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Regio- and chemoselective manipulation under mild conditions on glucosamine derivatives for oligosaccharide synthesis and its application toward *N*-acetyl-D-lactosamine and Lewis X trisaccharide

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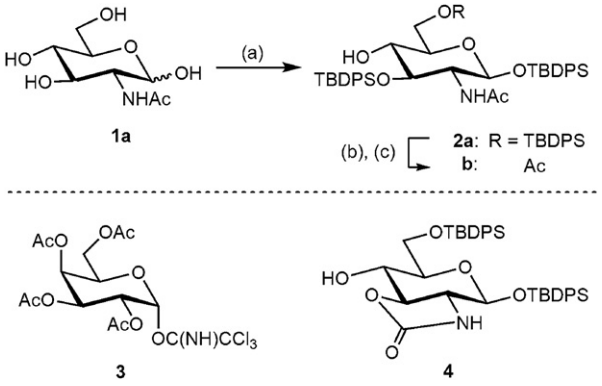
ABSTRACT

Special emphasis on regio- and chemoselective manipulation on a new glucosamine scaffold was laid, toward the short-step and efficient synthetic routes for oligosaccharides. First, the blocking of two hydroxyl groups at C-1 and C-6 positions of *N*-protected glucosamine at once by silylation followed by an oxazolidinone formation between C-3 hydroxyl and C-2 amino groups were established, to lead an expeditious way for a glycosyl acceptor for lactosamine synthesis. Second, without any effect on acetyl protective groups in the same molecule, the ring-opening of oxazolidinone and hydrolysis of resulting carbonate under mild conditions allowed the C-3 hydroxyl group to be free, which is indispensable for further extension to oligosaccharides, such as a LeX trisaccharide.

1. Introduction

Toward chemical syntheses of rare sugars and oligosaccharides, it is important to provide versatile key intermediates with specific free hydroxyl groups, on which introduction of other functional groups, oxidation, stereochemical inversion, and glycosyl bond formation are carried out. The protection and deprotection steps should be as few as possible for the synthesis of such intermediates to develop expeditious routes. Some years ago, we found an unexpected transformation, which would meet such approach for a new glucosamine derivative: a simultaneous TBDPS group protection of three hydroxyl groups on C-1, C-3, and C-6 positions of *N*-acetyl-D-glucosamine **1a**.[1] A tri-TBDPS ether **2a** was obtained in 70% yield, where remarkable regioselectivity was observed for the introduction of a silyl group at C-3 position leaving a free hydroxyl group at C-4. This was effectively derived to *N*-acetyl-D-galactosamine through a stereochemical inversion at the liberated C-4 position.

The above tri-TBDPS ether **2a** seemed attractive also as a lactosamine precursor by way of glycosylation, however, the reactivity of the free hydroxyl group turned out to be very low as an acceptor. For example, we hardly observed any glycosylated product between various galactosyl or glucosyl donors involving a trichloroactimidate **3**, under protic or Lewis acidic activating conditions. The observation was contrasting to the fact that C-3, C-6 dibenzyloxy glucosamine derivatives have been good glycosyl acceptors.[2,3] Then a less hindered glycosyl acceptor candidate **2b** was prepared, by substituting C-6 TBDPS group with acetyl group, through a regioselective deprotection[4] and the subsequent acetylation.[5] The attempted glycosylation, however, resulted in almost no reaction (Scheme 1). We realized that the TBDPS group at C-3 position should be replaced with sterically less hindered, but not too electron-withdrawing group. In this paper, we designed a sugar oxazolidinone **4** as a new acceptor, and the elaborated conditions on the preparation and its subsequent manipulation are described in detail.



Scheme 1. (a) TBDPSCl, imidazole, DMF, 70%; (b) AcCl, MeOH; (c) AcCl, collidine, 29%.

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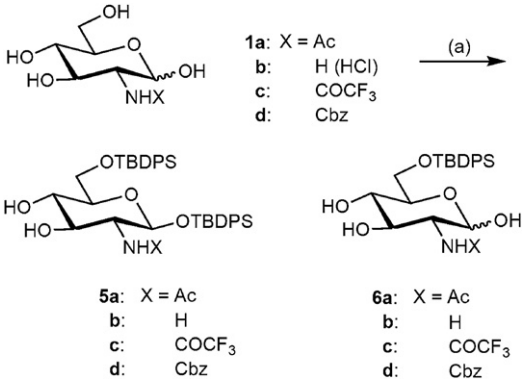
2. Results and discussion

2.1. Regioselective introduction of TBDPS ethers on C-1 and C-6 hydroxyl groups

The protection of hydroxyl groups located at C-6 and C-1 positions in one-shot with liberating C-3 and C-4 hydroxyl groups is the first task. In the course of our previous study on the silylation on GlcNAc **1a**,[1] at the very initial stage of the reaction, the desired di-TBDPS ether **5a** was observed by TLC analysis. The di-TBDPS ether **5a** was, however, quickly transformed into tri-TBDPS ether **2a** as the major product. This observation suggested that the electron-withdrawing nature of nitrogen function in C-2 position was expected to lower the nucleophilicity of C-3 hydroxyl group. Based on this consideration, our first attempt was the use of glucosamine hydrochloride (**1b**) as the substrate. Due to the scarce solubility of **1b** in the reaction mixture, the result was miserable, only to give complex mixture, and the silylated products **5b** as well as **6b** were only observed in trace amounts. Instead, the introduction of strongly withdrawing substituent, trifluoroacetyl group[6] on nitrogen atom (**1c**) turned the situation better, owing to the increase of solubility of the substrate in DMF. The major product was, however, monoprotected form **6c** (75%), only whose C-6 hydroxyl group was silylated, as the nucleophilicity of anomeric hydroxyl group turned very low.

Then we considered the enhancement of the concentration of in situ active silylating intermediate, TBDPS-imidazolinium chloride,[7] by increasing the equivalence of imidazole to TBDPSCl from 1.1 to 2.2. The desired C-1, C-6 silylated product **5c** became available in an excellent yield (89%, Scheme 2). We tried another substrate **1d** for silylation, whose amino group was protected by a less electron-withdrawing but sterically demanding Cbz group. The reaction proceeded in a similar way, however, the isolated yield (71%) of **6d** was substantially lower. In both cases, the orientation of anomeric TBDPS-oxy group exclusively settled in β, as had been observed for *N*-acetyl derivatives **2a**.[1] Similar observation has been well known for anomeric TMS ether formation in galactose.

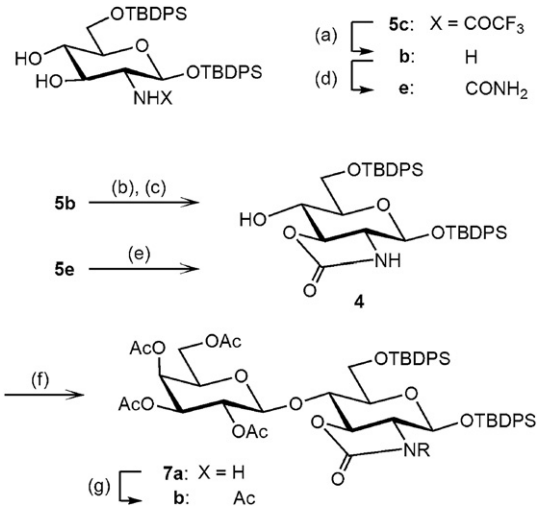


Scheme 2. (a) TBDPSCl, imidazole, DMF.

2.2. Elaboration to the oxazolidinone glycosyl acceptor

From recent literatures,[8,9] the introduction of 2,3-oxazolidinone functionality on 2-deoxyamino sugars do not interfere the glycosylation at C-4 hydroxyl group. In our case, labile *N*-trifluoroacetyl group in **5c** worked advantageously toward the oxazolidinone ring formation. Indeed, the protective group was easily removed to give **5b** in quantitative yield under mildly basic conditions, while two TBDPS protective groups were intact. Oxazolidinone formation worked well by treatment with *p*-nitrophenyl chloroformate to give **4** in 85% yield. On this occasion, the concomitantly formed *p*-nitrophenol, the leaving group, interferes the purification of **4**, due to the very similar chromatographic behavior of both products. Then zinc powder was added immediately after acidification of the reaction mixture to reduce *p*-nitrophenol into aminophenol, which enabled easier removal of the obstinate by-product. Alternatively, carbamylation–nitrosocyclization[10] by way of a urea **5e** provided the same oxazolidinone (**4**, 51%), and in this case, the inexpensiveness of reagents is advantageous. The oxazolidinone **4** was a crystalline material by virtue of the no contamination with the corresponding α-anomer.

The glycosylation reaction of oxazolidinone **4** with **3**[11] worked very well to give **7a** (87%) in exclusive formation of β-linkage between two sugars. Toward the introduction of the indispensable *N*-acyl moiety often observed in oligosaccharides, one-pot two-step transformation was also successful. Diisopropylethylamine followed by acetyl chloride were added to the reaction mixture, when the completion of the glycosylation was confirmed on TLC analysis. Acetylated oxazolidinone **7b** was obtained also as crystalline material, in 80% yield (Scheme 3).



Scheme 3. (a) LiOH, H_2O, THF, quant.; (b) *p*-$O_2N(C_6H_4)OCOCl$, $NaHCO_3$, MeCN, H_2O; (c) Zn, AcOH, 85%; (d) KCNO, H_2O; (e) $NaNO_2$, AcOH, H_2O, 51%; (f) **3**, TMSOTf, MS 4 Å, CH_2Cl_2; (g) AcCl, *i*-Pr_2NEt, CH_2Cl_2, 80%.

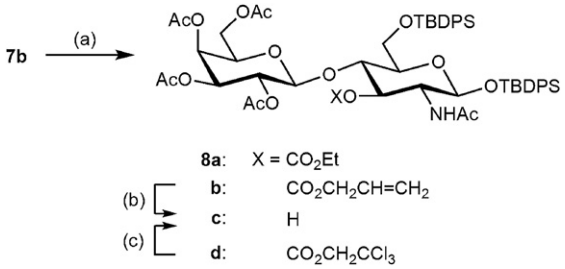
2.3. The chemoselective deprotection to give liberated C-3 hydroxyl group

Toward the further glycosylated oligosaccharides based on *N*-acetyl-D-lactosamine, the most important task is the liberation of C-3 hydroxyl group of GlcNAc by the hydrolysis of oxazolidinone ring. Kerns[12,13] and Crich[9,14] independently reported basic conditions such as Cs_2CO_3 in alcohol,[12,13] LiCl/LiOH,[13] and $Ba(OH)_2$.[9,14] In our case, the question is that under such strongly basic conditions, the hydrolysis of oxazolidinone heterocycle is possible or not, without any effect on many *O*-acetyl groups located in non-reducing galactose moiety. Crich emphasized the chelation of metal cation between *N*-acetyl carbonyl oxygen and β-oriented anomeric oxygen to enhance the electrophilicity at oxazolidinone carbonyl carbon.[9] We had also experienced strongly electron-donating property of the anomeric β-TBDPS oxygen atom in amino sugar derivative.[1] Our first attempt was then, the treatment of **7b** with a mixture of LiCl and LiOH[13] in aqueous THF solution by choosing small and strongly Lewis acidic lithium cation, however, gave no desired hydrolyzed product. The replacement of H_2O with H_2O_2 bearing an enhanced nucleophilicity,[13] disappointingly, gave similar result.

A very careful TLC analysis of the reaction was a clue to this obstacle. When ethanol was added as a co-solvent for making the reaction mixture to a homogeneous solution at the stage of the initial reaction operations, a remarkable spot other than the starting material appeared on TLC. The isolation and structural elucidation revealed that the new product was an ethyl carbonate at C-3 position (**8a**) in 53% yield. This result was quite strange, as the contrasting 'carbamate formation' had been reported[12] by treatment of some sugar oxazolidinones by Cs_2CO_3/ROH, but in our hands, a clearly observed downfield-shifted H-3 (δ 4.62) signal supported well the structure of **8a**. In previously reported Crich's experiments starting from acetylated oxazolidiones, no such carbonates had been observed, but those reactions were performed by applying $Ba(OH)_2$ in aqueous media at high temperature.[9,14]

We tried to put our experimental result into consideration. The ring-opening carbonate formation became very slow under the conditions that solid LiOH was added in a simple mixture of THF and ethanol. Recently Niwayama have reported a controlled action of alkali metal hydroxides in THF.[15] Our observation suggests the coordination of both of water and THF molecules on Lewis acidic metal cation, to certain extent, is necessary.

Then, alcohols for ring-opening reactions were screened, whose corresponding carbonates would selectively be removed under very mild conditions. In this point of view, the first candidate as the nucleophile was allyl alcohol. The reaction conditions were elaborated, eventually to provide allyl carbonate **8b** in 86% yield. The selective palladium-catalyzed deprotection of allyl carbonate[16] in **8b** afforded the *N*-acetyl-D-lactosamine derivative **8c** in 87% yield (Scheme 4). The reactivity of oxazolidinone carbonyl group toward nucleophilic alcohols was indeed very high. Even an electron-withdrawing and sterically hindered trichloroethanol[12] worked very well to give a trichloroethyl carbonate (Troc) **8d** in a quantitative yield. This carbonate **8d** could reductively cleaved by the addition of zinc powder with acetic acid to afford **8c** in two steps and 90% yield. The ring-opening reaction worked well by applying as low equivalent as 2.0 for trichloroethanol, and in this case, successive two operations, ring-opening and hydrolysis of the resulting carbonate were performed in one-pot. The attempt for the use of another electron-withdrawing nucleophile, trifluoroethanol was, however, unsuccessful, as the intermediates were too labile and the reaction turned to complex mixture. A bulky, electron-donating, *tert*-butyl alcohol did not work as the nucleophile.



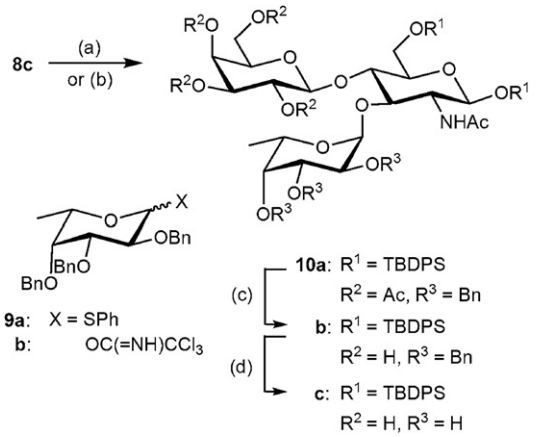
Scheme 4. (a) LiCl, LiOH, ROH, H_2O, THF; (b) $(Ph_3P)_4Pd$, morpholine, THF, 87%; (c); Zn, AcOH, quant.

2.4. Application of the disaccharide as the further glycosyl acceptor

Next, further glycosylation of above-mentioned disaccharide **8c** was examined. The target molecule is Lewis X trisaccharide,[17–28] and the fucosylation of **8c** would open a new route to provide derivatives with different protective groups on individual sugar components. The fucosylation was firstly performed with phenylthio fucoside **9a**.[29] A mixture of **9a** and **8c** was treated with *N*-iodosuccinimide (NIS, 3 equiv, based on **8c**) and catalytic amount of trifluoromethanesulfonic acid (TfOH, 0.1 equiv) in CH_2Cl_2 at 0 °C to room temperature to give a LeX trisaccharide derivative **10a** in 44% yield. The addition of benzene as the co-solvent (1:1) substantially improved the yield to be 77%. The moderate yield observed in less polar solvent was substantially due to the low reactivity of the free hydroxyl group through the hydrogen bond formation between the acetyl protective group on galactose moiety, which was suggested by the IR spectrum of **8c**. Furthermore, the 'inversed procedure', which had been proposed by Schmidt[30] for the highly active glycosylation intermediate, was very effective. The yield reached as high as quantitative. "Through the experiments, we observed that the acceptor **8c** was almost insoluble in benzene. The addition of donor...". phenylthio fucoside **9a** as benzene solution was necessary to a pre-mixed solution of acceptor **8c** and activators in CH_2Cl_2 so as to the reaction smoothly proceeds. The trichloroacetimidate donor **9b**[31] also worked well through the inversed procedure with a similar CH_2Cl_2–Et_2O solvent system, to give 92% yield of the desired **10a**.

Throughout changing reaction conditions, the anomeric ratio was constant (α/β=ca. 10:1) on the newly introduced fucosidic linkage, with this acceptor **8c**. The addition of DTBMP,[32] a proton scavenger, did not change either the yield or ratio, and in this case, the glycosyl triflate formation and the subsequent S_N2-like β-glycosylation pathway seems negligible.

As the major α-anomer was crystalline, the product **10a** was easily purified by simple recrystallization. This derivative **10a** carries different protective groups on different sugar component, Ac on Gal; Bn on Fuc; TBDPS on GlcNAc. Taking advantage of these properties, two new derivatives **10b** (92%) and **10c** (quantitative) were obtained, by treatment with sodium methoxide in methanol and catalytic debenzylation, sequentially. The use of trichloroacetoimidate fucosyl donor **9b** was advantageous at this later step, as the trace amount of sulfur contaminants, originated from phenylthio fucosyl donor **9a**, often interfered the smooth catalytic hydrogenolysis (Scheme 5).



Scheme 5. (a) **9a**, NIS, TfOH, C_6H_6, CH_2Cl_2, qunat.; (b) **9b**, NIS, TfOH, Et_2O, CH_2Cl_2, 92%; (c) MeONa, MeOH, 92%; (d) H_2, $Pd(OH)_2$, EtOH, quant.

3. Conclusion

We were successful to develop a route through a new amino sugar scaffold **4** toward 2-deoxy-2-acetamido oligosaccharides, on regioselective protection and chemoselective deprotection approach. The first key reaction was the protection of C-1, C-6 hydroxyl groups of glucosamine derivative at once with two TBDPS groups, to provide single β-anomer **5c** in high yield. In another key step, β-oriented anomeric TBDPS-oxy group played a crucial role for

the chemoselective deprotection of oxazolidinone ring in **7b**, which had not been available by treatment with conventionally basic conditions,[33] without any effect on other acetyl protective groups.

4. Experimental

4.1. Material and methods

Merck silica gel 60 F_{254} thin-layer plates (1.05744, 0.5 mm thickness) and silica gel 60 (spherical and neutral; 100–210 μm, 37560-79) from Kanto Chemical Co. were used for preparative thin-layer chromatography and column chromatography, respectively.

4.2. Analytical methods

All melting points are uncorrected. IR spectra were measured as films for oils or KBr disks for solids on a Jasco FT/IR-410 spectrometer. ^{1}H NMR spectra were measured in $CDCl_3$ at 400 MHz on a Jeol JNM GX-400 spectrometer and ^{13}C NMR spectra were measured in $CDCl_3$ at 100 MHz on a Jeol GX-400 spectrometer, unless otherwise stated. High resolution mass spectra were recorded on a Jeol JMS-GCmate spectrometer at 70 eV. Optical rotation values were recorded on a P-1010 polarimeter.

4.3. 2-Acetamido-6-*O*-acetyl-1,3-di-*O*-*tert*-butyldiphenylsilyl-2-deoxy-β-D-glucopyranose (2b)

AcCl (270.0 μL) was added dropwise to MeOH (6.6 mL) and the HCl solution obtained as above was cooled to 20 °C. A solution of the starting material **2a** (199.3 mg, 0.21 mmol) in Et_2O (6.6 mL) was added and the mixture was stirred at room temperature for 8 h. The reaction was monitored by silica gel TLC and developed with hexane–EtOAc (2:1). The reaction mixture was concentrated in vacuo. The residue was purified by silica gel column chromatography. Elution with hexane–EtOAc (4:1) afforded the corresponding partly desilylated product (56.5 mg, 38%). $[\alpha]_D^{20}$ −4.6 (*c* 1.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 1.03 (s, 18H, *t*-Bu), 1.31 (dd, $J_{6,OH}$=6.8 Hz, 1H, OH), 1.53 (s, 3H, Ac), 1.97 (d, $J_{4,OH}$=3.5 Hz, 1H, OH), 2.87 (m, 1H, H5), 3.50 (m, 3H, H3, H6, H6), 3.61 (ddd, $J_{3,4}$=8.8 Hz, $J_{4,5}$=8.8 Hz, 1H, H4), 3.95 (ddd, $J_{1,2}$=7.8 Hz, $J_{2,NH}$=9.3 Hz, $J_{2,3}$=9.1 Hz, 1H, H2), 4.44 (d, 1H, H1), 4.66 (d, 1H, NH), 7.30–7.69 (20H, aromatic); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*: 19.0, 19.6, 23.5, 26.7, 26.9, 58.1, 62.3, 72.0, 74.5, 76.5, 96.2, 127.3, 127.5, 127.8, 128.2, 129.7, 129.7, 129.9, 130.2, 132.2, 133.0, 133.5, 133.7, 135.3, 135.5, 135.6, 135.9, 169.4; the signals between 26.7 and 26.9 included totally 6 carbons, and ones between 127.3 and 135.9 included totally 24 carbons; IR ν_{max} 3566, 3367, 1668 cm^{-1}. This was employed for the next step without further purification. The above-mentioned desilylated product (106.8 mg, 0.15 mmol) was dissolved in CH_2Cl_2 (1.9 mL) at −78 °C. 2,4,6-Collidine (40.4 μL, 0.30 mmol, 2.0 equiv) and acetyl chloride (13.1 μL, 0.18 mmol, 1.2 equiv) were added to the solution with stirring. The reaction was monitored by silica gel TLC and developed with hexane–EtOAc (2:1). After stirring for 3 h at −78 °C and for 1 h at room temperature, the mixture was quenched by the addition of water, and the aqueous layer was extracted with EtOAc. The organic layers were combined, washed with saturated $NaHCO_3$ aq solution, water and brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by silica gel column chromatography. Elution with hexane–EtOAc (4:1) afforded **2b** (87.9 mg, 78%) as fine needles, mp 80.0–82.0 °C. $[\alpha]_D^{22}$ −8.2 (*c* 1.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 1.01 (s, 18H, *t*-Bu), 1.46 (s, 3H, Ac), 1.99 (s, 3H, Ac), 2.12 (d, $J_{4,OH}$=3.9 Hz, 1H, OH), 3.05 (ddd, $J_{4,5}$=9.0 Hz, $J_{5,6}$=4.3 Hz, $J_{5,6}$=4.3 Hz, 1H, H5), 3.50 (dd, $J_{2,3}$=9.2 Hz, $J_{3,4}$=8.9 Hz, 1H, H3), 3.55 (ddd, H4), 3.98 (ddd, $J_{1,2}$=7.8 Hz, $J_{2,NH}$=9.8 Hz, 1H, H2), 4.13 (m, 2H, H6a, H6b), 4.32 (d, 1H, H1), 4.59 (d, 1H, NH), 7.27–7.71 (20H, aromatic); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*: 19.0, 19.6, 20.8, 23.5, 26.6, 26.8, 57.9, 63.5, 71.8, 72.7, 76.3, 95.9, 127.1, 127.4, 127.7, 128.1, 129.5, 129.6, 129.8, 130.1, 132.3, 133.1, 133.1, 133.4, 135.3, 135.6, 135.8, 135.9, 169.4, 171.0; the signals between 26.6 and 26.8 included totally 6 carbons, and ones between 127.1 and 135.9 included totally 24 carbons; IR ν_{max} 3562, 3312, 1726, 1678 cm^{-1}. Anal. Calcd for $C_{42}H_{53}NO_7Si_2$+0.5H_2O: C, 67.35; H, 7.27; N, 1.89. Found: C, 67.60; H, 7.49; N, 1.83.

4.4. 1,6-Di-*O*-*tert*-butyldiphenylsilyl-2-deoxy-2-trifluoroacetoamido-β-D-glucopyranose (5c) and 6-*O*-*tert*-butyldiphenylsilyl-2-deoxy-2-trifluoroacetoamido-β-D-glucopyranose (6c)

2-Trifluoroacetyl-D-glucosamine[6] (**1c**, 2.24 g, 8.14 mmol) and imidazole (3.05 g, 44.8 mmol, 5.5 equiv) were dissolved in DMF (24 mL) containing MS 4 Å (2.3 g) under Ar. The mixture was stirred for 2 h at room temperature and *tert*-butyldiphenylsilyl chloride (TBDPSCl, 6.49 g, 23.6 mmol, 2.9 equiv) in DMF (10 mL) was added to the stirred solution. After stirring for 20 h at room temperature, the mixture was quenched by the addition of brine. The solids were filtered off and the filtrate was extracted with EtOAc, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by silica gel column chromatography (100 g). Elution with hexane–EtOAc (2:1) afforded **5c** (5.45 g, 89.0%) as amorphous solid, R_f 0.5 [hexane–EtOAc (3:2)]. $[\alpha]_D^{22}$ −7.1 (*c* 1.00, EtOH); ^{1}H NMR (270 MHz, $CDCl_3$) *δ*: 1.00 (s, 9H, *t*-Bu), 1.03 (s, 9H, *t*-Bu), 2.99 (dt, $J_{4,5}$=9.2 Hz, $J_{5,6}$=4.6 Hz, 1H, H5), 3.25 (d, *J*=2.2 Hz, 1H, OH), 3.45 (d, *J*=4.1 Hz, 1H, OH), 3.51–3.71 (m, 4H, H3, H4, H6, H6), 3.79 (ddd, $J_{1,2}$=7.9 Hz, $J_{2,3}$=10.1 Hz, $J_{2,NH}$=7.6 Hz, 1H, H2), 4.54 (d, 1H, H1), 6.49 (d, 1H, NH), 7.18–7.62 (20H, aromatic); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*: 19.1, 19.2, 26.8, 58.8, 64.1, 72.9, 73.8, 74.2, 95.2, 115.6, 127.4, 127.6, 127.8, 127.8, 129.8, 129.8, 129.8, 129.9, 132.3, 132.4, 132.5, 132.6, 135.4, 135.4, 135.6, 135.7, 157.8; the signal 26.8 included totally 6 carbons, and ones between 127.4 and 135.7 included totally 24 carbons; IR ν_{max} 3320, 2931, 1708 cm^{-1}; HRMS (EI): calcd for $C_{36}H_{59}F_3NO_6Si_2$ [M^+]: 694.2269; found *m*/*z*: 694.2268.

In another run by applying lower equivalents of reagents, monosilylated derivative **6c** became the major product. Chromatographic separation on silica gel with hexane–EtOAc (2:3) afforded **6c** (75%) as amorphous solid, R_f 0.2 [hexane–EtOAc (3:2)]. ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 1.04 (s, 9H, *t*-Bu), 5.22 (m, 1H, H1α, H1β). Upon acetylation, anomeric signals shifted to 5.65 (d, $J_{1,2}$=8.3 Hz, 1H, H1β) and 6.23 (d, $J_{1,2}$=3.9 Hz, 1H, H1α), respectively.

4.5. 2-*N*-Benzyloxycarbonyl-1,6-di-*O*-*tert*-butyldiphenysilyl-2-deoxy-β-D-glucopyranose (5d) and 2-*N*-benzyloxycarbonyl-6-*O*-*tert*-butyldiphenylsilyl-2-deoxy-β-D-glucopyranose (6d)

In the same manner as described for **5c**, *N*-Cbz-D-glucosamine[22] (**1d**, 454 mg, 1.45 mmol) was treated with TBDPSCl (1.34 g, 4.88 mmol, 3.4 equiv) and imidazole (516 mg, 7.58 mmol, 5.2 equiv) for 36 h. The crude residue was purified by silica gel column chromatography (20 g). Elution with hexane–EtOAc (1:1) afforded **5d** (847 mg, 71%) and **6d** (30.9 mg, 4%) as amorphous solid.

Compound **5d**: R_f 0.5 [hexane–EtOAc (1:1)]; $[\alpha]_D^{22}$ +3.6 (*c* 1.00, EtOH); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 1.01 (s, 9H, *t*-Bu), 1.04 (s, 9H, *t*-Bu), 3.00 (br, 1H, OH), 3.03 (br, 1H, H5), 3.43 (br, 1H, H3), 3.54 (br, 1H, H2), 3.58 (br, 1H, OH), 3.66–3.72 (m, 3H, H4, H6, H6), 4.42 (d, $J_{1,2}$=7.3 Hz, 1H, H1), 4.72 (d, $J_{2,NH}$=6.4 Hz, 1H, NH), 5.03 (d, *J*=18.6 Hz, 1H, Cbz), 5.03 (d, *J*=18.6 Hz, 1H, Cbz), 7.17–7.64 (25H, aromatic); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*: 19.2, 19.3, 26.8, 59.6, 64.1, 67.2, 72.6, 74.5, 75.4, 95.8, 127.4, 127.6, 127.7, 127.7, 128.1, 128.4, 129.7, 129.7, 129.8, 132.6, 132.7, 132.7, 135.4, 135.5, 135.7, 135.8, 136.0, 156.9; the signal 26.8 included totally 6 carbons, and ones between 127.4 and 136.0 included totally 30 carbons; IR ν_{max}: 3394,

1702 cm^{-1}. Anal. Calcd for $C_{46}H_{55}NO_7Si_2+0.5H_2O$: C, 69.14; H, 7.06; N, 1.75. Found: C, 69.20; H, 7.17; N, 1.66.

Compound **6d**: R_f 0.2 [hexane–EtOAc (1:2)]; ^1H NMR (400 MHz, $CDCl_3$) δ: 1.04 (s, 9H, *t*-Bu), 5.15 (br s, 1H, H1). In a similar manner for **7c**, upon acetylation, anomeric signal shifted to 5.58 (d, $J_{1,2}$=8.3 Hz, 1H, H1β) and 6.18 (d, $J_{1,2}$=3.4 Hz, 1H, H1α), respectively.

4.6. 2-Amino-1,6-di-*O*-*tert*-butyldiphenylsilyl-2-deoxy-β-D-glucopyranose (5b) and 1,6-di-*O*-*tert*-butyldiphenylsilyl-2-*N*,3-*O*-carbonyl-2-deoxy-β-D-glucopyranose (4)

To the stirred solution of silyl ether (**5c**, 5.35 g, 7.11 mmol) in THF (24 mL) at 0 °C, LiOH aq solution (2.0 M, 7.11 mL, 14.2 mmol, 2.0 equiv) was added. The mixture was stirred at 0 °C, the reaction was monitored by silica gel TLC, and developed with $CHCl_3$–MeOH (6:1). After 3.5 h, a small portion was extracted with EtOAc and the formation of **5b** was confirmed by the analysis of crude mixture. ^1H NMR (400 MHz, $CDCl_3$) δ: 0.95 (s, 9H, *t*-Bu), 1.00 (s, 9H, *t*-Bu), 2.67 (d, $J_{1,2}$=6.8 Hz, $J_{2,3}$=8.0 Hz, 1H, H2), 2.96 (ddd, $J_{4,5}$=9.2 Hz, $J_{5,6a}$=4.4 Hz, $J_{5,6b}$=4.6 Hz, 1H, H5), 3.22 (dd, $J_{3,4}$=8.3 Hz, 1H, H3), 3.56–3.63 (m, 3H, H4, H6a, H6b), 4.29 (d, 1H, H1), 7.13–7.58 (20H, aromatic); IR ν_{max} 3363, 2930 cm^{-1}. To the rest of the reaction mixture was added $NaHCO_3$ (1.20 g, 14.2 mmol, 2 equiv) and ice bath was removed. To the mixture, *p*-nitrophenyl chloroformate (2.87 g, 14.2 mmol, 2.0 equiv) in CH_3CN (10 mL) was added dropwise over 30 min. The reaction was monitored by silica gel TLC and developed with hexane–EtOAc (2:1). After addition, the reaction was further stirred for 2 h. AcOH (10 mL) and Zn dust (2.5 g) were added portionwise to the reaction mixture with stirring for 1 h. The mixture was then filtered to remove insoluble materials and the filtrate was concentrated in vacuo. The residue was diluted with Et_2O and washed with NaOH aq solution (1.0 M) three times and brine, dried over Na_2SO_4, and concentrated in vacuo. The crude brown oil was purified by silica gel column chromatography (200 g). Elution with hexane–EtOAc (4:1) afforded **4** (4.12 g, 85%) as colorless oil. This was recrystallized from hexane and EtOAc to afford **4** (3.88 g, 80%) as fine needles, mp 177–179 °C. $[\alpha]_D^{20}$ −15.0 (*c* 0.975, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ: 1.04 (s, 9H, *t*-Bu), 1.05 (s, 9H, *t*-Bu), 2.91 (s, 1H, OH), 3.19 (ddd, $J_{4,5}$=7.6 Hz, $J_{5,6a}$=4.0 Hz, $J_{5,6b}$=5.2 Hz, 1H, H5), 3.48 (dd, $J_{1,2}$=7.3 Hz, $J_{2,3}$=11.2 Hz, 1H, H2), 3.76 (dd, $J_{6a,6b}$=10.8 Hz, 1H, H6b), 3.80 (dd, 1H, H6a), 3.94 (dd, $J_{3,4}$=10.8 Hz, 1H, H3), 4.13 (dd, 1H, H4), 4.71 (d, 1H, H1), 4.96 (s, 1H, NH), 7.12–7.62 (20H, aromatic); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 19.1, 19.2, 26.8, 61.3, 63.9, 69.4, 76.7, 81.9, 96.2, 127.5, 127.8, 129.9, 129.9, 130.0, 130.1, 132.1, 132.3, 132.4, 132.5, 135.4, 135.4, 135.5, 135.6, 159.4; the signal 26.8 included totally 6 carbons, and ones between 127.5 and 135.6 included totally 24 carbons; IR ν_{max} 3367, 2931, 1774 cm^{-1}. Anal. Calcd for $C_{39}H_{47}NO_6Si_2$: C, 68.69; H, 6.95; N, 2.05. Found: C, 68.47; H, 6.88; N, 2.06.

The oxazolidinone was alternatively prepared by way of a urea intermediate **5e**. In this case, when the reaction for preparing free amine **5b** (from **5c**, 410 mg, 0.625 mmol) was completed, the mixture was acidified by the addition of AcOH (1.5 mL). Then, KCNO (505 mg, 6.25 mmol, 10.0 equiv) dissolved in water (1.0 mL) was added dropwise over 1 h. The reaction was monitored by silica gel TLC and developed with $CHCl_3$–MeOH (8:1). After stirring for 4 h at room temperature, the reaction was quenched by the addition of $NaHCO_3$ aq solution, and the aqueous layer was extracted with $CHCl_3$. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo to afford urea **5e** quantitatively. Small portion of **5e** was purified by preparative TLC [developed with $CHCl_3$–MeOH (8:1)] to give an analytical sample, mp 203–205 °C. ^1H NMR (270 MHz, $CDCl_3$) δ: 0.94 (s, 9H, *t*-Bu), 1.01 (s, 9H, *t*-Bu), 2.98 (m, 1H, H5), 3.28 (m, 1H, H2), 3.37 (dd, $J_{2,3}$=8.9 Hz, $J_{3,4}$=8.9 Hz, 1H, H3), 3.53 (dd, $J_{4,5}$=8.5 Hz, 1H, H4), 3.65 (br, 2H, H6, H6), 4.39 (d, $J_{1,2}$=7.2 Hz, 1H, H1), 7.12–7.60 (20H, aromatic); IR ν_{max} 3288, 1656, 1583 cm^{-1}. The crude urea **6e** as above was employed for next reaction without further purification and dissolved in AcOH (3.0 mL) under Ar. Then, a solution of $NaNO_2$ (65 mg, 0.94 mmol, 1.5 equiv) in water (0.1 mL) was added four times at every 2 h intervals with stirring. The reaction was monitored by silica gel TLC and developed with $CHCl_3$–MeOH (8:1). After stirring for 24 h at room temperature, the reaction was diluted with Et_2O and poured into NaOH aq solution (1.0 M). The aqueous layer was extracted with Et_2O and the combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by silica gel column chromatography (20 g). Elution with hexane–EtOAc (4:1) to EtOAc afforded **4** (217 mg, 51% from **5c**) as colorless fine needles together with the recovery of **5e** (91 mg, 21%). The physical and spectral data of **4** were coincided with those mentioned as above.

4.7. 2′,3′,4′,6′-Tetra-*O*-acetyl-β-D-galactopyranosyl-(1′-4)-1,6-di-*O*-*tert*-butyldiphenylsilyl-2-*N*,3-*O*-carbonyl-2-deoxy-β-D-glucopyranose (7a) and 2′,3′,4′,6′-tetra-*O*-acetyl-*N*-acetyl-β-D-galactopyranosyl-(1′-4)-1,6-di-*O*-*tert*-butyldiphenylsilyl-2-*N*,3-*O*-carbonyl-2-deoxy-β-D-glucopyranose (7b)

The oxazolidinone (**4**, 1.96 g, 2.87 mmol) and a trichloroacetimidate (**3**, 1.83 g, 3.72 mmol, 1.3 equiv) were dissolved in CH_2Cl_2 (35 mL) containing MS 4 Å (3.6 g) under Ar. After stirring for 4 h at room temperature, the reaction mixture was cooled to 0 °C and TMSOTf (0.1 mL, 0.574 mmol, 0.2 equiv) was added. The mixture was gradually warmed up to room temperature and stirring was continued for additional 2 h. After the complete consumption of the substrate was confirmed by TLC analysis, developed with hexane–EtOAc (1:1), the mixture was quenched by the addition of Et_3N. The solids were filtered off and the filtrate was concentrated in vacuo. The residue was purified by silica gel column chromatography (50 g). Elution with hexane–EtOAc (4:1) afforded **7a** (2.57 g, 87%) as colorless fine needles, mp 189–190 °C. $[\alpha]_D^{26}$ −17.1 (*c* 1.00, $CHCl_3$); ^1H NMR (270 MHz, $CDCl_3$) δ: 1.04 (s, 18H, *t*-Bu), 1.63 (s, 3H, Ac), 1.89 (s, 3H, Ac), 1.93 (s, 3H, Ac), 2.05 (s, 3H, Ac), 3.15 (m, 1H, H5), 3.45 (dd, $J_{1,2}$=7.4 Hz, $J_{2,3}$=11.0 Hz, 1H, H2), 3.74–3.76 (m, 3H, H3, H6, H6), 3.98–4.12 (m, 3H, H5′, H6′, H6′), 4.25 (dd, $J_{3,4}$=8.4 Hz, $J_{4,5}$=9.7 Hz, 1H, H4), 4.53 (d, $J_{1',2'}$=8.1 Hz, 1H, H1′), 4.66 (d, 1H, H1), 4.71 (s, 1H, NH), 4.82 (dd, $J_{2',3'}$=10.4 Hz, $J_{3',4'}$=3.5 Hz, 1H, H3′), 5.03 (dd, 1H, H2′), 5.25 (1H, H4′), 7.12–7.62 (20H, aromatic); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 19.2, 19.5, 20.5, 20.6, 20.7, 20.7, 26.8, 26.9, 61.3, 61.5, 61.6, 66.9, 68.8, 70.8, 70.9, 73.9, 77.5, 80.1, 95.8, 99.9, 127.7, 127.7, 127.8, 127.9, 129.7, 129.9, 130.1, 130.4, 132.0, 132.2, 132.4, 133.4, 135.3, 135.5, 135.6, 135.7, 158.8, 168.9, 169.8, 170.1, 170.3; the signals between 26.8 and 26.9 included totally 6 carbons, and ones between 127.7 and 135.7 included totally 24 carbons; IR ν_{max} 3367, 2932, 1779, 1754 cm^{-1}. Anal. Calcd for $C_{53}H_{65}NO_{15}Si_2+H_2O$: C, 61.79; H, 6.55; N, 1.36. Found: C, 61.84; H, 6.33; N, 1.37.

The glycosylation and the following N-acetylation could be performed in one pot. In this case, when the glycosylation completed, the reaction mixture was cooled to 0 °C and diisopropylethylamine (6.0 mL, 35.0 mmol, 12.0 equiv) was added. To the stirred solution, acetyl chloride (1.25 mL, 17.5 mmol, 6.0 equiv) was added dropwise over 1 h. The reaction was monitored by silica gel TLC and developed with hexane–EtOAc (3:2). After stirring for 24 h at room temperature, the mixture was quenched by the addition of saturated $NaHCO_3$ aq solution. The solids were filtered off and the filtrate was concentrated in vacuo. The residue was diluted with EtOAc and washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by silica gel column chromatography (100 g). Elution with hexane–EtOAc (3:1) afforded **7b** quantitatively as yellow gummy solid. This was recrystallized from hexane and EtOAc to give **7b** (2.42 g, 80%) as colorless fine needles, mp 105–109 °C. $[\alpha]_D^{20}$ −23.7 (*c* 0.950, EtOH); ^1H NMR (270 MHz,

$CDCl_3$) δ: 1.03 (s, 18H, *t*-Bu), 1.69 (s, 3H, Ac), 1.89 (s, 3H, Ac), 1.95 (s, 3H, Ac), 2.06 (s, 3H, Ac), 2.28 (s, 3H, Ac), 3.09 (dt, $J_{4,5}$=9.1 Hz, $J_{5,6}$=6.4 Hz, 1H, H5), 3.55 (t, $J_{5',6'}$=6.6 Hz, 1H, H5′), 3.65 (br, 2H, H6, H6), 3.77–4.10 (m, 4H, H2, H3, H6′, H6′), 4.19 (dd, $J_{3,4}$=6.6 Hz, 1H, H4), 4.47 (d, $J_{1',2'}$=8.1 Hz, 1H, H1′), 4.74–4.79 (m, 2H, H1, H3′), 5.02 (dd, $J'_{2,3'}$=10.2 Hz, 1H, H2′), 5.22 (d, $J_{3',4'}$=3.0 Hz, 1H, H4′), 7.14–7.60 (20H, aromatic); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 19.0, 19.5, 20.6, 20.7, 20.8, 20.8, 24.8, 26.7, 27.0, 61.2, 61.3, 61.6, 66.9, 68.8, 70.8, 70.8, 73.9, 77.2, 78.1, 97.0, 99.7, 127.3, 127.4, 127.8, 127.9, 129.7, 129.8, 129.9, 130.0, 132.3, 132.5, 132.8, 133.1, 135.4, 135.7, 135.9, 135.9, 154.0, 168.9, 169.8, 170.1, 170.1, 171.6; the signals between 26.7 and 27.0 included totally 6 carbons, and ones between 127.3 and 135.9 included totally 24 carbons; IR ν_{max} 3446, 1797, 1754 cm^{-1}. Anal. Calcd for $C_{55}H_{69}NO_{17}Si_2+H_2O$: C, 61.60; H, 6.49; N, 1.31. Found: C, 61.50; H, 6.42; N, 1.33.

4.8. 2′,3′,4′,6′-Tetra-*O*-acetyl-β-D-galactopyranosyl-(1′-4)-2-acetamido-3-*O*-ethoxycarbonyl-1,6-di-*O*-*tert*-butyldiphenylsilyl-2-deoxy-β-D-glucopyranose (8a)

The oxazolidinone (**7b**, 80.6 mg, 0.0765 mmol) and LiCl (9.7 mg, 0.0229 mmol, 3 equiv) were dissolved in a mixture of EtOH and THF (1:1, 3.2 mL). The mixture was cooled to −15 °C and LiOH aq solution (1.0 M, 0.01 mL, 1.3 equiv) was added. The reaction was monitored by silica gel TLC and developed with hexane–EtOAc (1:2). After stirring for 10 min, the mixture was poured into the saturated NH_4Cl solution and extracted with EtOAc. The organic phase was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by silica gel column chromatography (4 g). Elution with hexane–EtOAc (2:1) afforded **8a** (43.0 mg, 53%) as amorphous solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.01 (s, 9H, *t*-Bu), 1.04 (s, 9H, *t*-Bu), 1.23 (t, 3H, Et-CH_3), 1.64 (s, 3H, Ac), 1.75 (s, 3H, Ac), 1.89 (s, 3H, Ac), 1.97 (s, 3H, Ac), 2.02 (s, 3H, Ac), 2.93 (ddd, $J_{4,5}$=8.8 Hz, $J_{5,6a}$=2.0 Hz, $J_{5,6b}$=2.0 Hz, 1H, H5), 3.60 (dd, $J_{5',6a'}$=6.8 Hz, $J_{5',6b'}$=7.3 Hz, 1H, H5′), 3.65 (dd, $J_{6a,6b}$=11.2 Hz, 1H, H6a), 3.75 (dd, 1H, H6b), 3.97 (dd, $J_{6a',6b'}$=11.2 Hz, 1H, H6a′), 4.03 (dd, 1H, H6b′), 4.07–4.18 (m, 4H, H2, H4, Et–CH_2), 4.47 (d, $J_{1,2}$=7.8 Hz, 1H, H1), 4.51 (d, $J_{1',2}$=8.3 Hz, 1H, H1′), 4.62 (dd, $J_{2,3}$=10.3 Hz, $J_{3,4}$=8.8 Hz, 1H, H3), 4.72 (dd, $J_{3',4'}$=2.9 Hz, $J_{2',3'}$=10.4 Hz, 1H, H3′), 4.91 (d, 1H, H2′), 5.17 (d, $J_{2,NH}$=9.8 Hz, 1H, NH), 5.20 (d, 1H, H4′), 7.15–7.61 (20H, aromatic); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.3, 19.1, 19.5, 20.6, 20.7, 20.7, 20.7, 23.4, 26.7, 26.9, 55.2, 60.9, 61.2, 64.1, 66.8, 69.0, 70.4, 70.9, 74.1, 74.9, 76.5, 95.9, 100.0, 127.4, 127.6, 127.7, 127.9, 129.7, 129.8, 129.9, 132.1, 132.6, 132.8, 133.3, 135.4, 135.8, 135.8, 135.8, 155.0, 168.9, 169.6, 169.7, 170.0, 170.3; the signals between 26.7 and 26.9 included totally 6 carbons, and ones between 127.4 and 135.8 included totally 24 carbons; IR ν_{max} 2932, 1754, 1671 cm^{-1}.

4.9. 2′,3′,4′,6′-Tetra-*O*-acetyl-β-D-galactopyranosyl-(1′-4)-2-acetamido-3-*O*-allyloxycarbonyl-1,6-di-*O*-*tert*-butyldiphenylsilyl-2-deoxy-β-D-glucopyranose (8b)

In a similar manner as described above, the oxazolidinone (**7b**, 1.04 g, 0.984 mmol) and LiCl (125 mg, 2.95 mmol, 3 equiv) were dissolved in a mixture of allyl alcohol and THF (1:3, 15 mL). The mixture was cooled to 0 °C and LiOH aq solution (1.0 M, 1.0 mL, 1.0 equiv) was added. The reaction was monitored by silica gel TLC and developed with hexane–EtOAc (1:1). After stirring for 25 min, the mixture was quenched, and the extraction and chromatographic purification provided **8b** (928 mg, 86%) as colorless fine needles, mp 108–110 °C. $[\alpha]_D^{27}$ −31.5 (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.01 (s, 9H, *t*-Bu), 1.04 (s, 9H, *t*-Bu), 1.64 (s, 3H, Ac), 1.73 (s, 3H, Ac), 1.89 (s, 3H, Ac), 1.97 (s, 3H, Ac), 2.03 (s, 3H, Ac), 2.93 (ddd, $J_{4,5}$=8.8 Hz, 1H, H5), 3.60 (t, $J_{5',6'}$=6.8 Hz, 1H, H5′), 3.65 (dd, $J_{5,6a}$=2.0 Hz, $J_{6a,6b}$=11.2 Hz, 1H, H6), 3.75 (dd, $J_{5,6b}$=2.0 Hz, 1H, H6), 3.97–4.02 (m, 2H, H6′, H6′), 4.10–4.17 (m, 2H, H2, H4), 4.46 (d, $J_{1,2}$=7.8 Hz, 1H, H1), 4.49 (d, $J_{1',2'}$=7.8 Hz, 1H, H1′), 4.52–4.64 (m, 3H, H3, Alloc–CH_2), 4.72 (dd, $J_{2',3'}$=10.3 Hz, $J_{3',4'}$=3.4 Hz, 1H, H3′), 4.91 (dd, 1H, H2′), 5.14–5.20 (m, 3H, H4′, Alloc–C=CH, NH), 5.28 (dd, *J*=1.5, 17.1 Hz, 1H, Alloc–C=CH), 5.86 (ddt, *J*=5.4, 10.7 Hz, 1H, Alloc–CH=C), 7.15–7.62 (20H, aromatic); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 19.2, 19.5, 20.6, 20.6, 20.7, 20.7, 23.4, 26.7, 27.0, 55.2, 61.0, 61.2, 66.9, 68.5, 69.1, 70.5, 70.9, 74.1, 75.0, 76.8, 95.9, 100.0, 118.4, 127.5, 127.6, 127.7, 127.9, 129.7, 129.8, 129.9, 131.4, 132.1, 132.6, 132.8, 133.3, 135.4, 135.8, 135.8, 135.8, 154.9, 168.9, 169.6, 169.7, 170.0, 170.3; the signals between 26.7 and 27.0 included totally 6 carbons, and ones between 118.4 and 135.8 included totally 26 carbons; IR ν_{max} 2935, 1754, 1693 cm^{-1}. Anal. Calcd for $C_{58}H_{73}NO_{17}Si_2$: C, 62.63; H, 6.61; N, 1.26. Found: C, 62.30; H, 6.69; N, 1.18.

4.10. 2′,3′,4′,6′-Tetra-*O*-acetyl-β-D-galactopyranosyl-(1′-4)-2-acetamido-1,6-di-*O*-*tert*-butyldiphenylsilyl-2-deoxy-β-D-glucopyranose (8c)

Allyl carbonate (**8b**, 928 mg, 0.846 mmol) was dissolved in degassed THF (12 mL) under Ar. To the stirred solution, morpholine (2 mL) and a catalytic amount of $(Ph_3P)_4Pd$ were added, and the mixture was stirred at 45 °C for 12 h. The reaction was monitored by silica gel TLC and developed with hexane–EtOAc (1:5). The mixture was diluted with EtOAc and washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by silica gel column chromatography (40 g). Elution with hexane–EtOAc (3:1) and the subsequent recrystallization from hexane and EtOAc afforded **8c** (656 mg, 65% from **7b**) as colorless prisms, mp 222–223 °C. $[\alpha]_D^{27}$ −20.7 (*c* 0.950, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.08 (s, 9H, *t*-Bu), 1.10 (s, 9H, *t*-Bu), 1.68 (s, 3H, Ac), 1.86 (s, 3H, Ac), 1.96 (s, 3H, Ac), 2.05 (s, 3H, Ac), 2.11 (s, 3H, Ac), 2.99 (dd, $J_{4,5}$=9.3 Hz, $J_{5,6a}$=0.2 Hz, 1H, H5), 3.60 (dd, $J_{2,3}$=9.8 Hz, $J_{3,4}$=8.3 Hz, 1H, H3), 3.63 (s, 1H, OH), 3.65 (dd, $J_{6a,6b}$=11.2 Hz, 1H, H6a), 3.76 (d, 1H, H6b), 3.81 (t, $J_{5',6'}$=6.4 Hz, 1H, H5′), 3.85–3.96 (m, 2H, H2, H4), 4.09 (d, 2H, H6′, H6′), 4.59 (d, $J_{1',2'}$=7.8 Hz, 1H, H1′), 4.62 (d, $J_{1,2}$=7.8 Hz, 1H, H1), 4.85 (dd, $J_{2',3'}$=10.3 Hz, $J_{3',4'}$=3.4 Hz, 1H, H3′), 5.08 (dd, 1H, H2′), 5.15 (d, $J_{2,NH}$=8.8 Hz, 1H, NH), 5.30 (d, 1H, H4′), 7.20–7.68 (20H, aromatic); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 19.2, 19.5, 20.5, 20.6, 20.7, 20.7, 23.7, 26.8, 27.0, 57.8, 61.1, 61.4, 66.8, 68.7, 70.6, 71.1, 72.2, 74.5, 78.8, 95.7, 100.4, 127.4, 127.6, 127.7, 127.9, 129.7, 129.9, 132.2, 132.8, 133.0, 133.4, 135.4, 135.8, 135.8, 135.8, 169.0, 169.7, 169.9, 170.0, 170.3; the signals between 26.8 and 27.0 included totally 6 carbons, and ones between 127.4 and 135.8 included totally 24 carbons; IR ν_{max} 3405, 2932, 1757, 1736, 1692 cm^{-1}. Anal. Calcd for $C_{54}H_{69}NO_{15}Si_2$: C, 63.07; H, 6.76; N, 1.36. Found: C, 62.75; H, 6.81; N, 1.29.

4.11. 2′,3′,4′,6′-Tetra-*O*-acetyl-β-D-galactopyranosyl-(1′-4)-2-acetamido-3-*O*-trichloroethoxycarbonyl-1,6-di-*O*-*tert*-butyldiphenylsilyl-2-deoxy-β-D-glucopyranose (8d)

In a similar manner as described for **8a**, the oxazolidinone (**7b**, 824 mg, 0.782 mmol) and LiCl (130 mg, 3.13 mmol, 4 equiv) were dissolved in a mixture of 2,2,2-trichloroethanol (0.23 mL, 1.56 mmol, 2.0 equiv) and THF (8 mL). The mixture was cooled to 0 °C and LiOH aq solution (1.0 M, 0.78 mL, 1.0 equiv) was added. The reaction was monitored by silica gel TLC and developed with hexane–EtOAc (1:1). After stirring for 1 h, the mixture was quenched, and the extraction and chromatographic purification provided **8d** quantitatively. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.02 (s, 9H, *t*-Bu), 1.05 (s, 9H, *t*-Bu), 1.66 (s, 3H, Ac), 1.71 (s, 3H, Ac), 1.89 (s, 3H, Ac), 1.97 (s, 3H, Ac), 2.05 (s, 3H, Ac), 2.92 (ddd, $J_{4,5}$=8.8 Hz, $J_{5,6a}$=2.0 Hz, $J_{5,6b}$=2.0 Hz, 1H, H5), 3.59 (dd, $J_{5',6a'}$=6.8 Hz, $J_{5',6b'}$=6.8 Hz, 1H, H5′), 3.67 (dd, $J_{6a,6b}$=11.2 Hz, 1H, H6a), 3.75 (dd, 1H, H6b), 3.98 (dd, $J_{6a',6b'}$=11.2 Hz, 1H, H6a′), 4.05–4.19 (m, H2, H4, 3H, H6b′), 4.52 (d, $J_{1',2'}$=7.8 Hz, 1H, H1′), 4.56 (d, $J_{1,2}$=7.3 Hz, 1H, H1), 4.60 (d, *J*=11.7 Hz, 1H, Troc–CH_2), 4.70 (dd, $J_{2',3'}$=10.3 Hz, $J_{3',4'}$=3.4 Hz, 1H, H3′), 4.75

(dd, $J_{2,3}$=9.8 Hz, $J_{3,4}$=8.6 Hz, 1H, H3), 4.80 (d, 1H, Troc–CH_2), 4.89 (dd, 1H, H2′), 5.15 (d, 1H, $J_{2,NH}$=9.3 Hz, NH), 5.20 (d, 1H, H4′), 7.14–7.62 (20H, aromatic).

Without any quenching and isolation, the trichloroethyl carbonate **8d** as above was directly deprotected as follows. After stirring for 1 h of the mixture for preparing **8d**, AcOH (4 mL), and Zn dust (1.2 g) were added. After the complete consumption of the substrate was confirmed by TLC analysis, developed with hexane–EtOAc (1:5), the mixture was neutralized with saturated $NaHCO_3$ aq solution. The mixture was then filtered to remove insoluble materials and the filtrate was extracted with EtOAc. The organic solution was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was passed through a short column of silica gel, followed by the recrystallization from hot EtOAc afforded **8c** (720 mg, 90% from **7b**).

4.12. 2′,3′,4′,6′-Tetra-*O*-acetyl-β-D-galactopyranosyl-(1′-4)-2″,3″,4″-tri-*O*-benzyl-α-L-fucopyranosyl-(1″-3)-2-acetamido-1,6-di-*O*-*tert*-butyldiphenylsilyl-2-deoxy-β-D-glucopyranose (10a)

The acceptor (**8c**, 298 mg, 0.290 mmol) was dissolved in CH_2Cl_2 (6.0 mL) containing MS 4 Å (800 mg) under Ar. After stirring for 2 h, NIS (200 mg, 0.889 mmol) and TfOH (2 μL, 0.029 mmol) were added and the reaction mixture was cooled to 0 °C. To the mixture, the fucosyl donor (**9a**, 235 mg, 0.435 mmol) dissolved in benzene (6 mL) was added dropwise over 30 min. The reaction was monitored by silica gel TLC and developed with hexane–EtOAc (3:2). The reaction was quenched by addition of Et_3N. The solids were filtered off and the filtrate was concentrated in vacuo. The residue was diluted with EtOAc, washed with saturated $Na_2S_2O_3$ aq solution and brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by silica gel column chromatography (12 g). Elution with hexane–EtOAc (4:1) afforded inseparable anomeric mixture of **10a** (430 mg, ca. 10:1) quantitatively as amorphous solid. Recrystallization from hexane and EtOAc afforded pure α-anomer of **10a** in regard to fucosyl unit as fine needles, mp 93–95 °C. $[\alpha]_D^{28}$ −38.3 (*c* 1.20, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 0.97 (s, 9H, *t*-Bu), 1.04 (s, 9H, *t*-Bu), 1.10 (d, $J_{5″,6″}$=6.4 Hz, 3H, H6″), 1.46 (s, 3H, Ac), 1.67 (s, 3H, Ac), 1.78 (s, 3H, Ac), 1.86 (s, 3H, Ac), 1.95 (s, 3H, Ac), 2.85 (dd, $J_{4,5}$=8.3 Hz, $J_{5,6a}$=0.2 Hz, 1H, H5), 3.46 (dd, $J_{5′,6a′}$=6.4 Hz, $J_{5′,6b′}$=6.4 Hz, 1H, H5′), 3.52 (m, 1H, H2), 3.63 (d, $J_{3″,4″}$=2.0 Hz, 1H, H4″), 3.69 (dd, $J_{6a,6b}$=11.7 Hz, 1H, H6a), 3.75 (d, 1H, H6b), 3.88 (dd, $J_{6a′,6b′}$=10.7 Hz, 1H, H6′), 3.91 (dd, $J_{2″,3″}$=10.0 Hz, 1H, H3″), 3.90–4.09 (m, 5H, H1, H3, H4, H6′, H2″), 4.49 (1H, q, H5″), 4.50 (dd, $J_{2′,3′}$=10.3 Hz, $J_{3′,4′}$=4.4 Hz, 1H, H3′), 4.57 (d, $J_{1′,2′}$=8.8 Hz, 1H, H1′), 4.60–4.90 (m, 7H, H2′, Bn–CH_2×3), 4.96 (d, $J_{1″,2″}$=2.9 Hz, 1H, H1″), 5.15 (d, 1H, H4′), 5.46 (d, $J_{2,NH}$=7.8 Hz, 1H, NH), 7.06–7.61 (35H, aromatic); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 16.8, 19.2, 19.4, 20.5, 20.5, 20.6, 20.7, 23.3, 26.8, 26.9, 26.9, 29.4, 44.7, 60.5, 61.5, 66.2, 66.6, 66.6, 68.7, 70.2, 70.6, 72.6, 73.5, 74.0, 74.2, 75.0, 76.4, 77.2, 80.1, 97.8, 97.8, 98.9, 126.9, 127.2, 127.4, 127.4, 127.4, 127.6, 127.7, 128.0, 128.1, 128.2, 128.2, 128.4, 129.5, 129.6, 129.7, 130.0, 132.0, 132.7, 133.4, 133.5, 135.2, 135.6, 135.8, 135.9, 138.5, 138.8, 168.8, 169.6, 169.6, 169.7, 169.9; the signals between 26.8 and 29.4 included totally 6 carbons, and ones between 126.9 and 138.8 included totally 42 carbons; IR ν_{max} 2932, 1756, 1674 cm^{-1}. Anal. Calcd for $C_{81}H_{97}NO_{19}Si_2+H_2O$: C, 66.51; H, 6.82; N, 0.96. Found: C, 66.59; H, 7.04; N, 0.90.

4.13. β-D-Galactopyranosyl-(1′-4)-2″,3″,4″-tri-*O*-benzyl-α-fucopyranosyl-(1″-3)-2-acetamido-1,6-di-*O*-*tert*-butyldiphenylsilyl-2-deoxy-β-D-glucopyranose (10b)

To the stirred solution of trisaccharide **10a** (89.3 mg, 0.0618 mmol) in MeOH (2 mL), a catalytic amount of sodium methoxide was added. The reaction was monitored by silica gel TLC and developed with hexane–EtOAc (1:5). After stirring for 4 h at room temperature, the reaction was quenched by the addition of IR-120 resin (H^+ form). The insoluble materials were filtered off and the filtrate was concentrated in vacuo. The residue was passed through a short column of silica gel to afford pure **10b** (72 mg, 92%) as amorphous solid. $[\alpha]_D^{25}$ −78.0 (*c* 0.950, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 0.94 (s, 9H, *t*-Bu), 1.01 (s, 9H, *t*-Bu), 1.08 (d, $J_{5″,6″}$=6.8 Hz, 3H, H6″), 1.52 (s, 3H, Ac), 2.75 (d, $J_{4,5}$=9.3 Hz, 1H, H5), 2.96 ($J_{2′,3′}$=9.3 Hz, $J_{3′,4′}$=3.1 Hz, 1H, H3′), 3.07 (br, 1H, H4″), 3.33 (dd, $J_{1′,2′}$=7.8 Hz, 1H, H2′), 3.60–3.93 (m, 10H, H1, H2, H3, H6, H6, H4′, H5′, H6′, H6′, H3″), 3.99 (dd, $J_{1″,2″}$=2.5 Hz, $J_{2″,3″}$=9.8 Hz, 1H, H2″), 4.08 (dd, $J_{3,4}$=8.8, 1H, H4), 4.22 (q, 1H, H5″), 4.42 (d, 1H, H1′), 4.52–4.83 (m, 6H, Bn–CH_2×3), 5.38 (d, 1H, H1″), 5.45 (1H, d, $J_{2,NH}$=8.3 Hz, NH), 7.06–7.58 (35H, aromatic); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 16.8, 19.1, 19.5, 23.6, 26.7, 26.9, 27.0, 29.7, 61.6, 63.2, 67.3, 70.5, 71.7, 71.9, 72.7, 73.6, 74.3, 74.9, 75.1, 75.3, 76.2, 77.1, 77.2, 77.5, 79.8, 96.2, 96.7, 100.5, 127.1, 127.3, 127.3, 127.4, 127.5, 127.6, 127.6, 128.0, 128.0, 128.1, 128.2, 128.3, 128.3, 128.3, 128.5, 129.5, 129.6, 129.7, 132.5, 132.7, 133.4, 133.6, 135.5, 135.6, 135.6, 135.8, 135.8, 135.9, 137.7, 138.2, 138.3, 138.4, 138.5, 139.1, 170.0; the signals between 26.7 and 29.7 included totally 6 carbons, and ones between 127.1 and 139.1 included totally 42 carbons; IR ν_{max} 3411, 2931, 1658 cm^{-1}. Anal. Calcd for $C_{73}H_{89}NO_{15}Si_2+H_2O$: C, 67.72; H, 7.08; N, 1.08. Found: C, 67.97; H, 7.07; N, 1.17.

4.14. β-D-Galactopyranosyl-(1′-4)-α-L-fucopyranosyl-(1″-3)-2-acetamido-1,6-di-*O*-*tert*-butyldiphenylsilyl-2-deoxy-β-D-glucopyranose (10c)

A mixture of **10b** (87.0 mg, 0.0681 mmol) and $Pd(OH)_2$ (30 mg) in EtOH (8.0 mL) was vigorously stirred under H_2 at 40 °C. The reaction was monitored by silica gel TLC and developed with $CHCl_3$–MeOH (7:1). After stirring for 24 h, the catalyst was removed by filtration. The filtrate and washings were concentrated and the residue was passed through a short column of silica gel to afford **10c** (73 mg, quantitative) as colorless solid. This was recrystallized from hot EtOH to give **10c** (44.2 mg, 65%) as colorless prisms, mp 255–259 °C. $[\alpha]_D^{27}$ −49.8 (*c* 1.00, $CHCl_3$/MeOH=1:1); ^{1}H NMR (400 MHz, DMSO) *δ*: 0.94–0.98 (m, 12H, H6″, *t*-Bu), 1.01 (s, 9H, *t*-Bu), 1.76 (s, 3H, Ac), 2.83 (d, $J_{4,5}$=9.3 Hz, 1H, H5), 3.08 (t, $J_{5′,6′}$=6.4 Hz, 1H, H5′), 3.11 (dd, $J_{2′,3′}$=9.3 Hz, $J_{3′,4′}$=2.4 Hz, 1H, H3′), 3.26 (dd, $J_{1′,2′}$=7.8 Hz, 1H, H2′), 3.32–3.60 (m, 10H, H2, H3 H6a, H6b, H4′, H6′a, H6′b, H2″, H3″, H4″), 3.90 (d, $J_{3,4}$=8.8 Hz, 1H, H4), 4.19 (d, $J_{1,2}$=10.3 Hz, 1H, H1), 4.54 (d, 1H, H1′), 4.72 (q, $J_{5″,6″}$=6.8 Hz, 1H, H5″), 4.85 (d, $J_{1″,2″}$=3.4 Hz, 1H, H1″), 7.07–7.62 (20H, aromatic), 8.00 (d, $J_{2,NH}$=9.2 Hz, 1H, NH); ^{13}C NMR (100 MHz, DMSO) *δ*: 16.4, 18.8, 19.2, 23.1, 26.5, 26.7, 59.4, 59.4, 61.4, 65.6, 67.0, 68.3, 69.2, 70.7, 71.2, 72.8, 72.8, 73.4, 74.5, 75.3, 98.8, 98.8, 101.7, 127.3, 127.4, 127.7, 129.4, 129.5, 129.6, 129.7, 132.1, 132.2, 133.2, 133.2, 135.0, 135.1, 135.3, 135.4, 169.4; the signals between 26.5 and 26.7 included totally 6 carbons, and ones between 127.3 and 135.4 included totally 24 carbons; IR ν_{max} 3429, 2931, 1667 cm^{-1}. Anal. Calcd for $C_{52}H_{71}NO_{15}Si_2+H_2O$: C, 60.97; H, 7.18; N, 1.37. Found: C, 61.05; H, 7.26; N, 1.25.

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