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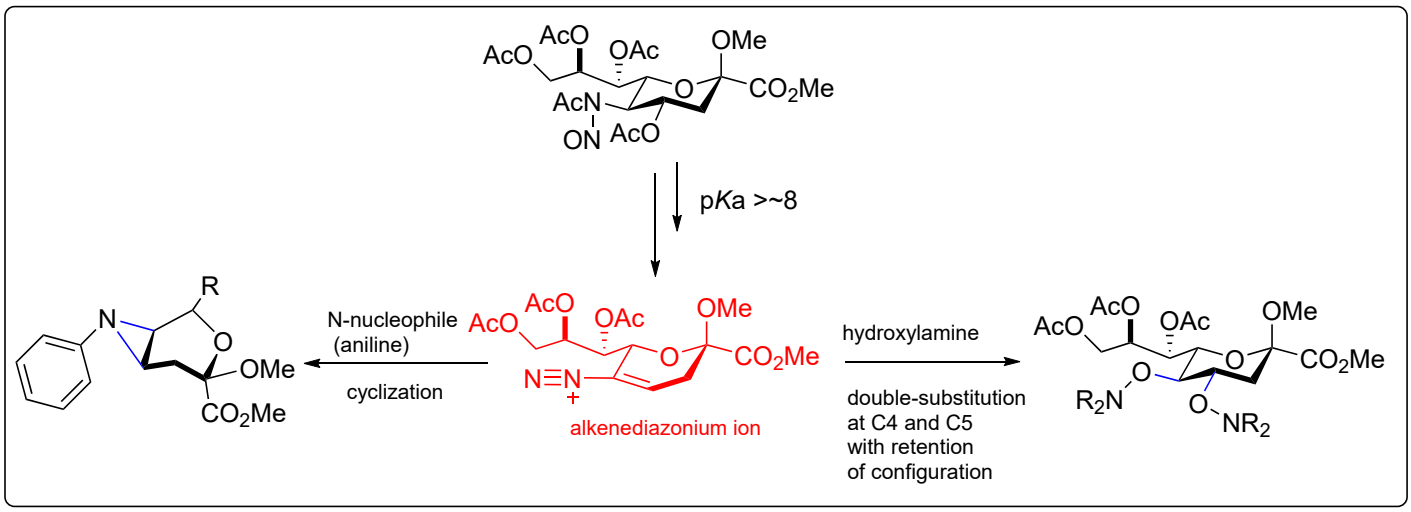
AcO
AcO
OAc
OMe
AcN
O
CO2Me
ON
AcO
pKa >~8
N-nucleophile
(aniline)
cyclization
alkenediazonium ion
hydroxylamine
double-substitution
at C4 and C5
with retention
of configuration
R2N
NR2

Use of Hydroxylamines, Hydroxamic Acids, Oximes and Amines as Nucleophiles in the Zbiral Oxidative Deamination of *N*-Acetyl Neuraminic Acid. Isolation and Characterization of Novel Mono- and Disubstitution Products

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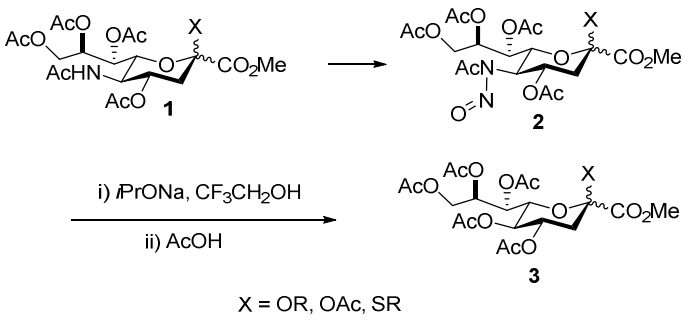
Abstract

The oxidative deamination of *N*-nitroso *N*-acetylneuraminic acid (NeuAc) derivatives is a useful reaction for the formation of 5-desamino-5-hydroxy NeuAc derivatives and their stereoisomers. We demonstrated previously that replacement of the classical nucleophile in these reactions, acetic acid, by phenols resulted in a novel double displacement process with substitution of the acetoxy group at the 4-position taking place in addition to that of the 5-acetamido group, for

which we postulated a mechanism centered on the formation of a highly reactive vinyl diazonium ion. We now extend these studies to encompass the use of hydroxylamine-based systems and weakly basic amines as nucleophile. We find that the nature of the product depends significantly on the p*K*a of the nucleophile, with the more acidic species typically affording only substitution at the 5-position, while the less acidic species give mixtures of elimination products and disubstitution products. The use of aniline as nucleophile is of particular note as it affords a novel aziridine spanning positions 4- and 5- of the neuraminic acid skeleton.

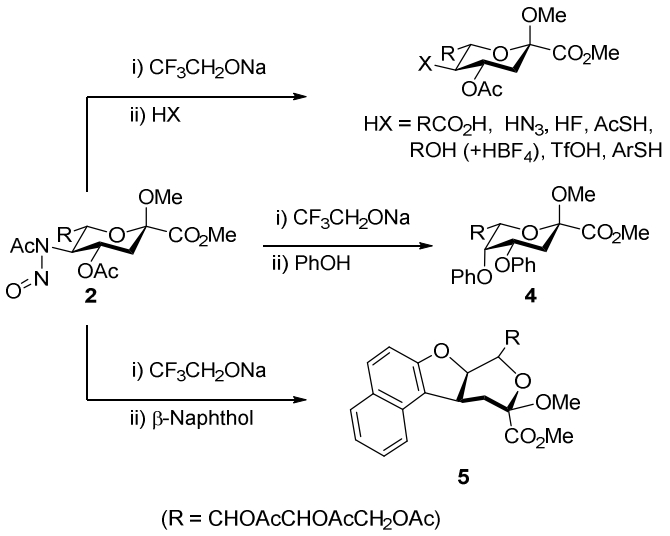
Introduction

The oxidative deamination of *N*-acetyl neuraminic acid (NeuAc) glycosides **1** by treatment of the corresponding *N*-nitrosoamides **2** with sodium trifluoroethoxide followed by the addition of acetic acid resulting in the replacement of the C-N bond by a C-O bond with retention of configuration is a practical and convenient synthesis of 3-deoxy-D-glycero-D-galacto-nonulosonic acid (KDN) glycosides **3** (Scheme 1, X = OAc) first described by Schreiner and Zbiral,[1] and extended to encompass NeuAc thioglycosides in our laboratory.[2] The overall transformation of **2** to **3** also may be achieved by simple thermolysis, also with retention of configuration, but such conditions with their seemingly narrower scope have been less widely explored.[3]



Scheme 1. Oxidative Deamination of NeuAc

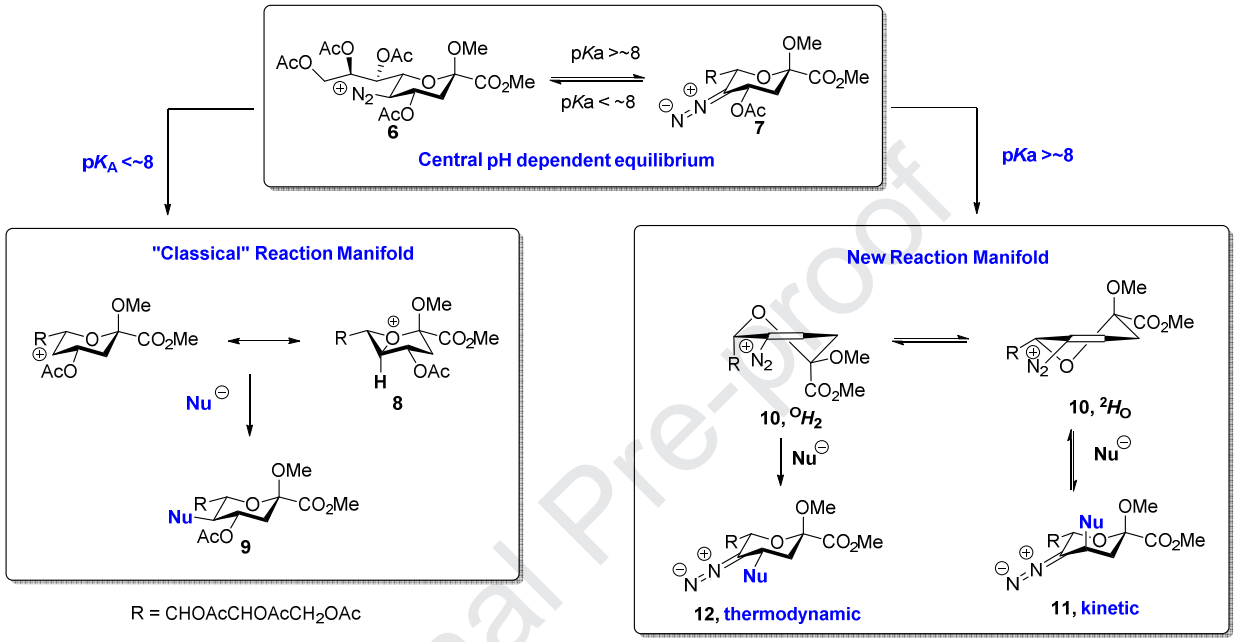
As originally described by Schreiner and Zbiral[1] the only nucleophiles employed were acetic acid (Scheme 1) and hydrogen azide, with the latter affording 5-azido-5-desacetamido-NeuAc derivatives, also with retention of configuration. In our laboratory we extended the range of nucleophiles to include alternate carboxylic acids (specifically levulinic acid),[4] hydrogen fluoride,[5] trifluoromethanesulfonic acid,[6] thioacetic acid,[5] thiophenols,[7] and provided the second step is conducted in the presence of fluoroboric acid, alcohols,[5] with each substitution taking place with retention of configuration (Scheme 2). In a series of experiments designed to probe mechanism of substitution with retention of configuration we conclusively eliminated stereodirecting participation by esters at the 4- or 7-positions from consideration and hypothesized that participation by the pyranosidic ring oxygen via an intermediate 1-oxabicyclo[3.1.0]oxahexanium ion underlies the stereochemical outcome of these reactions.[4] Seeking to further expand the range of nucleophiles compatible with the oxidative deamination we recently explored the use of phenols and uncovered a new reaction manifold with concomitant substitution at the 4-position. Thus, replacement of acetic acid as nucleophile by phenol under our otherwise standard conditions resulted in the isolation of the 4,5-disubstituted derivative **4** as major product with retention and inversion of configuration at the 4- and 5-positions, respectively. Conversely, the use of β-naphthol as nucleophile gave the crystallographically-established tricyclic system **5** as major product with inversion and retention of configuration at the 4- and 5-positions, respectively (Scheme 2).[7]



Scheme 2. Nucleophiles Employed Previously in the Deamination of NeuAc

We understand this ensemble of results in terms of the initial formation of a diazonium ion **6** on treatment of **2** with trifluoroethoxide that is in a pH dependent equilibrium with the diazoalkane **7** (Scheme 3). The intermediacy of the diazonium ion **6** is established by the isolation of a typical azo dye as byproduct (not shown) in the reaction with β-naphthol,[7] whereas the equilibrium **6** and **7** rests on the isolation of 5α-deuterio **3** (not shown) when deuterioacetic acid is used as nucleophile.[4] Addition of nucleophiles with p*K*a <~8 results in the loss of nitrogen with formation of the 1-oxabicyclo[3.1.0]hexanium ion **8**, and overall substitution with retention of configuration as in **9**, ie, the classical reaction described by Schreiner and Zbiral[1] and widely employed by ourselves and others as a means of entry into KDN and other sialosides.[2, 5, 8-10] With the less acidic phenols as nucleophiles the equilibrium favors the diazoalkane **7** resulting in the elimination of acetate from the 4-position giving an alkenediazonium ion **10**. Kinetic attack on the β-face of this alkenediazonium ion, perhaps via the ^2H_O half-chair conformer, gives an adduct **11** which following protonation and displacement of nitrogen affords the final products. The kinetic mode of reaction of **9** is exemplified by the use of β-naphthol as nucleophile

resulting ultimately in the isolation of **5**. Thermodynamic attack occurs on the α-face of the alkenediazonium ion **10**, perhaps via the $^{O}H_2$ half-chair conformer, to give an adduct **12** from which disubstituted products such as **4**, observed with phenol as nucleophile, flow (Scheme 3).[7]



Scheme 3. Classical and New Reaction Manifolds for the Deamination of NeuAc Dependent on the p*K*a of the Added Nucleophile

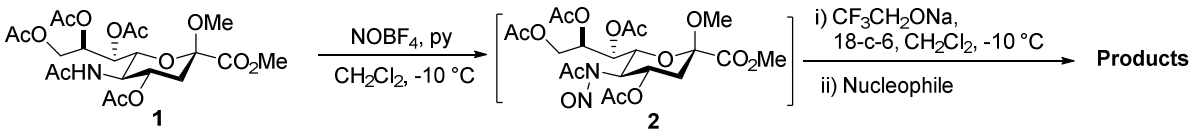
We now report on the on the use of further nucleophiles of varying p*K*a in the deamination of NeuAc with a view to providing further insight into the overall mechanistic scheme and increasing the variety of NeuAc-like structures available for medicinal chemistry purposes.

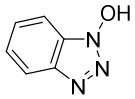
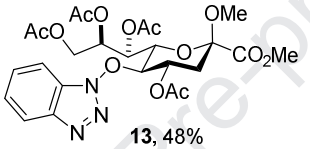
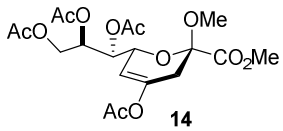
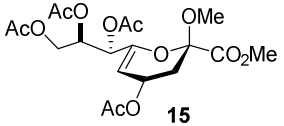
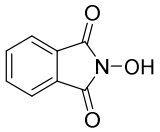
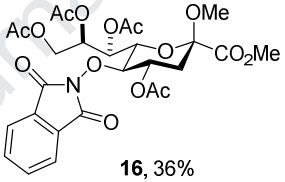
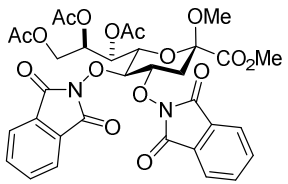
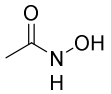
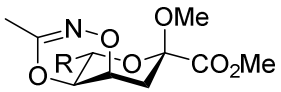
Results

The first nucleophile studied in this investigation, in view of its well-known and widely exploited nucleophilicity, was 1-hydroxybenzotriazole (HOBt). A single major product **13** was isolated in 48% yield that arose from substitution of the nitrosoacetamide function with retention

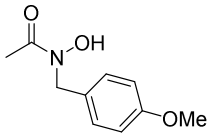
of configuration (Table 1, entry 1). A mixture of the two elimination products **14** and **15** was also formed in this reaction, as determined by mass spectrometry and NMR spectroscopy of the crude reaction mixture, albeit they were not isolated and quantified owing to the relative complexity of the reaction mixture, which is typical of the general reaction class. Turning to the use of *N*-hydroxyphthalimide as nucleophile, we isolated 36% of the standard Zbiral-type product **16**, and 32% of the disubstitution product **17**. Again, significant amounts of the elimination products **14** and **15** were formed in this reaction (Table 1, entry 2). With the less acidic acetohydroxamic acid[11] as nucleophile a bicyclic product **18** was formed in 21% yield alongside a single elimination product **15**, which was isolated in 28% yield (Table 1, entry 3). Use of *N*-(*p*-methoxybenzyl)acetohydroxamic acid as nucleophile on the other hand gave only 18% of the combined elimination products **14** and **15**, and 21% of the 4-deoxy-5-desacetamido non-4-eneulosonic acid derivative **19** (Table 1, entry 4), a class of sialic acid derivatives only previously accessed by Takahashi and coworkers by degradation of the NeuAc framework to a 7-carbon synthon, followed by reassembly.[12] With the more acidic *N*-hydroxyimide, *N*-Boc acetohydroxamic acid, the elimination products **14** and **15** were the predominant products isolated in a combined yield of 41%, while **19** was isolated as a minor product in 10% yield. An inseparable mixture of the ketone **21** and the enone **22** in 17% yield Table 1, entry 5) was also isolated. Turning to the use of oximes as nucleophiles, application of *p*-nitrophenylbenzaldehyde oxime afforded the adduct **20** in 26% yield along with a mixture of elimination products **14** and **15** in 24% yield, together with the inseparable mixture of the ketone **21** and the enone **22** in 8% yield Table 1, entry 6). With the less acidic and more hindered acetone oxime on the other hand only a mixture of the elimination products **14** and **15** could be isolated from the reaction mixture in 38% yield (Table 1, entry 7).

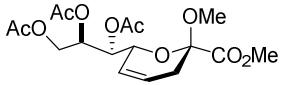
Table 1. Application of Hydroxylamine Derivatives and Amines as Nucleophiles in the Zbiral Reaction[a]



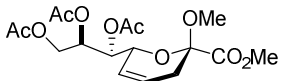
Entry	Nucleophile[b]	Products (% yield)[c]
1	*N*-Hydroxybenzotriazole 	 **13**, 48%  **14**  **15**
2	*N*-Hydroxyphthalimide 	 **16**, 36%  **17**, 32% **14** + **15** = 23%
3	Acetohydroxamic Acid 	 **18**, 21% R = CHOAcCHOAcCH$_2$OAc **15**, 28%

4 *N*-(*p*-Methoxybenzyl)acetohydroxamic acid

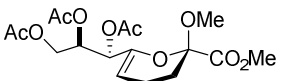




19, 21%



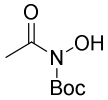
14

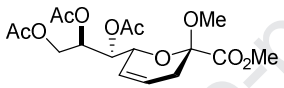


15

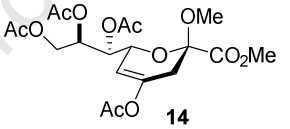
14 + **15** = 18%

5 *N*-Boc-Acetohydroxamic acid

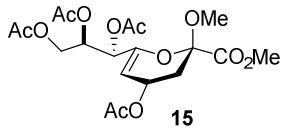




19, 10%

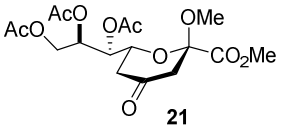


14

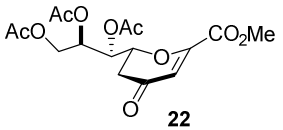


15

14 + **15** = 41%



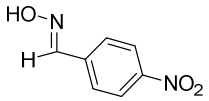
21

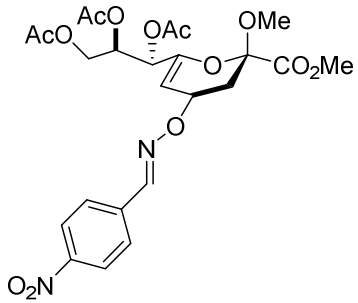


22

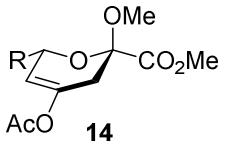
21 + **22** = 17%

6 *p*-Nitrobenzaldehyde oxime

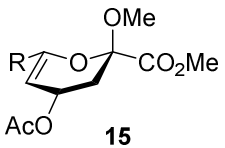




20, 26%



14

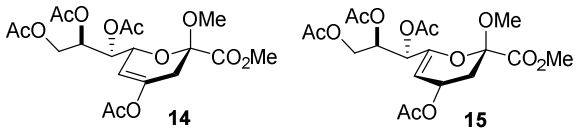


15

14 + **15** = 24%

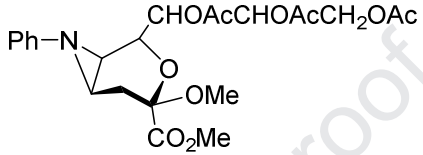
21 + **22** = 8%

7 Acetone oxime



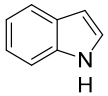
14 + **15** = 38%

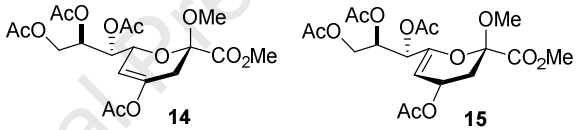
8 Aniline



23, 49%

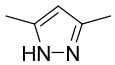
9 Indole



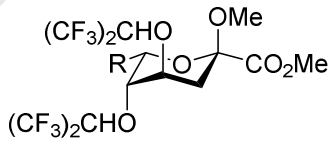


14 + **15** = 80%

10 3,5-Dimethylpyrazole



in $(CF_3)_2CHOH$



24, 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. .

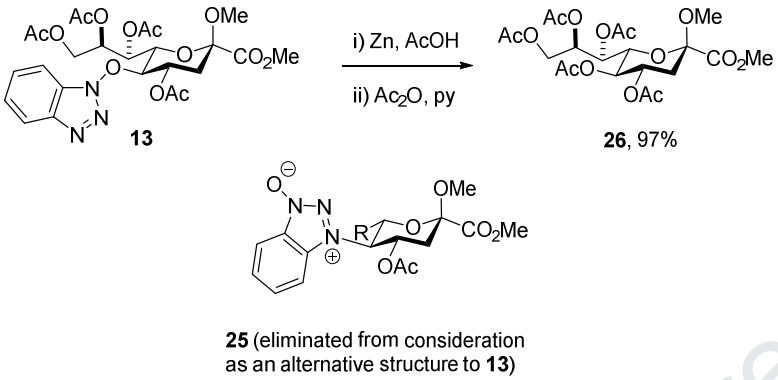
In addition to the use of hydroxylamine derivatives as nucleophiles we also briefly investigated that of the nitrogen nucleophiles aniline, indole, and 3,5-dimethylpyrazole. With aniline a complex reaction mixture was observed from which we isolated the aziridine **23** in 49% yield (Table 1, entry 8), while the use of indole afforded only the elimination products **14** and **15**, albeit with an excellent yield of 80% (Table 1, entry 9). 3,5-Dimethylpyrazole was not sufficiently soluble in dichloromethane for use as nucleophile, but was soluble in hexafluoroisopropanol, a weakly nucleophilic solvent[13-15] we had previously employed to good effect for the addition of the poorly soluble 6-hydroxyquinoline to the vinyldiazonium ion **20** and resulting in the isolation of a heterocyclic analog of tricyclic product **5** in good yield.[7] Unfortunately, addition of 3,5-dimethylpyrazole in hexafluoroisopropanol to a typical dichloromethane solution of the *N*-nitrosoamide **2** gave a complex reaction mixture from which none of the anticipated products could be recovered. We did, however, isolate from this mixture a product **24** resulting from the combination of two molecules of hexafluoroisopropanol with the activated nitrosoamide, albeit in only 9% yield (Table 1, entry 10).

Structural Elucidation

The structures of elimination products **14** and **15** was confirmed by comparison of their spectra with those of authentic samples,[7] while the structures of adducts **16**, **17**, and **19** follow without complication from inspection of their NMR spectroscopic and mass spectrometric data. The structure of the adduct **20** is assigned by comparison of its spectral data with that of **15** and an analogous product isolated from the application of 4-nitrophenol as nucleophile.[7] The structure of enone **22** was assigned by comparison with an authentic sample,[7] while that of ketone **21** follows from its gradual decomposition into **22**, which also prevented it from being isolated in pure form.

The configuration of the *N*-hydroxybenzotriazole adduct **13** is readily apparent from its ^{1}H NMR spectra, which reveal the all-equatorial nature of the substituents at the 4-,5-, and 6-positions around the

pyranoside ring. That **13** resulted from the attack of the ambident nucleophile *N*-hydroxybenzotriazole on oxygen and not nitrogen – resulting in the formation of betaine **25** – was ascertained by treatment with zinc in acetic acid followed by acetylation to give the known KDN derivative **26** in 97% overall yield (Scheme 4).



Scheme 4. Confirmation of the Structure of the *N*-Hydroxybenzotriazole Adduct **13**.

The structure of **18** is based on the HMBC correlation of the imidate carbonyl C with H5 and not with H4, which excludes the regioisomer **27** (Figure 1). The *cis*-fused ring junction and chair-like conformation of the pyranose ring in **18** is apparent from inspection of its NMR spectroscopic data including analysis of the complete set of ^{3}J proton-proton couplings in the H3a,e-H6 spin system. Finally, the fusion of the heterocylic ring to the β-face of the pyranose is confirmed by nOe correlations between H5 and H's 3 and 7 on the α-face of the molecule (Figure 1). Aziridine **23** was assigned on the basis of the nOe correlations between the side chain proton H7 and the ring protons H4 and H5, which place the aziridine ring on the opposite face of the pyranoside ring to the side chain. The exo-configuration is clear from the nOe correlations between the ortho-protons on the phenyl ring and H's 4 and 5 (Figure 2).

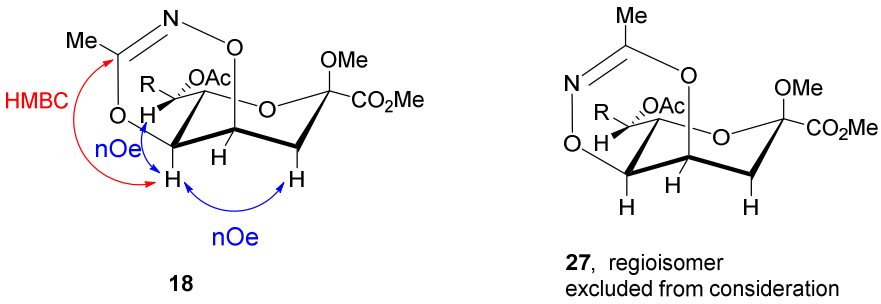


Figure 1. HMBC and Nuclear Overhauser Correlations Supporting the Structure of **18** as Compared to the Regioisomer **27**.

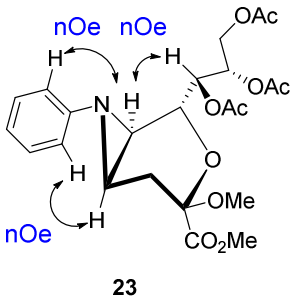


Figure 2. Nuclear Overhauser Correlations Establishing the Structure of **23**.

Finally, the configuration and conformation of the hexafluoroisopropanol adduct **24** are established by analysis of NMR coupling constants and nOe correlations. Thus, $^{3}J_{H4,H5}$ at 8.2 Hz indicates that H's 4 and 5 are either close to antiperiplanar or synperiplanar, while the $^{3}J_{H3ax,H4}$, $^{3}J_{H3eq,H4}$, and $^{3}J_{H5,H6}$ coupling constants of 6.1, 3.2, and 2.1 Hz, respectively, exclude axial orientations for both H4 and H5. This ensemble of information points to a chair-like conformation with axial substituents at C4 and C5, with twisting of the C4-C5 bond to minimize repulsion between the hexafluoroisopropyl groups, which forces the near-eclipsing of H's 4 and 5. In terms of spatial proximity, nOe correlations were observed between the 4-*O*-hexafluoroisopropyl proton and the ring protons H4 and H5. One of the two trifluoromethyl groups in the same 4-*O*-hexafluoroisopropyl ether also showed heteronuclear nOe

correlations with H4 in the HOESY (^{1}H-^{19}F) spectrum further supporting the assigned conformation (Figure 3).

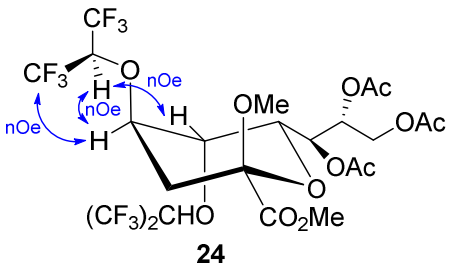
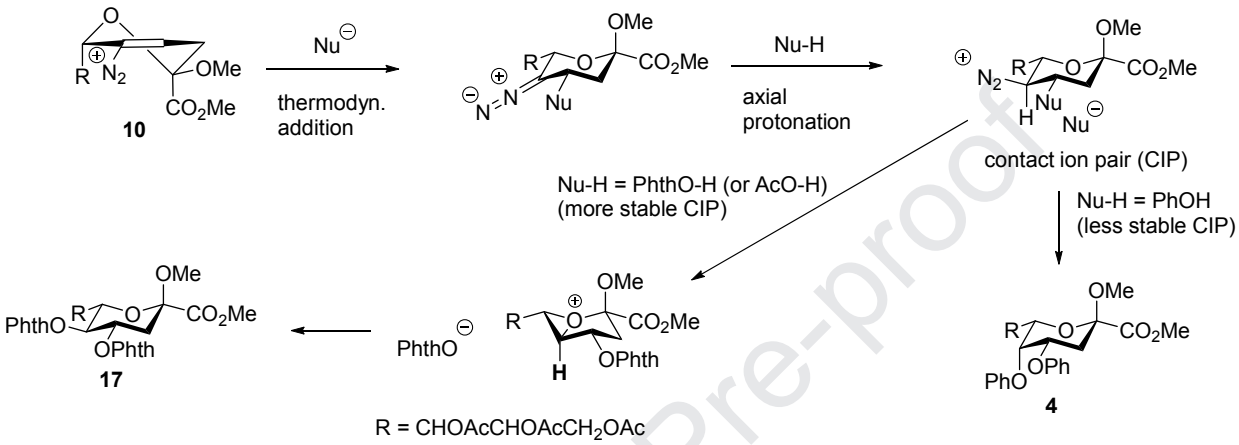


Figure 3. Nuclear Overhauser Correlations Establishing the Structure of **24**.

Discussion

With reported p*K*a's in aqueous solution varying between 4.53[16] and 7.39[17, 18] *N*-hydroxybenzotriazole performs similarly to acetic acid and delivers a moderate yield of the direct substitution product **13** with retention of configuration (Table 1, entry 1). The situation with *N*-hydroxyphthalimide (Table 1, entry 2) on the other hand is more complex: the direct substitution product **16**, expected to be the major product on the basis of the p*K*a (6.1) of the nucleophile,[19] was isolated in 36% yield. On the other hand, the double substitution product **17**, isolated in 32% yield, approximates more closely to the reactivity pattern observed with phenol (**4**, Scheme 2) and was not anticipated. Clearly, other factors intervene with *N*-hydroxyphthalimide to promote elimination of the acetoxy group from the 4-position giving rise to the vinyl diazonium ion **10**. Whatever the reason for the elimination, Michael addition of *N*-hydroxyphthalimide to **10** takes place under thermodynamic control as with phenol to give an equatorial adduct. Also as with phenol we propose that a second molecule of *N*-hydroxyphthalimide then protonates the diazoalkane axially on the α-face leading to a contact ion pair. However, unlike the phenol case where this contact ion pair collapses with loss of nitrogen and formation of the axial C-O

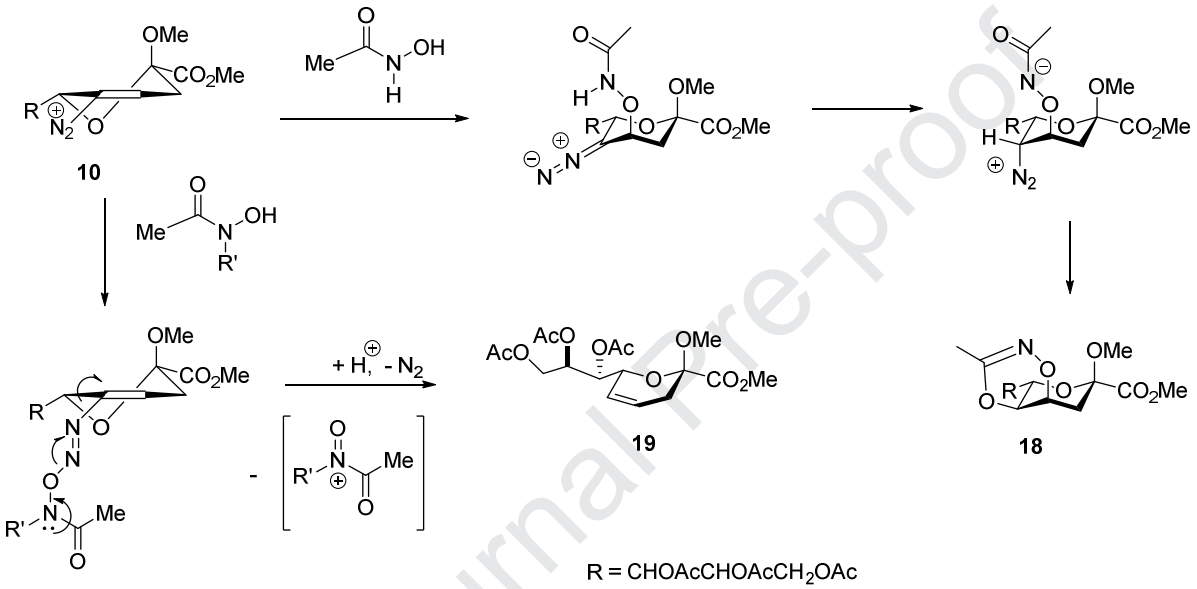
bond, this ion pair containing a more stable anion follows the pattern established with acetic acid as nucleophile and lives sufficiently long for participation by the ring oxygen leading ultimately to nucleophilic substitution on the β-face with overall retention of configuration at the 5-position (Scheme 5).



Scheme 5. Reaction of *N*-Hydroxyphthalimide with Vinyl Diazonium Ion **10**

Acetohydroxamic acid, with a p*K*a of 9.40,[11] favors the diazoalkane **7** over its conjugate acid, the diazonium ion **6**, leading to the formation of the vinyl diazonium ion **10**. Conjugate addition then occurs on the β-face leading to a kinetic adduct, which undergoes intramolecular proton transfer leading to a zwitterion followed by collapse with loss of nitrogen to give the observed *cis*-fused product **18** (Table 1, entry 3, Scheme 6) in close overall analogy to the mechanism postulated for the use of β-naphthol as nucleophile and leading to the formation of **5**.[7] Turning to the use of *N*-(4-methoxybenzyl)acetohydroxamic acid, with an expected p*K*a similar to that of acetohydroxamic acid itself,[11] no substitution products were isolated, rather the alkene **19** was observed for the first time (Table 1, entry 4). We speculate that this formal reduction product arises from competing nucleophilic attack of the bulky nucleophile of the terminal nitrogen of the vinyl diazonium ion leading to a complex intermediate. This intermediate presumably decomposes with loss of nitrogen and of an unstable acyl

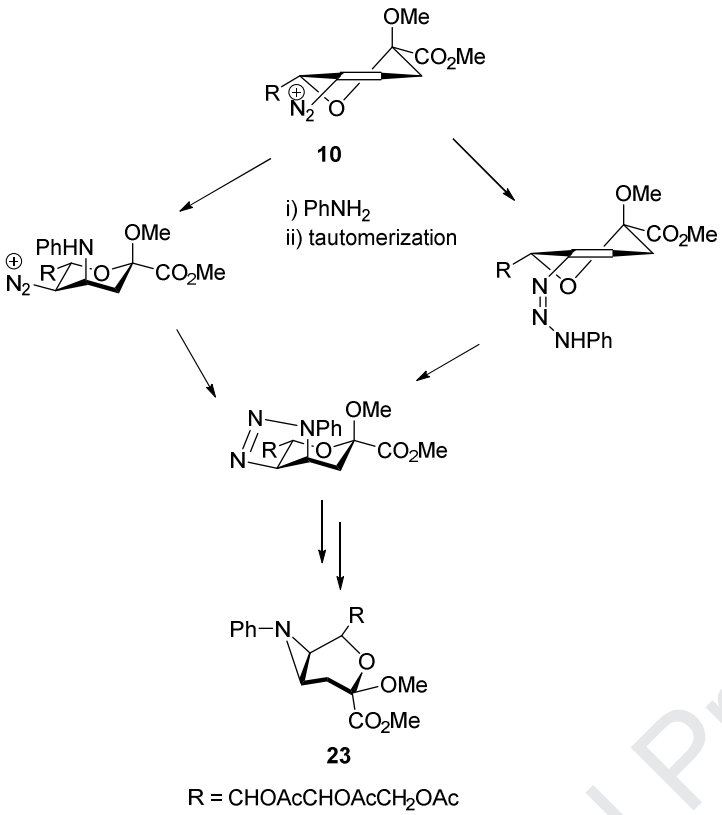
nitronium ion, resulting in the formation of a vinyl anion ready for protonation to give alkene **19** (Scheme **6**). Although *N*-Boc acetohydroxamic acid can be expected to have an acidity comparable to that of *N*-hydroxyphthalimide, it has considerable steric bulk and so might be expected to follow the same reaction path as *N*-(4-methoxybenzyl)acetohydroxamic acid resulting in the formation of alkene **19** rather than of any substitution product (Table 1, entry 5, Scheme **6**).



Scheme 6. Reaction of Hydroxamic Acids with Vinyl Diazonium Ion **10**.

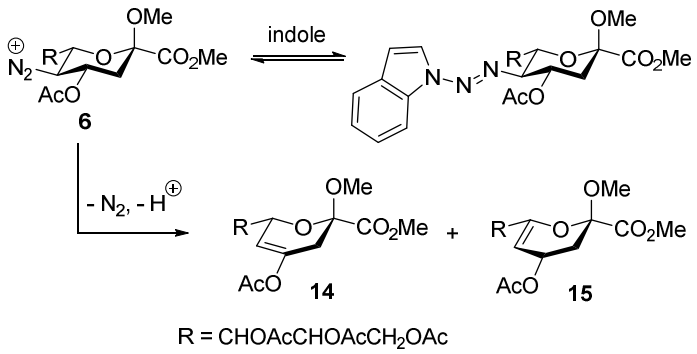
With *p*-nitrobenzaldehyde oxime (p*K*a 10.5)[11] as nucleophile the adduct **20**, isolated in 26% yield (Table 1, entry 6), must arise from conjugate addition of the nucleophile to the vinyl diazonium ion **10**, followed by protonation to the corresponding diazonium ion and explusion of nitrogen followed by deprotonation. Ketone **21** and, following elimination, α,β-unsaturated ketone **22** presumably arise by simple acid catalyzed hydrolysis of the relatively electron rich enol ether **20**. With acetone oxime (p*K*a 12.4) the comparable adduct to **20** will be even more electron-rich and so does not withstand the reaction conditions; ultimately only a 38% overall yield of elimination products **14** and **15** could be isolated from this reaction mixture (Table 1, entry 7).

The aziridine **23** formed on the use of aniline as nucleophile is consistent with a mechanism involving kinetic attack of the nucleophile on the β-face of the vinyl diazonium ion **10** followed by tautomerization and cyclization to afford a triazoline (Scheme **7**). Alternatively, by analogy with the well-known reaction of arene diazonium ions with amines,[20, 21] the triazoline may be formed by initial attack of the amine onto the terminal nitrogen position of the diazonium moiety to give a vinyl triazene, followed by tautomerization and ring closure. The formation of an intermediate triazoline is supported by examination of the crude reaction mixture by ESI mass spectrometry, which revealed a major ion of m/z 530 (M+Na) that diminished over time in favor of the aziridine (m/z 501, M+Na). Loss of nitrogen and formation of the corresponding aziridines in this manner is the standard mode of decomposition of 1,2,3-triazolines. This mechanism is further supported by the early work of Saalfrank and Ackerman who studied the reaction of primary amines with simple β-ethoxyvinyl diazonium ions, leading to the isolation of 1,2,3-triazoles – with the intermediate triazoline undergoing elimination of the ethoxy group and aromatization, rather than loss of nitrogen and aziridine formation.[22-24]



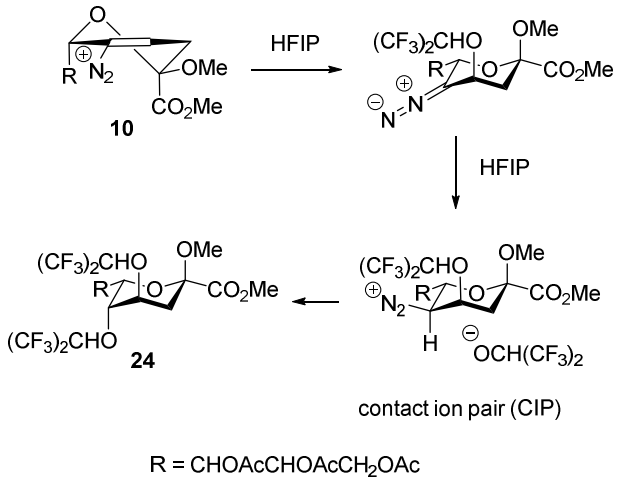
Scheme 7. Mechanism of Triazoline Formation and Subsequent Decomposition to Aziridine **23**

The attempted use of indole (p*K*a 16.2) as nucleophile gave a relatively clean reaction mixture from which was isolated a mixture of the two simple elimination products **14** and **15** in the unusually high yield of 80%. We suggest that this is the consequence of stabilization of the diazonium ion **6** in the form of an unstable triazene that retards elimination to the vinyl diazonium ion and ultimately decomposes with formation of the observed alkenes (Scheme 8). Related *N*-arylazoindoles have been isolated previously from the reaction of indole with arene diazonium salts under basic conditions.[25]



Scheme 8. Proposed stablization of Diazonium ion **6** by Triazene Formation

Finally, albeit the attempted use of 3,5-dimethylpyrazole as nucleophile in hexafluoroisopropanol afforded a complex reaction mixture from which no pyrazole-containing products could be isolated, the bis(hexafluoroisopropanol) adduct **24** was secured in 9% yield. This product is unusual and worthy of comment as, while there are numerous literature examples of the trapping of carbenium ions by hexafluoroisopropanol, often with support from X-ray crystal structures,[26-31] the formation of **24** requires hexafluoroisopropanol (p*K*a 9.3)[32] to act first as nucleophile in a conjugate addition to the vinyl diazonium ion **10**. Thus, **24** is envisaged as the product of kinetic addition of hexafluoroisopropanol to the β-face of **10**, axial protonation of the resulting diazoalkane on the α-face by a second molecule of hexafluoroisopropanol and collapse of the so-formed tight ion pair to afford **24** (Scheme **9**).



Scheme 9. Reaction of Hexafluoroisopropanol with the Vinyl Diazonium Ion **10**

The conformation of **24**, a flattened chair conformation with both hexafluoroiospropyl groups pseudoaxial, is presumably preferred because of unfavorable steric interactions between the hexafluoroisopropyl groups in alternate conformations that would enable them to benefit from the gauche effect. A similar effect is seen in the X-ray crystal structure of the formal glycol derivative **25** that adopts an antiperiplanar relationship of the two bulky ethers, even though this forces the two C-C bonds into a gauche relationship (Figure 4).[29]

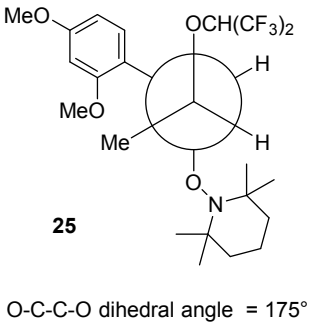


Figure 4. Solid State Conformation of Diether **25**

Conclusion

A variety of hydroxylamine derivatives and weakly basic amines have been examined as possible nucleophiles in the Zbiral-type deamination of *N*-nitroso-*N*-acetyl neuraminic acid. Depending on the nature of the nucleophile products arise either from direct substitution of the nitrosoamide moiety with retention of configuration, or from double substitution of the nitroamide and the vicinal acetoxy group. The double substitution products are considered to be formed by a multi-step process involving elimination of the acetoxy group to form a vinyl diazonium ion followed by Michael addition and finally displacement of nitrogen from the

resulting diazonium ion. The configuration at C5 is a function of the nature of the protonation step, inter or intramolecular, of the diazoalkane and of the tightness of the so-formed ion pair, which again is a function of the acidity of the nucleophile. Thus, intermolecular protonation takes place in the axial direction to afford a contact ion pair of the counterion with the equatorial diazo leaving group. When the ion pair is tight, ie, with counterions arising from less acidic nucleophiles (eg, phenol, hexafluoroisopropanol) the ion pair collapses with inversion of configuration and formation of an axial bond to the nucleophile. On the other hand, with more stable counterions (acetate, benzotriazole-1-oxide, phthalimide-1-oxide, etc) a looser ion pair is formed, the ring oxygen participates in explusion of nitrogen and the product is formed with overall retention of configuration.

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.

General procedure for 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 (5-20 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/HCl (1M) to remove excess 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.[33]

Methyl (methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-glycero-β-D-galacto-non 2-ulopyranosid)onate (1). Compound **1** (6 g, 95%) was obtained by a literature procedure[4] 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 (2). A solution of compound **1** (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 **2** as a yellowish foam which was carried forward for next reaction without further purification[4].

Methyl (methyl 4,7,8,9-tetra-*O*-acetyl-3-deoxy-5-*O*-(benzotriazol-1-yl)-D-glycero-β-D-galacto-non-2-ulopyranosid)onate (13). The nitrosyl sialoside **2** (150 mg, 0.3 mmol) in CH_2Cl_2 (3 mL) was deaminated using the general procedure for oxidative deamination with sodium 2,2,2-trifluoroethoxide (68 mg, 0.6 mmol), 18-crown-6 (74 mg, 0.3 mmol) in CH_2Cl_2 (2 mL) and HOBt (380 mg, 2.8 mmol, 10 equiv) in HFIP (2 mL) to afford **13** after flash column chromatography over silica gel eluting with hexane/ ethyl acetate (1:1), as a colorless oil (78 mg, 48 %); $[\alpha]_D^{20}$ + 45.7^o (*c* 0.45, CH_2Cl_2).^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.4 Hz, 1H, ArH), 7.49 (d, *J* = 3.5 Hz, 2H, ArH), 7.36 (dt, *J* = 8.0, 3.8 Hz, 1H, ArH), 5.91 (dd, *J* = 5.0, 2.3 Hz, 1H, H7), 5.60 (ddd, *J* = 11.0, 9.4, 5.5 Hz, 1H, H4), 5.39 (ddd, *J* = 7.3, 5.0, 2.6 Hz, 1H, H8), 4.95 (t, *J* = 9.7 Hz, 1H, H5), 4.76 (dd, *J* = 12.5, 2.6 Hz, 1H, H9), 4.40 (dd, *J* = 10.1, 2.2 Hz, 1H, H6), 4.20 (dd, *J* = 12.4, 6.8 Hz, 1H, H9'), 3.80 (s, 3H, CH_3), 3.34 (s, 3H, CH_3), 2.60 (dd, *J* = 13.1, 5.5 Hz, 1H, H3e), 2.32 (s, 3H, CH_3), 2.11 (s, 3H, CH_3), 2.04 (s, 3H, CH_3), 1.67 (dd, *J* = 13.1, 11.2 Hz, 1H, H3a), 1.12 (s, 3H, CH_3). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 170.8, 170.6, 170.0, 169.3, 166.9, 143.3, 128.4, 127.9, 124.8, 120.3, 108.8, 98.7, 82.8, 71.2, 70.0, 69.3, 68.5, 62.3, 52.9, 51.8, 36.8, 21.1, 21.0, 20.9, 20.1. ESI-HRMS Calcd. for $C_{25}H_{31}N_3NaO_{13}$:([M+Na]$^+$) m/z: 604.1755; found: 604.1756.

Methyl (methyl 4,7,8,9-tetra-*O*-acetyl-3-deoxy-5-*O*-(*N*-phthalimidoyl)-D-glycero-β-D-galacto-non-2-ulopyranosid)onate (16), Methyl (methyl 7,8,9-tri-*O*-acetyl-3-deoxy-4,5-di-*O*-(*N*-phthalimidoyl)-D-glycero-β-D-galacto-non-2-ulopyranosid)onate (17), 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 **2** (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 (90 mg, 0.7 mmol), 18-crown-6 (195 mg, 0.7 mmol) in CH_2Cl_2 (2 mL) and *N*-hydroxyphthalimide (1.2 g, 7.4 mmol, 20 equiv) to afford **16** after flash column chromatography over silica gel eluting with hexane/ ethyl acetate (1:1), as a colorless oil (115 mg, 36%) and **17** as a colorless oil (102 mg, 27%, and an inseparable mixture of elimination products **14** and **15** as a colorless oil (1:2.5 ratio, 53 mg, 23%).

Compound **16**: $[\alpha]_D^{20}$ – 52.0^o (*c* 0.4, $CHCl_3$).^{1}H NMR (600 MHz, $CDCl_3$) δ 7.82 (dd, *J* = 5.5, 3.1 Hz, 2H, ArH), 7.75 (dd, *J* = 5.5, 3.1 Hz, 2H, ArH), 5.80 (dd, *J* = 5.3, 2.0 Hz, 1H, H7), 5.53 (ddd, *J* = 11.0, 9.0, 5.4 Hz, 1H, H4), 5.39 (ddd, *J* = 6.7, 5.3, 2.7 Hz, 1H, H8), 4.67 (dd, *J* = 12.4, 2.7 Hz, 1H, H9), 4.44 (t, *J* = 9.4 Hz, 1H, H5), 4.23 (p, *J* = 9.8, 2.1 Hz, 1H, H6), 4.16 (dd, *J* = 12.4, 6.7 Hz, 1H, H9'), 3.78 (s, 3H, CH_3), 3.29 (s, 3H, CH_3), 2.66 (dd, *J* = 13.2, 5.4 Hz, 1H, H3e), 2.25 (s, 3H), 2.10 (s, 3H, CH_3), 2.04 (s, 3H, CH_3), 1.72 (s, 3H, CH_3), 1.69 (dd, *J* = 13.1, 11.0 Hz, 1H, H3a). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 170.8, 170.5, 170.2, 169.4, 167.3, 163.3, 134.8, 128.9, 123.7, 98.6, 79.5, 71.0, 70.2, 69.4, 68.9, 62.4, 52.8, 51.7, 36.4, 21.1, 21.1, 20.9, 20.8. ESI-HRMS Calcd. for $C_{27}H_{31}NNaO_{15}$:($[M+Na]^+$) m/z: 632.1591 ; found: 632.1592.

Compound **17**: $[\alpha]_D^{20}$ – 32.0 ^{o} (*c* 0.25, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.79 (dd, *J* = 5.5, 3.1 Hz, 2H, ArH), 7.73 – 7.68 (m, 4H, ArH), 7.67 (dd, *J* = 5.5, 3.0 Hz, 2H, ArH), 5.79 (dd, *J* = 5.7, 2.1 Hz, 1H, H7), 5.39 (td, *J* = 6.2, 2.7 Hz, 1H, H8), 5.17 (ddd, *J* = 10.5, 8.0, 5.5 Hz, 1H, H4), 4.86 (dd, *J* = 9.6, 7.9 Hz, 1H, H5), 4.67 (dd, *J* = 12.4, 2.7 Hz, 1H, H9), 4.23 (dd, *J* = 9.6, 2.1 Hz, 1H, H6), 4.16 (dd, *J* = 12.4, 6.5 Hz, 1H, H9'), 3.80 (s, 3H, CH_3), 3.23 (s, 3H, CH_3), 2.50 (dd, *J* = 13.4, 5.5 Hz, 1H, H3e), 2.32 (s, 3H, CH_3), 2.13 (dd, *J* = 13.4, 10.5 Hz, 1H, H3a), 2.10 (s, 3H,

CH_3), 2.03 (s, 3H, CH_3). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 170.9, 170.4, 170.2, 167.4, 163.6, 163.3, 134.7, 134.3, 129.3, 128.8, 123.8, 123.6, 98.9, 82.5, 78.8, 70.8, 69.2, 68.6, 62.3, 53.0, 51.5, 35.5, 21.2, 20.9, 14.3. ESI-HRMS Calcd. for $C_{33}H_{32}N_2NaO_{16}$:($[M+Na]^+$) m/z: 735.1650 ; found: 735.1650.

Compounds **14** and **15** (1:2.5 mixture) had NMR data consistant with the literature.[7]

Methyl (methyl 7,8,9-tri-*O*-acetyl-3-deoxy-4-*O*,5-*O*-(ethanimin-1-yl-*N*-yl)-D-glycero-β-D-talo-non-2-ulopyranosid)onate (18). The nitrosyl sialoside **2** (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 (3 mL) and acetoxyhydroxamic acid (555 mg, 7.4 mmol, 20 equiv) to afford **18** after flash column chromatography over silica gel eluting with hexane/ ethyl acetate (1:1), as a colorless oil (62 mg, 36%) and the single elimination product **15** as a colorless oil (46 mg, 28%). Compound **18**; $[\alpha]_D^{20}$ – 15.3^o (*c* 0.85, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 5.51 (dd, *J* = 5.6, 2.6 Hz, 1H, H7), 5.34 (td, *J* = 6.2, 2.6 Hz, 1H. H8), 4.57 (dd, *J* = 12.5, 2.7 Hz, 1H, H9), 4.33 (dd, *J* = 10.0, 2.6 Hz, 1H, H6), 4.22 (dd, *J* = 12.5, 6.3 Hz, 1H, H9'), 4.17 (dd, *J* = 10.0, 2.8 Hz, 1H, H5), 4.04 (dt, *J* = 4.2, 2.6 Hz, 1H, H4), 3.78 (s, 3H, CH_3), 3.23 (s, 3H, CH_3), 2.53 (dd, *J* = 15.5, 2.5 Hz, 1H, H3), 2.14 (s, 3H, CH_3), 2.10 (dd, *J* = 15.5, 4.2 Hz, 1H, H3'), 2.07 (s, 3H, CH_3), 2.03 (s, 3H. CH_3), 1.92 (s, 3H, CH_3). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 170.7, 170.3, 169.6, 167.9, 155.2, 97.7, 77.5, 77.2, 76.8, 70.5, 69.1, 68.8, 66.8, 66.1, 62.1, 52.8, 51.8, 34.9, 21.1, 20.8, 20.8, 17.4. ESI-HRMS Calcd. for $C_{19}H_{27}NNaO_{12}$:($[M+Na]^+$) m/z: 484.1431 ; found: 484.1400.

Methyl (methyl 7,8,9-tri-*O*-acetyl-3,4,5-trideoxy-β-D-arabino-non-4-en-2-ulopyranosid)onate (19). The nitrosyl sialoside **2** (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 *N*-(4-methoxybenzyl)acetyl hydroxamic caid (975 mg, 5 mmol, 10 equiv) in CH_2Cl_2 (5 mL) to afford **19** after flash column chromatography over silica gel eluting with hexane/ ethyl acetate (3:1), as a colorless oil (41 mg, 21%) and an inseparable mixture of elimination products **14** and **15** as a colorless oil (40 mg, 18%). $[\alpha]_D^{20}$ – 10.1° (*c* 1.3, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.82 (ddt, *J* = 10.0, 4.9, 2.3 Hz, 1H, H4), 5.63 (ddt, *J* = 10.5, 3.0, 1.5 Hz, 1H, H5), 5.45 (td, *J* = 6.2, 2.3 Hz, 1H, H8), 5.37 (dd, *J* = 6.2, 2.7 Hz, 1H, H7), 4.61 (dd, *J* = 12.5, 2.3 Hz, 1H. H9), 4.43 (tdq, *J* = 4.9, 2.6, 1.5, 0.9 Hz, 1H, H6), 4.22 (dd, *J* = 12.5, 6.1 Hz, 1H, H9'), 3.80 (s, 3H, CH_3), 3.28 (s, 3H, CH_3), 2.40 (ddt, *J* = 17.8, 4.0, 2.6 Hz, 1H, H3), 2.32 (dddd, *J* = 17.8, 4.8, 3.2, 1.4 Hz, 1H, H3'), 2.06 (s, 6H, $2CH_3$), 2.04 (s, 3H, CH_3). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 170.8, 170.1, 170.0, 169.0, 123.8, 123.8, 97.6, 71.3, 70.3, 69.2, 62.5, 52.6, 51.5, 32.1, 21.0, 20.9, 20.8.ESI-HRMS Calcd. for $C_{27}H_{24}NaO_{10}$:([M+Na]$^+$) m/z: 411.1262 ; found: 411.1248.

Deamination of nitrosyl sialoside 2 with *N*-(^{t}Butyloxycarbonyl)acetyl hydroxamic acid as nucleophile. Methyl (7,8,9-tri-*O*-acetyl-3,5-dideoxy-β-D-arabino-non-4-oxo-2-ulopyranosid)onate (21) and Methyl (7,8,9-tri-*O*-acetyl-2,3,5-trideoxy-β-D-arabino-non-2-en-4-oxo-2-ulopyranosid) onate (22). The nitrosyl sialoside **2** (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 *N*-(^{t}butyloxycarbonyl)acetyl hydroxamic acid (525 mg, 3 mmol, 6 equiv) in CH_2Cl_2 (5 mL) to afford **19** after flash column chromatography over silica gel eluting with hexane/ ethyl acetate (3:1), as a colorless oil (20 mg, 10%), an inseparable mixture of elimination products **14** and **15**

as a colorless oil (91 mg, 41%) and another inseparable mixture of compounds **21** and **22** (1.27:1 ratio, 35 mg, 17%) as a colorless oil.

Compound **22**;[7] ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.24 (d, *J* = 1.1 Hz, 1H, H3), 5.39 (ddd, *J* = 7.9, 5.3, 2.5 Hz, 1H, H8), 5.38 (dd, *J* = 7.9, 2.8 Hz, 1H, H7), 4.71 (ddd, *J* = 13.3, 4.1, 2.7 Hz, 1H, H6), 4.49 (dd, *J* = 12.5, 2.3 Hz, 1H, H9), 4.25 (m, 1H, H9), 3.87 (s, 3H, CH_3), 2.57 (dd, *J* = 16.9, 13.7 Hz, 1H, H5), 2.48 (dd, *J* = 16.9, 3.8 Hz, 1H, H5'), 2.14 (s, 3H, CH_3), 2.07 (s, 3H, CH_3), 2.06 (s, 3H, CH_3). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 191.8, 170.7, 170.0, 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.

Compound **21** was identified in the mixture by the following diagnostic signals; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.35 (ddd, *J* = 6.0, 5.7, 2.5 Hz, 1H, H8), 5.29 (dd, *J* = 6.0, 3.1 Hz, 1H, H7), 4.58 (dd, J=12.5, 2.6 Hz, 1H, H9), 4.25 (m, 1H, H6), 4.21 (dd, *J* = 12.5, 5.8 Hz, 1H, H9'), 3.82 (s, 3H, CH_3), 3.24 (s, 3H, CH_3), 2.74 (d, *J* = 14.9 Hz, 1H, H3), 2.61 (d, *J* = 14.9 Hz, 1H, H3'), 2.39 (br s, 1H, H5), 2.37 (br s, 1H, H5'), 2.13 (s, 3H, CH_3), 2.05 (s, 3H, CH_3), 2.04 (s, 3H, CH_3). ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 201.6, 170.7, 170.2, 169.8, 167.2, 100.2, 71.3, 70.2, 69.0, 62.0, 53.0, 51.5, 48.0, 42.1, 21.0, 20.8, 20.8.

Methyl (methyl 7, 8, 9-tri-*O*-acetyl-3,5-dideoxy-4-*O*-(4-nitrophenylmethanimin-*N*-yl)-β-D-arabino-non-4-en-2-ulopyranosid)onate (20). The nitrosyl sialoside **2** (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-nitrobenzaldehyde oxime (1.66 g, 10 mmol, 20 equiv) in THF (5 mL) to afford **20** after flash column chromatography over silica gel eluting with hexane/ ethyl acetate (1:1), as a colorless oil (72 mg, 26%), an inseparable mixture of elimination products **14** and **15** as a

colorless oil (53 mg, 24%) and another inseparable mixture of compounds **21** and **22** (17 mg, 8%) as a colorless oil. $[\alpha]_D^{20}$ – 15.5° (*c* 0.9, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.22 (d, *J* = 8.8 Hz, 2H, ArH), 8.02 (s, 1H, NCH), 7.73 (d, *J* = 8.8 Hz, 2H, ArH), 5.57 (ddd, *J* = 7.3, 4.5, 2.8 Hz, 1H, H8), 5.53 (dt, *J* = 4.6, 1.2 Hz, 1H, H7), 5.20 (d, *J* = 4.2 Hz, 1H, H5), 4.87 (dt, *J* = 6.4, 5.0 Hz, 1H, H4), 4.42 (dd, *J* = 12.2, 2.8 Hz, 1H, H9), 4.36 (dd, *J* = 12.1, 7.4 Hz, 1H, H9'), 3.74 (s, 3H, CH_3), 3.39 (s, 3H, CH_3), 2.56 (dd, *J* = 14.0, 4.8 Hz, 1H, H3), 2.25 (dd, *J* = 14.0, 5.2 Hz, 1H, H3'), 2.15 (s, 3H, CH_3), 2.07 (s, 3H, CH_3), 2.06 (s, 3H, CH_3). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 170.9, 170.1, 169.4, 167.8, 149.7, 148.6, 147.2, 138.2, 127.8 (2 Carbons), 124.1(2 Carbons), 99.4, 98.5, 72.3, 70.5, 70.5, 62.0, 52.7, 52.3, 34.7, 21.0, 20.9 (2 Carbons). ESI-HRMS Calcd. for $C_{24}H_{28}N_2NaO_{13}$:($[M+Na]^+$) m/z: 575.1484 ; found: 575.1486.

Deamination of nitrosyl sialoside 2 with acetone oxime as nucleophile. The nitrosyl sialoside **2** (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 acetone oxime (731 mg, 10 mmol, 20 equiv) in CH_2Cl_2 (5 mL) to afford **14** and **15**, after flash column chromatography over silica gel eluting with hexane/ ethyl acetate (1:1), as a colorless oil (84 mg, 38%).

Methyl (methyl 7,8,9-tri-*O*-acetyl-3,4,5-trideoxy-4-*N*,5-*N*-phenyliminyl-D-glycero-β-D-talo-non-2-ulopyranosid)onate (23). The nitrosyl sialoside **2** (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 aniline (0.83 mL, 9.2 mmol, 20 equiv) to afford **23**, after flash column chromatography over silica gel eluting with hexane/ ethyl acetate (1:1), as a yellowish oil (110 mg, 49%). $[\alpha]_D^{20}$ – 45.0° (*c* 0.5, CH_2Cl_2).^{1}H NMR (600 MHz, $CDCl_3$) δ 7.22 (dd, *J* = 8.5, 7.3 Hz, 2H, ArH), 6.98 –

6.94 (m, 3H, ArH), 5.69 (dd, *J* = 6.0, 3.9 Hz, 1H, H7), 5.52 (td, *J* = 5.9, 2.8 Hz, 1H, H8), 4.59 (dd, *J* = 12.5, 2.8 Hz, 1H, H9), 4.32 (dd, *J* = 12.5, 5.9 Hz, 1H, H9'), 4.16 (t, *J* = 3.6 Hz, 1H, H6), 3.80 (s, 3H, CH_3), 3.22 (s, 3H, CH_3), 2.51 (dd, *J* = 7.1, 3.4 Hz, 1H, H5), 2.47 (ddd, *J* = 7.1, 5.3, 1.7 Hz, 1H, H4), 2.37 (dd, *J* = 15.3, 1.8 Hz, 1H, H3pe), 2.26 (dd, *J* = 15.3, 5.3 Hz, 1H, H3pa), 2.15 (s, 3H, CH_3), 2.09 (s, 3H, CH_3), 2.08 (s, 3H, CH_3). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 170.8, 170.4, 170.2, 169.4, 153.4, 129.2, 123.1, 120.6, 97.6, 71.4, 70.3, 70.2, 62.2, 52.7, 52.0, 37.1, 35.3, 31.2, 21.1, 21.0, 20.9. ESI-HRMS Calcd. for $C_{23}H_{29}NNaO_{10}$:($[M+Na]^+$) m/z: 502.1689; found: 502.1682.

Deamination of nitrosyl sialoside 2 with indole as nucleophile. The nitrosyl sialoside **2** (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 indole (1.17 g, 10 mmol, 20 equiv) in CH_2Cl_2 (5 mL) to afford **14** and **15**, after flash column chromatography over silica gel eluting with hexane/ ethyl acetate (1:1), as a colorless oil (182 mg, 81%).

Methyl (methyl 7,8,9-tri-*O*-acetyl-3-deoxy-4,5-di-*O*-hexafluoroisopropyl-D-glycero-β-D-ido-non-2-ulopyranosid)onate (24). The nitrosyl sialoside **2** (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-dimethylpyrazole (960 mg, 10 mmol, 20 equiv) dissolved in HFIP (5 mL) to afford **24**, after flash column chromatography over silica gel eluting with hexane/ ethyl acetate (3:1), as a colorless oil (31 mg, 9%). $[\alpha]_D^{20}$ – 17.5° (*c* 1.5, CH_2Cl_2). ^1H NMR (600 MHz, $CDCl_3$) δ 5.24 (td, *J* = 6.0, 3.4 Hz, 1H, H8), 5.10 (p, *J* = 6.0 Hz, 1H, CH), 5.03 (t, *J* = 5.5 Hz, 1H, H7), 4.75 (p, *J* = 6.0 Hz, 1H, CH), 4.34 (dd, *J* = 12.3, 3.4 Hz, 1H, H9), 4.17 (dd, *J* = 12.3, 6.2 Hz, 1H, H9'), 3.80

(s, 3H, CH_3), 3.71 (ddd, *J* = 8.7, 6.0, 3.2 Hz, 1H, H4), 3.39 (s, 3H, CH_3), 3.11 (dd, *J* = 8.2, 2.1 Hz, 1H, H5), 3.02 (dd, *J* = 5.3, 2.1 Hz, 1H, H6), 2.49 (dd, *J* = 15.9, 6.1 Hz, 1H, H3a), 2.38 (dd, *J* = 15.9, 3.2 Hz, 1H, H3e), 2.11 (s, 3H, CH_3), 2.08 (s, 3H, CH_3), 2.05 (s, 3H, CH_3). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 170.6, 170.0, 169.7, 166.7, 101.1, 78.4, 73.5, 73.2, 73.0, 72.8, 72.6, 70.5, 69.8, 69.6, 69.4, 69.2, 68.9, 68.7, 61.6, 58.4, 53.2, 53.0, 52.7, 36.1, 20.7, 20.7. $^{13}C\{^{19}F,^1H\}$ NMR (126 MHz, $CDCl_3$) δ 170.7, 170.0, 169.7, 166.7, 121.7, 121.5, 121.3, 121.2, 101.2, 78.5, 73.1, 70.5, 69.8, 69.2, 61.6, 58.4, 53.3, 53.1, 52.7, 36.2, 20.8, 20.7. ^{19}F NMR (471 MHz, $CDCl_3$) δ -75.42 (q, *J* = 8.0, 7.1 Hz), -75.47 – -75.59 (m), -76.46 (h, *J* = 8.5, 7.3 Hz), -76.80 (qd, *J* = 9.2, 6.0 Hz). ESI-HRMS Calcd. for $C_{23}H_{26}F_{12}NaO_{12}$:($[M+Na]^+$) m/z: 745.1130 ; found: 745.1125.

Supporting Information.

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

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- Oxidative Deamination
- Double substitution
- Aziridine formation

Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: