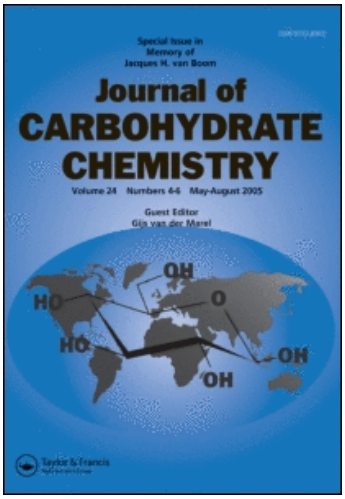

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Studies of the Synthesis of Rubranitrose and Crystal Structure of Methyl 2,3,6-Trideoxy-3-*C*-Methyl-3-Nitro-α-D-*Ribo*-Hexopyranoside

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STUDIES OF THE SYNTHESIS OF RUBRANITROSE AND CRYSTAL STRUCTURE OF METHYL 2,3,6-TRIDEOXY-3-*C*-METHYL-3-NITRO-α-D-*RIBO*-HEXOPYRANOSIDE

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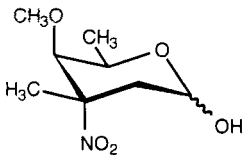
ABSTRACT

The branched-chain nitro sugar methyl 2,3,6-trideoxy-3-*C*-methyl-3-nitro-α-D-*ribo*-hexopyranoside **4** was investigated as a precursor to D-rubranitrose, a nitro sugar found in the antibiotic rubradirin. X-ray cyrstallographic analysis of **4** shows that the pyranose ring adopts the $^4C_1$ conformation with the methoxy group at C-1 and the nitro group at C-3 in a 1,3-diaxial relationship. There is an intermolecular hydrogen bond involving a nitro group oxygen of one monosaccharide residue and the C-4 hydroxyl group of the adjacent residue in the crystal lattice. This interaction results in a helical crystal packing. A series of nucleophilic displacement reactions was carried out on the triflate derivative of **4** in an attempt to introduce an axial carbon-oxygen bond at C-4 required for rubranitrose. Displacements with acetate and propionate gave as products the monosaccharide esters with the desired D-*xylo* configuration.

INTRODUCTION

The branched-chain nitro sugar rubranitrose **1** occurs in the antitumor antibiotic rubradirin, a member of the ansa macrolide class.[1] One of four known nitro sugars found in nature, rubranitrose contains *trans* diaxial nitro and methoxy groups at C-3 and C-4. A similar substitution pattern is found in the nitro sugar L-evernitrose in which the C-3 nitro and C-4 methoxy groups are *trans* diequatorial.[2] Control of the stereochemistry at these positions in the synthesis of the nitro sugars is a challenging synthetic problem, with most approaches

producing mixtures or requiring many steps.[3] Syntheses of both D-rubranitrose[4] and its L-enantiomer have been described.[3] We developed a synthesis of branched-chain amino sugar **2**,[5] a key intermediate in both the route to D-rubranitrose described by Brimacombe[4a] as well as in our synthesis of the nitro sugar, D-kijanose **3**.[6] In our synthesis of kijanose, methyl 2,3,6-trideoxy-3-*C*-methyl-3-nitro-α-D-*ribo*-hexopyranoside **4**, prepared from **2** by oxidation, was converted to methyl α-D-kijanoside by a sequence involving nucleophilic displacement of triflate **5** with azide and conversion of the azido group to the carbamate. In this study, introduction of an axial carbon-oxygen bond at C-4 in **5** by nucleophilic displacement of the triflate with oxygen nucleophiles was examined as a synthetic route to rubranitrose. Reactions of **5** with carboxylate anions gave ester derivatives **6** with the correct stereochemistry for rubranitrose. In addition, X-ray cystallographic analysis[7] was carried out on the nitro alcohol **4**, which was obtained from **2** by oxidation with dimethyldioxirane (DMDO). The X-ray analysis of **4** revealed a helical crystal packing involving an intermolecular hydrogen bond between a nitro group oxygen on one residue and the C-4 hydroxyl group of its neighbor. The pyranose ring of **4** adopts the $^4C_1$ conformation.



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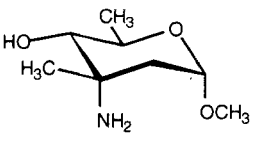

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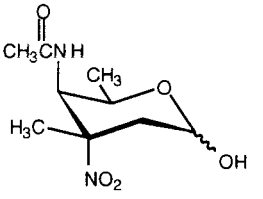

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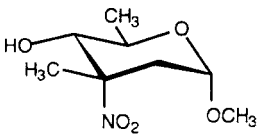

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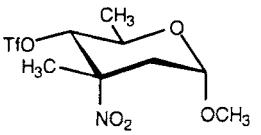

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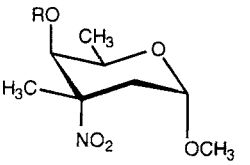


6a: R = MeCO
6b: R = EtCO

RESULTS AND DISCUSSION

Methyl 3-amino-2,3,6-trideoxy-3-*C*-methyl-α-D-*ribo*-hexopyanoside **2** was synthesized by the route developed in this laboratory[5] and oxidized to nitro sugar using MCPBA.[8] Yields were typically in the 40 - 50 % range for the peracid oxidation, so we investigated an alternative method for this transformation. Oxidations of amines with dimethyldioxirane (DMDO) have been studied by Zajac and coworkers[9] and a study involving amino sugars has been reported.[10] DMDO was viewed as an attractive method for

Table 1. Crystallographic Data for $C_8H_{15}NO_5$.*

formula	$C_8H_{15}NO_5$
formula weight	205.21
space group	$P2_1$
a, Å	7.780(1)
b, Å	6.006(2)
c, Å	11.253(2)
β, deg	100.842(9)
V, Å^3	516.5(2)
Z	2
cryst color	colorless
D(calc), g cm^{-3}	1.320
μ(MoKα), cm^{-1}	1.10
temp, K	298(2)
radiation	MoKα (λ = 0.71073 Å)
R(F), %[a]	3.73
R(wF^2), %[a]	7.11

[a] Quantity minimized = $R(wF^2) = \Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[(wF_o^2)^2]^{1/2}$; $R = \Sigma\Delta/\Sigma(F_o)$, $\Delta = |(F_o - F_c|$

*Tables of atomic coordinates, bond lengths, and bond angles have been deposited with the Cambridge Crystallographic Data Centre. These tables may be obtained on request from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK.

the oxidation of **2** since the 2-deoxy glycosidic linkage would be unaffected by the mild conditions and by-products (acetone). Generation of DMDO by procedure of Adam and coworkers[11] followed by addition of a solution of amino alcohol at 0 °C resulted in clean oxidation to nitro sugar **4** in 77% yield after further purification by flash chomatography. Inspection of the ^{1}H NMR spectrum of the crude oxidation product after evaporation of solvent showed no evidence of other products. Crystallization occurred during removal of solvent from the chromatographic fractions. Recrystallization from ethanol - hexane gave crystals of **4** suitable for X-ray analysis.

Crystallographic data were obtained on a Siemens P4 diffractometer. Crystal, data collection, and refinement parameters are given in Table 1. The ORTEP drawing of **4** (Figure 1) shows that the pyranose ring adopts the $^4C_1$ conformation in the solid state with the methoxy group at C-1 and the nitro group at C-3 both in axial positions. Selected dihedral angles are shown in Table 4. The ^{1}H NMR spectrum suggests that **4** adopts the same conformation in solution phase with $J_{1,2a}$ = 3.7 Hz, $J_{1,2e}$ = 1.3 Hz, and $J_{4,5}$ = 9.9 Hz (H-4

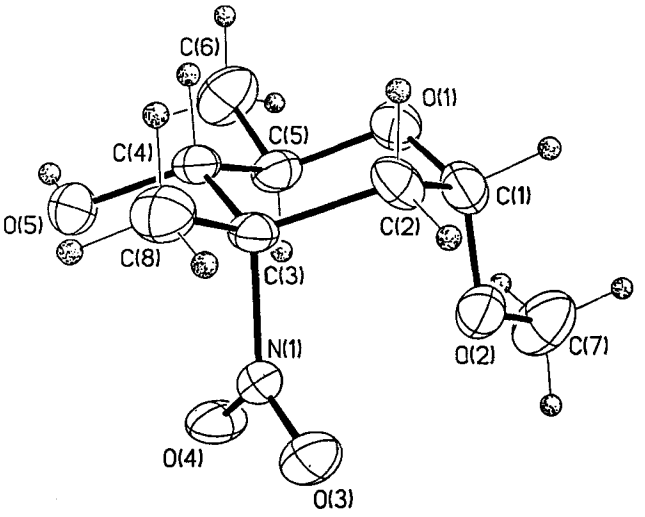


Figure 1. ORTEP diagram of **4** with atomic labeling scheme. Thermal ellipsoid at 30% probability.

and H-5*trans* diaxial). An intermolecular hydrogen bond between a nitro group oxygen and the C-4 hydroxyl group of the adjacent monosaccharide residue was observed in the crystal. The crystal packing is helical (Figure 2).

The conversion of nitro alcohol **4** to D-rubranitrose requires inversion of configuration at C-4 with introduction of a methoxy group at this position. A sequence consisting of oxidation of **4** to the nitro ketone followed by reduction with a bulky hydride donor was first attempted. The attempted reduction of the nitro ketone derived from **4** with L-selectride resulted in the cleavage of the C-3-C-4 bond to give products of ring-opening. By contrast, reduction of the ketone obtained by oxidation of the acetamido deriative of amino alcohol **2** gave the desired C-4 axial alcohol.[4a] Inversion of configuration in **4** by the Martin-modified Mitsunobo reaction also was investigated.[12] Treatment of **4** with *p*-nitrobenzoic acid in the presence of triphenylphosphine and diethylazodicarboxylate resulted in no observable reaction.

Epimerization of **4** under basic conditions was also investigated. We anticipated that a retro-aldol process might occur, followed by ring closure to give an isomeric nitro alcohol. There were no reports of the epimerization of a branched-chain nitro sugar; however, the process has been studied for nitro sugars lacking the C-3 methyl group.[3] These compounds are not good models for **4** because they possess an acidic α-proton at C-3. Epimerization by the retro-aldol process in such systems occurs to give the nitronate with the minimum of $A^{(1,3)}$ strain, and has been shown to result in the formation of the product with an axial orientation of hydroxyl groups on the adjacent carbons in the nitronate.[3] It was of interest to attempt the

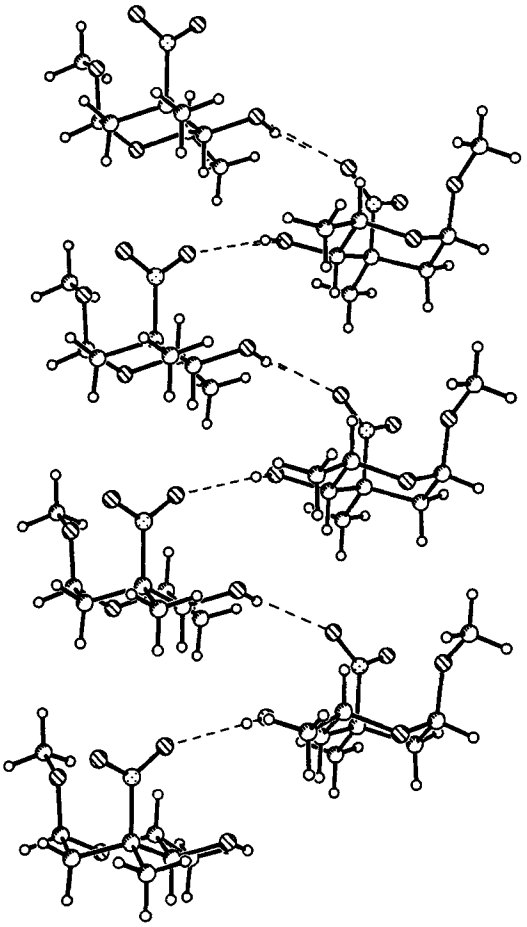


Figure 2. Packing diagram of **4** showing hydrogen bonding between a nitro group oxygen atom and the hydroxyl group of an adjacent residue. Interatomic separation: O(5)•••O(4), 2.886(3) Å.

analogous process on **4**, in which *cyclic* nitronate formation is precluded by the absence of the α-proton at C-3 of the pyranose ring. Treatment of **4** with sodium methoxide in methanol for 36 h at room temperature resulted in the formation of three new nitro sugars, **7** (27%), **8** (42%), and **9** (trace). Structures of **7** and **8** were assigned on the basis of their ^{1}H NMR spectra (Table 5). The resonance for the H-2 proton that is *cis* to the C-3 nitro group is significantly deshielded (H-2_{eq} in **4** and **9**; H-2_{ax} in **7** and **8**). While the desired epimerization at C-4 occurred in the formation of **8**, epimerization occurred at the C-3 position in *both* **7** and **8**. It is interesting that this thermodynamic preference is opposite to what would be expected on the basis of the naturally occurring nitro sugars, in which three of the four possess axial nitro groups, and is also opposite to what would be predicted from A-value for the methyl

Table 2. Atomic coordinates [Å x 10^4] and equivalent isotropic displacement parameters [$Å^2$ x 10^3] for **4**. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
N(1)	10952(3)	5802(3)	2840(2)	44(1)
O(1)	6791(2)	2824(3)	2242(1)	57(1)
O(2)	7765(2)	5770(3)	3557(2)	57(1)
O(3)	11806(2)	6398(3)	3807(1)	61(1)
O(4)	10435(3)	7075(3)	2004(1)	61(1)
O(5)	10326(2)	3446(3)	498(1)	60(1)
C(1)	7698(4)	3463(5)	3408(2)	54(1)
C(2)	9549(3)	2599(5)	3653(2)	50(1)
C(3)	10582(3)	3292(4)	2684(2)	40(1)
C(4)	9472(3)	2747(4)	1454(2)	43(1)
C(5)	7601(3)	3626(5)	1270(2)	51(1)
C(6)	6510(4)	2706(6)	104(2)	80(1)
C(7)	6075(4)	6806(7)	3448(3)	87(1)
C(8)	12386(3)	2193(5)	2857(2)	58(1)

Table 3. Bond lengths [Å] and angles [°] for **4**.

N(1)-O(3)	1.217(2)	N(1)-O(4)	1.220(2)
N(1)-C(3)	1.539(3)	O(1)-C(1)	1.421(3)
O(1)-C(5)	1.444(3)	O(2)-C(l)	1.395(4)
O(2)-C(7)	1.439(3)	O(5)-C(4)	1.430(2)
C(1)-C(2)	1.507(3)	C(2)-C(3)	1.529(3)
C(3)-C(4)	1.523(3)	C(3)-C(8)	1.530(3)
C(4)-C(5)	1.525(3)	C(5)-C(6)	1.526(3)
O(3)-N(1)-O(4)	123.4(2)	O(3)-N(1)-C(3)	116.7(2)
O(4)-N(1)-C(3)	119.9(2)	C(1)-O(1)-C(5)	113.4(2)
C(1)-O(2)-C(7)	113.9(2)	O(2)-C(1)-O(1)	112.3(2)
O(2)-C(1)-C(2)	107.9(2)	O(1)-C(1)-C(2)	111.6(2)
C(1)-C(2)-C(3)	112.8(2)	C(4)-C(3)-C(2)	107.8(2)
C(4)-C(3)-C(8)	111.9(2)	C(2)-C(3)-C(8)	112.6(2)
C(4)-C(3)-N(1)	112.1(2)	C(2)-C(3)-N(1)	107.3(2)
C(8)-C(3)-N(1)	105.1(2)	O(5)-C(4)-C(3)	110.9(2)
O(5)-C(4)-C(5)	111.3(2)	C(3)-C(4)-C(5)	114.3(2)
O(1)-C(5)-C(4)	108.9(2)	O(1)-C(5)-C(6)	106.2(2)
C(4)-C(5)-C(6)	110.7(2)		

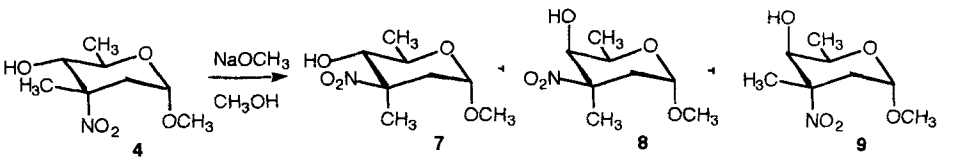
Table 4. Table of dihedral angles [°] for **4**.

O(2) - C(1) - C(2) - C(3)	-68.8 (2)	O(1) - C(1) - C(2) - C(3)	55.0 (3)
C(2) - C(1) - O(2) - C(7)	-175.1 (2)	O(1) - C(1) - O(2) - C(7)	61.5 (3)
C(2) - C(1) - O(1) - C(5)	-59.6 (3)	O(2) - C(1) - O(1) - C(5)	61.6 (3)
C(1) - C(2) - C(3) - C(4)	-49.5 (3)	C(1) - C(2) - C(3) - N(1)	71.4 (2)
C(1) - C(2) - C(3) - C(8)	-173.4 (2)	C(2) - C(3) - C(4) - C(5)	50.5 (3)
C(2) - C(3) - N(1) - O(3)	60.6 (3)	C(2) - C(3) - N(1) - O(4)	121.4 (2)
C(2) - C(3) - C(4) - O(5)	177.4 (2)	N(1) - C(3) - C(4) - C(5)	-67.4 (2)
N(1) - C(3) - C(4) - O(5)	59.5 (2)	C(8) - C(3) - C(4) - C(5)	174.8 (2)
C(8) - C(3) - C(4) - O(5)	-58.3 (3)	C(3) - C(4) - C(5) - C(6)	-171.2 (2)
C(3) - C(4) - C(5) - O(1)	-54.8 (3)	O(5) - C(4) - C(5) - C(6)	62.1 (3)
O(5) - C(4) - C(5) - O(1)	178.5 (2)	C(4) - C(5) - O(1) - C(1)	58.3 (3)
C(6) - C(5) - O(1) - C(1)	177.6 (2)		

Table 5. Comparison of ^{1}H NMR data for compound **4**, **7**, **8**, and **9**.

resonance	4	7	8	9	$J_{i,k}$ (Hz)	4	7	8	9
H-1	4.63	4.78	4.88	4.67	1, 2_{eq}	1.2	1.4	1.2	1.2
H-2_{eq}	2.87	2.40	2.13	2.71	1, 2_{ax}	3.6	4.3	4.8	4.2
H-2_{ax}	1.93	2.25	2.58	1.96	1, 5	0.7	0.6	0.6	0.7
3-C*H*$_3$	1.71	1.81	1.77	1.62	2_{eq}, 2_{ax}	15.0	13.8	14.2	15.2
H-4	3.27	3.92	3.94	4.06	2_{eq}, 4	--	--	1.2	1.2
4-O*H*	--	2.92	2.20	1.96	2_{ax}, 3-C*H*$_3$	--	0.8	0.8	--
H-5	4.13	3.70	4.04	4.24	4, 4-O*H*	--	2.5	7.9	8.9
H-6	1.37	1.36	1.32	1.36	4, 5	3.0	9.5	0.6	1.0
OC*H*$_3$	3.26	3.34	3.37	3.35	5, 6	6.3	6.1	6.6	6.6

(1.70 kcal/mol) and nitro (1.10 kcal/mol) groups.[13] Studies of cyclic β-nitro alcohols have shown that conformations in which the nitro and hydroxyl groups are *gauche* are preferred to conformations in which the groups are *anti*.[14] This preference, an example of the *gauche* effect,[15] may account for the low yield of the D-*xylo* isomer observed in the epimerization.



In view of the facile displacement of triflate **5** with azide observed in our previous study, we decided to survey the reactions of **5** with oxygen nucleophiles in a effort to obtain a

precursor to rubranitrose. Treatment of the nitro alcohol with trifluoromethanesulfonic anhydride in pyridine-dichloromethane gave crystalline triflate in 72% yield. Displacement with methoxide, which would give the desired product directly, resulted in decompostion, while displacements with sodium nitrite and sodium acetate did not occur at an observable rate. Cesium propionate has been used successfully as a nucleophile in cabohydrate systems. Treatment of triflate **5** with cesium propionate in DMF gave ester **6a** in 35% yield after purification. The use of cesium acetate under the same conditions did not give the corresponding acetate, perhaps due to the lower solubility of the reagent. However, treatment of **5** with cesium acetate in acetonitrile in the presence of 18-crown-6 gave ester **6b** in 40% yield.[17] Completion of the synthesis of D-rubranitrose from **6a** or **6b** will require deesterification and methylation of the C-4 hydroxyl group.

EXPERIMENTAL

General Methods. ^{1}H and ^{13}C NMR spectra were recorded on a Varian XL200 spectrometer at 200.06 and 50.3 MHz, respectively, in deuteriochloroform solution. Proton chemical shifts are relative to tetramethylsilane (0.00 ppm), and carbon chemical shifts are relative to deuteriochloroform (76.91 ppm). High resolution mass spectra were measured at the University of Pennsylvania under CI conditions using ammonia as the reagent gas. Flash chromatography was performed on Merck silica gel 60 using mixtures of ethyl acetate and petroleum ether as indicated. Visualization of TLC plates was carried out with 5% phosphomolybdic acid in ethanol. Anhydrous DMF and THF were purchased as such from Aldrich Chemical Co. Methanol was dried by distillation from magnesium.

Crystallographic Studies. Crystal, data collection, and refinement parameters are given in Table 1. The crystal of **4** ($C_8H_{15}NO_5$, MW 205.21) was colorless and belongs to the monoclinic crystal system with space group $P2_1$ (Table 1). A total of 2273 reflections were collected, and the structure was refined to R = 0.0373 for [$I>2\sigma(I)$] and to R = 0.0699 for all reflections. The range of 2θ is 5 to 60°. The part of the Ewald sphere measured was: h, from -1 to +10; k, from -1 to +8; l, from -15 to +15. The systematic absences in the diffraction data are consistent for P2, and $P2_1/m$. The absence of a molecular mirror plane or inversion center, and Z = 2 suggested the noncentric option which yielded computationally stable and chemically reasonable results. The structure was solved using direct methods, completed by subsequent difference Fourier syntheses and refined by full-matrix least squares procedures. Semi-empirical absorption corrections were not required because of the < 10% variation in the integrated ψ-scan intensities. While the absolute configuration could not be determined by crystallographic means alone due to ambiguities in the handedness tests that were applied, the handedness reported agrees with the compound's known configuration. All non-hydrogen atoms were refined with anisotropic displacement coefficients. Hydrogen atoms were treated as idealized contributions. All software and

sources of the scattering factors are contained in the SHELXTL (5.3) program library (G. Sheldrick, Siemens XRD, Madison, WI).

Methyl 2,3,6-trideoxy-3-*C*-methyl-3-nitro-α-D-*ribo*-hexopyranoside (4). Method 1 (MCPBA): Oxidation of the amino alcohol **2** to nitro alcohol **4** with MCPBA was carried out as described previously. Method 2 (DMDO): A solution of dimethyldioxirane (0.05 M, 200 mL) in acetone was prepared by the method of Adam, Hadjiarapoglu, and Smerz.[11] The concentration of the dimethyldioxirane solution was determined by ^{1}H NMR using the reported procedure.[18] Amino sugar **2** (52.6 mg, 0.3 mmol) in chloroform (3 mL) was added dropwise to a vigorously stirred solution of dimethyldioxirane (0.05 M, 60 mL, 3 mmol) in acetone at 0 °C. The reaction mixture was protected from light and stirred at 0 °C for 2 h. The solution was concentrated in vacuo and the residue was suspended in dichloromethane. The organic layer was separated, dried (sodium sulfate) and the solvent was removed under reduced pressure to give the nitro alcohol **4** (47.7 mg, 77%). See Table 5 and reference 5 for NMR and other data for **4**.

Methyl 2,3,6-trideoxy-4-*O*-trifluoromethanesulfonyl-3-*C*-methyl-3-nitro-α-D-*ribo*-hexopyranoside (5). To a solution of nitro alcohol **4** (39 mg, 0.12 mmol) in dry dichloromethane (4 mL) was added dry pyridine (160 μL), and the mixture was cooled to 0 °C. Trifluoromethanesulfonic anhydride (140 μL) in dry dichloromethane (1 mL) was added dropwise. Additional triflic anhydride (100 μL) in dichloromethane (0.5 mL) and pyridine (100 μL) were added after 1.5 h and the reaction was stirred for an additional hour. Water (10 mL) was added and the mixture was extracted with ether (3 x 5 mL). The combined ether extracts were washed with 10% aqueous sodium carbonate solution, 10% cupric sulfate solution, and saturated sodium chloride solution, dried (magnesium sulfate) and concentrated to give 46.3 mg (72%) of triflate **5** which matched that obtained previously:[5] ^{1}H NMR δ 4.56 (m, 3 H, H-1, H-4, and H-5), 3.21 (s, 3 H, OCH_3), 2.82 (dd, 1 H, $J_{2e,2a}$ = 15.3 Hz, $J_{1,2e}$ = 1.4 Hz, H-2e), 2.03 (dd, 1 H, $J_{1,2a}$ = 4.3 Hz, H-2a), 1.66 (s, 3 H, 3-CH_3), 1.33 (d, 3 H, $J_{5,6}$ = 6.1 Hz, H-6); ^{13}C NMR δ 95.88 (C-1), 86.63 (C-4), 84.30 (C-3), 63.17 (C-5), 54.92 (OCH_3), 41.53 (C-2), 25.73 (3-CH_3), 17.84 (C-6); HRMS Calcd for $C_9H_{18}N_2O_7SF_3$ ($M + NH_4^+$): 355.0787. Found: 355.0781.

Methyl 2,3,6-trideoxy-3-*C*-methyl-3-nitro-α-D-*arabino*-hexopyranoside (7), methyl 2,3,6-trideoxy-3-*C*-methyl-3-nitro-α-D-*lyxo*-hexopyranoside (8), and methyl 2,3,6-trideoxy-3-*C*-methyl-3-nitro-α-D-*xylo*-hexopyranoside (9). Freshly cut sodium (15 mg, 0.65 mmol) was added to dry methanol (2.5 mL) under nitrogen and the resulting solution was cooled to 0 °C. A solution of nitro alcohol **4** (18.4 mg, 0.09 mmol) in 1 mL of dry methanol was added dropwise; additional methanol was used to complete transfer of **4**, bringing the total volume of methanol to 5.0 mL. The reaction was stirred at room temperature for 2 h. Dichloromethane (40 mL) was added and the mixture was extracted with water; the aqueous fractions each were washed with dichloromethane (2 mL) and the combined dichloromethane extracts were dried (sodium sulfate), and

concentrated under reduced pressure to give 16.4 mg (89%) of crude nitro alcohols which were separated by flash chromatography (50 mL 88:12 hexane / ethyl acetate, then 100 mL 75:25) to give **7** (5.0 mg, 27%), **8** (7.7 mg, 42%), and **9** (<1mg). ^{1}H NMR data for **7**, **8**, and **9** are given in Table 5. Compound **7** had R_f 0.7 (3:2 hexane / ethyl acetate) and $[\alpha]_D^{24}$ +108° (*c* 0.5, chloroform). Compound **8** had R_f 0.52 (3:2 hexane / ethyl acetate) and $[\alpha]_D^{24}$+158° (c 0.7, chloroform). Compound **9** had R_f 0.34 (3:2 hexane / ethyl acetate). HRMS of **8** Calcd for $C_8H_{19}N_2O_5$ ($M + NH_4^+$): 223.1286. Found: 223.1294.

Methyl 4-*O*-acetyl-2,3,6-trideoxy-3-*C*-methyl-3-nitro-α-D-*xylo*-hexopyranoside (6a). Cesium acetate (0.27 g, 1.41 mmol) and 18-crown-6 were added to a solution of triflate **5** (102 mg, 0.30 mmol) in CH_3CN (5 mL) and the mixture was stirred at room temperature for 36 h. Dichloromethane (20 mL) was added and the mixture was washed with 0. 5 M HCl (3 x 6 mL), 10% aqueous sodium carbonate solution (3 x 6 mL) and water (3 x 6 mL), dried (magnesium sulfate) and concentrated under reduced pressure. Purification by column chromatography (4 / 3 petroleum ether / ethyl acetate, v/v) gave acetate **6a** as a syrup; yield, 29.8 mg (40%): $[\alpha]_D^{20}$ + 116° (*c* 0.4, chloroform); ^{1}H NMR δ 5.65 (bs, 1 H, H-4), 4.72 (bs, 1 H, H-1), 4.27 (m, 1 H, $J_{4,5}$ = 1.3 Hz, $J_{1,5}$ = 0.5 Hz, H-5), 3.25 (s, 3H, OCH_3), 2.71 (dd, 1 H, $J_{2e,4}$ = 1.5 Hz, $J_{2e,2a}$ = 15.3 Hz, H-2e), 2.18 (s, 3H, CH_3COO), 2.01 (dd, 1 H,$J_{1,2a}$ = 3.9 Hz, H-2a), 1.47 (s, 3H, 3-CH_3) and 1.16 (d, 3H, $J_{5,6}$ = 6.6 Hz, H-6); ^{13}C NMR δ 170.76 (*C*O), 97.49 (C-1), 84.63 (C-3), 70.10 (C-4), 62.92 (C-5), 55.73 (OCH_3), 35.73 (CH_3), 26.55 (3-CH_3), 21.43 (C-2), 17.33 (C-6). HRMS Calcd for $C_{10}H_{21}N_2O_6$ ($M + NH_4^+$): 265.1409. Found: 265.1400.

Methyl 2,3,6-trideoxy-3-*C*-methyl-3-nitro-4-*O*-propano-α-D-*xylo*-hexopyranoside (6b). To a cooled solution of nitro alcohol **4** (50 mg, 0.24 mmol) in dry dichloromethane (4 mL) was added pyridine (0.21 mL, 2.54 mmol). Then trifluoromethanesulfonic anhydride (0.18 mL, 1.07 mmol) in dry dichloromethane (3 mL) was added dropwise. The mixture was stirred at 0 °C for 2 h. The solvent was then evaporated to give 82 mg of crude triflate, to which was added dry DMF (6 mL) and cesium propionate (0.23 g, 1.12 mmol). The reaction mixture was stirred at room temperature for 24 h, then water (10 mL) was added and the mixture extracted with ether (4 x 15 mL). The combined ether extracts were dried (magnesium sulfate) and evaporated to give 52 mg of crude product which was purified by flash chromatography to give syrupy 4-*O*-propano ester **6b** (22 mg 35%): $[\alpha]_D^{20}$ + 36° (*c* 0.825, chlororform); ^{1}H NMR δ 5.70 (bs, 1 H, H-4), 4.72 (bd, 1 H, $J_{1,2a}$ = 3.8 Hz, $J_{1,5}$ = 0.7 Hz, H-1), 4.29 (m, 1 H, $J_{5,6}$ = 6.5 Hz, $J_{5,4}$ = 1.3 Hz, $J_{1,5}$ = 0.7 Hz, H-5), 3.25 (s, 3 H, OCH_3), 2.71 (dd, 1H, H-2e, $J_{2e,2a}$ = 15.0 Hz, $J_{1,2e}$ = 1.5 Hz, $J_{2e,3}$ = 1.5 Hz, H-2e), 2.49 and 2.44 (2H, J_{gem} = 11.5 Hz, J = 7.5 Hz, CH_3CH_2CO), 2.01 (dd, 1 H, $J_{2a,1}$ = 3.8 Hz, H-2a), 1.46 (s, 3 H, 3-CH_3), 1.21 (t, 3H, J = 7.5 Hz, CH_3CH_2), 1.15 (s, 3H, $J_{5,6}$ = 6.5 Hz, H-6); ^{13}C NMR δ 173.38 (*C*O), 96.57 (C-1), 86.58 (C-3), 68.91 (C-4), 62.06 (C-5), 54.79 (OCH_3), 40.78 (CH_2CH_3), 34.86 (3-CH_3), 25.62 (C-2), 16.41 (C-6), 9.18 (CH_3CH_2); HRMS Calcd for $C_{11}H_{23}N_2O_6$ ($M + NH_4^+$): 279.1551. Found: 279.1556.

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