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Efficient catalysis by pyridinium sulfonate in glycosylation involving an oxazoline intermediate derived from per-*O*-acetyl-*N*-acetyllactosamine and *N,N'*-diacetylchitobiose

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New and facile *N*-acetyllactosaminidation and *N,N'*-diacetylchitobiosylation with various alcohols, thiols, and sugar derivatives through the 1,2-oxazoline intermediates catalyzed by pyridinium *p*-toluenesulfonate were achieved.

Keywords: glycosylation, pyridinium *p*-toluenesulfonate, *N*-acetyllactosamine, *N,N'*-diacetylchitobiose

N-Acetyllactosamine (**1**) is one of the most abundant constituents of glycoconjugates; e.g., a basic constituent of lacto-series glycosphingolipids such as ABO and Ii blood group substances [1], and the terminal constituent of complex-type glycoproteins [2]. It has been reported that the *N*-acetyllactosamine structure in glycoconjugates is associated with biological functions such as an inhibitor for *Staphylococcus saprophiticus* [3], and also developmental and tumor-associated antigens [1, 4].

Chemically synthesized *N*-acetyllactosamine-containing oligosaccharides and glycoconjugates are expected to be used for the investigation of their biological functions. Such a background prompted us to reinvestigate *N*-acetyllactosaminidation. The result was then applied to glycosylation using *N,N'*-diacetylchitobiose (**2**), which is also an important constituent of glycoproteins.

Results and discussion

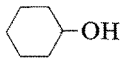
Compound **1** itself has been prepared in several ways; e.g., synthesis from each monosaccharide component [5], the conversion of per-*O*-acetyl-D-lactal to the 2-azido-2-deoxy-D-lactose derivative [6] or the modification of 3-*O*-*β*-D-galactosyl-D-arabinose by the cyanoamination method [7]. More recently, however, Usui and others reported an enzymatic method to prepare **1** on a practical scale [8], which was used for our experiment.

For the *β*-*N*-acetyllactosaminidation, per-*O*-acetyl-2-deoxy-2-*N*-phthaloyl-aminolactose as the halide [9, 10], trichloroacetimidate [11] or 1-S-methyl-glycoside [12] have been used as efficient glycosyl donors; however, each method requires long steps for the derivatization. On the other hand, *β*-hexosaminidation by the use of an oxazoline intermediate has been developed by Matta and other groups [13–18], in which sulfonic acids, Lewis acids, and more recently TMSOTf were used as catalysts. We now report here the milder and more efficient *β*-lactosaminidation using the 1,2-oxazoline derivative (**3**) [19] in the presence of a neutral catalyst, pyridinium *p*-toluenesulfonate(PPTS) [20]. The reaction was then compared with those obtained by using several sulfonic acids (Table 1).

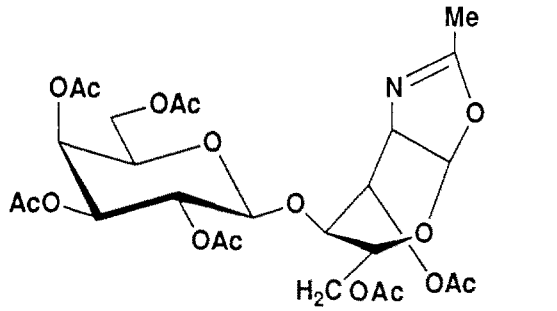
Among the results thus obtained, the lactosaminidation of allyl alcohol in 1,2-dichloroethane at reflux temperature demonstrated that PPTS gave the highest yield of the *β*-glycoside **5** (95%) in a shorter period than the sulfonic acid catalysts. Lactosaminidation of cyclohexanol under the same condition also gave the *β*-glycoside **6** in 86% yield. The effect of the molar ratio of cyclohexanol to **3** was examined for allyl alcohol and cyclohexanol, showing that 1.2 eq. molar acceptor alcohol was sufficient enough to give good yield.

These conditions were applied to the glycosylation for two acceptor sugars **10** and **11**, taking 4 and 3 hr to give the

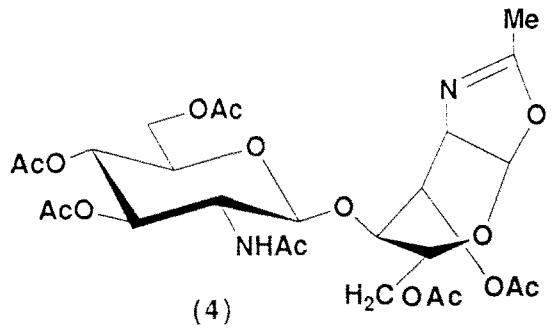
Table 1. Results of *N*-acetyllactosaminidation.

Acceptor (*RH*)	*Acceptor/ Donor* (*eq*)	*Catalyst*	*Solvent*[a] & *Temp.*	*Time*	*Yield* (%)	*Glycosides* [20]
AllOH	10	TsOH		8 h	50	
	10	CF_3SO_3H		5 h	65	
	10	CSA	A	20 min	70	(**5**)
	10	PPTS		20 min	95	
	1.2	PPTS		2 h	70	
	10	PPTS	A	3 h	86	(**6**)
	1.2	PPTS		2 h	68	
EtSH	10	TsOH		10 h	42	
	10	CF_3SO_3H	B	8 h	62	(**9**)
	10	CSA		10 h	31	
	10	PPTS		14 h	16	

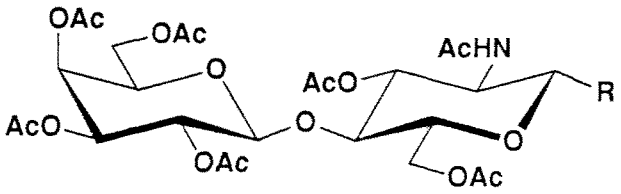
[a] A: $(CH_2Cl)_2$, reflux B: $CHCl_3$, reflux. CSA: 10-camphorsulfonic acid.



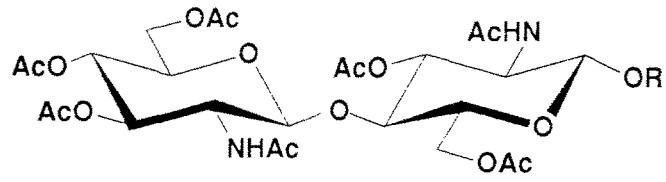
(3)



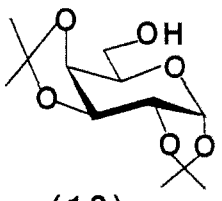
(4)



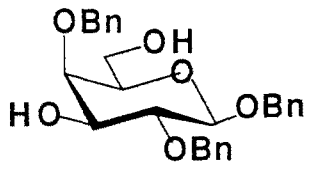
Glycosides (5) ~ (9)



Glycosides (12) ~ (15)



(10)



(11)

trisaccharide (**7** and **8**) with newly formed β(1–6) glycosidic linkage in 60 and 63% yields, respectively; ^{1}NMR data: δ 4.58(1H, d, H-1′, $J_{1,2}$ = 8.1 Hz) for **7**, and δ 4.48 (1H, d, H-1′, $J_{1,2}$ = 7.8 Hz) for **8**. The former result indicates that this method is feasible enough for an acceptor sugar bearing an acid labile *O*-isopropylidene group. The second one demonstrates that the glycosylation takes place preferentially at the primary hydroxy group.

Similarly, reaction of **3** with ethanethiol was carried out using three kinds of sulfonic acids and PPTS as catalysts (Table 1). The highest yield (62%) of ethyl *S*-thiolactosaminide **9** was obtained using triflic acid rather than PPTS. *S*-thio-glycosylation instead of PPTS required a longer time and gave unidentified products other than **9**.

The 'oxazoline-PPTS' method thus established was applied to the 1,2-oxazoline (**4**), which was derived from chitobiose hydrochloride through complete acetylation, followed by oxazoline formation with TMSOTf in 77% overall yield. Glycosylations of benzyl alcohol, allyl alcohol, methanol and cyclohexanol with **4** were carried out in the same way as with **3**, giving good yields of the corresponding β-alkyl *N*,*N*′-diacetylchitobiosides as shown in Table 2.

Table 2. Results of *N,N'-diacetylchitobiosylation.*

Acceptor (ROH)	*Acceptor/ Donor (eq)*	*Time*	*Glycosides*	*Yield (%)*
BnOH	10	1 h	(**12**)	87
	1.2	3 h		60
AllOH	10	1 h	(**13**)	88
MeOH	10	1 h	(**14**)	86
 –OH	1.2	3 h	(**15**)	59

In conclusion, the present method is useful for the preparation of β-alkyl *N*-acetyllactosaminides and *N,N'*-diacetylchitobiosides. In addition, glycosides containing trisaccharides with β(1–6) glycosidic linkage can be synthesized by this method.

Experimental

General methods

All melting points are uncorrected. The solutions were evaporated under reduced pressure at a bath temperature not exceeding 40 °C. The optical rotations were measured in a 0.5 dm tube with a JASCO DIP-140 polarimeter in chloroform. ^{1}H NMR spectra were recorded in C^2HCl_3 with a JEOL FX-200 spectrometer, with tetramethylsilane used as an internal standard. IR spectra were recorded with Hitachi 270-30 spectrometer. The chemical shifts, coupling constants, and IR frequencies were recorded in δ, Hz, and cm^{-1} units, respectively.

Allyl O-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-(1-4)-2-acetamido-3,6-di-O-acetyl-2-deoxy-β-D-glucopyranoside (**5**)

The solution of *O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-(1-4)-2-methyl-(3,6-di-*O*-acetyl-1,2 -dideoxy-α-D-glucopyrano)-[2,1-*d*]-2-oxazoline (**3**) (100 mg, 0.16 mmol), allyl alcohol (94 mg, 10 equiv.), and pyridinium *p*-toluenesulfonate (PPTS, 4.0 mg) in 1,2-dichloroethane (4.0 mL) was refluxed for 20 min under argon. The reaction mixture was neutralized with pyridine at room temperature and evaporated to give a syrup which was purified on a column of silica gel (Wakogel C-300, hexane-ethyl acetate; 2:3 by vol). Yield of **5** was 104 mg (95%).

In a similar manner as above, the reaction mixture of **3** (160 mg, 0.25 mmol), allyl alcohol (146 mg), and (*R, S*)-10-camphorsulfonic acid (5.0 mg) gave **5** (119 mg, 70%).

Mp 150–151° C (ethanol-hexane); $[\alpha]_D^{26}$-24.2° (c 1.0); IR (KBr disk): γ_{max} 1746, 1668, 1551, 1374, 1230, 1047, 756, and 606; ^{1}H NMR: δ = 5.96–5.74 (1H, m, allyl –CH=C), 5.84 (1H, d, $J_{NH,2}$ = 9.5, NH), 5.36 (1H, d, $J_{4',3'}$ = 2.4, $J_{4',5'}$ = 0, H-4'), 5.17 (1H, dd, $J_{3,4}$ = 8.3, $J_{3,2}$ = 10.0, H-3), 5.08 (1H, dd, $J_{2',1'}$ = 7.8, $J_{2',3'}$ = 10.3, H-2'), 5.00 (1H, dd, H-3'), 5.31–4.94 (2H, m, allyl=CH_2), 4.50 (1H, d, H-1'), 4.50 (1H, d, $J_{1,2}$ = 7.3, H-1), 4.35–4.00 (2H, m, allyl –CH_2–), 4.17–4.00 (5H, m, H-2, H-6a, H-6b, H-6'a, and H-6'b), 3.90 (1H, dd, $J_{5',6'a}$ = 6.6, $J_{5',6'b}$ = 6.6, H-5'), 3.80 (1H, dd, $J_{4,5}$ = 8.3, H-4), 3.63 (1H, m, H-5), 2.15, 2.12, 2.08, 2.06, and 1.97 (3H × 7, each s, NHAc and OAc × 6). Analytical data calculated for $C_{29}H_{42}O_{17}N$: C, 51.48; H, 6.26; N, 2.07%. Found: C, 51.36; H, 5.98; N, 2.08%.

Cyclohexyl O-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-(1-4)-2- acetamido-3,6-di-O-acetyl-2-deoxy-β-D-glucopyranoside (**6**)

In a similar manner as above, the reaction mixture of **3** (70 mg, 0.11 mmol), cyclohexanol (113 mg, 10 equiv.), and PPTS (4.0 mg) in 1,2-dichloroethane (3.0 mL) was refluxed for 3 h under argon. A similar work up of the reaction mixture and a purification on a column of silica gel (Wakogel C-300, hexane-ethyl acetate 1:3 by vol), gave **6** (70 mg, 86%).

Mp 196–198 °C (ethanol-hexane); $[\alpha]_D^{25}$-17.3° (c 1.2); IR (KBr disk): γ_{max} 3388, 2932, 2860, 1758, 1671, 1548, 1437, 1374, 1224, 1170, 1062, 957, 912, 603, and 492; ^{1}H NMR: δ = 5.65 (1H, d, $J_{NH,2}$ = 9.3, N-H), 5.36 (1H, d, $J_{4',3'}$ = 3.2, $J_{4',5'}$ = 0, H-4'), 5.13 (1H, dd, $J_{3,4}$ = 8.6, $J_{3,2}$ = 9.3, H-3), 5.12 (1H, dd, $J_{2',3'}$ = 10.3, $J_{2',1'}$ = 7.8, H-2'), 4.97 (1H, dd, H-3'), 4.58 (1H, d, $J_{1,2}$ = 7.8, H-1), 4.50 (1H, d, H-1'), 4.47 (1H, dd, $J_{6a,6b}$ = 9.0, $J_{6a,5}$ = 2.7, H-6a), 4.17–4.10 (3H, m, H-6b, H-6'a, and H-6'b), 4.04–3.86 (2H, m, H-2 and H-5), 3.77 (1H, dd, $J_{4,5}$ = 8.5, $J_{3,4}$ = 8.5, H-4), 3.65–3.57 (1H, m, H-5), 2.15, 2.11, 2.07, 2.06, 1.97, 1.95 (3H × 7, each s, NHAc and OAc × 6), 1.95–1.13 (11H, m, cyclohexane ring proton).

Analytical data calculated for $C_{32}H_{47}O_{17}N$: C, 53.25; H, 6.56; N, 1.94%. Found: C, 53.09; H, 6.68; N, 1.93%.

Ethyl O-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-(1-4)-2- acetamido-3,6-di-O-acetyl-2-deoxy-1-thio-β-D-glucopyranoside (**9**)

The reaction mixture of **3** (57 mg, 0.092 mmol), ethanethiol (57 mg), and trifluoromethanesulfonic acid (2.4 mL) in chloroform (2.0 mL) was refluxed for 8 h under argon. The reaction mixture was neutralized with pyridine at room temperature and evaporated to give a syrup which was purified on a column of silica gel (Wakogel C-300, hexane-ethyl acetate, 1:3 by vol). Crystallization from ethanol-hexane gave **9** (39 mg, 62%).

Mp 132–133 °C; $[\alpha]_D^{26}$-33.0° (c 0.9); IR (KBr disk): γ_{max} 2980, 1758, 1683, 1539, 1434, 1374, 1233, 1050, 915, and 606; ^{1}H NMR: δ = 5.93 (1H, d, $J_{NH,2}$ = 9.5, N-H), 5.36 (1H, d, $J_{4',3'}$ = 3.2, $J_{4',5'}$ = 0, H-4'), 5.10 (1H, dd, $J_{2',1'}$ = 7.8, $J_{2',3'}$ = 7.6, H-2'), 5.07 (1H, dd, $J_{3,4}$ = 9.3, $J_{3,2}$ = 7.8, H-3), 4.97 (1H, dd, H-3'), 4.51 (1H, d, H-1'), 4.55–4.44 (1H, m, H-6a), 4.46 (1H, d, $J_{1,2}$ = 11.0, H-1), 4.23–4.04 (4H, m, H-2, H-6b, H-6'a, and H-6'b), 3.89 (1H, dd, $J_{5',6'a}$ = 6.6, $J_{5',6'b}$ = 6.6, H-5'), 3.80 (1H, dd, $J_{4,5}$ = 9.5, H-4), 3.61 (1H, m, H-5), 2.69 (2H, dq, CH_2 of Et), 2.15, 2.11, 2.08, 2.06, 2.05,

1.97, and 1.96 (3H × 7, each s, NHAc and OAc × 6), 1.25 (3H, t, CH_3 of Et).

Analytical data calculated for $C_{28}H_{41}O_{16}NS$: C, 49.48; H, 6.08; N, 2.06%. Found: C, 49.39; H, 6.08; N, 2.04%.

O-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-(1-4)-2-acetamido-3,6-di-O-acetyl-2-deoxy-β-D-glucopyranosyl-(1-6)-1,2;3,4-di-O-isopropylidene-α-D-galactopyranose (**7**)

The reaction mixture of **3** (90 mg, 0.15 mmol), 1,2; 3,4-di-*O*-isopropylidene-α-D-galactopyranose (**10**) (45 mg, 1.2 equiv.), the PPTS (6.0 mg) in 1,2-dichloroethane (4.0 ml) was refluxed for 2 h under argon. The reaction mixture was neutralized with pyridine at room temperature and evaporated to give a syrup which was purified on a column of silica gel (Wakogel C-300, hexane-ethyl acetate 1:2 by vol). Crystallization from ethanol-hexane gave **7** (76 mg, 60%).

Mp 117–119 °C; $[\alpha]_D^{25}$-40.1° (c 1.0); IR (KBr disk): γ_{max} 3376, 2986, 1746, 1674, 1548, 1434, 1374, 1230, 1170, 1074, 960, 900, 756, 666, 603, and 510; ^{1}H NMR: δ = 5.64 (1H, $J_{N'H,2'}$ = 9.3, N'-H), 5.53 (1H, d, $J_{1,2}$ = 4.9, H-1), 5.35 (1H, d, $J_{4'',3''}$ = 2.4, $J_{4'',5''}$ = 0, H-4''), 5.12 (1H, dd, $J_{2'',3''}$ = 10.5, $J_{2'',1''}$ = 7.8, H-2''), 5.03 (1H, dd, H-3'), 4.96 (1H, dd, $J_{3'',2''}$ = 10.3, H-3''), 4.58 (1H, d, $J_{1',2'}$ = 8.1, H-1') 4.58 (1H, dd, $J_{3,2}$ = 3.2, $J_{3,4}$ = 7.8, H-3), 4.47 (1H, d, $J_{1'',2''}$ = 7.6, H-1''), 4.52–4.45 (1H, m, H-6'a), 4.31 (1H, dd, H-2), 4.16–4.01 (4H, m, H-2', H-6'b, H-6''a, and H-6''b), 3.95–3.63 (6H, m, H-4, H-5, H-6a, H-6b), 3.61–3.58 (1H, m, H-5'), 2.15, 2.12, 2.07, 2.06, 2.05, and 1.97 (3H × 7, each s, NHAc and OAc × 6, 1.50, 1.44, 1.32 (3H × 4, each s, CH_3 × 4).

Benzyl O-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-(1-4)-2-acetamido-3,6-di-O-acetyl-2-deoxy-β-D-glucopyranosyl)-(1-6)-2,4-di-O-benzyl-β-D-galactopyranoside (**8**)

The solution of **3** (54 mg, 0.087 mmol), benzyl 2,4-di-*O*-benzyl-β-D-galactopyranoside (**11**) (21 mg, 0.47 equiv.), and PPTS (4.0 mg) in 1,2-dichloroethane (2.0 ml) was refluxed for 3 h under argon. The reaction mixture was neutralized with pyridine at room temperature and evaporated to give a syrup which was purified on a column of silica gel (Wakogel C-300, hexane-ethyl acetate, 1:2 by vol). Yield of **8** was 72% (36 mg).

In a similar manner as above, the solution of **3** (35 mg, 0.056 mmol), **11** (31 mg, 1.2 equiv.), and PPTS (3.0 mg) in 1,2-dichloroethane (2.0 ml) gave **8** (38 mg, 61%).

IR (KBr disk): γ_{max} 3382, 2926, 1749, 1674, 1548, 1374, 1230, 1062, 957, 912, 753, 699, and 603; ^{1}H NMR: δ = 7.30–7.26 (5H × 3, m, Ph × 3), 5.49 (1H, d, $J_{N'H,2'}$ = 9.3, N'-H), 5.36 (1H, d, $J_{4'',3''}$ = 2.4, $J_{4'',5''}$ = 0, H-4''), 5.12 (1H, dd, $J_{2'',1''}$ = 7.6, $J_{2'',3''}$ = 10.3, H-2''), 5.02 (1H, dd, $J_{3',2'}$ = 10.0, $J_{3',4'}$ = 8.1, H-3'), 4.96–4.61 (2H × 3, each ABq, $-CH_2-$ of benzyl), 4.50–4.42 (4H, m, H-1, H-1', H-1'', and H-6''a), 4.12–4.07 (4H, m, H-2', H-6'a, H-6'b, and H-6''b), 3.90–3.61 (9H, m, H-2, H-3, H-4, H-5, H-6a, H-6b, H-4', H-5', and H-5''), 2.26 (1H, bs, OH), 2.15, 2.07, 2.06, 2.05, 2.03, 1.97, and 1.89 (3H × 7, each s, NHAc and OAc × 6).

3-O-Acetyl derivative of **11**: IR (NaCl neat): γ_{max} 1749, 1671, 1548, 1371, 1230, 1062, 912, 753, 702, and 603; ^{1}H NMR: δ = 7.36–7.26 (5H × 3, m, Ph × 3), 5.57 (1H, d, $J_{N'H,2'}$ = 8.3, N'-H), 5.36 (1H, d, $J_{4'',3''}$ = 3.7, $J_{4'',5''}$ = 0, H-4''), 5.17–4.44 (2H × 3, each ABq, $-CH_2-$ of benzyl), 4.98 (1H, dd, $J_{2'',1''}$ = 7.3, $J_{2'',3''}$ = 8.9, H-2''), 4.98–4.82 (2H, m, H-3' and H-3), 4.85 (1H, dd, H-3''), 4.69–4.44 (4H, m, H-1, H-1', H-1'', and H-6'a), 4.14–3.90 (4H, m, H-2', H-6'b, H-6''a, and H-6''b), 3.87–3.48 (8H, m, H-2, H-4, H-5, H-6a, H-6b, H-4', H-5', and H-5''), 2.15, 2.07, 2.06, 2.05, 1.97, 1.90, and 1.88 (3H × 8, each s, NHAc and OAc × 7).

Benzyl O-(2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-(1-4)-2-acetamido-3,6-di-O-acetyl-2-deoxy-β-D-glucopyranoside (**12**)

The solution of *O*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1-4)-2-methyl-(3,6-di-*O*-acetyl-1,2-dideoxy-α-D-glucopyrano)-[2,1-d]-2-oxazoline (**4**) (215 mg, 0.35 mmol), benzyl alcohol (377 mg, 10 equiv.), and PPTS (6.0 mg) in 1,2-dichloroethane (8.0 ml) was refluxed for 1 h under argon. The reaction mixture was neutralized with pyridine at room temperature and evaporated to give a syrup which was purified on a column of silica gel (Wakogel C-300, chloroform-methanol 50:1 by vol). Crystallization from ethanol gave **12** (221 mg, 87%).

Mp 280–282 °C; $[\alpha]_D^{26}$-52.0° (c 1.0); IR (KBr disk): γ_{max} 3310, 1746, 1665, 1539, 1377, 1233, 1119, 1050, 921, 738, 699, 600, and 564; ^{1}H NMR: δ = 7.32–7.27 (5H, m, Ph), 6.19 (1H, d, $J_{NH,2}$ = 8.5, N-H), 5.73 (1H, d, $J_{N'H,2'}$ = 9.3, N'-H), 5.19 (1H, dd, $J_{3',2'}$ = 10.3, $J_{3',4'}$ = 10.3, H-3'), 5.05 (1H, dd, $J_{3,2}$ = 10.0, $J_{3,4}$ = 10.0, H-3), 5.04 (1H, dd, $J_{4',5'}$ = 10.3, H-4'), 4.86–4.57 (2H, ABq, CH_2 of benzyl), 4.56 (1H, d, $J_{1,2}$ = 8.5, H-1), 4.46 (1H, d, $J_{1',2'}$ = 7.8, H-1'), 4.43–4.32 (3H, m, H-6'a, H-6'b, and H-6b), 4.16–3.90 (3H, m, H-2, H-2', and H-6a), 3.75 (1H, dd, H-4), 3.70–3.64 (2H, m, H-5 and H-5'), 2.16, 2.08, 2.00, 1.96, and 1.93 (3H × 7, each s, NHAc × 2 and OAc × 5).

Analytical data calculated for $C_{33}H_{44}O_{16}N_2$: C, 54.70; H, 6.12; N, 3.87%. Found: C, 54.58; H, 6.09; N, 3.79%.

Allyl O-(2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-(1-4)-2-acetamido-3,6-di-O-acetyl-2-deoxy-β-D-glucopyranoside (**13**)

The solution of **4** (58 mg, 0.094 mmol), allyl alcohol (52 mg, 10 equiv.), and PPTS 3.0 mg) in 1,2-dichloroethane (3.0 ml) was refluxed for 1 h under argon. The reaction mixture was neutralized with pyridine at room temperature and evaporated to give a syrup which was purified on a column of silica gel (Wakogel C-300, Chloroform-methanol 50:1 by vol). Crystallization from ethanol gave **13** (56 mg, 88%).

Mp 257–259 °C; $[\alpha]_D^{26}$-38° (c 0.7) {lit [20]: mp 254 °C; $[\alpha]_D^{22}$-42° (c 0.4, $CHCl_3$)}; IR (KBr disk): γ_{max} 3310, 2938, 1746, 1665, 1548, 1377, 1233, 1047, and 600; ^{1}H NMR data are identical with that reported [21].

Methyl O-(2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-(1-4)-2-acetamido,3,6-di-O-acetyl-2-deoxy-β-D-glucopyranoside (**14**)

The solution of **4** (60 mg, 0.097 mmol), methanol (32 mg, 10 equiv.), and PPTS (3.0 mg) in 1,2-dichloroethane (3.0 ml) was refluxed for 1 h under argon. The reaction mixture was neutralized with pyridine at room temperature and evaporated to give a syrup which was purified on a column of silica gel (Wakogel C-300, chloroform-methanol 50:1 by vol). Crystallized from ethanol gave **14** (54 mg, 86%).

Mp (284–286 °C $[\alpha]_D^{26}$-42° (c 0.7) {lit. [21]: mp 284 °C; $[\alpha]_D^{22}$-44° (c 0.55, $CHCl_3$)}; IR (KBr disk): γ_{max} 3310, 2944, 1743, 1659, 1551, 1434, 1380, 1233, 1167, 1050, 909, 705, and 603; 1H NMR data are identical with that reported [21].

Cyclohexyl O-(2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-(1-4)-2-acetamido-3,6-di-O-acetyl-2-deoxy-β-D-glucopyranoside (**15**)

The solution of **4** (55 mg, 0.09 mmol), cyclohexanol (11 mg, 1.2 equiv.), and PPTS (3.0 mg) in 1,2-dichloroethane (4.0 ml) was refluxed for 3 h under argon. The reaction mixture was neutralized with pyridine at room temperature and evaporated to give a syrup which was purified on a column of silica gel (Wakogel C-300, chloroform-methanol 50:1 by vol). Crystallization from ethanol-hexane gave **15** (38 mg, 59%).

Mp 174–175 °C; $[\alpha]_D^{24}$-1.3° (c 0.3); IR (KBr disk): γ_{max} 2932, 1746, 1665, 1551, 1374, 1230, 1047, and 603; ^{1}H NMR: δ = 6.41 (1H, d, $J_{NH,2}$ = 8.8, N-H), 6.02 (1H, d, $J_{N'H,2'}$ = 9.0, N'-H), 5.26 (1H, dd, $J_{3,2}$ = 9.5, $J_{3,4}$ = 9.5, H-3), 5.10 (1H, dd, $J_{3',2'}$ = 9.3, $J_{3',4'}$ = 9.3, H-3'), 5.04 (1H, dd, $J_{4',5'}$ = 9.3, H-4'), 4.70 (1H, d, $J_{1,2}$ = 8.1, H-1), 4.68 (1H, d, $J_{1',2'}$ = 8.1, H-1'), 4.38 (1H, dd, $J_{6b,5}$ = 3.8, $J_{6b,6a}$ = 12.5, H-6b), 4.41–4.13 (2H, m, H-2 and H-6'b), 4.22 (1H, dd, $J_{6a,5}$ = 4.0, H-6a), 4.01 (1H, dd, $J_{6'a,5'}$ = 2.4, $J_{6'a,6'b}$ = 12.0, H-6'a), 3.88–3.73 (3H, m, H-5, H-5', and H-4), 2.13, 2.08, 2.06, 2.00, 1.95, and 1.94 (3H × 7, each s, NHAc × 2 and OAc × 5), 1.85–1.23 (11H, m, cyclohexane ring proton).

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