92 mg, 34%); $[\alpha]_D^{20}$ – 79.8° (*c* 0.93, CH_2Cl_2).^{1}H NMR (600 MHz, $CDCl_3$) δ 6.02 (d, *J* = 2.0 Hz, 1H, ArH), 5.97 (d, *J* = 2.0 Hz, 1H, ArH), 5.59 (dd, *J* = 6.4, 4.6 Hz, 1H, H7), 5.39 (td, *J* = 6.1, 2.6 Hz, 1H, H8), 4.70 (t, *J* = 9.4 Hz, 1H, H5), 4.41 (dd, *J* = 12.3, 2.7 Hz, 1H, H9), 4.28 (dd, *J* = 12.4, 5.8 Hz, 1H, H9'), 4.03 (dd, *J* = 9.4, 4.6 Hz, 1H, H6), 3.82 (s, 3H, CH_3), 3.73 (s, 3H, CH_3), 3.72 (s, 3H, CH_3), 3.47 (ddd, *J* = 12.9, 9.1, 5.4 Hz, 1H, H4), 3.25 (s, 3H, CH_3), 2.63 (dd, *J* = 14.9, 5.4 Hz, 1H, H3pe), 2.14 (s, 3H, CH_3), 2.06 (s, 6H, CH_3), 1.79 (dd, *J* = 14.9, 12.9 Hz, 1H, H3pa). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 170.7, 170.1, 169.7, 169.4, 162.1, 161.1, 157.1, 107.5, 99.4, 91.8, 88.7, 79.5, 70.2, 69.7, 69.2, 61.7, 55.6, 55.3, 52.8, 51.5, 35.2, 33.7, 21.0, 20.8. ESI-HRMS Calcd. for ($C_{25}H_{32}NaO_{13}$) :($[M+Na]^+$) m/z: 563.1741 ; found: 563.1715.

Deamination of nitrosyl sialoside 5 with 2-quinolinol as nucleophile. The nitrosyl sialoside **5** (306 mg, 0.6 mmol) in CH_2Cl_2 (5 mL) was deaminated using the general procedure for oxidative deamination with sodium 2,2,2-trifluoroethoxide (140 mg, 1.1 mmol), 18-crown-6 (300 mg, 1.1 mmol) in CH_2Cl_2 (3 mL) and 2-quinolinol (165 mg, 1.1 mmol) in Et_2O (10 mL) to afford, after flash column chromatographic separation over silica gel (hexane/ethyl acetate 1:1), a mixture of compounds **14** and **15** (1:2.5 ratio; 220 mg, 86%).

Methyl (methyl 7,8,9-tri-*O*-acetyl-3,5-dideoxy-4-*O*-(quinolin-3-yl)-β-D-arabino-non-4-en-2-ulopyranosid)onate (24) and Methyl (methyl 7,8,9-tri-*O*-acetyl-3,5-dideoxy-4-*O*-(quinolin-3-yl)-β-D-ribo-non-5-en-2-ulopyranosid)onate (25). The nitrosyl sialoside **5** (330 mg, 0.6 mmol) in CH_2Cl_2 (5 mL) was deaminated using the general procedure for oxidative deamination with sodium 2,2,2-trifluoroethoxide (146 mg, 1.2 mmol), 18-crown-6 (317 mg, 1.2 mmol) in CH_2Cl_2 (3 mL) and 3-quinolinol (1.2 g, 8.5 mmol) in Et_2O (10 mL) to afford, after flash column chromatography over silica gel eluting with (hexane/ethyl acetate 1:2), **24** as a colorless oil in (68 mg, 21%) and **25** as a colorless oil in (40 mg, 12%).

Compound **24**; $[\alpha]_D^{20}$ – 42.1° (*c* 0.28, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (d, *J* = 2.8 Hz, 1H, ArH), 8.11 (d, *J* = 8.5 Hz, 1H, ArH), 7.77 (d, *J* = 8.2 Hz, 1H, ArH), 7.73 (d, *J* = 2.7 Hz, 1H, ArH), 7.67 (ddd, *J* = 8.4, 6.7, 1.5 Hz, 1H, ArH), 7.56 (t, *J* = 7.5 Hz, 1H, ArH), 5.46 (td, *J* = 6.3, 2.5 Hz, 1H, H8), 5.29 (dd, *J* = 6.5, 2.8 Hz, 1H, H7), 4.89 (t, *J* = 2.0 Hz, 1H, H5), 4.56 (dd, *J* = 12.5, 2.4 Hz, 1H, H9), 4.52 (q, *J* = 2.7 Hz, 1H, H6), 4.21 (dd, *J* = 12.5, 6.0 Hz, 1H, H9'), 3.84 (s, 3H, CH_3), 3.34 (s, 3H, CH_3), 2.73 (ddd, *J* = 17.0, 3.7, 2.1 Hz, 1H, H3), 2.61 (dd, *J* = 17.1, 2.4 Hz, 1H, H3'), 2.12 (s, 3H, CH_3), 2.04 (s, 3H, CH_3), 2.03 (s, 3H, CH_3). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 170.8, 170.0, 169.8, 168.1, 150.6, 148.1, 145.6, 129.4, 128.5, 127.5, 127.3, 122.9, 101.3,

98.4, 71.1, 70.0, 69.3, 62.4, 52.8, 51.7, 34.3, 21.0, 20.9, 20.8. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{26}H_{29}NO_{11}Na$ 554.1638; Found: 554.1636.

Compound **25**; $[\alpha]_D^{20}$ – 26.2° (*c* 0.2, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$) δ 8.57 (d, *J* = 2.8 Hz, 1H, ArH), 8.03 (d, *J* = 8.3 Hz, 1H, ArH), 7.72 (d, *J* = 8.1 Hz, 1H, ArH), 7.57 (t, *J* = 7.6 Hz, 1H, ArH), 7.51 (t, *J* = 7.5 Hz, 1H, ArH), 7.40 (d, *J* = 2.9 Hz, 1H, ArH), 5.58 – 5.53 (m, 2H, H8 and H7), 5.24 (d, *J* = 3.8 Hz, 1H, H5), 5.06 (tdd, *J* = 5.3, 3.7, 1.3 Hz, 1H, H4), 4.43 (dd, *J* = 12.2, 2.8 Hz, 1H, H9), 4.36 (dd, *J* = 12.1, 7.2 Hz, 1H, H9'), 3.80 (s, 3H, CH_3), 3.42 (s, 3H, CH_3), 2.51 (dd, *J* = 13.8, 5.4 Hz, 1H, H3), 2.40 (dd, *J* = 13.8, 5.3 Hz, 1H, H3'), 2.13 (s, 3H, CH_3), 2.06 (s, 6H, CH_3). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 170.8, 170.1, 169.4, 167.5, 150.2, 149.6, 128.7, 127.5, 126.9, 99.4, 98.3, 70.5, 70.4, 66.8, 61.9, 53.0, 52.4, 34.4, 21.0, 20.9, 20.9. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{26}H_{29}NO_{11}Na$ 554.1638; Found: 554.1636.

Methyl (methyl 7,8,9-tri-*O*-acetyl-3,4-dideoxy-4-*C*,5-*O*-(quinolin-5,6-diyl)-D-glycero-β-D-talo-non-2-ulopyranosid)onate (26). The nitrosyl sialoside **5** (200 mg, 0.4 mmol) in CH_2Cl_2 (4 mL) was deaminated using the general procedure for oxidative deamination with sodium 2,2,2-trifluoroethoxide (91 mg, 0.7 mmol), 18-crown-6 (195 mg, 0.7 mmol) in CH_2Cl_2 (3 mL) and 6-quinolinol (1.1 g, 7.6 mmol) in hexafluoroisopropanol (3 mL), to afford, after flash column chromatography over silica gel eluting with (hexane/ethyl acetate 1:2), **26** as light yellow oil (105 mg, 53%) and an inseparable mixture of **14** and **15** as a colorless oil (25 mg, 11%).

Compound **26**; $[\alpha]_D^{20}$ – 85.1° (*c* 0.37, CH_2Cl_2).^1H NMR (600 MHz, $CDCl_3$) δ 8.78 (dd, *J* = 4.2 Hz, 1H, ArH), 8.01 (d, *J* = 9.0 Hz, 1H, ArH), 7.91 (d, *J* = 8.3 Hz, 1H, ArH), 7.39 (dd, *J* = 8.4, 4.2 Hz, 1H, ArH), 7.34 (d, *J* = 9.0 Hz, 1H, ArH), 5.68 (dd, *J* = 6.1, 5.0 Hz, 1H, H7), 5.46 (td, *J* = 6.0, 2.6 Hz, 1H, H8), 4.99 (dd, *J* = 9.3, 8.9 Hz, 1H, H5), 4.48 (dd, *J* = 12.3, 2.7 Hz, 1H, H9), 4.34 (dd, *J* =

12.3, 6.0 Hz, 1H, H9'), 4.21 (dd, *J* = 9.3, 5.0 Hz, 1H, H6), 3.91 (s, 3H, CH_3), 3.88 (ddd, *J* = 13.4, 8.9, 5.1 Hz, 1H, H4), 3.31 (s, 3H, CH_3), 2.78 (dd, *J* = 14.9, 5.1 Hz, 1H, H3pe), 2.18 (s, 3H, CH_3), 2.10 (s, 3H), 2.09 (s, 3H), 1.92 (dd, *J* = 14.9, 13.4 Hz, 1H, H3pa). ^{13}C {^1H} NMR (151 MHz, $CDCl_3$) δ 170.8, 170.3, 169.9, 169.2, 157.3, 147.3, 133.2, 131.6, 130.4, 125.5, 121.9, 119.8, 115.9, 99.2, 80.5, 70.5, 69.8, 69.5, 61.7, 53.1, 51.8, 36.9, 34.3, 21.2, 21.1, 21.0. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{26}H_{29}NO_{11}Na$ 554.1638; Found: 554.1634.

Methyl (methyl 7,8,9-tri-*O*-acetyl-3,4-dideoxy-4-*C*,5-*O*-(indol-4,5-diyl)-D-glycero-β-D-talo-non-2-ulopyranosid)onate (27) and Methyl (methyl 4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-5-(5-hydroxyindol-4-diazenyl)-D-glycero-β-D-galacto-non-2-ulopyranosid)onate (28). The nitrosyl sialoside **5** (267 mg, 0.5 mmol) in CH_2Cl_2 (5 mL) was deaminated using the general procedure for oxidative deamination with sodium 2,2,2-trifluoroethoxide (122 mg, 1 mmol), 18-crown-6 (291 mg, 1.1 mmol) in CH_2Cl_2 (2.5 mL) and 5-hydroxyindole (1.33 g, 10 mmol, 20 eq) in THF (5 mL) to afford, after flash column chromatography over silica gel eluting with (hexane/ethyl acetate 1:1), **27** as a colorless oil (72 mg, 27%), **28** (28 mg, 9%) as deep yellow crystals from methanol/CH_2Cl_2, and an inseparable mixture of **14** and **15** (16 mg, 7%).

Compound **27**; colorless oil, $[\alpha]_D^{20}$ – 104.8° (*c* 0.4, CH_2Cl_2). ^1H NMR (600 MHz, $CDCl_3$) δ 8.13 (s, 1H, NH), 7.22 (t, *J* = 2.9 Hz, 1H, ArH), 7.17 (d, *J* = 8.6 Hz, 1H, ArH), 6.74 (d, *J* = 8.6 Hz, 1H, ArH), 6.32 (ddd, *J* = 3.1, 2.0, 1.0 Hz, 1H, ArH), 5.67 (dd, *J* = 6.1, 5.0 Hz, 1H, H7), 5.47 (td, *J* = 6.1, 2.8 Hz, 1H, H8), 4.82 (dd, *J* = 9.4, 8.8 Hz, 1H, H5), 4.46 (dd, *J* = 12.3, 2.8 Hz, 1H, H9), 4.32 (dd, *J* = 12.3, 6.1 Hz, 1H, H9'), 4.12 (dd, *J* = 9.4, 5.0 Hz, 1H, H6), 3.88 (s, 3H), 3.77 (ddd, *J* = 12.8, 8.8, 5.5 Hz, 1H, H4), 3.28 (s, 3H, CH_3), 2.72 (dd, *J* = 14.9, 5.5 Hz, 1H, H3pe), 2.17 (s, 3H, CH_3), 2.09 (s, 3H, CH_3), 2.07 (s, 3H, CH_3), 2.02 (dd, *J* =14.9, 12.8 Hz, 1H, H3pa). ^{13}C {^1H} NMR (151 MHz, $CDCl_3$) δ 170.9, 170.3, 169.9, 169.6, 153.3, 132.3, 126.0, 124.5, 116.9, 110.9, 106.0,

99.5, 99.4, 78.7, 70.7, 69.9, 69.6, 61.9, 53.0, 51.6, 37.6, 34.2, 21.1, 21.0. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{25}H_{29}NNaO_{11}$ 542.1638; Found: 542.1637.

Compound **28**; m.p = 209-2010 °C; $[\alpha]_D^{20}$ – 51.1° (*c* 0.45, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$) δ 11.44 (s, 1H), 8.31 (s, 1H, ArH), 7.36 (d, *J* = 8.7, 0.9 Hz, 1H, ArH), 6.94 (ddd, *J* = 2.9, 2.0, 0.8 Hz, 1H, ArH), 6.82 (d, *J* = 8.8 Hz, 1H, ArH), 6.00 (ddd, *J* = 11.4, 9.9, 5.1 Hz, 1H, H4), 5.42 (td, *J* = 6.1, 2.6 Hz, 1H, H8), 5.34 (dd, *J* = 6.3, 1.9 Hz, 1H, H7), 4.61 (dd, *J* = 12.5, 2.5 Hz, 1H, H9), 4.44 (dd, *J* = 10.4, 1.9 Hz, 1H, H6), 4.14 (dd, *J* = 12.5, 6.0 Hz, 1H, H9'), 4.02 (t, *J* = 10.1 Hz, 1H, H5), 3.84 (s, 3H, CH_3), 3.32 (s, 3H, CH_3), 2.65 (dd, *J* = 12.9, 5.1 Hz, 1H, H3e), 2.17 (s, 3H, CH_3), 2.02 (s, 3H, CH_3), 1.97 (s, 3H, CH_3), 1.87 (dd, *J* = 12.8, 11.6 Hz, 1H, H3a), 1.85 (s, 3H, CH_3). ^{13}C $\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 170.9, 170.2, 169.9, 169.5, 167.7, 149.3, 130.6, 128.9, 126.6, 118.1, 113.2, 101.4, 99.1, 74.2, 70.4, 70.2, 69.1, 67.5, 62.2, 52.9, 51.5, 36.5, 21.1, 20.9, 20.9, 20.9. UV-vis λ_{max} = 365 nm (dichloromethane, ε = 2391 $M^{-1}cm^{-1}$). HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{27}H_{33}N_3NaO_{13}$ 630.1911; Found: 630.1904.

Methyl (methyl 4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-5-phenylthio-D-glycero-β-D-galacto-non-2-ulopyranosid)onate (29) and Methyl (methyl 4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-β-D-gluco-non-2-ulopyranosid)onate (30). The nitrosyl sialoside **5** (200 mg, 0.4 mmol) in CH_2Cl_2 (4 mL) was deaminated using the general procedure for oxidative deamination with sodium 2,2,2-trifluoroethoxide (90 mg, 0.7 mmol), 18-crown-6 (97 mg, 0.4 mmol) in CH_2Cl_2 (2 mL) and thiophenol (0.8 mL, 7.4 mmol) to afford **29** (48 mg, 23%) and **30** (32 mg, 19%) after flash column chromatography over silica gel eluting with (hexane/ethyl acetate 1:1).

Compound **29**: yellow oil, $[\alpha]_D^{20}$ –59.4° (*c* 0.5, $CHCl_3$).^1H NMR (600 MHz, $CDCl_3$) δ 7.45 – 7.40 (m, 3H, ArH), 7.36 – 7.32 (m, 2H, ArH), 5.98 (dd, *J* = 4.7, 1.8 Hz, 1H, H7), 5.29 (td, *J* = 10.9, 5.0

Hz, 1H, H4), 5.23 (ddd, *J* = 7.2, 4.7, 2.6 Hz, 1H, H8), 4.71 (dd, *J* = 12.4, 2.5 Hz, 1H, H9), 4.12 (dd, *J* = 12.4, 7.1 Hz, 1H, H9'), 3.87 (dd, *J* = 11.1, 1.9 Hz, 1H, H6) , 3.78 (s, 3H), 3.17 (s, 3H), 2.88 (t, *J* = 10.9 Hz, 1H, H5), 2.53 (dd, *J* = 12.8, 4.9 Hz, 1H, H3e), 2.08 (s, 3H), 2.04 (s, 3H), 2.00 (s, 3H), 1.92 (s, 3H), 1.73 (dd, *J* = 12.8, 11.1 Hz, 1H, H3a). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 170.6, 170.4, 169.6, 169.5, 167.4, 134.8, 133.8, 132.09, 132.03, 131.3, 122.3, 98.5, 71.7, 71.3, 69.7, 69.0, 62.2, 52.6, 51.3, 48.7, 37.9, 29.6, 20.96, 20.91, 20.7, 20.3. ESI-HRMS Calcd. for ($C_{25}H_{32}NaO_{12}S$) :($[M+Na]^+$) m/z: 579.1512; found: 579.1519.

Compound **30**: colorless oil, $[\alpha]_D^{20}$ –21.9° (*c* 2.1, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.33 (td, *J* = 6.0, 2.6 Hz, 1H, H8), 5.26 (dd, *J* = 6.2, 3.2 Hz, 1H, H7), 5.20 (m 1H, H4), 4.56 (dd, *J* = 12.8, 2.6 Hz, 1H, H9) , 4.22 (dd, *J* = 12.6, 5.9 Hz, 1H, H9), 3.99 (dd, *J* = 11.9, 3.2 Hz, 1H, H6), 3.78 (s, 3H, CH_3), 3.19 (s, 3H, CH_3), 2.35 (dd, *J* = 12.8, 4.9 Hz, 1H, H3e), 2.14 (s, 3H, CH_3), 2.07 (s, 3H, CH_3), 2.04 (s, 3H, CH_3), 2.02 (s, 3H, CH_3), 1.64 – 1.56 (m, 2H, H5e and H3a), 1.38 (q, *J* = 12.0 Hz, 1H, H5a). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 170.7, 170.2, 170.1, 170.1, 168.1, 99.4, 71.7, 70.3, 68.2, 66.5, 62.0, 52.7, 50.9, 37.3, 32.2, 21.2, 21.0, 20.8, 20.8. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{28}NaO_{12}$ 471.1478; Found: 471.1479.

Methyl (methyl 4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-5-(2-aminophenylthio)-D-glycero-β-D-galacto/gulo-non-2-ulopyranosid)onate (31) and Methyl (methyl 4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-β-D-gluco-non-2-ulopyranosid)onate (30). The nitrosyl sialoside **5** (267 mg, 0.5 mmol) in CH_2Cl_2 (5 mL) was deaminated using the general procedure for oxidative deamination with sodium 2,2,2-trifluoroethoxide (122 mg, 1 mmol), 18-crown-6 (291 mg, 1.1 mmol) in CH_2Cl_2 (2.5 mL) and 2-aminothiophenol (1.25 g, 10 mmol, 20 eq) in CH_2Cl_2 (5 mL) to afford, after flash column chromatography over silica gel eluting with (hexane/ethyl acetate 2:1), **31** (167 mg, 58%) as a mixture of two isomers (ratio; axial/equatorial = 1:3) and **30** (64 mg, 28%).

Compound **31;** ESI-HRMS Calcd. for ($C_{25}H_{33}NNaO_{12}S$): ($[M+Na]^+$) m/z: 594.1621; found: 594.1621. Major isomer (D-glycero-D-galacto): colorless oil, ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33 (dd, *J* = 7.7, 1.5 Hz, 1H, ArH), 7.09 (ddd, *J* = 8.0, 7.3, 1.5 Hz, 1H, ArH), 6.67 (dd, *J* = 8.1, 1.3 Hz, 1H, ArH), 6.65 (td, *J* = 7.6, 1.2 Hz, 1H, ArH), 5.97 (dd, *J* = 5.1, 1.5 Hz, 1H, H7), 5.27 (ddd, *J* = 6.8, 5.1, 2.5 Hz, 1H, H8), 5.22 (td, *J* = 10.6, 5.0 Hz, 1H, H4), 4.67 (dd, *J* = 12.5, 2.5 Hz, 1H, H9), 4.14 (dd, *J* = 12.5, 6.9 Hz, 1H, H9'), 3.96 (dd, *J* = 11.1, 1.6 Hz, 1H, H6), 3.75 (s, 3H, CH_3), 3.15 (s, 3H, CH_3), 2.94 (t, *J* = 10.7 Hz, 1H, H5), 2.51 (dd, *J* = 12.8, 5.1 Hz, 1H, H3e), 2.07 (s, 3H, CH_3), 2.03 (s, 3H, CH_3), 2.02 (s, 3H, CH_3), 1.89 (s, 3H, CH_3), 1.63 (dd, *J* = 12.8, 10.9 Hz, 1H, H3a). ^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$) δ 170.7, 170.5, 170.0, 169.8, 167.5, 136.7, 130.6, 118.7, 115.4, 113.7, 98.5, 71.7, 71.7, 70.1, 70.0, 62.4, 52.6, 51.3, 47.0, 37.6, 21.1, 20.9, 20.6. Minor isomer (D-glycero-D-gulo): ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.44 (dd, *J* = 8.3, 1.4 Hz, 1H, ArH), 7.04 (td, *J* = 7.7, 1.5 Hz, 1H, ArH), 5.86 (dd, *J* = 7.6, 4.1 Hz, 1H, H7), 5.41 (dt, *J* = 6.0, 4.6 Hz, 1H), 4.37 (dd, *J* = 12.0, 4.8 Hz, 1H, H9), 4.18 (dd, *J* = 12.0, 5.9 Hz, 1H, H9'), 4.09 (dd, *J* = 7.6, 1.7 Hz, 1H, H6), 3.80 (s, 3H, CH_3), 3.21 (s, 3H, CH_3), 2.66 (dd, *J* = 12.9, 12.0 Hz, 1H, H3), 2.10 (s, 3H, CH_3), 2.09 (s, 3H, CH_3), 2.05 (s, 3H, CH_3), 1.46 (s, 3H, CH_3). ^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$) δ 170.3, 170.0, 167.5, 148.8, 137.0, 129.8, 118.8, 116.5, 115.5, 98.9, 71.2, 70.3, 69.5, 61.4, 52.8, 51.0, 48.0, 32.7, 21.0, 20.9, 20.8, 20.2.

Methyl (methyl 4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-5-(naphthalen-2-thio)-D-glycero-β-D-galacto/gulo-non-2-ulopyranosid)onate (32) and Methyl (methyl 4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-gluco-non-2-ulopyranosid)onate (30). The nitrosyl sialoside **5** (267 mg, 0.5 mmol) in CH_2Cl_2 (5 mL) was deaminated using the general procedure for oxidative deamination with sodium 2,2,2-trifluoroethoxide (122 mg, 1 mmol), 18-crown-6 (291 mg, 1.1 mmol) in CH_2Cl_2 (2.5 mL) and 2-naphthalenethiol (1.60 g, 10 mmol, 20 eq) in CH_2Cl_2 (5 mL) to afford, after flash

column chromatography over silica gel eluting with (hexane/ethyl acetate 3:1), **32a** as colorless oil (92 mg, 30%), a mixture of **32a** and its stereoisomer **32b** as a colorless oil (76 mg, 25%) axial/equatorial ratio; 1:4 by ^{1}H NMR and **30** (30 mg, 13%).

Compound **32a** (D-glycero-D-galacto); colorless oil, (92 mg, 30%), $[\alpha]_D^{20}$ – 34.7^o (*c* 2.5, CH_2Cl_2). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97 (d, *J* = 1.8 Hz, 1H, ArH), 7.79 (dd, *J* = 7.8, 1.6 Hz, 2H, ArH), 7.77 (d, *J* = 8.5 Hz, 1H, ArH), 7.52 (dd, *J* = 8.6, 1.9 Hz, 1H, ArH), 7.48 (m, 2H, ArH), 6.08 (dd, *J* = 4.8, 1.9 Hz, 1H, H7), 5.38 (td, *J* = 1 0.9, 5.0 Hz, 1H, H4), 5.25 (ddd, *J* = 7.2, 4.8, 2.6 Hz, 1H, H8), 4.69 (dd, *J* = 12.4, 2.6 Hz, 1H, H9), 4.12 (dd, *J* = 12.4, 7.1 Hz, 1H, H9), 3.94 (dd, *J* = 11.0, 1.9 Hz, 1H, H6), 3.77 (s, 3H, CH_3), 3.12 (s, 3H, CH_3), 3.03 (t, *J* = 10.9 Hz, 1H, H5), 2.54 (dd, *J* = 12.9, 5.1 Hz, 1H, H3e), 2.03 (s, 3H, CH_3), 2.01 (s, 3H, CH_3), 1.96 (s, 3H, CH_3), 1.80 (s, 3H, CH_3), 1.76 (dd, *J* = 12.9, 11.1 Hz, 1H, H3a). ^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$) δ 170.7, 170.6, 169.8, 169.5, 167.6, 133.6, 132.9, 132.7, 130.3, 129.4, 128.7, 127.7, 127.7, 126.8, 126.7, 98.7, 71.8, 71.7, 70.0, 69.4, 62.5, 52.7, 51.4, 48.8, 38.1, 21.0, 21.0, 20.9, 20.4. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{29}H_{34}O_{12}SNa$ 629.1669; Found: 629.1669.

The minor D-glycero-D-gulo isomer **32b** was identified from a mixture with the major isomer by the following signals: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 1.8 Hz, 1H, ArH), 7.81-7.75 (m, 3H, ArH), 7.59 (dd, *J* = 8.6, 1.9 Hz, 1H, ArH), 7.48-7.43 (m, 2H, ArH), 5.94 (dd, *J* = 4.8, 1.9 Hz, 1H, H7), 5.52 (ddd, *J* = 7.2, 4.8, 2.6 Hz, 1H, H8), 5.38 (m, 1H, H4), 4.46 (dd, *J* = 12.4, 2.6 Hz, 1H, H9), 4.18-4.10 (m, 2H, H6 & H9), 3.95 (m, 1H, H5), 3.82 (s, 3H, CH_3), 3.24 (s, 3H, CH_3), 2.60 (dd, *J* = 12.9, 11.1 Hz, 1H, H3), 2.16 (dd, *J* = 12.9, 5.1 Hz, 1H, H3), 2.12 (s, 3H, CH_3), 2.09 (s, 3H, CH_3). ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 170.8, 170.4, 170.2, 169.7, 167.4, 133.7, 132.7, 132.0, 131.1, 129.4, 129.3, 128.2, 127.3, 126.6, 126.2, 98.9, 71.8, 70.7, 69.7, 68.9, 61.6, 52.8, 50.9, 49.9, 29.7, 20.8, 20.7, 20.6, 20.1.

Methyl (methyl 7,8,9-tri-*O*-acetyl-3,5-dideoxy-4,4-*O*-ethylidene)-β-D-arabino-non-2-ulopyranosid)onate (33). Dry ethylene glycol (20 μL) and a few crystals of dry *p*-toluenesulfonic acid were added to compound **20** (30 mg, 0.06 mmol) dissolved in CH_2Cl_2 (5 mL). The mixture was stirred at rt until the substrate was consumed (25 h). The reaction mixture was diluted with DCM (5 mL), and the organic layer was washed with sat. $NaHCO_3$, brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by column chromatography over silica gel eluting with (hexane/ethyl acetate 1:1) then gave compound **33** as a colorless oil (11 mg, 42 %); $[\alpha]_D^{20}$ – 16.4° (*c* 0.45, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.35 (td, *J* = 6.0, 2.5 Hz, 1H, H8), 5.29 (dd, *J* = 5.9, 3.3 Hz, 1H, H7), 4.60 (dd, *J* = 12.5, 2.5 Hz, 1H, H9), 4.23 (dd, *J* = 12.5, 6.0 Hz, 1H, H9), 4.19 (ddd, *J* = 12.2, 3.4, 2.1 Hz, 1H, H6), 4.10 – 3.86 (m, 4H), 3.78 (s, 3H, CH_3), 3.23 (s, 3H, CH_3), 2.19 (dd, *J* = 14.2, 2.2 Hz, 1H, H5), 2.13 (s, 3H, CH_3), 2.07 (s, 3H, CH_3), 2.03 (s, 3H, CH_3), 1.89 (d, *J* = 14.1 Hz, 1H, H5'), 1.71 (dt, *J* = 13.2, 2.2 Hz, 1H, H3e), 1.58 (dd, *J* = 13.1, 12.1 Hz, 1H, H3a).^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$) δ 170.8, 170.3, 170.2, 168.5, 105.8, 99.3, 71.9, 70.5, 68.0, 65.5, 64.1, 62.0, 52.7, 51.5, 40.5, 35.8, 21.1, 20.9. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{28}NaO_{12}$ 471.1478; Found: 471.1471.

Methyl (7,8,9-tri-*O*-acetyl-2,3,5-trideoxy-β-D-arabino-non-2-en-4-oxo-2-ulopyranosid) onate (36). A solution of compound **20** (25 mg, 0.05 mmol), a few drops of wet methanol and a few crystals of *p*-toluenesulfonic acid in CH_2Cl_2 (5 mL) was stirred at rt until TLC showed complete consumption of the starting material (4 h). The reaction mixture was diluted with CH_2Cl_2 (5 mL), and the organic layer was washed with sat. $NaHCO_3$, brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by column chromatography over silica gel eluting with (toluene/ethyl acetate 4:1) gave compound **36** as a colorless oil (10 mg, 55 %); $[\alpha]_D^{20}$ –26.8° (*c* 0.2,$CHCl_3$).^{1}H NMR (600 MHz, $CDCl_3$) δ 6.24 (d, *J* = 1.1 Hz, 1H, H3), 5.41 (ddd, *J* =

7.3, 4.9, 2.5 Hz, 1H, H8), 5.38 (dd, *J* = 7.1, 2.8 Hz, 1H, H7), 4.71 (ddd, *J* = 13.5, 3.8, 2.8 Hz, 1H, H6), 4.49 (dd, *J* = 12.6, 2.5 Hz, 1H, H9), 4.25 (dd, *J* = 12.6, 4.9 Hz, 1H, H9), 3.88 (s, 3H, CH_3), 2.58 (dd, *J* = 16.9, 13.6 Hz, 1H, H5), 2.49 (ddd, *J* = 16.9, 3.8, 1.1 Hz, 1H, H5'), 2.14 (s, 3H, CH_3), 2.08 (s, 3H, CH_3), 2.06 (s, 3H, CH_3). ^{13}C {^1H} NMR (151 MHz, $CDCl_3$) δ 191.8, 170.7, 169.8, 161.7, 158.3, 109.5, 77.7, 77.4, 77.2, 76.9, 70.1, 69.5, 61.7, 53.4, 37.8, 21.0, 20.8, 20.6. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{20}NaO_{10}$ 395.0954; Found: 395.0950.

Supporting Information. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.8b01645.

Copies of the ^1H and ^{13}C NMR spectra of all new compounds (PDF)

X-Crystallographic Structure of Compound **18** (CCDC 1941624)

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