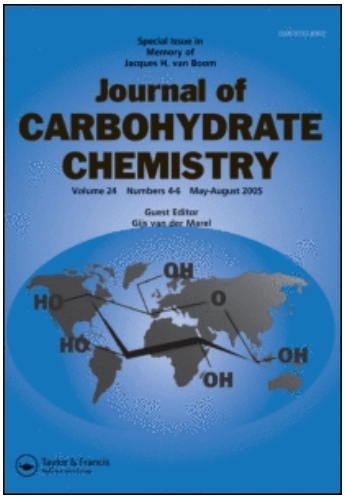

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STUDIES ON GLYCAN PROCESSING INHIBITORS: SYNTHESIS OF N-ACETYLHEXOSAMINE ANALOGS AND CYCLIC CARBAMATE DERIVATIVES OF 1-DEOXYNOJIRIMYCIN

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ABSTRACT

1-Deoxynojirimycin (1,5-dideoxy-1,5-imino-D-glucitol) was converted, *via* epoxide intermediates, into a series of *N*-acetylhexosamine analogs, i. e., 2-acetamido-1,2,5-trideoxy-1,5-imino-D-glucitol, 2-acetamido-1,2,5-trideoxy-1,5-imino-D-mannitol, 2-acetamido-1,2,5-trideoxy-1,5-imino-D-galactitol, and their isomers. The cyclic 5-*N*,6-*O*-carbamoyl derivatives of 1-deoxynojirimycin were also prepared.

INTRODUCTION

1-Deoxynojirimycin (1) initially obtained by catalytic degradation of nojirimycin[1] and chemical synthesis from L-sorbofuranose,[2] has widely been found in nature[3-6] as a potent inhibitor of glucosidases.[7] In the past decade, many analogs and derivatives of 1 have been synthesized,[8-14] designed as the specific inhibitors against various glycosidases that participate in the carbohydrate metabolism. In this connection, the syntheses of 2-acetamido-1,2,5-

trideoxy-1,5-imino-D-glucitol[10,12] and its manno analog,[10] potent inhibitors of N-acetylhexosaminidases, have also been reported. We now describe a facile preparation of the N-acetylhexosamine analogs of 1 by chemical modification.

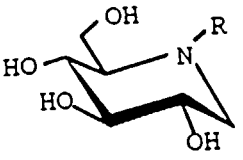
RESULTS AND DISCUSSION

Treatment of 1 with 2-(tert-butoxycarbonylthio)-4,6-dimethylpyrimidine in 1,4-dioxane gave crystalline 2 in an almost quantitative yield. Benzylidenation of 2, and partial chloroacetylation afforded 4 (49%) and 5 (25%), which were converted, by methanesulfonylation and following treatment with methanolic sodium methoxide, into the corresponding epoxides 11 and 12 in high yields, respectively. Epoxide 11 was also obtained by a similar treatment of 10 which was prepared from 5 via 8 and 9.

The cleavage of epoxides 11 and 12 with azide group was achieved by use of sodium azide in N,N-dimethylformamide (DMF), to yield 13 (59%) and 15 (31%), and 17 (58%) and 19 (22%), respectively. This result indicates that the attack of azide anion took place preferentially at the less-hindered C-2 position.

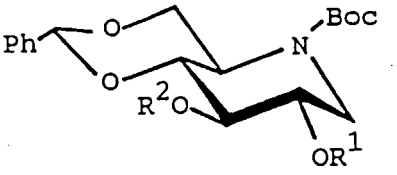
For preparing the mannosamine analog, compound 5 was converted, by successive benzoylation, dechloroacetylation and methanesulfonylation, into 10, which underwent nucleophilic replacement by azide ion to afford 21.

The selective reduction of the azide group of 13, 15, 17, 19, and 21 with 10% palladium-on-carbon and ammonium formate in methanol, and treatment of the products with acetic anhydride gave the corresponding acetamide derivatives 14, 16, 18, 20, and 22, respectively. Compound 23 was obtained by treatment of 22 with methanolic sodium methoxide. Finally, the butoxycarbonyl and benzylidene group were simultaneously cleaved by treatment with trifluoroacetic acid, to give the desired 1-deoxynojirimycin analogs that have the structures related to N-acetyl-D-glucosamine (33), N-acetyl-D-mannosamine (34), and their isomers 36, 37 and 38, in quantitative yields.



1 R = H
2 R = Boc

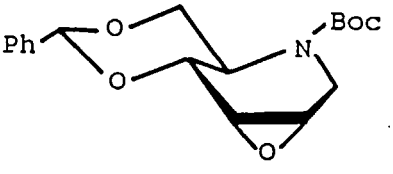
Boc = t-butoxycarbonyl



3 $R^{1,2}$ = H
4 R^1 = H, R^2 = ClAc
5 R^1 = ClAc, R^2 = H
6 R^1 = Ms, R^2 = ClAc
7 R^1 = ClAc, R^2 = Ms
8 R^1 = ClAc, R^2 = Bz
9 R^1 = H, R^2 = Bz
10 R^1 = Ms, R^2 = Bz

ClAc = chloroacetyl
Ms = methanesulfonyl
Bz = benzoyl

11



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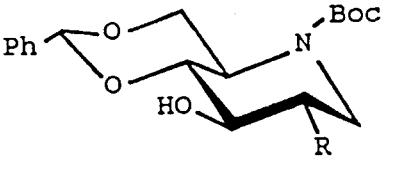
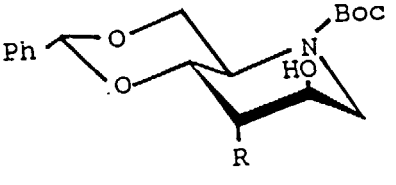
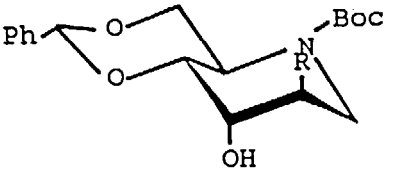


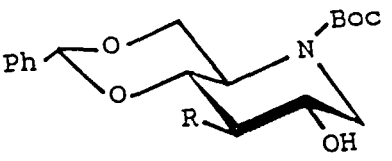
13 R = N_3
14 R = NHAc



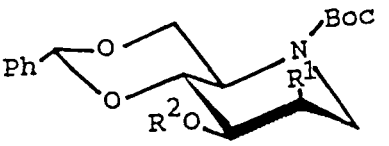
15 R = N_3
16 R = NHAc



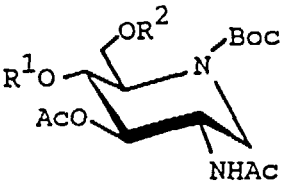
17 R = N_3
18 R = NHAc



19 R = N_3
20 R = NHAc

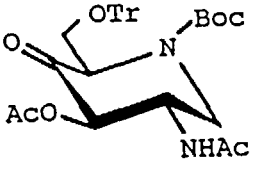


21 R^1 = N_3, R^2 = Bz
22 R^1 = NHAc, R^2 = Bz
23 R^1 = NHAc, R^2 = H



24 $R^{1,2}$ = benzylidene
25 $R^{1,2}$ = H
26 R^1 = H, R^2 = Tr

Tr = trityl



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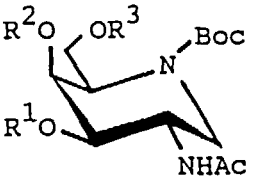
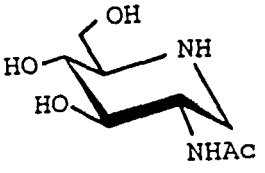


28 R^1 = Ac, R^2 = H
R^3 = Tr
29 $R^{1,2}$ = Ac, R^3 = Tr
30 R^1 = Ac, $R^{2,3}$ = H
31 $R^{1,3}$ = H, R^2 = Ac
32 R^{1-3} = H



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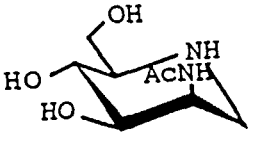

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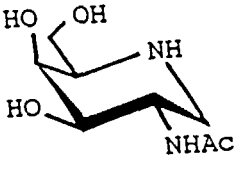

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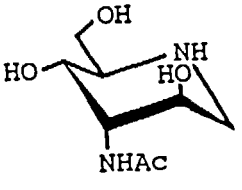

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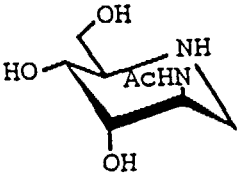

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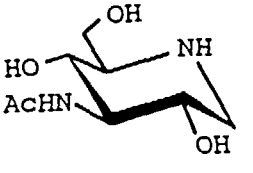

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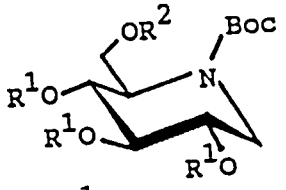
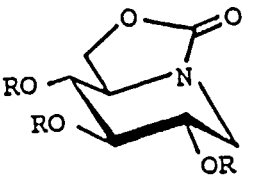
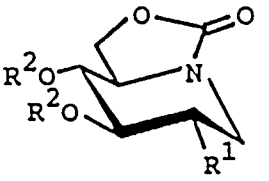


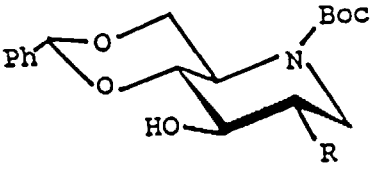
39 R^1 = Bz
R^2 = TBDMS
40 R^1 = Bz, R^2 = H
TBDMS = t-butyldimethylsilyl



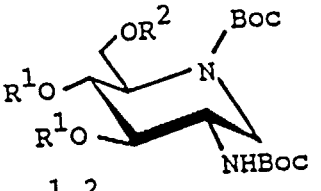
41 R = Bz
42 R = H



48 R^1 = NHBoc
R^2 = Bz
49 R^1 = NHBoc
R^2 = H
50 R^1 = NH_2·TFA
R^2 = H
51 R^1 = NHAc
R^2 = H
TFA = CF_3CO_2H



43 R = NH_2
44 R = NHBoc



45 $R^{1,2}$ = H
46 R^1 = Bz
R^2 = TBDMS
47 R^1 = Bz, R^2 = H

The selective hydrogenolysis of 13, as described for 14, and acetylation of the product with acetic anhydride in pyridine gave 24, which was converted stepwise into 25 and then 26. Oxidation of the hydroxyl group at C-4 with pyridinium dichromate, to give crystalline 27 (92%), and the following treatment with sodium borohydride afforded 28. The structure of 28 was characterized from the ^1H NMR spectrum of its 3,4-di-O-acetyl derivative 29. Hydrogenolytic detritylation of 28 and O-deacetylation gave 32, which was then treated with trifluoroacetic acid as described for 33 and 34, to give 2-acetamido-1,2,5-trideoxy-1,5-imino-D-galactitol (35). This compound could also be prepared by simultaneous hydrolysis of the butoxycarbonyl and trityl group after O-deacetylation.

Compound 40 was prepared from 2 via the 6-O-tert-butyldimethylsilyl derivative 39 and converted, by treatment with a mixture of iodine-triphenylphosphine-imidazole, to the cyclic carbamate deriva-

tive 41 and then 42 in good yields. A similar treatment of 45, which was prepared stepwise from 13 via 43 and 44, gave the corresponding cyclic carbamate derivative 48 in 73% yield. The benzoyl groups of 48 were cleaved by Zemplen's method and the resulting 49 was converted, by treatment with trifluoroacetic acid, to 50 which was then acetylated to afford 51.

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 IR spectra were recorded with a JASCO A-100 spectrophotometer. ^{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.

N-(tert-Butoxycarbonyl)-1,5-dideoxy-1,5-imino-D-glucitol (2). To a solution of 1 (2 g) in water (1 mL) were added triethylamine (1.6 mL), and 2-(tert-butoxycarbonyl)thio-4,6-dimethylpyrimidine (11.6 g) in 1,4-dioxane (1 mL). The mixture was stirred overnight at 60 °C, and the solvents were removed by evaporation. The residue was chromatographed on a column of silica gel with (a) 100:1 (b) 50:1, and (c) 20:1 dichloromethane-methanol. Eluant (c) gave crystalline 2 (98%): mp 123-125 °C; $[\alpha]_D$ -8.5° (c 0.5, methanol); IR (Nujol) 1660 cm^{-1} (carbonyl); ^{1}H NMR ($CDCl_3$+CD_3OD) δ 1.47 (s, 9H, CH_3).

Anal. Calcd for $C_{11}H_{21}NO_6$ (263.29): C, 50.18; H, 8.04; N, 5.32. Found: C, 50.29; H, 8.12; N, 5.31.

4,6-O-Benzylidene-N-(tert-butoxycarbonyl)-1,5-dideoxy-1,5-imino-D-glucitol (3). To a solution of 2 (3.2 g) in N,N-dimethylformamide (DMF, 30 mL) were added benzaldehyde dimethyl acetal (5.5 mL) and a catalytic amount of p-toluenesulfonic acid monohydrate,

and the mixture was stirred for 10 h at room temperature. After treatment with Amberlite IRA-410 (OH^-) ion-exchange resin, the solvent was removed by evaporation. The residue was chromatographed on a column of silica gel with (a) dichloromethane and (b) 100:1 dichloromethane-methanol. Eluant (b) gave syrupy 3 (80%), which was crystallized from ethyl acetate-n-hexane solution: mp 156-157 °C; $[\alpha]_D$ +7° (c 0.6, dichloromethane); ^1H NMR ($CDCl_3$) δ 1.46 (s, 9H, CH_3), 4.38 (t, 1H, $J_{gem} = J_{5,6a}$ = 10.6 Hz, H-6a), 4.75 (dd, 1H, $J_{5,6e}$ = 4.4 Hz, H-6e), 5.53 (s, 1H, CHPh), and 7.26-7.5 (m, 5H, Ph-H).

Anal. Calcd for $C_{18}H_{25}NO_6$ (351.40): C, 61.53; H, 7.17; N, 3.99. Found: C, 61.38; H, 7.21; N, 4.00.

4,6-O-Benzylidene-N-(tert-butoxycarbonyl)-3-O-(chloroacetyl)-1,5-dideoxy-1,5-imino-D-glucitol (4) and 4,6-O-Benzylidene-N-(tert-butoxycarbonyl)-2-O-(chloroacetyl)-1,5-dideoxy-1,5-imino-D-glucitol (5). To a solution of 3 (1 g) in dichloromethane (25 mL) were added, at 0 °C, 2,6-lutidine (3.6 mL), triethylamine (0.5 mL), and chloroacetic anhydride (0.58 g), and the mixture was stirred for 1 h at 0 °C. The reaction mixture was poured into ice-water and extracted with dichloromethane. The extract was washed with ice-cold 2M hydrochloric acid and water, dried (anhydrous sodium sulfate), and the solvent was evaporated to leave a syrup, which was chromatographed on a column of silica gel with (a) dichloromethane, (b) 400:1, and (c) 300:1 dichloromethane-methanol. Eluants (b) and (c) gave 5 (0.3 g, 25%) and 4 (0.6 g, 49%), respectively.

Compound 4 had $[\alpha]_D$ +13° (c 0.5, dichloromethane); IR 1750 and 1690 cm^{-1} (carbonyl); ^1H NMR ($CDCl_3$) δ 1.48 (s, 9H, CH_3) 2.99 (dd, 1H, J_{gem} = 13.9, $J_{1a,2}$ = 9.2 Hz, H-1a), 3.35 (m, 1H, H-5), 3.77 (m, 1H, H-2), 3.81 (t, 1H, J = 9-10 Hz, H-4), 4.12 (dd, 1H, $J_{1e,2}$ = 4.4 Hz, H-1e), 4.13 (s, 2H, CH_2Cl), 4.32 (t, 1H, $J_{gem} = J_{5,6a}$ = 10.6 Hz, H-6a), 4.78 (dd, 1H, $J_{5,6e}$ = 4.4 Hz, H-6e), 5.03 (dd, 1H, $J_{2,3}$ = 7.7, $J_{3,4}$ = 9 Hz, H-3), 5.53 (s, 1H, CHPh), and 7.3 - 7.5 (m, 5H, Ph-H).

Anal. Calcd for $C_{20}H_{26}NO_7Cl$ (427.49): C, 56.19; H, 6.13; N, 3.28. Found: C, 56.34; H, 6.06; N, 3.14.

Compound 5 had $[\alpha]_D$ -6° (c 1.4, dichloromethane); IR 1750 and 1690 cm^{-1} (carbonyl); ^1H NMR ($CDCl_3$) δ 1.48 (s, 9H, CH_3), 3.14 (dd, 1H, J_{gem} = 13.6, $J_{1a,2}$ = 8.4 Hz, H-1a), 3.32 (m, 1H, H-5), 3.73 (t, 1H, J = 9-10 Hz, H-4), 3.84 (t, 1H, J = 9 Hz, H-3), 4.07 (dd, 1H, $J_{1e,2}$ = 4.4 Hz, H-1e), 4.11 (s, 2H, CH_2Cl), 4.26 (t, 1H, J_{gem} = $J_{5,6a}$ = 11.4 Hz, H-6a), 4.78 (dd, 1H, $J_{5,6e}$ = 4.4 Hz, H-6e), 4.91 (m, 1H, H-2), 5.59 (s, 1H, CHPh), and 7.3-7.55 (m, 5H, Ph-H).

Anal. Found: C, 56.31; H, 6.15; N, 3.32.

4,6-O-Benzylidene-N-(tert-butoxycarbonyl)-3-O-(chloroacetyl)-1,5-dideoxy-1,5-imino-2-O-methanesulfonyl-D-glucitol (6) and 4,6-O-Benzylidene-N-(tert-butoxycarbonyl)-2-O-(chloroacetyl)-1,5-dideoxy-1,5-imino-3-O-methanesulfonyl-D-glucitol (7). Methanesulfonyl chloride (0.21 mL) was added to a solution of 4 or 5 (0.61 g) in dry pyridine (3 mL) at -20 °C, and the mixture was stirred for 5 h at 0 °C. The product was extracted with dichloromethane, and the extract was washed with ice-cold 2M hydrochloric acid and water, dried, and the solvent was evaporated to leave 6 or 7 (quantitative).

Compound 6 had $[\alpha]_D$ -3.4° (c 1, dichloromethane); ^1H NMR ($CDCl_3$) δ 3.08 (s, 3H, CH_3SO_2), 3.19 (dd, 1H, J_{gem} = 13.6, $J_{1a,2}$ = 9.2 Hz, H-1a), 4.13 (s, 2H, CH_2Cl), 4.33 (dd, 1H, $J_{1e,2}$ = 4.4 Hz, H-1e), 4.68 (m, 1H, H-2), and 5.27 (t, 1H, J = 8 Hz, H-3)

Anal. Calcd for $C_{21}H_{28}NO_9ClS$ (505.57): C, 49.89; H, 5.58; N, 2.77. Found: C, 50.14; H, 5.37; N, 2.59.

Compound 7 had $[\alpha]_D$ -14.4° (c 1, dichloromethane); ^1H NMR ($CDCl_3$) δ 2.93 (s, 3H, CH_3SO_2), 2.99 (dd, 1H, J_{gem} = 13.6, $J_{1a,2}$ = 9.2 Hz, H-1a), 4.13, 4.18 (2d, 2H, CH_2Cl), 4.30 (dd, 1H, $J_{1e,2}$ = 4.4 Hz, H-1e), and 5.04 (m, 1H, H-2).

Anal. Found: C, 50.21; H, 5.40; N, 2.86.

3-O-Benzoyl-4,6-O-benzylidene-N-(tert-butoxycarbonyl)-2-O-(chloroacetyl)-1,5-dideoxy-1,5-imino-D-glucitol (8) and 3-O-Benzoyl-4,6-O-benzylidene-N-(tert-butoxycarbonyl)-1,5-dideoxy-1,5-imino-D-glucitol (9). Benzoyl chloride (2 mL) was added to a solution of 5 (3 g) in 2:1 dichloromethane-pyridine (15 mL) at -20 °C, and the mixture was stirred for 1 h at -20 °C. After work-up as described for 7, the product was triturated in n-hexane and decanted to give 8

(quantitative): $[\alpha]_D$ -19° (c 0.5, dichloromethane); ^1H NMR ($CDCl_3$) δ 4.02 (s, 2H, $C\underline{H}_2Cl$), 5.16 (m, 1H, H-2), 5.46 (dd, 1H, J = 9.2, 6.2 Hz, H-3), and 7.25-8.2 (m, 10H, Ph-H).

A solution of 8 (0.32 g) in pyridine (20 mL) was heated for 24 h at 50 °C, and then pyridine was evaporated. The residue was taken up in dichloromethane, and washed with ice-cold 2M hydrochloric acid and water, dried, and the solvent was evaporated to leave a syrup. The product was chromatographed on a column of silica gel with 200:1 dichloromethane-methanol, to give 9 (0.25 g, 89%): $[\alpha]_D$ -48° (c 0.8, 5:1 dichloromethane-methanol); ^1H NMR ($CDCl_3$+CD_3OD) δ 1.50 (s, 9H, $C\underline{H}_3$), 3.07 (dd, 1H, J_{gem} = 13.9, $J_{1a,2}$ = 9.2 Hz, H-1a), 3.44 (m, 1H, H-5), 3.84 (m, 1H, H-2), 3.96 (t, 1H, J = 9.9 Hz, H-4), 4.13 (dd, 1H, $J_{1e,2}$ = 4.4 Hz, H-1e) 4.34 (t, 1H, J = 10.6, H-6a), 4.80 (dd, 1H, J = 10.6, 4.4 Hz, H-6e), 5.22 (t, 1H, J = 8.8 Hz, H-3), 5.57 (s, 1H, C<u>H</u>Ph), and 7.25-8.1 (m, 10H, Ph-H)

Anal. Calcd for $C_{25}H_{29}NO_7$ (455.51): C, 65.92; H, 6.42; N, 3.07. Found: C, 65.73; H, 6.34; N, 3.10.

3-O-Benzoyl-4,6-O-benzylidene-N-(tert-butoxycarbonyl)-2-O-methanesulfonyl-1,5-dideoxy-1,5-imino-D-glucitol (10). Compound 9 (0.87 g) was treated with methanesulfonyl chloride (1 mL) in pyridine (20 mL), to give 10 (quantitative): $[\alpha]_D$ -2.3° (c 1, dichloromethane); ^1H NMR ($CDCl_3$) δ 3.03 (s, 3H, $C\underline{H}_3SO_2$).

Anal. Calcd for $C_{26}H_{31}NO_9S$ (533.60): C, 58.52; H, 5.86; N, 2.62. Found: C, 58.76; H, 5.80; N, 2.48.

2,3-Anhydro-4,6-O-benzylidene-N-(tert-butoxycarbonyl)-1,5-dideoxy-1,5-imino-D-mannitol (11). Compound 6 (1.5 g) in dry 1,4-dioxane (0.5 mL) and methanol (2 mL) was treated with methanolic sodium methoxide (28%, 3 mL) for 2 h at room temperature. Solvents were evaporated and the residue was taken up in dichloromethane, washed with water, dried, and the solvent was evaporated. The residue was crystallized from n-hexane to afford 11 (quantitative): mp 124.5-126 °C; $[\alpha]_D$ +44° (c 0.5, chloroform); ^1H NMR ($CDCl_3$): δ 1.47 (s, 9H, $C\underline{H}_3$), 3.00 (m, 1H, J = 10.3, 10.3, 4.4 Hz, H-5), 3.19 (near d, 1H, $J_{2,3}$ = 2.9 Hz, H-2), 3.32 (dd, 1H, J = 15, 1.1 Hz, H-1a), 3.33 (d, 1H, H-3), 4.03 (d, 1H, $J_{4,5}$ = 10.3 Hz, H-4), 4.43 (dd, 1H,

J = 7, 4.4 Hz, H-6e), 4.45 (d, 1H, H-1e), 4.70 (broad dd, J = 10.3, 7 Hz, H-6a), 5.64 (s, 1H, CHPh), and 7.25-7.55 (m, 5H, Ph-H)

Anal. Calcd for $C_{18}H_{23}NO_5$ (333.38): C, 64.85; H, 6.95; N, 4.20. Found: C, 64.65; H, 7.03; N, 4.21.

2,3-Anhydro-4,6-O-benzylidene-N-(tert-butoxycarbonyl)-1,5-dideoxy-1,5-imino-D-allitol (12). Compound 7 (1.2 g) in 4:1 methanol-1,4-dioxane (2.5 mL) was treated with methanolic sodium methoxide as described for 11, to give 12 (94%): $[\alpha]_D$ +31° (c 1.3, dichloromethane); ^1H NMR ($CDCl_3$) δ 1.46 (s, 9H, CH_3), 3.48 (m, 1H, J = 10.3, 10.3, 4.4 Hz, H-5), 3.67 (d, 1H, J = 15 Hz, H-1a), 3.94 (dd, 1H, J = 15, 2.9 Hz, H-1e), 4.12 (d, 1H, $J_{4,5}$ = 9.9 Hz, H-4), 4.24 (t, 1H, J = 10.6 Hz, H-6a), 4.65 (dd, 1H, J = 10.6, 4.4 Hz, H-6e), 5.54 (s, 1H, CHPh), and 7.25-7.55 (m, 1H, Ph-H).

Anal. Found: C, 64.98; H, 7.12; N, 4.09.

2-Azido-4,6-O-benzylidene-N-(tert-butoxycarbonyl)-1,2,5-trideoxy-1,5-imino-D-glucitol (13) and 3-Azido-4,6-O-benzylidene-N-(tert-butoxycarbonyl)-1,3,5-trideoxy-1,5-imino-D-altritol (15). A mixture of 11 (0.2 g) and sodium azide (0.45 g) in DMF (5 mL) was heated for 6 h at 110 °C, and the solvent was removed by evaporation. The residual syrup was taken up in dichloromethane, washed with water, dried, and the solvent was evaporated. The residue was chromatographed on a column of silica gel with dichloromethane to give 13 (59%) and 15 (31%).

Compound 13 crystallized from n-hexane: mp 104-105 °C; $[\alpha]_D$ -33° (c 1.2, dichloromethane); IR 2100 cm^{-1} (N_3); ^1H NMR ($CDCl_3$) δ 3.64 (dd, 1H, J = 13.6, $J_{1a,2}$ = 11 Hz, H-1a) 3.16 (m, 1H, J_{gem} = $J_{5,6a}$ = 10.3, $J_{5,6e}$ = 4.8 Hz, H-5), 3.49 (m, 1H, $J_{2,3}$ = 8.8, $J_{1e,2}$ = 4.8 Hz, H-2), 4.23 (dd, 1H, H-1e), 4.39 (t, 1H, J = 11.4 Hz, H-6a), and 4.76 (dd, 1H, H-6e).

Anal. Calcd for $C_{18}H_{24}N_4O_5$ (376.41): C, 57.44; H, 6.43; N, 14.88. Found: C, 57.24; H, 6.58; N, 15.04.

Compound 15 had $[\alpha]_D$ -3° (c 1, dichloromethane); IR 2100 cm^{-1} (N_3); ^1H NMR ($CDCl_3$) δ 3.19 (dd, 1H, J_{gem} = 15, $J_{1a,2}$ = 1.5 Hz, H-1a), 3.67 (m, 1H, H-5), 3.89 (m, 1H, H-2), 4.02 (m, 1H, $J_{1e,2}$ = 3.3, $J_{1e,3}$ = 1.5 Hz, H-1e), 4.03 (t, 1H, H-3), 4.28 (dd, 1H, $J_{4,5}$ = 9.9,

$J_{3,4}$ = 3.3 Hz, H-4), 4.47 (t, 1H, J = 11.4 Hz, H-6a), and 4.73 (dd, 1H, $J_{5,6e}$ = 4.8 Hz, H-6e).

Anal. Found: C, 57.68; H, 6.32; N, 14.74.

2-Azido-4,6-O-benzylidene-N-(tert-butoxycarbonyl)-1,2,5-trideoxy-1,5-imino-D-altritol (17) and 3-Azido-4,6-O-benzylidene-N-(tert-butoxycarbonyl)-1,3,5-trideoxy-1,5-imino-D-glucitol (19). Compound 12 (0.8 g) was treated with sodium azide (1.6 g) as described for the preparation of 13 and 15. The products were purified by chromatography on a column of silica gel with (a) dichloromethane and (b) 200:1 dichloromethane-methanol. Eluant (a) gave 17 (58%) and eluant (b) gave 19 (22%).

Compound 17 crystallized from n-hexane: mp 128-129 °C $[\alpha]_D$ -52° (c 1, dichloromethane); IR 2100 cm^{-1} (N_3); ^1H NMR ($CDCl_3$) δ 2.71 (m, 1H, J_{gem} = 13.6, $J_{1a,2}$ = 9.2 Hz, H-1a), 3.70 (t, 1H, J = 9.2 Hz, H-3), and 4.27 (dd, 1H, $J_{1e,2}$ = 3.3 Hz, H-1e).

Compound 19 had $[\alpha]_D$ +38° (c 0.5, dichloromethane); IR 2100 cm^{-1} (N_3); ^1H NMR ($CDCl_3$) δ 2.71 (m, 1H, J_{gem} = 13.6, $J_{1a,2}$ = 9.2 Hz, H-1a), 3.70 (t, 1H, J = 9.2 Hz, H-3), and 4.27 (dd, 1H, $J_{1e,2}$ = 3.3 Hz, H-1e).

Anal. Found: C, 57.65; H, 6.26; N, 15.00.

2-Acetamido-4,6-O-benzylidene-N-(tert-butoxycarbonyl)-1,2,5-trideoxy-1,5-imino-D-glucitol (14) and 3-Acetamido-4,6-O-benzylidene-N-(tert-butoxycarbonyl)-1,3,5-trideoxy-1,5-imino-D-altritol (16). To a solution of compound 13 or 15 (0.3 g) in 1:1 methanol-acetic anhydride (4 mL) were added 10% palladium-on-carbon (Pd-C) catalyst (0.1 g) and ammonium formate (0.15 g), and the mixture was stirred at room temperature. The catalyst was filtered off and washed with methanol-dichloromethane. The filtrate and washings were combined, and concentrated. The residue was taken up in dichloromethane, and washed with water, dried, and the solvent was evaporated, to leave the title compounds.

Compound 14 had mp 184.5-185.5 °C; $[\alpha]_D$ -15.5° (c 1.8, dichloromethane); IR 1660 and 1550 cm^{-1} (amide) ; ^1H NMR ($CDCl_3$) δ 1.47 (s, 9H, CH_3), 1.99 (s, 3H, $COCH_3$), 2.64 (dd, 1H, J_{gem} = 13.6,

$J_{1a,2}$ = 10.3 Hz, H-1a), 3.19(m, 1H, H-5), 3.82 (m, 1H, H-2), 5.56 (s, 1H, CHPh), and 7.3-7.55 (m, 5H, Ph-H).

Anal. Calcd for $C_{20}H_{28}N_2O_6$ (392.45): C, 61.21; H, 7.19; N, 7.14. Found: C, 61.45; H, 7.24; N, 7.10.

Compound 16 had $[\alpha]_D$ +1° (c 1.4, dichloromethane); IR 1670 and 1550 cm^{-1} (amide); ^1H NMR ($CDCl_3$) δ 1.48 (s, 9H, CH_3), 2.03 (s, 3H, $COCH_3$), 3.19 (dd, 1H, J_{gem} = 14.5, $J_{1a,2}$ = 3.7 Hz, H-1a), 3.54 (m, 1H, H-5), 3.99 (m, 1H, H-2), 5.62 (s, 1H, CHPh), and 7.3-7.55 (m, 5H, Ph-H).

Anal. Found: C, 61.53; H, 7.28; N, 7.04.

2-Acetamido-4,6-O-benzylidene-N-(tert-butoxycarbonyl)-1,2,5-trideoxy-1,5-imino-D-altritol (18) and 3-Acetamido-4,6-O-benzylidene-N-(tert-butoxycarbonyl)-1,3,5-trideoxy-1,5-imino-D-glucitol (20). Compounds 17 and 19 were converted to the corresponding acetamido derivatives 18 and 20, respectively, as described for 14 and 16.

Compound 18 had $[\alpha]_D$ +35° (c 1.6, dichloromethane): IR 1670 and 1550 cm^{-1} (amide); ^1H NMR ($CDCl_3$) δ 1.49 (s, 9H, CH_3) and 7.3-7.55 (m, 5H, Ph-H).

Anal. Found: C, 61.49; H, 7.13; N, 7.22.

Compound 20 had $[\alpha]_D$ -26° (c 1.7, dichloromethane); IR 1660 and 1550 cm^{-1} (amide); 1H NMR ($CDCl_3$) δ 1.46 (s, 9H, CH_3), 2.04 (s, 3H, $COCH_3$), and 7.25-7.55 (m, 5H, Ph-H).

Anal. Found: C, 60.87; H, 7.24; N, 7.01.

2-Azido-3-O-benzoyl-4,6-O-benzylidene-N-(tert-butoxycarbonyl)-1,2,5-trideoxy-1,5-imino-D-mannitol (21). A mixture of 10 (1 g) and sodium azide (3.6 g) in DMF was heated overnight at 100 °C and worked up as described for 13 and 15. The title compound 21 (35%) was obtained by chromatography on a column of silica gel with 300:1 dichloromethane-methanol: mp 142-144 °C, $[\alpha]_D$ -20° (c 0.5, dichloromethane); IR 2100 cm^{-1} (N_3); ^1H NMR ($CDCl_3$) δ 1.50 (s, 9H, CH_3), 3.08 (dd, 1H, J_{gem} = 14.7, $J_{1a,2}$ = 1.5 Hz, H-1a), 3.31 (m, 1H, H-5), 4.26 (m, 1H, H-2), 4.31 (t, 1H, J = 9.9 Hz, H-4), 4.44 (dd, 1H, J = 2.9 Hz, H-1e), 5.31 (dd, 1H, $J_{3,4}$ = 9.9, $J_{2,3}$ = 4 Hz, H-3), 5.63 (s, 1H, CHPh), and 7.2-8.2 (m, 10H, Ph-H).

Anal. Calcd for $C_{25}H_{28}N_4O_6$ (480.52): C, 62.49; H, 5.87; N, 11.66. Found: C, 62.23; H, 6.01; N, 11.54.

2-Acetamido-3-O-benzoyl-4,6-O-benzylidene-N-(tert-butoxycarbonyl)-1,2,5-trideoxy-1,5-imino-D-mannitol (22). To a solution of 21 (0.3 g) in 1:1 methanol-ethanol (10 mL) were added 10% Pd-C catalyst (0.5 g) and ammonium formate (0.2 g), and the mixture was stirred for 30 min at room temperature. The catalyst was filtered off, and the filtrate was concentrated to dryness. The residue was treated with acetic anhydride in pyridine to afford 22 (70%): mp 95-97 °C; $[\alpha]_D$ -68° (c 2, dichloromethane); ^1H NMR ($CDCl_3$) δ 1.95 (s, 3H, $COCH_3$), 2.99 (dd, 1H, J_{gem} = 14.3, $J_{1a,2}$ = 1.5 Hz, H-1a), 3.23 (m, 1H, H-5), 3.9 (t, 1H, J = 9.9 Hz, H-4), 4.36 (dd, 1H, $J_{1e,2}$ = 2.9 Hz, H-1e), 4.46 (t, 1H, J = 10.6 Hz, H-6a), 4.64 (m, 1H, H-2), 4.73 (dd, 1H, $J_{5,6e}$ = 4.8 Hz, H-6e), 5.03 (dd, 1H, $J_{2,3}$ = 4.8 Hz, H-3), 5.51 (s, 1H, CHPh), 6.35 (d, 1H, J = 6.4 Hz, NH), and 7.2-7.8 (m, 10H, Ph-H).

Anal. Calcd for $C_{27}H_{32}N_2O_7$ (496.56): C, 65.31; H, 6.50; N, 5.64. Found: C, 65.52; H, 6.44; N, 5.62.

2-Acetamido-4,6-O-benzylidene-N-(tert-butoxycarbonyl)-1,2,5-trideoxy-1,5-imino-D-mannitol (23). Treatment of 22 (0.2 g) with methanolic sodium methoxide at 0 °C gave crystalline 23 (quantitative): mp 211-214 °C; $[\alpha]_D$ -103° (c 1, 4:1 methanol-dichloromethane); IR 1630 and 1530 cm^{-1} (amide); ^1H NMR ($CDCl_3$) δ 3.93 (dd, 1H, $J_{3,4}$ = 9.2, $J_{2,3}$ = 4.4 Hz, H-3) and complete loss of the peaks due to a benzoyl group.

Anal. Calcd for $C_{20}H_{28}N_2O_6$ (392.45): C, 61.21; H, 7.19; N, 7.14. Found: C, 61.41; H, 7.20; N, 7.14.

2-Acetamido-3-O-acetyl-4,6-O-benzylidene-N-(tert-butoxycarbonyl)-1,2,5-trideoxy-1,5-imino-D-glucitol (24). To a solution of 13 (1.4 g) in methanol (10 mL) were added 10% Pd-C catalyst (2 g) and ammonium formate (1.3 g), and the mixture was stirred for 10 min at room temperature. After usual work up, the product was treated with acetic anhydride in pyridine, to give crystalline 24 (90%): mp 189-192 °C; $[\alpha]_D$ -16° (c 0.9, dichloromethane); IR 1670, 1540 (amide), and 1740 cm^{-1} (ester); ^1H NMR ($CDCl_3$) δ 1.95 (s, 3H, NCO-

CH_3), and 2.10 (s, 3H, $OCOCH_3$). The physical properties and spectral data were the same as those of the title compound prepared by acetylation of 14.

Anal. Calcd for $C_{22}H_{30}N_2O_7$ (434.49): C, 60.82; H, 6.96; N, 6.45. Found: C, 61.01; H, 6.88; N, 6.39.

2-Acetamido-3-O-acetyl-N-(tert-butoxycarbonyl)-1,2,5-trideoxy-1,5-imino-D-glucitol (25). To a solution of 24 (1.4 g) in 2:1 acetic acid-methanol (15 mL) was added 10% Pd-C catalyst, and the mixture was stirred for 2 days at room temperature in a hydrogen atmosphere. The catalyst was filtered off, and the filtrate was concentrated. The residue was chromatographed on a column of silica gel with (a) 100:1 and (b) 20:1 dichloromethane-methanol. Eluant (b) gave amorphous 25 (60%): $[\alpha]_D$ +30° (c 0.5, 2:1 dichloromethane-methanol); ^1H NMR data ($CDCl_3$+CD_3OD) showed complete loss of the peaks due to a phenyl group.

Anal. Calcd for $C_{15}H_{26}N_2O_7$ (346.38): C, 52.01; H, 7.57; N, 8.09. Found: C, 52.30; H, 7.41; N, 8.11.

2-Acetamido-3-O-acetyl-N-(tert-butoxycarbonyl)-1,2,5-trideoxy-1,5-imino-6-O-(triphenylmethyl)-D-glucitol (26) and 2-Acetamido-3-O-acetyl-N-(tert-butoxycarbonyl)-1,2,5-trideoxy-1,5-imino-6-O-(triphenylmethyl)-D-xylo-hex-4-ulitol (27). To a solution of 24 (0.12 g) in pyridine (10 mL) was added triphenylmethyl chloride (0.2 g), and the mixture was heated overnight at 60 °C. After work-up, the product was purified by chromatography on a column of silica gel with 50:1 dichloromethane-methanol, to give amorphous 26 (90%): $[\alpha]_D$ +34° (c 0.5, dichloromethane). A mixture of chromium trioxide (0.13 g) and pyridine (0.1 g) in dichloromethane (5 mL) was stirred for 1 h at 0 °C. A solution of 26 (0.19 g) in dichloromethane (2 mL) was added, and the mixture was stirred for another 1.5 h at 0 °C. The reaction mixture was chromatographed on a column of silica gel with ethyl acetate, to afford crystalline 27 (92%): mp 123-127 °C; $[\alpha]_D$ -41° (c 0.6, dichloromethane); IR 1780, 1740, 1690 (carbonyl), and 1650 and 1520 cm^{-1} (amide).

Anal. Calcd for $C_{34}H_{38}N_2O_7$ (586.69): C, 69.61; H, 6.53; N, 4.77. Found: C, 69.84; H, 6.61; N, 4.73.

2-Acetamido-3-O-acetyl-N-(tert-butoxycarbonyl)-1,2,5-trideoxy-1,5-imino-6-O-(triphenylmethyl)-D-galactitol (28) and 2-Acetamido-3,4-di-O-acetyl-N-(tert-butoxycarbonyl)-1,2,5-trideoxy-1,5-imino-6-O-(triphenylmethyl)-D-galactitol (29). To a solution of 27 (0.14 g) in 6:1 methanol-ethanol (3.5 mL) was added sodium borohydride (40 mg), and the mixture was stirred for 30 min at 0 °C. Work-up and evaporation gave a syrup which was chromatographed on a column of silica gel with (a) 100:1 and (b) 50:1 dichloromethane-methanol. Eluant (b) gave amorphous 28 (61%): [α] -18° (c 1, dichloromethane).

Compound 28 was acetylated with acetic anhydride and pyridine to afford 29: ^{1}H NMR ($CDCl_3$) δ 1.97 (s, 3H, $NCOCH_3$), 2.01, 2.14 (2s, 6H, $OCOCH_3$), 5.18 (m, 1H, H-4), and 5.34 (dd, 1H, $J_{2,3}$ = 8.8, $J_{3,4}$ = 1.5 Hz, H-3).

Anal. Calcd for $C_{36}H_{42}N_2O_8$ (630.74): C, 68.55; H, 6.71; N, 4.44. Found: C, 68.32; H, 6.58; N, 4.43.

2-Acetamido-3-O-acetyl-N-(tert-butoxycarbonyl)-1,2,5-trideoxy-1,5-imino-D-galactitol (30), 2-Acetamido-4-O-acetyl-N-(tert-butoxycarbonyl)-1,2,5-trideoxy-1,5-imino-D-galactitol (31) and 2-Acetamido-N-(tert-butoxycarbonyl)-1,2,5-trideoxy-1,5-imino-D-galactitol (32). To a solution of 28 (0.27 g) in 2:1 acetic acid-methanol (15 mL) was added 10% Pd-C catalyst (0.15 g), and the mixture was stirred for 3 days at room temperature in a hydrogen atmosphere. Work-up and evaporation gave a residue which was chromatographed on a column of silica gel with (a) 40:1, (b) 20:1, and (c) 10:1 dichloromethane-methanol. Eluant (b) gave 31 (45%) and eluant (c) gave 30 (32%).

Compound 30 had $[\alpha]_D$ -38° (c 0.9, methanol); IR 1740, 1670 (carbonyl), and 1640 and 1530 cm^{-1} (amide), ^{1}H NMR (s, 3H, $OCOCH_3$), and 5.04 (dd, 1H, $J_{2,3}$ = 9.9, $J_{3,4}$ =1.5 Hz, H-3).

Compound 31 had mp 157-159 °C; $[\alpha]_D$ +10° (c 1.2, methanol); IR 1740, 1660 (carbonyl), and 1640 and 1530 cm^{-1} (amide); ^{1}H NMR (CD_3OD) δ 2.05 and 2.08 (2s, 3H, $COCH_3$).

O-Deacetylation of 30 and 31 was performed by Zemplen's method to give 32 (quantitative): mp 156-160 °C; $[\alpha]_D$ -2° (c 0.9,

methanol); IR 1670 (carbonyl), and 1640 and 1540 cm^{-1} (amide); ^1H NMR (CD_3OD) δ 1.50 (s, 9H,CH_3) and 2.07 (s, 3H, $COCH_3$).

Anal. Calcd for $C_{13}H_{24}N_2O_6$ (304.34): C, 51.31; H, 7.95; N, 9.20. Found: C, 51.56; H, 8.07; N, 9.18.

2-Acetamido-1,2,5-trideoxy-1,5-imino-D-glucitol (33), 2-Acetamido-1,2,5-trideoxy-1,5-imino-D-mannitol (34) and 2-Acetamido-1,2,5-trideoxy-1,5-imino-D-galactitol (35). To a cooled, and stirred solution of 14, 23 or 32 (0.1-0.2 g) in trifluoroacetic acid (1-2 mL) was added a small amount of ice; stirring was continued for 2 h at room temperature. The mixture was concentrated, and the residue was triturated with ether. After decantation, the residue was treated with Amberlite IR-410 (OH^-) ion exchange resin in methanol. The resin was filtered off and the filtrate was concentrated, to give 32, 33, and 34 in quantitative yields.

Compound 33 had mp 226 °C (ref. 10 and 12a, 227-228 °C; ref. 12b, 224 °C); $[\alpha]_D$ +23° (c 0.8, methanol); IR 1660 and 1550 cm^{-1} (amide).

Anal. Calcd for $C_8H_{16}N_2O_4$ (204.23): C, 47.05; H, 7.90; N, 13.72. Found: C, 47.21; H, 8.03; N, 13.68.

Compound 34 had mp 208 °C (ref. 10, 203-207 °C); $[\alpha]_D$ -50° (c 1.3, methanol); IR 1650 and 1540 cm^{-1} (amide).

Anal. Found: C, 47.30; H, 8.12; N, 13.65.

Compound 35 had mp 230 °C; $[\alpha]_D$ +35° (c 0.9, methanol); IR 1650 and 1560 cm^{-1} (amide).

Anal. Found: C, 47.28; H, 7.96; N, 13.55.

3-Acetamido-1,3,5-trideoxy-1,5-imino-D-altritol (36), 2-Acetamido-1,2,5-trideoxy-1,5-imino-D-altritol (37) and 3-Acetamido-1,3,5-trideoxy-1,5-imino-D-glucitol (38). Compounds 16, 18, and 20 were treated with trifluoroacetic acid as described for the preparation of 32-34, to afford quantitative yields of 35, 36, and 37, respectively.

Compound 36 had $[\alpha]_D$ +1.4° (c 0.7, methanol); IR 1660 and 1550 cm^{-1} (amide).

Anal. Found: C, 46.76; H, 7.74; N, 13.50.

Compound 37 had $[\alpha]_D$ +14° (c 0.4, methanol); IR 1660 and 1550 cm^{-1} (amide).

Anal. Found: C, 46.81; H, 7.72; N, 13.63.

Compound 38 had $[\alpha]_D$ +40° (c 0.8, methanol); IR 1660 and 1550 cm^{-1} (amide)

Anal. Found: C, 47.33; H, 7.85; N, 13.75.

2,3,4-Tri-O-benzoyl-N-(tert-butoxycarbonyl)-1,5-dideoxy-1,5-imino-D-glucitol (40). To a solution of 2 (0.49 g) in pyridine (5 mL) was added tert-butyldimethylsilyl chloride (0.5 g), and the mixture was stirred for 1.5 h at room temperature. The mixture was cooled to 0 °C, and benzoyl chloride (3 mL) was added; stirring was continued for 3 h at 0 °C. The mixture was poured into ice-water, and extracted with dichloromethane. The extract was successively washed with ice-cold, 2M hydrochloric acid and water, dried, and the solvent was evaporated. The residual crude 39 was dissolved in 4:1 80% aq. acetic acid-1,4-dioxane (25 mL), and the mixture was kept for 5 h at 40 °C. The solvents were evaporated, and the residual syrup was chromatographed on a column of silica gel with 100:1 dichloromethane-methanol, to give crystalline 40 (84%): mp 188.5 °C; $[\alpha]_D$ -1.8° (c 1, dichloromethane); ^1H NMR (C_6D_6) δ 1.22 (s, 9H, CH_3), 3.34 (dd, 1H, J = 15.8, 1.5 Hz, H-1a), 3.76 (dd, 1H, J = 11.4, 5.9 Hz, H-6a), 3.84 (dd, 1H, J = 11.4, 8.1 Hz, H-6b), 4.45 (d, 1H, J = 15.8 Hz, H-1e), 4.73 (m, 1H, H-5), 5.10 (narrow m, 1H, H-4), 5.37 (narrow m, 1H, H-2), 5.72 (near t, 1H, J = 3.3-3.7 Hz, H-3), and 7-8.1 (m, 15H, ph-H).

Anal. Calcd for $C_{32}H_{33}NO_9$ (575.61): C, 66.77; H, 5.78; N, 2.43. Found: C, 66.54; H, 5.62; N, 2.41.

2,3,4-Tri-O-benzoyl-5-N,6-O-carbamoyl-1,5-dideoxy-1,5-imino-D-glucitol (41). To a solution of 40 (0.1 g) in pyridine (2 mL) were added iodine (0.14 g), triphenylphosphine (0.24 g) and imidazole (80 mg), and the mixture was stirred for 1 h at 45 °C. Ice was added and the product was extracted with dichloromethane. The extract was successively washed with aq. $Na_2S_2O_3$, ice-cold 2M hydrochloric acid and water, dried, and concentrated. The residue was chromatographed on a column of silica gel with 400:1 dichloromethane-methanol, to

give crystalline 41 (62%): mp 227 °C. $[\alpha]_D$ +7° (c 0.5, dichloromethane); IR 1760 and 1720 cm^{-1}(carbonyl); ^1H NMR (C_6D_6) δ 2.74 (dd, 1H, J = 13.2, 10.3 Hz, H-1a), 3.39 (m, 1H, H-5), 3.96 (dd, 1H, J = 9.2, 7.7 Hz, H-6a), 4.17 (dd, 1H, J = 9.2, 5.1 Hz, H-6e), 4.38 (dd, 1H, J = 13.2, 5.9 Hz, H-1e), 5.16 (t, J = 9.5 Hz, H-4), 5.25 (m, 1H, H-2), 5.74 (t, 1H, J = 9.5 Hz, H-3), and 7-8 (m, 15H, Ph-H).

Anal. Calcd for $C_{28}H_{23}NO_8$ (501.49): C, 67.06; H, 4.62; N, 2.79. Found: C, 67.35; H, 4.48; N, 2.87.

5-N,6-O-Carbamoyl-1,5-dideoxy-1,5-imino-D-glucitol (42). To a solution of 41 (0.1 g) in 2:1 methanol-1,4-dioxane (7.5 mL) was added one drop of 28% methanolic sodium methoxide at 0 °C. The mixture was stirred for 10 min at 0 °C, and then treated with Amberlite IR-120 (H^+) ion-exchange resin to remove the base. The resin was filtered off, and the filtrate was concentrated to dryness. The residue was triturated with toluene and decanted, to give hygroscopic 42 (81%): $[\alpha]_D$ +29° (c 0.5, methanol); IR 1730 cm^{-1} (carbonyl); ^1H NMR (CD_3OD) δ 2.84 (dd, 1H, J = 13.2, 10.6 Hz, H-1a), 3.2-3.7 (m, 4H, H-2,3,4 and 5), 3.92 (dd, 1H, J = 13.2, 5.5 Hz, H-1e), 4.31 (dd, 1H, J = 9, 4.4 Hz, H-6e), 4.50 (t, 1H, J = 9 Hz, H-6a), and complete disappearance of the peaks due to two benzoyl groups.

Anal. Calcd for $C_7H_{11}NO_5$ (189.17): C, 44.45; H, 5.86; N, 7.40. Found: C, 44.72; H, 5.69; N, 7.44.

4,6-O-Benzylidene-2,5-di-N-(tert-butoxycarbonyl)-1,2,5-trideoxy-1,5-imino-D-glucitol (44). To a solution of 13 (0.41 g) in 2:1 methanol-acetic acid (12 mL) was added 10% Pd-C catalyst (0.2 g), and the mixture was stirred for 40 min in a hydrogen atmosphere. The usual work-up gave a solid of 43, which was treated with 2-(tert-butoxycarbonyl)thio-4,6-dimethylpyrimidine (0.39 g) in water (2 mL)-1,4-dioxane (1 mL)-triethylamine (0.3 mL) overnight at 50 °C. The product was purified by chromatography on a column of silica gel with 400:1 dichloromethane-methanol to afford 44 (89%): $[\alpha]_D$ -15° (c 1.1, dichloromethane); ^1H NMR ($CDCl_3$) δ 1.45, 1.47 (2s, 18H, CH_3), 5.56 (s, 1H, CHPh), and 7.3-7.55 (m, 5H, Ph-H).

Anal. Calcd for $C_{23}H_{34}N_2O_7$ (450.53): C, 61.32; H, 7.61; N, 6.22. Found: C, 61.58; H, 7.43; N, 6.16.

3,4-Di-O-benzoyl-2,5-di-N-(tert-butoxycarbonyl)-1,2,5-trideoxy-1,5-imino-D-glucitol (47). A solution of 44 (0.2 g) in 90% aq. AcOH (5 mL) was kept overnight at 35 °C, and the solvent was removed by evaporation. The residue was chromatographed on a column of silica gel with 10:1 dichloromethane-methanol to give 45 (quantitative), $[\alpha]_D$ +49° (c 1.2, 1:1 dichloromethane-methanol): ^{1}H NMR ($CDCl_3$+CD_3OD) δ 1.45, 1.47 (2s, 18H, CH_3), and complete disappearance of the peaks due to a phenyl group. Compound 45 (0.17 g) was successively treated with tert-butyldimethylsilyl chloride, benzoyl chloride and aq. acetic acid as described for 40 to afford 47 (86%): $[\alpha]_D$ -46° (c 0.9, dichloromethane); ^{1}H NMR (C_6D_6): δ 1.31, 1.39 (2s, 18H, CH_3), and 7-8.1 (m, 10H, Ph-H).

Anal. Calcd for $C_{30}H_{38}N_2O_9$ (570.64): C, 63.15; H, 6.71; N, 4.91. Found: C, 63.37; H, 6.86; N, 5.04.

3,4-Di-O-benzoyl-2-(tert-butoxycarbonyl)amino-5-N,6-O-carbamoyl-1,2,5-trideoxy-1,5-imino-D-glucitol (48). To a solution of 47 (0.19 g) in pyridine (5 mL) were added iodine (0.32 g), triphenylphosphine (0.53 g) and imidazole (0.17 g), and the mixture was heated for 1 h at 60 °C. The work-up as described for 41 and chromatography on a column of silica gel gave 48 (73%): $[\alpha]_D$ -53° (c 0.5, dichloromethane); ^{1}H NMR ($CDCl_3$) δ 1.24 (s, 9H, CH_3), 3.0 (t, 1H, J = 12-13 Hz, H-1a), 4.28 (dd, 1H, J = 13.5 Hz, H-1e), 5.39, 5.50 (2t, 2H, J = 9.2 Hz, H-3 and H-4), and 7.2-8.0 (m, 10H, Ph-H).

Anal. Calcd for $C_{26}H_{28}N_2O_8$ (496.52): C, 62.90; H, 5.68; N, 5.64. Found: C, 63.15; H, 5.79; N, 5.61.

2-(tert-Butoxycarbonyl)amino-5-N,6-O-carbamoyl-1,2,5-trideoxy-1,5-imino-D-glucitol (49). Compound 48 (0.11 g) was treated with methanolic sodium methoxide as described for 42 to give crystalline 13 (85%): mp 234 °C, $[\alpha]_D$ +11° (c 1, 2:1 dichloromethane-methanol); ^{1}H NMR ($CDCl_3$+CD_3OD) complete loss of the peaks due to the phenyl groups.

Anal. Calcd for $C_{12}H_{20}N_2O_6$ (288.30): C, 49.99; H, 6.99; N, 9.72. Found: C, 50.23; H, 6.79; N, 9.70.

2-Amino-5-N,6-O-carbamoyl-1,2,5-trideoxy-1,5-imino-D-glucitol trifluoroacetate (50) and 2-acetamido-5-N,6-O-carbamoyl-1,2,5-

trideoxy-1,5-imino-D-glucitol (51). A solution of 49 (50 mg) in trifluoroacetic acid (2 mL) was stirred for 1 h at room temperature, and then concentrated. The residue was triturated with ether-n-hexane, and decanted to give hygroscopic 50, $[\alpha]_D$ +18° (c 0.6, methanol).

Anal. Calcd for $C_9H_{13}N_2O_6F_3$ (302.21): C, 35.77; H, 4.34; N, 9.27. Found: C, 36.04; H, 4.25; N, 9.32.

Compound 50 (50 mg) in methanol (5 mL) was treated with Amberlite IR-410 (OH^-) ion-exchange resin to remove the acid. The resulting amine was treated with acetic anhydride (2 mL) in methanol (2 mL) for 40 min at room temperature to afford 51 (quantitative): $[\alpha]_D$ +11° (c 0.4, methanol); IR 1740 (carbonyl), and 1650 and 1560 cm^{-1} (amide); ^1H NMR (CD_3OD) δ 1.90 (s, 3H, $COCH_3$), 2.70 (dd, 1H, J = 12.8, 5.9 Hz, H-1e), 4.19 (dd, 1H, J = 8.8, 4.4 Hz, H-6a), and 4.38 (t, 1H, J = 8.8 Hz, H-6e).

Anal. Calcd for $C_9H_{14}N_2O_5$ (230.22): C, 46.95; H, 6.13; N, 12.17. Found: C, 47.23; H, 6.05; N, 12.29.

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