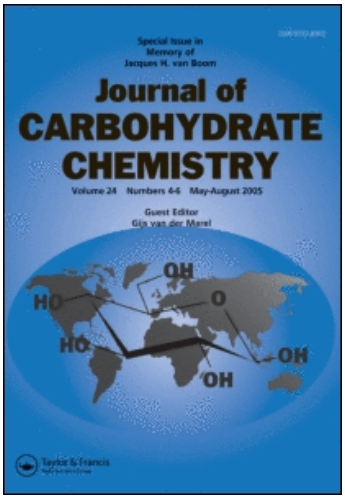

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Synthesis and Reactions of 3,4-Di-*O*-Acetyl-6-amino-6-deoxy-and 6-Acetamido-3,4-Di-*O*-acetyl-6-deoxy-d-glucal[1]

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SYNTHESIS AND REACTIONS OF 3,4-DI-*O*-ACETYL-6-AMINO-6-DEOXY- AND 6-ACETAMIDO-3,4-DI-*O*-ACETYL-6-DEOXY-D-GLUCAL[1]

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ABSTRACT

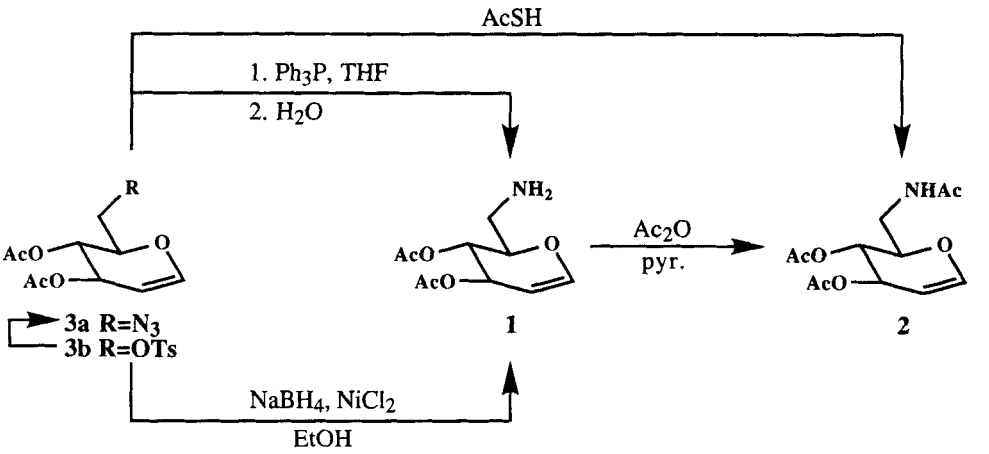
The reduction of 3,4-di-*O*-acetyl-6-azido-6-deoxy-D-glucal (**3a**) with nickel boride gives the aminoglycal **1**; whereas reduction with thiolacetic acid leads directly to the amidoglycal **2**. The aminoglycal **1** is sensitive to aqueous acid and rearranges to (1*R*)-(2-furyl)-2-acetamidoethanol (**4**). This furan gives a Diels-Alder adduct **5** with *N*-phenylmaleimide in which the nitrogen and oxygen on the side chain have interchanged positions. In contrast, the amidoglycal **2** reacts with ammonium nitrate in trifluoroacetic anhydride and with acidic mercuric sulfate to give (*E*)-5-acetamido-(3*S*)-acetoxy-(4*R*)-formoxy-1-nitro-1-pentene (**6**) and 6-acetamido-4-*O*-acetyl-2,3,6-trideoxy-*aldehydo*-D-*erythro*-*trans*-hex-2-enose (**7**) respectively. The amidoglycal **2** also undergoes an intramolecular palladium (II) catalyzed cyclization reaction leading to a pair of diastereomeric (4*R*)-acetoxy-7-acetyl-7-aza-2-oxabicyclo[3.2.1]oct-5-enes (**8**).

INTRODUCTION

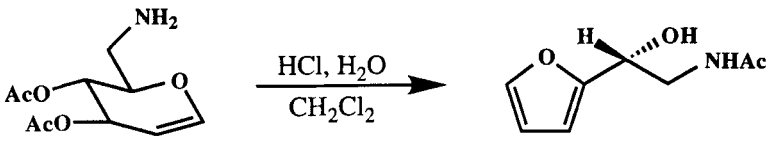
Reactions at the double bond of glycals make these unsaturated sugars useful intermediates in carbohydrate synthesis[2] including the synthesis of oligosaccharides.[3] Our interest in glycals centers around cleavage reactions between C-1 and the ring oxygen and between C-1 and C-2 which we have previously reported.[4] The products from these types of reactions lead to chiral acyclic compounds which are potentially useful in natural product synthesis. In a projected synthesis of (-)anisomycin[5] and its various epimers from such chiral acyclic precursors we needed glycals substituted with a nitrogen functionality at C-6. This paper describes the synthesis of 3,4-di-*O*-acetyl-6-amino-6-deoxy-D-glucal (**1**), an improved synthesis of 6-acetamido-3,4-di-*O*-acetyl-6-deoxy-D-glucal[6] (**2**), and some reactions of these nitrogen containing glycals.

RESULTS AND DISCUSSION

Synthesis of 3,4-Di-*O*-acetyl-6-amino-6-deoxy- and 6-Acetamido-3,4-di-*O*-acetyl-6-deoxy-D-glucal (1 & 2). We chose as our starting material 3,4-di-*O*-acetyl-6-azido-6-deoxy-D-glucal (**3a**) which was readily prepared by azide ion displacement of the tosylate group of 3,4-di-*O*-acetyl-6-*O*-tosyl-D-glucal[7] (**3b**) according to the procedure of Dunkerton *et al.*[6] The tosylate in turn can be prepared in 86% yield from D-glucose by two consecutive one-pot reactions using the procedure of Miljkovic *et al.*[8] After trying a number of agents to reduce the azide **3a** to the amine **1**, we settled on employing nickel boride[9] as the reducing agent and prepared 3,4-di-*O*-acetyl-6-amino-6-deoxy-D-glucal (**1**) in 95% yield from the azide **3a**. Only a 41% yield of the amine **1** was obtained when the Staudinger reaction[10] was used for reduction of the azide **3a**. The amine **1** was quantitatively *N*-acetylated to give **2**. This compound had been previously prepared by the reacetylation of the lithium aluminum hydride reduction product of the azide **3a**.[6] Prompted by the work of Rosen *et al.*,[11] we developed a convenient one step reductive acylation method for the direct transformation of the azide **3a** to the amide **2** using thiolacetic acid.



Reactions of 3,4-Di-*O*-acetyl-6-amino-6-deoxy-D-glucal (1). As mentioned previously, the amine **1** can be acetylated with acetic anhydride in pyridine in quantitative yield. However, under acidic conditions the amine **1** appears to be quite labile. We observed a rearrangement reaction when we attempted purification of a chloroform solution of the amine **1** by extraction with 10% HCl. The structure of the rearranged product was assigned as (1*R*)-(2-furyl)-2-acetamidoethanol (**4**) by ^{1}H NMR. The *R*



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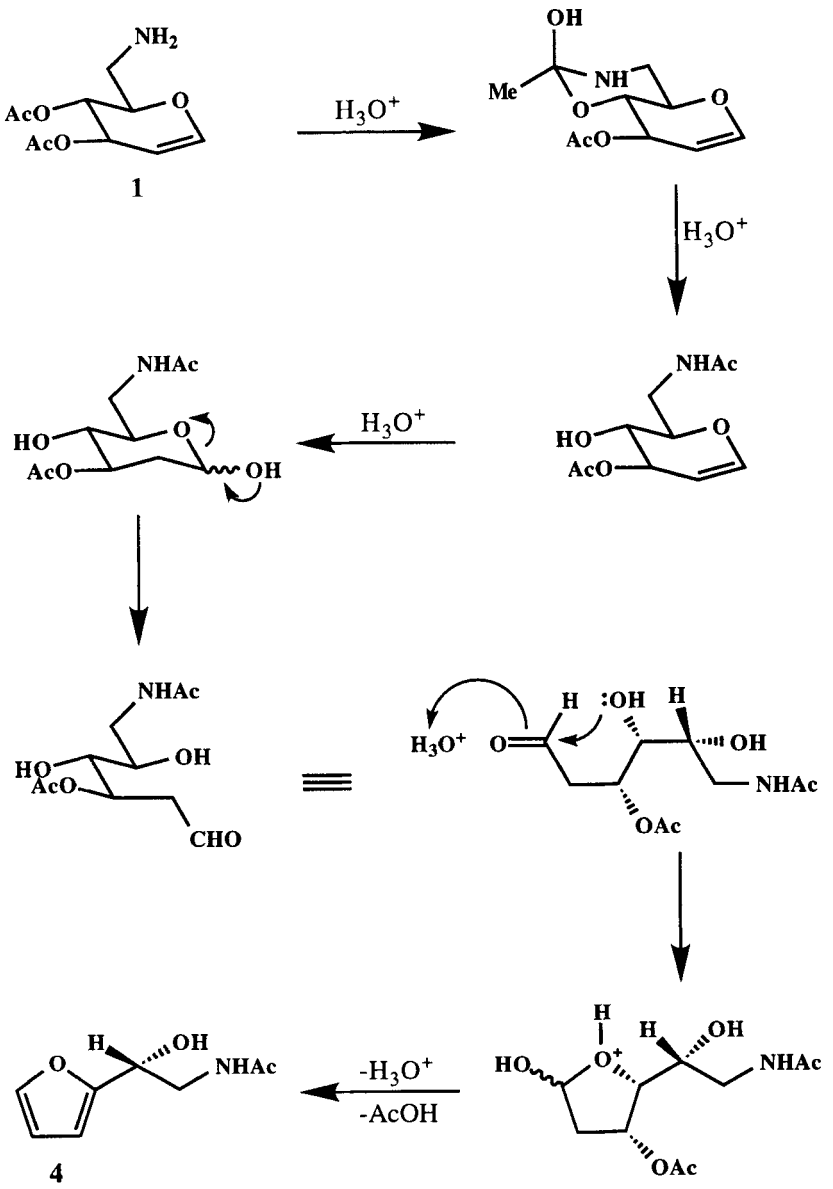
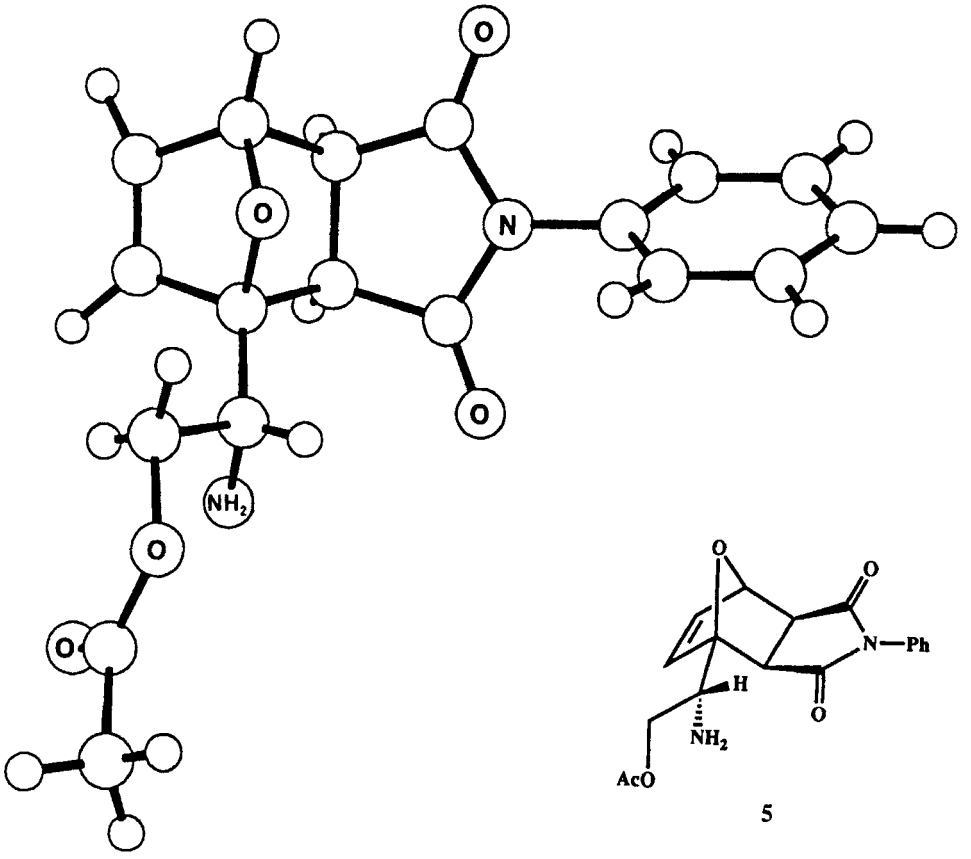
configuration was assigned to the lone stereocenter based upon the configuration of the starting material and the proposed mechanism of formation (Scheme 1).



Scheme 1

Under acidic conditions, glycals have been observed to lead to similar types of rearrangement products.[12] We carried out a Diels-Alder reaction of the furan **4** with *N*-phenylmaleimide in refluxing toluene[13] in an attempt to obtain a crystalline derivative suitable for a X-ray structure determination. From the X-ray structure, the configuration of the stereocenter could then be conclusively determined. A Diels-Alder adduct **5**, whose X-ray structure is shown below, shows that the rearranged product was indeed a furan. To our surprise, however, the nitrogen and oxygen atoms on the side chain have

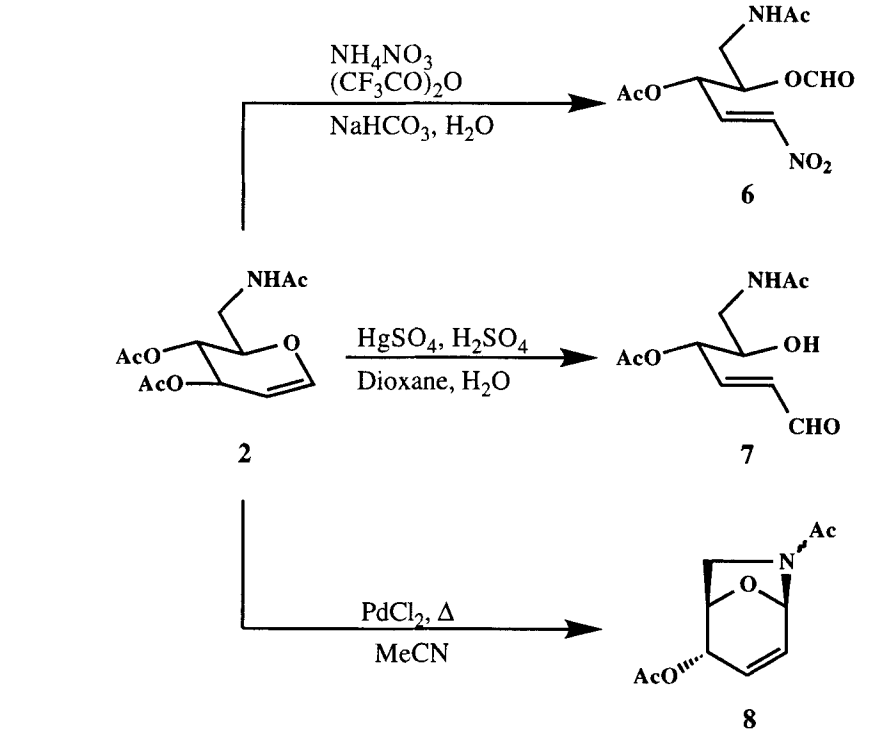


5

interchanged positions with retention of configuration at the stereocenter. This discrepancy between the amido-alcohol structure **4** indicated by NMR and the amino-ester structure **5** determined by X-ray can be explained by another rearrangement. The fact that there is retention of configuration at the stereocenter on the side chain eliminates the possibility of an intramolecular S_N2 reaction leading to an aziridine which is opened

with acetate or acetic acid. This mechanism would require an inversion of configuration. However, the small amount of acid which is usually present in commercial *N*-phenylmaleimide[14] could catalyze the formation of an aziridine via a S_N1 pathway. Two diastereomeric adducts with the exo configuration should be observed. We cannot rule out the S_N1 process because we only isolated a single diastereomer as a crystalline adduct in only 33% yield. It is also possible that a single diastereomer is produced due to asymmetric induction by the stereocenter adjacent to the cationic site during the course of the reaction. The Diels-Alder reaction of the furan **4** needs to be studied in more detail before a definitive mechanism can be proposed.

Reactions of 6-Acetamido-3,4-Di-*O*-acetyl-6-deoxy-D-glucal (2). Unlike 3,4-di-*O*-acetyl-6-amino-6-deoxy-D-glucal (**1**), 6-acetamido-3,4-di-*O*-acetyl-6-deoxy-D-glucal (**2**) smoothly underwent reactions at the double bond. When the amidoglycal **2**



was treated with trifluoroacetic anhydride and ammonium nitrate, the expected cleavage product,[4] (*E*)-5-acetamido-(3*S*)-acetoxy-(4*R*)-formoxy-1-nitro-1-pentene (**6**) was obtained in 65% yield. The expected acyclic product, 6-acetamido-4-*O*-acetyl-2,3,6-trideoxy-*aldehydo*-D-*erythro*-*trans*-hex-2-enose (**7**), was obtained in 95% yield when the

amidoglycal **2** was reacted with aqueous acidic mercury(II) sulfate according to the procedure of Perlin.[13] Although the amidoglycal **2** did not react with palladium (0), the π-allyl complex formed with palladium (II) underwent an intramolecular attack by the amide nitrogen at the anomeric carbon to give a pair of diastereomeric (4*R*)-acetoxy-7-acetyl-7-aza-2-oxabicyclo[3.2.1]oct-5-enes (**8**). This diastereoisomerism is due to a high barrier of rotation about the amide linkage. The 2:1 mixture (by ^{1}H NMR) of stereoisomers could not be separated by column chromatography.

CONCLUSION

In this paper we have presented efficient syntheses of the aminoglycal **1** and the amidoglycal **2**. In contrast to the amidoglycal **2**, which undergoes reactions at the double bond under acidic conditions, the aminoglycal **1** is labile under acidic conditions.

EXPERIMENTAL

General Procedures. Melting points were determined on a Haake-Buchler melting point apparatus and were uncorrected. Optical rotations were determined with a Perkin-Elmer 241 polarimeter at room temperature. Infrared spectra were recorded on an Analect FX-6160 infrared spectrophotometer. ^{1}H NMR spectra were recorded on a Varian XL-200 spectrometer at 200.05 MHz. Chemical shifts for ^{1}H resonances were recorded relative to tetramethylsilane (0.00 ppm). ^{13}C NMR spectra were recorded on a Varian XL-200 spectrometer at 50.3 MHz with complete proton decoupling. Chemical shifts for ^{13}C resonances were recorded relative to deuteriochloroform (76.91 ppm). Coupling data were recorded using the distortionless enhancement by polarization transfer method. High resolution mass spectra were recorded on a VG Fisons ZAB-DE spectrometer at the Mass Spectrometry Center, University of Pennsylvania. The X-ray structure was determined by Dr. Herman L. Ammon at the Department of Chemistry and Biochemistry, University of Maryland, College Park. The progress of reactions was monitored by thin layer chromatography using aluminum supported plates of silica gel 60 (0.2 mm, F-254, E. Merck). Solvent systems consisted of ethyl acetate and petroleum ether in volume:volume ratios as indicated following the R_f value. Components were detected by observation under short wavelength ultraviolet light, spraying with concentrated sulfuric acid, or immersion in Hanessian dip [90 mL H_2O, 10 mL H_2SO_4,

2 g $(NH_4)_2MoO_4$, 1 g $Ce(SO_4)_2$], and charring with a heat gun. Flash chromatography was performed on silica gel (40μm particle size). Acetonitrile and tetrahydrofuran were both purchased anhydrous from Aldrich Chemical Company and used as received. Dimethyl sulfoxide and triethylamine were dried by distillation from sodium hydroxide. Methylene chloride was dried by passing through a column of basic alumina (pH = 7.3). Pyridine was dried by distillation from barium oxide and sodium hydroxide.

3,4-Di-*O*-acetyl-6-amino-6-deoxy-D-glucal (1). In a 100 mL round-bottom flask, 0.40 g (1.6 mmol) of 3,4-di-*O*-acetyl-6-azido-6-deoxy-D-glucal[6] **(3a)** was dissolved in 4.5 mL of ethanol and cooled to 0°C in an ice bath. The solution was treated with 0.08 g (2 mmol) of sodium borohydride which caused the evolution of some gas. Then 0.28 g of nickel (II) chloride was added. The reaction mixture turned black while bubbling vigorously. The ice bath was removed, a drying tube was installed, and the reaction mixture was stirred for 1 h at room temperature. The reaction mixture was poured over 8.0 mL of 5% sodium bicarbonate solution and extracted with three 20 mL portions of ethyl acetate. The extracts were combined, dried over anhydrous sodium sulfate, filtered, and concentrated to give a golden taffy (0.34 g, 95%): R_f = 0.56 (MeCN); $[\alpha]^{23}_D$ -80.7° (*c* 1, $CHCl_3$); IR (cm^{-1}, neat): 3297 (N-H), 3059 (C-H), 1740 (C=O), 1651 (C=C), 1190 (C-O), 1119 (C-N), 1067 (C-C); ^1H NMR ($CDCl_3$) δ 6.40 (bs, 2H, NH_2), 6.35 (dd, 1H, $J_{1,2}$ = 6.0 Hz, $J_{1,3}$ = 1.7 Hz, H-1), 5.38 (ddd, $J_{2,3}$ = 2.0 Hz, $J_{3,4}$ = 7.7 Hz, H-3), 4.73 (dd, 1H, H-2), 4.06 (ddd, 1H, $J_{5,6}$ = 2.4 Hz, $J_{6,6'}$ = 15.0 Hz, $J_{6,N}$ = 8.1 Hz, H-6), 3.82 (ddd, 1H, $J_{4,5}$ = 10.4 Hz, $J_{5,6'}$ = 2.8 Hz, H-5), 3.63 (dd, 1H, H-4), 3.24 (ddd, 1H, $J_{6',N}$ = 5.0 Hz, H-6′), 2.10 (s, 3H, CH_3), 2.09 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$) δ 172.77 (s, C=O), 171.07 (s, C=O), 145.31 (d, C-1), 100.34 (d, C-2), 77.67 (d, C-3), 71.42 (d, C-4), 66.28 (d, C-5), 39.30 (t, C-6), 22.58 (q, CH_3), 21.00 (q, CH_3); HRMS Calcd for $C_{10}H_{16}NO_5$: 230.1032, Found: 230.1057 (MH^+).

6-Acetamido-3,4-di-*O*-acetyl-6-deoxy-D-glucal[6] (2). In a 25 mL round-bottom flask, 5.00 g (19.6 mmol) of 3,4-di-*O*-acetyl-6-azido-6-deoxy-D-glucal[6] **(3a)** was dissolved in 5.6 mL (78 mmol) of thiolacetic acid and stirred for 4 h at room temperature. The stirring bar was removed, and the reaction mixture was concentrated. The crude product was purified by flash chromatography to give an orange syrup (3.47 g, 65%): R_f = 0.46 (MeCN); IR (cm^{-1}, neat): 3386 (N-H), 2931 (C-H), 1739 (C=O), 1653 (C=C), 1233 (C-O), 1370 (C-N), 1030 (C-C); ^1H NMR ($CDCl_3$) δ 6.44 (dd, 1H, $J_{1,2}$ = 6.1 Hz, $J_{1,3}$ = 1.5 Hz, H-1), 5.79 (bs, 1H, NH), 5.41 (ddd, 1H, $J_{2,3}$ = 2.8 Hz, $J_{3,4}$ = 6.5 Hz, H-3), 5.13 (dd, 1H, $J_{4,5}$ = 9.1 Hz, H-4), 4.82 (dd, 1H, H-2), 4.07 (ddd, 1H, $J_{5,6}$ = 3.1 Hz, $J_{5,6'}$ = 6.1 Hz, H-5), 3.68 (ddd, 1H, $J_{6,6'}$ = 14.6 Hz, $J_{6,N}$ = 6.3 Hz, H-6), 3.48 (ddd, 1H, $J_{6',N}$ = 6.0 Hz, H-6′), 2.11 (s, 3H, CH_3), 2.05 (s, 3H, CH_3), 2.00 (s, 3H, CH_3); ^{13}C NMR

($CDCl_3$) δ 170.02 (s, C=O), 169.73 (s, C=O), 169.12 (s, C=O), 144.92 (d, C-1), 98.60 (d, C-2), 74.32 (d, C-3), 67.37 (d, C-4), 67.25 (d, C-5), 37.92 (t, C-6), 22.12 (q, CH_3), 20.23 (q, CH_3), 20.07 (q, CH_3).

(1*R*)-(2-Furyl)-2-acetamidoethanol (4). In a 25 mL round-bottom flask, 0.09 g (0.4 mmol) of 3,4-di-*O*-acetyl-6-amino-6-deoxy-D-glucal **(1)** was dissolved in 150 μL of methylene chloride, and 10.0 mL of 10% hydrochloric acid solution was added. The reaction mixture was stirred vigorously for 3 h at room temperature. The reaction mixture was neutralized with sodium carbonate and extracted with three 10.0 mL portions of methylene chloride. The extracts were combined, dried over anhydrous sodium sulfate, filtered and concentrated to give a golden syrup (0.02 g, 30%): R_f = 0.38 (MeCN); $[\alpha]^{27}_D$ +18.1° (*c* 1, $CHCl_3$); IR (cm^{-1}, neat): 3313 (O-H, N-H), 2973 (C-H), 1653 (C=O), 1542 (C=C), 1371 (C-N), 1231 (C-O), 1040 (C-C); ^1H NMR ($CDCl_3$) δ 7.36 (dd, 1H, $J_{4,5}$ = 1.8 Hz, $J_{3,5}$ = 0.8 Hz, H-5), 6.54 (bs, 1H, NH), 6.32 (dd, 1H, $J_{3,4}$ = 3.3 Hz, H-4), 6.28 (dd, 1H, H-3), 4.81 (dd, 1H, $J_{1,2}$ = 3.8 Hz, $J_{1,2'}$ = 7.6 Hz, H-1), 4.29 (bs, 1H, OH), 3.73 (ddd, 1H, $J_{2,2'}$ = 13.9 Hz, $J_{2,N}$ = 6.4 Hz, H-2), 3.49 (ddd, 1H, $J_{2',N}$ = 5.5 Hz, H-2'), 1.98 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$) δ 171.61 (s, C=O), 154.26 (s, C), 141.89 (d, C-5), 110.07 (d, C-4), 106.35 (d, C-3), 66.67 (d, C-1), 44.24 (t, C-2), 22.73 (q, CH_3); HRMS Calcd for $C_8H_{11}NO_3$: 169.0739, Found: 169.0760 (M^+).

Diels-Alder Adduct of (1*R*)-(2-Furyl)-2-acetamidoethanol and *N*-Phenylmaleimide (5). A 50 mL round-bottom flask was flushed with nitrogen and charged with 0.18 g (1.1 mmol) of (1*R*)-(2-furyl)-2-acetamidoethanol **(4)**. The starting material was dissolved in 25 mL of dry benzene, and 1.88 g (10.9 mmol) of *N*-phenylmaleimide was added. The reaction mixture was heated to reflux and stirred under nitrogen for 30 h at 95°C. After heating, the reaction mixture was allowed to cool. The stirring bar was removed, and the reaction mixture was concentrated. The crude product was purified by flash chromatography to give a white crystalline solid (0.12 g, 33%): mp = 167-170°C; R_f = 0.29 (MeCN).

(*E*)-5-Acetamido-(3*S*)-acetoxy-(4*R*)-formoxy-1-nitro-1-pentene (6). A 25 mL round-bottom flask was flushed with nitrogen and charged with 0.40 g (1.5 mmol) of 6-acetamido-3,4-di-*O*-acetyl-6-deoxy-D-glucal **(2)** and 0.14 g (1.7 mmol) of ammonium nitrate. The mixture was dissolved in 1.5 mL of trifluoroacetic anhydride, and a drying tube was installed. The reaction mixture was stirred for 15 min at room temperature when it became clear. The solution was stirred for an additional 50 min at room temperature. The solution was then treated with 6.0 mL of 5% sodium bicarbonate solution. Bubbling and a white vapor were observed above the reaction mixture which was stirred for 15 min at room temperature. The reaction mixture was extracted with

three 25 mL portions of methylene chloride. The extracts were combined and washed with 75 mL of 5% sodium bicarbonate solution. The extracts were then washed with 9.0 mL of saturated sodium chloride solution, dried over anhydrous sodium sulfate, filtered, and concentated to give a golden syrup (0.25 g, 62%): R_f = 0.82 (MeCN); $[\alpha]^{23}_D$ +16.9° (*c* 1, $CHCl_3$); IR (cm^{-1}, neat): 3297 (N-H), 2928 (C-H), 1735 (C=O), 1654 (C=C), 1534 (N=O), 1433 (C-N), 1358 (N-O), 1229 (C-O), 1039 (C-C); ^1H NMR ($CDCl_3$) δ 8.09 (s, 1H, CHO), 7.24 (dd, 1H, $J_{1,2}$ = 13.4 Hz, $J_{2,3}$ = 4.2 Hz, H-2), 7.19 (dd, 1H, $J_{1,3}$ = 0.8 Hz, H-1), 5.78 (bs, 1H, NH), 5.71 (ddd, 1H, $J_{3,4}$ = 4.1 Hz, H-3), 5.27 (ddd, 1H, $J_{4,5}$ = 5.7 Hz, $J_{4,5'}$ = 6.2 Hz, H-4), 3.69 (ddd, 1H, $J_{5,5'}$ = 14.7 Hz, $J_{5,N}$ = 5.7 Hz, H-5), 3.40 (ddd, 1H, $J_{5',N}$ = 6.2 Hz, H-5′), 2.16 (s, 3H, CH_3), 2.00 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$) δ 170.99 (s, C=O), 169.24 (s, C=O), 159.71 (d, CHO), 141.86 (d, C-1), 133.97 (d, C-2), 71.52 (d, C-3), 68.16 (d, C-4), 38.48 (t, C-5), 22.67 (q, CH_3), 20.42 (q, CH_3); HRMS Calcd for $C_{10}H_{14}N_2O_7$: 274.0801, Found: 274.0828 (M^+).

6-Acetamido-4-*O*-acetyl-2,3,6-trideoxy-*aldehydo*-D-*erythro-trans*-hex-2-enose (7). In a 10 mL round-bottom flask, 0.20 g (0.74 mmol) of 6-acetamido-3,4-di-*O*-acetyl-6-deoxy-D-glucal (**2**) was dissolved in 1.0 mL of 1,4-dioxane. The solution was acidified with 4.0 mL of 5 mM sulfuric acid, and 0.01 g of mercuric sulfate was added. The reaction mixture was stirred for 3 h at room temperature. The solution was neutralized by adding 0.01 g of barium carbonate and stirring for 30 min at room temperature. The mixture was diluted with 50 mL of methylene chloride. The solution was dried over anhydrous sodium sulfate, filtered, and concentrated to give a yellow syrup (0.16 g, 95%): R_f = 0.83 (MeCN); $[\alpha]^{23}_D$ -15.7° (*c* 1, $CHCl_3$); IR (cm^{-1}, neat): 3345 (O-H), 3297 (N-H), 2918 (C-H), 1744 (C=O), 1690 (C=C), 1432 (C-N), 1235 (C-O), 1036 (C-C); ^1H NMR ($CDCl_3$) δ 9.60 (d, 1H, $J_{1,2}$ = 7.8 Hz, H-1), 7.00 (dd, 1H, $J_{2,3}$ = 15.9 Hz, $J_{3,4}$ = 4.4 Hz, H-3), 6.26 (ddd, 1H, $J_{2,4}$ = 1.7 Hz, H-2), 6.20 (bs, 1H, NH), 5.50 (ddd, 1H, $J_{4,5}$ = 7.4 Hz, H-4), 3.85 (ddd, 1H, $J_{5,6}$ = 2.7 Hz, $J_{5,6'}$ = 5.7 Hz, H-5), 3.70 (ddd, 1H, $J_{6,6'}$ = 14.6 Hz, $J_{6,N}$ = 8.4 Hz, H-6), 3.18 (ddd, 1H, $J_{6',N}$ = 5.6 Hz, H-6′), 2.17 (s, 3H, CH_3), 2.07 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$) δ 192.96 (d, C-1), 172.71 (s, C=O), 169.92 (s, C=O), 150.98 (d, C-2), 132.47 (d, C-3), 72.60 (d, C-4), 72.08 (d, C-5), 42.25 (t, C-6), 22.70 (q, CH_3), 20.69 (q, CH_3); HRMS Calcd for $C_{10}H_{16}NO_5$: 230.1028, Found: 230.1060 (MH^+).

(4*R*)-Acetoxy-7-acetyl-7-aza-2-oxabicyclo[3.2.1]oct-5-ene (8). A 100 mL three-necked flask was flushed with nitrogen and charged with 0.02 g of palladium chloride and 35 mL of dry acetonitrile. The mixture was heated to reflux and stirred for 1 h under nitrogen. The solution was allowed to cool back to room temperature, and 0.20 g (0.74 mmol) of 6-acetamido-3,4-di-*O*-acetyl-6-deoxy-D-glucal (**2**) was added as a

solution in 1.0 mL of dry acetonitrile. The reaction mixture was heated again to reflux and stirred for 2 h under nitrogen. The reaction mixture was allowed to cool and was concentrated. The residue was dissolved in 25 mL of methylene chloride and filtered. The filtrate was concentrated to give 0.16 g of an amber syrup. The crude product was purified on a prep. plate to give a yellow syrup (0.07 g, 40%): R_f = 0.48 (MeCN); IR (cm^{-1}, neat): 2960 (C-H), 1735 (C=O), 1651 (C=C), 1424 (C-N), 1240 (C-O), 1034 (C-C); ^1H NMR ($CDCl_3$) Major isomer: δ 6.51 (dd, 1H, $J_{1,6}$ = 3.9 Hz, $J_{5,6}$ = 9.6 Hz, H-6), 5.99 (d, 1H, H-1), 5.81 (ddd, 1H, $J_{3,5}$ = 1.6 Hz, $J_{4,5}$ = 4.1 Hz, H-5), 4.86 (dd, 1H, $J_{3,4}$ = 1.1 Hz, H-4), 4.83 (ddd, 1H, $J_{3,8}$ = 7.3 Hz, $J_{3,8'}$ = 1.0 Hz, H-3), 3.81 (dd, 1H, $J_{8,8'}$ = 9.7 Hz, H-8), 3.27 (dd, 1H, H-8′), 2.14 (s, 3H, CH_3), 2.04 (s, 3H, CH_3); Minor isomer: δ 6.38 (dd, 1H, $J_{1,6}$ = 3.5 Hz, $J_{5,6}$ = 9.7 Hz, H-6), 5.87 (ddd, 1H, $J_{3,5}$ = 1.6 Hz, $J_{4,5}$ = 4.1 Hz, H-5), 5.60 (d, 1H, H-1), 4.86 (dd, 1H, $J_{3,4}$ = 1.1 Hz, H-4), 4.78 (ddd, 1H, $J_{3,8}$ = 7.5 Hz, $J_{3,8'}$ = 1.0 Hz, H-3), 3.91 (dd, 1H, $J_{8,8'}$ = 11.7 Hz, H-8), 3.15 (dd, 1H, H-8′), 2.14 (s, 3H, CH_3), 2.11 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$) Major isomer: δ 170.34 (s, C=O), 167.07 (s, C=O), 133.44 (d, C-6), 122.34 (d, C-5), 79.39 (d, C-1), 76.64 (d, C-4), 67.68 (d, C-3), 45.16 (t, C-8), 22.00 (q, CH_3), 20.86 (q, CH_3); Minor isomer: δ 170.44 (s, C=O), 170.16 (s, C=O), 131.84 (d, C-6), 123.22 (d, C-5), 80.82 (d, C-1), 75.68 (d, C-4), 67.37 (d, C-3), 43.46 (t, C-8), 22.22 (q, CH_3), 20.86 (q, CH_3); HRMS Calcd for $C_{10}H_{14}NO_4$: 212.0923, Found: 212.0904 (MH^+).

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