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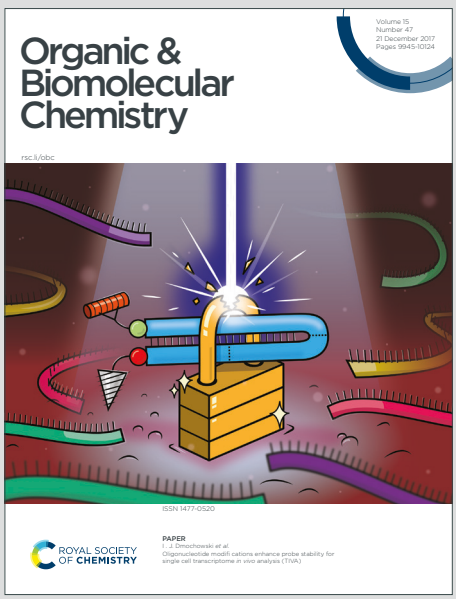

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ARTICLE

Synthesis of hyaluronic acid oligosaccharides with GlcNAc–GlcA repeating pattern and their binding affinity with CD44

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Hyaluronic acid (HA) is a ubiquitious glycosaminoglycan in the extracellular matrix and a substrate of CD44, a transmembrane glycoprotein that is important in cell migration. Crystal and NMR studies found the hexasaccharide of the pattern (GlcA–GlcNAc)$_3$ as the shortest HA that could bind to CD44, but molecular dynamics simulations indicated that a tetrasaccharide of the pattern (GlcNAc–GlcA)$_2$ is the key structure interacting with CD44. Access to oligomers with such a repeat pattern is crucial in binding studies with CD44. Here we developed a synthetic procedure to afford the HA oligosaccharides with GlcNAc–GlcA repeating unit and measured the binding interaction between these sugars and hCD44 by isothermal titration calorimetry (ITC). During the chemical synthesis, we successfully generated the β-glycosidic bond in the absence of neighbouring group participation and overcome the issues in the oxidation step. In addition, ammonia-free dissolving metal reduction for debenzylation and azido reduction was applied in carbohydrate synthesis for the first time. ITC analysis revealed that the HA tetrasaccharide (GlcNAc–GlcA)$_2$ could indeed interact and bind to the human CD44.

Introduction

Hyaluronic acid (HA) is an anionic, linear nonsulfated glycosaminoglycan and a major component of the extracellular matrix. It is composed of alternating β(1→3) D-glucuronic acid (GlcA) and β(1→4) *N*-acetyl-D-glucosamine (GlcNAc) and can weigh up to several million daltons. HA can take in water several times heavier than itself to form a cushion and keep tissues moist. It is elastic and lubricating enough to prevent the impacts between bones in the articular cartilage and avoid frictions in organs.[1] Besides the physical properties, it has an essential contribution to biological processes such as cell adhesion,[2] proliferation,[3] inflammation,[4] and cell migration.[5] In the process of wound healing, for example, coagulation is enabled by the HA–fibrin matrix formed.[6] HA is hydrolysed later into oligosaccharides for interaction with proteins, including CD44, to induce inflammation and cell migration.

CD44 is a transmembrane glycoprotein with multiple glycoforms differentiated by *N*- or *O*-glycosylation.[7] Complex splicing of the gene transcripts also results in different isoforms.[8] It plays an important role in neuronal axon guidance,[9] lymphocyte activation,[10] and cell migration.[11] Interaction of HA with CD44 induces a conformational change in the protein that that increases its affinity to HA.[12–14] This event results in signal transduction, followed by cell migration. The process occurs not only in common cells, but also in tumour cells, especially, those with highly expressed CD44 on the surface.[15]

Although the interaction of CD44 and HA has been studied for quite a while, the key structure is still unclear. Crystal and NMR studies of CD44 and HA show that the latter must be at least a hexasaccharide.[16,17] On the other hand, theoretical calculation indicated that the key HA structure of the interaction is the tetrasaccharide (GlcNAc-GlcA)$_2$.[14] However, this sequence pattern does not exist in human body because hyaluronidases degrade HA mainly into the (GlcA-GlcNAc)$_n$-type oligosaccharides (Fig. 1). Only leech has so far been found able to produce (GlcNAc-GlcA)$_n$-type sugar in nature.[18] We became curious as to whether the (GlcNAc-GlcA)$_2$ tetrasaccharide is indeed the shortest length of HA for binding to CD44. After a thorough search, this compound and its homologous variants are neither commercially available nor are they accessible by degradation even though there are new methods that can control the degradation of high-molecular-weight HA into homogeneous oligosaccharides.[19] In the end, we decided to develop a chemical strategy to obtain these sugars.

Several chemical methods of preparation of HA have been reported previously.[20] These methods may be classified on the basis of the reducing end sugar: GlcA,[21–26] GlcNAc,[27–32] or involving both.[33–36] From these reports, a number of challenges for the synthesis of HA oligosaccharides with (GlcNAc-GlcA)$_n$

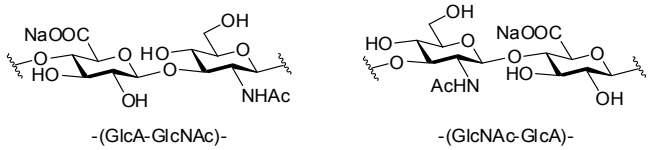

Fig. 1 Sequence possibilities for the oligosaccharide repeating unit.

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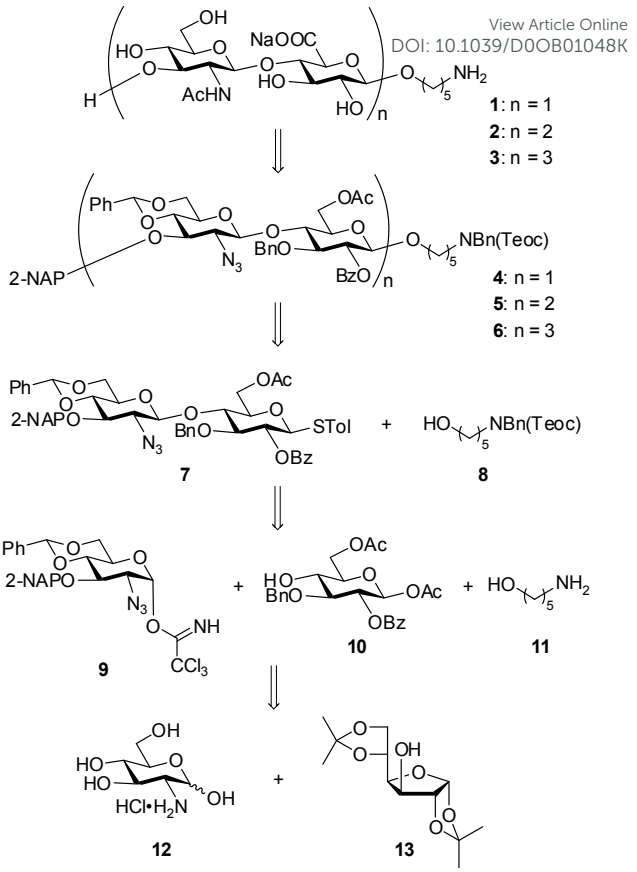
pattern are highlighted. Use of glucuronic acid backbones at the reducing end of glycosyl donors expected for such synthesis encumbers the elongation procedures because of low reactivity.[20,27] However, using the more reactive glucose backbone in donors may face difficult oxidation of multiple primary alcohols at the late stage of the synthesis.[26,34,35] Another challenge is building the β-glycosidic bond of glucosamine. Although previous studies reported that the neighbouring group effect is effective in making the β-glycosidic bond,[26–28,30] there are problems concerning the oxazoline formation,[25,28] purification, or NMR analysis.[37] Using the azido group can avoid those problems, but control of stereoselectivity in glycosylation is not easy. Protecting groups also need to be judiciously selected such that these moieties could be selectively removed to form the precursor of glycosylation or enable functional group transformation and remain inert in the reaction environment when required by the process.

In this paper, we conceived a synthetic procedure for the chemical preparation of HA disaccharide, tetrasaccharide, and hexasaccharide with the $(GlcNAc\text{-}GlcA)_n$ repeat pattern. Along the way, ammonia-free dissolving metal reduction for the debenzylation and azido reduction in carbohydrates was successfully implemented. The generated oligosaccharides were examined for their binding interaction with human CD44 protein, in which observed the tetrasaccharide as the shortest HA fragment that could bind to CD44

Results and discussion

We envisioned that the preparation of the desired HA oligosaccharides **1**, **2**, and **3** can be approached from HA oligosaccharide skeletons **4**, **5**, and **6** through selective alcohol oxidation and final transformations (Scheme 1). The skeletons would be elongated by β-glycosylation of the linker derivative **8** and the disaccharide surrogate **7**. The latter has a benzoyl (Bz) group at O2 to give neighbouring group effect in forming the β-glycosidic bond. We also opted for the glucose backbone, which is considerably more reactive than that with glucuronic acid during glycosylation. Compound **7** is equipped with orthogonal protecting groups to permit proper chain extension and functionalization. The 2-naphthylmethyl (2-NAP) group could be selectively cleaved by 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) to give a glycosyl acceptor without affecting the benzyl (Bn) and benzylidene groups. Removal of acetyl (Ac) groups at primary positions facilitated by $Mg(OMe)_2$ should have higher reaction rate than the cleavage of Bz esters and the 2-(trimethylsilyl)ethoxycarbonyloxy (Teoc) group. In contrast to the phthalimido, trichloroacetyl, and trichloroethylcarbamate protecting groups, the azido group can survive strongly basic environments and can be reduced by hydrogenolysis or Staudinger reaction.[38] To build the β-glycosidic bond of compound **7**, 4,6-*O*-benzylidene would be installed on the 2-azido-2-deoxy-glucosamine **9** to reduce steric hindrance of the β-face during glycosylation. Linker **8**, the glucosamine-derived **9** and the glucose-derived **10** can be prepared from the commercially available compounds **11**–**13**.



Scheme 1 Retrosynthesis of the target compounds.

Scheme 2 illustrates our preparation of the disaccharide building block **7**. The known 3-alcohol **14**[39] was obtained from glucosamine hydrochloride (**12**) by using the typical diazo transfer procedure,[40] thioglycosylation,[41] and benzylidene formation.[39] Further installation of a 2-NAP group gave the thioglycoside **15** in 93% yield. The benzylglucofuranose **16**, obtained by typical benzylation of the diacetonide **13**,[42] was hydrolysed and then rearranged by an acidic ion-exchange resin, which does not require neutralization. Then, regioselective diacetylation provided the 2,4-diol **17** in 53% yield over two steps. To affect selective benzoylation, the diacetylglucose **17** was dissolved in pyridine and slowly treated with BzCl, giving the 2-benzoylglucose **10** in 61% yield.

Bearing the necessary functional groups, the thioglycoside **15** could already be used as glycosyl donor and form a link with the acceptor **10**. Nevertheless, the condensation of **10** and **15** using the promoter tandem *N*-iodosuccinimide (NIS) and trifluoromethanesulfonic acid (TfOH) in the presence or absence of the β-inducing nitrile solvent[43] could only provide low to moderate yields and a nearly one-to-one proportion of the α and β isomers. The alternate use of 1-benzenesulfinyl piperidine (BSP), 2,4,6-tri-*tert*-butyl pyrimidine (TTBP), and trifluoromethanesulfonic anhydride (Tf_2O) promoter system, which was used to enable β-mannosylation,[44] could adjust neither the α/β ratio nor the yield for the disaccharide (24%, α/β=1.5/1).

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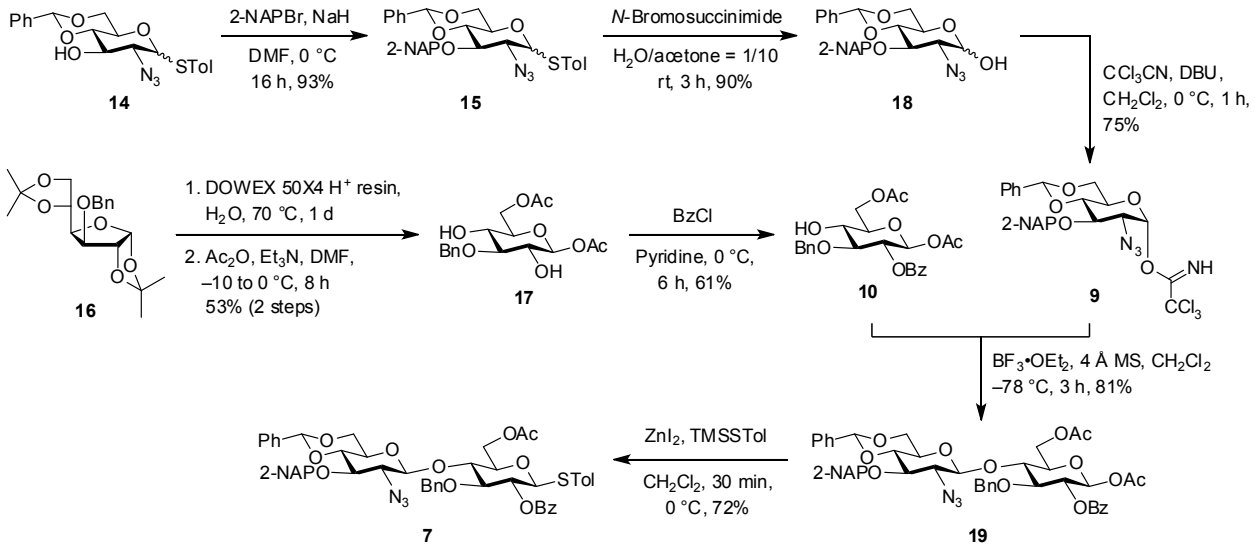
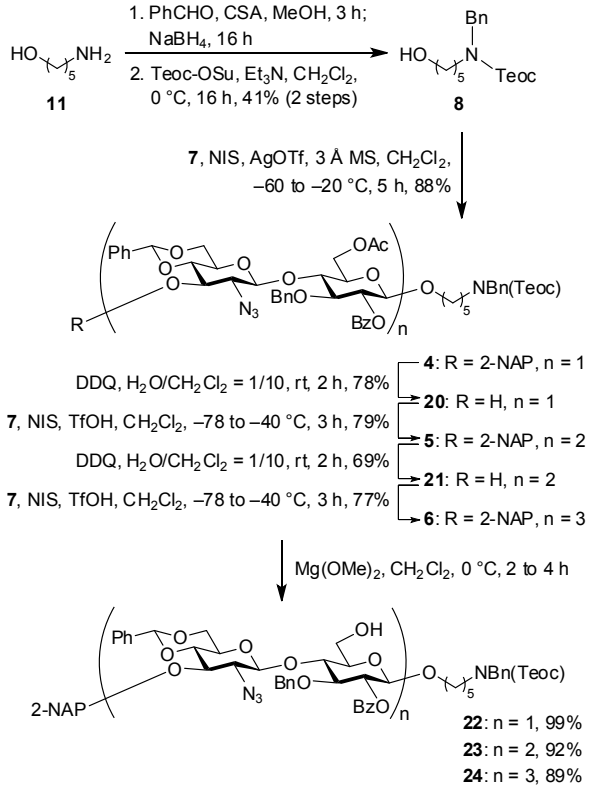


Scheme 2 Preparation of the disaccharide donor **7**. DMF, *N*,*N*-dimethylformamide.

With such a predicament, we opted to convert the thioglycoside **15** into an α-imidate that could proceed by an S_N2-like mechanism at glycosylation by using $BF_3{\cdot}OEt_2$ as promoter.[45] The thioglycoside underwent hydrolysis and reaction with trichloroacetonitrile in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) to form the imidate with α/β = 5/1 (^{1}H NMR: $\delta_{H1\alpha}$ = 6.38 ppm, $^3J_{H1,H2}$ = 3.7 Hz; $\delta_{H1\beta}$ = 5.70 ppm, $^3J_{H1,H2}$ = 6.6 Hz). The β-isomer can be recycled, that is, hydrolysed back into compound **18**. The condensation of the α-imidate **9** and acceptor **10** fortunately led to the β-disaccharide **19** (^{1}H NMR: $\delta_{H1'}$ = 4.37 ppm, $^3J_{H1',H2'}$ = 8.3 Hz) in 81% yield without the α-product. Using 1 equivalent ZnI_2 in tandem with trimethyl(4-methylphenylthio)silane (TMSSTol) to transform the glycosyl acetate **19** into the thioglycoside **7** avoided the hydrolysis of the benzylidene acetal.

The linker **8** was produced by installing Teoc group on the benzylamine generated by reductive amination of 5-aminopentanol (**11**) (Scheme 3). With NIS and silver trifluoromethanesulfonate (AgOTf) as promoter, the glycosylation of acceptor **8** and donor **7** offered the disaccharide derivative **4** in 88% yield without orthoester formation (^{1}H NMR: δ_{H1} = 4.49 ppm, $^3J_{H1,H2}$ = 7.8 Hz). Compound **4** was treated with DDQ to form the disaccharide acceptor **20** in 78% yield. Successive elongation of this acceptor with the thioglycoside donor **7** punctuated by 2-NAP cleavage successfully delivered the tetrasaccharide **5** and hexasaccharide **6**. Selective hydrolysis of the acetate groups at the primary position by $Mg(OMe)_2$ furnished the compounds **22–24** in 89–99% yield.



Scheme 3 Synthesis of HA-based oligomers and oxidation precursors. CSA, 10-camphorsulfonic acid; Teoc-OSu, 1-[2-(trimethylsilyl)ethoxycarbonyloxy]pyrrolidin-2,5-dione.

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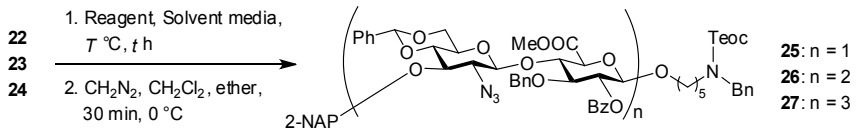
Table 1 Oxidation of HA skeletons



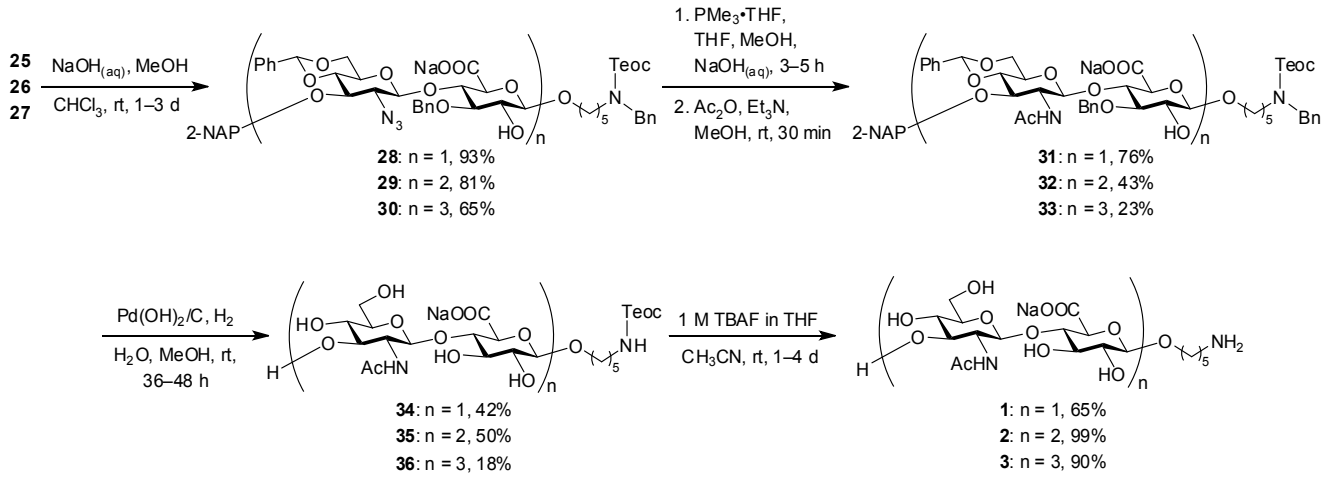
Entry	Compound	Reagent	Solvent media	*T*	*t*	Product	Yield (%)[a]
1	**22**	TEMPO, NaClO	NaBr, TBAB, $NaHCO_3$, H_2O, CH_2Cl_2	0	2	**25**	44
2	**23**	TEMPO, NaClO	NaBr, TBAB, $NaHCO_3$, H_2O, CH_2Cl_2	0	2	**26**	53
3	**24**	TEMPO, NaClO	NaBr, TBAB, $NaHCO_3$, H_2O, CH_2Cl_2	0	2	**27**	0
4	**24**	TEMPO, NaClO, $NaClO_2$	Toluene, phosphate buffer pH 6.8	rt	2	**27**	0[b]
5	**24**	PDC, Ac_2O	CH_2Cl_2	rt	2	**27**	6
6	**24**	TEMPO, BAIB	CH_2Cl_2/H_2O = 10/1	rt	48	**27**	29
7	**24**	TEMPO, BAIB	CH_3CN/H_2O = 10/1	rt	5	**27**	53
8	**22**	TEMPO, BAIB	CH_3CN/H_2O = 10/1	rt	2	**25**	84
9	**23**	TEMPO, BAIB	CH_3CN/H_2O = 10/1	rt	2	**26**	71

[a] Isolated yield. [b] No reaction. TBAB, tetrabutylammonium bromide.

For the oxidation of the primary alcohol, the 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) free radical, NaClO, and $NaClO_2$ combination was utilized as recommended in a previous HA synthesis.[35] We later discovered that the oxidation could proceed toward the carboxylic acid even without $NaClO_2$. Because of the difficult purification and NMR analysis of the carboxylate compound, subsequent methylation was carried out to afford the methyl esters **25**–**27** (Table 1). Although the stated oxidation condition provided the desired disaccharide **25** (entry 1, 44%) and tetrasaccharide **26** (entry 2, 53%), hexasaccharide **27** was not obtained even when the solvent was replaced by toluene and phosphate buffer (entries 3 and 4).[46]

Alternatively, we treated the hexasaccharide **24** with TEMPO and [bis(acetoxy)iodo]benzene (BAIB) or pyridinium dichromate (PDC) and Ac_2O.[32] The case with TEMPO and BAIB gave better yield of compound **27** (29%, entry 6). Surprisingly, the yield of compound **27** increased to 53% when the solvent in the oxidation step was changed from CH_2Cl_2 to CH_3CN (entry 7). Furthermore, the yields of disaccharide **25** and tetrasaccharide **26** also increased considerably to 84% and 71%, respectively, under such condition (entries 8 and 9).

Hydrolysis of the esters in compounds **25**–**27** supplied the carboxylates **28**–**30** in 65–93% yield (Scheme 4). Staudinger reaction, followed by *N*-acetylation produced the acetamides **31**–**33** in 23–76% yield. Hydrogenolysis of **31**–**33** under $Pd(OH)_2/C$ promotion produced compounds **34**–**36** in 18–50% yield. Finally, the Teoc group was eliminated by tetrabutylammoium fluoride (TBAF) to get the target molecules **1**–**3** in 65–99% yield.



Scheme 4 Synthesis of the target molecules **1**–**3**.

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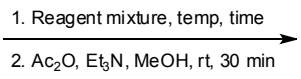
Table 2 Alternate procedure toward compounds **34**–**36**.



Entry	S.M.[a]	Reagent mixture[b]	temp	time (h)	Product	Yield (%)[c]
1	**28**	**A**	rt	36	**34**	31
2	**29**	**A**	rt	36	**35**	15
3	**30**	**A**	rt	36	**36**	0
4	**28**	**B**	rt	48	**34**	58
5	**29**	**B**	rt	48	**35**	–[d]
6	**30**	**B**	rt	48	**36**	–[d]
7	**29**	**C**	0 °C	1	**35**	37
8	**29**	**C**	–50 °C	1	**35**	47
9	**30**	**C**	–50 °C	1	**36**	38
10	**30**	**C**	–50 °C	3	**36**	62

[a] Starting material. [b] **A**: $Pd(OH)_2/C$, H_2, H_2O, MeOH; **B**: Pd black, H_2, H_2O, MeOH; **C**: $Na_{(s)}$, 15-crown-5, tetrahydrofuran. [c] Isolated yields. [d] No product because of probable Pd black conjugation.

Although the syntheses of the HA-based compounds **1**–**3** were successful, the yields of Staudinger reaction and hydrogenolysis dropped significantly as the sugar length increased. Consequently, we modified the synthetic pathway at these stages by first performing the simultaneous removal of the benzyl-type and benzylidene groups and reduction of the azido group and then, installation of the acetyl group on the amino moiety. Thus, hydrogenolysis of the HA skeletons **28**–**30** by $Pd(OH)_2/C$ and then *N*-acetylation is expected to produce the acetamides **34**–**36** (Table 2). The yield of disaccharide **34** is similar to the yield of the original pathway (31% overall, entry 1), but the results for the tetrasaccharide **35** and, most especially, the hexasaccharide **36** are not satisfactory (entries 2 and 3). These outcomes may be caused by the absorption of the product by the activated carbon.[47] When Pd black was used instead of $Pd(OH)_2/C$, the yield for the disaccharide **34** improved to 58% (entry 4), which is higher than that of the initial route (32%, **28**→**31**→**34**). Unfortunately, no target products were observed for the tetrasaccharide and hexasaccharide possibly due to Pd black conjugation (entries 5 and 6).

The feasibility of ammonia-free dissolving metal reduction, which uses $Na_{(s)}$ and 15-crown-5,[48] was alternatively examined for the transformation of compounds **29** and **30**. It took 1 h to remove all of the benzyl-type and benzylidene groups from sugar at 0 °C. After quenching the reaction, the sodium salt was easily separated by a C-18 column by virtue of the less polar Teoc group. Then, the crude residue underwent *N*-acetylation to provide the acetamide **35** in 37% yield (entry 7). Considering that the reduction condition maybe too harsh 0 °C, we set up the reaction at a temperature low enough for adequate stirring. A reaction temperature controlled to –50 °C allowed the solution to be stirred smoothly, and the tetrasaccharide **29** reacted completely in 1 h with 47% yield (entry 8). Applying the same reaction condition to the hexasaccharide **30** supplied the product **36** in 38% yield (entry 9). We noted here that the low yield is caused by the incomplete debenzylation of the hexasaccharide. Extending the reaction time from 1 h to 3 h generated **36** in a far better 62% yield (entry 10). In the end, we successfully improved the yield for the disaccharide, tetrasaccharide, and hexasaccharide by using Pd black and ammonia free dissolving metal reduction.

Table 3 Dissociation constants of the binding of HA-based sugars to hCD44 determined through ITC.[a]

Sugar	Sugar-to-protein ratio	K_D (μM)[b]
Disaccharide **1**	0	–[c]
Tetrasaccharide **2**	1.05 (±0.05)	3.5 (±1.4)
Hexasaccharide **3**	0.90 (±0.08)	29 (±6)
LMW-HA (8–15 kDa)	0.17 (±0.02)	9.2 (±1.1)

[a] The values reported are averages of results from three experiments with standard deviations indicated in parentheses. [b] Measured as association constant, the inverse of K_D. [c] No binding detected.

For the binding affinity measurements, isothermal titration calorimetry (ITC) was used to detect the interaction between the HA sugars and a commercially acquired hCD44. Binding for disaccharide **1** is not evident, but exothermic binding to hCD44 are observable for tetrasaccharide **2** and hexasaccharide **3**. In Table 3, the binding ratios of tetrasaccharide and hexasaccharide to hCD44 are both close to one. In contrast, that of low-molecular-weight (LMW)-HA (8–15 kDa, about 40–75 sugar units per molecule) is 0.17, which suggests that one LMW-HA molecule can interact with approximately six hCD44 units.

CD44 transitions between two stable conformations: an ordered conformation with low affinity to HA and a conformation with partially disordered C-terminal exhibiting high affinity to HA.[12] Guvench et al.[14] showed in their molecular dynamics simulations that an HA tetrasaccharide segment of the sequence $(GlcNAc–GlcA)_2$ forms close associations with the binding domain in CD44 with nearly similar minimum distances for both the ordered and partially disordered states. Additional sugar residues at the reducing and non-reducing ends are relatively farther away from the protein. Our K_D value for the tetrasaccharide **2** (3.5 μM) corroborates these observations. The disaccharide **1** is indeed far too short to display any meaningful association with CD44. Previous measurements of binding affinity with polymeric HA showed a K_D range of 13–27 μM,[17,49] which is quite consistent with our results (9.2 μM). That the tetrasaccharide **2** could fit closely to the binding groove may

be the reason for the higher affinity. We also suspect that the notably lower affinity of our hexasaccharide **3** (29 μM) and the longer oligosaccharides of previous measurements[17,50] have to do with the extended sugar residues and their secondary interaction with the protein that may influence the switching between the ordered and partially disordered states. We hope to investigate this behaviour in future studies.

Conclusions

We successfully assembled HA-based disaccharide, tetrasaccharide, and hexasaccharide with $(GlcNAc\text{-}GlcA)_n$ repeat pattern. In this synthesis work, we were able to form the β-glycosidic bond between the glucosamine-derived donor **9** and the glucose-based acceptor **10** by S_N2-like reaction without neighbouring group effect. Our method for late-stage oxidation worked well and the turnover at the debenzylation stage was improved. After reviewing previous research papers, we believe that this is the first application of ammonia-free dissolving metal reduction ($Na_{(s)}$ and 15-crown-5) in the carbohydrate field. Our ITC binding experiments also confirmed that the tetrasaccharide 2 bearing the GlcNAc-GlcA repeat unit could indeed effectively bind CD44 and, thus far, is the shortest HA oligomer to exhibit this property.

Experimental Section

ITC measurements

hCD44 (Gln21–Pro220) was brought from Acrobiosystem. LMW-HA (molecular weight: 8–15 kDa) was brought from Carbosynth. All ITC experiments were carried out at 25 °C with sodium phosphate buffer [phosphate (50 mM), NaCl (62.3 mM), pH 7.4]. The hCD44 protein solution (60-70 μM) was placed in the calorimeter cell and titrated with the sugar solution (1–1.4 mM, 2 μL injections with 3 min spacing). The results of the protein titration were subtracted by the data for the sugar solution titrated into the buffer without protein and then fitted by One site model.

General synthetic method

CH_2Cl_2 was purified and dried from a safe purification system filled with anhydrous Al_2O_3. All other reagents were obtained from commercial sources and used without further purification. Water was either distilled or Milli-Q-purified. Flash column chromatography was carried out on Silica Gel 60 (230–400 mesh, E. Merck). TLC was performed on glass plates pre-coated with Silica Gel 60 F_{254} (0.25 mm, E. Merck); detection was executed by spraying with a solution of $Ce(NH_4)_2(NO_3)_6$, $(NH_4)_6Mo_7O_{24}$, and H_2SO_4 in water followed subsequent heating on a hot plate. Specific rotations were taken at ambient conditions and reported in $10^{-1}\cdot deg\cdot cm^2\cdot g^{-1}$; the sample concentrations are in $g\cdot dL^{-1}$. ^1H and ^{13}C NMR spectra were recorded on 600 MHz spectrometers. Chemical shifts are in ppm and *J* values are given in Hz. The hydrogen multiplicities of carbon peaks were determined using DEPT-90 and DEPT-135 experiments, the spectra of which were herein provided together with the power-gated-decoupled ^{13}C NMR spectrum.

Experimental procedures and characterization data

4-Methylphenyl 2-azido-4,6-*O*-(benzylidene)-2-deoxy-3-*O*-(2-naphthylmethyl)-1-thio-D-glucopyranoside (15). NaH (0.12 g, 3.0 mmol) was slowly added to the solution of compound **14** (1.0 g, 2.5 mmol) and BnBr (0.47 mL, 3.0 mmol) in anhydrous DMF (15 mL) under nitrogen atmosphere at 0 °C. After 16 h, the mixture was quenched with H_2O (50 mL) and then extracted with ethyl acetate. The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (ethyl acetate/ hexane = 1/8, v/v) to yield the product **15** (1.3 g, 93%). For the α-isomer: $[\alpha]_D^{24}$ +71.1 (*c* 0.79 in $CHCl_3$); IR (thin film): ν_{max}/cm^{-1} 3056, 2867, 2110, 1492, 1371, 1275, 1171, 1099; ^1H NMR (400 MHz, $CDCl_3$): δ 7.81-7.78 (3H, m, Ar-H), 7.76-7.73 (1H, m, Ar-H), 7.51-7.48 (3H, m, Ar-H), 7.45-7.43 (2H, m, Ar-H), 7.39-7.36 (5H, m, Ar-H), 7.13-7.11 (2H, m, Ar-H), 5.59 (1H, s, PhC*H*), 5.49 (1H, d, *J* 4.8, 1-H), 5.10-4.98 (2H, m, $ArCH_2$), 4.44 (1H, td, *J* 9.9, 4.9, 5-H), 4.22 (1H, dd, *J* 10.3, 5.0, 6-H_a), 4.03-3.95 (2H, m, 2-H, 3-H), 3.79-3.73 (2H, m, 4-H, 6-H_b), 2.32 (3H, s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.4 (C), 137.2 (C), 135.2 (C), 133.3 (C), 133.1 (CH), 130.0 (CH), 129.1 (CH), 128.3 (CH), 128.2 (CH), 128.0 (CH), 127.7 (CH), 127.0 (CH), 126.1 (CH), 126.0 (CH), 125.9 (CH), 101.6 (CH), 88.2 (CH), 82.8 (CH), 77.9 (CH), 77.2 (CH), 75.2 (CH_2), 68.7 (CH_2), 63.8 (CH), 21.1 (CH_3); HRMS (ESI): *m/z* calcd for $C_{31}H_{29}N_3O_4NaS$ ($[M+Na]^+$): 562.1776, found 562.1768. For the β-isomer: $[\alpha]_D^{24}$ –171.6 (*c* 4.86 in $CHCl_3$); IR (thin film): ν_{max}/cm^{-1} 3480, 3030, 2919, 2873, 2111, 1494, 1346, 1277, 1078; ^1H NMR (400 MHz, $CDCl_3$): δ 7.81-7.74 (4H, m, Ar-H), 7.50-7.44 (7H, m, Ar-H), 7.40-7.38 (3H, m, Ar-H), 7.16-7.14 (2H, m, Ar-H), 5.57 (1H, s, PhC*H*), 5.05-4.95 (2H, m, $ArCH_2$), 4.43 (1H, d, *J* 10.2, 1-H), 4.38 (1H, dd, *J* 10.5, 5.0, 6-H_a), 3.78 (1H, t, *J* 10.3, 6-H_b), 3.69 (1H, t, *J* 9.1, 3-H), 3.63 (1H, t, *J* 9.2, 4-H), 3.43 (1H, dd, *J* 9.5, 5.0, 5-H), 3.36 (1H, t, *J* 9.4 Hz, 2-H), 2.35 (3H, s, Ar-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.1 (C), 137.1 (C), 135.0 (C), 134.5 (CH), 133.2 (C), 133.1 (C), 129.9 (CH), 129.1 (CH), 128.3 (CH), 128.2 (CH), 128.0 (CH), 127.7 (CH), 127.2 (CH), 126.6 (C), 126.1 (CH), 126.0 (CH), 125.96 (CH), 101.3 (CH), 86.7 (CH), 81.3 (CH), 80.9 (CH), 75.1 (CH_2), 70.4 (CH), 68.5 (CH), 64.7 (CH), 21.2 (CH_3).

2-Azido-4,6-*O*-benzylidene-2-deoxy-3-*O*-(2-naphthylmethyl)-D-glucopyranose (18). NBS (8.3 g, 46 mmol) was added to a solution of the thioglycoside **15** (5.0 g, 9.3 mmol) in the mixture of H_2O and THF (1/10, v/v, 495 mL) at room temperature. After 3 h, the reaction was quenched with $Na_2S_2O_{3(aq)}$ and $NaHCO_{3(aq)}$. THF was removed under reduced pressure. The mixture was extracted with ethyl acetate. The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (ethyl acetate/ hexane = 1/3, v/v) to yield compound **18** (3.6 g, 90%, α/β = 1/1). $[\alpha]_D^{24}$ –78.9 (*c* 1.0 in $CHCl_3$); IR (thin film): ν_{max}/cm^{-1} 3434, 3055, 1921, 1874, 2211, 2114, 1634, 1451, 1367, 1347, 1254, 1168, 1138, 1123, 1095, 1039, 1005, 962, 852, 815, 793, 770, 747, 695, 652, 473; ^1H NMR (600 MHz, $CDCl_3$): δ 7.82-7.79 (6H, m, Ar-H), 7.76-7.74 (2H, m, Ar-H), 7.51-7.43 (10H, m, Ar-H), 7.40-7.38 (6H, m, Ar-H), 5.60 (1H, s), 5.57 (1H, s), 5.26 (1H, m), 5.10 (1H, m), 5.06 (1H, m), 4.97 (1H, m), 4.96

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(1H, m), 4.58 (1H, m), 4.31-4.26 (2H, m), 4.15-4.09 (2H, m), 3.78-3.71 (4H, m), 3.63-3.60 (2H, m), 3.49 (1H, m), 3.42-3.37 (2H, m), 3.07 (1H, m); ^{13}C NMR (150 MHz, $CDCl_3$): δ 137.1 (C), 137.0 (C), 135.2 (C), 135.1 (C), 133.2 (C), 133.2 (C), 133.1 (C), 129.13 (CH), 129.10 (CH), 128.3 (CH), 128.19 (CH), 128.16 (CH), 128.0 (CH), 127.66 (CH), 127.64 (CH), 127.1 (CH), 126.1 (CH), 126.04 (CH), 126.00 (CH), 125.95 (CH), 125.92 (CH), 101.5 (CH), 101.4 (CH), 96.5 (CH), 92.7 (CH), 82.7 (CH), 81.5 (CH), 78.8 (CH), 76.2 (CH), 75.1 (CH_2), 74.9 (CH_2), 68.9 (CH_2), 68.4 (CH_2), 67.3 (CH), 66.3 (CH), 63.6 (CH), 62.7 (CH); HRMS (ESI): *m/z* calcd for $C_{13}H_{18}N_3O_4S$ ([M+H]$^+$): 434.1710, found: 434.1712.

2-Azido-4,6-*O*-benzylidene-2-deoxy-3-*O*-(2-naphthylmethyl)-α-D-glucopyranosyl trichloroacetimidate (9). DBU (33.6 µL, 0.225 mmol) was added to a solution of the compound **18** (196 mg. 0.452 mmol) and trichloroacetonitrile (CCl_3CN, 226 µL, 2.25 mmol) in CH_2Cl_2 (2 mL) at 0 °C. After 1 h, the reaction was concentrated under reduced pressure and then purified by silica gel chromatography (ethyl acetate/hexane = 1/7, v/v) to give the α-trichloroacetimidate derivative **9** (196 mg, 75%); IR (thin film): ν_{max}/cm^{-1} 3340, 3058, 2925, 2867, 2112, 1673, 1509, 1454, 1372, 1328, 1281, 1234, 1213, 1172, 1135, 1091, 1070, 1022, 990, 911, 856, 834, 819, 795, 754, 698, 646, 476; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.73 (1H, s, N-H), 7.82-7.81 (3H, m, Ar-H), 7.77 (1H, m, Ar-H), 7.53-7.50 (3H, m, Ar-H), 7.48-7.45 (2H, m, Ar-H), 7.40-7.38 (3H, m, Ar-H), 6.38 (1H, d, *J* 3.7, 1-H), 5.62 (1H, s, PhC*H*), 5.17 (1H, d, *J* 11.2, ArCH_2), 5.01 (1H, d, *J* 11.2, ArCH_2), 4.34 (1H, dd, *J* 10.5, 4.8, 6-H$_a$), 4.07 (1H, td, *J* 10.0, 5.0, 5-H), 3.85 (1H, t, *J* 9.4, 4-H), 3.78 (1H, t, *J* 10.4, 6-H$_b$), 3.74 (1H, dd, *J* 9.9, 3.7, 2-H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 160.8 (C), 136.8 (C), 135.0 (C), 133.2 (C), 133.0 (C), 129.2 (CH), 128.3 (CH), 128.2 (CH), 128.0 (CH), 127.6 (CH), 127.0 (CH), 126.1 (CH), 126.0 (CH), 126.0 (CH), 125.9 (CH), 101.5 (CH), 94.8 (CH), 90.6 (C), 82.1 (CH), 76.4 (CH), 75.2 (CH_2), 68.5 (CH_2), 65.2 (CH), 62.5 (CH); HRMS (ESI): *m/z* calcd for $C_{26}H_{24}Cl_3N_4O_5$ ([M+H]$^+$): 577.0807, found: 577.0795.

6-*O*-Acetyl-3-*O*-benzyl-β-D-glucopyranosyl acetate (17). A solution of glucofuranose **16** (1.5 g, 4.3 mmol) in H_2O (15 mL) was mixed with DOWEX 50WX4 H$^+$ ion-exchange resin (1.5 g) and was heated to 70 °C. After 1 day, the reaction was filtered through filter paper, concentrated under reduced pressure, and dried *in vacuo*. The crude residue and Et_3N (2.1 mL, 15 mmol) was dissolved in anhydrous DMF (10 mL) under nitrogen atmosphere at –10 °C. A solution of Ac_2O (0.70 mL, 7.4 mmol) in anhydrous CH_2Cl_2 (20 mL) was slowly added to the solution of the crude residue at –10 °C. The reaction was gradually warm to 0 °C and kept going for 8 h. The reaction was quenched with MeOH (1.0 mL). The mixture was concentrated under reduced pressure and purified by silica gel chromatography (ethyl acetate/hexane = 3/1, v/v) to give the product **17** (0.8 g, 53% in 2 steps); $[\alpha]_D^{24}$ –8.0 (*c* 5.2 in $CHCl_3$); IR (thin film): ν_{max}/cm^{-1} 3444, 1738, 1368, 1239, 1070; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.36-7.30 (4H, m, Ar-H), 7.41-7.27 (1H, m, Ar-H), 5.48 (1H, d, *J* 8.2, 1-H), 4.85 (1H, d, *J* 11.7, PhCH_2), 4.83 (1H, d, *J* 11.7, PhCH_2), 4.35 (1H, dd, *J* 12.3, 4.6, 6-H$_a$), 4.20 (1H, dd, *J* 2.0, 12.3, 6-H$_b$), 3.55 (1H, dd, *J* 7.7, 8.2, 2-H), 3.50 (1H, ddd, *J* 9.2, 4.6, 2.0, 5-H), 3.47-3.39 (2H, m, 3-H, 4-H), 3.14 (1H, d, *J* 3.5, 4-OH), 2.93 (1H, s, 2-OH), 2.08 (3H, s, OCOCH_3), 2.03 (3H, s, OCOCH_3); ^{13}C NMR (150 MHz, $CDCl_3$): δ 171.7 (C), 169.5 (C), 138.0 (C), 128.4 (CH), 127.8 (CH), 93.7 (CH), 83.5 (CH), 74.7 (CH_2),74.4 (CH),72.4 (CH), 69.2 (CH), 62.8 (CH_2), 20.8 (CH_3), 20.6 (CH_3); HRMS (ESI): *m/z* calcd for $C_{17}H_{22}O_8Na$ ([M+Na]$^+$): 377.1212, found 377.1209.

6-*O*-Acetyl-2-*O*-benzoyl-3-*O*-benzyl-β-D-glucopyranosyl acetate (10). A solution of BzCl (0.30 mL, 2.9 mmol) in anhydrous CH_2Cl_2 (20 mL) was slowly added to a solution of the compound **17** (1.0 g, 2.8 mmol) in pyridine (10 mL) under nitrogen atmosphere at 0 °C. After 6 h, the reaction was quenched with MeOH (1.0 mL). The mixture was concentrated under reduced pressure and purified by silica gel chromatography (ethyl acetate/hexane = 1/10, v/v) to give the product **10** (0.8 g, 62%). $[\alpha]_D^{24}$ +20.4 (*c* 3.5 in $CHCl_3$); IR (thin film): ν_{max}/cm^{-1} 3485, 1726, 1454, 1367, 1268, 1244; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.98 (2H, m, Ar-H), 7.58 (1H, m, Ar-H), 7.46-7.42 (2H, m, Ar-H), 7.19-7.14 (5H, m, Ar-H), 5.78 (1H, d, *J* 8.3, 1-H), 5.33 (1H, dd, *J* 9.1, 8.3, 2-H), 4.70 (2H, d, *J* 12, PhCH_2), 4.53 (1H, dd, *J* 3.1, 12.3, 6-H$_a$), 4.25 (1H, d, *J* 12.3, 6-H$_b$), 3.74-3.68 (1H, m, 3-H), 3.66-3.62 (2H, m, 4-H, 5-H), 2.85-2.83 (1H, m, 4-OH), 2.12 (3H, s, OCOCH_3), 1.99 (3H, s, OCOCH_3); ^{13}C NMR (150 MHz, $CDCl_3$): δ 171.9 (C), 169.3 (C), 165.1 (C), 137.5 (C), 133.5 (CH), 129.8 (CH), 129.3 (C), 128.53 (CH), 128.46 (CH), 128.1 (CH), 128.0 (CH), 92.1 (CH), 81.5 (CH), 74.92 (CH), 74.89 (CH_2), 72.2 (CH), 69.7 (CH), 62.5 (CH_2), 20.8 (CH_3); HRMS (ESI): *m/z* calcd for $C_{24}H_{26}O_9Na$ ([M+Na]$^+$): 481.1475, found 481.1476.

6-*O*-Acetyl-[2-azido-4,6-*O*-benzylidene-2-deoxy-3-*O*-(2-naphthylmethyl)-β-D-glucopyranosyl]-(1→4)-2-benzoyl-3-benzyl-β-D-glucopyranosyl acetate (19). *Method A*: A mixture of thioglycoside **15** (72.3 mg, 0.134 mmol) and acceptor **10** (50.2 mg, 0.109 mmol) in anhydrous CH_2Cl_2 (3 mL) was added to a reaction flask containing freshly dried AW-300 (180 mg) at room temperature under nitrogen atmosphere and stirred for 1 h. The reaction flask was cooled to –40 °C and then NIS (36.2 mg, 0.161 mmol) and TfOH (3.8 uL, 0.0436 mmol) were sequentially added. After 3 h, the donor **15** was consumed completely. The reaction was quenched with Et_3N and $Na_2S_2O_{3(aq)}$ and filtered through Celite. The crude target product was extracted with CH_2Cl_2. The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (ethyl acetate/ hexane = 1/3, v/v) to yield compound **19** (39.2 mg, 41%, α/β=1.2/1). *Method B*: A solution of thioglycoside **15** (73.0 mg, 0.135 mmol) in anhydrous CH_2Cl_2 (3.0 mL) was added to a reaction flask containing freshly dried 3 Å molecular sieves (180 mg) at room temperature under nitrogen atmosphere and stirred for 1 h. The reaction flask was cooled to -78 °C and then BSP (34.0 mg, 0.177 mmol), TTBP (49 mg, 0.197 mmol), and Tf_2O (26 uL, 0.158 mmol) were sequentially added. After 30 min, the acceptor **10** (50.3 mg, 0.109 mmol) was added to the reaction vessel. After 3 h, the donor **15** was consumed completely. The reaction was quenched with Et_3N and $Na_2S_2O_{3(aq)}$ and filtered through Celite. The mixture was extracted with CH_2Cl_2. The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (ethyl acetate/ hexane = 1/3, v/v) to yield

compound **19** (23.0 mg, 24%, α/β=1.5/1). *Method C*: A mixture of imidate **9** (84.5 mg, 0.146 mmol) and acceptor **10** (53.6 mg, 0.117 mmol) in anhydrous CH_2Cl_2 (1.4 mL) was added to a reaction flask containing freshly dried 3 Å molecular sieves (80 mg) at room temperature under nitrogen atmosphere. After stirring for 1 h, the reaction flask was cooled to –78 °C and $BF_3{\cdot}Et_2O$ (0.2 M in CH_2Cl_2, 292 μL, 0.0730 mmol) was slowly added. After 3 h, the donor **9** was consumed completely. The reaction was quenched with Et_3N and filtered through Celite. The mixture was concentrated under reduced pressure. The residue was purified by silica gel chromatography (ethyl acetate/ hexane = 1/3, v/v) to yield compound **19** (19.2 mg, 94%). $[\alpha]_D^{24}$ –34.0 (*c* 1.8 in $CHCl_3$); IR (thin film): ν_{max}/cm^{-1} 2877, 3223, 1738, 1602, 1453, 1368, 1267, 1231, 1175, 1094, 1064, 1004, 857, 820, 754, 699, 563, 476; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.93 (2H, m, Ar-H), 7.81-7.78 (2H, m, Ar-H), 7.76-7.73 (2H, m, Ar-H), 7.56 (1H, m, Ar-H), 7.48-7.40 (7H, m, Ar-H), 7.37-7.36 (3H, m, Ar-H), 7.12 (5H, m, Ar-H), 5.80 (1H, d, *J* 8.2, 1-H), 5.48 (1H, s, PhC*H*), 5.34 (1H, t, *J* 8.8, 2-H), 5.04 (1H, d, *J* 11.3, ArCH_2), 4.93 (1H, d, *J* 11.3, ArCH_2), 4.77 (1H, d, *J* 11.3, ArCH_2), 4.62 (1H, d, *J* 11.3, ArCH_2), 4.57 (1H, dd, *J* 12.2, 1.7, 6-H_a), 4.37 (1H, d, *J* 8.3, 1'-H), 4.34 (1H, dd, *J* 8.0, 4.3 Hz, 6-H_b), 4.08 (1H, dd, *J* 10.6, 4.9, 1H; 6'-H_a), 4.01 (1H, t, *J* 9.1, 4-H), 3.85-3.81 (2H, m, 3-H, 5-H), 3.65-3.62 (2H, m, 3'-H, 4'-H), 3.45-3.40 (2H, m, 2'-H, 6'-H_b), 3.23 (1H, m, 5'-H), 2.10 (3H, s, OCOCH_3); 1.99 (3H, s, OCOCH_3); ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.5 (C), 169.3 (C), 165.0 (C), 137.8 (C), 137.0 (C), 135.0 (C), 133.4 (CH), 133.2 (C), 133.0 (C), 129.8 (CH), 129.2 (C), 129.2 (CH), 128.5 (CH), 128.3 (CH), 128.2 (CH), 128.0 (CH), 127.7 (CH), 127.6 (CH), 127.5 (CH), 127.12 (CH), 126.09 (CH), 126.06 (CH), 126.0 (CH), 102.1 (CH), 101.3 (CH), 91.9 (CH), 81.5 (CH), 80.3 (CH), 79.2 (CH), 77.5 (CH), 75.0 (CH_2), 74.8 (CH_2), 73.9 (CH), 71.8 (CH), 68.3 (CH_2), 66.7 (CH), 66.2 (CH), 62.1 (CH_2), 20.9 (CH_3), 20.9 (CH_3), HRMS (ESI): *m/z* calcd for $C_{48}H_{48}N_3O_{13}$ ([M+H]$^+$): 874.3182, found: 874.3159.

4-Methylphenyl [2-azido-4,6-*O*-benzylidene-2-deoxy-3-*O*-(2-naphthylmethyl)-β-D-glucopyranosyl]-(1→4)-6-acetyl-2-benzoyl-3-benzyl-1-thio-β-D-glucopyranoside (7). ZnI_2 (365 mg, 1.14 mmol) was added to a solution of the compound **19** (1.00 g, 1.14 mmol) and TMSSTol (674 mg, 3.43 mmol) in anhydrous CH_2Cl_2 (20 mL) at 0 °C. After stirring for 30 min, the reaction was filtered through Celite and then quenched with Et_3N. The mixture was concentrated under reduced pressure and purified by silica gel chromatography (ethyl acetate/hexane = 1/5, v/v) to give thioglycoside **7** (774 mg, 72%). $[\alpha]_D^{24}$ –39.8 (*c* 2.0 in $CHCl_3$); IR (thin film): ν_{max}/cm^{-1} 3062, 3028, 2920, 2872, 2112, 1732, 1601, 1584, 1493, 1452, 1367, 1315, 1265, 1173, 1093, 1030, 1003, 915, 856, 814, 754, 710, 698, 666, 562, 475; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.03 (2H, m, Ar-H), 7.83-7.75 (3H, m, Ar-H), 7.58 (1H, m, Ar-H), 7.51-7.43 (7H, m, Ar-H), 7.39-7.37 (5H, m, Ar-H), 7.15-7.14 (5H, m, Ar-H), 7.08 (2H, m, Ar-H), 5.50 (1H, s, PhC*H*), 5.21 (1H, t, *J* 9.4 Hz, 2-H), 5.07 (1H, d, *J* 11.3, ArCH_2), 4.95 (1H, d, *J* 11.3, ArCH_2), 4.78 (1H, d, *J* 11.0, ArCH_2), 4.73 (2H, m, 1-H, 6-H_a), 4.60 (1H, d, *J* 11.0, ArCH_2), 4.39 (1H, d, *J* 8.1, 1'-H), 4.32 (1H, dd, *J* 11.9, 4.7, 6-H_b), 4.08 (1H, dd, *J* 10.4, 4.7, 6'-H_a), 3.94 (1H, t, *J* 9.2, 4-H), 3.80 (1H, t, *J* 8.8, 3-H), 3.71 (1H, m, 5-H), 3.66 (2H, m, 3'-H, 4'-H), 3.46 (1H, t, *J* 5.7, 2'-H), 3.41 (1H, t, *J* 10.3, 6'-H_b), 3.25 (1H, m, 5'-H), 2.33 (3H, s, Ar-CH_3), 2.12 (3H, s, OCOCH_3); ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.4 (C), 165.0 (C), 138.3 (C), 137.9 (C), 136.9 (C), 135.0 (C), 133.7 (CH), 133.1 (CH), 133.0 (CH), 129.8 (CH), 129.7 (CH), 129.4 (CH), 129.1 (CH), 128.4 (CH), 128.34 (CH), 128.25 (CH), 128.13 (CH), 128.06 (CH), 127.9 (CH), 127.6 (CH), 127.4 (CH), 127.4 (CH), 127.0 (CH), 126.03 (CH), 126.00 (CH), 125.94 (CH), 102.0 (CH), 101.3 (CH), 85.9 (CH), 82.0 (CH), 81.5 (CH), 79.1 (CH), 77.8 (CH), 77.0 (CH), 74.92 (CH_2), 74.89 (CH_2), 71.8 (CH), 68.2 (CH_2), 66.7 (CH), 66.1 (CH), 62.3 (CH_2), 21.1 (CH_3), 20.9 (CH_3), HRMS (ESI): *m/z* calcd for $C_{53}H_{51}N_3O_{11}SNa$ ([M+Na]$^+$): 960.3137, found: 960.3137.

***N*-Benzyl-*N*-2-(trimethylsilyl)ethoxycarbonyl-5-aminopentanol (8).** CSA (45 mg, 0.097 mmol) was added to the solution of 5-amino-pentanol **11** (2.0 g, 9.7 mmol) and benzaldehyde (2.4 mL, 12 mmol) in MeOH (100 mL) at 0 °C. After 3 h, the reaction was treated with $NaBH_4$ (1.7 g, 23 mmol). The reaction was concentrated under reduced pressure after 16 h and then dried *in vacuo*. Et_3N (5.4 mL, 19 mmol) and Teoc-OSu (5.0 g, 9.7 mmol) were sequentially added to the solution of the dried crude residue anhydrous CH_2Cl_2 (30 mL) at 0 °C. After stirring 16 h, the reaction was quenched with H_2O (50 mL) and the crude product was extracted with CH_2Cl_2. The organic layer was dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel chromatography (ethyl acetate/hexane = 1/2, v/v) to provide the pentanol **8** (2.7g, 41% for 2 steps). IR (thin film): ν_{max}/cm^{-1} 3444, 3089, 3065, 3031, 2951, 2863, 1694, 1682, 1495, 1471, 1454, 1422, 1364, 1305, 1249, 1177, 1125, 1092, 937, 857, 837, 769, 751, 731, 699, 666, 616, 457; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.30-7.18 (5H, m, Ar-H), 4.46 (2H, s, ArCH_2), 4.19 (2H, s, CH_2), 3.57 (2H, m, CH_2), 3.18 (2H, d, CH_2), 1.52 (4H, s, CH_2), 1.30 (2H, s, CH_2), 0.99 (2H, s, CH_2), 0.01 (9H, s × 2, TMS);^{13}C NMR (150 MHz, $CDCl_3$): δ 156.8 (C), 138.1 (C), 127.7 (CH), 127.2 (CH), 63.6 (CH_2), 62.6 (CH_2), 49.9 (CH_2), 46.5 (CH_2), 32.3 (CH_2), 27.3 (CH_2), 22.9 (CH_2), 22.8 (CH_2), 17.8 (CH_2), -1.5 (CH_3); HRMS (ESI): *m/z* calcd for $C_{18}H_{31}NO_3SiNa$ ([M+Na]$^+$): 360.1965, found: 360.1966.

***N*-Benzyl-*N*-2-(trimethylsilyl)ethoxycarbonyl-5-aminopentyl [2-azido-4,6-*O*-benzylidene-2-deoxy-3-*O*-(2-naphthylmethyl)-β-D-glucopyranosyl]-(1→4)-6-acetyl-2-benzoyl-3-benzyl-β-D-glucopyranose (4).** A mixture of donor **7** (504 mg, 0.538 mmol) and acceptor **8** (363 mg, 1.08 mmol) in anhydrous CH_2Cl_2 (17 mL) was added to a reaction flask containing freshly dried 3 Å molecular sieves (500 mg) at room temperature under nitrogen atmosphere. After stirring for 1 h, the reaction flask was cooled to –60 °C. The reaction flask was sequentially added with NIS (145 mg, 0.645 mmol) and AgOTf (152 mg, 0.588 mmol) and was gradually warmed to –20 °C. After 5 h, the donor **7** was consumed completely. The reaction was filtered through Celite and quenched with $NaHCO_{3(aq)}$ and $Na_2S_2O_{3(aq)}$. The crude target material was extracted with CH_2Cl_2. The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified by silica gel chromatography (ethyl acetate/ hexane = 1/3, v/v) to yield compound **4** (545 mg, 88%). $[\alpha]_D^{24}$ –43.7 (*c* 3.4 in $CHCl_3$); IR (thin film): ν_{max}/cm^{-1} 3456, 3063, 3030, 2951, 2870, 2112, 1732, 1693, 1603, 1585, 1496, 1469, 1453, 1421, 1367, 1314, 1267, 1249, 1173, 1094, 1094, 1031, 1002, 857, 838, 754, 710, 698, 666, 602,

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560, 475; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.92 (2H, m, Ar-H), 7.81-7.73 (4H, m, Ar-H), 7.48-7.43 (6H, m, Ar-H), 7.36-7.34 (5H, m, Ar-H), 7.30-7.27 (2H, m, Ar-H), 7.23-7.21 (1H, m, Ar-H), 7.16-7.13 (7H, m, Ar-H), 5.48 (1H, s, PhC*H*), 5.19 (1H, t, *J* 7.9, 2-H), 5.04 (1H, d, *J* 11.3, ArCH_2), 4.93 (1H, d, *J* 11.3, ArCH_2), 4.75 (1H, d, *J* 11.3, ArCH_2), 4.61-4.60 (2H, m, 6-H_a, ArCH_2), 4.49 (1H, d, *J* 7.8, 1-H), 4.39 (1H, d, *J* = 8.1, 1'-H), 4.34-4.30 (3H, m, 6-H_b, ArCH_2), 4.16-4.13 (2H, m, ArCH_2), 4.07 (1H, dd, *J* 10.6, 4.8, 6'-H_a), 3.96 (1H, t, *J* 9.1, 4-H), 3.81-3.75 (2H, m, 3-H, CH_2), 3.63-3.61 (3H, m, 3'-H, 5-H, 4'-H), 3.45-3.36 (3H, m, 2'-H, 6'-H_b, CH_2), 3.24-3.22 (1H, m, 5'-H), 2.98-2.87 (2H, m, CH_2), 2.08 (3H, s, OCOCH_3); 1.44 (2H, m, CH_2), 1.32 (2H, m, CH_2), 1.10 (2H, m, CH_2), 0.95 (2H, m, CH_2), 0.01-0.01 (9H, m, TMS); ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.5 (C), 165.0 (C), 157.0 (C), 138.1 (C), 138.0 (C), 137.0 (C), 135.0 (C), 133.2 (C), 133.0 (CH), 129.8 (C), 129.6 (CH), 129.1 (CH), 128.4 (CH), 128.3 (CH), 128.2 (CH), 128.1 (CH), 127.9 (CH), 127.6 (CH), 127.5 (CH), 127.4 (CH), 127.1 (CH), 126.1 (CH), 126.0 (CH), 126.0 (CH), 125.9 (CH), 102.0 (CH), 101.3 (CH), 101.0 (CH), 81.5 (CH), 80.5 (CH), 79.2 (CH), 77.9 (CH), 77.2 (CH), 76.8 (CH), 75.0 (CH_2), 74.5 (CH_2), 73.1 (CH), 73.0 (CH), 69.8 (CH_2), 68.3 (CH_2), 66.7 (CH), 66.2 (CH), 63.5 (CH_2), 62.4 (CH_2), 50.2 (CH), 46.6 (CH_2), 29.0 (CH_2), 27.2 (CH_2), 23.0 (CH_2), 20.9 (CH_3), 17.8 (CH_2), -1.5 (CH_3); HRMS (ESI): *m/z* calcd for $C_{64}H_{74}N_4O_{14}SiNa$ ([M+Na]$^+$): 1173.4863, found: 1173.4877.

***N*-Benzyl-*N*-2-(trimethylsilyl)ethoxycarbonyl-5-aminopentyl [2-azido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranosyl]-(1→4)-6-acetyl-2-benzoyl-3-benzyl-β-D-glucopyranoside (20).** A solution of compound **4** (518 mg, 0.450 mmol) in a mixed solvent CH_2Cl_2 and water (10/1, v/v, 5.5 mL) was added with DDQ (153 mg, 2.01 mmol) in three equal portions and in half-hour intervals at room temperature. After 2 h, the reaction was quenched with $NaHCO_{3(aq)}$ and $Na_2S_2O_{3(aq)}$. The crude product was extracted with CH_2Cl_2. The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (ethyl acetate/hexanes = 1/2, v/v) to give 3'-alcohol **20** (349 mg, 78%). $[\alpha]_D^{24}$ –4.4 (*c* 2.1 in $CHCl_3$); IR (thin film): ν_{max}/cm^{-1} 3444, 3064, 3031, 2951, 2113, 1732, 1688, 1603, 1496, 1453, 1422, 1367, 1314, 1267, 1250, 1171, 1093, 1056, 1029, 996, 838, 753, 711, 699, 665, 603, 555; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.94 (2H, m, Ar-H), 7.48-7.42 (3H, m, Ar-H), 7.36-7.22 (8H, m, Ar-H), 7.17-7.12 (7H, m, Ar-H), 5.41 (1H, s, PhC*H*), 5.22 (1H, dd, *J* 9.0, 8.9, 2-H), 4.77 (1H, d, *J* 11.3, ArCH_2), 4.63 (1H, d, *J* 11.3, ArCH_2), 4.60 (1H, d, *J* 11.9, 6-H_a), 4.52 (1H, d, *J* 7.9, 1-H), 4.41 (1H, d, *J* 8.1, 1'-H), 4.35-4.32 (2H, m, ArCH_2), 4.33 (1H, dd, *J* 12.1, 4.6, 6-H_b), 4.17 (2H, m, CH_2), 4.08 (1H, dd, *J* 10.6, 4.9, 6'-H_a), 3.98 (1H, t, *J* 9.1, 4-H), 3.81 (1H, m, CH_2), 3.79 (1H, t, *J* 8.8, 3-H), 3.68-3.64 (2H, m, 5-H, 3'-H), 3.44-3.34 (4H, m, 2'-H, 4'-H, 6'H_b, CH_2), 3.22-3.18 (2H, m, 5'-H, CH_2), 3.00-2.89 (2H, m, CH_2), 2.09 (3H, s, OCOCH_3); 1.45 (2H, m, CH_2), 1.33 (2H, m, CH_2), 1.10 (2H, m, CH_2), 0.97 (2H, m, CH_2), 0.02 (9H, m, TMS); ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.5 (C), 165.0 (C), 157.0 (C), 138.03 (C), 137.99 (C), 136.7 (C), 133.0 (CH), 129.7 (C), 129.6 (CH), 129.3 (CH), 128.3 (CH), 128.2 (CH), 128.0 (CH), 127.6 (CH), 127.4 (CH), 127.0 (CH), 126.1 (CH), 101.9 (CH), 101.8 (CH), 100.9 (CH), 80.5 (CH), 80.3 (CH), 77.8 (CH), 74.4 (CH_2), 73.0 (CH), 72.3 (CH), 69.7 (CH_2), 68.2 (CH_2), 67.0 (CH), 66.1 (CH), 63.4 (CH_2), 62.40 (CH_2), 50.1 (CH_2), 46.5 (CH_2), 28.9 (CH), 27.6 (CH_2), 22.9 (CH_2), 20.8 (CH_3), 17.7 (CH_2), -1.6 (CH_3); HRMS (ESI): *m/z* calcd for $C_{13}H_{18}N_3O_4SNa$ ([M+H]$^+$): 1033.4237, found: 1033.4240.

***N*-Benzyl-*N*-2-(trimethylsilyl)ethoxycarbonyl-5-aminopentyl [2-azido-4,6-*O*-benzylidene-2-deoxy-3-*O*-(2-naphthylmethyl)-β-D-glucopyranosyl]-(1→4)-(6-acetyl-2-benzoyl-3-benzyl-β-D-glucopyranosyl)-(1→3)-[2-azido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranosyl]-(1→4)-6-acetyl-2-benzoyl-3-benzyl-β-D-glucopyranose (5).** A mixture of donor **7** (2.77 g, 2.95 mmol) and acceptor **20** (2.44 g, 2.46 mmol) in anhydrous CH_2Cl_2 (60 mL) was added to a reaction flask containing freshly dried 3 Å molecular sieves (1.50 g) at room temperature under nitrogen atmosphere. After stirring for 1 h, the reaction flask was cooled to –78 °C and NIS (776 mg, 3.45 mmol) and TfOH (44.0 μL, 0.492 mmol) were sequentially added. The reaction was gradually warmed to –40 °C and kept going for 3 h. The reaction was filtered through Celite and quenched with $NaHCO_{3(aq)}$ and $Na_2S_2O_{3(aq)}$. The crude product was extracted with CH_2Cl_2. The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (ethyl acetate/hexane = 1/2, v/v) to yield compound **5** (3.52 g, 79%). $[\alpha]_D^{24}$ –26.5 (*c* 2.4 in $CHCl_3$); IR (thin film): ν_{max}/cm^{-1} 3063, 3031, 2950, 2874, 2112, 1738, 1732, 1693, 1602, 1585, 1496, 1454, 1418, 1367, 1314, 1267, 1249, 1174, 1094, 1030, 1003, 839, 753, 710, 699, 666, 604, 552, 476; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.07(2H, m, Ar-H), 7.96 (2H, m, Ar-H), 7.83-7.76 (4H, m, Ar-H), 7.58 (1H, m, Ar-H), 7.53-7.43 (10H, m, Ar-H), 7.40-7.35 (8H, m, Ar-H), 7.33-7.30 (2H, m, Ar-H), 7.26 (1H, m, Ar-H), 7.20-7.16 (12H, m, Ar-H), 5.52 (1H, s, PhC*H*), 5.50 (1H, s, PhC*H*), 5.32 (1H, t, *J* 8.8, 2''-H), 5.22 (1H, t, *J* 8.4, 2-H), 5.07 (1H, d, *J* 11.4, ArCH_2), 4.96 (1H, d, *J* 11.4, ArCH_2), 4.85 (1H, d, *J* 7.9, 1''-H), 4.80 (1H, d, *J* 11.3, ArCH_2), 4.74 (1H, d, *J* 11.2, ArCH_2), 4.65 (1H, d, *J* 11.3, ArCH_2), 4.60 (1H, d, *J* 11.2, ArCH_2), 4.53 (1H, d, *J* 11.0, 6-H_a), 4.49 (1H, d, *J* 7.9, 1-H), 4.40-4.35 (5H, m, 1'-H, 1'''-H, 6-H_b, 6''-H_a, CH_2), 4.22-4.09 (6H, m, 6'-H_a, 6''-H_b, 6'''-H_a, CH_2), 4.01 (1H, t, *J* 9.2, 4''-H), 3.97 (1H, t, *J* 8.9, 4-H), 3.81 (1H, m, CH_2), 3.81 (2H, m, 3''-H, CH_2), 3.75 (1H, t, *J* 8.8, 3-H), 3.68-3.61 (5H, m, 3'-H, 3'''-H, 4'''-H, 5-H, 5''-H), 3.48-3.43 (4H, m, 2'''-H, 4'-H, 6'-H_b, 6'''H_b), 3.38 (1H, s, CH_2), 3.34 (1H, t, *J* 8.7, 2'-H), 3.25-3.21 (2H, m, 5'-H, 5'''-H), 3.03-2.94 (2H, m, CH_2), 2.07 (3H, s, OCOCH_3), 2.02 (3H, s, OCOCH_3), 1.46 (2H, m, CH_2), 1.36 (2H, m, CH_2), 1.13 (2H, m, CH_2), 1.01 (2H, m, CH_2), 0.05 (9H, m, TMS); ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.2 (C), 170.1 (C), 164.9 (C), 164.8 (C), 156.8 (C), 137.9 (C), 137.82 (C), 137.75 (C), 136.8 (C), 136.7 (C), 134.9 (C), 133.0 (C), 132.89 (C), 132.85 (CH), 129.6 (C), 129.6 (C), 129.4 (CH), 129.4 (CH), 129.1 (CH), 128.9 (CH), 128.22 (CH), 128.19 (CH), 128.11 (CH), 128.07 (CH), 128.0 (CH), 127.9 (CH), 127.7 (CH), 127.5 (CH), 127.4 (CH), 127.31 (CH), 127.27 (CH), 127.24 (CH), 127.20 (CH), 126.9 (CH), 126.8 (CH), 125.9 (CH), 125.80 (CH), 125.76 (CH), 101.9 (CH), 101.7 (CH), 101.3 (CH), 101.1 (CH), 100.8 (CH), 100.7 (CH), 81.3 (CH), 80.3 (CH), 80.0 (CH), 79.2 (CH), 79.1 (CH), 78.9 (CH), 77.4 (CH), 77.3 (CH), 74.7 (CH_2), 74.4 (CH_2), 73.2 (CH), 72.9 (CH), 72.8 (CH), 69.5 (CH_2), 68.1 (CH_2), 66.5 (CH), 66.2 (CH), 66.1 (CH), 66.0 (CH), 63.3 (CH_2), 62.0 (CH_2), 61.8 (CH_2), 50.0 (CH_2), 46.4 (CH_2), 28.8 (CH), 27.4 (CH_2), 22.8 (CH_2), 20.7

(CH_3), 20.6 (CH_2), 17.6 (CH_3), -1.7 (CH_3); HRMS (ESI): *m/z* calcd for $C_{99}H_{109}N_7O_{25}SiNa$ ([M+Na]$^+$): 1847.7165, found: 1847.7163.

_N_-Benzyl-_N_-2-(trimethylsilyl)ethoxycarbonyl-5-aminopentyl [2-azido-4,6-_O_-benzylidene-2-deoxy-β-D-glucopyranosyl]-(1→4)-6-(acetyl-2-benzoyl-3-benzyl-β-D-glucopyranosyl)-(1→3)-[2-azido-4,6-_O_-benzylidene-2-deoxy-β-D-glucopyranosyl]-(1→4)-6-acetyl-2-benzoyl-3-benzyl-β-D-glucopyranose (21). DDQ (150 mg, 0.661 mmol) was added to a solution of compound **5** (265 mg, 0.145 mmol) in a mixed solvent CH_2Cl_2 and water (10/1, v/v, 4.4 mL) in three equal portions and in half-hour intervals at room temperature. After 2 h, the reaction was quenched with the addition of $NaHCO_{3(aq)}$ and $Na_2S_2O_{3(aq)}$. The crude product was extracted with CH_2Cl_2. The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (ethyl acetate/hexanes = 2/3, v/v) to give the 3'''-alcohol **21** (168 mg, 69%). $[\alpha]_D^{24}$ –1.9 (*c* 2.1 in $CHCl_3$); IR (thin film): ν_{max}/cm^{-1} 3444, 2952, 2113, 1731, 1682, 1645, 1497, 1453, 1422, 1367, 1315, 1267, 1173, 1093, 1030, 1002, 838, 753, 699, 666; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.02 (2H, m, Ar-H), 7.92 (2H, d, *J* 7.3, Ar-H), 7.56 (1H, m, Ar-H), 7.47-7.41 (7H, m, Ar-H), 7.35-7.32 (8H, m, Ar-H), 7.30-7.27 (2H, m, Ar-H), 7.23 (1H, m, Ar-H), 7.16-7.10 (12H, m, Ar-H), 5.47 (1H, s, PhC*H*), 5.41 (1H, s, PhC*H*), 5.27 (1H, dd, *J* 8.9, 8.2, 2''-H), 5.15 (1H, t, *J* 9.1, 2-H), 4.80 (1H, d, *J* 7.9 Hz, 1''-H), 4.75 (1H, d, *J* 11.3, ArCH_2), 4.69 (1H, d, *J* 11.2, ArCH_2), 4.60 (1H, d, *J* 11.2, ArCH_2), 4.55 (1H, d, *J* 11.3, ArCH_2), 4.48 (1H, d, *J* 11.3, 6-H$_a$), 4.45 (1H, d, *J* 7.9, 1-H), 4.34-4.31 (5H, m, 1'-H, 1'''-H, 6-H$_b$, 6''-H$_a$, CH_2), 4.17-4.04 (6H, m, 6'-H$_a$, 6''-H$_b$, 6'''-H$_a$, CH_2), 3.96 (1H, t, *J* 9.1, 4''-H), 3.92 (1H, t, *J* 9.0, 4-H), 3.77 (1H, m, CH_2), 3.76 (1H, t, *J* 8.9, 3''-H), 3.71 (1H, t, *J* 8.8, 3-H), 3.65-3.54 (4H, m, 3'-H, 3'''-H, 5-H, 5''-H), 3.44-3.37 (4H, m, 2'''-H, 4'-H, 6'-H$_b$, 6'''H$_b$), 3.34-3.27 (3H, m, 2'-H, 4'''-H, CH_2), 3.20-3.15 (2H, m, 5'-H, 5'''-H), 3.00 (1H, s, CH_2), 2.89 (1H, m, CH_2), 2.04 (3H, s, OCOCH_3), 1.99 (3H, s, OCOCH_3), 1.42 (2H, m, CH_2), 1.31 (2H, m, CH_2), 1.10 (2H, m, CH_2), 0.96 (2H, m, CH_2), 0.01 (9H, m, TMS); ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.4 (C), 170.3 (C), 165.1 (C), 164.9 (C), 156.5 (C), 138.1 (C), 137.9 (C), 137.9 (C), 136.8 (C), 136.6 (C), 133.03 (CH) 133.00 (CH) 129.8 (C), 129.7 (C), 129.59 (CH) 129.55 (CH) 129.30 (CH) 129.25 (CH) 128.36 (CH) 128.33 (CH) 128.28 (CH) 128.25 (CH) 128.1 (CH) 127.6 (CH) 127.5 (CH) 127.4 (CH) 127.1 (CH) 126.1 (CH) 126.0 (CH) 102.0 (CH) 101.84 (CH) 101.79 (CH) 101.5 (CH) 101.0 (CH) 100.9 (CH) 80.5 (CH) 80.4 (CH) 80.2 (CH) 79.4 (CH) 79.3 (CH) 77.5 (CH) 77.3 (CH) 74.54 (CH_2), 74.51 (CH_2), 73.3 (CH) 73.1 (CH) 72.9 (CH) 72.2 (CH) 69.7 (CH_2), 68.2 (CH_2), 67.0 (CH) 66.4 (CH) 66.3 (CH) 66.2 (CH) 63.5 (CH_2), 62.2 (CH_2), 62.0 (CH_2), 60.3 (CH_2), 50.2 (CH_2), 45.9 (CH_2), 28.9 (CH_2), 27.6 (CH_2), 22.9 (CH_2), 20.8 (CH_3), 20.8 (CH_3), 17.7 (CH_2), 14.1 (CH_3), -1.6 (CH_3); HRMS (ESI): *m/z* calcd for $C_{88}H_{101}N_7O_{25}SiNa$ ([M+Na]$^+$): 1707.6539, found: 1707.6544.

_N_-Benzyl-_N_-2-(trimethylsilyl)ethoxycarbonyl-5-aminopentyl [2-azido-4,6-_O_-benzylidene-2-deoxy-3-_O_-(2-naphthylmethyl)-β-D-glucopyranosyl]-(1→4)-(6-acetyl-2-benzoyl-3-benzyl-β-D-glucopyranosyl)-(1→3)-[2-azido-4,6-_O_-(benzylidene)-2-deoxy-β-D-glucopyranosyl]-(1→4)-(6-acetyl-2-benzoyl-3-benzyl-β-D-glucopyranosyl)-(1→3)-[2-azido-4,6-_O_-(benzylidene)-2-deoxy-β-D-glucopyranosyl]-(1→4)-6-acetyl-2-benzoyl-3-benzyl-β-D-glucopyranose (6). A mixture of donor **7** (85.7 mg, 91.4 μmol) and acceptor **21** (126 mg, 74.8 μmol) in anhydrous CH_2Cl_2 (4.6 mL) was added to a reaction flask containing freshly dried 3 Å molecular sieves (115 mg) at room temperature under nitrogen atmosphere. After stirring for 1 h, the reaction flask was cooled to –78 °C and NIS (24.0 mg, 107 μmol) and TfOH (1.3 μL, 18 μmol) were sequentially added. The reaction was gradually warmed up to –40 °C and kept going for 3 h. After the donor **7** was consumed completely, the reaction was filtered through Celite and quenched with $NaHCO_{3(aq)}$ and $Na_2S_2O_{3(aq)}$. The crude product was extracted with CH_2Cl_2. The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (ethyl acetate/ hexane = 1/2, v/v) to yield compound **6** (145 mg, 77%). $[\alpha]_D^{24}$ –16.0 (*c* 1.7 in $CHCl_3$); IR (thin film): ν_{max}/cm^{-1} 3064, 3031, 2925, 2873, 2113, 1738, 1732, 1693, 1602, 1585, 1496, 1454, 1417, 1367, 1315, 1267, 1250, 1174, 1094, 1031, 1003, 918, 839, 753, 710, 699, 666, 603, 552, 476; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.02(2H, m, Ar-H), 8.00 (2H, m, Ar-H), 7.92 (2H, m, Ar-H), 7.82-7.79 (4H, m, Ar-H), 7.60-7.55 (2H, m, Ar-H), 7.49-7.41 (14H, m, Ar-H), 7.37-7.33 (8H, m, Ar-H), 7.30-7.28 (4H, m, Ar-H), 7.23 (1H, m, Ar-H), 7.18-7.09 (18H, m, Ar-H), 5.48 (1H, s, PhC*H*), 5.47 (1H, s, PhC*H*), 5.45 (1H, s, PhC*H*), 5.26 (1H, t, *J* 8.5, 2''''-H), 5.21 (1H, t, *J* 8.7, 2''-H), 5.15 (1H, t, *J* 8.7, 2-H), 5.04 (1H, d, *J* 11.4, ArCH_2), 4.93 (1H, d, *J* 11.4, ArCH_2), 4.79-4.73 (3H, m, 1''-H, 1''''-H, ArCH_2), 4.70-4.67 (2H, m, ArCH_2), 4.61 (1H, d, *J* 11.2, ArCH_2), 4.55 (1H, d, *J* 11.8, ArCH_2), 4.53 (1H, d, *J* 11.6, ArCH_2), 4.47 (1H, d, *J* 11.6, 6-H$_a$), 4.45 (1H, d, *J* 7.9, 1-H), 4.35-4.30 (5H, m, 1'''-H, 1'''''-H, 6-H$_b$, 6''-H$_a$, CH_2), 4.23-4.04 (9H, m, 1'-H, 6'-H$_a$, 6''-H$_b$, 6'''-H$_a$, 6''''-H$_a$, 6'''''-H$_a$, CH_2), 3.96 (1H, t, *J* 9.1, 4''-H), 3.93-3.89 (2H, m, 4-H, 4''''-H), 3.86 (1H, m, 6''''-H), 3.78-3.74 (2H, m, 3''''-H, CH_2), 3.70 (1H, t, *J* 8.9, 3-H), 3.68 (1H, t, *J* 8.9, 3''-H), 3.65-3.53 (7H, m, 3'-H, 3'''-H, 3'''''-H, 4'-H, 4'''-H, 4'''''-H 5-H), 3.44-3.38 (5H, m, 2'''''-H, 5''-H, 6'-H$_b$, 6'''-H$_b$, 6'''''-H$_b$), 3.34 (1H, s, CH_2), 3.30-3.13 (6H, m, 2'-H, 2'''-H, 5'-H, 5'''-H, 5''''-H, 5'''''-H), 2.99-2.89 (2H, m, CH_2), 2.04 (3H, s, OCOCH_3), 1.98 (3H, s, OCOCH_3), 1.94 (3H, s, OCOCH_3), 1.42 (2H, m, CH_2), 1.30 (2H, m, CH_2), 1.08 (2H, m, CH_2), 0.97 (2H, m, CH_2), 0.01 (9H, m, TMS); ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.4 (C), 170.3 (C), 170.2 (C), 165.08 (C), 165.06 (C), 164.9 (C), 156.5 (C), 138.1 (C), 138.0 (C), 137.9 (C), 137.8 (C), 136.9 (C), 136.8 (C), 135.0 (C), 133.2 (C), 133.0 (CH), 129.8 (C), 129.8 (C), 129.63 (CH), 129.59 (CH), 129.3 (CH), 129.2 (CH), 129.1 (CH), 128.4 (CH), 128.34 (CH), 128.27 (CH), 128.26 (CH), 128.13 (CH), 128.09 (CH), 128.07 (CH), 127.9 (CH), 127.63 (CH), 127.58 (CH), 127.57 (CH), 127.5 (CH), 127.4 (CH), 127.1 (CH), 127.0 (CH), 126.02 (CH), 125.98 (CH), 125.95 (CH), 102.0 (CH), 101.93 (CH), 101.89 (CH), 101.49 (CH), 101.47 (CH), 101.3 (CH), 101.1 (CH), 101.0 (CH), 100.9 (CH), 81.5 (CH), 80.5 (CH), 80.3 (CH), 80.2 (CH), 79.4 (CH), 79.34 (CH), 79.29 (CH), 79.1 (CH), 77.5 (CH), 77.4 (CH), 77.1 (CH), 74.9 (CH_2), 74.7 (CH_2), 74.57 (CH_2), 74.56 (CH_2), 73.4 (CH), 73.2 (CH), 73.1 (CH), 73.03 (CH), 72.96 (CH), 69.7 (CH_2), 68.29 (CH_2), 68.25 (CH_2), 66.7 (CH), 66.4 (CH), 66.3 (CH), 66.2 (CH), 63.5 (CH_2), 62.2 (CH_2), 62.0 (CH_2), 61.7 (CH_2), 50.2 (CH_2), 46.6 (CH_2), 29.6 (CH_2), 29.0 (CH_2), 27.6 (CH_2), 23.0 (CH_2), 20.83 (CH_3), 20.80 (CH_3), 20.77

(CH_3), 17.8 (CH_2), -1.5 (CH_3); HRMS (ESI): *m/z* calcd for $C_{134}H_{144}N_{10}O_{36}SiNa$ ([M+Na]$^+$): 2520.9417, found: 2520.9437.

_N_-Benzyl-_N_-2-(trimethylsilyl)ethoxycarbonyl-5-aminopentyl [2-azido-4,6-_O_-benzylidene-2-deoxy-3-_O_-(2-naphthylmethyl)-β-D-glucopyranosyl]-(1→4)-2-benzoyl-3-benzyl-β-D-glucopyranoside (22). Magnesium methoxide (7–8%) in MeOH (2.00 mL, 1.63 mmol) was added to a solution of compound **4** (188 mg, 0.163 mmol) in CH_2Cl_2 (4 mL) under nitrogen atmosphere at 0 °C. After 2 h, the reaction was quenched with $HCl_{(aq)}$ until the solution was neutral. The organic solvent was removed under reduced pressure. The crude product was extracted with CH_2Cl_2. The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (ethyl acetate/ hexane = 1/2, v/v) to give alcohol **22** (179 mg, 99%). $[\alpha]_D^{24}$ –49.5 (*c* 3.1 in $CHCl_3$); IR (thin film): ν_{max}/cm^{-1} 3444, 2953, 2111, 1729, 1660, 1645, 1634, 1453, 1421, 1367, 1314, 1268, 1172, 1093, 1030, 1001, 837, 752, 698, 666; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.95 (2H, m, Ar-H), 7.83-7.75 (4H, m, Ar-H), 7.52-7.45 (6H, m, Ar-H), 7.38-7.35 (5H, m, Ar-H), 7.32-7.30 (2H, m, Ar-H), 7.26-7.25 (1H, m, Ar-H), 7.16-7.14 (7H, m, Ar-H), 5.50 (1H, s, PhC*H*), 5.20 (1H, t, *J* 8.5 Hz, 2-H), 5.07 (1H, d, *J* 11.4, ArCH_2), 4.95 (1H, d, *J* 11.4, ArCH_2), 4.81 (1H, d, *J* 11.4, ArCH_2), 4.65 (1H, d, *J* 11.4, ArCH_2), 4.59 (1H, d, *J* 8.0, 1'-H), 4.54 (1H, d, *J* 7.9, 1-H), 4.37-4.34 (2H, m, ArCH_2), 4.21-4.12 (3H, m, 6'-H_a, CH_2), 4.12 (1H, t, *J* 9.2, 4-H), 4.03-3.98 (2H, m, 6-H_a, 6-H_b), 3.82 (1H, m, CH_2), 3.79 (1H, t, *J* 9.2, 3-H), 3.69-3.65 (2H, m, 3'-H, 4'-H), 3.51-3.35 (5H, m, 2'-H, 5-H, 5'-H 6'H_b, CH_2), 3.03-2.92 (2H, m, CH_2), 1.47 (2H, m, CH_2), 1.35 (2H, m, CH_2), 1.14 (2H, m, CH_2), 0.99 (2H, m, CH_2), 0.03 (9H, m, TMS); ^{13}C NMR (150 MHz, $CDCl_3$): δ 164.9 (C), 156.5 (C), 138.2 (C), 138.1 (C), 137.1 (C), 135.1 (C), 133.2 (C), 133.0 (C), 132.94 (CH), 129.85 (C), 129.6 (CH), 129.0 (CH), 128.4 (CH), 128.2 (CH), 128.1 (CH), 128.0 (CH), 127.9 (CH), 127.6 (CH), 127.3 (CH), 127.1 (CH), 127.0 (CH), 126.1 (CH), 126.0 (CH), 125.9 (CH), 101.7 (CH), 101.3 (CH), 101.1 (CH), 81.7 (CH), 80.2 (CH), 79.1 (CH), 75.3 (CH), 74.9 (CH_2), 74.3 (CH_2), 73.1 (CH), 69.6 (CH_2), 68.4 (CH), 66.8 (CH), 65.9 (CH), 63.5 (CH_2), 60.8 (CH_2), 49.9 (CH_2), 46.6 (CH_2) 29.0 (CH_2), 27.0 (CH_2), 22.9 (CH_2), 17.8 (CH_2), -1.5 (CH_3); HRMS (ESI): *m/z* calcd for $C_{62}H_{72}N_4O_{13}SiNa$ ([M+Na]$^+$): 1159.4707, found: 1131.4775.

_N_-Benzyl-_N_-2-(trimethylsilyl)ethoxycarbonyl-5-aminopentyl [2-azido-4,6-_O_-benzylidene-2-deoxy-3-_O_-(2-naphthylmethyl)-β-D-glucopyranosyl]-(1→4)-(2-_O_-benzoyl-3-_O_-benzyl-β-D-glucopyranosyl)-(1→3)-[2-azido-4,6-_O_-benzylidene-2-deoxy-β-D-glucopyranosyl]-(1→4)-2-_O_-benzoyl-3-_O_-benzyl-β-D-glucopyranoside (23). Magnesium methoxide (7-8%) in MeOH (630 µL, 576 µmol) was added to a solution of compound **5** (52.6 mg, 28.8 µmol) in CH_2Cl_2 (2 mL) under nitrogen atmosphere at 0 °C. After 2 h, the reaction was quenched with $HCl_{(aq)}$ until the solution was neutral. The organic solvent was removed under reduced pressure. The crude product was extracted with CH_2Cl_2. The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (ethyl acetate/ hexane = 2/3, v/v) to give compound **23** (46.8 mg, 92%). $[\alpha]_D^{24}$ –14.8 (*c* 2.0 in $CHCl_3$); IR (thin film): ν_{max}/cm^{-1} 3440, 2953, 2111, 1726, 1645, 1634, 1496, 1453, 1420, 1367, 1315, 1269, 1175, 1095, 1071, 1002, 913, 837, 819, 752, 699, 666; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.04 (2H, m, Ar-H), 7.91 (2H, d, *J* 7.4, Ar-H), 7.82-7.74 (4H, m, Ar-H), 7.57 (1H, m, Ar-H), 7.49-7.28 (10H, m, Ar-H), 7.37-7.33 (8H, m, Ar-H), 7.30-7.28 (2H, m, Ar-H), 7.23 (1H, m, Ar-H), 7.12-7.09 (12H, m, Ar-H), 5.48 (1H, s, PhC*H*), 5.42 (1H, s, PhC*H*), 5.23 (1H, t, *J* 8.6 Hz, 2''-H), 5.12 (1H, t, *J* 8.9, 2-H), 5.03 (1H, d, *J* 11.5, ArCH_2), 4.92 (1H, d, *J* 11.5, ArCH_2), 4.79-4.75 (2H, m, 1''-H, ArCH_2), 4.71 (1H, d, *J* 11.3, ArCH_2), 4.60 (1H, d, *J* 11.3, ArCH_2), 4.53 (2H, m, 1'''-H, ArCH_2), 4.47-4.44 (2H, m, 1-H, 1'-H), 4.35 (2H, m, CH_2), 4.42-4.11 (4H, m, 6'-H_a, 6'''-H_a, CH_2), 4.06 (1H, t, *J* 9.2, 4-H), 4.01 (1H, t, *J* 9.2, 4''-H), 3.90 (1H, d, *J* 11.94, 6-H_a), 3.74-3.73 (3H, m, 3-H, 6-H_b, CH_2), 3.69-3.65 (3H, m, 3''-H, 6''-H_a, 6''-H_b), 3.63 (1H, t, *J* 10.2, 3'-H), 3.60 (1H, t, *J* 9.2, 4'-H), 3.55 (1H, t, *J* 9.2, 3'''-H), 3.51 (1H, t, *J* 9.1, 4'''-H), 3.44-3.37 (5H, m, 2'-H, 5-H, 6'-H_b, 6'''-H_b, CH_2), 3.32-3.27 (3H, m, 5'-H, 5''-H, 5'''-H), 3.25 (1H, t, *J* = 8.7 Hz, 2'''-H), 3.01-2.89 (2H, m, CH_2), 1.43 (2H, m, CH_2), 1.31 (2H, m, CH_2), 1.11 (2H, m, CH_2), 0.97 (2H, m, CH_2), 0.01 (9H, m, TMS); ^{13}C NMR (150 MHz, $CDCl_3$): δ 165.2 (C), 165.0 (C), 156.6 (C), 138.2 (C), 138.1 (C), 137.08 (C), 137.05 (C), 135.1 (C), 133.2 (C), 133.1 (C), 133.0 (CH), 129.9 (C), 129.8 (C), 129.7 (CH), 129.6 (CH), 129.4 (CH), 129.1 (CH), 128.42 (CH), 128.39 (CH), 128.34 (CH), 128.28 (CH), 128.26 (CH), 128.14 (CH), 128.04 (CH), 128.01 (CH), 127.95 (CH), 127.7 (CH), 127.64 (CH), 127.60 (CH), 127.4 (CH), 127.12 (CH), 127.07 (CH), 126.1 (CH), 126.03 (CH), 125.99 (CH), 125.9 (CH), 102.0 (CH), 101.71 (CH), 101.66 (CH), 101.5 (CH), 101.3 (CH), 101.2 (CH), 81.7 (CH), 80.3 (CH), 80.0 (CH), 79.4 (CH), 79.1 (CH), 79.0 (CH), 76.4 (CH), 75.2 (CH), 75.1 (CH), 74.9 (CH_2), 74.5 (CH_2), 74.4 (CH_2), 73.4 (CH), 73.0 (CH), 69.6 (CH_2), 68.4 (CH_2), 68.3 (CH_2), 66.8 (CH), 66.6 (CH), 66.4 (CH), 66.0 (CH), 63.5 (CH_2), 60.7 (CH_2), 49.9 (CH_2), 46.6 (CH_2), 29.0 (CH_2), 27.0 (CH_2), 22.9 (CH_2), -1.5 (CH_3); HRMS (ESI): *m/z* calcd for $C_{95}H_{105}N_7O_{23}SiNa$ ([M+Na]$^+$): 1763.6954, found: 1763.6958.

_N_-Benzyl-_N_-2-(trimethylsilyl)ethoxycarbonyl-5-aminopentyl [2-azido-4,6-_O_-benzylidene-2-deoxy-3-_O_-(2-naphthylmethyl)-β-D-glucopyranosyl]-(1→4)-(2-_O_-benzoyl-3-_O_-benzyl-β-D-glucopyranosyl)-(1→3)-[2-azido-4,6-_O_-benzylidene-2-deoxy-3-_O_-(2-nathphylmethyl)-β-D-glucopyranosyl]-(1→4)-(2-_O_-benzoyl-3-_O_-benzyl-β-D-glucopyranosyl)-(1→3)-[2-azido-4,6-_O_-benzylidene-2-deoxy-β-D-glucopyranosyl]-(1→4)-2-_O_-benzoyl-3-_O_-benzyl-β-D-glucopyranoside (24). Magnesium methoxide (7-8%) in MeOH (15.2 mL, 12.4 mmol) was added to a solution of compound **6** (1.02 g, 0.413 mmol) in CH_2Cl_2 (15.2 mL) under nitrogen atmosphere at 0 °C. After 4 h, the reaction was quenched with $HCl_{(aq)}$ until the solution was neutral. The organic solvent was removed under reduced pressure. The crude product was extracted with CH_2Cl_2. The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (ethyl acetate/ hexane=3/4, v/v) to give compound **24** (877 mg, 89%). $[\alpha]_D^{24}$ –38.4 (*c* 4.2 in $CHCl_3$); IR (thin film): ν_{max}/cm^{-1} 3418, 3064, 3031, 2929, 2881, 2222, 2112, 1728, 1694, 1603, 1585, 1496, 1453, 1418, 1367, 1315, 1269, 1176, 1095, 1030, 1003, 839, 753, 699, 667, 620, 553, 477; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.06-8.03 (4H, m, Ar-H), 7.92 (2H, m, Ar-H), 7.83-7.75 (4H, m, Ar-H), 7.59-7.55 (2H, m, Ar-H), 7.50-7.42 (14H, m, Ar-H), 7.37-7.32 (11H, m, Ar-

H), 7.31-7.29 (2H, m, Ar-H), 7.25 (1H, m, Ar-H), 7.17-7.09 (17H, m, Ar-H), 5.49 (1H, s, PhC*H*), 5.42 (1H, s, PhC*H*), 5.41 (1H, s, PhC*H*), 5.24 (1H, t, *J* 8.5, 2''''-H), 5.20 (1H, t, *J* 8.8, 2''-H), 5.14 (1H, t, *J* = 8.8 Hz, 2-H), 5.05 (1H, d, *J* 11.5, ArCH_2), 4.93 (1H, d, *J* 11.5, ArCH_2), 4.80 (1H, d, *J* 11.3, ArCH_2), 4.75-4.70 (4H, m, 1''-H, 1''''-H, ArCH_2), 4.62 (1H, d, *J* 11.3, ArCH_2), 4.55-4.52 (3H, m, 1'-H, ArCH_2), 4.47-4.45 (2H, m, 1-H, 1'''''-H), 4.42 (1H, d, *J* 8.0, 1'''-H), 4.36 (2H, m, CH_2), 4.19-4.13 (5H, m, 6'-H_a, 6'''-H_a, 6'''''-H_a, CH_2), 4.06 (1H, t, *J* 9.2, 4-H), 4.01 (1H, t, *J* 9.2, 4''''-H), 3.98 (1H, t, *J* 9.2, 4''-H), 3.90 (1H, d, *J* 11.7, 6-H_a), 3.78-3.72 (3H, m, 3''''-H, 6-H_b, CH_2), 3.70-3.48 (7H, m, 3-H, 3''-H, 3'''''-H, 4'''''-H, 6''-H_a, 6''''-H_a, 6''-H_b), 3.56-3.48 (4H, m, 3'-H, 3'''-H, 4'-H, 4'''-H), 3.47-3.36 (7H, m, 2'''''-H, 5-H, 6'-H_b, 6'''-H_b, 6''''-H, 6'''''-H_b, CH_2), 3.33-3.20 (7H, m, 2'-H, 2'''-H, 5'-H, 5''-H, 5'''-H, 5''''-H, 5'''''-H), 3.01-2.90 (2H, m, CH_2), 1.43-1.30 (4H, m, CH_2), 1.13-1.10 (2H, m, CH_2), 0.99-0.96 (2H, m, CH_2), 0.02 (9H, m, TMS); ^{13}C NMR (150 MHz, $CDCl_3$): δ 165.14 (C), 165.10 (C), 164.9 (C), 156.5 (C), 138.2 (C), 138.1 (C), 138.0 (C), 137.1 (C), 137.0 (C), 135.1 (C), 133.2 (C), 133.03 (C), 132.99 (CH), 129.81 (C), 129.77 (C), 129.74 (C), 129.69 (CH), 129.6 (CH), 129.4 (CH), 129.3 (CH), 129.0 (CH), 128.40 (CH), 128.37 (CH), 128.29 (CH), 128.26 (CH), 128.2 (CH), 128.1 (CH), 128.02 (CH), 127.97 (CH), 127.9 (CH), 127.7 (CH), 127.62 (CH), 127.55 (CH), 127.4 (CH), 127.1 (CH), 127.0 (CH), 126.1 (CH), 126.00 (CH), 125.95 (CH), 125.9 (CH), 102.00 (CH), 101.7 (CH), 101.6 (CH), 101.43 (CH), 101.41 (CH), 101.3 (CH), 101.1 (CH), 101.0 (CH), 100.9 (CH), 81.6 (CH), 80.3 (CH), 80.0 (CH), 79.3 (CH), 79.3 (CH), 79.0 (CH), 79.0 (CH), 76.6 (CH), 76.5 (CH), 75.2 (CH), 75.1 (CH), 75.0 (CH), 74.9 (CH_2), 74.5 (CH_2), 74.4 (CH_2), 73.4 (CH), 73.3 (CH), 73.00 (CH), 69.6 (CH_2), 68.4 (CH_2), 68.3 (CH_2), 66.8 (CH), 66.54 (CH), 66.48 (CH), 66.32 (CH), 66.29 (CH), 65.9 (CH), 63.5 (CH_2), 60.7 (CH_2), 60.6 (CH_2), 50.2 (CH_2), 46.6 (CH_2), 29.0 (CH_2), 27.0 (CH_2), 22.9 (CH_2), 17.8 (CH_2), -1.5 (CH_3); HRMS (ESI): *m/z* calcd for $C_{128}H_{139}N_{10}O_{33}Si$ ([M+H]$^+$): 2372.9301, found: 2372.9293.

***N*-Benzyl-*N*-2-(trimethylsilyl)ethoxycarbonyl-5-aminopentyl [2-azido-4,6-*O*-benzylidene-2-deoxy-3-*O*-(2-naphthylmethyl)-β-D-glucopyranosyl]-(1→4)-methyl 2-benzoyl-3-benzyl-β-D-glucopyranosyluronate (25).** TEMPO (13.9 mg, 88.8 μmol) and BAIB (286 mg, 888 μmol) were added to a solution of disaccharide **22** (395 mg, 0.356 mmol) in mixed solvent of CH_3CN and H_2O (10/1, v/v, 10.5 mL) at 0 °C. After 2 h, the reaction was quenched with $Na_2S_2O_{3(aq)}$ and $NaHCO_{3(aq)}$. The crude product was extracted with ethyl acetate. The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. A solution of the crude product in CH_2Cl_2 (10 mL) was added to a solution of diazomethane in ether (12 mL, 2.14 mmol) at 0 °C. After 20 min, the reaction was quenched with acetic acid. The resulting mixture was concentrated under reduced pressure and purified by silica gel column chromatography (ethyl acetate/hexanes = 1/3, v/v) to yield the methyl ester **25** (341 mg, 84% in 2 steps). $[\alpha]_D^{24}$ –43.7 (*c* 1.5 in $CHCl_3$); IR (thin film): ν_{max}/cm^{-1} 3456, 3063, 3030, 2951, 2870, 2112, 1732, 1693, 1603, 1585, 1496, 1469, 1453, 1421, 1367, 1314, 1267, 1249, 1173, 1094, 1094, 1031, 1002, 857, 838, 754, 710, 698, 666, 602, 560, 475; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.92 (2H, m, Ar-H), 7.81-7.73 (4H, m, Ar-H), 7.49-7.43 (6H, m, Ar-H), 7.37-7.35 (5H, m, Ar-H), 7.30-7.28 (2H, m, Ar-H), 7.23 (1H, m, Ar-H), 7.22-7.12 (7H, m, Ar-H), 5.47 (1H, s, PhC*H*), 5.21 (1H, t, *J* 7.8, 2-H), 5.03 (1H, d, *J* 11.5, ArCH_2), 4.91 (1H, d, *J* 11.5, ArCH_2), 4.78 (1H, d, *J* 11.4, ArCH_2), 4.62 (1H, d, *J* 11.4, ArCH_2), 4.59 (1H, d, *J* 7.5, 1-H), 4.50 (1H, d, *J* 8.0, 1'-H), 4.36 (2H, m, ArCH_2), 4.30 (1H, t, *J* 8.9, 4-H), 4.18-4.15 (2H, m, CH_2), 4.11 (1H, dd, *J* 10.4, 4.7, 6'-H_a), 4.07 (1H, d, *J* 9.2, 5-H), 3.83-3.78 (5H, m, 3-H, CH_2, OCH_3), 3.61 (1H, t, *J* 9.2, 4'-H), 3.56 (1H, t, *J* 9.2, 3'-H), 3.43-3.67 (3H, m, 2'-H, 6'-H_b, CH_2), 3.30 (1H, td, *J* 7.4, 4.9, 5'-H), 3.01-2.91 (2H, m, CH_2), 1.44 (2H, m, CH_2), 1.34 (2H, m, CH_2), 1.11 (2H, m, CH_2), 0.96 (2H, m, CH_2), 0.01 (9H, m, TMS); ^{13}C NMR (150 MHz, $CDCl_3$): δ 168.7 (C), 164.9 (C), 157.0 (C), 138.1 (C), 138.0 (C), 137.1 (C), 135.2 (C), 133.2 (C), 133.1 (C), 133.0 (C), 129.73 (C), 129.66 (CH), 129.1 (CH), 128.4 (CH), 128.31 (CH), 128.26 (CH), 128.1 (CH), 127.9 (CH), 127.7 (CH), 127.6 (CH), 127.5 (CH), 127.1 (CH), 126.9 (CH), 126.0 (CH), 125.9 (CH), 102.2 (CH), 101.4 (CH), 101.3 (CH), 81.5 (CH), 79.5 (CH), 79.0 (CH), 75.0 (CH_2), 74.5 (CH), 74.4 (CH_2), 72.9 (CH), 69.9 (CH), 68.3 (CH), 66.7 (CH), 66.1 (CH), 63.5 (CH_2), 52.8 (CH_3), 49.9 (CH_2), 45.9 (CH_2), 29.0 (CH_2), 27.3 (CH_2), 23.0 (CH_2), 17.8 (CH_2), -1.5 (CH_3); HRMS (ESI): *m/z* calcd for $C_{64}H_{74}N_4O_{14}SiNa$ ([M+Na]$^+$): 1173.4863, found: 1173.4877.

***N*-Benzyl-*N*-2-(trimethylsilyl)ethoxycarbonyl-5-aminopentyl [2-azido-4,6-*O*-benzylidene-2-deoxy-3-*O*-(2-naphthylmethyl)-β-D-glucopyranosyl]-(1→4)-(methyl 2-benzoyl-3-*O*-benzyl-β-D-glucopyranosyluronate)-(1→3)-[2-azido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranosyl]-(1→4)-methyl 2-*O*-benzoyl-3-*O*-benzyl-β-D-glucopyranosyluronate (26).** TEMPO (7.7 mg, 49.3 μmol) and BAIB (159 mg, 492 μmol) were added to a solution of tetrasaccharide **23** (172 mg, 98.5 μmol) in mixed solvent of CH_3CN and H_2O (10/1, v/v, 3.7 mL) at 0 °C. After 2 h, the reaction was quenched with $Na_2S_2O_{3(aq)}$ and $NaHCO_{3(aq)}$. The crude product was extracted with ethyl acetate. The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. A solution of the crude product in CH_2Cl_2 (5 mL) was added to a solution of diazomethane in ether (8 mL, 0.591 mmol) at 0 °C. After 20 min, the reaction solution was quenched with acetic acid. The resulting mixture was concentrated under reduced pressure and purified by silica gel column chromatography (ethyl acetate/hexanes = 1/3, v/v) to yield the methyl ester **26** (126 mg, 71% in 2 steps). $[\alpha]_D^{24}$ –32.8 (*c* 1.2 in $CHCl_3$); IR (thin film): ν_{max}/cm^{-1} 3063, 3030, 2952, 2925, 2856, 2222, 2114, 1955, 1732, 1693, 1602, 1496, 1454, 1439, 1421, 1373, 1315, 1267, 1223, 1174, 1094, 1029, 1003, 915, 857, 839, 755, 710 ,699, 666, 551, 476; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.01 (2H, m, Ar-H), 7.90 (2H, m, Ar-H), 7.82-7.74 (4H, m, Ar-H), 7.55 (1H, m, Ar-H), 7.48-7.43 (10H, m, Ar-H), 7.36-7.33 (8H, m, Ar-H), 7.29-7.28 (2H, m, Ar-H), 7.23 (1H, m, Ar-H), 7.17-7.10 (12H, m, Ar-H), 5.47 (1H, s, PhC*H*), 5.42 (1H, s, PhC*H*), 5.30 (1H, t, *J* 8.7, 2''-H), 5.17 (1H, t, *J* 8.8, 2-H), 5.03 (1H, d, *J* 11.5, ArCH_2), 4.91 (1H, d, *J* 11.5, ArCH_2), 4.85 (d, *J* 7.9, 1''-H), 4.75 (1H, d, *J* 11.4, ArCH_2), 4.71 (1H, d, *J* 11.4, ArCH_2), 4.59 (1H, d, *J* 11.4, ArCH_2), 4.54 (1H, d, *J* 11.3, ArCH_2), 4.51 (1H, d, *J* 7.5, 1-H), 4.42 (1H, d, *J* 8.0, 1'''-H), 4.39 (1H, d, *J* 8.0, 1'-H), 4.35 (2H, m, CH_2), 4.27 (1H, t, *J* 8.8, 4''-H), 4.21-4.15 (3H, m, 4-H, CH_2), 4.11-4.07 (2H, m, 6'-H_a, 6'''-H_a), 3.94-3.92 (2H, m, 5-H, 5''-H), 3.78-3.75 (2H, m, 3''-H, CH_2), 3.70 (1H, t, *J* 8.9, 3-H), 3.66 (3H, s, OCH_3), 3.62-3.51 (6H, m, 3'-H, 3'''-H, 4'''-H, OCH_3), 3.41-3.33 (4H, m, 2'''-H, 6'-H, 6'''-H, CH_2), 3.30-3.20 (3H, m,

2'-H, 5'-H, 5'''-H), 3.00-2.90 (3H, m, CH_2), 1.41 (2H, m, CH_2), 1.30 (2H, m, CH_2), 1.08 (2H, m, CH_2), 0.96 (2H, m, CH_2, 0.01 (9H, m, TMS); ^{13}C NMR (150 MHz, $CDCl_3$): δ 168.6 (C), 168.4 (C), 164.90 (C), 164.86 (C), 156.5 (C), 138.1 (C), 137.94 (C), 137.89 (C), 137.04 (C), 136.98 (C), 135.22 (C), 133.19 (C), 133.1 (CH), 133.04 (C), 132.96 (CH), 129.9 (C), 129.7 (CH), 129.6 (CH), 129.1 (CH), 128.9 (CH), 128.41 (CH), 128.37 (CH), 128.30 (CH), 128.25 (CH), 128.2 (CH), 128.12 (CH), 128.08 (CH), 128.05 (CH), 127.9 (CH), 127.7 (CH), 127.6 (CH), 127.4 (CH), 127.1 (CH), 127.0 (CH), 126.9 (CH), 126.1 (CH), 126.0 (CH), 125.9 (CH), 102.3 (CH), 102.1 (CH), 101.5 (CH), 101.4 (CH), 101.3 (CH), 101.0 (CH), 81.5 (CH), 79.5 (CH), 79.5 (CH), 79.3 (CH), 79.0 (CH), 78.9 (CH), 78.8 (CH), 75.0 (CH_2), 74.5 (CH_2), 74.4 (CH), 74.3 (CH_2), 74.2 (CH), 73.1 (CH), 72.8 (CH), 69.9 (CH_2), 68.3 (CH_2), 68.1 (CH_2), 66.7 (CH), 66.1 (CH), 66.0 (CH), 63.5 (CH_2), 52.6 (CH_3), 52.4 (CH_3), 50.2 (CH_2), 45.9 (CH_2), 28.9 (CH_2), 27.6 (CH_2), 23.0 (CH_2), 17.8 (CH_2), -1.5 (CH_3); HRMS (ESI): *m/z* calcd for $C_{97}H_{105}N_7O_{25}SiNa$ ([M+Na]$^+$): 1819.6852, found: 1819.6849.

***N*-Benzyl-*N*-2-(trimethylsilyl)ethoxycarbonyl-5-aminopentyl [2-azido-4,6-*O*-benzylidene-2-deoxy-3-*O*-(2-naphthylmethyl)-β-D-glucopyranosyl]-(1→4)-(methyl 2-benzoyl-3-*O*-benzyl-β-D-glucopyranosyluronate)-(1→3)-[2-azido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranosyl]-(1→4)-(methyl 2-benzoyl-3-*O*-benzyl-β-D-glucopyranosyluronate)-(1→3)-[2-azido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranosyl]-(1→4)-methyl 2-*O*-benzoyl-3-*O*-benzyl-β-D-glucopyranosyluronate (27).** TEMPO (19.2 mg, 0.123 mmol) and BAIB (384 mg, 1.19 mmol) were added to a solution of hexasaccharide **26** (362 mg, 0.153 mmol) in mixed solvent of CH_3CN and H_2O (10/1, v/v, 33 mL) at 0 °C. After 5 h, the reaction was quenched with $Na_2S_2O_{3(aq)}$ and $NaHCO_{3(aq)}$. The crude product was extracted with ethyl acetate. The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. A solution of crude product in CH_2Cl_2 (30 mL) was added to a solution of diazomethane in ether (10 mL, 0.765 mmol). After 20 min, the reaction was quenched with acetic acid. The mixture was concentrated under reduced pressure and purified by silica gel column chromatography (ethyl acetate/hexanes = 1/2, v/v) to yield the methyl ester **27** (199 mg, 53% in 2 steps). $[\alpha]_D^{24}$ –32.5 (*c* 5.3 in $CHCl_3$); IR (thin film): ν_{max}/cm^{-1} 3032, 2951, 2115, 1735, 1691, 1602, 1497, 1453, 1368, 1315, 1267, 1223, 1174, 1094, 1072, 1029, 1004, 840, 753, 710, 699, 551, 476; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.01 (2H, m, Ar-H), 7.97 (2H, m, Ar-H), 7.88 (2H, m, Ar-H), 7.81-7.73 (4H, m, Ar-H), 7.58-7.52 (2H, m, Ar-H), 7.47-7.39 (12H, m, Ar-H), 7.38-7.31 (13H, m, Ar-H), 7.30-7.26 (2H, m, Ar-H), 7.21-7.21 (1H, m, Ar-H), 7.11-7.05 (17H, m, Ar-H), 5.46 (1H, s, PhC*H*), 5.40 (1H, s, PhC*H*), 5.38 (1H, s, PhC*H*), 5.28 (1H, t, *J* 8.6, 2''''-H), 5.23 (1H, t, *J* 8.8, 2''-H), 5.15 (1H, t, *J* 8.4, 2-H), 5.02 (1H, d, *J* 11.5, ArCH_2), 4.90 (1H, d, *J* 11.5, ArCH_2), 4.83 (1H, d, *J* 7.9, 1''''-H), 4.77-4.74 (2H, m, 1''-H, ArCH_2), 4.68 (1H, d, *J* 11.2, ArCH_2), 4.67 (1H, d, *J* 11.2 Hz, ArCH_2), 4.49 (1H, d, *J* 11.4, ArCH_2), 4.53-4.48 (3H, m, 1-H, ArCH_2), 4.41 (1H, d, *J* 8.1, 1'-H), 4.36-4.28 (4H, m, 1'''-H, 1'''''-H, CH_2), 4.25 (1H, t, *J* 8.9, 4''''-H), 4.18-4.13 (4H, m, 4-H, 4''-H, CH_2), 4.09 (1H, dd, *J* 9.8, 4.9, 6'''''-H_a), 4.07-4.04 (2H, m, 6'-H_a, 6'''-H_a), 3.92-3.90 (2H, m, 5-H, 5''-H), 3.79-3.73 (3H, m, 3''''-H, 5''-H, CH_2), 3.69-3.64 (5H, m, 3-H, 3''-H, OCH_3), 3.60 (1H, t, *J* 9.2, 4'-H), 3.55-3.43 (8H, m, 3'-H, 3'''-H, 3'''''-H, 4'''-H, 4'''''-H, OCH_3), 3.39 (1H, t, *J* 10.3, 6'-H_b), 3.36-3.25 (8H, m, 2'-H, 5'-H, 6'''-H_b, 6'''''-H_b, CH_2, OCH_3), 3.20-3.15 (4H, m, 2'''-H, 2'''''-H, 5'''-H, 5'''''-H), 3.98-2.87 (2H, m, CH_2), 1.42-1.38 (2H, m, CH_2), 1.28 (2H, m, CH_2), 1.08-1.03 (2H, m, CH_2), 0.95-0.91 (2H, m, CH_2), 0.01 (m, 9H; TMS); ^{13}C NMR (150 MHz, $CDCl_3$): δ 168.6 (C), 168.4 (C), 168.3 (C), 164.90 (C), 164.87 (C), 157.0 (C), 138.1 (C), 137.93 (C), 137.86 (C), 137.04 (C), 136.97 (C), 135.2 (C), 133.2 (C), 133.10 (CH), 133.05 (C), 133.0 (C), 129.9 (C), 129.8 (C), 129.70 (C), 129.66 (CH), 129.6 (CH), 129.1 (CH), 128.94 (CH), 128.85 (CH), 128.42 (CH), 128.37 (CH), 128.31 (CH), 128.28 (CH), 128.25 (CH), 128.2 (CH), 128.10 (CH), 128.07 (CH), 128.05 (CH), 128.0 (CH), 127.9 (CH), 127.7 (CH), 127.63 (CH), 127.60 (CH), 127.5 (CH), 127.4 (CH), 127.1 (CH), 126.9 (CH), 126.04 (CH), 126.03 (CH), 125.94 (CH), 125.91 (CH), 125.86 (CH), 102.3 (CH), 102.2 (CH), 102.1 (CH), 101.6 (CH), 101.5 (CH), 101.4 (CH), 101.3 (CH), 101.0 (CH), 100.9 (CH), 81.5 (CH), 79.54 (CH), 79.51 (CH), 79.4 (CH), 79.3 (CH), 79.1 (CH), 78.90 (CH), 78.85 (CH), 75.0 (CH_2), 74.6 (CH_2), 74.5 (CH_2), 74.40 (CH), 74.35 (CH_2), 74.2 (CH), 74.1 (CH), 73.0 (CH), 72.9 (CH), 72.7 (CH), 70.0 (CH_2), 68.3 (CH_2), 68.1 (CH_2), 66.7 (CH), 66.0 (CH), 63.5 (CH_2), 52.7 (CH_3), 52.4 (CH_3), 52.3 (CH_3), 50.2 (CH_2), 45.9 (CH_2), 29.7 (CH_2), 28.9 (CH_2), 27.2 (CH_2), 23.0 (CH_2), 17.8 (CH_2), -1.5 (CH_3); HRMS (ESI): *m/z* calcd for $C_{131}H_{140}N_{10}O_{36}Si$ ([M+2H$^+$]): 1228.9611, found: 1228.9610.

***N*-Benzyl-*N*-2-(trimethylsilyl)ethoxycarbonyl-5-aminopentyl [2-azido-4,6-*O*-benzylidene-2-deoxy-3-*O*-(2-naphthylmethyl)-β-D-glucopyranosyl]-(1→4)-3-benzyl-β-D-glucopyranosyluronate sodium salt (28).** A mixture of 5 N $NaOH_{(aq)}$, H_2O, and MeOH (1/2/15, v/v/v, 50 mL) was added to a solution of compound **25** (341 mg, 299 μmol) in $CHCl_3$ (10 mL) at room temperature. After 1 day, H_2O (50 mL) was added to the reaction. The organic solvent was removed under reduced pressure. The crude product was extracted with CH_2Cl_2. The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by Sephadex LH-20 column (MeOH) and then passed through a column of Biorad 50X80 Na^+ resin (MeOH/H_2O = 20/1) to give the carboxylate **28** (291 mg, 93%). ^{1}H NMR (600 MHz, CD_3OD): δ 7.69-7.57 (4H, m, Ar-H), 7.36-7.11 (18H, m, Ar-H), 5.44 (1H, m, PhC*H*), 4.90-4.86 (3H, m, ArCH_2), 4.72-4.70 (1H, m, ArCH_2), 4.63 (1H, d, *J* 7.6, 1'-H), 4.36-4.35 (2H, m, ArCH_2), 4.22 (1H, d, *J* 7.7, 1-H), 4.10 (2H, s, CH_2), 4.00-3.97 (2H, m, 4-H), 3.76-3.74 (1H, m, 5-H), 3.69 (1H, m, CH_2), 3.57-3.53 (2H, m, 3'-H, 5'-H), 3.45-3.37 (4H, m, 3-H, 4'-H, 6'-H_b, CH_2), 3.30-3.25 (2H, m, 2-H, 2'-H), 3.08 (2H, m, CH_2), 1.46-1.39 (2H, m, CH_2), 1.18 (2H, m, CH_2), 0.92-0.87 (2H, m, CH_2), -0.07 (9H, m, TMS); ^{13}C NMR (150 MHz, CD_3OD): δ 175.5 (C), 158.5 (C), 140.6 (C), 139.5 (C), 139.2 (C), 137.2 (C), 134.8 (C), 134.6 (C), 130.1 (CH), 129.8 (C), 129.33 (CH), 129.26 (CH), 129.1 (CH), 128.8 (CH), 128.5 (CH), 128.0 (CH), 127.5 (CH), 127.3 (CH), 127.2 (CH), 127.1 (CH), 104.8 (CH), 102.8 (CH), 102.7 (CH), 84.2 (CH), 83.0 (CH), 80.3 (CH), 79.6 (CH), 77.8 (CH), 76.0 (CH_2), 75.7 (CH_2), 75.0 (CH), 71.6 (CH_2), 71.0 (CH_2), 69.7 (CH_2), 68.4 (CH), 67.5 (CH_2), 65.1 (CH_2), 51.4 (CH_2), 47.5 (CH_2), 30.9 (CH_2), 29.0 (CH_2) 24.4 (CH_2), 18.8 (CH_2), -1.3 (CH_3); HRMS (ESI): *m/z* calcd for $C_{55}H_{66}N_4O_{13}SiNa$ ([M+H]$^+$): 1041.4288, found: 1041.4286.

***N*-Benzyl-*N*-2-(trimethylsilyl)ethoxycarbonyl-5-aminopentyl [2-azido-4,6-*O*-benzylidene-2-deoxy-3-*O*-(2-naphthylmethyl)-β-D-**

glucopyranosyl]-(1→4)-(3-*O*-benzyl-β-D-glucopyranosyluronate)-(1→3)-[2-azido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranosyl]-(1→4)-3-*O*-benzyl-β-D-glucopyranosyluronate disodium salt (29). A mixture of 5 N $NaOH_{(aq)}$, H_2O, and MeOH (1/2/15, v/v/v, 4mL) was added to a solution of compound **26** (126 mg, 69.9 μmol) in $CHCl_3$ (1.6 mL) at room temperature. After 2 days, H_2O (10 mL) was added to the reaction. The organic solvent was removed under reduced pressure. The crude product was extracted with CH_2Cl_2. The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by Sephadex LH-20 column (MeOH) and then passed through a column of Biorad 50X80 Na^+ resin (MeOH/H_2O = 20/1) to give the carboxylate **29** (90.4 mg, 81%). ^{1}H NMR (600 MHz, CD_3OD): δ 7.77-7.65 (4H, m, Ar-H), 7.41-7.19 (28H, m, Ar-H), 5.51 (1H, s, PhC*H*), 5.45 (1H, s, PhC*H*), 4.95-4.78 (4H, m, ArCH_2), 4.62-4.54 (5H, m, 1'-H, 1''-H, 1'''-H, ArCH_2), 4.44 (2H, s, ArCH_2), 4.27 (1H, m, 1-H), 4.17 (1H, s, CH_2), 4.08-4.05 (4H, m, 4-H, 4''-H, 6'-H_a, 6'''-H_a), 3.81-3.73 (3H, m, 5-H, 5''-H, CH_2), 3.66-3.44 (12H, m, 2'-H, 3-H, 3'-H, 3''-H, 3'''-H, 4'-H, 4'''-H, 5'-H, 5'''-H, 6'-H_b, 6'''-H_b, CH_2), 3.36-3.27 (3H, m, 2-H, 2'-H, 2'''-H), 3.17 (2H, m, CH_2), 1.53-1.47 (4H, m, CH_2), 1.24 (2H, m, CH_2), 1.00-0.95 (2H, m, CH_2), 0.02 (9H, m, TMS); ^{13}C NMR (150 MHz, CD_3OD): δ 176.2 (C), 175.5 (C), 159.0 (C), 140.7 (C), 140.6 (C), 139.5 (C), 139.2 (C), 138.9 (C), 137.1 (C), 134.8 (C), 134.7 (C), 130.1 (CH), 130.0 (CH), 129.8 (CH), 129.31 (CH), 129.29 (CH), 129.23 (CH), 129.19 (CH), 129.12 (CH), 129.11 (CH), 128.90 (CH), 128.8 (CH), 128.6 (CH), 128.5 (CH), 128.1 (CH), 127.6 (CH), 127.5 (CH), 127.4 (CH), 127.2 (CH), 127.1 (CH), 105.0 (CH), 103.0 (CH), 102.8 (CH), 102.5 (CH), 84.3 (CH), 84.1 (CH), 83.0 (CH), 80.2 (CH), 80.1 (CH), 79.3 (CH), 78.9 (CH), 78.8 (CH), 76.1 (CH_2), 75.7 (CH_2), 75.6 (CH_2), 75.0 (CH), 74.8 (CH), 70.9 (CH_2), 69.7 (CH_2), 68.5 (CH), 68.4 (CH), 68.3 (CH), 68.1 (CH), 65.1 (CH_2), 51.3 (CH_2), 48.2 (CH_2), 30.5 (CH_2), 28.6 (CH_2), 24.4 (CH_2), 18.8 (CH_2), -1.3 (CH_3); HRMS (ESI): *m/z* calcd for $C_{81}H_{92}N_7O_{23}Si$ ($[M+H]^+$): 1604.5804, found: 1604.5808.

***N*-Benzyl-*N*-2-(trimethylsilyl)ethoxycarbonyl-5-aminopentyl [2-azido-4,6-*O*-benzylidene-2-deoxy-3-*O*-(2-naphthylmethyl)-β-D-glucopyranosyl]-(1→4)-(3-*O*-benzyl-β-D-glucopyranosyluronate)-(1→3)-[2-azido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranosyl]-(1→4)-(3-*O*-benzyl-β-D-glucopyranosyluronate)-(1→3)-[2-azido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranosyl]-(1→4)-3-*O*-benzyl-β-D-glucopyranosyluronate trisodium salt (30).** A mixture of 5 N $NaOH_{(aq)}$, H_2O, and MeOH (1/2/15, v/v/v, 1mL) was added to a solution of compound **27** (10 mg, 4.07 μmol) in $CHCl_3$ (0.5 mL) at room temperature. After 3 days, H_2O (10 mL) was added to the reaction. The organic solvent was removed under reduced pressure. The crude product was extracted with CH_2Cl_2. The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by Sephadex LH-20 column (MeOH) and then passed through a column of Biorad 50X80 Na^+ resin (MeOH/H_2O = 20/1) to give the carboxylate acid **30** (5.7 mg, 65%). ^{1}H NMR (600 MHz, CD_3OD): δ 7.68 (1H, m, Ar-H), 7.64-7.63 (2H, m, Ar-H), 7.58 (1H, m, Ar-H), 7.38-7.30 (15H, m, Ar-H), 7.25-7.12 (23H, m, Ar-H), 5.42 (1H, s, PhC*H*), 5.39 (1H, s, PhC*H*), 5.37 (1H, s, PhC*H*), 4.87-4.80 (4H, m, ArCH_2), 4.71 (3H, m, 1'-H, 1'''-H, 1''''-H), 4.67-4.60 (6H, m, 1''-H, 1''''-H, ArCH_2), 4.36 (2H, s, ArCH_2), 4.17 (1H, d, *J* = 7.8 Hz, 1-H), 4.10-4.02 (8H, m, 4-H, 4''-H, 4''''-H, 6'-H_a, 6'''-H_a, 6''''-H_a, CH_2), 3.69-3.62 (6H, m, 3''-H, 3''''-H, 5-H, 5''-H, 5''''-H, CH_2), 3.55-3.33 (15H, m, 2''-H, 2'''-H, 2''''-H, 2'''''-H, 3-H, 3''-H, 3''''-H, 3'''''-H, 4'-H, 4'''-H, 4''''-H, 6'-H_b, 6'''-H_b, 6''''-H_b, CH_2), 3.28-3.25 (5H, m, 2-H, 2'-H, 5'-H, 5'''-H, 5'''''-H), 3.14-3.09 (2H, m, CH_2), 1.46-1.40 (4H, m, CH_2), 1.19-1.18 (2H, m, CH_2), 0.93 (2H, m, CH_2), -0.05--0.01 (9H, m, TMS); ^{13}C NMR (150 MHz, CD_3OD): δ 175.9 (C), 175.4 (C), 175.3 (C), 159.0 (C), 140.9 (C), 140.79 (C), 140.75 (C), 139.6 (C), 139.3 (C), 139.0 (C), 137.3 (C), 134.9 (C), 134.7 (C), 130.1 (CH), 129.8 (CH), 129.34 (CH), 129.26 (CH), 129.19 (CH), 129.16 (CH), 129.13 (CH), 129.06 (CH), 128.9 (CH), 128.8 (CH), 128.5 (CH), 128.4 (CH), 128.0 (CH), 127.7 (CH), 127.5 (CH), 127.4 (CH), 127.1 (CH), 127.0 (CH), 104.8 (CH), 104.3 (CH), 104.1 (CH), 102.8 (CH), 102.5 (CH), 102.5 (CH), 102.2 (CH), 84.4 (CH), 84.2 (CH), 83.1 (CH), 80.8 (CH), 80.7 (CH), 80.5 (CH), 79.6 (CH), 79.4 (CH), 79.3 (CH), 79.3 (CH), 79.20 (CH), 79.17 (CH), 75.8 (CH_2), 75.6 (CH_2), 75.5 (CH_2), 75.1 (CH), 74.9 (CH), 70.7 (CH_2), 69.8 (CH_2), 69.7 (CH_2), 68.7 (CH), 68.4 (CH), 67.7 (CH), 67.5 (CH), 65.1 (CH_2), 51.4 (CH_2), 48.2 (CH_2), 47.6 (CH_2), 30.6 (CH_2), 29.2 (CH_2), 24.5 (CH_2), 18.8 (CH_2), -1.3 (CH_3); HRMS (ESI): *m/z* calcd for $C_{107}H_{121}N_{10}O_{33}Si$ ($[M+H^+]$): 2100.7746, found: 2100.7766.

***N*-Benzyl-*N*-2-(trimethylsilyl)ethoxycarbonyl-5-aminopentyl [2-acetamido-4,6-*O*-benzylidene-2-deoxy-3-*O*-(2-naphthylmethyl)-β-D-glucopyranosyl]-(1→4)-3-benzyl-β-D-glucopyranosyluronate sodium salt (31).** PMe_3 (1.0 M in THF, 0.656 mL, 0.656 mmol), MeOH (82 μL), and 0.1 N $NaOH_{(aq)}$ (82 μL) were sequentially added to a solution of carboxylate **28** (17.2 mg, 16.5 μmol) in THF (656 μL). After 3 h, the reaction was concentrated under reduced pressure and dried *in vacuo*. To a solution of the dried crude residue and Et_3N (69.0 μL, 496 μmol) in MeOH (1.0 mL) was added Ac_2O (23.4 μL, 248 μmol) in three equal portions and in half-hour intervals at room temperature. After 1.5 h, the reaction was concentrated under reduced pressure and purified by silica gel column chromatography (MeOH/$CHCl_3$ = 1/15, v/v) and then passed through a column of Biorad 50X80 Na^+ resin (MeOH/H_2O = 20/1) to yield the acetamide **31** (13.2 mg, 76%). HRMS (ESI): *m/z* calcd for $C_{57}H_{70}N_2NaO_{14}Si$ ($[M+H^+]$): 1057.4489, found: 1057.4481.

***N*-Benzyl-*N*-2-(trimethylsilyl)ethoxycarbonyl-5-aminopentyl [2-acetamido-4,6-*O*-benzylidene-2-deoxy-3-*O*-(2-naphthylmethyl)-β-D-glucopyranosyl]-(1→4)-(3-*O*-benzyl-β-D-glucopyranosyluronate)-(1→3)-[2-acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranosyl]-(1→4)-3-*O*-benzyl-β-D-glucopyranosyluronate disodium salt (32).** PMe_3 (1.0 M in THF, 40 μL, 40 μmol), MeOH (40 μL), and 0.1 N $NaOH_{(aq)}$ (40 μL) were sequentially added to a solution of carboxylate **29** (6.4 mg, 4.0 μmol) in THF (0.32 mL). After 3 h, the reaction was concentrated under reduced pressure and dried *in vacuo*. To a solution of dried crude residue and Et_3N (37 μL, 240 μmol) in MeOH (1.0 mL) was added Ac_2O (11 μL, 120 μmol) in three equal portions and in half-hour intervals at room temperature. After 1.5 h, the reaction was concentrated under reduced pressure and purified by silica gel column chromatography (MeOH/$CHCl_3$ = 1/12, v/v) and then passed through a column of Biorad 50X80 Na^+ resin (MeOH/H_2O = 20/1) to yield the acetamide

32 (2.8 mg, 43%). HRMS (ESI): *m/z* calcd for $C_{85}H_{102}N_3O_{25}Si$ ([M+H$^+$]): 1592.6566, found: 1592.6575.

***N*-Benzyl-*N*-2-(trimethylsilyl)ethoxycarbonyl-5-aminopentyl [2-acetamido-4,6-*O*-benzylidene-2-deoxy-3-*O*-(2-naphthylmethyl)-β-D-glucopyranosyl]-(1→4)-(3-*O*-benzyl-β-D-glucopyranosyluronate)-(1→3)-[2-acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranosyl]-(1→4)-(3-*O*-benzyl-β-D-glucopyranosyluronate)-(1→3)-[2-acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranosyl]-(1→4)-3-*O*-benzyl-β-D-glucopyranosyluronate trisodium salt (33).** PMe_3 (1.0 M solution in THF, 98.8 μL, 98.8 μmol), MeOH (98.8 μL), and 0.1 N $NaOH_{(aq)}$ (98.8 μL) were sequentially added to a solution of carboxylate **30** (14.3 mg, 6.59 μmol) in THF (800 μL). After 5 h, the reaction was concentrated under reduced pressure and dried *in vacuo*. To a solution of dried crude residue and Et_3N (92.6 μL, 594 μmol) in MeOH (1.0 mL) was added with Ac_2O (27.9 μL, 297 μmol) in three equal portions and in half-hour intervals at room temperature. After 1.5 h, the reaction was concentrated under reduced pressure and purified by silica gel column chromatography (MeOH/$CHCl_3$ = 1/8, v/v) and then passed through a column of Biorad 50X80 Na^+ resin (MeOH/H_2O = 20/1) to yield the acetamide **33** (3.4 mg, 23%). HRMS (ESI): *m/z* calcd for $C_{113}H_{134}N_4O_{36}Si$ ([M+2H$^+$]): 1075.4268, found: 1075.4259.

***N*-2-(Trimethylsilyl)ethoxycarbonyl-5-aminopentyl [2-acetamido-2-deoxy-β-D-glucopyranosyl]-(1→4)-β-D-glucopyranosyluronate sodium salt (34).** *Method A*: A mixture of the acetamide **31** (13.2 mg, 12.5 μmol) and 20% $Pd(OH)_2$ on carbon (39.6 mg) in a MeOH (1 mL) was equipped with a hydrogen balloon at room temperature. After 16 h, H_2O (5 mL) was added to the reaction and kept going for 1 day under hydrogen. The mixture was filtered through Celite and the filtrate was concentrated under reduced pressure. The residue was purified by Sephadex G-10 (H_2O) and then passed through a column of Biorad 50X80 Na^+ resin (H_2O) to give disaccharide **34** (3.9 mg, 42%). *Method B*: A mixture of compound **28** (19.1 mg, 18.3 μmol) and 20% $Pd(OH)_2$ on carbon (57.3 mg) in MeOH (1 mL) was equipped with a hydrogen balloon at room temperature. After 16 h, H_2O (5 mL) was added to the reaction and kept going for 1 day under hydrogen. The mixture was filtered through Celite, and the filtrate was concentrated under reduced pressure. Ac_2O (25.8 μL, 275 μmol) and Et_3N (85.6 μL, 0.549 mmol) were added to the solution of the crude residue in MeOH (1 mL) in three equal portions and in 10-min intervals. After 30 min, the mixture was concentrated under reduced pressure. The residue was purified by Sephadex G-10 (H_2O) and then passed through a column of Biorad 50X80 Na^+ resin (H_2O) to give disaccharide **36** (4.2 mg, 31%). *Method C*: A mixture of compound **28** (9.7 mg, 9.3 μmol) and Pd black (50 mg) in a MeOH (1.5 mL) was equipped with a hydrogen balloon at room temperature. After 16 h, H_2O (7.5 mL) was added to the reaction and kept going for 1 day under hydrogen. The mixture was filtered through Celite, and the filtrate was concentrated under reduced pressure. Ac_2O (13.1 μL, 140 μmol) and Et_3N (43.5 μL, 280 μmol) were added to the solution of crude residue in MeOH (1 mL) in three equal portions and in 10-min intervals. After 30 min, the mixture was concentrated under reduced pressure. The residue was purified by Sephadex G-10 (H_2O) and then passed through a column of Biorad 50X80 Na^+ resin (H_2O) to give disaccharide **34** (4.0 mg, 58%).^{1}H NMR (600 MHz, D_2O): δ 4.53 (1H, d, *J* 8.5 Hz, 1'-H), 4.43 (1H, d, *J* 8.0 Hz, 1-H), 4.17 (2H, m, CH_2), 3.92-3.86 (2H, m, 6'-H_a, CH_2), 3.77-3.62 (5H, m, 2'-H, 4-H, 5-H, 6'-H_b, CH_2), 3.57 (1H, t, *J* 9.2, 3-H), 3.51 (1H, t, *J* 8.7, 3'-H), 3.46-3.45 (2H, m, 4'-H, 5'-H), 3.31 (1H, t, *J* 8.2, 2-H), 3.01 (2H, t, *J* 6.7, CH_2), 2.04 (3H, s, OCOCH_3), 1.61 (2H, m, CH_2), 1.49 (2H, m, CH_2), 1.36 (2H, m, CH_2), 0.98 (2H, t, *J* 7.9, CH_2), 0.02 (9H, s, TMS); ^{13}C NMR (150 MHz, D_2O): δ 175.2 (C), 174.7 (C), 159.3 (C), 102.7 (CH), 101.1 (CH), 80.3 (CH), 77.0 (CH), 76.2 (CH), 74.2 (CH), 74.1 (CH), 73.1 (CH), 70.9 (CH_2), 70.0 (CH), 64.3 (CH_2), 60.8 (CH_2), 55.7 (CH), 40.5 (CH_2), 28.9 (CH_2), 28.7 (CH_2), 22.7 (CH_3), 22.5 (CH_2), 12.3 (CH_2), -2.1 (CH_3); HRMS (ESI): *m/z* calcd for $C_{32}H_{52}N_2O_{14}SiNa$ ([M+H]$^+$): 717.3270, found: 717.3261.

***N*-2-(Trimethylsilyl)ethoxycarbonyl-5-aminopentyl [2-acetamido-2-deoxy-β-D-glucopyranosyl]-(1→4)-(β-D-glucopyranosyluronate)-(1→3)-[2-acetamido-2-deoxy-β-D-glucopyranosyl]-(1→4)-β-D-glucopyranosyluronate disodium salt (35).** *Method A*: A mixture of the acetamide **32** (2.8 mg, 1.7 μmol) and 20% $Pd(OH)_2$ on carbon (8.4 mg) in a MeOH (1 mL) was equipped with a hydrogen balloon at room temperature. After 16 h, H_2O (5 mL) was added to the reaction and kept going for 1 day under hydrogen. The mixture was filtered through Celite and the filtrate was concentrated under reduced pressure. The residue was purified by Sephadex G-10 (H_2O) and then passed through a column of Biorad 50X80 Na^+ resin (H_2O) to give disaccharide **35** (0.9 mg, 50%). *Method B*: A mixture of compound **29** (22.0 mg, 0.0137 mmol) and 20% $Pd(OH)_2$ on carbon (75.0 mg) in MeOH (1 mL) was equipped with a hydrogen balloon at room temperature. After 16 h, H_2O (5 mL) was added to the reaction and kept going for 1 day under hydrogen. The mixture was filtered through Celite, and the filtrate was concentrated under reduced pressure. Ac_2O (38.9 μL, 0.411 mmol) and Et_3N (129 μL, 0.822 mmol) were added to the solution of the crude residue in MeOH (1 mL) in three equal portions and in 10-min intervals. After 30 min, the whole mixture was concentrated under reduced pressure. The residue was purified by Sephadex G-10 (H_2O) and then passed through a column of Biorad 50X80 Na^+ resin (H_2O) to give the tetrasaccharide **35** (2.3 mg, 15%). *Method C*: A solution of $Na_{(s)}$ dispersion in oil (0.34 mL, 5.7 mmol) and 15-crown-5 (1.0 mL, 5.1 mmol) in THF (1 mL) was added to a solution of compound **29** (9.8 mg, 6.1 μmol) in THF (0.5 mL) at –50 °C. After 1 h, the reaction was quenched by sequential addition of isopropyl alcohol, MeOH, and 2 N $HCl_{(aq)}$. The organic solvent was removed under reduced pressure. The mixture was washed by $CHCl_3$. The water layer was concentrated under reduced pressure and purified by C-18 column (H_2O/MeOH = 1/0 and 0/1) to give a crude residue. To a solution of the crude residue in a mixed solvent of 5 N $NaOH_{(aq)}$, H_2O and MeOH (1/2/15, v/v/v, 2 mL) was added Ac_2O (17.3 μL, 183 μmol) in three equal portions and in 10-min intervals at room temperature. After 30 min, the reaction mixture was concentrated under reduced pressure and sequentially purified by C-18 column (H_2O/MeOH=1/0 and 9/1), Biorad 50X80 Na^+ resin column (H_2O), and Sephadex G-10 column (H_2O) to give product **35** (3 mg, 47%). ^{1}H NMR (600 MHz, D_2O): δ 4.57-4.52 (2H, m, 1'-H, 1'''-H), 4.49-4.46 (2H, m, 1-H, 1''-H), 4.18 (2H, m, CH_2), 3.92-3.82 (4H, m, 2'''-H, 6'-H_a, 6'''-H_a, CH_2), 3.78-

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3.66 (9H, m, 2'-H, 3'-H, 3'''-H, 4-H, 4''-H, 5-H, 5''-H, 6'-H_b, 6'''-H_b, CH_2), 3.59 (2H, m, 3-H, 3''-H), 3.10 (2H, m, CH_2), 2.08 (3H, s, OCOCH_3), 2.04 (3H, s, OCOCH_3), 2.01 (3H, s, OCOCH_3), 1.61 (2H, m, CH_2), 1.49 (2H, m, CH_2), 1.36 (2H, m, CH_2), 0.99 (2H, m, CH_2), 0.03 (9H, m, TMS); ^{13}C NMR (150 MHz, D_2O): δ 174.8 (C), 173.6 (C), 103.0 (CH), 102.3 (CH), 100.80 (CH), 100.75 (CH), 82.3 (CH), 80.1 (CH), 79.8 (CH), 75.8 (CH), 75.6 (CH), 75.3 (CH), 75.2 (CH), 73.8 (CH), 73.7 (CH), 73.5 (CH), 72.6 (CH), 72.2 (CH), 70.6 (CH_2), 69.6 (CH), 68.3 (CH), 63.9 (CH_2), 60.4 (CH_2), 55.3 (CH), 54.3 (CH), 40.1 (CH_2), 28.5 (CH_2), 28.3 (CH_2), 22.4 (CH_3), 22.3 (CH_3), 22.1 (CH), 16.9 (CH_2), -2.5 (CH_3); HRMS (ESI): *m/z* calcd for $C_{39}H_{67}N_3Na_2O_{25}Si$ ([M+H]$^+$): 1050.3545, found: 1050.3539.

***N*-2-(Trimethylsilyl)ethoxycarbonyl-5-aminopentyl [2-acetamido-2-deoxy-β-D-glucopyranosyl]-(1→4)-(β-D-glucopyranosyluronate)-(1→3)-[2-acetamido-2-deoxy-β-D-glucopyranosyl]-(1→4)-(β-D-glucopyranosyluronate)-(1→3)-[2-acetamido-2-deoxy-β-D-glucopyranosyl]-(1→4)-β-D-glucopyranosyluronate trisodium salt (36).** *Method A*: A mixture of the acetamide **33** (3.4 mg, 1.5 μmol) and 20% $Pd(OH)_2$ on carbon (10 mg) in MeOH (1 mL) was equipped with a hydrogen balloon at room temperature. After 16 h, H_2O (5 mL) was added to the reaction and kept going for 1.5 day under hydrogen. The mixture was filtered through Celite and the filtrate was concentrated under reduced pressure. The residue was purified by Sephadex G-10 (H_2O) and then passed through a column of Biorad 50X80 Na^+ resin (H_2O) to give disaccharide **36** (0.4 mg, 18%). *Method B*: A solution of $Na_{(s)}$ dispersion in oil (0.340 mL, 5.74 mmol) and 15-crown-5 (1.00 mL, 5.05 mmol) in THF (1 mL) was added to a solution of compound 29 (14.5 mg, 6.69 μmol) in THF (0.5 mL) at –50 °C. After 3 h, the reaction was quenched by sequentially adding IPA, MeOH and 2 N $HCl_{(aq)}$. The organic solvent was removed under reduced pressure. The mixture was washed by $CHCl_3$. The water layer was concentrated under reduced pressure and purified by C-18 column (H_2O/MeOH = 1/0 and 0/1) to give a crude residue. To a solution of the crude residue in a mixed solvent of 5 N $NaOH_{(aq)}$, H_2O and MeOH (1/2/15, v/v/v, 2 mL) was added Ac_2O (28.5 μL, 301 μmol) in three equal portions and in 10-min intervals at room temperature. After 30 min, the reaction mixture was concentrated under reduced pressure and sequentially purified by C-18 column (H_2O/MeOH = 1/0 and 0/1), Biorad 50X80 Na^+ resin column (H_2O), and Sephadex G-10 column (H_2O) to give the product **36** (5.3 mg, 62%) ^{1}H NMR (600 MHz, D_2O): δ 4.56-4.52 (3H, m, 1'-H, 1'''-H, 1'''''-H), 4.47-4.43 (3H, m, 1-H, 1''-H, 1''''-H), 4.19-4.18 (2H, m, CH_2), 3.92-3.88 (4H, m, 6'-H_a, 6'''-H_a, 6'''''-H_a, CH_2), 3.85-3.82 (2H, m, 2'''-H, 2'''''-H), 3.77-3.64 (14H, m, 2'-H, 3'-H, 3'''-H, 3'''''-H, 4-H, 4''-H, 4''''-H, 5-H, 5''-H, 5''''-H, 6'-H_b, 6'''-H_b, 6'''''-H_b, CH_2), 3.59-3.56 (3H, m, 3-H, 3''-H, 3''''-H), 3.54-3.45 (6H, m, 4'-H, 4'''-H, 4'''''-H, 5'-H, 5'''-H, 5'''''-H), 3.36-3.30 (3H, m, 2-H, 2''-H, 2''''-H), 3.11-3.09 (2H, m, CH_2), 2.05-2.02 (9H, m, OCOCH_3), 1.63-1.60 (2H, m, CH_2), 1.51-1.48 (2H, m, CH_2), 1.39-1.35 (2H, m, CH_2), 1.01-0.99 (2H, m, CH_2), 0.04-0.03 (9H, m, TMS); ^{13}C NMR (150 MHz, D_2O): δ 175.1 (C), 174.4 (C), 171.2 (C), 161.1 (C), 103.4 (CH), 102.5 (CH), 100.8 (CH), 82.8 (CH), 80.3 (CH), 80.1 (CH), 79.9 (CH), 76.9 (CH), 76.5 (CH), 76.1 (CH), 75.5 (CH), 74.1 (CH), 73.7 (CH), 73.0 (CH), 72.7 (CH), 70.7 (CH_2), 69.9 (CH), 68.6 (CH), 64.2 (CH_2), 60.7 (CH_2), 55.6 (CH), 54.5 (CH), 40.3 (CH_2), 28.7 (CH_2), 28.5 (CH_2), 22.6 (CH_3), 22.4 (CH_3), 17.1 (CH_2), -2.2 (CH_3); HRMS (ESI): *m/z* calcd for $C_{53}H_{86}N_4O_{36}Si$ ([M+H]$^+$): 1451.4479, found: 1451.4486.

5-Aminopentyl [2-acetamido-2-deoxy-β-D-glucopyranosyl]-(1→4)-β-D-glucopyranosyluronate sodium salt (1). TBAF (1.0 M in THF, 65 μL, 65 μmol) was added to a solution of compound **34** (1.9 mg, 2.6 μmol) in CH_3CN (2 mL) at room temperature. After 1 day, the mixture was concentrated under reduced pressure, purified by Sephadex G-10 column (H_2O), and then passed through a column of Biorad 50X80 Na^+ resin (H_2O) to provide product **1** (0.80 mg, 65%). ^{1}H NMR (600 MHz, D_2O): δ 4.57 (1H, d, *J* 8.4, 1'-H), 4.48 (1H, d, *J* 7.9, 1-H), 3.96-3.91 (2H, m, 6'-H_a, CH_2), 3.80-3.71 (5H, m, 2'-H, 4-H, 5-H, 6'-H_b, CH_2), 3.61 (1H, t, *J* 9.1, 3-H), 3.55 (1H, t, *J* 9.5 Hz, 3'-H), 3.49-3.48 (2H, m, 4'-H, 5'-H), 3.35 (1H, t, *J* 8.5, 2-H), 3.01 (2H, m, CH_2), 2.07 (3H, s, OCOCH_3), 1.69 (4H, m, CH_2), 1.47 (2H, m, CH_2); ^{13}C NMR (150 MHz, D_2O): δ 175.3 (C), 174.7 (C), 102.7 (CH), 101.2 (CH), 80.4 (CH), 77.1 (CH), 76.2 (CH), 74.3 (CH), 74.2 (CH), 73.1 (CH), 70.6 (CH_2), 70.1 (CH), 60.9 (CH_2), 55.7 (CH), 39.7 (CH_2), 28.5 (CH_2), 26.7 (CH_2), 22.8 (CH_3), 22.3 (CH_2); HRMS (ESI): *m/z* calcd for $C_{19}H_{35}N_2O_{12}$ ([M+H]$^+$): 483.2195, found: 483.2191.

5-Aminopentyl [2-acetamido-2-deoxy-β-D-glucopyranosyl]-(1→4)-(β-D-glucopyranosyluronate)-(1→3)-[2-acetamido-2-deoxy-β-D-glucopyranosyl]-(1→4)-β-D-glucopyranosyluronate disodium salt (2). TBAF (1.0 M in THF, 230 μL, 230 μmol) was added to a solution of compound **35** (9.6 mg, 9.1 μmol) in CH_3CN (5 mL) under room temperature. After 1 day, the mixture was concentrated under reduced pressure, purified by Sephadex G-10 column (H_2O), and then passed through a column of Biorad 50X80 Na^+ resin (H_2O) to provide product **2** (8.0 mg, 99%). ^{1}H NMR (600 MHz, D_2O): δ 4.60-4.55 (2H, m, 1'-H, 1'''-H), 4.50-4.47 (2H, m, 1-H, 1''-H), 3.96-3.85 (4H, m, 2'''-H, 6'-H_a, 6'''-H_a, CH_2), 3.81-3.70 (9H, m, 2'-H, 3'''-H, 4-H, 4''-H, 5-H, 5''-H, 6'-H_b, 6'''-H_b, CH_2), 3.62-3.59 (2H, m, 3-H, 3''-H), 3.57-3.48 (5H, m, 3'-H, 4'-H, 4'''-H, 5'-H, 5'''-H), 3.39-3.34 (2H, m, 2-H, 2'-H), 3.02 (2H, m, CH_2), 2.08 (3H, s, OCOCH_3), 2.05 (3H, s, OCOCH_3), 1.69 (4H, m, CH_2), 1.48 (2H, m, CH_2); ^{13}C NMR (150 MHz, D_2O): δ 175.3 (C), 174.6 (C), 103.5 (CH), 102.8 (CH), 101.1 (CH), 101.0 (CH), 82.8 (CH), 80.5 (CH), 80.2 (CH), 77.1 (CH), 76.7 (CH), 76.3 (CH), 75.7 (CH), 74.3 (CH), 74.2 (CH), 73.9 (CH), 73.1 (CH), 72.9 (CH), 70.6 (CH_2), 70.1 (CH), 68.8 (CH), 60.9 (CH_2), 55.8 (CH), 54.7 (CH), 39.7 (CH_2), 28.5 (CH_2), 26.6 (CH_2), 22.8 (CH_3), 22.8 (CH_3), 22.3 (CH_2); HRMS (ESI): *m/z* calcd for $C_{13}H_{18}N_3O_4SNa$ ([M+H]$^+$): 884.3145, found: 884.3119.

Aminopentyl [2-acetamido-2-deoxy-β-D-glucopyranosyl]-(1→4)-(β-D-glucopyranosyluronate)-(1→3)-[2-acetamido-2-deoxy-β-D-glucopyranosyl]-(1→4)-(β-D-glucopyranosyluronate)-(1→3)-[2-acetamido-2-deoxy-β-D-glucopyranosyl]-(1→4)-β-D-glucopyranosyluronate trisodium salt (3). TBAF (1.0 M in THF, 38 μL, 38 μmol) was added to a solution of compound **36** (2.1 mg, 1.5 μmol) in CH_3CN (0.7 mL) at room temperature. After 1 day, the mixture was concentrated under reduced pressure, purified by Sephadex G-10 column (H_2O), and then passed through a column of Biorad 50X80 Na^+ resin (H_2O) to provide product **3** (1.7 mg, 90%). ^{1}H NMR (600 MHz, D_2O): δ 4.57-4.52 (3H, m, 1'-H, 1'''-H, 1'''''-H), 4.47-

4.44 (3H, m, 1-H, 1''-H, 1''''-H), 3.92-3.88 (4H, m, 6'-H_a, 6'''-H_a, 6'''''-H_a, CH_2), 3.85-3.82 (2H, m, 2'''-H, 2'''''-H), 3.77-3.67 (13H, m, 2'-H, 3'''-H, 3'''''-H, 4-H, 4''-H, 4''''-H, 5-H, 5''-H, 5''''-H, 6'-H_b, 6'''-H_b, 6'''''-H_b, CH_2), 3.59-3.56 (3H, m, 3-H, 3''-H, 3''''-H), 3.54-3.45 (7H, m, 3'-H, 4'-H, 4'''-H, 4'''''-H, 5'-H, 5'''-H, 5'''''-H), 3.36-3.30 (3H, m, 2-H, 2''-H, 2''''-H), 2.99-2.97 (2H, m, CH_2), 2.05-2.02 (9H, m, OCOCH_3), 1.70-1.63 (4H, m, CH_2), 1.46-1.43 (2H, m, CH_2); ^{13}C NMR (150 MHz, D_2O): δ 174.90 (C), 174.84 (C), 174.2 (C), 103.1 (CH), 102.3 (CH), 100.6 (CH), 100.5 (CH), 82.5 (CH), 82.3 (CH), 80.1 (CH), 79.9 (CH), 79.7 (CH), 76.7 (CH), 76.3 (CH), 73.9 (CH), 73.8 (CH), 73.5 (CH), 72.7 (CH), 72.4 (CH), 70.2 (CH_2), 69.6 (CH), 68.4 (CH), 60.5 (CH_2), 55.3 (CH), 54.2 (CH), 39.3 (CH_2), 28.1 (CH_2), 26.2 (CH_2), 22.4 (CH_3), 22.3 (CH_3), 21.9 (CH_2); HRMS (ESI): *m/z* calcd for $C_{47}H_{74}N_4O_{34}Si$ ([M+H$^+$]): 1307.3872, found: 1307.3831.

Conflicts of interest

There are no conflicts to declare.

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Table of Contents

A practical route for the synthesis of hyaluronic acid oligosaccharides was developed and a tetrasaccharide (GlcNAcβ1→4GlcAβ1→3GlcNAcβ1→4GlcAβ1→) was identified to be the minimum sugar unit to bind with human CD44 (K_D = 3.5 μM) through the measurement of Isothermal Titration Calorimeter.