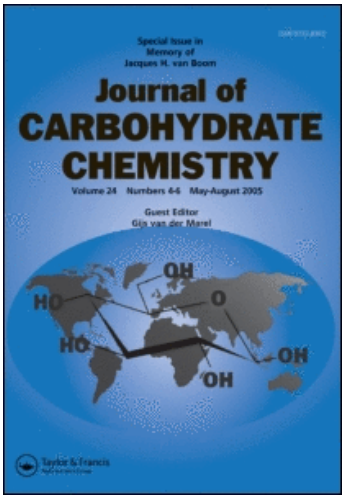

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Studies on 1-Deoxynojirimycin-Containing Glycans: Synthesis of Novel Disaccharides Related to Lactose, Lactosamine, and Chitobiose

Makoto Kiso[a]; Hideki Katagiri[a]; Hiroyasu Furui[a]; Akira Hasegawa[a]
[a] Department of Applied Bioorganic Chemistry, Gifu University, Gifu, Japan

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STUDIES ON 1-DEOXYNOJIRIMYCIN-CONTAINING GLYCANS: SYNTHESIS OF NOVEL DISACCHARIDES RELATED TO LACTOSE, LACTOSAMINE, AND CHITOBIOSE

Makoto Kiso, Hideki Katagiri, Hiroyasu Furui, and Akira Hasegawa

Department of Applied Bioorganic Chemistry, Gifu University,
Gifu 501-11, Japan

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ABSTRACT

Suitably protected 1-deoxynojirimycin (1,5-dideoxy-1,5-imino-D-glucitol; DNJ) and its 2-acetamido derivative, i.e., 2,3,6-tri-*O*-benzyl-*N*-benzyloxycarbonyl-1,5-dideoxy-1,5-imino-D-glucitol (**6**) and 2-acetamido-3,6-di-*O*-benzyl-*N*-benzyloxycarbonyl-1,2,5-trideoxy-1,5-imino-D-glucitol (**14**) were each coupled with methyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranoside (**15**) in the presence of dimethyl(methylthio)-sulfonium triflate (DMTST) as a promoter, to give **16** and **18**, which were converted to the novel disaccharides (**20, 21**) related to lactose and lactosamine. Coupling of **14** with methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (**22**) gave a chitobiose analog (**25**). *O*-(β-D-Galactopyranosyl)-(1→3)-DNJ derivatives (**38, 39**) and *O*-(β-D-glucopyranosyl)-(1→3)-DNJ (**45**) were also synthesized. Conformational analysis of a variety of DNJ derivatives, based on the ^{1}H NMR data, is also discussed.

INTRODUCTION

Polyhydroxylated piperidine alkaloids, such as 1-deoxynojirimycin (DNJ) and related compounds have been shown[1-6] not only to be potent inhibitors of α-glucosidases and glycoprotein-processing enzymes, but also to be of potential clinical value as antidiabetic, anti-neoplastic and anti-HIV agents. In addition, much attention is now focused on cell-surface complex carbohydrates because of their newly discovered involvement in cell-cell recognition, cell growth, differentiation, adhesion, oncogenesis, immune reactions, and so on.

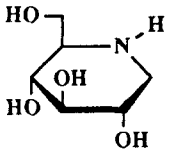
In the preceding papers,[7,8] we have reported the synthesis of some DNJ derivatives designed as the specific enzyme inhibitors and immunoadjuvant active compounds. Yoshikuni *et al.*[9] reported an enzymatic synthesis and α-glucosidase inhibitory activity of the 4-*O*-α-D-glucopyranosyl-DNJ derivatives. The present paper describes the synthesis of novel, DNJ-containing disaccharides structurally related to lactose, lactosamine and chitobiose, which are important disaccharide components of cell-surface glycolipids and glycoproteins.

RESULTS AND DISCUSSION

Compound **1**, prepared by acetylation of *N*-(*tert*-butoxycarbonyl)-1,5-dideoxy-1,5-imino-D-glucitol,[8] was treated with trifluoroacetic acid in dichloromethane, and the resulting product was then benzyloxycarbonylated to give **2**. Zemplen's *O*-deacetylation of **2** at 0 °C and treatment of the product **3** with benzaldehyde dimethyl acetal in the presence of a catalytic amount of *p*-toluenesulfonic acid monohydrate in *N,N*-dimethylformamide gave crystalline **4** in high yield. Benzylation of **4** and reductive ring opening of the benzylidene group of **5** afforded **6** as a glycosyl acceptor. 3-*O*-Benzylation of 2-acetamido-4,6-*O*-benzylidene-*N*-(*tert*-butoxycarbonyl)-1,2,5-trideoxy-1,5-imino-D-glucitol[8] (**7**) and following treatment with 80% acetic acid gave **9**, which was then acetylated to afford **10**. The conversion of **10** into another glycosyl acceptor **14**, *via* **11**, **12** and **13**, was achieved as just described for the preparation of **6**.

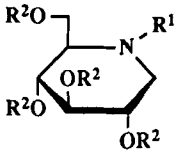
Coupling of a glycosyl donor **15**[10] with **6** or **14** was performed using dimethyl(methylthio)sulfonium triflate (DMTST)[11,12] as a thiophilic promoter to give **16** (78%) or **18** (65%), respectively. Zemplen's *O*-deacetylation of the protected disaccharides at 0 °C and following hydrogenolytic removal of the benzyloxycarbonyl (Z) and benzyl (Bn) groups in the presence of 10% Pd-C catalyst gave the novel disaccharides (**20** and **21**) which are structurally related to lactose and lactosamine, respectively, important disaccharide components of sphingoglycolipids such as gangliosides and various glycoproteins.

The glycosylation of **14** with another glycosyl donor **22**[10] was performed as described for the preparation of **16** or **18**, to give the desired disaccharide **23** (83%). *O*-Deacetylation of **23** and simultaneous cleavage of the phthaloyl and benzyloxycarbonyl group with hydrazine hydrate, followed by *N*-acetylation in methanol, afforded **25** which is structurally related to chitobiose, the core disaccharide component of asparagin-linked glycans.

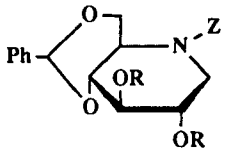


1-deoxynojirimycin

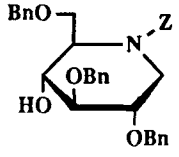
(DNJ)



	R^1	R^2
1	Boc	Ac
2	Z	Ac
3	Z	H



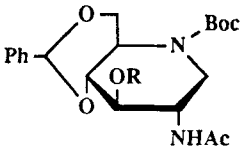
	R
4	H
5	Bn



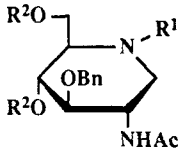
6

Boc =*tert*-butoxycarbonyl Bn = benzyl

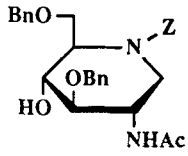
Z = benzyloxycarbonyl



	R
7	H
8	Bn



	R^1	R^2
9	Boc	H
10	Boc	Ac
11	Z	Ac
12	Z	H
13	Z	benzylidene



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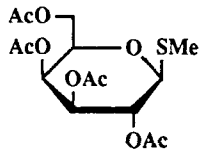

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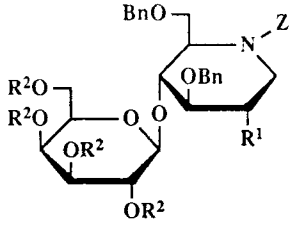
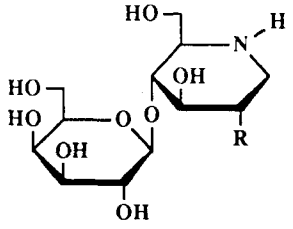
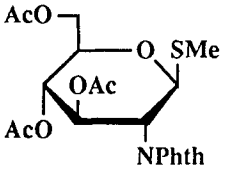


	R^1	R^2
16	OBn	Ac
17	OBn	H
18	NHAc	Ac
19	NHAc	H



	R
20	OH
21	NHAc



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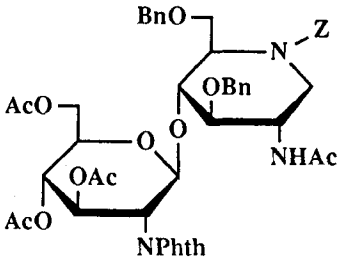

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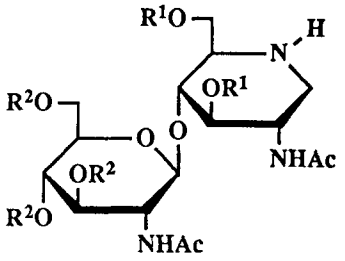
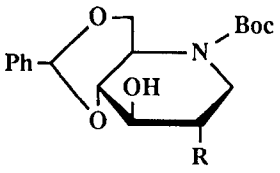
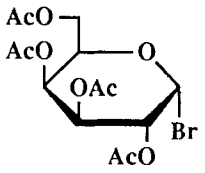


	R^1	R^2
24	Bn	H
25	H	H



	R
26	OClAc
27	N_3



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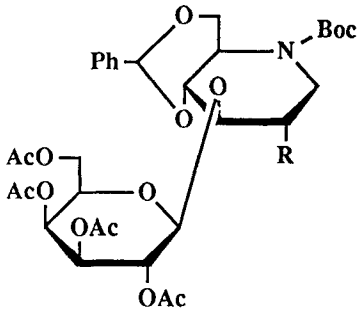
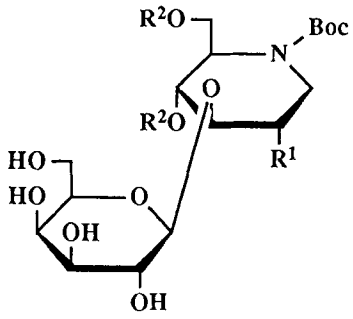
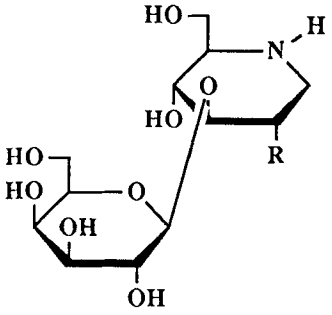


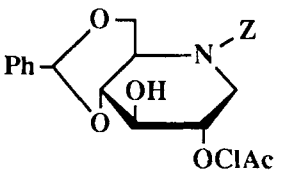
	R
29	OClAc
30	OH
31	N_3
32	NH_2
33	NHAc



	R^1	R^2
34	OH	benzylidene
35	NHAc	benzylidene
36	OH	H
37	NHAc	H



	R
38	OH
39	NHAc



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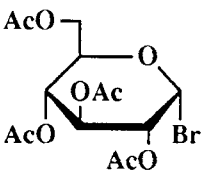

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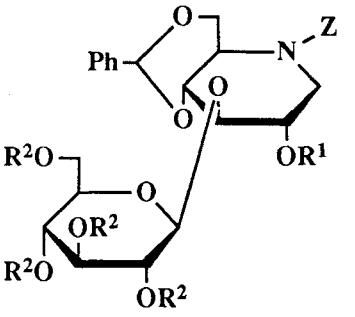
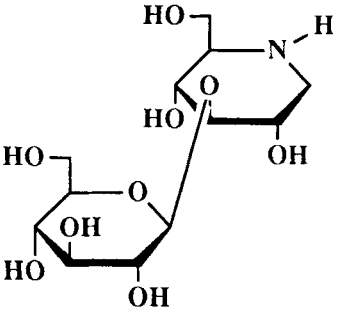


	R^1	R^2
42	ClAc	Ac
43	H	Ac
44	H	H



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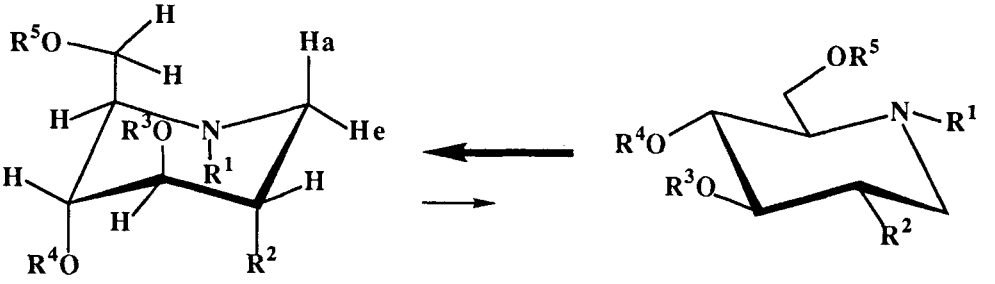

$^1C_4$ $^4C_1$

	R^1	R^2	R^3	R^4	R^5
46	Boc	OAc	Ac	H	Bz
47	Boc	N_3	Ac	H	Bz
48	Boc	OBn	Bn	Ac	Ac
49	Boc	N_3	Ac	Ac	Ac
50[8]	Boc	OBz	Bz	Bz	H
51	Z	OBn	Bn	Ac	Ac
52	Z	N_3	Bn	Ac	Ac

O-(β-D-Galactopyranosyl)-(1→3)-DNJ derivatives (**38** and **39**) were synthesized as follows. 2-*O*-Chloroacetyl (**26**) and 2-azido (**27**) derivatives[8] of DNJ were each coupled with acetobromogalactose (**28**) in the presence of silver carbonate and silver perchlorate in dichloromethane to give **29** (86%) and **31** (75%). The chloroacetyl group of **29** was removed by treatment with aq. pyridine to give **30**, which successively underwent Zemplen's *O*-deacetylation, hydrogenolytic cleavage of the benzylidene group, and acid hydrolysis of the *tert*-butoxycarbonyl (Boc) group to afford **38**. Selective hydrogenolysis of the azido group in **31**, and following *N*-acetylation gave **33** in a quantitative yield. The conversion of **33** into **39** was achieved as described for the synthesis of **38**. Compound **40**, prepared by partial chloroacetylation of **4**, was coupled with acetobromoglucose (**41**), as described for the preparation of **29**, to afford **42** (76%). After removal of the chloroacetyl and acetyl groups in **42**, the benzylidene and benzyloxycarbonyl group were simultaneously cleaved by hydrogenolysis. The product was purified by chromatography on a column of Sephadex LH-20 to give crystalline **45**.

In the ^{1}H NMR data of *N*-*tert*-butoxycarbonyl (Boc) and *N*-benzyloxycarbonyl (Z) derivatives of DNJ, such as **1** and **2** (see Experimental section) and **46-52** (see Table 1), all of the ring protons H-1~H-4 had the small vicinal coupling constants ($J_{1a,2}$ = 1.5-3.1, $J_{1e,2} < 2$, $J_{2,3} \cong J_{3,4} \cong J_{4,5}$ = 3-4 Hz) to strongly suggest that the preferred conformation of these *N*-protected DNJ derivatives is $^1C_4$. Even in the disaccharide derivatives, such as **16** and **17**, the preferred conformation of the DNJ moiety appeared to be $^1C_4$. However, for DNJ itself,[13,14] *N*-benzyl[15] or *N*-alkyl[4,14] derivatives of DNJ, and the 4,6-*O*-benzylidene derivatives such as **4, 5, 8, 13, 26, 27, 29~33, 42~44** (see Experimental section), the usual $^4C_1$ conformation is predominant. The chemical and biological[16] reactivity of the DNJ derivatives may be dependent upon such conformational properties.

EXPERIMENTAL

General Procedures. Melting points were determined with a Yanagimoto micro melting-point apparatus and are uncorrected. Specific rotations were determined with a Union PM-201 polarimeter, and ^{1}H NMR spectra were recorded at 270 MHz with a JEOL JNM-GX270 spectrometer. Preparative TLC was performed on silica gel 60 (Merck Co.), and column chromatography on silica gel (Wako Co.; 200 mesh) was accomplished with the solvent systems (v/v) specified. Concentrations and evaporations were conducted *in vacuo*.

TABLE 1. ^{1}H NMR Data of Some N-Protected 1-Deoxynojirimycin(DNJ) Derivatives (**46-52**)

Compound (Solvent)	Chemical Shifts (ppm) and Coupling Constants (Hz)							
	H-1a	H-1e	H-2	H-3	H-4	H-5	H-6	H-6'
46 ($CDCl_3$)	3.34(dd) $J_{1a,2}$=2.2 J_{gem}=15.4	4.26(~d) $J_{1e,2}$<2	4.91(m)	5.04(~t) J =~4	3.91(~t) J =~4	4.58-4.7(m)	4.48(dd) $J_{5,6}$=3.5 J_{gem}=9.5	4.68(dd) $J_{5,6'}$=7.3
47 ($CDCl_3$)	3.44(dd) $J_{1a,2}$=2.6 J_{gem}=15.0	4.26(~d) $J_{1e,2}$<2	3.78(m)	4.98(~t) J =3~4	3.85(~t) J =~3	4.7-4.78(m)	4.42(dd) $J_{5,6}$=4 J_{gem}=9.9	4.42(dd) $J_{5,6'}$=8.8
48 ($CDCl_3$)	3.26(dd) $J_{1a,2}$=2.2 J_{gem}=15.0	4.23(~d) $J_{1e,2}$<2	3.58(m)	3.72(~t) J =3~4	4.99(~t) J =~3	4.48-4.58(m)	4.20(dd) $J_{5,6}$=5.5 J_{gem}=11	4.42(dd) $J_{5,6'}$=8.1
49 ($CDCl_3$)	3.40(dd) $J_{1a,2}$=3.1 J_{gem}=15.2	4.21(~d) $J_{1e,2}$<2	3.52(m)	— 4.89,4.99(~t) — J=3.3~3.4		4.60(m)	4.19(dd) $J_{5,6}$=6.2 J_{gem}=11.4	4.41(dd) $J_{5,6'}$=8.1
50 (C_6D_6)	3.34(dd) $J_{1a,2}$=1.5 J_{gem}=15.8	4.45(~d) $J_{1e,2}$<2	5.37(m)	— 5.72,5.10(~t) — J=3~4		4.73(m)	3.76(dd) $J_{5,6}$=5.9 J_{gem}=11.4	3.84(dd) $J_{5,6'}$=8.1
51 ($CDCl_3$)	3.32(~d) J_{gem}=14.7 $J_{1a,2}$<2		3.57(m)	3.74(~t) J =~3	4.99(bs)		4.21(dd) $J_{5,6}$=5.9 J_{gem}=11.4	4.47(dd) $J_{5,6'}$=8.4
52 ($CDCl_3$)	3.42(dd) $J_{1a,2}$=2.9 J_{gem}=15.0	4.25(~d) $J_{1e,2}$<2	3.59(m)	— 4.90,5.01(~t) — J=~3		4.67(m)	4.20(dd) $J_{5,6}$=5.9 J_{gem}=11.7	4.42(dd) $J_{5,6'}$=8.6

2,3,4,6-Tetra-*O*-acetyl-*N*-(*tert*-butoxycarbonyl)-1,5-dideoxy-1,5-imino-D-glucitol (1) and 2,3,4,6-Tetra-*O*-acetyl-*N*-benzyloxycarbonyl-1,5-dideoxy-1,5-imino-D-glucitol (2). Acetylation of *N*-(*tert*-butoxycarbonyl)-1,5-dideoxy-1,5-imino-D-glucitol[8] with acetic anhydride in pyridine gave **1** (quant): $[\alpha]_D$ +0.7° (*c* 0.84, dichloromethane); ^{1}H NMR ($CDCl_3$) δ 1.46 (s, 9H, 3 x C*H*$_3$), 2.07 (6H), 2.08 (3H), 2.10 (3H) (3s, 12H, 4 x C*H*$_3$CO), 3.29 (dd, 1H, J = 15.4, 1.4 Hz, H-1a), 4.23 (dd, 1H, J = 11.4, 5.9 Hz, H-6), 4.24 (dd, 1H, J = 15.4, 1-2 Hz, H-1e), 4.33 (dd, 1H, J = 11.4, 7.3 Hz, H-6'), 4.57 (m, 1H, H-5), 4.78 (narrow m, 1H, H-2), and 4.92 (~t, 1H, J = 3.7-3.9 Hz, H-3 or 4). These NMR data show that compound **1** is present in the ^{1}C$_4$ conformation in chloroform-*d* solution.

Compound **1** (21 g) was treated with trifluoroacetic acid (19 mL) in dichloromethane (30 mL) overnight at room temperature, and the mixture was concentrated. The residual syrup was triturated with ether and decanted. The solid residue was dissolved in methanol and treated with Amberlite IR-410 (OH^-) to remove the acid. The resin was filtered off and the filtrate was concentrated to a syrup, which was then treated with benzyl chloroformate (23 g) in dichloromethane (40 mL) and pyridine (15 mL) overnight at room temperature. Methanol was added and the mixture was concentrated. The residue was taken up in dichloromethane, and washed successively with 2 M hydrochloric acid and water, dried and concentrated. The residual syrup was chromatographed on a column of silica gel with dichloromethane to give **2** (21.53 g, 92%): $[\alpha]_D$ -6.1° (*c* 1, dichloromethane); ^{1}H NMR ($CDCl_3$) δ 1.93, 1.96, 1.99, 2.10 (4s, 12H, 4 x C*H*$_3$CO), 3.38 (near d, 1H, J = 15.4 Hz, H-1a), 4.24 (dd, 1H, J = 11.7, 5.9 Hz, H-6), 4.30 (near d, 1H, J = 15.4 Hz, H-1e), 4.38 (dd, 1H, J = 11.7, 8 Hz, H-6'), 4.66 (m, 1H, H-5), 4.80 (narrow m, 1H, H-2), 4.91 (narrow t, 1H, H-3 or 4), 5.03 (t, 1H, J = 3.7 Hz, H-3 or 4), 5.18 (broad s, 2H, PhC*H*$_2$), and 7.3-7.4 (m, 5H, Ph-*H*).

Anal. Calcd for $C_{22}H_{27}NO_{10}$ (465.46): C, 56.77; H, 5.85; N, 3.01. Found: C, 57.03; H, 5.87; N, 3.09.

4,6-*O*-Benzylidene-*N*-benzyloxycarbonyl-1,5-dideoxy-1,5-imino-D-glucitol (4). *O*-Deacetylation of **2** with methanolic sodium methoxide was achieved at 0 °C to give **3** (85%); $[\alpha]_D$ -13.6° (*c* 0.7, methanol). Treatment of **3** with benzaldehyde dimethyl acetal in the presence of a catalytic amount of *p*-toluenesulfonic acid monohydrate in *N,N*-dimethylformamide (DMF) gave **4**, which was crystallized from ethyl acetate-*n*-hexane: mp 134-135 °C; $[\alpha]_D$ +8.7° (*c* 0.7, dichloro-methane); ^{1}H NMR ($CDCl_3$-CD_3OD) δ 2.89 (dd, 1H, Jgem = 13.6, $J_{1a,2}$ = 9.5 Hz, H-1a), 3.31 (m, 1H, H-5), 3.4-3.7 (m, 3H, H-2~4), 4.15 (dd, 1H, $J_{1e,2}$ = 4.0 Hz, H-1e), 4.36 (t, 1H, J =

10.6 Hz, H-6a), 4.74 (dd, 1H, $J_{5,6e}$ = 4.4 Hz, H-6e), 5.10 (s, 2H, PhC*H*$_2$O), 5.57 (s, 1H, PhC*H*), and 7.3-7.5 (m, 10H, Ph-*H*).

Anal. Calcd for $C_{21}H_{23}NO_6$ (385.42): C, 65.44; H, 6.02; N, 3.63. Found: C, 65.53; H, 5.72; N, 3.42.

2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-*N*-benzyloxycarbonyl-1,5-dideoxy-1,5-imino-D-glucitol (5). To a solution of **4** (9.15 g) in DMF (40 mL) was added sodium hydride in oil (2.85 g, 60% of sodium hydride by weight) at -45 °C, and the mixture was stirred for 1 h at -45 °C. Benzyl bromide (8.47 mL) was added and the mixture was stirred for 5 h at -45 °C. The mixture was poured into ice-water and extracted with dichloromethane. The extract was washed with ice-cold 2 M hydrochloric acid and water, dried, and the solvent was evaporated to leave a syrup, which was chromatographed on a column of silica gel with dichloromethane to give syrupy **5** (65%) : $[\alpha]_D$ -18.4° (*c* 1, chloroform); ^{1}H NMR ($CDCl_3$) δ 3.48 (m, 1H, $J_{4,5} = J_{5,6a}$ = 10.3, $J_{5,6e}$ = 4.4 Hz, H-5), 3.51 (dd, 1H, H-1a), 3.59 (m, 1H, $J_{1a,2}$ = 7.3, $J_{1e,2}$ = 2.6, $J_{2,3}$ = 4.4 Hz, H-2), 3.69 (dd, 1H, $J_{3,4}$ = 8.8 Hz, H-3), 3.78 (dd, 1H, Jgem = 13.56, $J_{1e,2}$ = 2.6 Hz, H-1e), 3.89 (dd, 1H, $J_{4,5}$ = 10.3 Hz, H-4), 4.07 (~t, 1H, Jgem = 11, $J_{5,6a}$ = 10.6 Hz, H-6a), 4.50-4.61 (m, 2H, PhC*H*$_2$), 4.71, 4.79 (2d, 2H, PhC*H*$_2$), 4.82 (dd, 1H, Jgem = 11, $J_{5,6}$ = 4.4 Hz, H-6e), 5.05-5.15 (m, 2H, PhC*H*$_2$ of Z), and 7.15-7.55 (m, 15H, Ph-*H*).

Anal. Calcd for $C_{35}H_{35}NO_6$ (565.67): C, 74.32; H, 6.24; N, 2.48. Found: C, 74.12; H, 6.38; N, 2.65.

2,3,6-Tri-*O*-benzyl-*N*-benzyloxycarbonyl-1,5-dideoxy-1,5-imino-D-glucitol (6). To a stirred mixture of **5** (0.13 g), sodium cyanoborohydride (0.2 g) and molecular sieves 3Å (0.1 g) in tetrahydrofuran (4.2 mL) was dropwise added saturated hydrogen chloride solution in dry diethyl ether until the evolution of gas ceased. Dichloromethane and ice-cold water were added, and the mixture was filtered. The filtrate was washed with water, dried, and concentrated to a syrup, which was chromatographed on a column of silica gel with 4:1 *n*-hexane-ethyl acetate to give syrupy **6** (80%): $[\alpha]_D$ +21° (*c* 1, dichloromethane) ; ^{1}H NMR ($CDCl_3$-CD_3OD) δ 3.16 (d, 1H, Jgem = 15 Hz, H-1a), 5.14, 5.20 (2d, 2H, Jgem = 12.5 Hz, PhC*H*$_2$ of Z), and 7.15-7.4 (m, 20H, Ph-*H*).

Anal. Calcd for $C_{35}H_{37}NO_6$ (567.68): C, 74.05; H, 6.57; N, 2.47. Found: C, 73.78; H, 6.63; N, 2.35.

2-Acetamido-3-*O*-benzyl-4,6-*O*-benzylidene-*N*-(*tert*-butoxycarbonyl)-1,2,5-trideoxy-1,5-imino-D-glucitol (8). Compound **7**[8] (2.34 g) was treated with sodium hydride (1.5 mol equiv) in DMF (25 mL) for one hour at room temperature.

Benzyl bromide (1.5 mol equiv) was added, and the mixture was stirred for 5 h at room temperature. The mixture was cooled to 0 °C and then methanol was added to decompose excess reagents. After concentration, the residue was taken up in dichloromethane and washed with water, dried, and the solvent was evaporated. The residual syrup was chromatographed on a column of silica gel with (a) *n*-hexane, (b) 4:1 and (c) 2:1 *n*-hexane-ethyl acetate. Eluant (c) gave **8** (2.64 g, 91%): $[\alpha]_D$ +19° (*c* 1, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.46 (s, 9H, C*H*$_3$ of Boc), 1.82 (s, 3H, C*H*$_3$CO), 2.76 (dd, 1H, Jgem = 13.6, $J_{1a,2}$ = 9.5 Hz, H-1a), 3.24 (m, 1H, $J_{4,5}$ = $J_{5,6a}$ = 10.3, $J_{5,6e}$ = 4.4 Hz, H-5), 3.47 (t, 1H, $J_{2,3}$ = $J_{3,4}$ = 8.4 Hz, H-3), 3.79 (m, 1H, H-2), 3.92 (dd, 1H, H-4), 4.21 (dd, 1H, Jgem = 13.6, $J_{1e,2}$ = 4.4, H-1e), 4.43 (~t, 1H, J = 11 Hz, H-6a), 4.76 (dd, 1H, Jgem = 10.6, $J_{5,6e}$ = 4.8, H-6e), 4.71, 4.90 (2d, 2H, PhC*H*$_2$), 5.07 (d, 1H, J = 5.5 Hz, NH), 5.64 (s, 1H, PhC*H*), and 7.25-7.6 (m, 10H, Ph-*H*).

Anal. Calcd for $C_{27}H_{34}N_2O_6$ (482.58): C, 67.20; H, 7.10; N, 5.81. Found: C, 66.99; H, 6.89; N, 5.98.

2-Acetamido-3-*O*-benzyl-*N*-(*tert*-butoxycarbonyl)-1,2,5-trideoxy-1,5-imino-D-glucitol (9) and 2-Acetamido-4,6-di-*O*-acetyl-3-*O*-benzyl-*N*-(*tert*-butoxycarbonyl)-1,2,5-trideoxy-1,5-imino-D-glucitol (10). A mixture of **8** (2.47 g) and 80 % acetic acid (16 mL) was stirred overnight at 40 °C, and the solvent was evaporated. The product **9** (quant.) was purified by chromatography on a column of silica gel: $[\alpha]_D$ +33° (*c* 0.84, methanol); ^{1}H NMR ($CDCl_3$ - CD_3OD) δ 1.45 (s, 9H, C*H*$_3$ of Boc), 1.88 (s, 3H, C*H*$_3$CO), 3.28 (dd, 1H, J = 13.9, 1.8 Hz, H-1), 4.56 4.62 (2d, 2H, Jgem = 11.7 Hz, PhC*H*$_2$), and 7.2-7.4 (m, 5H, Ph-*H*).

A mixture of **9** (2 g) in pyridine (10 mL) and acetic anhydride (5 mL) was stirred overnight at room temperature. After work up, the product was purified by chromatography on a column of silica gel with 300:1 ~ 250:1 dichloromethane-methanol to give **10** (quant.): $[\alpha]_D$ -17° (*c* 0.8, dichloromethane); ^{1}H NMR ($CDCl_3$) δ 1.47 (s, 9H, C*H*$_3$ of Boc), 1.96 (s, 3H, AcN), 2.03, 2.06 (2s, 6H, AcO), 3.39 (~d, J = 14.7 Hz, H-1a), 6.07 (d, 1H, J = 8.4 Hz, NH), and 7.2-7.4 (m, 5H, Ph-*H*).

Anal. Calcd for $C_{24}H_{34}N_2O_8$ (478.54): C, 60.24; H, 7.16; N, 5.85. Found: C, 60.12; H, 7.29; N, 5.62.

2-Acetamido-4,6-di-*O*-acetyl-3-*O*-benzyl-*N*-benzyloxycarbonyl-1,2,5-trideoxy-1,5-imino-D-glucitol (11) and 2-Acetamido-3-*O*-benzyl-*N*-benzyloxycarbonyl-1,2,5-trideoxy-1,5-imino-D-glucitol (12). A mixture of **10** (1.7 g) and trifluoroacetic acid (1.4 mL) in dichloromethane (15 mL) was stirred overnight at room temperature. Work up and the *N*-benzyloxycarbonylation were performed as described for **2**. The product was purified by chromatography on a column of silica gel with (a) *n*-hexane, (b) 4:1 and (c) 1:1 *n*-hexane-ethyl acetate.

Eluant (c) gave **11** (1.6 g, 86%): $[\alpha]_D$ -16° (*c* 1, dichloromethane); ^1H NMR ($CDCl_3$) δ 5.3 (~s, 2H, PhC*H*$_2$OCO), 7.25-7.45 (m, 10H, Ph-*H*), and complete disappearance of C*H*$_3$ of Boc).

Compound **11** (1.5 g) was treated with methanolic sodium methoxide for 2 h at 0 °C. After work up, the product was purified by chromatography on a column of silica gel with 150:1~100:1 dichloromethane-methanol, to give **12** (1.2 g, 94%): $[\alpha]_D$ +31° (*c* 0.7, chloroform); ^1H NMR ($CDCl_3$-CD_3OD) δ 1.78 (s, 3H, AcN), 3.38 (dd, 1H, J = 14, 2 Hz, H-1a), 3.56 (~s, 1H), 3.75-3.9 (m, 2H), 4.08 (~s, 1H), 4.13 (d, 1H, J = 14 Hz, H-1e), 4.21 (~s, 1H), 4.53, 4.65 (2d, 2H, Jgem =11.7 Hz, PhC*H*$_2$ of OBn), 5.04, 5.18 (2d, 2H, Jgem = 12.6 Hz, PhC*H*$_2$ of Z), and 7.2-7.4 (m, 10H, Ph-*H*). These NMR data show that the $^1C_4$ conformation is predominant for **11** and **12**.

Anal. Calcd for $C_{23}H_{28}N_2O_6$ (428.49): C, 64.47; H, 6.59; N, 6.54. Found: C, 64.32; H, 6.55; N, 6.80.

2-Acetamido-3-*O*-benzyl-4,6-*O*-benzylidene-*N*-benzyloxycarbonyl-1,2,5-trideoxy-1,5-imino-D-glucitol (13). A mixture of **12** (0.58 g), benzaldehyde dimethyl acetal (0.81 mL), drierite (0.58 g) and a catalytic amount of *p*-toluenesulfonic acid in DMF was stirred overnight at room temperature. Work up and solvent evaporation gave a syrup which was chromatographed on a column of silica gel with (a) dichloromethane and (b) 300:1 dichloromethane-methanol. Eluant (b) gave **13** (80%): $[\alpha]_D$ -1.3° (*c* 0.8, 2:1 chloroform-methanol); ^1H NMR ($CDCl_3$-CD_3OD) δ 1.85 (s, 3H, AcN), 3.01 (dd, 1H, J = 13.6, 8.8 Hz, H-1a), 3.35 (m, 1H, H-5), 3.55 (t, 1H, J = 8.8, H-3), 3.92 (dd, 1H, J = 9, 8.8 Hz, H-4), 4.14 (dd, 1H, J = 13.6, 4.4 Hz, H-1e), 4.34 (t, 1H, J = 11 Hz, H-6a), 4.69, 4.84 (2d, 2H, J = 11.7, PhC*H*$_2$ of OBn), 4.81 (dd, 1H, J = 11, 4.8 Hz, H-6e), 5.05, 5.14 (2d, 2H, J = 12 Hz, PhC*H*$_2$ of Z), 5.62 (s, 1H, PhC*H* 2), and 7.2-7.55 (m, 15H, Ph-*H*).

Anal. Calcd for $C_{30}H_{32}N_2O_6$ (516.59): C, 69.75; H, 6.24; N, 5.42. Found: C, 69.56; H, 5.96; N, 5.64.

2-Acetamido-3,6-di-*O*-benzyl-*N*-benzyloxycarbonyl-1,2,5-trideoxy-1,5-imino-D-glucitol (14). Compound **13** (0.7 g) was treated with sodium cyanoborohydride and hydrogen chloride-ether in tetrahydrofuran as described for **6**. After usual work up, the product was purified by chromatography on a column of silica gel with (a) dichloromethane and (b) 300:1~150:1 dichloromethane-methanol. Eluant (b) gave **14** (98%): $[\alpha]_D$ +23° (*c* 0.8, chloroform); ^1H NMR ($CDCl_3$) δ 1.78 (s, 3H, AcN), 3.20 (dd, 1H, J = 15.2 Hz, H-1a), 3.53 (near s, 1H), 3.66 (dd, 1H, J = 10.7 Hz, H-6), 3.73 (near t, 1H, J = 10.8 Hz, H-6'), 4.05 (near s, 1H), 4.09 (d, 1H, J = 15 Hz, H-1e), 4.16 (near s, 1H), 4.37, 4.46, 4.47, 4.59 (4d, 4H, J = 12 Hz, PhC*H*$_2$ of OBn), 5.03, 5.18 (2d, 2H, J = 12.5 Hz, PhC*H*$_2$ of Z), 7.09 (d, 1H, J = 8 Hz, NH), and 7.1-7.4 (m, 15H, Ph-*H*). These NMR data indicate that the preferred conformation of **14** is $^1C_4$.

Anal. Calcd for $C_{30}H_{34}N_2O_6$ (518.61): C, 69.48; H, 6.61; N, 5.40. Found: C, 69.24; H, 6.82; N, 5.55.

***O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-*N*-benzyloxycarbonyl-1,5-dideoxy-1,5-imino-D-glucitol (16).** A mixture of **6** (181.5 mg), methyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranoside (**15**, 242.8 mg) and molecular sieves 4Å (500 mg) in dichloromethane (3 mL) was stirred overnight. The mixture was cooled to 0 °C and dimethyl(methylthio)sulfonium triflate (about 6 molar equiv.) was added; the mixture was stirred overnight at 23 °C. Molecular sieves were filtered off and washed with dichloromethane. The filtrate and washings were combined and washed with M sodium carbonate and water, dried, and concentrated. The residue was chromatographed on a column of silica gel with dichloromethane, to give **16** (234 mg, 78%): $[\alpha]_D$ -4° (*c* 1, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.93, 1.97, 1.99, 2.12 (4s, 12H, AcO), 3.42 (dd, 1H, J = 14, 3.5 Hz, H-1a), 3.86 (t, 1H, J = 3.7 Hz, H-3 or 4), 4.23 (t, 1H, J = 3.3 Hz, H-3 or 4), 4.45, 4.68 (2d, 2H, J = 11.7 Hz, PhC*H*$_2$ of OBn), 4.52 (d, 1H, J = 8.1 Hz, H-1') 4.93 (dd, 1H, J = 10.3, 3.3 Hz, H-3'), 5.07, 5.13 (2d, 2H, J = 12 Hz, PhC*H*$_2$ of Z), 5.18 (dd, 1H, J = 10.3, 8.1 Hz, H-2'), 5.35 (near s, 1H, H-4'), and 7.2-7.4 (m, 20H, Ph-*H*).

Anal. Calcd for $C_{49}H_{55}NO_{15}$ (897.97): C, 65.54; H, 6.17; N, 1.56. Found: C, 65.42; H, 5.92; N, 1.36.

***O*-(β-D-Galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-*N*-benzyloxycarbonyl-1,5-dideoxy-1,5-imino-D-glucitol (17) and *O*-(β-D-Galactopyranosyl)-(1→4)-1,5-dideoxy-1,5-imino-D-glucitol (20).** Zemplen's *O*-deacetylation of **16** was carefully performed at 0 °C as described for **3** and **12**, to give **17** (95%): ^{1}H NMR ($CDCl_3$-CD_3OD) δ 3.24 (dd, 1H, J = 15, 2.2 Hz, H-1a), 3.57 (dd, 1H, J = 10.7 Hz, H-2'), 3.90 (d, 1H, J = 2.6 Hz), 3.94 (near s, 1 H), 4.14 (d, 1H, J = 15 Hz, H-1e), 4.16 (near s, 1H), 4.29 (d, 1H, J = 7 Hz, H-1'), and 7.2-7.4 (m, 20H, Ph-*H*).

Compound **17** (51.4 mg) was hydrogenolyzed in ethanol (5 mL) and acetic acid (3 mL) in the presence of 10% Pd-C catalyst, and the resulting **20** (quant.) was purified by chromatography on a column of Sephadex LH-20: $[\alpha]_D$ -1° (*c* 0.6, methanol); ^{1}H NMR ($CDCl_3$) δ 2.25 (t, 1H, J = 10.6 Hz), 2.32 (t, 1H, J = 8.3 Hz), 2.79 (m, 1H), 2.86-3.03 (m, 2H), 4.04 (near d, 1H, J = 11.7 Hz), and 4.42 (d, 1H, J = 7 Hz, H-1').

Anal. Calcd for $C_{12}H_{23}NO_9$ (325.31): C, 44.31; H, 7.13; N, 4.31. Found: C, 44.50; H, 7.30; N, 4.25.

***O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2-acetamido-3,6-di-*O*-benzyl-*N*-benzyloxycarbonyl-1,2,5-trideoxy-1,5-imino-D-glucitol (18).** Condensation of **15** with **14** was performed as described for the preparation

of **16**, to give **18** (65%); $[\alpha]_D$ -2° (*c* 0.5, dichloromethane): ^1H NMR ($CDCl_3$) δ 1.94, 1.98, 1.99, 2.05, 2.15 (5s, 15H, AcN, AcO), 3.23 (dd, 1H, J = 14, 2 Hz, H-1a), 3.60 (dd, J = 9, 7 Hz), 3.67 (near s, 1H), 3.78 (t, 1H, J = 9 Hz), 3.85 (near t, J = 7 Hz), 4.27 (dd, 1H, $J_{2,NH}$ = 9 Hz, H-2), 4.43 (d, 1H, J = 7 Hz, H-1'), 4.45, 4.53, 4.54, 4.60 (4d, 4H, PhC*H*$_2$ of OBn), 5.08, 5.20 (2d, 2H, PhC*H*$_2$ of Z), 5.40 (narrow d, 1H, H-4'), 6.75 (d, 1H, J = 9 Hz, NH), and 7.2-7.4 (m, 15H, Ph-*H*).

Anal. Calcd for $C_{44}H_{52}N_2O_{15}$ (848.90): C, 62.26; H, 6.17; N, 3.30. Found: C, 62.53; H, 6.39; N, 3.35.

***O*-(β-D-Galactopyranosyl)-(1→4)-2-acetamido-1,2,5-trideoxy-1,5-imino-D-glucitol (21).** Zemplen's *O*-deacetylation of **18**, to give **19**: $[\alpha]_D$ +32° (*c* 1, methanol) and hydrogenolytic removal of the Z and Bn groups as described for **20** gave the title compound **21** (quant.): $[\alpha]_D$ +22° (*c* 0.8, methanol); ^1H NMR (CD_3OD) δ 1.86 (s, 3H, AcN), 2.92 (dd, 1H, Jgem = 11.3, $J_{1a,2}$ = 4.8 Hz, H-1a), 3.34 (near t, 1H, J = 10.3, 9 Hz), 3.97 (dd, 1H, J = 12, 2 Hz), and 4.35 (d, 1H, J = 7.3 Hz, H-1')

Anal. Calcd for $C_{14}H_{26}N_2O_9$ (366.37): C, 45.90; H, 7.15; N, 7.65. Found: C, 45.84; H, 7.37; N, 7.98.

***O*-(2-Acetamido-2-deoxy-β-D-glucopyranosyl)-(1→4)-2-acetamido-1,2,5-trideoxy-1,5-imino-D-glucitol (25).** Condensation of **14** (200 mg) with methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (**22**) (460 mg) in dichloromethane was performed as described for the preparation of **16** or **18**, to afford **23** (83%). After Zemplen's *O*-deacetylation, the product was treated with hydrazine hydrate in ethanol at the reflux temperature. The mixture was filtered and the filtrate was concentrated to a syrup, which was then treated with acetic anhydride in methanol. After work-up, the product was purified by chromatography on a column of silica gel with acetone to give **24** (85%): $[\alpha]_D$ -1° (*c* 1, methanol). Treatment of **24** (90 mg) in methanol (10 mL) with formic acid (2 mL) and activated palladium black gave **25** (quant.), which was finally purified by chromatography on a column of Sephadex LH-20.

Compound **25** had $[\alpha]_D$ +11° (*c* 0.7, methanol); ^1H NMR (CD_3OD) δ 1.94, 2.01 (2s, 6H, AcN), 2.95 (dd, 1 H, J_{gem} = 11.5, $J_{1a,2}$ = 4.7 Hz, H-1a), 3.45 (near t, 1H, J = 9, 8.4 Hz), 3.61 (t, 1H, J = 9.3 Hz), 3.65 (dd, 1H, J = 12, 5.8 Hz), 3.71 (near d, 1H, J = 11~12 Hz), 3.76 (dd, 1H, J = 10, 8.4 Hz), and 4.54 (d, 1H, J = 8.4 Hz, H-1')

Anal. Calcd for $C_{16}H_{29}N_3O_9$ (407.42): C, 47.17; H, 7.17; N, 10.31. Found: C, 47.22; H, 7.45; N, 10.60.

***O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→3)-4,6-*O*-benzylidene-*N*-(*tert*-butoxycarbonyl)-2-*O*-chloroacetyl-1,5-dideoxy-1,5-imino-D-glucitol (29) and *O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galacto-pyranosyl)-(1→**

3)-4,6-*O*-benzylidene-*N*-(*tert*-butoxycarbonyl)-1,5-dideoxy-1,5-imino-D-glucitol (30). Acetobromogalactose (**28**) (0.72 g), which was stirred with molecular sieves 4Å (0.5 g) overnight in dichloromethane (3 mL), was added to a mixture of **26** (0.46 g), silver carbonate (0.32 g), silver perchlorate (0.24 g) and molecular sieves 4Å (0.5 g) in dichloromethane (5 mL). The mixture was stirred for 3.5 h in the dark at room temperature and filtered through Celite. The solvent was evaporated and the residue was chromatographed on a column of silica gel with dichloro-methane to give **29** (0.7 g, 86%): $[\alpha]_D$ -9.5° (*c* 0.8, dichloromethane); ^{1}H NMR ($CDCl_3$) δ 1.48 (s, 9H, C*H*$_3$ of Boc), 1.97 (s, 6H, 2AcO), 2.04, 2.13 (2s, 6H, 2AcO), 3.30 (dd, 1H, J = 14, 8 Hz, H-1a), 3.34 (m, 1H, H-5), 3.76 (t, 1H, J = 7 Hz), 3.90 (dd, 1H, J = 14, 3.6 Hz, H-1e), 4.20 (t, 1H, J = 10.6 Hz, H-6a), 4.78 (dd, 1H, J = 11.7, 3.7 Hz, H-6e), 4.79 (d, 1H, J = 8 Hz, H-1'), 4.92 (m, 1H, H-2), 4.96 (dd, 1H, J = 10, 3.5 Hz, H-3'), 5.22 (dd, 1H, J = 10, 8 Hz, H-2'), 5.35 (m, 1H, H-4'), 5.6 (s, 1H, PhC*H* <), and 7.35-7.55 (m, 5H, Ph-*H*)

A mixture of **29** (0.7 g), pyridine (20 mL) and water (5 mL) was stirred overnight at room temperature. The mixture was poured into ice-water and extracted with dichloromethane. The extract was successively washed with ice-cold 2 M hydrochloric acid and water, dried, and concentrated. The residue was chromatographed on a column of silica gel with dichloromethane to give **30** (quant.): $[\alpha]_D$ +3.5° (*c* 0.8, dichloromethane); ^{1}H NMR ($CDCl_3$) δ 1.46 (s, 9H, C*H*$_3$ of Boc), 1.93, 1.97, 2.01, 2.12 (4s, 12H, 4AcO), 2.70 (dd, 1H, J_{gem} = 13, $J_{1a,2}$ = 10 Hz, H-1a), 2.78 (d, 1H, OH), 3.22 (m, 1H, $J_{4,5}$ = $J_{5,6a}$ = 10, $J_{5,6e}$ = 4.4 Hz, H-5), 3.82 (near t, 1H, J = 9.5, 7.7 Hz), 3.88, 4.07 (2dd, 2H, J_{gem} = 11, $J_{5,6'}$ = 5.9, 7.7 Hz, H-6'), 4.23 (dd, 1H, J = 13, 4.6 Hz, H-1e), 4.50 (t, 1H, J = 11.4 Hz, H-6a), 4.72 (dd, 1H, J = 11.4, 4.4 Hz, H-6e), 4.78 (d, 1H, J = 8 Hz, H-1'), 4.97 (dd, 1H, J = 10.3, 3.5 Hz, H-3'), 5.21 (dd, 1H, J = 10.3, 8 Hz, H-2'), 5.30 (m, 1H, H-4'), 5.57 (s, 1H, PhC*H*), and 7.35-7.5 (m, 5H, Ph-*H*<).

Anal. Calcd for $C_{32}H_{43}NO_{15}$ (681.69): C, 58.38; H, 6.36; N, 2.05. Found: C, 56.60; H, 6.10; N, 2.31.

***O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→3)-2-azido-4,6-*O*-benzylidene-*N*-(*tert*-butoxycarbonyl)-1,2,5-trideoxy-1,5-imino-D-glucitol (31).** A mixture of **27** (0.38 g), silver carbonate (0.37 g), silver perchlorate (0.28 g) and molecular sieves 4Å (0.5 g) was stirred overnight in the dark. Acetobromogalactose (**28**) (0.82 g) was also treated with molecular sieves (0.5 g) in dichloromethane (5 mL) overnight, and then added to the mixture of **27** and glycosyl promoters. The reaction mixture was stirred for a day in the dark at room temperature and worked up as described for **29**, to afford **31** (0.55 g, 75%): $[\alpha]_D$ -18° (*c* 1, dichloromethane); ^{1}H NMR ($CDCl_3$) δ 1.48 (s, 9H, Boc-C*H*$_3$), 1.95, 1.97, 2.07, 2.12 (4s, 12H, 4AcO),

2.80 (dd, 1H, Jgem = 14, $J_{1a,2}$ = 10 Hz, H-1a), 3.21 (m, 1H, $J_{4,5}$ = $J_{5,6a}$ = 10, $J_{5,6e}$ = 4.4 Hz, H-5), 3.5-3.59 (m, 1H, H-2), 3.86 (t, 1H, J = 9 Hz, H-3), 3.89, 4.08 (2dd, 2H, J_{gem} = 11, $J_{5,6'}$ = 7.7, 5.9 Hz, H-6'), 4.18 (dd, 1H, J = 14, 4.8 Hz, H-1e), 4.38 (t, 1H, J = 11 Hz, H-6a), 4.71 (dd, 1H, J = 11, 4.4 Hz, H-6e), 4.80 (d, 1H, J = 8 Hz, H-1'), 4.97 (dd, 1H, J = 10, 3.5 Hz, H-3'), 5.24 (dd, 1H, J = 10, 8 Hz, H-2'), 5.32 (m, 1H, H-4), 5.58 (s, 1H, PhC*H*), and 7.35-7.55 (m, 5H, Ph-*H*).

Anal. Calcd for $C_{32}H_{42}N_4O_{14}$ (706.70): C, 54.39; H, 5.99; N, 7.93. Found: C, 54.46; H, 6.25; N, 7.97.

***O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→3)-2-amino-4,6-*O*-benzylidene-*N*-(*tert*-butoxycarbonyl)-1,2,5-trideoxy-1,5-imino-D-glucitol (32) and *O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→3)-2-acetamido-4,6-*O*-benzylidene-*N*-(*tert*-butoxycarbonyl)-1,2,5-trideoxy-1,5-imino-D-glucitol (33).** Hydrogenolysis of **31** (0.45 g) in the presence of 10% Pd-C catalyst in ethanol gave **32** (quant.): $[\alpha]_D$ -3° (*c* 0.5, dichloromethane); ^1H NMR ($CDCl_3$) δ 2.59 (dd, 1H, J_{gem} = 13.4, $J_{1a,2}$ = 10 Hz, H-1a), 3.01 (m, 1H, J = 11, 9, 4.4 Hz, H-2), 3.24 (m, 1 H, $J_{4,5}$ = $J_{5,6a}$ = 10, $J_{5,6e}$ = 4.4 Hz, H-5), and 4.10 (dd, 1H, J = 13.4, 4.4 Hz, H-1e). Other peaks are very similar to those of **31**.

Acetylation of **32** (215 mg) with acetic anhydride (1.5 mL) and pyridine (3 mL) gave **33** (quant.): $[\alpha]_D$ -29° (*c* 0.6, dichloromethane); ^1H NMR ($CDCl_3$) δ 1.48 (s, 9H, Boc-C*H*$_3$), 1.97 (s, 6H, AcN, AcO), 1.99, 2.04, 2.12 (3s, 9H, AcO), 3.25 (dd, 1H, J_{gem} = 14, $J_{1a,2}$ = 8 Hz, H-1a), 4.03 (dd, 1H, J = 14, 3.3 Hz, H-1e), 4.89 (d, 1H, J = 8 Hz, H-1'), and 5.63 (d, 1H, J = 5.5 Hz, NH).

Anal. Calcd for $C_{34}H_{46}N_2O_{15}$ (722.74): C, 56.50; H, 6.42; N, 3.88. Found: C, 56.54; H, 6.22; N, 4.13.

***O*-(β-D-Galactopyranosyl)-(1→3)-4,6-*O*-benzylidene-*N*-(*tert*-butoxycarbonyl)-1,5-dideoxy-1,5-imino-D-glucitol (34), *O*-(β-D-Galacto-pyranosyl)-(1→3)-*N*-(*tert*-butoxycarbonyl)-1,5-imino-D-glucitol (36) and *O*-(β-D-Galactopyranosyl)-(1→3)-1,5-dideoxy-1,5-imino-D-glucitol (38).** Zemplen's *O*-deacetylation of **30** (0.45 g) gave **34** (quant.): $[\alpha]_D$ -16° (*c* 1, methanol); ^1H NMR ($CDCl_3$-CD_3OD) δ 1.44 (s, 9H, Boc-C*H*$_3$), 2.53 (near t, 1H, J = 11 Hz, H-1a), 4.11 (near d, 1H, J = 11 Hz, H-1e), 4.45 (d, 1H, J = 7.7 Hz, H-1'), 5.52 (s, 1H, PhC*H*<), and 7.25-7.55 (m, 5H, Ph-*H*).

Hydrogenolytic cleavage of the benzylidene group in the presence of 10% Pd-C catalyst in acetic acid afforded **36** (quant.): $[\alpha]_D$ -10° (*c* 0.5, methanol); ^1H NMR ($CDCl_3$-CD_3OD) δ 1.47 (s, 9H, Boc-C*H*$_3$), 3.38 (dd, 1H), 3.54 (near t, 1H, J = 7.7, 4 Hz), 4.04 (near t, 1H, J = 3-4 Hz), 4.10 (m, 1H), and 4.39 (d, 1H, J = 7.3 Hz, H-1'). Compound **36** was treated with 50% acetic acid for three days at 45 °C and the solvent

was removed by evaporation. The residue was triturated with ether and decanted several times to give a solid, which was then treated with Amberlite IR-410 (OH^-) to remove the acid. The product **38** had $[\alpha]_D$ +27° (*c* 0.5, methanol); ^1H NMR (CD_3OD) δ 4.49 (d, 1H, J = 7.7 Hz, H-1') and the disappearance of Boc-C*H*$_3$.

Anal. Calcd for $C_{12}H_{23}NO_9$ (325.31): C, 44.31; H, 7.13; N, 4.31. Found: C, 44.49; H, 7.34; N, 4.34.

***O*-(β-D-Galactopyranosyl)-(1→3)-2-acetamido-4,6-*O*-benzylidene-*N*-(*tert*-butoxycarbonyl)-1,2,5-trideoxy-1,5-imino-D-glucitol (35), *O*-(β-D-Galactopyranosyl)-(1→3)-2-acetamido-*N*-(*tert*-butoxycarbonyl)-1,2,5-trideoxy-1,5-imino-D-glucitol (37) and *O*-(β-D-Galactopyranosyl)-(1→3)-2-acetamido-1,2,5-trideoxy-1,5-imino-D-glucitol (39).** Zemplen's *O*-deacetylation of **33** (174 mg) at 0 °C gave **35** in a quantitative yield: $[\alpha]_D$ -9° (*c* 0.8, methanol); ^1H NMR ($CDCl_3$-CD_3OD) δ 1.48 (s, 9H, Boc-C*H*$_3$), 1.98 (s, 3H, AcN), 3.06 (dd, 1H, H-1a), 4.29 (t, 1H, J = 10.6 Hz, H-6a), 4.44 (d, 1H, J = 7.7 Hz, H-1'), 4.71 (dd, 1H, J = 10.6, 4.4 Hz, H-6e), 5.64 (s, 1H, Ph-C*H*<), and 7.3-7.6 (m, 5H, Ph-*H*).

Hydrogenolytic removal of the benzylidene group in **35**, as described for **36**, afforded **37** (quant.): $[\alpha]_D$ +27° (*c* 0.4, methanol); ^1H NMR ($CDCl_3$-CD_3OD) δ 1.46 (s, 9H, Boc-C*H*$_3$), 1.97 (s, 3H, AcN) and the complete loss of Ph-*H* and Ph-C*H*<.

Treatment of **37** with 50% acetic acid and work-up as described for **38** gave **39** in a quantitative yield: $[\alpha]_D$ +6.7° (*c* 0.45, methanol); ^1H NMR (CD_3OD) δ 1.96 (s, 3H, AcN), 3.15 (dd, 1H, J = 12-13, 4.4-4.8 Hz, H-1a), and 4.37 (d, 1H, J = 7.3 Hz, H-1').

Anal. Calcd for $C_{14}H_{26}N_2O_9$ (366.37): C, 45.90; H, 7.15; N, 7.65. Found: C, 45.92; H, 7.09; N, 7.60.

***O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)-(1→3)-4,6-*O*-benzylidene-*N*-benzyloxycarbonyl-2-*O*-chloroacetyl-1,5-dideoxy-1,5-imino-D-glucitol (42).** Compound (**40**) (209 mg), which was prepared by partial chloroacetylation of **4** according to the procedure described in ref. 8, was coupled with acetobromoglucose (334 mg) in the presence of silver carbonate (125 mg), silver perchlorate (94 mg) and molecular sieves 4Å (400 mg) in dichloromethane as described for **29**. After work-up, the product was purified by chromatography on a column of silica gel with 400:1 dichloromethane-methanol to give **42** (76%): $[\alpha]_D$ -24° (*c* 0.9, chloroform); ^1H NMR ($CDCl_3$) δ 1.98, 1.985, 1.99, 2.01 (4s, 12H, AcO), 3.9-4.0 (2H, C*H*$_2$ClCO-), 4.81 (d, 1H, J = 7.7 Hz, H-1'), 5.0-5.2 (2d, 2H, Jgem = 12 Hz, Ph-C*H*$_2$CO-), 5.58 (s, 1H, Ph-C*H*<) and 7.3-7.5 (m, 10H, Ph-*H*).

Anal. Calcd for $C_{37}H_{42}ClNO_{16}$ (792.19): C, 56.10; H, 5.34; N, 1.77. Found: C, 55.96; H, 5.26; N, 1.83.

***O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)-(1→3)-4,6-*O*-benzylidene-*N*-benzyloxycarbonyl-1,5-dideoxy-1,5-imino-D-glucitol (43), *O*-(β-D-Glucopyranosyl)-(1→3)-4,6-*O*-benzylidene-*N*-benzyloxycarbonyl-1,5-dideoxy-1,5-imino-D-glucitol (44) and *O*-(β-D-Glucopyranosyl)-(1→3)-1,5-dideoxy-1,5-imino-D-glucitol (45).** A mixture of **43** (0.89 g) and pyridine containing a small amount of water was stirred overnight at room temperature, and the product was extracted with dichloromethane. The extract was successively washed with ice-cold 2 M HCl and water, dried and concentrated to a syrup, which was chromatographed on a column of silica gel with dichloromethane to give **43** (quant.): $[\alpha]_D$ -13° (*c* 0.7, 1:1 chloroform-methanol). Zemplen's *O*-deacetylation of **43** (0.65 g) at 0 °C and chromatography on a column of silica gel afforded **44** (86%): $[\alpha]_D$ +0.2° (*c* 1.3, 1:1 chloroform-methanol); ^1H NMR ($CDCl_3$-CD_3OD) δ 2.85 (dd, 1H, Jgem = 13-14, $J_{1a,2}$ = 9.9 Hz, H-1a), 4.27 (dd, 1H, $J_{1e,2}$ = 4 Hz, H-1e), 4.4 (t, 1H, J = 11 Hz, H-6a), 4.56 (d, 1H, J = 7' Hz, H-1'), 4.79 (dd, 1H, $J_{5,6e}$ = 4.4 Hz, H-6e), 5.11 (s, 2H, Ph-C*H*$_2$CO), 5.59 (s, 1H, Ph-C*H*<), and 7.3-7.55 (m, 10H, Ph-*H*).

Hydrogenolytic removal of the benzylidene and benzyloxycarbonyl group in **44** was achieved by using 10% Pd-C catalyst in 1:1 ethanol-acetic acid, and the final product was purified by chromatography on a column of Sephadex LH-20, to give crystalline **45** (97%): mp 227 °C; ^1H NMR (CD_3OD) δ 4.52 (d, 1H, J = 7 Hz, H-1').

Anal. Calcd for $C_{12}H_{23}NO_9$ (325.31): C, 44.31; H, 7.13; N, 4.31. Found: C, 44.16; H, 7.25; N, 4.48.

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