Pergamon

Tetrahedron, Vol. 52, No. 42, pp. 13315-13326, 1996

0040-4020/96 $15.00 + 0.00

PII: S0040-4020(96)00791-0

Synthetic Studies on a Potential Endoglycosidase Inhibitor: Chemical Conversion of *N,N'*-Diacetylchitobiose into a Pseudodisaccharide Containing 2-Acetamido-1,2-Dideoxynojirimycin

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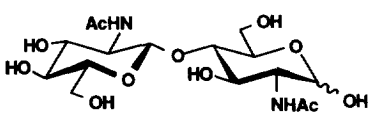
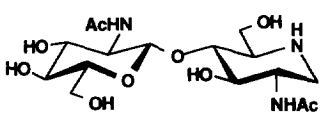
Abstract: The usefulness of *N,N'*-diacetylchitobiose (**1**) as a starting material for syntheses of biologically active compounds was shown by converting allyl chitobioside **5** into *O*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→4)-2-acetamido-1,2,5-trideoxy-1,5-imino-D-glucitol (**2**), which would be a potential glycosidase inhibitor. The conversion includes a discriminative modification of two amino groups existing in the disaccharide intermediate **8**, regioselective introduction of an azide group and construction of a piperidine ring utilizing an intramolecular aminocyclization.

Recently, we have established an efficient method for the preparation of β-(1→4)-linked amino sugar disaccharide, *N,N'*-diacethylchitobiose (**1**) through a limited enzymatic degradation of chitin.[1] The use of **1** as a key starting material is of grate advantage to the syntheses of various bioactive and/or biologically important pseudosugar chains,[2] because the step of laborious glycosidation will be able to cut down. In the preceding papers, we have reported total syntheses of some chitinase inhibitors from **1**.[3] In order to extend the utility of **1**, our attention has next been directed towards azachitobiose **2**, in which the ring oxygen and the anomeric hydroxyl group at the reducing end of **1** were replaced by an imino group and a hydrogen atom, respectively. This type of pseudooligosaccharide[4] is expected to inhibit endo-glycosidases which bind at the interior of polysaccharides and cleave randomly their glycosidic bonds, since many polyhydroxylated piperidine alkaloids, as represented by 1-deoxynojirimycin **3**, have showed powerful inhibitory activity against glycosidases.[5] A constituent of **2**, 2-acetamido-1,2-dideoxynojirimycin **4**, has also been known to inhibit powerfully a number of β-*N*-acetylglucosaminidases.[6] Hasegawa et al. has reported total synthesis of **2** via a coupling reaction of two components derived from D-glucosamine and 1-deoxynojirimycin.[4e] In this paper, we would like to describe an alternative synthesis of **2** employing **1** based on our strategy without the glycosidation reaction.[7]



1



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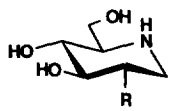
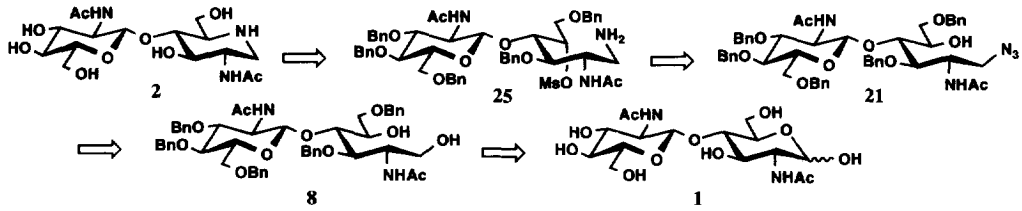


3: R = OH
4: R = NHAc

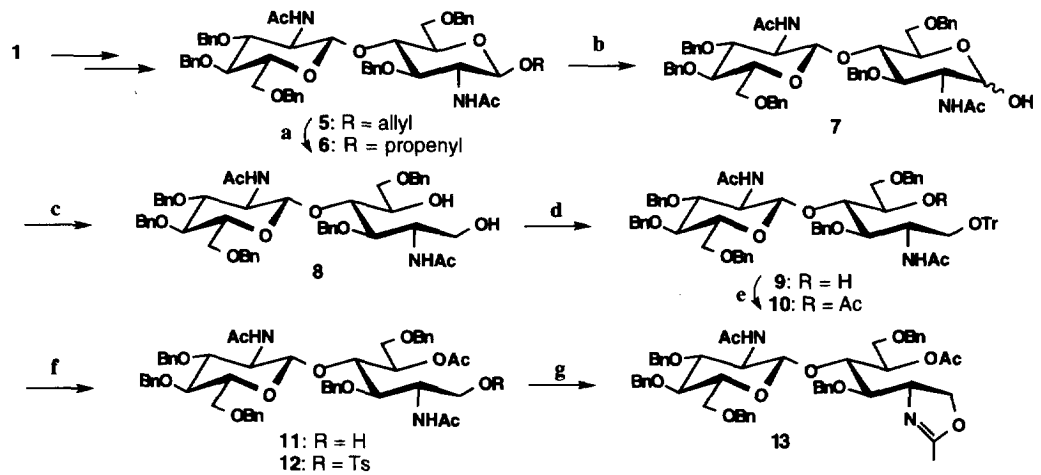
Our synthetic plan of **2** is shown in Scheme 1. In order to construct the piperidine ring in **2**, we have designed an intramolecular aminocyclization reaction of an aminomesylate **25**. This compound would be synthesized from an azido alcohol **21** via stereoinversion of a hydroxyl group at the C-5 position in **21**,

followed by reduction of an azido group at C-1. An introduction of the azido group might be possible by taking advantage of difference between the reactivities of two hydroxyl groups in a diol **8**, which would be readily obtainable from **1** by the simple manipulations.



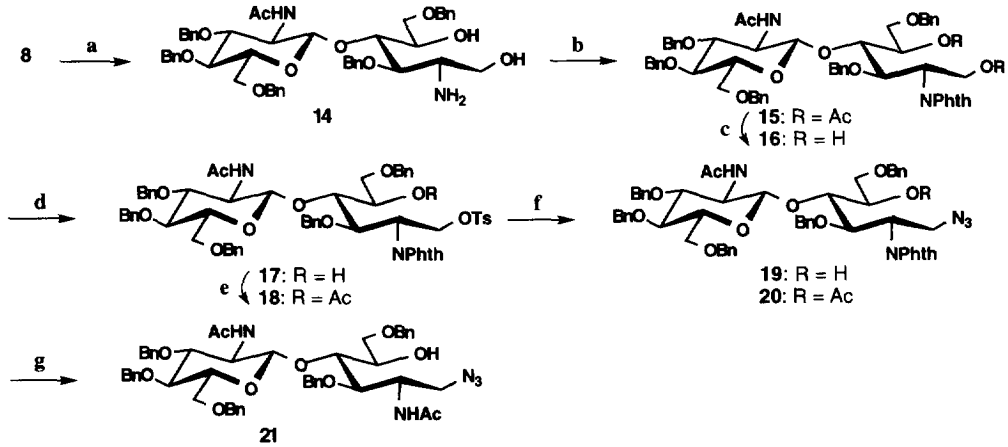
Scheme 1: A retrosynthetic scheme.

Firstly, allyl chitobioside **5**[1] prepared from **1**, was isomerized by treating it with potassium *t*-butoxide[8] in DMF to give an isopropenyl isomer **6** in high yield (Scheme 2). This was hydrolyzed with dil. HCl in chloroform-methanol to provide a hemiacetal **7** in 76% yield from **5**. Attempts to obtain **7** from **5** in a single step with palladium chloride-NaOAc[9] or selenium dioxide[10] in aq. acetic acid gave unsatisfactory results arised from the yields (~50%) and the lack of reproducibility of the reaction. The hemiacetal moiety in **7** was readily reduced with sodium borohydride ($NaBH_4$) to giving **8** in good yield. Unexpectedly the C-1 monotosylation of the diol **8** under standard reaction conditions gave a complicated reaction mixture. Even when a C-5 acetyl protected alcohol **11**, prepared via C-1 tritylated compounds **9**[11] and **10**, was treated with a small excess of p-toluenesulfonyl chloride (p-TsCl) in pyridine at room temperature, the reaction proceeded very sluggishly to give a complex mixture after a prolonged reaction time. The use of triethylamine and *N,N*-dimethylaminopyridine (DMAP) as additive bases improved the reaction, but a major product obtained was not a desired 1-*O*-monotosylate **12** but an oxazoline **13**, which was formed by a neighboring group participation of an acetamido group at C-2 in **12**. Methanesulfonylation of **11** in pyridine also gave **13** in a moderate yield.



Scheme 2: a) KO*t*-Bu, DMF, 75 °C; b) 2M HCl, $CHCl_3$-MeOH, rt, 76% from **5**; c) $NaBH_4$, EtOH-THF, -20 °C → rt, 72%; d) TrCl, pyr., 60 °C; e) Ac_2O, pyr., rt; f) 2M HCl, MeOH-$CHCl_3$, rt, 64% from **8**; g) p-TsCl, Et_3N, DMAP, $(CH_2Cl)_2$, rt, 71% or MsCl, pyr., 0 °C, 65%.

Therefore, we designed to replace the acetyl group of amino functionality in the acyclic moiety of **8** by a phthaloyl residue, which conducting as an *N*-protecting group, lacking of the neighboring participation. To do this an effective, selective deprotection of the acetyl group at C-2 in **8** was required. After making trial of several basic reaction conditions, we found that treatment of **8** with sodium hydroxide in aq. 2-methoxyethanol at 90 °C provided a monoamino derivative **14** in high yield (scheme 3). The presence of an *N*-acetyl group remained at C-2' position was confirmed by ^{1}H-NMR analyses including decoupling experiments. This regioselectivity in the hydrolysis seemed to be responsible for a neighboring group participation of the hydroxyl function at C-1 in **8**.[12] According to the Lemieux's procedure,[13] **14** was converted into a phthaloyl derivative **15** in 64% yield. After Zemplene de-*O*-acetylation, the resulting diol **16** was submitted to regioselective tosylation with p-TsCl and triethylamine in the presence of DMAP in CH_2Cl_2. As anticipated, this reaction proceeded nicely to afford a tosylate **17** in high yield. While **17** reacted slowly with sodium azide in DMF at 100 °C to provide a desired azide **19**[11] in low yield (~30%), a 5-*O*-acetylated derivative **18** gave the corresponding azide **20** in good yield under the same reaction condition. After simultaneous hydrolysis of *N*-phthaloyl and *O*-acetyl groups in **20** had been conducted under mild conditions using methylamine[14] in aq. ethanol, the resulting amino alcohol was acetylated to afford the key intermediate **21** in 85% yield.

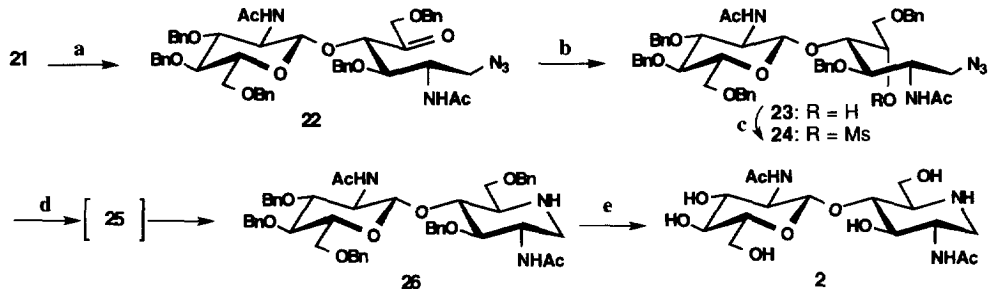


Scheme 3: a) 1M NaOH, 2-methoxyethanol, 90 °C, quant.; b) phthalic anhydride, Et_3N, MeOH, rt; then Ac_2O, pyr., 80 °C, 64%; c) NaOMe, MeOH, rt, quant.; d) p-TsCl, Et_3N, DMAP, CH_2Cl_2, rt, 81%; e) Ac_2O, pyr., rt, quant.; f) NaN_3, DMF, 100 °C, 74%; g) 40% CH_3NH_2, EtOH, rt; then Ac_2O, MeOH, rt, 85%.

The final stage of synthesis of **2** involved a S_N2 inversion of a free secondary hydroxyl group in **21** (scheme 4). Attempts to apply one-pot inversion methods including the Mitsunobu reaction[15] to **21** gave unsatisfactory results.[11] We chose, therefore, an oxidation-reduction process. Thus, **21** was initially oxidized with tetrapropylammonium perruthenate[16] and *N*-methylmorphorine *N*-oxide in the presence of molecular sieves 4A in CH_2Cl_2 at 23 °C to give an unstable 5-ulose **22** in high yield.[17] Next, reduction of the ketone function in **22** was examined under several conditions. Conventional sodium borohydride ($NaBH_4$) reduction in ethanol at 23 °C gave a L-ido alcohol **23** in 23% yield together with D-gluco isomer **21** (59% yield recovery) after silica-gel column chromatography. A reversed selectivity (**23**/**21** = 53/47, 75% yield) was observed when cerium chloride heptahydrate was used as an additive. The reduction at low temperature (-60 °C) was also effective;

59% yield of **23** was attained along with **21**(29%). However, warming to room temperature was required in order to complete the reaction. A high selectivity (**23**/**21** = 84/16) was obtained by the reduction of **22** with lithium tri *t*-butoxy aluminium hydride in THF at 0 °C albeit in low yield (total 34%). After sulfonylation of **23** under standard conditions, the resulting mesylate **24** was treated successively with triphenylphosphine, water and triethylamine in THF to give rise to the intermediate **25**, which cyclized spontaneously to afford a cyclic amine **26** in 89% yield. Finally, **26** was hydrogenated over 10% palladium on carbon in acetic acid-aqueous ethanol under hydrogen atmosphere, producing **2** in good yield.

In conclusion, the synthesis of the biologically interesting pseudodisaccharide **2** was achieved without a glycosidation reaction starting from *N,N'*-diacetylchitobiose **1**, which was readily available from enzymatic degradation of chitin.



Scheme 4: a) Tetrapropylammonium perruthenate, *N*-methylmorpholine *N*-oxide, MS4A, CH_2Cl_2, rt, 82%; b) $NaBH_4$, $CeCl_3 \cdot 7H_2O$, MeOH, -60 °C → rt, 59% for **23** and 29% for **21**; c) methanesulfonyl chloride, Et_3N, CH_2Cl_2, 0 °C, 70%; d) triphenylphosphine, THF, 50 °C; then Et_3N, H_2O, 65 °C, 89%; e) 10% Pd/C, H_2, AcOH-EtOH-H_2O, 83%.

Experimental

General Procedures. Melting points were determined in a capillary with an Ishii melting-point apparatus and are uncorrected. Optical rotations were measured with a JASCO DIP-370 polarimeter at 23±2 °C. IR spectra were recorded with a Shimadzu-FTIR-8100M spectrophotometer. ^{1}H-NMR spectra were recorded at 400 MHz or 500 MHz with JEOL JNM-α 400 or GX 500 spectrometers, using tetramethylsilane as the internal standard. Column chromatography was performed on silica gel 60 (230-400 mesh; E. Merck, Darmstadt, Germany). Merck precoated silica gel 60 F_{254} plates, 0.25 or 1.0 mm thickness, were used for analytical or preparative thin-layer chromatography respectively.

1-Propenyl 2-Acetamido-4-*O*-(2-acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside (6). To a stirred solution of **5** (5.0 g, 5.5 mmol) in *N,N*-dimethylformamide (100 ml) was added potassium *t*-butoxide (10 g, 89 mmol) under argon (Ar) and then the mixture was stirred at 75 °C for 3hr. After cooling, the resulting solution was poured into ice-water with stirring. The precipitate was collected by filtration, washed with water, and dried to give **6** (4.9 g, 98%) as a white solid, which was employed to the next step without further purification; mp 181~183 °C (EtOH); $[\alpha]_D$ -35.3° (*c* 0.51, $CHCl_3$); $\delta_H(CDCl_3)$ 1.44 (3H, dd, *J* = 6.7 and 1.5 Hz, Me), 1.72, 2.03, (6H, each s, NAc), 6.04 (1H, dd, *J* = 6.4 and 1.5 Hz, OC*H*=CH).

Found: C, 70.73; H, 6.80; N, 3.03%. Calcd for $C_{54}H_{62}O_{11}N_2$: C, 70.88; H, 6.83; N, 3.06%.

2-Acetamido-4-*O*-(2-acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-3,6-di-*O*-benzyl-2-deoxy-D-glucopyranose (7). To a stirred solution of **6** (4.9 g, 5.4 mmol) in chloroform-methanol (1:1, 300 ml) was added 2M hydrochloric acid solution (75 ml). The mixture was stirred at room temperature (rt) for 20hr, diluted with chloroform, washed with sat. $NaHCO_3$ solution, water, brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residual syrup was chromatographed on silica gel with chloroform-methanol (40 : 1, v/v) as eluent to give **7** (3.65 g, 76% from **5**); $[\alpha]_D$ +28.1° (*c* 0.53, $CHCl_3$); $\delta_H(CDCl_3)$ 1.67, 1.78, (1.98H, each s, β-NAc), 1.71, 1.80 (4.02H, each s, α-NAc), 3.75 (0.67H, brq, α-H-2'), 3.85 (0.33H, brq, β-H-2'), 3.90-3.92 (1.34H, brd, α-H-4, 5), 4.02 (0.33H, t, $J_{3,4} = J_{4,5}$ = 8.3 Hz, β-H-4), 4.09 (0.67H, dt, $J_{1,2}$ = 3.4 Hz, $J_{2,3}$ = 9.2 Hz, $J_{2,NH}$ = 8.8 Hz, α-H-2), 4.30 (0.67H, d, $J_{1,OH}$ = 4.4 Hz, α-OH), 4.36 (0.33H, d, $J_{1',2'}$ = 8.3 Hz, β-H-1'), 4.42 (0.33H, dd, $J_{1,2}$ = 8.3 Hz, $J_{1,OH}$ = 6.4 Hz, β-H-1), 4.43 (0.67H, d, $J_{1',2'}$ = 8.3 Hz, α-H-1'), 4.89 (0.67H, d, $J_{2',NH'}$ = 9.2 Hz, α-NH'), 5.21 (0.67H, dd, α-H-1), 5.48 (0.33H, d, $J_{2,NH}$ = 5.8 Hz, β-NH), 5.73 (0.67H, d, $J_{2,NH}$ = 8.8 Hz, α-NH), 5.98 (0.33H, d, β-OH); $\delta_C(CDCl_3)$ 90.9 (α-C-1), 97.7 (β-C-1), 100.4 (α-C-1'), 100.6 (β-C-1').

Found: C, 69.62; H, 6.62; N, 3.19%. Calcd for $C_{51}H_{58}O_{11}N_2$: C, 70.00; H, 6.68; N, 3.20%.

2-Acetamido-4-*O*-(2-acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-3,6-di-*O*-benzyl-2-deoxy-D-glucitol (8). To a stirred solution of **7** (437 mg, 0.5 mmol) in ethanol-tetrahydrofuran (2:1, 12 ml) was added sodium borohydride (58 mg, 1.5 mmol) at -20 °C and then the mixture was stirred at -20 °C→rt for 18hr. Acetic acid (0.5 ml) was added and the resulting solution was concentrated *in vacuo*. The residue was treated with water and then extracted with chloroform. The extracts were washed with water, brine, and dried ($MgSO_4$), evaporated. The residual syrup was chromatographed on silica gel with chloroform-methanol (50 : 1, v/v) as eluent to give **8** (316 mg, 72%); $[\alpha]_D$ +3.0° (*c* 0.20, $CHCl_3$); $\nu_{max}(CHCl_3)$ 3400, 3250, 1650 cm^{-1}; $\delta_H(CDCl_3)$ 1.74, 1.86, (6H, each s, NAc), 3.03 (1H, br.s, OH), 3.34 (1H, brs, OH), 3.45~3.86 (10H, m, H-1, 6, 2', 3', 4', 5', 6'), 3.96 (2H, brs, H-4, 5), 4.05 (1H, brt, *J* = 4.4Hz, H-3), 4.27 (1H, m, H-2), 4.44~4.80 (10H, m, CHPh), 4.72 (1H, d, $J_{1',2'}$ = 8.3 Hz, H-1'), 5.62 (1H, d, $J_{2',NH'}$ = 1.5 Hz, NH'), 6.33 (1H, d, $J_{2,NH}$ = 8.3 Hz, NH), 7.16-7.36 (25H, m, Ph).

Found: C, 68.94; H, 6.83; N, 3.09%. Calcd for $C_{51}H_{60}O_{11}N_2 \cdot 0.5H_2O$: C, 69.13; H, 6.94; N, 3.16%.

2-Acetamido-4-*O*-(2-acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-3,6-di-*O*-benzyl-2-deoxy-1-*O*-trityl-D-glucitol (9) . To a stirred solution of **8** (1.98 g, 2.26 mmol) in pyridine (50 ml) was added trityl chloride (690 mg, 2.48 mmol) and then the mixture was stirred at 60 °C for 2 days under Ar. After more addtional trityl chloride (300 mg, 1.08 mmol) being added, stirring was further continued for 18 hr. After cooling, the reaction mixture was poured into ice-water, and then extracted with chloroform. The extracts were washed with water, brine, and dried ($MgSO_4$), evaporated. The residual syrup was chromatographed on silica gel with chloroform-methanol (80 : 1, v/v) as eluent to give **9** (1.71 g, 67%); $[\alpha]_D$ +5.4° (*c* 0.65, $CHCl_3$); $\nu_{max}(CHCl_3)$: 3300, 1675, 1650 cm^{-1}; $\delta_H(CDCl_3)$ 1.75, 1.77, (6H, each s, NAc), 2.88 (1H, d, *J* = 5.2 Hz, OH), 3.25~3.42 (6H, m, H-1, 2', 4', 5', 6'a), 3.51 (2H, brd, H-6), 3.55 (1H, dd, $J_{5',6'a}$ = 1.5 and $J_{6'a,6'b}$ = 11 Hz, H-6'b), 3.89 (1H, t, *J* = 9.5 Hz, H-3), 3.93 (1H, dd, $J_{3,4}$ = 4.9 and $J_{4,5}$ = 5.1 Hz, H-4), 3.98 (1H, m, H-5), 4.05 (1H, dd, $J_{2,3}$ = 4.6 Hz, H-3), 4.28~4.49 (6H, m, PhCH), 4.63~4.68 (3H, m, H-2, PhCH), 4.73~4.80 (2H, m, PhCH), 4.86 (1H, d, $J_{1',2'}$ = 8.2 Hz, H-1'), 5.75 (1H, d, $J_{2',NH'}$ = 7.6 Hz, NH'), 6.10 (1H, d, $J_{2,NH}$ = 8.5 Hz, NH), 7.11-7.41 (40H, m, Ph).

Found: C, 74.27; H, 6.61; N, 2.46%. Calcd for $C_{70}H_{74}O_{11}N_2 \cdot H_2O$: C, 73.92; H, 6.74; N, 2.46%.

2-Acetamido-4-*O*-(2-acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-5-*O*-acetyl-3,6-di-*O*-benzyl-2-deoxy-1-*O*-trityl-D-glucitol (10). Compound **9** (404 mg, 0.36 mmol) was acetylated with acetic anhydride (1 ml) in pyridine (2 ml) at rt for 3hr. Methanol was added at 0 °C and the resulting mixture was stirred for several minutes, evaporated and then co-evaporated with toluene to give **10** (419 mg, quantitative). An analytical sample was prepared by chromatography on silica gel with chloroform-methanol-triethylamine (200 : 2 : 1, v/v/v) as eluent. **10**; $[\alpha]_D$ +0.2° (*c* 0.68, $CHCl_3$); $\nu_{max}(CHCl_3)$: 1740, 1650 cm^{-1}; $\delta_H(CDCl_3)$ 1.74, 1.79, 1.97, (9H, each s, Ac), 3.05 (1H, m, H-2'), 3.21~3.28 (2H, m, H-1a, 4'), 3.36~3.40 (3H, m, H-1b, 5', 6'a), 3.52 (1H, dd, $J_{5,6a}$ = 4.8 and $J_{6a,6b}$ = 11 Hz, H-6a), 3.56 (1H, brd, $J_{6'a,6'b}$ = 10 Hz, H-6'b), 3.66 (1H, dd, $J_{5,6b}$ = 3.9 Hz, H-6b), 4.03 (1H, dd, $J_{2,3}$ = 3.9 and $J_{3,4}$ = 4.4 Hz, H-3), 4.13 (1H, t, *J* = 9.5 Hz, H-3'), 4.22 (1H, dd, $J_{4,5}$ = 5.4 Hz, H-4), 4.31 (2H, brs, PhCH), 4.38~4.82 (8H, m, PhCH), 4.78 (1H, m, H-2), 4.89 (1H, d, $J_{1',2'}$ = 8.3 Hz, H-1'), 5.21 (1H, m, H-5), 5.51 (1H, d, $J_{2',NH'}$ = 7.8 Hz, NH'), 6.18 (1H, d, $J_{2,NH}$ = 7.8 Hz, NH), 7.11-7.45 (40H, m, Ph).

Found: C, 74.46; H, 6.54; N, 2.40%. Calcd for $C_{72}H_{76}O_{12}N_2$: C, 74.46; H, 6.60; N, 2.41%.

2-Acetamido-4-*O*-(2-acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-5-*O*-acetyl-3,6-di-*O*-benzyl-2-deoxy-D-glucitol (11). a) To a stirred solution of **10** (254 mg, 0.22 mmol) in methanol-chloroform (1 : 1; 20 ml) was added 2 M HCl solution (5 ml). The mixture was stirred for 3 hr at rt and then diluted with chloroform, washed with sat. $NaHCO_3$ solution, water, brine, dried ($MgSO_4$) and concentrated. The residual syrup was chromatographed on silica gel with chloroform-methanol (75 : 1, v/v) as eluent to give **11** (165 mg, 83%).

b) A mixture of **8** (900mg, 1.03 mmol) and trityl chloride (572 mg, 2.05 mmol) in pyridine (12 ml) was stirred at 70 °C for 12 hr under Ar, and then cooled. Ac_2O (0.5 ml) was added and stirring was further continued for 3 hr. The resulting mixture was poured into ice-water with stirring, and extracted with chloroform. The extracts were washed with sat. $NaHCO_3$ solution, water, brine, dried ($MgSO_4$) and concentrated to give a syrup (1.50 g), which was dissolved in methanol-chloroform-2M HCl (2 : 2 : 1; 100 ml) and treated as described above to give **11** (604 mg, 64% from **8**); $[\alpha]_D$ +4.5° (*c* 0.20, $CHCl_3$); $\nu_{max}(CHCl_3)$: 1730, 1650 cm^{-1}; $\delta_H(CDCl_3)$ 1.76, 1.89, 1.98, (9H, each s, Ac), 2.72 (1H, m, OH), 3.38 (1H, q, H-2'), 3.46~3.75 (7H, m, H-1, 6, 4', 5', 6'), 3.92 (1H, dd, $J_{2,3}$ = 4.4 and $J_{3,4}$ = 4.9 Hz, H-3), 4.01 (1H, $J_{2',3'}$ = 8.3 and $J_{3',4'}$ = 10 Hz,, H-3'), 4.18 (1H, t, *J* = 4.9 Hz, H-4), 4.32 (1H, m, H-2), 4.43~4.82 (10H, m, PhCH), 4.84 (1H, d, $J_{1',2'}$ = 8.3 Hz, H-1'), 5.27 (1H, m, H-5), 5.43 (1H, d, $J_{2',NH'}$ = 7.8 Hz, NH'), 6.28 (1H, d, $J_{2,NH}$ = 8.3 Hz, NH), 7.16-7.35 (25H, m, Ph).

Found: C, 67.66; H, 6.69; N, 2.95%. Calcd for $C_{53}H_{62}O_{12}N_2 \cdot H_2O$: C, 67.93; H, 6.88; N, 2.99%.

5-*O*-Acetyl-4-*O*-(2-acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-3,6-di-*O*-benzyl-2-deoxy-1,2-(2-methyl-1-oxa-3-azaprop-2-eno)-D-glucitol (13). To a stirred solution of **11** (10 mg, 0.01 mmol), triethylamine (9 μl, 0.06 mmol) and *N,N*-dimethylaminopyridine (1.3 mg, 0.01 mmol) in 1,2-dichloroethane (0.25 ml) was added p-toluenesulfonyl chloride (6.2 mg, 0.03 mmol) at rt. The mixture was stirred at room temperature for 7.8 hr, poured into ice-water, and then stirred vigorously for 2hr. The resulting mixture was extracted with chloroform. The extracts was washed successively with 10 % hydrochloric acid, sat. $NaHCO_3$ solution, water and brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residual syrup was chromatographed on silica gel with chloroform-methanol (50 : 1, v/v) as eluent to give **13** (7 mg, 71%); $[\alpha]_D$ +4.4° (*c* 0.27, $CHCl_3$); $\nu_{max}(CHCl_3)$ 1740, 1672, 1655 cm^{-1}; $\delta_H(CDCl_3)$ 1.76 (3H, s, Ac), 1.95 (3H, s, oxazoline Me), 1.97, (3H, each s, Ac), 3.34 (1H, q, H-2'), 3.39 (1H, m, H-5'), 3.50 (1H, dd, $J_{2,3}$ = 7.8 and

$J_{3,4}$ = 2.9 Hz, H-3), 3.56 (1H, t, J = 9,3 Hz, H-4'), 3.60~3.65 (3H, m, H-6a, 6'), 3.76 (1H, dd, $J_{5,6b}$ = 2.9 and $J_{6a,6b}$ = 11 Hz, H-6b), 3.92 (1H, dd, $J_{1a,1b}$ = 8.8 and $J_{1a,2}$ = 8.3 Hz, H-1a), 4.05 (1H, dd, $J_{2',3'}$ = 8.8 and $J_{3',4'}$ = 9.3 Hz, H-3'), 4.09 (1H, $J_{4,5}$ = 6.0 Hz, H-4), 4.32 (1H, dd, $J_{1b,2}$ = 9.8 Hz, H-1b), 4.44~4.64 (8H, m, H-2, PhCH), 4.75~4.86 (3H, m, PhCH), 4.83 (1H, d, $J_{1',2'}$ = 8.3 Hz, H-1'), 5.29 (1H, m, H-5), 5.49 (1H, d, $J_{2',NH'}$ = 7.8 Hz, NH'), 7.17-7.34 (25H, m, Ph); $\delta_C(CDCl_3)$ 14.0 (Me), 21.2 (OAc), 23.5 (NAc), 57.5 (C-2'), 67.7 (C-6), 67.8 (C-2), 68.7 (C-6'), 69.7 (C-1), 72.5 (C-5), 74.6 (C-5'), 74.9 (C-4), 78.6 (C-4'), 80.7 (C-3), 80.8 (C-3'), 99.0 (C-1'), 165.4 (*C*=N), 170.1 (O*C*OMe), 170.3 (N*C*OMe); FAB-MS m/z 901.5 $(M+H)^+$ (nitrobenzyl alcohol matrix).

Found: C, 70.19; H, 6.73; N, 3.12%. Calcd for $C_{53}H_{60}O_{11}N_2$: C, 70.65; H, 6.71; N, 3.11%.

4-*O*-(2-Acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-2-amino-3,6-di-*O*-benzyl-2-deoxy-D-glucitol (14). Compound **8** (5.2 g, 5.93 mmol) was heated in a mixture of M NaOH solution (65 ml) and 2-methoxyethanol (91 ml) while stirring at 90 °C for 8hr under Ar. After cooling, acetic acid (4.0 ml) was added and then the resulting solution was concentrated *in vacuo*. The residue was treated with water and extracted with chloroform. The extarcts were washed with dil. NaOH solution, water and brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was co-evaporated with toluene to give crude **14** (5.0 g), which was employed to the next step without further purification, $\nu_{max}(CHCl_3)$ 3200, 1650, 1560 cm^{-1}; $\delta_H(CDCl_3)$ 1.76 (3H, s, Ac), 3.08 (1H, brt, J = 5.8 Hz, H-2), 3.36 (1H, brdd, $J_{1a,1b}$ = 11Hz, $J_{1a,2}$ = 5.8 Hz, H-1a), 3.45 (1H, m, H-2'), 3.89 (1H, brs, H-3), 4.69 (1H, d, $J_{1',2'}$ = 7.8 Hz, H-1'), 5.99 (1H, brs, NH').

4-*O*-(2-Acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-1,5-di-*O*-acetyl-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-D-glucitol (15). Compound **14** (5.0 g) was treated with phthalic anhydride (1.76 g, 11.9 mmol) and triethylamine (1.23 ml, 8.9 mmol) in methanol (30 ml) to give the phthalamido derivative, which was reacted with acetic anhydride (12 ml) in pyridine (20 ml) at 80 °C for 7 h. The reaction mixture was poured into ice-water, and allowed to stand overnight. The resulting solution was extracted with ethyl acetate. The extracts was washed successively with 10 % hydrochloric acid, sat. $NaHCO_3$ solution, water and brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residual syrup was chromatographed on silica gel with hexane-ethyl acetate (1 : 1, v/v) as eluent to give **15** (4.0 g, 64%); $[\alpha]_D$ +23.7° (*c* 0.43, $CHCl_3$); $\nu_{max}(CHCl_3)$ 1748, 1715, 1650 cm^{-1}; $\delta_H(CDCl_3)$ 1.84, 1.86, 2.09 (9H, each s, Ac), 3.47 (1H, m, H-5'), 3.60 (1H, q, H-2'), 3.62 (1H, dd, $J_{3',4'}$ = 9.5 and $J_{4',5'}$ = 8.9 Hz, H-4'), 3.69 (2H, brd, H-6'), 3.78 (2H, brd, H-6), 4.03 (1H, dd, $J_{2',3'}$ = 9.2 Hz, H-3'), 4.20 (1H, d, J = 11 Hz, PhCH), 4.33 (1H, dd, $J_{3,4}$ = 2.5 and $J_{4,5}$ = 6.8 Hz, H-4), 4.49~4.69 (9H, m, H-1a, 3, PhCH), 4.70 (1H, dd, $J_{1a,1b}$ = 12 and $J_{1b,2}$ = 7.0 Hz, H-1b), 4.78 (1H, d, J = 11 Hz, PhCH), 4.83 (1H, d, J = 11 Hz, PhCH), 4.99 (1H, d, $J_{1',2'}$ = 7.9 Hz, H-1'), 5.00 (1H, m, H-2), 5.48 (1H, m, H-5), 5.79 (1H, d, J =7.9 Hz, NH'), 6.86-7.73 (29H, m, Ph).

Found: C, 69.68; H, 6.20; N, 2.61%. Calcd for $C_{61}H_{64}O_{14}N_2$: C, 70.00; H, 6.11; N, 2.65%.

4-*O*-(2-Acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-1-*O*-tosyl-D-glucitol (17). To a stirred solution of diacetate **15** (163 mg, 0.16 mmol) in methanol (5 ml) was added sodium methoxide (11 mg, 0.2 mmol), and the solution was stirred for 2 h at rt, made neutral with Dowex 50W X-8 (H^+) resin, the mixture filtered, and the filtrate evaporated, and then co-evaporated with toluene to give **16** (140 mg, 95%). To a stirred solution of the above diol **16** (91 mg, 0.1 mmol), triethylamine (0.4 ml, 2.9 mmol) and *N,N*-dimethylaminopyridine (12 mg, 0.1 mmol) in dichloromethane (4 ml) was added p-toluenesulfonyl chloride (72 mg, 0.38 mmol) and the mixture was stirred for 4 hr at rt. To the mixture was added a Na_2CO_3 solution and the resulting suspension was vigorously

stirred for 1hr, then extracted with chloroform. The extracts were washed with dil. HCl solution, sat. $NaHCO_3$ solution, water, brine, and dried ($MgSO_4$) and concentrated *in vacuo*. The residual syrup was chromatographed on silica gel with toluene-ethyl acetate (3 : 1, v/v) as eluent to give **17** (85 mg, 80%); $[\alpha]_D$ +31.5° (*c* 0.27, $CHCl_3$); $\nu_{max}(CHCl_3)$: 3400, 1714, 1670, 1361, 1176 cm^{-1}; $\delta_H(CDCl_3)$ 1.83 (3H, s, Ac), 2.28 (3H, s, Ts), 2.87 (1H, d, J = 4.9 Hz, OH), 3.40 (1H, m, H-5'), 3.58 (1H, dd, $J_{3',4'}$ = 8.9 and $J_{4',5'}$ = 9.5 Hz, H-4'), 3.61 (1H, q, H-2'), 3.60~3.70 (4H, m, H-6, 6'), 3.83 (1H, dd, $J_{3,4}$ = 2.8 and $J_{4,5}$ = 8.2 Hz, H-4), 3.87 (1H, dd, $J_{2',3'}$ = 9.8 and $J_{3',4'}$ = 8.6 Hz, H-3'), 4.13 (1H, m, H-5), 4.22 (1H, d, J = 11 Hz, PhCH), 4.44 (1H, dd, $J_{1a,1b}$ = 11 and $J_{1a,2}$ = 3.7 Hz, H-1a), 4.47 (1H, dd, $J_{2,3}$ = 10 and $J_{3,4}$ = 2.8 Hz, H-3), 4.50~4.59 (6H, m, PhCH), 4.69 (1H, d, J = 11 Hz, PhCH), 4.78 (1H, d, J = 11 Hz, PhCH), 4.80 (1H, dd, $J_{1b,2}$ = 10 Hz, H-1b), 4.83 (1H, d, J = 11 Hz, PhCH), 4.90 (1H, d, $J_{1',2'}$ = 8.4 Hz, H-1'), 4.99 (1H, m, H-2), 5.88 (1H, d, J = 8.9 Hz, NH'), 6.83-7.60 (33H, m, Ph).

Found: C, 68.64; H, 6.01; N, 2.51; S, 2.84%. Calcd for $C_{64}H_{56}O_{14}N_2S$: C, 68.68; H, 5.94; N, 2.50; S, 2.86%.

4-*O*-(2-Acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-5-*O*-acetyl-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-1-*O*-tosyl-D-glucitol (18). Alcohol **17** was acetylated with acetic anhydride in pyridine to give acetate **18** (quantitative); $[\alpha]_D$ +17.5° (*c* 0.69, $CHCl_3$); $\nu_{max}(CHCl_3)$ 1749, 1715, 1650, 1360, 1175 cm^{-1}; $\delta_H(CDCl_3)$ 1.87, 2.12 (6H, each s, Ac), 2.26 (3H, s, Ts), 3.51 (1H, m, H-5'), 3.58 (1H, brq, H-2'), 3.60 (1H, dd, $J_{3',4'}$ = 9.7 and $J_{4',5'}$ = 8.8 Hz, H-4'), 3.65~3.78 (4H, m, H-6, 6'), 3.97 (1H, dd, $J_{2',3'}$ = 9.3 Hz, H-3'), 4.10 (1H, d, J = 11 Hz, PhCH), 4.23 (1H, dd, $J_{3,4}$ = 2.9 and $J_{4,5}$ = 5.9 Hz, H-4), 4.27 (1H, dd, $J_{2,3}$ = 9.7 Hz, H-3), 4.40 (1H, d, J = 11 Hz, PhCH), 4.45~4.70 (6H, m, PhCH), 4.56 (1H, dd, $J_{1a,1b}$ = 11 and $J_{1a,2}$ = 3.4 Hz, H-1a), 4.67 (1H, dd, $J_{1b,2}$ = 11 Hz, H-1b), 4.78~4.86 (2H, m, PhCH), 4.87 (1H, d, $J_{1',2'}$ = 8.3 Hz, H-1'), 5.08 (1H, dt, H-2), 5.42 (1H, brq, H-5), 5.67 (1H, d, $J_{2',NH'}$ = 8.3 Hz, NH'), 6.77~7.65 (33H, m, Ph).

Found: C, 68.15; H, 5.93; N, 2.33; S, 2.82%. Calcd for $C_{66}H_{68}O_{15}N_2S$: C, 68.26; H, 5.90; N, 2.46; S, 2.76%.

4-*O*-(2-Acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-5-*O*-acetyl-1-azido-3,6-di-*O*-benzyl-1,2-dideoxy-2-phthalimido-D-glucitol (20). To a stirred solution of **18** (1.0 g, 0.86 mmol) in *N,N*-dimethylformamide (50 ml) was added sodium azide (560 mg, 8.6 mmol). The mixture was stirred at 100 °C for 8 h, and cooled, poured into ice-water. The resulting solution was extracted with ether. The extracts were washed with water, brine, and dried ($MgSO_4$) and concentrated *in vacuo*. The residual syrup was chromatographed on silica gel with toluene-ethyl acetate (5 : 1, v/v) as the eluent to give **20** (660 mg, 71%); $[\alpha]_D$ +12.0° (*c* 1.0, $CHCl_3$); $\nu_{max}(CHCl_3)$: 2100, 1748, 1713, 1653 cm^{-1}; $\delta_H(CDCl_3)$ 1.82, 2.11 (6H, each s, Ac), 3.49~3.55 (2H, m, H-2', 5'), 3.57 (1H, dd, $J_{3',4'}$ = 9.8 and $J_{4',5'}$ = 9.3 Hz, H-4'), 3.66 (1H, dd, $J_{5',6'a}$ = 5.4 and $J_{6'a,6'b}$ = 11 Hz, H-6'a), 3.70 (1H, dd, $J_{5',6'b}$ = 2.0 Hz, H-6'b), 3.72 (1H, dd, $J_{5,6a}$ = 5.4 and $J_{6a,6b}$ = 11 Hz, H-6a), 3.77 (1H, dd, $J_{5,6b}$ = 3.4 Hz, H-6b), 3.91~3.99 (2H, m, H-1), 4.06 (1H, dd, $J_{2',3'}$ = 8.8 Hz, H-3'), 4.16 (1H, d, J = 11 Hz, PhCH), 4.25 (1H, dd, $J_{3,4}$ = 2.4 and $J_{4,5}$ = 6.3 Hz, H-4), 4.36 (1H, dd, $J_{2,3}$ = 10 Hz, H-3), 4.45~4.85 (9H, m, PhCH), 4.90 (1H, m, H-2), 4.94 (1H, d, $J_{1',2'}$ = 8.3 Hz, H-1'), 5.38 (1H, m, H-5), 5.62 (1H, d, $J_{2',NH'}$ = 8.3 Hz, NH'), 6.83~7.74 (29H, m, Ph).

Found: C, 68.35; H, 5.99; N, 6.66%. Calcd. for $C_{59}H_{61}O_{12}N_5$: C, 68.66; H, 5.96; N, 6.79%.

2-Acetamido-4-*O*-(2-acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-1-azido-3,6-di-*O*-benzyl-1,2-dideoxy-D-glucitol (21). To a stirred solution of **20** (210 mg, 0.21 mmol)

in ethanol (5 ml) was added dropwise a 40 % CH_3NH_2 solution (3.5 ml). The mixture was stirred at rt for 42 hr, evaporated, and then co-evaporated with toluene. The residue was dissolved in methanol (3 ml) containing acetic anhydride (60 µl) and the mixture was stirred at rt for 10 min, evaporated, and then co-evaporated with toluene. The residual syrup was chromatographed on silica gel with toluene-ethyl acetate (1 : 1, v/v) as eluent to give **21** (157 mg, 85%); $[\alpha]_D$ +6.5° (*c* 0.34, $CHCl_3$); $\nu_{max}(CHCl_3)$ 3300, 2100, 1652 cm^{-1}; $\delta_H(CDCl_3)$ 1.78, 1.83 (6H, each s, Ac), 3.05 (1H, brd, J = 6.1 Hz, OH), 3.37 (1H, dd, $J_{1a,1b}$ = 13 and $J_{1a,2}$ = 4.7 Hz, H-1a), 3.45 (1H, m, H-2'), 3.46~3.56 (4H, m, H-6, 4', 6'a), 3.59 (1H, m, H-5'), 3.61 (1H, dd, $J_{1b,2}$ = 8.2 Hz, H-1b), 3.68 (1H, dd, $J_{5',6'b}$ = 1.5 and $J_{6'a,6'b}$ = 11 Hz, H-6'b), 3.91 (1H, m, H-5), 3.92~4.02 (3H, m, H-3, 4, 3'), 4.41~4.54 (6H, m, H-2, PhCH), 4.55~4.83 (5H, m, PhCH), 4.90 (1H, d, $J_{1',2'}$ = 8.2 Hz, H-1'), 5.68 (1H, d, $J_{2',NH'}$ = 7.9 Hz, NH'), 6.35 (1H, d, $J_{2,NH}$ = 8.6 Hz, NH), 7.23~7.49 (25H, m, Ph).

Found: C, 67.76; H, 6.62; N, 7.63%. Calcd. for $C_{51}H_{59}O_{10}N_5$: C, 67.91; H, 6.59; N, 7.76%.

2-Acetamido-4-*O*-(2-acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-1-azido-3,6-di-*O*-benzyl-1,2-dideoxy-D-xylo-*hex*-5-ulose (22). To a stirred solution of **21** (146 mg, 0.15 mmol), *N*-methylmorphorine *N*-oxide (35 mg, 0.30 mmol) and molecular sieves 4A in dichloromethane (4 ml) was added n-tetrapropylammonium perruthenate (6 mg, 0.02 mmol) and the mixture was stirred for 1 hr at rt. Then a trace amount of *N*-methylmorphorine *N*-oxide and n-tetrapropylammonium perruthenate were added to the reaction mixture and stirring was further continuted for 1h. The mixtrure was diluted with dichloromethane, filtered through a pad of Celite, concentrated *in vacuo*. Flash chromatography with toluene-ethyl acetate (3 : 1, v/v) as eluent gave **22** (120 mg, 82%), which was employed to the next step without further purification, $\nu_{max}(CHCl_3)$ 3250, 2104, 1732, 1670, 1651 cm^{-1}; $\delta_H(CDCl_3)$ 1.80, 1.86 (6H, each s, Ac), 3.45 (1H, m, H-2'), 3.62 (1H, t, J = 7.8 Hz, H-3'), 3.92 (1H, d, $J_{6'a,6'b}$ = 17 Hz, H-6a), 4.05 (1H, d, H-6b), 4.19 (1H, dd, $J_{2,3}$ = 4.9 and $J_{3,4}$ = 3.4 Hz, H-3), 4.58 (1H, m, H-2), 4.62 (1H, d, H-4), 4.66 (1H, d, $J_{1',2'}$ = 8.3 Hz, H-1'), 5.66 (1H, d, $J_{2',NH'}$ = 7.8 Hz, NH'), 6.22 (1H, d, $J_{2,NH}$ = 7.8 Hz, NH); $\delta_C(CDCl_3)$ 170.3, 171.2 (*N*COMe), 205.7 (*C*O).

2-Acetamido-4-*O*-(2-acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-1-azido-3,6-di-*O*-benzyl-1,2-dideoxy-L-iditol (23). To a stirred solution of **22** (17 mg, 0.02 mmol) and cerium chloride heptahydrate (7 mg, 0.02 mmol) in methanol (0.5 ml) was added sodium borohydride (3 mg, 0.08 mmol) at -60 °C. The mixture was stirred for 4.5h at -60 °C and then gradually warmed to rt. After adding acetic acid (0.1 ml), the reaction mixture was directly concentrated, co-evaporated with toluene, diluted with dichloromethane and poured into a column of silica gel. Elution with toluene-acetone (3:1 → 1:1, v/v) gave **21** (5 mg, 29%) and **23** (10 mg, 59%); $[\alpha]_D$ +7.3° (*c* 0.23, $CHCl_3$); $\delta_H(CDCl_3)$ 1.81 (6H, s, Ac), 2.94 (1H, brd, OH), 3.18 (1H, dd, $J_{5,6a}$ = 4.9 and $J_{6a,6b}$ = 9.9 Hz, H-6a), 3.30 (1H, dd, $J_{5,6b}$ = 4.4 Hz, H-6b), 3.43 (1H, t, $J_{3',4'} = J_{4',5'}$ = 8.3 Hz H-4'), 3.48~3.70 (6H, m, H-1, 6, 5', 6'), 3.58 (1H, q, H-2'), 3.70 (1H, dd, $J_{2',3'}$ = 9.8 Hz, H-3'), 3.78 (1H, m, H-3), 3.83 (1H, dd, $J_{3,4}$ = 9.3 and $J_{4,5}$ = 3.9 Hz H-4), 3.88 (1H, m, H-5), 4.36~4.76 (10H, m, PhCH), 4.56 (1H, m, H-2), 4.83 (1H, d, $J_{1',2'}$ = 8.3 Hz, H-1'), 5.84 (1H, d, $J_{2',NH'}$ = 7.3 Hz, NH'), 6.48 (1H, d, $J_{2,NH}$ = 8.3 Hz, NH), 7.26~7.37 (25H, m, Ph).

Found: C, 66.65; H, 6.62; N, 7.49%. Calcd. for $C_{51}H_{59}O_{10}N_5 \cdot H_2O$: C, 66.58; H, 6.68; N, 7.61%.

2-Acetamido-4-*O*-(2-acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-1-azido-3,6-di-*O*-benzyl-1,2-dideoxy-5-*O*-mesyl-L-iditol (24). To a stirred solution of **23** (20 mg, 0.02 mmol) and triethylamine (0.05 ml) in dichloromethane (0.5 ml) was added methanesulfonyl chloride (10 µl, 0.13 mmol) at 0 °C. The mixture was stirred at 0 °C for 1.5 hr, and then poured into ice-water. The

resulting mixture was extracted with chloroform. The extracts was washed successively with water, sat. $NaHCO_3$ solution, water and brine, dried ($MgSO_4$) and concentrated *in vacuo*. Purification by preparative TLC with chloroform-methanol (20 : 1, v/v) gave **24** (16 mg, 70%); $[\alpha]_D$ -11° (*c* 0.10, $CHCl_3$); $\nu_{max}(CHCl_3)$ 2100, 1670, 1650, 1362 cm^{-1}; $\delta_H(CDCl_3)$ 1.88, 1.91 (6H, each s, Ac), 2.94 (3H, s, Ms), 3.10 (1H, dd, $J_{5,6a}$ = 5.8 and $J_{6a,6b}$ = 12 Hz, H-6a), 3.31 (1H, brd, H-6b), 3.51~3.70 (7H, m, H-1a, 3, 3', 4', 5', 6'), 3.86 (1H, dd, $J_{1a,1b}$ = 14 and $J_{1b,2}$ = 9.5 Hz, H-1b), 4.05 (1H, q, H-2'), 4.08 (1H, dd, $J_{3,4}$ = 2.4 and $J_{4,5}$ = 8.6 Hz, H-4), 4.18~4.65 (7H, m, PhCH), 4.69 (1H, m, H-2), 4.69~4.74 (3H, m, PhCH), 4.76 (1H, d, $J_{1',2'}$ = 8.2 Hz, H-1'), 5.03 (1H, m, H-5), 6.23 (1H, d, $J_{2',NH'}$ = 9.5 Hz, NH'), 6.58 (1H, d, $J_{2,NH}$ = 8.6 Hz, NH), 7.06~7.37 (25H, m, Ph).

Found: C, 62.92; H, 6.24; N, 6.86; S, 3.10 %. Calcd. for $C_{52}H_{61}O_{12}N_5S \cdot H_2O$: C, 62.57; H, 6.35; N, 7.02; S, 3.21%.

2-Acetamido-4-*O*-(2-acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-3,6-di-*O*-benzyl-1,2,5-trideoxy-1,5-imino-D-glucitol (26). A mixture of **24** (113 mg, 0.12 mmol) and triphenylphosphine (31 mg, 0.12 mmol) in THF (3.5 ml) were stirred at 55 °C for 9hr. Triethylamine-water (0.9 ml, 1:1, v/v) was added, and then the mixture was heated under reflux for 14 hr, concentrated *in vacuo*. The residue was diluted with dichloromethane, washed with dil. NaOH solution, water and brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residual syrup was chromatographed on silica gel with chloroform-methanol (30 : 1, v/v) as eluent to give **26** (88 mg, 89%) as a crystalline solid; mp. 220-220.5 °C (EtOH-$CHCl_3$); $[\alpha]_D$ +4.6° (*c* 0.46, $CHCl_3$); $\delta_H(CDCl_3)$ 1.73, 1.92 (6H, each s, Ac), 2.38 (1H, dd, $J_{1a,1b}$ = 13 and $J_{1a,2}$ = 5.6 Hz, H-1a), 2.77 (1H, m, H-5), 3.20 (1H, dd, $J_{1b,2}$ = 3.7 Hz, H-1b), 3.38 (1H, m, H-5'), 3.45 (1H, dd, $J_{2,3}$ = 5.1 and $J_{3,4}$ = 9.5 Hz, H-3), 3.46 (1H, dd, $J_{4,5}$ = 5.1 Hz, H-4), 3.51 (1H, dd, $J_{2',3'}$ = 8.1 and $J_{3',4'}$ = 10 Hz, H-3'), 3.65~3.75 (5H, m, H-6, 4', 6'), 3.76 (1H, q, $J_{1',2'}$ = 8.1 and $J_{2',NH'}$ = 7.3 Hz, H-2'), 3.93 (1H, m, H-2), 4.25 (1H, d, H-1'), 4.40~4.84 (11H, m, NH, PhCH), 4.80 (1H, d, NH'), 6.30 (1H, brs, NH), 7.21~7.39 (25H, m, Ph); $\delta_C(CDCl_3)$ 23.3, 23.5, 43.5, 47.8, 55.6, 57.3, 68.3, 68.7, 72.5, 73.5, 74.4, 74.8, 75.2, 77.2, 77.6, 78.6, 80.8, 100.7, 127.7, 127.8, 127.9, 128.1, 128.4, 128.5, 128.6, 137.8, 138.0, 138.1, 138.2, 138.5, 170.2, 170.3.

Found: C, 71.06; H, 6.91; N, 4.82%. Calcd. for $C_{51}H_{59}O_9N_3$: C, 71.39; H, 6.93; N, 4.90%.

2-Acetamido-4-*O*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-1,2,5-trideoxy-1,5-imino-D-glucitol (2). A mixture of **26** (61 mg, 0.07 mmol) and 10% Pd-C (20 mg) in acetic acid-ethanol-water (3 ml; 1:1:1; v/v/v) was stirred at rt under hydrogen atmosphere for 70 hr. The catalyst was then filtered off and washed with aq. methanol. The filtrate and washings were combined, and concentrated *in vacuo*. The residual syrup was chromatographed on silica gel with ethanol-chloroform-water (4 : 2 : 1, v/v/v) as eluent to give **2** (24 mg, 83%) as a solid, which was crystallized from methanol. Recrystallization from methanol gave **2** (14 mg)[19] as needles; mp. 259 °C (dec.); $[\alpha]_D$ -2.0° (*c* 0.21, H_2O) {lit.[4e] $[\alpha]_D$ +11° (*c* 0.70, MeOH)}; $\delta_H(D_2O)$ 1.99, 2.06 (6H, each s, Ac), 2.40 (1H, t, $J_{1a,1b}$ = $J_{1a,2}$ = 12 Hz, H-1a), 2.61 (1H, ddd, H-5), 3.05 (1H, dd, $J_{1b,2}$ = 4.9 Hz, H-1b), 3.44 (1H, dd, $J_{3,4}$ = 8.8 and $J_{4,5}$ = 9.3 Hz , H-4), 3.47 (1H, t, $J_{3',4'}$ = $J_{4',5'}$ = 9.8 Hz, H-4'), 3.52 (1H, m, H-5'), 3.54 (1H, dd, $J_{2,3}$ = 9.7 Hz, H-3), 3.57 (1H, t, $J_{2',3'}$ = $J_{3',4'}$ = 9.8 Hz, H-3'), 3.58 (1H, dd, $J_{5,6a}$ = 5.4 and $J_{6a,6b}$ = 12 Hz, H-6a), 3.73 (1H, ddd, H-2), 3.75 (1H, dd, $J_{5',6'a}$ = 5.4 and $J_{6'a,6'b}$ = 12 Hz, H-6'a), 3.77 (1H, dd, $J_{5,6b}$ = 2.4 Hz, H-6b), 3.77 (1H, dd, $J_{1',2'}$ = 8.3 Hz, H-2'), 3.91 (1H, dd, $J_{5',6'b}$ = 1.5 Hz, H-6'b), 4.57 (1H, d, H-1'); $\delta_C(D_2O)$ 22.8, 22.9 (Me), 47.3 (C-1), 52.7 (C-2), 56.4 (C-2'), 60.2 (C-5), 61.2 (C-6'), 61.3 (C-6), 70.4 (C-4'), 74.3 (C-3'), 75.1 (C-3), 76.7 (C-5'), 83.0 (C-4), 102.4 (C-1'),

175.1, 175.5 (C=O); HRFAB-MS (glycerol matrix) m/z 408.1990 $(M+H)^+$ (Calcd for $C_{16}H_{31}O_9N_3$: 408.1982).

ACKNOWLEDGMENTS

We thank Drs. J. Uzawa and H. Koshino in RIKEN for measurement of 2D-NMR spectra, and Ms. M. Yoshida and her collaborators in RIKEN for the elemental analyses. We also thank Dr. T. Nakata and Ms. K. Harata in RIKEN for mass spectral measurements. This work was supported by Grant-in-Aid for Encouragement of Young Scientists from the Ministry of Education, Science and Culture, Japan (No. 07760121 and 08760119).

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(*Received in Japan* 8 *August* 1996; *accepted* 4 *September* 1996)