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One-Pot Synthesis of *N*-Glycooxazolines, *N*-Glycoaminooxazolines, and *N*-Glycothiazolines from Glycals

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Dedicated to the memory of Dr. Frank Pellegrini

Keywords: Carbohydrates / Heterocycles / Natural products / Synthetic methods

Novel one-pot syntheses of *N*-glycooxazolines (N at C-1), *N*-glycoaminooxazolines, and *N*-glycothiazolines have been developed. Thus, the reaction of tri-*O*-benzyl-D-glucal or tri-*O*-benzyl-D-galactal with aryl amides, heteroaryl amides, thioamides, and substituted ureas in the presence of *N*-iodosuccinimide (NIS) in dry propionitrile at 45 °C afforded the cyclized products in good yields. When tris(*O*-*tert*-butyldimethylsilyl)-D-glucal was employed, the 2-deoxy-2-iodoglycosylamide was isolated instead. Treatment of this newly formed glycosylamide with an anhydrous base afforded the *O*-glycooxazoline (O at C-1) in high to moderate yields. Product outcomes and the overall stereoselectivity of the reactions were found to be highly dependent on the nature of the sugar protecting group, the nature of the substituent on the amide, and the reaction temperature.

Introduction

The use and applications of carbohydrate-based oxazolines cannot be understated. Carbohydrate-fused oxazolines have been prepared with the oxygen atom at the C-1 position (*O*-glycooxazolines), and these molecules have been used as glycosyl donors in the synthesis of oligosaccharides,[1] as activated donor substrates in the enzymatic synthesis of glycoconjugates,[2] and as protecting groups of the anomeric center.[3] However, recently there has been interest in the preparation of carbohydrate-based oxazolines due to their occurrence in natural products such as the chitinase inhibitor Allosamidin (**1**)[4] and the trehalase inhibitor Trehazolin (**2**) (Figure 1).[5] Chitinases are enzymes that hydrolyze chitin, a polysaccharide that consists of repeating β-(1–4)-linked *N*-acetyl-D-glucosamine units. Chitin is the second most abundant polysaccharide in nature and is commonly found in insects, plants, bacteria, and fungi.[6] Allosamidin can inhibit the biosynthesis of chitin, and as such it has been used as an antifungal agent and as a pesticide.[7] Although chitin is not synthesized by humans, chitinases are produced by human white blood cells and have been linked to inflammation and airway constriction during asthma attacks.[8] Thus, it has been proposed that chitinase inhibitors may also be useful as chemotherapeutics in the treatment of asthma.[9] Allosamidin is a pseudotrisaccharide featuring an aminooxazoline fused to a cyclopentitol. Several analogues of Allosamidin have been isolated from nature, and all of them contain the aminoxazoline moiety.[10–12] X-ray crystal structures of Allosamidin bound to hevamine, a plant chitinase/lysozyme, have shown that the aminooxazoline moiety interacts directly with the catalytic machinery of the enzyme, and it has been proposed to play a crucial role in the inhibition of chitinase.[13] This suggests that the aminooxazoline may be the minimal subunit

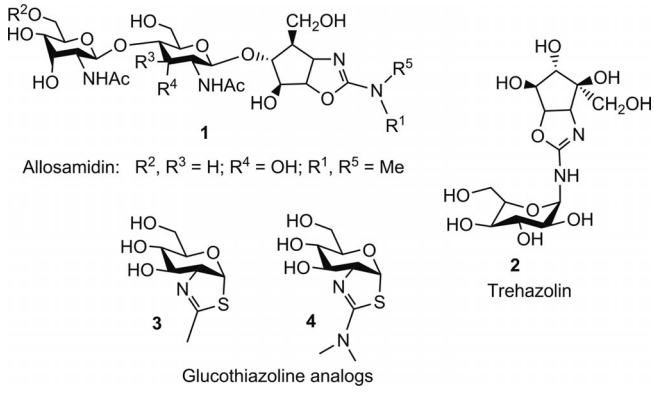

Figure 1. Carbohydrate-based heterocyclic compounds.

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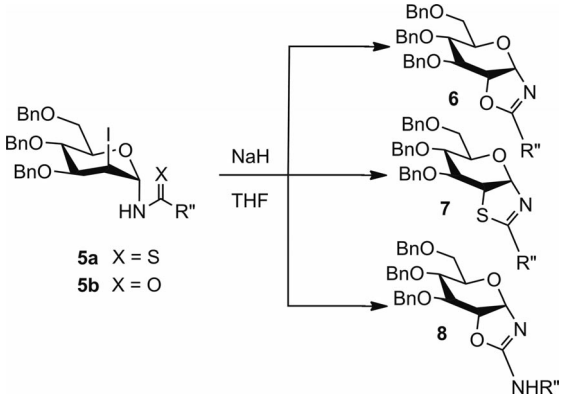
required for binding to the enzyme. Trehazolin is a pseudodisaccharide that also features an aminooxazoline fused to a cyclopentitol. It is a powerful inhibitor of trehalases, which are widespread in nature, including in invertebrates.[14] Just as with Allosamidin, the aminooxazoline moiety found in Trehazolin binds directly to the active site of the enzyme and is capable of mimicking the high-energy intermediate implicated in the hydrolysis of the native substrate trehalose.[15]

As part of our ongoing research aimed at the generation of carbohydrate-fused heterocyclic compounds, we became interested in the development of a convergent approach to the synthesis of a small library of carbohydrate-fused substituted oxazolines. Compounds of this kind have the potential to be powerful glycosidase inhibitors. Our study targeted the less common *N*-glycooxazolines **6** (N at C-1), *N*-glycothiazolines **7**, and *N*-glycoaminooxazolines **8** (Scheme 1) based on the frameworks of Allosamidin and Trehazolin. We envisioned being able to access the latter constructs by using 2-deoxy-2-iodoglycosylthioamides **5a** and 2-deoxy-2-iodoglycosylureas **5b** as precursors. Cyclization under basic conditions by deprotonation of the nitrogen atom of the amide followed by *O*- or *S*-alkylation and displacement of the iodine atom at the C-2 position of the sugar should furnish our targeted compounds.



Scheme 1. Targeted *N*-glycooxazoline, *N*-glycothiazoline, and *N*-glycoaminooxazoline.

Although the total syntheses of Allosamidin and Trehazolin are well documented,[16–19] the preparation of monosaccharides bearing a fused aminooxazoline or -thiazoline based on the same frameworks remains relatively unexplored. Knapp and co-workers prepared glucothiazoline **3** and aminothiazoline **4** (Figure 1), derivatives based on the structure of Allosamidin. These constructs were found to competitively inhibit jack bean *N*-acetylhexoaminidase.[20,21] In contrast, several methods exist for the preparation of *O*-glycooxazolines. Access to these constructs has been achieved by using haloglycosides as starting materials. Their preparation has been accomplished by the displacement of the halogen atom at the anomeric center followed by *O*-alkylation of the neighboring acetamide using a mixture of Ag salts and collidine[3] or $NaHCO_3$.[22] On the other hand, only a few reports exist for the preparation of *N*-glycooxazolines. Common approaches include Ritter-like addition reactions of acetonitrile to anhydrosugars in the presence of $ZnCl_2$[23] and of fructopyranose and furanose 1,2-*O*-acetonide derivatives with various nitriles and triflic acid.[24] Glycosyl azides have also been treated with trialkylphosphanes to prepare *N*-glycooxazolines.[25] In general, *N*-glycooxazolines have been used as precursors in the preparation of β-glycosyl isothiocyanates[26] and as a way of constructing glycosylamides for the preparation of *N*-glycopeptides. Therefore, there is still a need for a convergent approach that will allow the preparation of a small library of carbohydrate-fused oxazolines, thiazolines, and aminooxazolines. Having access to these constructs will facilitate their rapid screening against various glycosidases, including the all important chitinases.

We herein report a novel one-pot procedure for the direct preparation of *N*-glycooxazolines and the extension of this methodology to the preparation of *N*-glycoaminooxazolines and *N*-glycothiazolines by the iodonium-mediated addition of heteroaryl amides, thioamides, and substituted ureas to glycals. The effects of the sugar protecting group, the nature of the substituent on the amide, and the reaction temperature on the product outcomes will also be discussed.

Results and Discussion

We have previously reported the preparation of 2-deoxy-2-iodoglycosylamides from glycals as well as their use as precursors in the preparation of both *O*- and *N*-glycooxazolines by basic cyclization.[27,28] In this two-step procedure, the product outcome of the initial addition reaction was found to be highly dependent on different factors, including the nature of the protecting group on the sugar hydroxy moieties, the substituent on the amide, and the reaction temperature. In the preparation of 2-deoxy-2-iodoglycosylamides, the best overall yields and stereoselectivities were obtained when the bulky *tert*-butyldimethylsilyl ether (TBDMS) and benzyl ether were used as protecting groups on the sugar. Analysis of the ^1H NMR coupling constants of adjacent protons suggested that the TBDMS-protected glycosylamides exist in the $^1C_4$ chair conformation, whereas the benzyl-protected glycosylamide exists in the $^4C_1$ conformation. The *trans*-2-deoxy-2-iodoglycosylamide was obtained as the major addition product in both cases. Alkyl, aryl, and heteroaryl amides gave the best yields, whereas the less nucleophilic trichloroacetamide and acetamide gave poor yields and mixtures of diastereomers. The best overall stereoselectivity was obtained when the reactions were carried out at –78 °C in dry propionitrile or at 0 °C in dry DMF.[29] In our previous study we did not explore the addition of thioamides and substituted ureas. However, we envisioned the construction of *N*-glycoaminooxazolines and *N*-glycothiazolines by using glycosylthioamides and glycosylureas as precursors. Cyclization under basic conditions

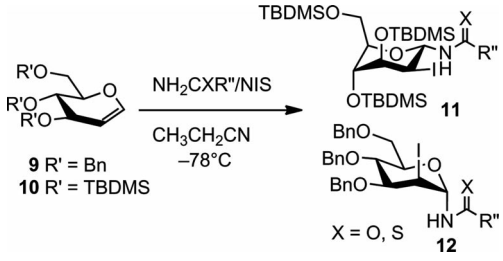
Table 1. Proportions of diastereomeric iodoamides obtained from the glucals.[a]

Entry	Sugar R′	Amide	α-Manno	β-Manno	α-Gluco	β-Gluco	Yield [%][b]
1	TBDMS	NH_2CSCH_3	1	traces	1	10	46
2	TBDMS	NH_2CSPh	0	1	1	8	53
3	Bn	NH_2CSCH_3	1	traces	1	2	55
4	Bn	NH_2CSPh	1	traces	2	4	52
5	TBDMS	$NH_2CONHPh$	1	0	0	0	80
6	TBDMS	$NH_2CON(CH_3)_2$	1	0	0	0	88
7	TBDMS	1-(trimethylsilyl)pyrrolidin-2-one	1	0	0	0	95
8	Bn	NH_2COOBn	–	–	–	–	–
9	TBDMS	NH_2COOBn	–	–	–	–	–

[a] Dry propionitrile was used as solvent. The reaction was performed at –78 °C for 8 h and then at room temp. for 48 h. The proportions of products were determined by integration of the signals of the anomeric protons in the ^{1}H NMR spectrum. [b] Yields of product after recovery by extractive workup and subsequent chromatographic purification on SiO_2.

should furnish our targeted compounds. The addition of other amides, including benzyl carbamates and secondary silylated amides, was also examined.

We began our studies by attempting the addition of thioacetamide and thiobenzamide to both tri-*O*-benzyl-D-glucal (**9**) and tris(*O*-*tert*-butyldimethylsilyl)-D-glucal (**10**) in the presence of NIS and dry propionitrile at –78 °C (Scheme 2). Consistent with our previous results with acetamide and benzamide, we anticipated the formation of the glycosylamides **11** and **12** (Scheme 2), but instead the reaction proceeded very sluggishly, and poor yields and mixtures of diastereoisomers were obtained (Table 1, Entries 1–4).



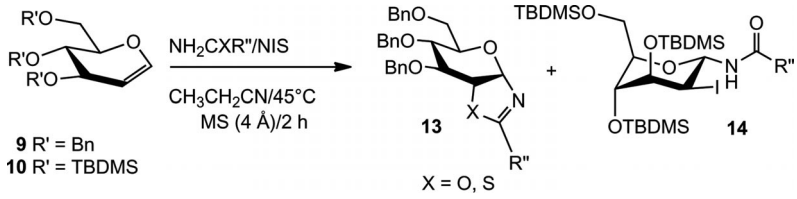
Scheme 2. Preparation of 2-deoxy-2-iodoglycosylamides.

Furthermore, the halohydrin byproduct that can result from the addition of adventitious water found in the system was isolated after flash column chromatography (data not shown) as a minor product. These results were rather surprising, because thioamides have quite a high nucleophilicity and have been used extensively in the synthesis of a wide variety of heterocycles.[30] We also attempted the addition of benzyl carbamate to both the benzyl- and TBDMS-protected glucals (Table 1, Entries 8 and 9). Unfortunately, this addition reaction failed, and starting material was isolated exclusively.

However, in spite of the poor results obtained with the thioamides and benzyl carbamate, other functionalities added quite readily under these reaction conditions. Monosubstituted phenylurea and disubstituted 1,1-dimethylurea added to the TBDMS-protected glucal **10**, and 1-(2-deoxy-2-iodo-α-D-mannopyranosyl)-3-phenylurea **11a** and 1-(2-deoxy-2-iodo-α-D-mannopyranosyl)-3,3-dimethylurea **11b** were obtained exclusively in good yields (Scheme 2; Table 1, Entries 5 and 6). The TBDMS glucal was also treated with the secondary amide 1-(trimethylsilyl)-2-pyrrolidinone to yield 1-[3,4,6-tris(*O*-*tert*-butyldimethylsilyl)-2-deoxy-2-iodo-α-D-mannopyranosyl]-2-pyrrolidinone (**11c**) in 95% yield (Table 1, Entry 7). This is not a surprise, because *N*-silylated amides have been used before in the direct addition of amides to 1-hydroxyglycosyl donors in the presence of trifluoromethanesulfonic anhydride and diphenyl sulfoxide.[31]

We noted that thioamides, ureas, and heteroaryl amides (previous study) are only partially soluble in propionitrile at –78 °C resulting in heterogeneous mixtures. We reasoned that such a lack of solubility may lead to lengthy reaction times and in some cases poor yields and stereoselectivity. To optimize the reaction conditions and improve the reaction times we decided to carry out the addition reaction at a higher temperature. Therefore, a new procedure was developed that involved the mixing of the glucal in dry propionitrile followed by the addition of the amide (6 equiv.). The reaction mixture was heated at 45 °C until the amide had completely dissolved. This was followed by the addition of pre-activated molecular sieves (4 Å) to the reaction mixture as a scavenger of water to prevent the formation of the halohydrin byproduct.

Finally, NIS (2 equiv.) was added to the reaction mixture at 45 °C, and the reaction was monitored by TLC until complete disappearance of the starting material (Scheme 3). Under these new reaction conditions we did not observe any improvement in the addition of both thioacetamide and thiobenzamide to the TBDMS-protected glucal (data not shown). However, when benzamide, heteroaryl amides, phenylurea, and 1,1-dimethylurea were added to the TBDMS-protected glucal **10**, the 2-deoxy-2-iodoglycosylamides **14** were isolated exclusively (Scheme 3; Table 2, Entries 1–6). ^{1}H NMR analysis suggests that all the newly prepared 2-deoxy-2-iodoglycosylamides exist in the $^1C_4$ chair conformation due to the large values of ^3J obtained for the protons at C-1 and C-2, ranging from 10 to 12 Hz, and the medium to small values of ^3J observed for the rest of the protons in the pyranose ring, ranging from 1 to 5 Hz. The total time for the completion of the reaction was just 2 h. This represents a major improvement over our previously reported methodology in which a total of 48 h was required



Scheme 3. Addition of various amides to glycals in the presence of *N*-iodosuccinimide at 45 °C.

Table 2. One-pot preparation of *N*-glycooxazolines, *N*-glycoaminooxazolines, and *N*-thiazolines.

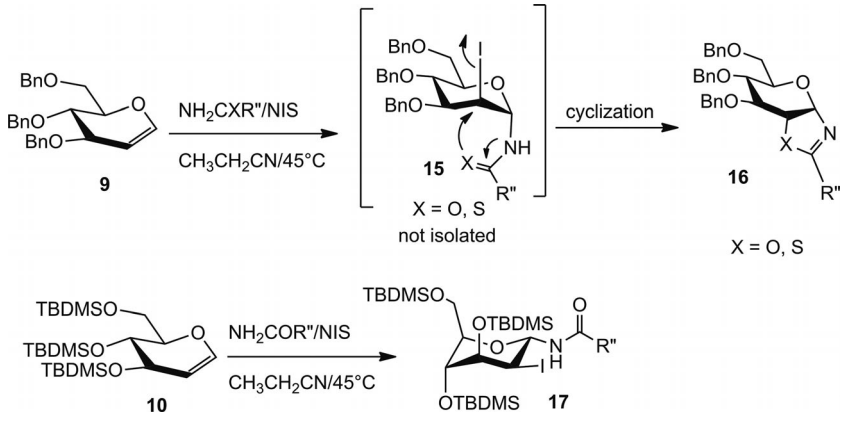
Entry	Sugar R'	Amide (R")	α-Manno	*N*-Oxazoline	*N*-Thiazoline
1	TBDMS	**14a**	88%	–	–
2	TBDMS	**14b**	93%	–	–
3	TBDMS	**14c**	86%	–	–
4	TBDMS	**14d**	88%	–	–
5	TBDMS	**14e**	86%	–	–
6	TBDMS	**14f**	92%	–	–
7	Bn	**13a**	–	70%	–
8	Bn (Gal)	**13b**	–	58%	–
9	Bn	**13c**	–	73%	–
10	Bn	**13d**	–	71%	–
11	Bn	**13e**	–	–	72%
12	Bn	**13f**	–	71%	–
13	Bn	**13g**	–	75%	–

for the reaction to be completed. One can reason that such an improvement must be correlated to the increased solubility of the amides at 45 °C, which results in a homogeneous reaction mixture.

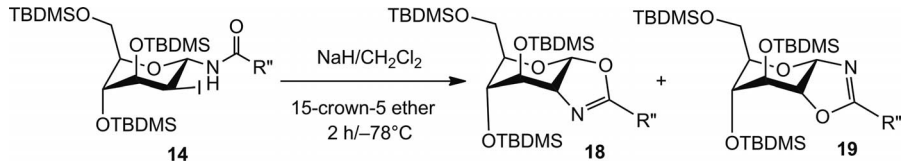
To our surprise, when benzamide was added to the benzyl-protected glucal **9** and galactal derivatives, *N*-glycooxazolines **13a** and **13b** were isolated exclusively in just one step (Scheme 3; Table 2, Entries 7 and 8). Heteroaryl amides, thiobenzamide, phenylurea, and 1,1-dimethylurea were also added to **9** to yield the corresponding heteroaryl *N*-glycooxazolines **13c** and **13d** (Table 2, Entries 9 and 10), *N*-glycothiazoline **13e** (entry 11), and *N*-glycoaminooxazolines **13f** and **13g** (Entries 12 and 13). The direct formation of *O*-glycooxazoline was never observed with the TBDMS-protected glucal, instead the glycosylamide or diastereomeric mixtures of the glycosylthioamide (data not shown) were isolated exclusively.

The results obtained indicate that the temperature and nature of the protecting group on the sugar may play a crucial role in the outcomes of the reaction. It seems that at high temperatures the in situ formation of *N*-glycooxazoline is favored with the benzyl-protected glucal. We reasoned that a combination of the reverse anomeric effect and the preference for the $^4C_1$ chair conformation by the benzyl-protected glycosylamide will favor the formation of 1,2-*cis*-*N*-glycooxazoline. In previous studies, ^{1}H NMR analysis of **15** indicated that the $^4C_1$ chair conformation is preferred by the benzyl-protected glycosylamide (Scheme 4).[27]

It is our hypothesis that the initial formation of the *trans*-2-deoxy-2-iodoglycosylamide **15** takes place at 45 °C. In the



Scheme 4. Product outcomes for the addition of amides at 45 °C to various protected glucals.



Scheme 5. *O*- and *N*-glycooxazolines from 2-deoxy-2-iodoglycosylamides.

$^4C_1$ chair conformation the amide group at C-1 and the iodine atom at C-2 will have the *anti* coplanar conformation required for ring-closure through *O*-alkylation leading to the formation of the oxazoline **16**. One can envision that cyclization may also be favored due to the preference of the amide to occupy the equatorial position rather than the axial position attained in **15** due in part to the reverse anomeric effect.[32] That is not true for the TBDMS-protected glycosylamide **17** (Scheme 4). In this case the $^1C_4$ chair conformation is favored due to the preference of the bulky silyloxy protecting groups to occupy the axial position.[33] In this particular chair conformation the amide group at C-1 and the iodine atom at C-2 will not be able to assume the *anti* coplanar conformation observed in compound **15** thereby preventing the in situ formation of the oxazoline.

Note that the TBDMS-protected glycosylamides **14** were subjected to cyclization through the use of a heterogeneous mixture of NaH in DCM and 15-crown-5 ether at –78 °C (Scheme 5). The *O*-glycooxazolines **18** were obtained in good to excellent yields along with the *N*-glycooxazolines **19** as minor products (Table 3, Entries 1–4). As previously reported, the latter is formed by the migration of the nitrogen atom from C-1 to C-2 through an *N*-acylaziridino sugar intermediate.[27] The aziridine rearranges by nucleophilic ring-opening at the anomeric center by the amide carbonyl oxygen atom to form the *O*-glycooxazoline. To rule out the possibility of an equilibrium between the *N*- and *O*-glycooxazolines, the latter was stirred in a suspension of NaH and CH_2Cl_2 at room temperature, but this did not lead to equilibration.

Table 3. Preparation of *O*-glycooxazolines.

Entry	Sugar R'	Amide (R")	*N*-Oxazoline	*O*-Oxazoline
1	TBDMS	 **18a**	traces	91%
2	TBDMS	 **18b**	–	92%
3	TBDMS	 **18c**	11%	88%
4	TBDMS	 **18d**	25%	73%

Conclusions

We have reported herein a practical one-pot synthesis of various carbohydrate-based heterocycles, including *N*-glycooxazolines, *N*-glycoaminooxazolines, and *N*-glycothiazolines. Direct access to these constructs was achieved by the addition of various aryl and heteroaryl amides, substituted ureas, and thiobenzamide to tri-*O*-benzyl-D-glucal in the presence of NIS and dry propionitrile at 45 °C. When tris(*O*-*tert*-butyldimethylsilyl)-D-glucal was used the 2-deoxy-2-iodoglycosylamides were isolated instead. Cyclization by using a suspension of NaH in CH_2Cl_2 at –78 °C furnished some *N*-glycooxazoline with *O*-glycooxazoline as the major product. The preparation of glycosylureas and glycosylamides through the use of secondary silylated amides in the presence of NIS and propionitrile at –78 °C has also been reported. Further mechanistic studies are in progress to validate the proposed pathway. In addition, the final deprotection and biological screening of the compounds described in this paper are underway, and the results will be reported in due course.

Experimental Section

General Synthetic Methods: Column chromatography was performed on silica gel 60 (EM Science, 70–230 mesh). Reactions were monitored by TLC on Kieselgel 60 F254 (EM Science), and the compounds were detected by examination under UV light and by charring with 10% sulfuric acid in MeOH. Solvents were removed under reduced pressure at <40 °C. CH_2Cl_2 was distilled from CaH_2 and stored over molecular sieves (3 Å). Molecular sieves (4 Å) used in the reactions were crushed and activated in vacuo at 390 °C for 8 h in the first instance and then at 390 °C for 2–3 h directly prior to application. ^1H and ^{13}C NMR spectra were recorded with Varian spectrometers (models Inova 300 and 500) equipped with Sun workstations and an ECS 400 MHz JEOL spectrometer. ^1H NMR spectra were recorded in [D_6]acetone and are referenced to residual CH_3COCH_3 at δ = 2.04 ppm, and ^{13}C NMR spectra are referenced to the peak at δ = 205 ppm. ^1H NMR spectra recorded in $CDCl_3$ are referenced to residual $CHCl_3$ at δ = 7.24 ppm, and ^{13}C NMR spectra are referenced to the central peak of $CDCl_3$ at δ = 77.0 ppm. Assignments were made by standard gCOSY and gHSQC experiments. HRMS data were obtained with a Bruker Ultraflex MALDI-TOF mass spectrometer. Tri-*O*-benzyl-D-glucal, tri-*O*-benzyl-D-galactal, 3,4,6-tris(*O*-*tert*-butyldimethylsilyl)-D-glucal, and *N*-iodosuccinimide (NIS) were purchased from Aldrich. Amides, heteroaryl amides, and thiobenzamide were also purchased from Aldrich Chemical Co., whereas phenylurea and 1,1-dimethylurea were purchased from TCI America.

General Procedure for the Preparation of *N*-[3,4,6-Tris(*O*-*tert*-butyldimethylsilyl)-2-deoxy-2-iodo-α-D-mannopyranosyl]amides at –78 °C: 3,4,6-Tris(*O*-*tert*-butyldimethylsilyl)-D-glucal (**10**) (0.150 g, 0.30 mmol) was diluted in freshly distilled propionitrile (3.0 mL) and mixed under N_2. The amide (0.615 mmol) was added to the reaction flask followed by *N*-iodosuccinimide (0.138 g, 0.61 mmol). The reaction mixture was stirred at –78 °C for 8 h and then warmed to room temp. and mixed for 48 h. The reaction was monitored by TLC until complete disappearance of the starting material was observed. The reaction was quenched with distilled water and the

mixture diluted in DCM (50 mL). The crude mixture was washed with a saturated solution of $Na_2S_2O_3$ (100 mL) and distilled water (3 × 100 mL). The organic layer was dried with $MgSO_4$ and the solvent removed in vacuo.

1-Phenyl-3-[3,4,6-tris(*O*-*tert*-butyldimethylsilyl)-2-deoxy-2-iodo-α-D-mannopyranosyl]urea (11a): The crude mixture (0.250 g) was purified by flash column chromatography on silica gel (hexane/ethyl acetate, 3:1, v/v), to give a colorless solid (0.184 g, 80%). R_f = 0.40. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50 (s, 1 H, N*H*-Ph), 7.29 (d, J = 7.6 Hz, 2 H, Ar), 7.20 (t, J = 7.8 Hz, 2 H, Ar), 6.98 (t, J = 7.08 Hz,1 H, Ar), 5.92 (d, J_{NH-1} = 8.24 Hz, 1 H, N*H*), 5.56 (dd, J_{1-NH} = 9.16, J_{1-2} = 9.1 Hz, 1 H, 1-H), 4.61 (br. d, J_{2-1} = 12.8 Hz, 1 H, 2-H), 4.18 (dd, J_{5-4} = 11.0, J_{5-6} = 10.8 Hz, 1 H, 5-H), 4.04 (s, 1 H, 4-H), 3.93–3.89 (m, 3 H, 3-H, 6-H), 0.97–0.84 [m, 27 H, $(CH_3)_3C$], 0.15–0.1 (m, 18 H, CH_3Si) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.99 (C=O), 138.33, 129.11, 128.95, 128.59, 126.28, 123.57 (Ar), 81.85 (C-3), 76.86 (C-5), 76.47 (C-1), 69.18 (C-4), 61.38 (C-6), 33.99 (C-2), 32.04, 32.03, 29.81, 29.80, 26.37, 26.36, 26.08, 26.04, 22.80, 18.42, 18.19, 14.27 [$(CH_3)_3C$], –3.46, –4.47, 4.56 (CH_3Si) ppm. HRMS (MALDI-TOF): calcd. for $C_{31}H_{59}IN_2O_5Si_3$ 750.2776 [M + H]$^+$; found 751.2855.

1,1-Dimethyl-3-[3,4,6-tris(*O*-*tert*-butyldimethylsilyl)-2-deoxy-2-iodo-α-D-mannopyranosyl]urea (11b): The crude mixture (0.240 g) was purified by flash column chromatography on silica gel (hexane/ethyl acetate, 4:1, v/v) to give a white solid (0.189 g, 88%). R_f = 0.41. ^{1}H NMR (500 MHz, [D$_6$]acetone): δ = 5.86 (d, J_{N-H1} = 9.60 Hz, 1 H, N*H*), 5.49 (dd, J_{1-NH} = 9.90, J_{1-2} = 9.75 Hz, 1 H, 1-H), 4.69 (dd, J_{2-1} = 5.10, J_{2-3} = 2.41 Hz, 1 H, 2-H), 4.22–4.14 (m, 1 H, 5-H), 4.02 (s, 1 H, 4-H), 3.86 (dd, J_{3-2} = 1.80, J_{3-4} = 1.80 Hz, 1 H, 3-H), 3.74–3.66 (m, 2 H, 6-H), 2.76 (s, 3 H, C*H*$_3$), 2.71 (s, 3 H, C*H*$_3$), 0.91–0.88 [m, 7 H, $(CH_3)_3C$], 0.82–0.78 [m, 20 H, $(CH_3)_3C$], 0.16–0.12 (m, 9 H, CH_3Si), 0.03–0.00 (m, 9 H, CH_3Si) ppm. ^{13}C NMR (125 MHz, [D$_6$]acetone): δ = 156.79 (C=O), 81.18 (C-3), 77.45 (C-5), 75.27 (C-1), 69.61 (C-4), 61.80 (C-6), 35.78 (C-2), 29.42, 29.17, 28.91, 28.65, 28.40, 26.11, 25.71, 25.51, 25.40, 18.28, 18.18, 17.91 [$(CH_3)_3C$], –3.71, –5.02, –5.07, –5.14, –5.64, –5.66 (CH_3Si) ppm. HRMS (MALDI-TOF): calcd. for $C_{27}H_{59}IN_2O_5Si_3$ 702.2776 [M + Na]$^+$; found 725.2546.

1-[3,4,6-Tris(*O*-*tert*-butyldimethylsilyl)-2-deoxy-2-iodo-α-D-mannopyranosyl]-2-pyrrolidinone (11c): The crude mixture (0.220 g) was purified by flash column chromatography on silica gel (hexane/ethyl acetate, 3:1, v/v) to give a clear oil (0.20 g, 95%). R_f = 0.38. ^{1}H NMR (400 MHz, [D$_6$]acetone): δ = 5.65 (d, J_{NH-1} = 10.5 Hz, 1 H, N*H*), 4.69 (br. d, J_{1-NH} = 11.0 Hz, 1 H, 1-H), 4.14 (dd, J_{2-1} = 2.62, J_{2-3} = 1.34 Hz, 2 H, 2-H, 5-H), 3.91 (d, J_{3-2} = 3.2 Hz, 1 H, 3-H), 3.86–3.85 (m, 3 H, 4-H, 6-H), 3.41–3.36 (m, 2 H, $COCH_2CH_2CH_2$), 2.24–2.22 (m, 2 H, $COCH_2CH_2CH_2$), 2.02–2.01 (m, 2 H, $COCH_2CH_2CH_2$), 0.91–0.87 [m, 27 H, $(CH_3)_3C$], 0.24–0.0 (m, 18 H, CH_3Si) ppm. ^{13}C NMR (100 MHz, [D$_6$]acetone): δ = 175.09 (C=O), 82.24 (C-3), 77.11 (C-5), 74.01 (C-1), 69.70 (C-4), 61.93 (C-6), 41.38 (C-2), 32.55, 31.59, 26.62, 26.26, 26.01, 18.78, 18.38 [$(CH_3)_3C$], –3.25, –4.59, –5.10 (CH_3Si) ppm. HRMS (MALDI-TOF): calcd. for $C_{27}H_{59}IN_2O_5Si_3$ 699.2667 [M + H]$^+$; found 700.2746.

General Procedure for the Preparation of 3,4,6-Tris(*O*-*tert*-butyldimethylsilyl)-2-deoxy-2-iodo-α-D-mannopyranosyl Amides at 45 °C: 3,4,6-Tris(*O*-*tert*-butyldimethylsilyl)-D-glucal (**10**) (0.150 g, 0.30 mmol) was diluted in freshly distilled propionitrile (3.0 mL) and stirred under N_2. The amide (0.615 mmol) was added to the reaction flask, and the reaction mixture was heated at 45 °C until it became a homogeneous solution. Activated molecular sieves (4 Å) in powder form (0.100 g) were added. After 10 min, *N*-iodosuccinimide (0.138 g, 0.61 mmol) was added to the flask, which was then wrapped in aluminium foil, and the reaction mixture was stirred at 45 °C for 2 h. The reaction was monitored by TLC, and upon disappearance of the starting material the following workup was carried out to isolate the crude product. The reaction was quenched with distilled water, and the mixture was diluted in CH_2Cl_2 (50 mL). The crude mixture was filtered and washed with a saturated aqueous solution of $Na_2S_2O_3$ (100 mL) and distilled water (3 × 100 mL). The organic layer was dried with $MgSO_4$, and the solvent was removed in vacuo.

***N*-[3,4,6-Tris(*O*-*tert*-butyldimethylsilyl)-2-deoxy-2-iodo-α-D-mannopyranosyl]pyridine-2-carboxamide (14a):** The crude mixture (0.235 g) was purified by flash column chromatography on silica gel (hexane/ethyl acetate, 8:1, v/v) to give a clear oil (0.197 g, 88%). R_f = 0.29. ^{1}H NMR (400 MHz, [D$_6$]acetone): δ = 8.59 (dd, J = 2.52, J = 0.92 Hz, 1 H, Ar), 8.09 (d, J = 0.56 Hz, 1 H, Ar), 7.98 (dd, J = 2.32, J = 1.36 Hz, 1 H, Ar), 7.57 (dd, J = 2.76, J = 2.06 Hz, 1 H, Ar), 5.86 (t, J_{N-H1} = 6.88, J_{NH-2} = 5.04 Hz, 1 H, N*H*), 5.10 (dd, J_{1-NH} = 6.16, J_{1-2} = 2.88 Hz, 1 H, 1-H), 3.96 (dd, J_{2-3} = 5.04, J_{2-1} = 2.28 Hz, 1 H, 2-H), 4.14 (s, 1 H, 5-H), 3.97 (dd, J_{4-3} = 2.08, J_{4-5} = 1.72 Hz, 1 H, 4-H), 3.92 (dd, J_{3-2} = 5.96, J_{3-4} = 4.78 Hz, 1 H, 3-H), 3.90–3.85 (m, 2 H, 6-H), 0.90–0.86 [m, 27 H, $(CH_3)_3C$], 0.13–0.07 (m, 18 H, CH_3Si) ppm. ^{13}C NMR (100 MHz, [D$_6$]acetone): δ = 149.22, 138.42, 127.49, 123.0 (Ar), 81.90 (C-3), 77.27 (C-5), 70.02 (C-1), 62.16 (C-6), 34.98 (C-2), 26.69, 26.27, 26.06, 18.85, 18.73, 18.45 [$(CH_3)_3C$], –3.14, –4.50, –5.07 (CH_3Si) ppm. HRMS (MALDI-TOF): calcd. for $C_{30}H_{57}IN_2O_5Si_3$ 736.2620 [M + H]$^+$; found 737.2698.

***N*-[3,4,6-Tris(*O*-*tert*-butyldimethylsilyl-2-deoxy-2-iodo-α-D-mannopyranosyl]pyrazincarboxamide (14b):** The crude mixture (0.240 g) was purified by flash column chromatography on silica gel (hexane/ethyl acetate, 7:1, v/v) to give a yellowish oil (0.210 g, 93%). R_f = 0.34. ^{1}H NMR (400 MHz, [D$_6$]acetone): δ = 9.22 (s,1 H, Ar), 8.22 (d, J = 2.28 Hz, 1 H, Ar), 8.63 (d, J = 1.84 Hz,1 H, Ar), 5.87 (d, J_{NH-1} = 10.0 Hz, 1 H, N*H*), 5.13 (dd, J_{1-NH} = 10.0, J_{1-2} = 6.2 Hz, 1 H, 1-H), 4.20 (br. d, J_{2-1} = 7.8 Hz, 1 H, 2-H), 4.14 (s, 1 H, 5-H), 3.97 (dd, J_{4-3} = 1.6, J_{4-5} = 1.3 Hz, 1 H, 4-H), 3.93–3.90 (m, 3 H, 3-H, 6-H), 0.90–0.86 [m, 27 H, $(CH_3)_3C$], 0.26–0.07 (m, 18 H, CH_3Si) ppm. ^{13}C NMR (100 MHz, [D$_6$]acetone): δ = 160.75 (C=O), 148.03, 144.42, 144.31, 143.35 (Ar), 81.29 (C-3), 76.63 (C-1), 69.32 (C-4), 61.43 (C-6), 32.0 (C-2), 29.28, 29.09, 28.90, 28.70, 28.50, 25.54, 19.0, 18.80, 14.0 [$(CH_3)_3C$], –3.86, –5.27, –5.80 (CH_3Si) ppm. HRMS (MALDI-TOF): calcd. for $C_{29}H_{56}IN_3O_5Si_3$ 737.2572 [M + H]$^+$; found 738.2659.

***N*-[3,4,6-Tris(*O*-*tert*-butyldimethylsilyl)-2-deoxy-2-iodo-α-D-mannopyranosyl]thiophenecarboxamide (14c):** The crude mixture (0.245 g) was purified by flash column chromatography on silica gel (hexane/ethyl acetate, 9:1, v/v) to give a white solid (0.197 g, 86%). R_f = 0.25. ^{1}H NMR (400 MHz, [D$_6$]acetone): δ = 7.54–7.48 (m, 2 H, Ar), 7.06 (d, J = 9.2 Hz, 1 H, Ar), 6.37 (d, J_{NH-1} = 9.2 Hz, 1 H, N*H*), 5.77 (dd, J_{1-NH} = 10.0, J_{1-2} = 9.84 Hz, 1 H, 1-H), 4.64 (dd, J_{2-1} = 10.0, J_{2-3} = 2.4 Hz, 1 H, 2-H), 4.25 (m, 1 H, 5-H), 4.07 (s, 1 H, 4-H), 3.92 (dd, J_{3-2} = 2.76, J_{3-4} = 1.2 Hz, 1 H, 3-H), 3.85–3.83 (m, 2 H, 6-H), 0.97–0.76 [m, 27 H, $(CH_3)_3C$], 0.22–0.04 (m, 18 H, CH_3Si) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.16 (C=O), 138.24, 130.99, 128.82, 127.72 (Ar), 81.83 (C-3), 73.17 (C-1), 68.81 (C-4), 61.18 (C-6), 33.96 (C-2), 29.79, 26.30, 26.01, 25.90, 25.73, 25.66, 18.37, 18.28, 18.09, 14.23, 13.90 [$(CH_3)_3C$], –4.58, –4.65, –5.17 (CH_3Si) ppm. HRMS (MALDI-TOF): calcd. for $C_{29}H_{56}INO_5Si_3$ 741.2232 [M + Na]$^+$; found 764.2234.

***N*-[3,4,6-Tris(*O*-*tert*-butyldimethylsilyl-2-deoxy-2-iodo-α-D-mannopyranosyl]benzamide (14d):** The crude mixture (0.250 g) was puri-

fied by flash column chromatography on silica gel (hexane/ethyl acetate, 10:1, v/v) to give a clear oil (0.200 g, 88%). R_f = 0.35. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.79 (d, J = 6.88 Hz, 2 H, Ar), 7.49 (t, J = 6.88 Hz, 1 H, Ar), 7.41 (t, J = 6.88 Hz, 2 H, Ar), 6.51 (d, J = 9.16 Hz, 1 H, NH), 5.81 (dd, $J_{1\text{-NH}}$ = 10.0, $J_{1\text{-}2}$ = 9.76 Hz, 1 H, 1-H), 4.67 (dd, $J_{2\text{-}1}$ = 5.24, $J_{2\text{-}3}$ = 2.76 Hz, 1 H, 2-H), 4.29 (dd, $J_{5\text{-}4}$ = 11.6, $J_{5\text{-}6}$ = 11.4 Hz, 1 H, 5-H), 4.08 (s, 1 H, 4-H), 3.95 (dd, $J_{3\text{-}2}$ = 3.24, $J_{3\text{-}4}$ = 1.20 Hz, 1 H, 3-H), 3.87 (m, 2 H, 6-H), 0.98–0.84 [m, 27 H, $(CH_3)_3C$], 0.23–0.04 (m, 18 H, CH_3Si) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.75 (C=O), 133.93, 132.00, 128.66, 127.32 (Ar), 81.76 (C-3), 73.15 (C-1), 68.85 (C-4), 61.22 (C-6), 34.26 (C-2), 26.02, 25.89, 18.39, 18.07 [$(CH_3)_3C$], –4.58, –4.65, –5.17 (CH_3Si) ppm. HRMS (MALDI-TOF): calcd. for $C_{31}H_{58}INO_5Si_3$ 735.2784 $[M + Na]^+$; found 758.2786.

Compounds **11a** and **11b** are identical to compounds **14e** and **14f** found in Table 2.

General Procedure for the Preparation of the α-D-Glucopyrano[1,2-*d*]-[1,3]oxazolines: 3,4,6-Tri-*O*-benzyl-D-glucal (**9**) (0.200 g, 0.48 mmol) was diluted in freshly distilled propionitrile (3.0 mL) and stirred under N_2. The amide (2.88 mmol) was added to the reaction flask, and the reaction mixture was heated at 45 °C until it became a homogeneous solution. Then preactivated molecular sieves (4 Å) in powder form (0.100 g) were added. After 10 min, *N*-iodosuccinimide (0.216 g, 0.96 mmol) was added to the reaction flask while heating at 45 °C. The reaction was monitored by TLC, and complete disappearance of the starting material was detected after 2 h. The reaction was quenched with distilled water, and the mixture was diluted in DCM (50.0 mL). The crude mixture was filtered and washed with a saturated aqueous solution of $Na_2S_2O_3$ (100 mL) and distilled water (3 × 100 mL). The organic layer was dried with $MgSO_4$, and the solvent was removed in vacuo.

2-Phenyl-1,3-oxazoline 13a: The crude mixture (0.355 g) was purified by flash column chromatography on silica gel (hexane/ethyl acetate, 6:1–3:1, v/v) to give a clear oil (0.180 g, 70%). R_f = 0.35. ^{1}H NMR (500 MHz, [D$_6$]acetone): δ = 7.99 (d, J = 7.0 Hz, 2 H, Ar), 7.57 (t, J = 6.5 Hz, 1 H, Ar), 7.50–7.43 (m, 5 H, Ar), 7.39–7.24 (m, 12 H, Ar), 6.01 (d, $J_{1\text{-}2}$ = 7.0 Hz, 1 H, 1-H), 4.87 (dd, $J_{2\text{-}1}$ = 5.5, $J_{2\text{-}3}$ = 4.75 Hz, 1 H, 2-H), 4.83–4.77 (m, 2 H, Ph-CH_2), 4.75–4.50 (m, 4 H, Ph-CH_2), 3.99 (dd, $J_{3\text{-}2}$ = 5.0, $J_{3\text{-}4}$ = 4.5 Hz, 1 H, 3-H), 3.80 (dd, $J_{5\text{-}4}$ = 9.5, $J_{5\text{-}6}$ = 9.0 Hz, 1 H, 5-H), 3.74–3.54 (m, 3 H, 4-H, 6-H) ppm. ^{13}C NMR (125 MHz, [D$_6$]acetone): δ = 165.47 (C=N), 138.90, 138.66, 138.53, 138.37, 132.20, 128.54, 128.45, 128.31, 128.22, 128.20, 128.16, 128.14, 128.00, 127.87, 127.79, 127.77, 127.67, 127.64, 127.58, 127.51, 127.44, 127.36, 127.27, 127.15 (Ar), 93.35 (C-1), 79.05 (C-2), 78.74 (C-3), 76.61 (C-5), 76.25 (C-4), 74.97 (C-6), 74.58, 72.90, 72.84, 72.63, 71.86, 71.33, 70.12, 70.05, 69.43 ppm. HRMS (MALDI-TOF): calcd. for $C_{34}H_{33}NO_5$ 535.2359 $[M + H]^+$; found 536.2437.

2-Phenyl-1,3-oxazoline 13b: The crude mixture (0.300 g) was purified by flash column chromatography on silica gel (hexane/ethyl acetate, 6:1–3:1, v/v) to give a clear oil (0.150 g, 58%). R_f = 0.37. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99 (d, J = 11.0 Hz, 2 H, Ar), 7.40–7.27 (m, 18 H, Ar), 5.97 (d, $J_{1\text{-}2}$ = 5.0 Hz, 1 H, 1-H), 4.82 (dd, $J_{2\text{-}1}$ = 9.15, $J_{2\text{-}3}$ = 8.8 Hz, 1 H, 2-H), 4.93 (dd, J = 14.0, J = 13.5 Hz, 2 H, Ph-CH_2), 4.66 (dd, J = 14.1, J = 14.0 Hz, 2 H, Ph-CH_2), 4.45 (dd, J = 13.5, J = 13.0 Hz, 2 H, Ph-CH_2), 4.08 (dd, $J_{3\text{-}2}$ = 6.8, $J_{3\text{-}4}$ = 5.76 Hz, 1 H, 3-H), 4.00 (s, 1 H, 5-H), 3.74–3.67 (m, 3 H, 4-H, 6-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.61 (C=N), 138.48, 137.98, 128.57, 128.48, 128.41, 127.66 (Ar), 93.94 (C-1), 79.93 (C-2), 74.73 (C-3), 73.57 (C-5), 73.40 (C-4), 72.86 (C-6), 71.56, 68.04, 60.5, 29.80, 21.17, 14.30 ppm. HRMS (MALDI-TOF): calcd. for $C_{34}H_{33}NO_5$ 535.2359 $[M + H]^+$; found 536.2437.

2-(2-Thienyl)-1,3-oxazoline 13c: The crude mixture (0.280 g) was purified by flash column chromatography on silica gel (hexane/ethyl acetate, 6:1–3:1, v/v) to give a white solid (0.190 g, 73%). R_f = 0.34. ^{1}H NMR (500 MHz, [D$_6$]acetone): δ = 7.78–7.72 (m, 2 H, Ar), 7.44 (d, J = 7.0 Hz, 1 H, Ar), 7.37–7.71 (m, 15 H, Ar), 5.98 (d, $J_{1\text{-}2}$ = 7.5 Hz, 1 H, 1-H), 4.81–4.75 (m, 3 H, Ph-CH_2, 2-H), 4.69 (d, J = 11.5 Hz, 2 H, Ph-CH_2), 4.57–4.49 (m, 2 H, Ph-CH_2), 3.98 (dd, $J_{3\text{-}2}$ = 4.5, $J_{3\text{-}4}$ = 4.5 Hz, 1 H, 3-H), 3.73–3.66 (m, 3 H, 4-H, 5-H, 6-H), 3.56–3.55 (m, 1 H, 6-H) ppm. ^{13}C NMR (125 MHz, [D$_6$]acetone): δ = 161.25 (C=N), 138.65, 138.52, 138.31, 131.69, 129.45, 128.31, 128.19, 128.14, 128.02, 128.00, 127.74, 127.68, 127.65, 127.43, 127.36, 127.77 (Ar), 93.33 (C-1), 78.98 (C-2), 78.72 (C-3), 74.92 (C-5), 72.82 (C-4), 72.56 (C-6), 71.82, 71.30, 70.04 ppm. HRMS (MALDI-TOF): calcd. for $C_{32}H_{31}NO_5S$ 541.1923 $[M + H]^+$; found 542.2001.

2-(2-Pyridyl)-1,3-oxazoline 13d: The crude mixture (0.290 g) was purified by flash column chromatography on silica gel (hexane/ethyl acetate, 6:1–3:1, v/v) to give a clear oil (0.185 g, 71%). R_f = 0.30. ^{1}H NMR (500 MHz, [D$_6$]acetone): δ = 8.62 (d, J = 4.0 Hz, 1 H, Ar), 8.14 (d, J = 7.5 Hz, 1 H, Ar), 8.03–8.0 (m, 1 H, Ar), 7.63–7.60 (m, 1 H, Ar), 7.44 (d, J = 7.5 Hz, 1 H, Ar), 7.33–7.25 (m, 14 H, Ar), 6.05 (d, $J_{1\text{-}2}$ = 6 Hz, 1 H, 1-H), 5.13–5.11 (m, 1 H, 2-H), 4.76–4.73 (m, 2 H, Ph-CH_2), 4.68–4.53 (m, 4 H, Ph-CH_2), 3.91 (dd, $J_{3\text{-}2}$ = 5.5, $J_{3\text{-}4}$ = 5.5 Hz, 1 H, 3-H), 3.87–3.80 (m, 3 H, 4-H, 5-H, 6-H), 3.79–3.76 (m, 1 H, 6-H) ppm. ^{13}C NMR (125 MHz, [D$_6$]-acetone): δ = 163.71 (C=N), 148.48, 138.82, 138.53, 137.93, 137.75, 128.26, 128.21, 128.16, 128.08, 127.86, 127.83, 127.70, 127.53, 127.51, 127.26, 126.93, 122.36 (Ar), 86.24 (C-1), 78.34 (C-2), 77.31 (C-3), 74.87 (C-5), 74.65 (C-4), 72.93 (C-6), 72.90, 71.66, 68.69 ppm. HRMS (MALDI-TOF): calcd. for $C_{33}H_{32}N_2O_5$ 536.2311 $[M + H]^+$; found 537.2389.

2-Phenyl-1,3-thiazoline 13e: The crude mixture (0.300 g) was purified by flash column chromatography on silica gel (hexane/ethyl acetate, 3:1, v/v) to give a yellowish oil (0.190 g, 72%). R_f = 0.38. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.00–7.26 (m, 20 H, Ar), 6.05 (s, 1 H, 1-H), 4.88–4.42 (m, 6 H, Ph-CH_2), 4.11 (d, $J_{2\text{-}1}$ = 7.5 Hz, 1 H, 2-H), 3.99 (d, $J_{3\text{-}2}$ = 8.5 Hz, 1 H, 3-H), 3.77 (d, $J_{4\text{-}5}$ = 11 Hz, 1 H, 5-H), 3.68–3.64 (m, 3 H, 4-H, 6-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.06, 137.70, 128.61, 128.47, 128.04, 128.01 (Ar), 88.25 (C-1), 73.52 (C-2), 72.78 (C-3), 71.48 (C-5), 60.54 (C-4), 52.10 (C-6), 69.0, 60.54, 52.10 ppm. HRMS (MALDI-TOF): calcd. for $C_{34}H_{33}NO_4S$ 551.2130 $[M + H]^+$; found 552.2209.

2-(Phenylamino)-1,3-oxazoline 13f: The crude mixture (0.315 g) was purified by flash column chromatography on silica gel (ethyl acetate/hexane, 2:1, v/v) to give a clear oil (0.183 g, 71%). R_f = 0.44. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 11.74 (s, 1 H, N*H*-Ph), 7.60 (d, J = 4.5 Hz, 1 H, Ar), 7.35–7.24 (m, 19 H, Ar), 6.43 (d, $J_{1\text{-}2}$ = 5.96 Hz, 1 H, 1-H), 4.67–4.63 (m, 3 H, Ph-CH_2, 2-H), 4.54 (dd, J = 11.5, J = 11.0 Hz, 2 H, Ph-CH_2), 4.38 (d, J = 14.5 Hz, 1 H, Ph-CH_2), 4.06 (dd, $J_{3\text{-}2}$ = 3.6, $J_{3\text{-}4}$ = 3.2 Hz, 1 H, 3-H), 3.83–3.68 (m, 4 H, 4-H, 5-H, 6-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.71, 143.57, 138.21, 137.88, 137.75, 137.29, 128.56, 128.46, 128.14, 128.11, 128.00 (Ar), 119.9 (C-1), 80.21 (C-2), 75.62 (C-3), 74.20 (C-5), 73.72 (C-4), 72.77 (C-6), 72.64, 72.45, 70.0 ppm. HRMS (MALDI-TOF): calcd. for $C_{34}H_{34}N_2O_5$ 550.2468 $[M + H]^+$; found 551.2546.

2-(Dimethylamino)-1,3-oxazoline 13g: The crude mixture (0.300 g) was purified by flash column chromatography on silica gel (ethyl acetate/hexane, 3:1, v/v) to give a white solid (0.180 g, 75%). R_f = 0.48. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.31–7.23 (m, 15 H, Ar), 6.70 (s, 1 H, 1-H), 4.62–4.32 (m, 8 H, Ph-CH_2, 2-H, 3-H), 3.93 (s, 1 H, 5-H), 3.84 (dd, $J_{4\text{-}5}$ = 5.84, $J_{4\text{-}3}$ = 5.52 Hz, 1 H, 4-H), 3.54–

3.48 (m, 2 H, 6-H), 3.00 [s, 6 H, $(CH_3)_2$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.37 (C=O), 141.32, 138.29, 138.02, 137.65, 128.49, 127.94 (Ar), 81.0 (C-1), 74.00 (C-2), 73.45 (C-3), 70.76 (C-5), 70.54 (C-4), 69.00 (C-6), 37.83 (CH_3) ppm. HRMS (MALDI-TOF): calcd. for $C_{30}H_{34}N_2O_5$ 502.2468 $[M + H]^+$; found 503.2546.

2-(2-Pyridyl)-1,3-oxazoline 18a: Compound **14a** (0.197 g, 0.26 mmol) was added to a heterogeneous solution of NaH (14.0 mg, 0.42 mmol) in dry DCM (2.0 mL) under N_2. 15-Crown-5 ether (0.1 mL) was subsequently added, and the mixture was allowed to react at –78 °C for 2 h. Upon addition of the crown ether fizzing was observed along with a change in color of the reaction mixture from white to yellow. The reaction mixture was monitored by TLC, and upon disappearance of the starting material the reaction was quenched with distilled water. The reaction mixture was diluted in DCM (50.0 mL) and washed with distilled water (3 × 100 mL). The organic layer was dried with $MgSO_4$, and the solvent was removed in vacuo. The crude mixture (0.175 g) was purified by flash column chromatography on silica gel (hexane/ethyl acetate, 7:1, v/v) to give a white solid (0.150 g, 91%). R_f = 0.34. ^{1}H NMR (500 MHz, [D$_6$]acetone): δ = 8.66 (d, J = 4.5 Hz, 1 H, Ar), 8.08 (d, J = 8.0 Hz, 1 H, Ar), 7.91 (dd, J = 4.5, J = 4.0 Hz, 1 H, Ar), 7.52 (dd, J = 3.5, J = 3.2 Hz,1 H, Ar), 6.25 (d, $J_{1\text{-}2}$ = 8.0 Hz, 1 H, 1-H), 4.34 (dd, $J_{2\text{-}1}$ = 2.50, $J_{2\text{-}3}$ = 1.50 Hz, 1 H, 2-H), 4.30 (dd, $J_{3\text{-}2}$ = 1.25, $J_{3\text{-}4}$ = 1.0 Hz, 1 H, 3-H), 3.92 (d, $J_{4\text{-}5}$ = 7.0 Hz, 1 H, 5-H), 3.78–3.73 (m, 3 H, 4-H, 6-H), 0.95–0.82 [m, 27 H, $(CH_3)_3C$], 0.23–0.06 (m, 18 H, CH_3Si) ppm. ^{13}C NMR (125 MHz, [D$_6$]acetone): δ = 161.99 (C=N), 146.64, 143.02, 139.45, 126.23, 122.36 (Ar), 100.17 (C-1), 74.44 (C-2), 72.64 (C-3), 71.32 (C-5), 69.52 (C-4), 68.47 (C-6), 23.0, 22.0, 17.69, 17.46 [$(CH_3)_3C$], –5.13, –5.77, –5.86 (CH_3Si) ppm. HRMS (MALDI-TOF): calcd. for $C_{30}H_{56}N_2O_5Si_3$ 608.3497 $[M + H]^+$; found 609.3575.

2-Pyrazinyl-1,3-oxazoline 18b: Compound **14b** (0.210 g, 0.28 mmol) was added to a heterogeneous solution of NaH (14.0 mg, 0.42 mmol) in dry DCM (2.0 mL) under N_2. 15-Crown-5 ether (0.1 mL) was subsequently added, and the mixture was allowed to react at –78 °C for 2 h. Upon addition of the crown ether fizzing was observed along with a change in color of the reaction mixture from white to yellow. The reaction mixture was monitored by TLC, and upon disappearance of the starting material the reaction was quenched with distilled water. The reaction mixture was diluted in DCM (50.0 mL) and washed with distilled water (3 × 100 mL). The organic layer was dried with $MgSO_4$, and the solvent was removed in vacuo. The crude mixture (0.200 g) was purified by flash column chromatography on silica gel (hexane/ethyl acetate, 6:1, v/v) to give a white solid (0.155 g, 92%). R_f = 0.35. ^{1}H NMR (400 MHz, [D$_6$]-acetone): δ = 9.18 (s, 1 H, Ar), 8.72 (d, J = 2.28 Hz, 1 H, Ar), 8.70 (d, J = 2.32 Hz, 1 H, Ar), 6.27 (d, $J_{1\text{-}2}$ = 7.80 Hz, 1 H, 1-H), 4.37 (dd, $J_{2\text{-}1}$ = 1.40, $J_{2\text{-}3}$ = 1.36 Hz, 1 H, 2-H), 4.26 (dd, $J_{3\text{-}4}$ = 6.0, $J_{3\text{-}2}$ = 1.36 Hz, 1 H, 3-H), 3.72–3.68 (m, 2 H, 4-H, 5-H), 3.35–3.28 (m, 2 H, 6-H), 0.86–0.77 [m, 27 H, $(CH_3)_3C$], 0.22–0.01 (m, 18 H, CH_3Si) ppm. ^{13}C NMR (100 MHz, [D$_6$]acetone): δ = 161.83 (C=N), 146.64, 145.02, 144.45, 142.47 (Ar), 101.17 (C-1), 74.44 (C-2), 71.64 (C-3), 70.32 (C-5), 69.52 (C-4), 67.47 (C-6), 25.50, 25.33, 25.14, 17.69, 17.46 [$(CH_3)_3C$], –5.13, –5.77, –5.86 (CH_3Si) ppm. HRMS (MALDI-TOF): calcd. for $C_{29}H_{55}N_3O_5Si_3$ 609.3450 $[M + Na]^+$; found 632.3455.

2-(2-Thienyl)-1,3-oxazoline 18c: Compound **14c** (0.197 g, 0.26 mmol) was added to a heterogeneous solution of NaH (10.0 mg, 0.39 mmol) in dry DCM (2.0 mL) under N_2. 15-Crown-5 ether (0.1 mL) was subsequently added, and the mixture was allowed to react at –78 °C for 2 h. Upon addition of the crown ether fizzing was observed along with a change in color of the reaction mixture from white to yellow. The reaction was monitored by TLC, and upon disappearance of the starting material the reaction was quenched with distilled water. The reaction mixture was diluted in DCM (50.0 mL) and washed with distilled water (3 × 100 mL). The organic layer was dried with $MgSO_4$, and the solvent was removed in vacuo. The crude mixture (0.180 g) was purified by flash column chromatography on silica gel (hexane/ethyl acetate, 7:1, v/v) to give a white solid (0.140 g, 88%). R_f = 0.41. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.61 (d, J = 3.68 Hz, 1 H, Ar), 7.44 (dd, J = 3.68, J = 2.58 Hz, 1 H, Ar), 7.06 (dd, J = 3.68, J = 2.55 Hz, 1 H, Ar), 6.11 (d, $J_{1\text{-}2}$ = 6.84 Hz, 1 H, 1-H), 4.19 (dd, $J_{2\text{-}1}$ = 6.88, $J_{2\text{-}3}$ = 1.36 Hz, 1 H, 2-H), 3.73–3.69 (m, 4 H, 3-H, 4-H, 6-H), 3.31 (m, 1 H, 5-H), 0.88–0.81 [m, 27 H, $(CH_3)_3C$], 0.11–0.03 (m, 18 H, CH_3Si) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.99 (C=N), 130.55, 130.12, 129.90, 127.46 (Ar), 100.00 (C-1), 74.37 (C-2), 70.23 (C-3), 67.46 (C-5), 63.84 (C-4), 25.91, 25.66, 18.36, 17.83, 17.68 [$(CH_3)_3C$], –4.03, –4.55, –4.99, –5.22 (CH_3Si) ppm. HRMS (MALDI-TOF): calcd. for $C_{29}H_{55}NO_5SSi_3$ 613.3109 $[M + H]^+$; found 614.3187.

2-Phenyl-1,3-oxazoline 18d: Compound **14d** (0.200 g, 0.27 mmol) was added to a heterogeneous solution of NaH (14.0 mg, 0.41 mmol) in dry DCM (2.0 mL) under N_2. 15-Crown-5 ether (0.1 mL) was subsequently added, and the mixture was allowed to react at –78 °C for 2 h. Upon addition of the crown ether fizzing was observed along with a change in color of the reaction mixture from white to yellow. The reaction was monitored by TLC, and upon disappearance of the starting material the reaction was quenched with distilled water. The reaction mixture was diluted in DCM (50 mL) and washed with distilled water (3 × 100 mL). The organic layer was dried with $MgSO_4$, and the solvent was removed in vacuo. The crude mixture (0.180 g) was purified by flash column chromatography on silica gel (hexane/ethyl acetate, 10:1, v/v) to give a white solid (0.120 g, 73%). R_f = 0.40. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.95 (d, J = 6.84 Hz, 2 H, Ar), 7.42 (t, J = 6.58, J = 4.50 Hz, 1 H, Ar), 7.39 (d, J = 7.0 Hz, 2 H, Ar), 6.14 (d, $J_{1\text{-}2}$ = 3.68 Hz, 1 H, 1-H), 4.22 (dd, $J_{2\text{-}1}$ = 1.40, $J_{2\text{-}3}$ = 1.36 Hz, 1 H, 2-H), 3.74–3.70 (m, 1 H, 3-H), 3.67 (d, $J_{3\text{-}4}$ = 2.72 Hz, 1 H, 4-H) 3.68–3.61 (m, 1 H, 5-H), 3.29–3.25 (m, 2 H, 6-H), 0.98–0.84 [m, 27 H, $(CH_3)_3C$], 0.23–0.04 (m, 18 H, CH_3Si) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.32 (C=N), 131.54, 127.29 (Ar), 100.60 (C-1), 74.30 (C-2), 71.85 (C-3), 70.47 (C-5), 67.67 (C-4), 63.91 (C-6), 18.46, 17.95, 17.78 [$(CH_3)_3C$], –3.93, –4.86, –5.08, –5.12 (CH_3Si) ppm. HRMS (MALDI-TOF): calcd. for $C_{31}H_{57}NO_5Si_3$ 607.3545 $[M + H]^+$; found 608.2984.

Supporting Information (see footnote on the first page of this article): NMR spectra of the compounds synthesized.

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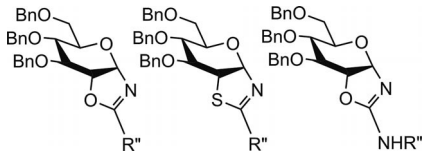
A novel one-pot synthesis of *N*-glycooxazolines, *N*-glycothiazolines, and *N*-glycoaminooxazolines has been developed based on the frameworks of the natural products Allosamidin and Trehazolin. Access to these constructs was possible by the addition of heteroaryl amides, thiobenzamide, and substituted ureas to glycals in the presence of *N*-iodosuccinimide and propionitrile at high temperatures.



Carbohydrate Heterocycles

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