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Oxidation of 3-*C*-(2-amino-2-deoxy-D-glucopyranosyl)-1-propene compounds and the structure of 3-*C*-(2-amino-2-deoxy-D-glucopyranosyl)-1,2-propanediol derivatives for a synthesis of 2,3-didehydro-2,7-dideoxy-*N*-acetylneuraminic acid

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Dedicated to Professor Derek Horton on the occasion of his 70th birthday

Abstract

Oxidation of 5-acetamido-4,8-anhydro-1,2,3,5-tetradeoxy-D-*glycero*-D-*ido*-non-1-enitol [3-*C*-(2-amino-2-deoxy-β-D-glucopyranosyl)-1-propene] was studied to search for preparative routes to aminodeoxy didehydro nonulosonic acid derivatives. Since only moderate chiral induction was observed with osmium tetroxide dihydroxylation as well as with peracid epoxidation, the catalytic asymmetric dihydroxylation conditions were applied to give the stereocontrolled formation of 1,2-propanediol derivatives. The structures of these diastereoisomeric 1,2-propanediol derivatives were determined by X-ray crystallographic analyses. The formation of diastereoisomeric 1,2-propanediols also varied with the nature of 2-substituent on the aminodoexy glycosyl moiety. Thus 5-acetamido-4,8-anhydro-3,5-dideoxy-D-*erythro*-L-*ido*-nonitol [(2*S*)-3-*C*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-1,2-propanediol] was obtained predominantly up to 70% from 3-*C*-(2-acetamido-2-deoxyglycosyl)-1-propene by the use of ADmixβ reagent. The (2*S*)-propanediol derivative was transformed in a five-step reaction sequence to 2,3-didehydro-2,7-dideoxy-*N*-acetylneuraminic acid. © 2002 Elsevier Science Ltd. All rights reserved.

Keywords: 3-*C*-(2-Amino-2-deoxyglycosyl)-1,2-propanediol; 5-Acetamido-4,8-anhydro-1,2,3,5-tetradeoxy-D-*glycero*-D-*ido*-non-1-enitol; Stereocontrolled dihydroxylation; X-Ray crystallographic analysis; 2,3-Didehydro-2,7-dideoxy-*N*-acetylneuraminic acid

1. Introduction

Preparative routes for the anomerically specific C-allylation of 2-amino-2-deoxy sugars were evaluated in a comparative study and established by Cui and Horton.[1] These 1-C-allylated amino sugar derivatives have good possibilities as intermediates to lead to analogues linked through C-1 that may be useful glycomimetics that would be stable to glycoprocessing enzymes. 1-C-Linked glycosyl analogues of *N*-acetyl-α-D-glucosamine 1-phosphate have been derived from 1-α-C-allylated derivatives of 2-acetamido-2-deoxy-α-D-glucose.[2] As one such approach that would lead to biologically important compounds, we have attempted to derive aminononose derivatives by oxidation of anomerically pure 1-C-allylated amino sugar derivatives. Synthetic access to *N*-acetylneuraminic acid, a widely distributed aminononose derivative, has been designed on the basis of its known biosynthetic pathway via an aldol condensation starting from *N*-acetyl-D-mannosamine.[3] Since 2,3-didehydro-2-deoxy-*N*-acetylneuraminic acid deriva-

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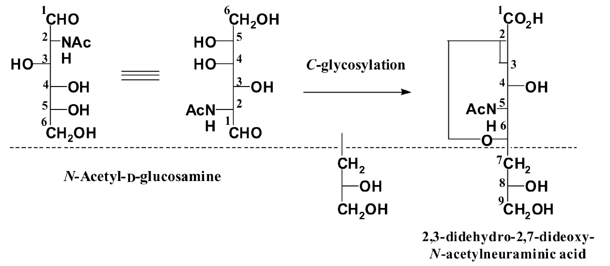
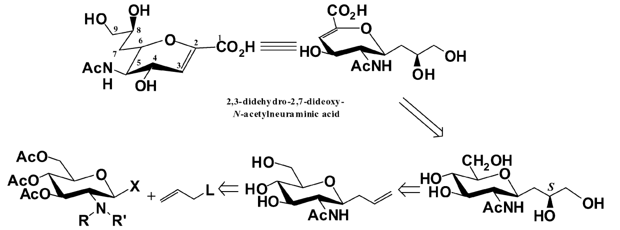


Scheme 1. Synthetic access to 2,3-didehydro-2,7-dideoxy-*N*-acetylneuraminic acid.



Scheme 2. Retrosynthesis of 2,3-didehydro-2,7-dideoxy-*N*-acetylneuraminic acid.

Table 1
Crystal data and structure refinement for **2*S***

Empirical formula	$C_{26}H_{33}NO_{11}$
Formula weight	535.55
Crystal color, system	colorless, prism
Crystal dimension (mm)	0.40 × 0.10 × 0.08
Lattice type	primitive
No. of reflections used for unit cell determination (2θ range) (°)	24264 (3.4–50.7)
Lattice parameters	
a (Å)	14.256(1)
b (Å)	21.133(2)
c (Å)	8.977(1)
V (Å^3)	2704.4(4)
Space group	$P2_12_12_1$ (#19)
Z value	4
D_{calcd} (g/cm^{-3})	1.305
F000	1136
μ(Mo K$_\alpha$) (cm^{-1})	1.03
Temperature (°C)	−160.0
No. of reflections measured	16392/2760 (R_{int} = 0.105)
Refinement	full-matrix least-squares
No. observations	1643
No. variables	322
Residuals: R; R_w	0.075; 0.078
Goodness of fit indicator	1.31
Max shift/error in final cycle	0.001

tives act as anti-influenza agents,[4] those derived from *N*-acetylneuraminic acid have garnered much attention, and an improved method without using the expensive *N*-acetyl-D-mannosamine is considered highly desirable. Although the epimerization of inexpensive *N*-acetyl-D-glucosamine to *N*-acetyl-D-mannosamine is not effective chemically, the simultaneous use of *N*-acetylneuraminate lyase and *N*-acetyl-D-glucosamine 2-epimerase and feeding of pyruvate has realized a practical synthesis of *N*-acetylneuraminic acid.[5] The development of a preparative-scale synthesis of *N*-acetylneuraminic acid prompts the effort in preparing its analogs for use as potential medicinally interesting compounds.

In this paper we describe the stereoselectivity in oxidation of 1-C-allylated amino sugar derivatives and a new synthetic approach to the synthesis of *N*-acetylneuraminic acid derivatives (Schemes 1 and 2).

2. Results and discussion

Conventional peroxyacid oxidation of 3-(3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-1-propene (**1**) afforded a mixture of two diastereoisomeric 1,2-epoxypropane derivatives **2** in a ratio of 2:1, identified by their ^{1}H NMR spectra. Fractional crystallization of 2 afforded single crystals of a major component, whose structure was determined to be (*S*)-1,2-epoxide **2*S*** by X-ray crystallographic analysis. The crystal structure of **2*S*** was solved by the direct method (SIR97[6]), and a summary of crystallographic data, data collection, and structure refinement is presented in Table 1. An ORTEP view of **2*S*** in the crystal is presented in Fig. 1. In the crystal, **2*S*** adopts a $^4C_1$ chair conformation, where the oxirane ring lies in a remote position to the phthalimido group, and the faces of both rings are essentially vertical against glycosyl ring structure. O-2 (oxirane) is spaced deep in the α-site of the glycosyl ring, which suggests α-facial selection for delivery of electrophilic oxygen from MCPBA. The coordinates of all atoms are presented in Table 2, and a selection of important geometric parameters for **2*S*** is tabulated in Table 3.

Dihydroxylation of **1** using osmium tetroxide only gave a 50:50 mixture of 1,2-propanediols. Such a poor chiral induction under the conventional dihydroxylation conditions was dependent on the nature of 3-*C*-(glycosyl)-1-propene, whose terminal vinyl group was positioned one methylene apart from the chiral center on the glycosyl moiety. Thus, asymmetric dihydroxylation conditions that have been successful for terminal olefins[7] were applied to obtain diastereomerically pure 1,2-propanediol derivatives. Compound **1** was treated with ADmixα reagent [contains chiral ligand $(DHQ)_2$-PHAL, $K_3Fe(CN)_6$, K_2CO_3, and $K_2OsO_4 \cdot 2H_2O$], and

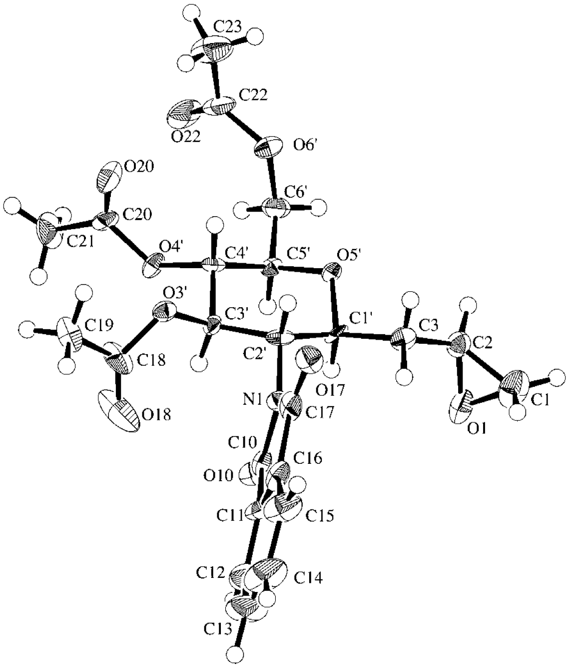


Fig. 1. Structure of 3-(3′,4′,6′-tri-*O*-acetyl-2′-deoxy-2′-phthalimido-β-D-glucopyranosyl)-1,2-epoxypropene (**2*S***).

the resulting diastereoisomeric 1,2-propanediol derivatives were transformed to their *O*-isopropylidene derivatives, which were then separated by column chromatography. A major product was crystallized and afforded a single crystal, whose structure was solved as (2*S*)-1,2-*O*-isopropylidene-1,2-propanediol (**4*S***) by X-ray crystallographic analysis. The crystal structure of **4*S*** was analyzed by the direct method (SIR97[6]), and a summary of crystallographic data, data collection, and structure refinement is presented in Table 4. An ORTEP view of **4*S*** in the crystal is presented in Fig. 2. In the crystal, **4*S*** adopts a $^4C_1$ chair conformation, where the1,3-dioxolane ring lies close to phthalimido group, and the facial relationship of both rings are essentially vertical. Interestingly, O-3 (1,3-dioxolane) and N-1 (phthalimido) are in close proximity to one another (2.87 Å), which suggests an attractive interaction. The coordinates of the atoms are presented in Table 5, and a selection of important geometric parameters of **4*S*** is tabulated in Table 6. In a similar manner (2*R*)-1,2-di-*O*-isopropylidene-1,2-propanediol (**4*R***) was predominantly obtained via the dihydroxylation using ADmixβ reagent [contains chiral ligand (DHQD)$_2$-PHAL, $K_3Fe(CN)_6$, K_2CO_3, and $K_2OsO_4 \cdot 2H_2O$].

Cleavage of the 2-phthalimido group of **4*S*** with hydrazine,[8] followed by acetylation, gave (2*S*)-3-*C*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-1,2-di-*O*-isopropylidene-1,2-propanediol (**7*S***). By the use of authentic **7*S***, the stereoselectivity in dihydroxylation of 3-*C*-(2-acetamido-2-deoxyglycosyl)-1-propene (**5**), derived from **1** by treatment with sodium borohydride,[9] was studied. The stereoselectivity in the dihydroxylation was varied and was shown to depend on the nature of 2-substituent on the sugar moiety. Dihydroxylation of 3-*C*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy)-1-propene (**5**) under the conditions using ADmixβ, followed by O-isopropylidenation and separation, afforded (2*S*)-1,2-*O*-isopropylidene-1,2-diol derivative **7*S*** with much improved stereoselectivity and yield (**7*S***:**7*R*** = 3.5:1; **7*S*** in 69.2% isolated yield from **5**). Even via conventional osmium tetroxide dihydroxylation of **5**, **7*S*** formed predominantly with 2:1 stereoselectivity. On the other

Table 2
Atomic coordinates ($\times 10^4$) for **2*S***

Atom	*x*	*y*	*z*	Atom	*x*	*y*	*z*
O-1	0.0358(5)	0.8528(3)	1.0712(7)	C-4′	0.0646(5)	1.0501(4)	0.6279(9)
O-3′	0.0804(4)	0.9940(3)	0.3989(6)	C-5′	0.0553(5)	1.0444(4)	0.7952(9)
O-4′	0.1376(4)	1.0960(3)	0.5983(6)	C-6′	0.0257(6)	1.1053(4)	0.873(1)
O-5′	−0.0105(3)	0.9953(3)	0.8283(6)	C-10	0.1632(5)	0.8515(4)	0.5818(9)
O-6′	−0.0536(4)	1.1317(3)	0.7944(7)	C-11	0.1724(6)	0.7935(5)	0.491(1)
O-10	0.2202(4)	0.8763(3)	0.6628(8)	C-12	0.2481(8)	0.7534(5)	0.470(1)
O-17	−0.0627(4)	0.8377(3)	0.4376(7)	C-13	0.2365(9)	0.7019(6)	0.379(1)
O-18	0.2217(5)	0.9534(5)	0.3581(8)	C-14	0.150(1)	0.6887(6)	0.314(1)
O-20	0.0478(4)	0.1507(3)	0.4360(8)	C-15	0.0720(8)	0.7276(5)	0.338(1)
O-22	0.0236(5)	1.2255(3)	0.7701(9)	C-16	0.0868(6)	0.7811(4)	0.4262(10)
N-1	0.0719(5)	0.8730(3)	0.5612(8)	C-17	0.0212(7)	0.8314(5)	0.4698(9)
C-1	−0.0531(8)	0.8185(5)	1.076(1)	C-18	0.1535(6)	0.9777(5)	0.310(1)
C-1′	0.0223(6)	0.9342(4)	0.7849(10)	C-19	0.1324(6)	0.9921(5)	0.153(1)
C-2	−0.0475(6)	0.8796(5)	1.004(1)	C-20	0.1209(6)	1.1425(4)	0.499(1)
C-2′	0.0334(5)	0.9334(4)	0.6158(9)	C-21	0.2048(7)	1.1837(5)	0.489(1)
C-3	−0.0444(6)	0.8856(4)	0.840(1)	C-22	−0.0431(7)	1.1925(5)	0.747(1)
C-3′	0.0932(5)	0.9875(4)	0.5582(9)	C-23	−0.1259(8)	1.2112(6)	0.654(1)

Table 3
Selected bond lengths (Å), bond angles (°) and torsion angles (°) for **2*S***

Bond lengths		Bond angles		Torsion angles	
C-1–C-2	1.44(1)	C-1–O-1–C-2	59.5(6)	O-5′–C-1′–C-2′–C-3′	53.0(9)
C-1′–C-2′	1.53(1)	C-3′–O-3′–C-18	117.3(6)	C-1′–C-2′–C-3′–C-4′	−46.7(9)
C-1′–C-3	1.49(1)	C-1′–O-5′–C-5′	112.6(6)	O-6′–C-6′–C-5′–C-4′	48.0(9)
C-2–C-3	1.48(1)	C-2′–N-1–C-10	126.0(7)	O-5′–C-5′–C-4′–C-3′	−56.5(8)
C-2′–C-3′	1.52(1)	C-2′–N-1–C-17	123.1(7)	C-1′–O-5′–C-5′–C-4′	66.4(8)
C-3′–C-4′	1.52(1)	O-1–C-1–C-2	59.7(6)	C-1–C-2–C-3–C-1′	−139.1(9)
C-4′–C-5′	1.51(1)	O-5′–C-1′–C-2′	108.4(7)	O-1–C-2–C-3–C-1′	−69(1)
C-5′–C-6′	1.52(1)	O-5′–C-1′–C-3	108.9(7)	C-1–O-1–C-2–C-3	−113.5(10)
C-10–C-11	1.48(1)	C-2′–C-1′–C-3	113.0(7)	O-1–C-1–C-2–C-3	103.0(9)
C-11–C-12	1.39(1)	O-1–C-2–C-1	60.8(7)	C-2–C-3–C-1′–C-2′	172.5(7)
C-11–C-16	1.38(1)	O-1–C-2–C-3	114.9(7)	O-5′–C-1′–C-3–C-2	−67.0(9)
C-12–C-13	1.37(2)	C-1–C-2–C-3	121.4(9)	C-3–C-1′–O-5′–C-5′	172.9(7)
C-13–C-14	1.39(2)	N-1–C-2′–C-1′	112.3(7)	C-3–C-1′–C-2′–C-3′	173.8(7)
C-14–C-15	1.40(2)	N-1–C-2′–C-3′	109.3(6)	N-1–C-2′–C-1′–C-3	−62.2(9)
C-15–C-16	1.40(1)	C-1′–C-2′–C-3′	112.8(7)		
C-16–C-17	1.47(1)	C-1′–C-3–C-2	114.3(8)		
C-18–C-19	1.48(1)	C-2′–C-3′–C-4′	111.4(7)		
C-20–C-21	1.48(1)	C-3′–C-4′–C-5′	111.2(7)		
C-22–C-23	1.50(2)	C-4′–C-5′–C-6′	114.2(7)		
O-1–C-1	1.46(1)	O-6′–C-6′–C-5′	108.8(7)		
O-1–C-2	1.45(1)				
O-3′–C-3′	1.45(1)				
O-3′–C-18	1.35(1)				
O-4′–C-4′	1.447(10)				
O-4′–C-20	1.35(1)				
O-5′–C-1′	1.43(1)				
O-5′–C-5′	1.431(10)				
O-6′–C-6′	1.44(1)				
O-6′–C-22	1.36(1)				
O-10–C-10	1.21(1)				
O-17–C-17	1.24(1)				
O-18–C-18	1.18(1)				
O-20–C-20	1.20(1)				
O-22–C-22	1.20(1)				
N-1–C-2′	1.47(1)				
N-1–C-10	1.39(1)				
N-1–C-17	1.40(1)				

hand, no stereoselectivity was observed in the dihydroxylation of **5** using ADmixα. Asymmetric dihydroxylation for terminal olefins was reported to be (2*S*)-diol selective for ADmixα, and (2*R*)-diol for ADmixβ.[7] Although the 3-glycosyl-1-propene having a phthalimido group as the 2-substituent on the glycosyl moiety influenced the usual (2*S*)-diol selectivity for ADmixα (**2*S***:**2*R*** = 2:1), the analogous 3-(2-acetamido-glycosyl)-1-propene showed unusual selectivity in that ADmixβ gave the (2*S*)-diol preferentially (**7*S***:**7*R*** = 3.5:1) (Table 7). Such a difference in enantioselectivity under the dihydroxylation using ADmix reagents is presumably dependent on the relative orientation of the alkenes to the chiral glycosyl moiety.

O-Deacetylation, followed by selective catalytic oxidation at 6-OH on the glycosyl moiety (9-OH with anhydrononitol numbering) of the 1,2-*O*-isopropylidene-1,2-propanediol derivative **7*S***, furnished a synthesis of 5-acetamido-2,6-anhydro-nonanoic acid derivative **8** (Scheme 3). Treatment of **8** with DBU effected elimination[10] across the C-2–C-3 bond and afforded 2,3-didehydro-2,7-dideoxy-*N*-acetylneuraminic acid derivative **9**, whose 4-substituted derivatives are expected to be potentially active as inhibitors of sialidase.

3. Experimental

General methods.—Melting points were determined in open glass capillaries in a Yazawa (Japan) apparatus,

Table 4
Crystal data and structure refinement for **4S**

Empirical formula	$C_{26}H_{31}NO_{11}$
Formula weight	533.53
Crystal color, system	colorless, prism
Crystal dimensions	0.35 × 0.20 × 0.07 nm
Crystal system	monoclinic
Lattice type	primitive
No. of reflections used for unit cell determination (2θ range)	9012 (6.9–54.9)
Lattice parameters	
a (Å)	9.2794(4)
b (Å)	7.7682(2)
c (Å)	17.9395(6)
V (Å^3)	1289.00(8)
Space group	$P2_1$ (#4)
Z value	2
D_{calcd} (g/cm^3)	1.375
$F000$	564
μ(Mo K$_\alpha$) (cm^{-1})	1.08
Temperature (°C)	−160.0
No. of reflection measured	12602/3161 ($R_{\mathrm{int}} = 0.028$)
Refinement	full-matrix least-squares
No. observations	3157
No. variables	344
Residuals: R; R_w	0.066; 0.087
Goodness of fit indicator	1.05
Max shift/error in final cycle	0.001

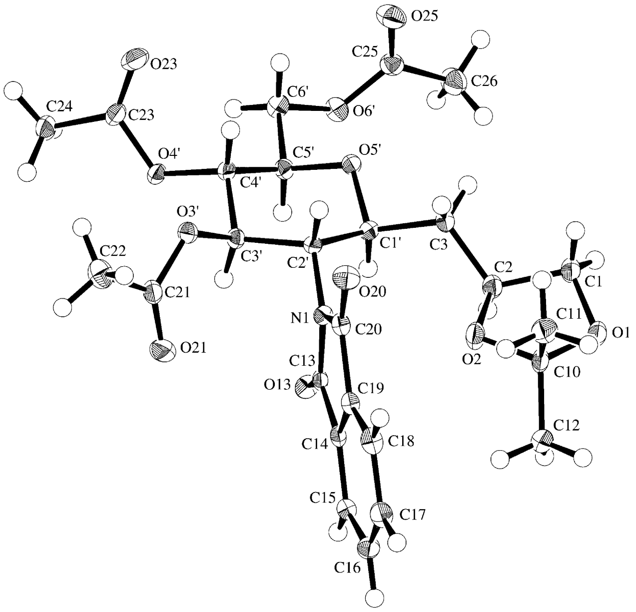


Fig. 2. Structure of 3-(3′,4′,6′-tri-*O*-acetyl-2′-deoxy-2′-phthalimido-β-D-glucopyranosyl)-1,2-di-*O*-isopropylidene-1,2-propanediol (**4*S***).

and are uncorrected. Specific rotations were determined at room temperature (rt) with a JASCO (Japan) Model DIP 1000 polarimeter. ^{1}H and ^{13}C NMR spectra were recorded with a JEOL (Japan) JNM-A500 (500 MHz ^{1}H, 125 MHz ^{13}C) spectrometer. Chemical shifts (ppm) are relative to Me_4Si as the internal standard. Hydrogen- and carbon-atom numbering is based on the 3-*C*-(glycosyl)propane skeleton. Mass spectra were recorded on a JEOL (Japan) JMS-GC BU25 spectrometer in the electron impact mode. X-Ray crystallographic analyses were performed on a Rigaku AXIS-RAPID imaging plate diffractometer with graphite-monochromated Mo K$_\alpha$ radiation. Elemental analyses were performed on a Perkin–Elmer 2400II Organic Elemental Analyzer.

*6,7,9-Tri-*O*-acetyl-1,2:4,8-dianhydro-5-deoxy-5-phthalimido-*D-erythro-L-ido- *and* D-erythro-L-gulo-*nonitol [(2*S *and 2*R*)-3-*C*-(3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-*D-*glucopyranosyl)-1,2-epoxypropane]* (**2*S*** and **2*R***).—To a solution of 3-(3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-1-propene[1] (**1**) (1.0 g, 2.18 mmol) in CH_2Cl_2 (20 mL) was added *m*-chloroperoxybenzoic acid (MCPBA, 1.22 g, 4.96 mmol), and the mixture was stirred for 20 h at rt. The solution was washed successively with 10% sodium thiosulfate, brine, dried (Na_2SO_4) and evaporated to a syrup, which was chromatographed on a column of silica gel with 8:1 toluene–acetone to give a mixture of 1,2-epoxypropane derivatives in a crystalline state. Crude products were recrystallized from 2-PrOH to afford **2*S*** as white crystals (545 mg, 53%): mp 108–110 °C; $[\alpha]_D$ +53° (c 1.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.85 and 7.75 (m, 4H, Phth), 5.84 (dd, 1H, $J_{2',3'}$ 10.4 Hz, $J_{3',4'}$ 9.2 Hz, H-3′), 5.16 (dd, 1H, $J_{4',5'}$ 7.0 Hz, H-4′), 4.61 (ddd, 1H, $J_{1',2'}$ 10.4 Hz, $J_{1',3b}$ 1.8 Hz, $J_{1',3a}$ 3.4 Hz, H-1′), 4.32 (dd, 1H, $J_{6'a,6'b}$ 12.3 Hz, H-6′b), 4.23 (t, 1H, H-2′), 4.15 (dd, 1H, $J_{5',6'a}$ 2.1 Hz, H-6′a), 3.88 (ddd, 1H, H-5′), 3.07 (ddd, 1H, $J_{1a,2}$ 2.4 Hz, $J_{1b,2}$ 4.3 Hz, $J_{2,3a}$ 4.0 Hz, $J_{2,3b}$ 3.0 Hz, H-2), 2.73 (dd, 1H, H-1b), 2.38 (dd, 1H, H-1a), 2.11 and 2.04 (2s, 2 × 3H, 2OAc), 1.87 (ddd, 1H, $J_{3a,3b}$ 4.0 Hz, H-3b), 1.84 (s, 3H, NAc), 1.46 (ddd, 1H, H-3a). ^{13}C NMR: δ 170.71, 170.18 ($3OCOCH_3$), 167.65 (2-Phth-CO), 134.53, 134.27, 131.52, 131.03, 123.75, 123.67 (Phth), 75.67 (C-5′), 73.05 (C-1′), 71.49 (C-3′), 69.15 (C-4′), 62.31 (C-6′), 54.86 (C-2′), 48.70 (C-2), 47.34 (C-1), 35.77 (C-3), 20.77, 20.65, 20.42 ($3OCOCH_3$). EIMS: m/z 475 [M$^+$]. Anal. Calcd for $C_{23}H_{25}NO_{10}$: C, 58.10; H, 5.30; N, 2.95. Found: C, 58.30; H, 5.48; N, 2.92. For X-ray crystallographic data see Tables 1–3.

From the mother liquor of the above recrystallization, **2*R*** was obtained as a syrup (282 mg, 27%): ^{1}H NMR ($CDCl_3$): δ 7.85 and 7.75 (m, 4H, Phth), 5.76 (dd, 1H, $J_{2',3'}$ 10.4 Hz, $J_{3',4'}$ 9.2 Hz, H-3′), 5.15 (t, 1H, $J_{4',5'}$ 10.1 Hz, H-4′), 4.57 (ddd, 1H, $J_{1',3a}$ 3.1 Hz, $J_{1',3b}$ 4.0 Hz, H-1′), 4.29 (dd, 1H, $J_{5',6'b}$ 5.2 Hz, H-6′b), 4.23 (t, 1H, H-2′), 4.15 (dd, 1H, $J_{5',6'a}$ 2.1 Hz, H-6′a), 3.85 (ddd, 1H, H-5′), 3.07 (dddd, 1H, $J_{1a,2}$ 2.8 Hz, $J_{1b,2}$ 4.3

Table 5
Atomic coordinates (-10^4) for **4*S***

Atom	*x*	*y*	*z*	Atom	*x*	*y*	*z*
O-1	−1.2795(1)	−0.2989(7)	−0.57473(7)	C-2	−1.1992(2)	−0.0969(7)	−0.6568(1)
O-2	−1.0834(1)	−0.2125(7)	−0.63475(8)	C-3	−1.2035(2)	−0.0495(7)	−0.73885(10)
O-3′	−0.7579(1)	0.0411(7)	−0.86893(7)	C-10	−1.1357(2)	−0.3481(7)	−0.58915(10)
O-4′	−0.8551(1)	0.3778(7)	−0.90356(7)	C-11	−1.1353(2)	−0.5167(7)	−0.6321(1)
O-5′	−1.1613(1)	0.1828(7)	−0.81945(7)	C-12	−1.0445(2)	−0.3539(7)	−0.5158(1)
O-6′	−1.2802(1)	0.5067(7)	−0.84240(7)	C-13	−0.8081(2)	−0.0127(7)	−0.66359(9)
O-13	−0.8145(1)	0.1386(7)	−0.64886(7)	C-14	−0.7397(2)	−0.1550(7)	−0.61784(10)
O-20	−0.8842(2)	−0.3648(7)	−0.77976(7)	C-15	−0.6709(2)	−0.1516(7)	−0.5462(1)
O-21	−0.5814(2)	0.0566(7)	−0.77515(8)	C-16	−0.6252(2)	−0.3100(7)	−0.5158(1)
O-23	−0.9405(2)	0.3437(7)	−1.02400(8)	C-17	−0.6478(2)	−0.4636(7)	−0.5551(1)
O-25	−1.4439(2)	0.3476(7)	−0.91203(8)	C-18	−0.7159(2)	−0.4647(7)	−0.6276(1)
N-1	−0.8690(2)	−0.0903(7)	−0.72918(8)	C-19	−0.7607(2)	−0.3077(7)	−0.65714(10)
C-1′	−1.0909(2)	0.0819(7)	−0.76037(9)	C-20	−0.8449(2)	−0.2682(7)	−0.7298(1)
C-2′	−0.9545(2)	0.0000(7)	−0.78918(9)	C-21	−0.6213(2)	0.0177(7)	−0.8383(1)
C-3′	−0.8589(2)	0.1321(7)	−0.82572(9)	C-22	−0.5299(2)	−0.0627(7)	−0.8941(1)
C-4′	−0.9489(2)	0.2452(7)	−0.87994(9)	C-23	−0.8607(2)	0.4144(7)	−0.97771(10)
C-5′	−1.0726(2)	0.3228(7)	−0.83927(10)	C-24	−0.7572(2)	0.5569(7)	−0.9907(1)
C-6′	−1.1655(2)	0.4487(7)	−0.88628(10)	C-25	−1.4124(2)	0.4372(7)	−0.8586(1)
C-1	−1.3318(2)	−0.1964(7)	−0.6368(1)	C-26	−1.5141(2)	0.4869(7)	−0.8014(1)

Hz, $J_{2,3a}$ 2.4, H-2), 2.70 (t, 1H, H-1b), 2.40 (dd, 1H, H-1a), 1.91 (m, 1H, H-3b), 1.60 (ddd, 1H, H-3a). ^{13}C NMR: δ 170.18, 169.60, 169.52 (3O*C*OCH$_3$), 167.65 (2-Phth-*C*O), 134.53, 134.27, 131.52, 131.03, 123.54 (Phth), 75.77 (C-5′), 72.92 (C-1′), 71.69 (C-3′), 69.9 (C-4′), 62.36 (C-6′), 54.35 (C-2′), 48.59 (C-2), 46.38 (C-1), 34.44 (C-3), 20.77, 20.65, 20.42 (3OCO*C*H$_3$). EIMS: *m*/*z* 475 [M$^+$].

*6,7,9-Tri-*O*-acetyl-4,8-anhydro-5-deoxy-1,2-*O*-isopropylidene-5-phthalimido-*D-erythro-L-ido- *and* D-erythro-L-gulo-*nonitol [(2*S *and* 2R*-1,2-*O*-isopropylidene-3-*C*-(3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-*D*-glucopyranosyl)-1,2-propanediol]* (**4*S*** and **4*R***)

Via dihydroxylation of **1** *with ADmixα*. To a solution of ADmixα (30.5 g) in 3:5 *t*-BuOH–H$_2$O (149 mL) was added **1** (10 g, 22 mmol) in *t*-BuOH (69 mL) portion by portion, and the mixture was stirred at 0 °C for 9 h. Sodium sulfite (33 g) was added to decompose the oxidizing agent, and the mixture was stirred for a further 0.5 h at rt. The reaction mixture was mixed with EtOAc (200 mL) and separated. The aqueous layer was extracted with EtOAc (3 × 90 mL), and the combined organic layers were washed with brine, dried (Na$_2$SO$_4$) and evaporated to a syrup, which was separated by column chromatography on silica gel with 18:1 CHCl$_3$–MeOH. The fraction, R_f 0.45 (10:1 CHCl$_3$–MeOH), was evaporated to give a major component of diastereomeric isomers of 1,2-diol as a syrup (4.91 g, 46%) and the fraction R_f 0.46, a minor component (2.84 g, 27%): Data for **3*S***: R_f 0.45 (10:1 CHCl$_3$–MeOH); $[\alpha]_D$ +49° (*c* 1.8, MeOH); ^{1}H NMR (CDCl$_3$): δ 7.47 and 7.85 (m, 4H, Phth), 5.82 (dd, 1H, $J_{3',4'}$ 9.2 Hz, H-3′), 5.14 (t, 1H, $J_{4',5'}$ 9.7 Hz, H-4′), 4.64 (ddd, 1H, $J_{1',2'}$ 10.2 Hz, H-1′), 4.27 (dd, 1H, $J_{5',6'a}$ 3.6 Hz, $J_{6'a,6'b}$ 12.2 Hz, H-6′a), 4.25 (t, 1H, $J_{2',3'}$ 10.4 Hz, H-2′), 4.18 (dd, 1H, $J_{5',6'b}$ 2.4 Hz, H-6′b), 3.93–3.97 (m, 1H, H-2), 3.87 (ddd, 1H, H-5′), 3.62 (dd, 1H, $J_{2,3b}$ 3.7 Hz, $J_{3a,3b}$ 10.9 Hz, H-3b), 3.42 (dd, 1H, $J_{3a,1'}$ 6.1 Hz, H-3a), 1.64 (ddd, 1H, $J_{3a,1'} = J_{3b,1'}$ 3.1 Hz, $J_{3a,3b}$ 14.7 Hz, H-3a), 1.57 (ddd, 1H, $J_{2,3a} = J_{2,3b}$ 8.6 Hz, H-3b), 1.84, 2.04 and 2.12 (3s, 3 × 3H, 3OAc). EIMS: *m*/*z* 493 [M$^+$].

Data for **3*R***: R_f 0.46 (10:1 CHCl$_3$–MeOH); $[\alpha]_D$ +58° (*c* 1.6, MeOH); ^{1}H NMR (CDCl$_3$): δ 7.75 and 7.86 (m, 4H, Phth), 5.78 (dd, 1H, $J_{3',4'}$ 9.2 Hz, H-3′), 5.11 (t, 1H, $J_{4',5'}$ 9.7 Hz, H-4′), 4.65 (ddd, 1H, $J_{1',2'}$ 10.4 Hz, H-1′), 4.32 (dd, 1H, $J_{5',6'b}$ 1.9 Hz, $J_{6'a,6'b}$ 12.2 Hz, H-6′b), 4.24 (t, 1H, $J_{2',3'}$ 10.4 Hz, H-2′), 4.14 (dd, 1H, $J_{5',6'b}$ 6.1 Hz, H-6′a), 3.89–3.94 (m, 2H, H-5′, H-2), 3.61 (dd, 1H, $J_{2,3b}$ 3.7 Hz, H-3b), 3.42 (dd, 1H, $J_{2,3a}$ 6.8 Hz, H-3a), 1.64 (ddd, 1H, $J_{3a,1'} = J_{3b,1'}$ 3.1 Hz, $J_{3a,3b}$ 14.7 Hz, H-3a), 1.57 (ddd, 1H, $J_{2,3a} = J_{2,3b}$ 8.6 Hz, H-3b), 1.84, 2.04 and 2.12 (3s, 3 × 3H, 3OAc). EIMS: *m*/*z* 493 [M$^+$].

The syrup **3*S*** (R_f 0.45, 4.80 g) was treated with 2,2-dimethoxypropane (2.9 mL, 14.9 mmol) in DMF (24 mL) in the presence of *p*-TsOH (19 mg). The crude product was purified by column chromatography on silica gel with 10:1 toluene–acetone and crystallized from 2-PrOH to give (*S*)-1,2-*O*-isopropylidene-3-*C*-(3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)1,2-propanediol (**4*S***) as colorless needles (4.72 g, 41% from **1**): mp 110–112 °C; $[\alpha]_D$ +51° (*c* 1.5, CHCl$_3$); ^{1}H NMR (CDCl$_3$): δ 7.74 and 7.84 (m, 4H, Phth), 5.82 (dd, 1H, $J_{3',4'}$ 10.4 Hz, H-3′), 5.11 (t, 1H,

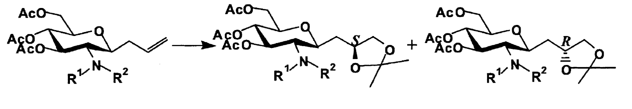
$J_{4',5'}$ 10.4 Hz, H-4′), 4.50 (dt, 1H, $J_{1',2'}$ 9.8 Hz, H-1′), 4.25 (dd, 1H, $J_{5',6'a}$ 4.9 Hz, $J_{6'a,6'b}$ 12.2 Hz, H-6′a), 4.1–4.2 (m, 3H, H-2, H-2′, H-6′b), 4.04 (dd, 1H, $J_{1a,2}$ 6.1 Hz, $J_{1a,1b}$ 8.6 Hz, H-1a), 3.84 (ddd, 1H, H-5′), 3.50 (dd, 1H, $J_{1b,2}$ 6.7 Hz, H-1b), 1.75 (ddd, 1H, $J_{3a,1'}$ 2.4 Hz, $J_{2,3a}$ 9.8 Hz, $J_{3a,3b}$ 14.7 Hz, H-3a), 1.67 (ddd, 1H, $J_{3b,1'}$ 5.5 Hz, $J_{2,3b}$ 9.1 Hz, H-3b), 1.84, 2.03 and 2.11 (3s, 3 × 3H, 3OAc), 1.18 and 1.22 (2s, 2 × 3H, Ip-C*H*$_3$). ^{13}C NMR: δ 170.70, 170.22, 169.63 (3*C*OCH$_3$), 167.60 (Phth-*C*O), 134.54, 134.29, 131.61, 131.13, 123.63 (Phth), 108.5 (Ip-Me$_2$*C*O$_2$-), 75.59 (C-5′), 73.47 (C-2), 72.98 (C-1′), 71.45 (C-3′), 69.80 (C-1), 69.28 (C-4′), 62.50 (C-6′), 54.98 (C-2′), 36.69 (C-3), 26.77, 25.60 (2 × Ip-*C*H$_3$), 20.81, 20.68 and 20.48 (3CO*C*H$_3$). EIMS: *m*/*z* 533 [M$^+$]. Anal. Calcd for $C_{26}H_{31}NO_{11}$: C, 58.53; H, 5.86; N, 2.63. Found: C, 58.71; H, 5.88; N, 2.70. For X-ray crystallographic data see Tables 4–6.

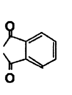
The syrup **3*R*** (R_f 0.46, 1.55 g) was O-isopropylidenated analogously to give (*R*)-1,2-*O*-isopropylidene-3-*C*-(3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-1,2-propanediol (**4*R***) as colorless needles (0.98 g, 16% from **1**): mp 122–125 °C; [α]$_D$ +42° (*c* 1.2, CHCl$_3$); ^{1}H NMR (CDCl$_3$): δ 7.74 and 7.81 (m, 4H, Phth), 5.75 (t, 1H, $J_{3',4'}$ 9.8 Hz, H-3′), 5.14 (t, 1H,

Table 6
Selected bond lengths (Å), bond angles (°) and torsion angles (°) for **4*S***

Bond lengths		Bond angles		Torsion angles	
O-3′–C-3′	1.447(4)	C-1′–O-5′–C-5′	111.3(2)	O-5′–C-1′–C-2′–C-3′	50.5(4)
O-3′–C-21	1.352(2)	C-2–O-2–C-10	109.6(2)	C-1′–C-2′–C-3′–C-4′	−47.2(3)
O-4′–C-4′	1.435(6)	C-1–O-1–C-10	105.8(2)	C-2′–C-3′–C-4′–C-5′	53.0(4)
O-4′–C-23	1.357(3)	C-3′–O-3′–C-21	118.3(2)	O-5′–C-5′–C-4′–C-3′	−64.2(3)
O-5′–C-1′	1.433(4)	C-2′–N-1–C-13	124.7(5)	C-1′–O-5′–C-5′–C-4′	71.6(3)
O-5′–C-5′	1.426(6)	C-2′–N-1–C-20	123.0(3)	O-5′–C-1′–C-3–C-2	−144.9(3)
O-6′–C-6′	1.446(3)	O-5′–C-1′–C-2′	108.4(2)	C-2′–C-1′–C-3–C-2	96.2(3)
O-6′–C-25	1.350(4)	O-5′–C-1′–C-3	105.7(2)	C-1′–C-3–C-2–C-1	167.6(4)
O-2–C-2	1.432(5)	N-1–C-2′–C-1′	111.2(2)	O-2–C-2–C-3–C-1′	−76.5(5)
O-2–C-10	1.422(5)	N-1–C-2′–C-3′	109.6(2)	C-3–C-2–O-2–C-10	−135.2(3)
O-1–C-1	1.431(3)	C-1′–C-2′–C-3′	112.6(4)	O-1–C-1–C-2–C-3	151.4(4)
O-13–C-13	1.207(7)	C-2′–C-3′–C-4′	110.7(2)	C-2–O-2–C-10–C-12	−124.7(3)
O-20–C-20	1.203(5)	C-2′–C-1′–C-3	113.9(4)	C-2–C-1–O-1–C-10	−36.0(5)
O-21–C-21	1.202(3)	C-3′–C-4′–C-5′	108.6(2)	C-1–O-1–C-10–C-11	−90.1(4)
O-23–C-23	1.200(4)	C-4′–C-5′–C-6′	113.8(2)	C-1–O-1–C-10–C-12	144.9(4)
O-25–C-25	1.202(5)	C-1′–C-3–C-2	116.2(2)	O-2–C-10–O-1–C-1	28.1(4)
N-1–C-2′	1.464(4)	O-2–C-2–C-3	112.4(2)	C-2–O-2–C-10–C-11	111.3(3)
N-1–C-13	1.400(4)	O-2–C-2–C-1	102.7(4)	O-2–C-2–C-1–O-1	29.9(4)
N-1–C-20	1.400(8)	C-3–C-2–C-1	113.2(2)	C-3′–C-2′–C-1′–C-3	167.8(1)
C-1′–C-2′	1.542(4)	O-1–C-1–C-2	103.7(2)	C-5′–O-5′–C-1′–C-3	173.7(3)
C-1′–C-3	1.531(5)	O-2–C-10–O-1	105.6(4)	N-1–C-2′–C-1′–C-3	−68.6(3)
C-2′–C-3′	1.537(5)	O-1–C-10–C-12	108.5(2)		
C-3′–C-4′	1.512(5)	O-2–C-10–C-11	109.1(2)		
C-4′–C-5′	1.531(4)	C-11–C-10–C-12	113.1(4)		
C-5′–C-6′	1.515(5)	O-6′–C-6′–C-5′	108.0(2)		
C-3–C-2	1.515(3)				
C-2–C-1	1.520(5)				
C-10–C-11	1.520(7)				
C-10–C-12	1.507(3)				
C-13–C-14	1.488(6)				
C-14–C-15	1.388(2)				
C-14–C-19	1.386(7)				
C-15–C-16	1.398(7)				
C-16–C-17	1.393(7)				
C-17–C-18	1.400(3)				
C-18–C-19	1.380(7)				
C-19–C-20	1.497(3)				
C-21–C-22	1.499(4)				
C-23–C-24	1.496(6)				
C-25–C-26	1.498(4)				

Table 7
Dihydroxylation of 3-*C*-(2-aminoglycosyl)-1-propene



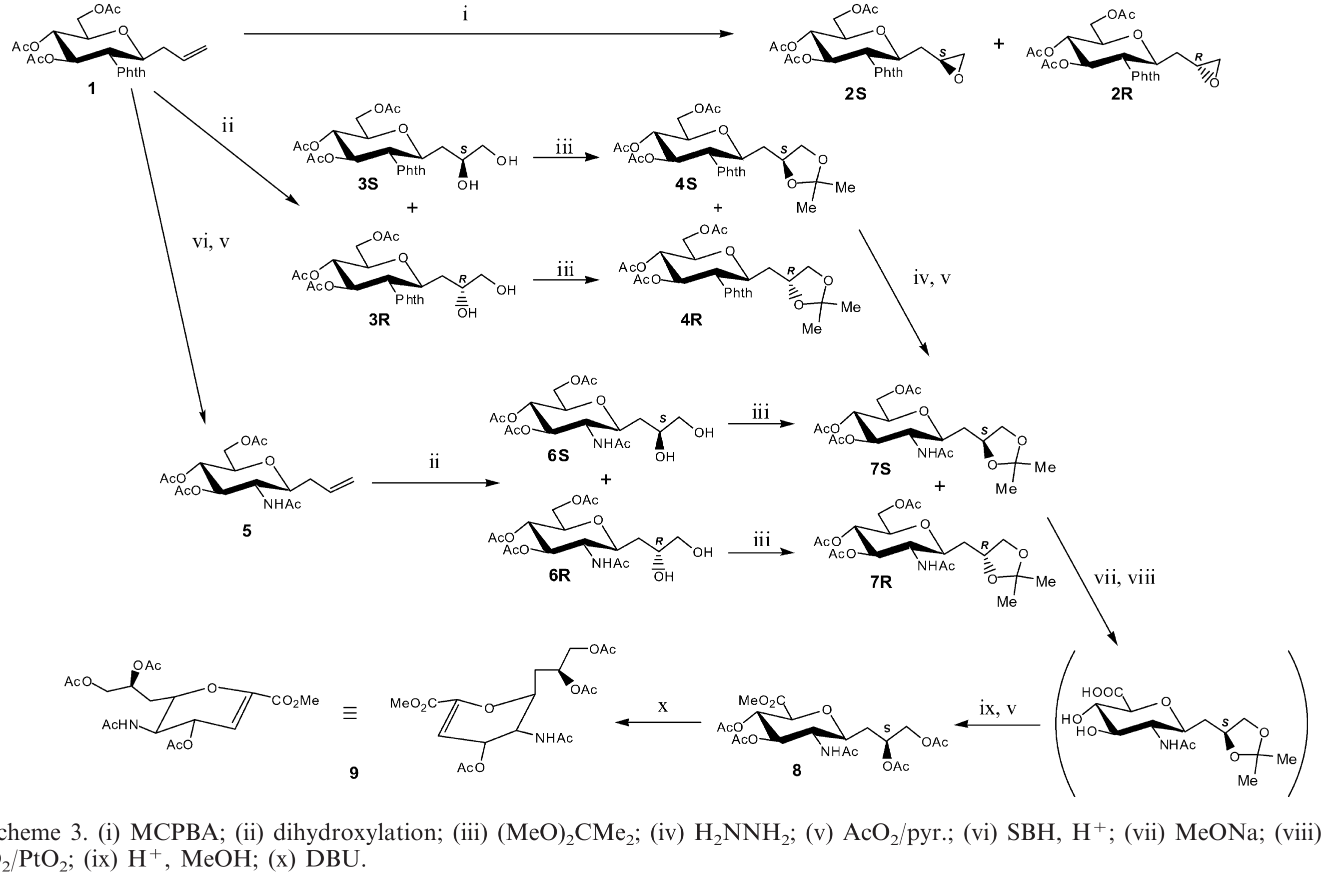
2-Substituent	Reagent	Yield		Ratio
		4*S*	4*R*	4*S*/4*R*
$R^1= R^2=$ 	OsO$_4$	35%[a]	34%[a]	1:1[a]
	ADmixa	41%	16%	2.6:1
	ADmixb	27%	40%	1:1.5
		7*S*	7*R*	7*S*/7*R*
R^1= Ac, R^2= H	OsO$_4$	20%	10%	2:1
	ADmixa	27%	29%	1:1
	ADmixb	69%	20%	3.5:1

a. Yields and Ratio were given as diol derivatives.

$J_{4',5'}$ 9.8 Hz, H-4′), 4.53 (dt, 1H, $J_{1',2'}$ 9.8 Hz, H-1′), 4.2–4.3 (m, 3H, H-2, H-2′, H-6′a), 4.14 (dd, 1H, $J_{5',6'b}$ 4.9 Hz, $J_{6'a,6'b}$ 12.2 Hz, H-6′b), 4.02 (dd, 1H, $J_{1a,2}$ 5.5 Hz, $J_{1a,1b}$ 8.5 Hz, H-1a), 3.81 (ddd, 1H, H-5′), 3.55 (dd, 1H, $J_{1b,2}$ 7.9 Hz, H-1b), 1.89 (ddd, 1H, $J_{3a,1'}$ 4.8 Hz, $J_{2,3a}$ 9.7 Hz, $J_{3a,3b}$ 14.6 Hz, H-3a), 1.72 (ddd, 1H, $J_{3ab,1'}$ 3.1 Hz, $J_{2,3b}$ 11.6 Hz, H-3b), 1.84, 2.03 and 2.11 (3s, 3 × 3H, 3OAc), 1.29, 1.27 (2s, 2 × 3H, Ip-CH_3). ^{13}C NMR: δ 170.71, 170.26, 169.55 (3 × CH$_3$*C*O), 167.91, 167.42 (Phth-*C*O), 134.48, 134.30, 123.67, 123.57 (Phth), 75.75 (C-5′), 72.29 (C-1′), 71.87 (C-2), 71.78 (C-3′), 69.07 (C-4′), 68.96 (C-1), 62.36 (C-6′), 54.28 (C-2′), 34.77 (C-3), 26.58, 25.38 (2 × Ip-*C*H$_3$), 20.77, 20.65, 20.44 (3-CO*C*H$_3$). EIMS: *m*/*z* 533 [M$^+$]. Anal. Calcd for $C_{26}H_{31}NO_{11}$: C, 58.53; H, 5.86; N, 2.63. Found: C, 58.90; H, 5.90; N, 2.75.

Via dihydroxylation of **1** *with ADmixβ*. Compound **1** (0.46 g, 1.0 mmol) was treated with ADmixβ (1.4 g) as described in Section 3.3.1 (**1** with ADmixβ). The crude product was purified by column chromatography, and a mixture of the diastereomeric isomers of 1,2-diol (**3*S*** and **3*R***) as a syrup (0.4 g, 82%) was O-isopropylidenated as described above. After purification by column chromatography, (*S*)-1,2-*O*-isopropylidene-1,2-propanediol (**4*S***) (89 mg, 27% from **1**) and (*R*)-1,2-*O*-isopropylidene-1,2-propanediol (**4*R***) (133 mg, 40% from **1**) were obtained.

Via dihydroxylation of **1** *with osmium tetroxide*. To a solution of **1** (6.5 g, 14 mmol) in 8:1 acetone–water (71 mL) was added OsO$_4$ (0.18 mg, 0.71 mmol) and 4-methylmorpholine *N*-oxide (3.33 g, 28 mmol), and the mixture was stirred 6 h at rt. The reaction mixture was diluted with CHCl$_3$ (150 mL), and the solution was washed successively with 1 M HCl, aq. sodium metabisulfite, brine, dried (Na$_2$SO$_4$) and evaporated to a syrup, which was chromatographed on a column of silica gel with 15:1 CHCl$_3$–MeOH to give a 1:1 mixture



Scheme 3. (i) MCPBA; (ii) dihydroxylation; (iii) (MeO)$_2$CMe$_2$; (iv) H$_2$NNH$_2$; (v) AcO$_2$/pyr.; (vi) SBH, H$^+$; (vii) MeONa; (viii) O$_2$/PtO$_2$; (ix) H$^+$, MeOH; (x) DBU.

of 1,2-propanediol derivatives, **3*S*** and **3*R***, as a syrup (5.5 g, 79%). R_f 0.45 and R_f 0.46 (10:1 $CHCl_3$–MeOH) for **3*S*** and **3*R***.

*5-Acetamido-4,8-anhydro-1,2,3,5-tetradeoxy-*D-glycero-D-ido-*non-1-enitol [3-*C*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-*D*-glucopyranosyl)-1-propene]* (**5**).—To a solution of **1** (2.65 g, 5.8 mmol) in 6:1 2-PrOH–water (66 mL) was added $NaBH_4$ (1.53 g, 40 mmol), and the mixture was stirred at rt for 3 h. After being acidified by the addition of 1 M HCl (58 mL), the reaction mixture was heated at 80 °C for 5 h. The resulting solution was evaporated, and the residue was acetylated with Ac_2O (23 mL) in pyridine (46 mL) for 3 h. The reaction mixture was diluted with water (210 mL) and extracted with $CHCl_3$ (3 × 43 mL), and then the $CHCl_3$ solution was washed successively with $NaHSO_4$, water, $NaHCO_3$ and water, then dried and evaporated. The residue was chromatographed on silica gel with 8:1 $CHCl_3$–acetone and crystallized from EtOH to give colorless needles (1.33 g, 62%): mp 180–181 °C; $[\alpha]_D$ −30° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 5.84 (dddd, 1H, H-2), 5.50 (d, 1H, $J_{NH,2'}$ 9.8 Hz, NH), 5.10 (m, 2H, H-1a, H-1b), 5.07 (t, 1H, $J_{3',4'}$ 9.8 Hz, H-4′), 5.01 (t, 1H, $J_{2',3'}$ 9.8 Hz, H-3′), 4.23 (dd, 1H, $J_{5',6'a}$ 5.5 Hz, $J_{6'a,6'b}$ 12.2 Hz, H-6′a), 4.10 (dd, 1H, $J_{5',6'b}$ 2.45, H-6′b), 4.04 (td, 1H, $J_{1',2'}$ 10.4 Hz, H-2′), 3.59 (ddd, 1H, H-5′), 3.34 (ddd, 1H, $J_{3a,1'}$ 3.7 Hz, $J_{3b,1'}$ 7.9 Hz, H-1′), 2.35 (ddd, 1H, H-3a), 2.34 (ddd, 1H, $J_{3a,3b}$ 14.3 Hz, H-3b), 2.08, 2.04 and 2.03, (3s, 3 × 3H, 3OAc), 1.95 (s, 3H, NAc) EIMS: *m*/*z* 371 [M^+]. Anal. Calcd for $C_{17}H_{25}NO_8$: C, 54.98; H, 6.97; N, 3.77. Found: C, 55.32; H, 6.85; N, 3.80.

*5-Acetamido-6,7,9-tri-*O*-acetyl-4,8-anhydro-5-deoxy-1,2-*O*-isopropylidene-*D-erythro-L-ido- *and* D-erythro-L-gulo-*nonitol [(2*S *and* 2*R)-3-*C*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-*D*-glucopyranosyl)-1,2-*O*-isopropylidene-1,2-propanediol]* (**7*S*** and **7*R***)

From **4S**. To a solution of **4S** (3.9 g, 7.3 mmol) in EtOH (195 mL) was added hydrazine monohydrate (4.64 mL, 95 mmol), and the solution was heated to reflux for 17 h. After cooling to rt, insoluble matter was removed by filtration. The filtrate was evaporated, and the residue was dried and then subjected to acetylation with Ac_2O (17.5 mL) in pyridine (35 mL). The reaction mixture was diluted with water (150 mL) and extracted with $CHCl_3$ (3 × 120 mL). The $CHCl_3$ layers were combined and washed with $NaHCO_3$, then with brine. The solution was dried over anhydrous Na_2SO_4 and evaporated to dryness. The residue was purified by chromatography on silica gel with 4:1 $CHCl_3$–acetone and by crystallization from EtOH to give **7*S*** as colorless needles (2.5 g, 77%): mp 165–167 °C; $[\alpha]_D$ −26° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 5.48 (bd, 1H, NHAc), 5.07 (dd, 1H, $J_{4',5'}$ 9.5 Hz, H-4′), 4.99 (dd, 1H, $J_{3',4'}$ 9.8 Hz, H-3′), 4.24 (m, 1H, H-2), 4.21 (dd, 1H, $J_{5',6'a}$ 5.2 Hz, $J_{6'a,6'b}$ 12.2 Hz, H-6′a), 4.10 (dd, 1H, $J_{5',6'b}$ 2.4 Hz H-6′b), 4.06 (dd, 1H, $J_{1a,2}$ 7.2 Hz, $J_{1a,1b}$ 8.2 Hz, H-1a), 4.02 (t, 1H, $J_{2',3'}$ 10.1 Hz, H-2′), 3.63 (ddd, 1H, H-5′), 3.53 (dd, 1H, $J_{1b,2}$ 7.0 Hz, H-1b), 3.46 (td, 1H, $J_{1',3a}$ 1.8 Hz, $J_{1',2'} = J_{1',3b}$ 10.1 Hz, H-1′), 2.08, 2.04 and 2.04 (3s, 3 × 3H, 3OAc), 1.95 (s, 3H, NAc), 1.85 (ddd, 1H, $J_{2,3a}$ 8.5 Hz, $J_{3a,3b}$ 14.4 Hz, H-3a), 1.71 (ddd, 1H, $J_{2,3b}$ 4.6 Hz, H-3b), 1.37 and 1.34 (2s, 2 × 3H, 2 × Ip-CH_3). ^{13}C NMR: δ 71.64, 170.67, 170.11, 169.31 ($NHCOCH_3$ and $3OCOCH_3$), 108.64 (Ip-Me_2CO_2), 76.67 (C-1′), 75.63 (C-5′), 74.33 (C-3′), 72.80 (C-2), 69.63 (C-1), 68.38 (C-4′), 62.42 (C-6′), 53.87 (C-2′), 36.22 (C-3), 27.04, 25.75 (2 × Ip-CH_3), 23.22 ($NHCOCH_3$), 20.75, 20.69, 20.61 ($3OCOCH_3$). EIMS: *m*/*z* 445 [M^+]. Anal. Calcd for $C_{23}H_{31}NO_{10}$: C, 53.92; H, 7.01; N, 3.14. Found: C, 54.23; H, 7.12; N, 3.13.

Via dihydroxylation of **5** *with ADmixβ*. To a suspension of ADmixβ (12.2 g) in water (43.5 mL) were added **5** (3.23 g, 8.70 mmol) and *t*-BuOH (43.5 mL). The mixture was stirred at 0 °C for 10 h and treated with sodium sulfite until the color of the reaction mixture turned to gray from orange–yellow. The reaction mixture was extracted with EtOAc (87 mL, then 3 × 44 mL), and the combined extracts were washed with brine (130 mL) and then dried (Na_2SO_4). The EtOAc solution was evaporated, and the residue was triturated with 2-Pr_2O (3 × 20 mL). Crude products of 1,2-propanediol derivatives (2.30 g, 5.7 mmol), 2,2-dimethoxypropane (1.66 mL, 8.5 mmol) and *p*-TsOH (11 mg, 0.07 mmol) were dissolved in DMF (11.5 mL), and the reaction solution was heated at 70 °C for 5 h. The solution was evaporated, and the residue was separated by column chromatography on silica gel with 4:1 $CHCl_3$–acetone. The fraction having R_f 0.43 (4:1 $CHCl_3$–acetone) was collected and evaporated to give pure **7*S*** (1.75 g, 69% from **5**), which was recrystallized from EtOH to afford colorless needles: mp 165–167 °C; $[\alpha]_D$ −26° (*c* 1.0, $CHCl_3$).

From the fraction having R_f 0.38, **7*R*** was obtained as colorless needles (0.50 g, 20% from **5**): mp 150–152 °C; $[\alpha]_D$ −23° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 5.67 (bd, 1H, NHAc), 5.08 (dd, 1H, $J_{3',4'}$ 9.5 Hz, H-3′), 5.03 (t, 1H, $J_{4',5'}$ 9.5 Hz, H-4′), 4.28 (m, 1H, H-2), 4.18 (dd, 1H, $J_{5',6'a}$ 5.5 Hz, $J_{6'a,6'b}$ 12.2 Hz, H-6′a), 4.09 (dd, 1H, $J_{5',6'b}$ 2.1 Hz H-6′b), 4.02 (t, 1H, $J_{1',2'} = J_{2',3'}$ 10.1 Hz, H-2′), 4.00 (dd, 1H, $J_{1a,1b}$ 8.2 Hz, $J_{1a,2}$ 6.1 Hz, H-1a), 3.70 (dd, 1H, $J_{1b,2}$ 7.6 Hz, H-1b), 3.61 (ddd, 1H, H-5′), 3.56 (ddd, 1H, $J_{1',3a}$ 4.9 Hz, $J_{1',3b}$ 5.5 Hz, H-1′), 2.09, 2.04 and 2.03 (3s, 3 × 3H, 3OAc), 1.95 (s, 3H, $NHCOCH_3$), 1.92 (m, 2H, H-3a and H-3b), 1.40 and 1.35 (2s, 2 × 3H, 2 × Ip-CH_3). ^{13}C NMR δ 171.44, 170.73, 170.22, 169.40 ($NH\mathit{C}OCH_3$ and $3O\mathit{C}OCH_3$), 108.50 (Ip-$Me_2\mathit{C}O_2$), 75.72 (C-1′), 75.61 (C-5′), 74.36 (C-3′), 72.60 (C-2), 68.75 (C-1), 68.60 (C-4′), 62.53 (C-6′), 53.68 (C-2′), 34.15 (C-3), 26.78, 25.66 (2 × Ip-$\mathit{C}H_3$), 23.29 ($NHCO\mathit{C}H_3$), 20.76, 20.73, 20.65 ($3OCO\mathit{C}H_3$). EIMS: *m*/*z* 533 [M^+]. Anal. Calcd for

$C_{23}H_{25}NO_{10}$: C, 53.92; H, 7.01; N, 3.14. Found: C, 53.72; H, 7.16; N, 3.11.

Via dihydroxylation with ADmixα. To a solution of ADmixα (1.9 g) in 1:1 *t*-BuOH–H_2O (13.4 mL) was added **5** (0.5 g, 1.34 mmol), and the reaction mixture was worked up as described above. After the purification by column chromatography on silica gel with 8:1 $CHCl_3$–MeOH, a mixture of 1,2-propanediols derivatives, **6*S*** and **6*R***, was obtained as a solid (0.31 g, 58%). The mixture of 1,2-propandiols (0.2 g, 0.5 mmol) was treated with 2,2-dimethoxypropane (0.4 mL, 0.7 mmol) in DMF (1.0 mL) in the presence of *p*-TsOH (0.1 mg). The crude product was purified by column chromatography on silica gel with 8:1 $CHCl_3$–acetone and crystallized from 2-PrOH to give **7*S*** (0.10 g, 27% from **5**) and **7*R*** (0.11 g, 29% from **5**) both as colorless needles. **7*S***: mp 165–167 °C; $[\alpha]_D$ −26° (*c* 1.0, $CHCl_3$). **7*R***: mp 150–152 °C; $[\alpha]_D$ −23° (*c* 1.0, $CHCl_3$).

Via dihydroxylation of **5** *with osmium tetroxide*. Compound 5 (400 mg, 1.1 mmol) was treated with OsO_4 (14 mg, 0.054 mmol) and 4-methylmorpholine *N*-oxide (250 mg, 2.2 mmol). After the workup as described for the dihydroxylation of **1** previously, a mixture of diols, **6*S*** and **6*R***, was obtained as a syrup (151 mg, 34%). The resulting diols (135 mg, 0.33 mmol) were O-isopropylidenated with 2,2-dimethoxypropane (0.1 mL, 0.51 mmol) and *p*-TsOH (0.6 mg) in DMF (1.3 mL). After the purification by column chromatography as described for Section 3.5.2, **7*S*** (98 mg, 20% from **5**) and **7*R*** (49 mg, 10% from **5**) were isolated.

*Methyl 5-acetamido-2,6-anhydro-5,7-dideoxy-*D-glycero-L-gluco-*nonanoate [(2*S*)-1,2-di-*O-*acetyl-3-*C-*(methyl 2-acetamido-3,4,6-tri-*O-*acetyl-2-deoxy-β-*D-*glucuronat-1-yl)-1,2-propanediol]* (**8**)*.*—To a solution of **7*S*** (2.3 g, 5.2 mmol) in MeOH (23 mL) was added 28% sodium methoxide in MeOH (1.1 mL, 5.2 mmol), and the solution was stirred at rt for 1.5 h. The solution was neutralized by the addition of Amberlite IR-120B resin and evaporated to give a syrupy residue. To the residue in water (80 mL) were added $NaHCO_3$ (0.72 g, 8.6 mmol) and prehydrogenated PtO_2 (0.26 g). Oxygen was passed through the solution at 90 °C for 22 h. After the catalyst was removed by filtration, the filtrate was neutralized by the addition of Amberlite IR-120B resin and then evaporated to dryness. The residue was dissolved in MeOH, and the insoluble salts were removed by filtration. Amberlyst-15E (2.8 g) was added to the filtrate, and the mixture was refluxed at 70 °C for 8 h. After the resin was filtered off, the filtrate was evaporated, and the residue was acetylated with Ac_2O (15 mL) in pyridine (30 mL). The reaction mixture was evaporated, and the residue was chromatographed on silica gel with 4:1 $CHCl_3$–acetone. The fraction having R_f 0.59 (10:1 $CHCl_3$–MeOH) was evaporated to a white solid, which was crystallized from EtOH to give **8** as colorless needles (1.56 g, 37% overall yield from **7*S***): mp 129–132 °C; $[\alpha]_D$ −22° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 5.53 (d, 1H, $J_{2',NH}$ 9.15 Hz, NH), 5.25 (m, 1H, H-2), 5.16 (t, 1H, $J_{4',5'}$ 9.76 Hz, H-4′), 5.03 (t, 1H, $J_{3',4'}$ 9.76 Hz, H-3′), 4.26 (dd, 1H, $J_{1b,2}$ 3.66 Hz, $J_{1a,1b}$ 12.2 Hz, H-1b), 4.2–4.09 (m, 2H, H-2, H-1a), 3.88 (d, 1H, H-5′), 3.74 (s, 3H, CO_2CH_3), 3.36 (ddd, 1H, $J_{1',2'}$ 11.6 Hz, H-1′), 1.87 (m, 2H, H-3a and H-3b), 2.07, 2.06, 2.05 and 2.02 (4s, 4 × 3H, 4OAc), 1.97 (s, 3H, NAc). ^{13}C NMR: δ 171.60, 170.58, 170.38, 170.22, 169.27, 167.44 (4$OCOCH_3$, $NHCOCH_3$ and CO_2CH_3), 76.31 (C1′), 73.40 (C3′), 69.37, 68.88, 65.13, 53.48, 52.73 (CO_2CH_3), 33.06 (C3), 23.20, 21.01, 20.73, 20.66, 20.46 ($NHCOCH_3$ and 4$OCOCH_3$). EIMS: *m*/*z* 475 [M^+]. Anal. Calcd for $C_{20}H_{28}NO_{12}$: C, 50.63; H, 5.95; N, 2.95. Found: C, 50.57; H, 6.14; N, 2.95.

*Methyl 5-acetamido-4,8,9-tri-*O-*acetyl-2,6-anhydro-5,7-dideoxy-*D-manno-*non-2-enoate (methyl 4,8,9-tri-*O-*acetyl-2,3-didehydro-2,7-dideoxy-*N-*acetylneuraminate)* (**9**).—To a solution of **8** (1.4 g, 3.0 mmol) in $CHCl_3$ (dried over CaH_2, 22 mL) was added DBU (1.76 mL, 1.81 g, 12 mmol), and the reaction solution was refluxed at 70 °C for 5 h. The solution was washed with 2 M HCl and brine, then dried and evaporated. Column chromatography on silica gel (1:1 hexane–acetone) of the residue gave a syrup (0.94 g) that was crystallized from EtOH to give **9** as colorless needles (0.81 g, 66%): mp 124–126 °C; $[\alpha]_D$ +108° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 6.05 (d, 1H, $J_{3,4}$ 4.47 Hz, H-3), 5.90 (bs, 1H, NH), 5.29 (m, 1H, H-4), 5.25 (m, 1H, H-8), 4.35 (dd, 1H, $J_{8,9a}$ 3.35 Hz, H-9a), 4.26 (m, 2H, H-5, H-6), 4.10 (dd, 1H, $J_{8,9b}$ 5.5 Hz, $J_{9a,9b}$ 12.2 Hz, H-9b), 3.81 (s, 3H, CO_2CH_3), 2.14 (ddd, 1H, H-7b), 2.08, 2.08 and 2.06 (3s, 3 × 3H, 3OAc), 1.99 (s, 3H, NAc), 1.94 (ddd, 1H, $J_{7a,7b}$ 15.0 Hz, H-7b). ^{13}C NMR: δ 170.56, 170.31, 170.26, 169.88, 161.97 (3$OCOCH_3$, $NHCOCH_3$ and CO_2CH_3), 74.98 (C-6), 68.64 (C-8), 66.49 (C-4), 64.91 (C-9), 52.57 (CO_2CH_3), 49.53 (C-5), 31.36 (C-7), 23.11, 20.97, 20.84, 20.67 ($NHCOCH_3$, 3$OCOCH_3$). EIMS: *m*/*z* 415 [M^+]. Anal. Calcd for $C_{18}H_{25}NO_{10}$: C, 52.05; H, 6.07; N, 3.27. Found: C, 52.03; H, 6.24; N, 3.23.

4. Supplementary material

Full crystallographic details, excluding structure features, have been deposited with the Cambridge Crystallographic Data Centre. These data may be obtained, on request, from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Tel.: +44-1223-336408; fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk) on quoting CCDC-188233 for (*S*)-1,2-*O*-isopropylidene-3-*C*-(3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-1,2-propanediol (**4*S***) and CCDC-188234 for (*S*)-3-*C*-(3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-1,2-epoxypropane (**2*S***).

References

1. Cui, J.; Horton, D. *Carbohydr. Res.* **1998**, *309*, 319–330.
2. Gaurat, O.; Xie, J.; Valery, J.-M. *Tetrahedron Lett.* **2000**, *41*, 1187–1189.
3. Wu, W.-Y.; Jin, B.; Kong, D. C. M.; von Itzstein, M. *Carbohydr. Res.* **1997**, *300*, 171–174.
4. Wilson, J. C.; Thomson, R. J.; Dyson, J. C.; Florio, P.; Quelch, K. J.; Abo, S.; von Itzstein, M. *Tetrahedron: Asymmetry* **2000**, *11*, 53–73 and references cited therein.
5. Maru, I.; Ohnishi, J.; Ohta, Y.; Tsukada, Y. *Carbohydr. Res.* **1998**, *306*, 575–578.
6. Altomare, A.; Burla, M. C.; Camalli, M.; Cascarano, G. L.; Giacovazzo, C.; Guagliardi, A.; Moliterni, A. G. G.; Polidori, G.; Spagna, R. *J. Appl. Crystallogr.* **1999**, *32*, 115–119.
7. Sharpless, K. B.; Amberg, W.; Bennani, Y. L.; Crispino, G. A.; Hartung, J.; Jeong, K.-S.; Kwong, H.-L.; Morikawa, K.; Wang, Z.-M.; Xu, D.; Zhang, X.-L. *J. Org. Chem.* **1992**, *57*, 2768–2771.
8. Kanno, K.; Kobayashi, Y.; Nishimura, S.; Kuzuhara, H.; Hatanaka, K. *J. Carbohydr. Chem.* **1995**, *14*, 481–490.
9. Roe, B. A.; Boojamura, C. G.; Griggs, J. L.; Bertozzi, C. R. *J. Org. Chem.* **1996**, *61*, 6442–6445.
10. Bamford, M. J.; Pichel, J. C.; Husman, W.; Patel, B.; Storer, R.; Weir, N. G. *J. Chem. Soc., Perkin Trans. 1* **1995**, 1181–1187.