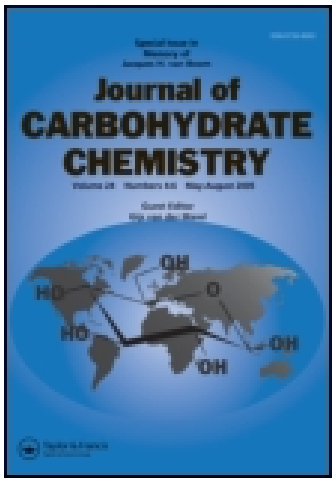

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SYNTHESIS OF NEW GLYCOPOLYMERS CONTAINING β-D-MANNOPYRANOSE, AND *C*-2-SUBSTITUTED β-D-MANNOPYRANOSE RESIDUES AS A NEW CLASS OF INHIBITOR

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ABSTRACT

New styryl monomers containing β-D-mannopyranose, 2-acetamido-2-deoxy-β-D-mannopyranose, 2-deoxy-2-fluoro-β-D-mannopyranose, and 2-deoxy-β-D-*arabino*-hexopyranose on their side chains, were efficiently synthesized as a new class of a potent inhibitor resistant to *exo*-α-mannosidase digestion. The binding affinity of the carbohydrate polymers obtained from those mannopyranosyl styryl monomers by radical polymerization with Concanavalin A were evaluated. A binding assay indicated that the multivalency effect and the affinity enhancement attained by modification at the *C*-2 position of the β-D-mannopyranoside residue resulted in the β-D-mannopyranosyl polymer which has the same affinity as that of the α-D-mannopyranosyl polymer.

*Corresponding author.

INTRODUCTION

Concanavalin A (Con A) binds α-D-mannopyranoside in preference to other mono-carbohydrate ligands and this specificity has been extensively investigated.[1] The 3-, 4-, and 6-hydroxyl groups of D-mannopyranoside are essential for Con A binding. On the other hand, the Con A binding affinity toward β-D-mannopyranoside is only one-fortieth that of α-D-mannopyranoside[1] due to steric hindrance of the glycosyl bond in the binding site.[1] In addition, X-ray crystallographic analysis showed that the oxygen atom at the anomeric position and the 2-hydroxyl group of α-D-mannopyranoside is positioned out of the binding site of Con A.[2] This result suggests that the 2-hydroxyl group is not specifically recognized.

In order to synthesize an effective inhibitor against carbohydrate-processing enzymes, for use as in *in vivo* assays, resistance toward *exo*-glycosidase digestion is essential. With this goal in mind, several inhibitors such as *S*- or *C*-glycosyl analogues have been synthesized by other researchers.[3,4] In our work, we planned to synthesize a new class of inhibitor based on a β-D-mannopyranoside scaffold, which can resist *exo*-α-D-mannosidase, which is relatively abundant compared with the low levels of β-D-mannosidase present in the *in vivo* assay environment. However, the binding affinity of β-D-mannopyranoside is significantly less than that of the α-isomer, as mentioned above. In order to enhance the low binding affinity of a β-D-mannopyranoside scaffold, several methods were considered.

Recently, two approaches for enhancement of the binding affinity of carbohydrate ligands have been reported. One is the use of a multivalent glycoconjugate to take advantage of the multivalency effect.[5–16] The other approach is to modify the carbohydrate ligand with an enhancer[17] for binding affinity. Specifically, one of the hydroxyl groups positioned away from the binding site of the receptor, is modified with an enhancer. We thought that these two approaches could be combined effectively to enhance the binding affinity of carbohydrate ligands to receptors. However, such a combined approach had not been reported. Therefore, we set out to determine whether a combined multivalency effect and enhancer modification would result in β-D-mannopyranoside possessing sufficient binding affinity toward Con A. We expected the substitution of the 2-hydroxyl group of β-D-mannopyranoside with an enhancer to result in increased binding affinity. In this work, we examined substitution of the 2-hydroxyl with hydrogen (deoxy),[18,19] fluoro,[18,19] and acetamide groups, because hydrogen atoms are known to enhance binding affinity through hydrophobic interactions and fluorine acts as a proton acceptor for hydrogen bonds. The acetamide group is thought to act as both a proton donor and a proton acceptor in addition to participating in hydrophobic interactions.

In this paper, we describe the synthesis and the Con A binding ability of several styryl polymers containing β-D-mannopyranoside analogues containing binding enhancers to illustrate this approach for the construction of novel inhibitors.

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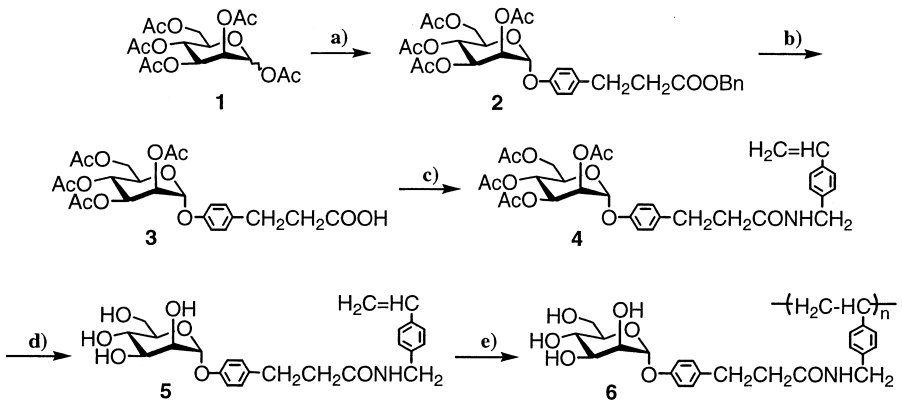
RESULTS AND DISCUSSION

Synthesis

For the synthesis of glycopolymers, we selected a styryl derivative as the monomer. Further, 3-(*p*-hydroxyphenyl)propionic acid was selected as the spacer, since an aromatic ring at the anomeric position of D-mannopyranoside increases the binding affinity over that of the methyl glycoside.[1] In addition, the propionic acid residue was used to distance the polymer backbone from the carbohydrate residue and thus enable efficient binding with Con A.

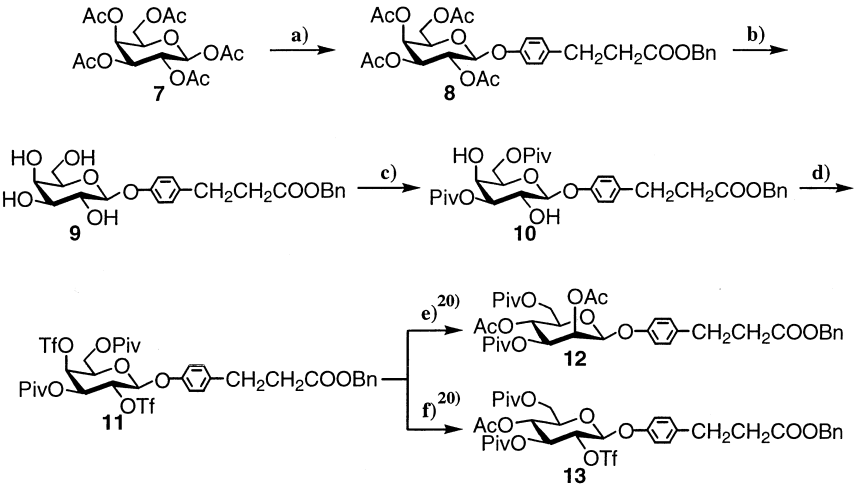
We started by synthesizing the glycopolymers **6** containing the spacer-armed α-D-mannopyranoside as the standard compound for the Con A binding assay. The α-D-mannopyranoside derivative **2** was prepared by glycosylation of 1,2,3,4,6-penta-*O*-acetyl-D-mannopyranose with benzyl 3-(*p*-hydroxyphenyl)propionate in 83% yield, and then reduced in the presence of 10% $Pd(OH)_2$-C/H_2 in EtOH to give the corresponding carboxylic acid derivative **3** in 97% yield. Condensation of **3** with *p*-vinylbenzylamine[16] by the use of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (WSC) in dichloromethane gave the corresponding amide derivative **4** in 73% yield. Subsequently, *O*-deacetylation of **4** with NaOMe/MeOH gave *p*-[2-(*N*-*p*-vinylbenzyl)carbamoyl]ethyl]phenyl α-D-mannopyranoside **5**, in 97% yield, as a glycomonomer containing the α-D-mannopyranoside residue on its side chain. Finally, the α-D-mannopyranosyl polymer **6** was obtained *via* radical polymerization of **5** by treatment with 2,2′-azobisisobutyronitrile (AIBN), in 98% yield (Scheme 1).

For the synthesis of the β-D-mannopyranoside derivatives, we employed a method developed previously in our laboratory to form the β-D-mannopyranosyl linkage (Scheme 2).[20] In this way, we synthesized glycomonomers containing the



a) TMSOTf, HO-C_6H_4-CH_2CH_2COOBn (34) / CH_2Cl_2, 0 °C (y. 83%); b) 10% $Pd(OH)_2$-C, H_2 / EtOH, rt (y. 97%); c) H_2N-CH_2-C_6H_4-CH_2=CH_2, WSC / CH_2Cl_2, 0 °C (y. 73%); d) NaOMe /MeOH, rt (y. 97%); e) AIBN / DMSO, 65 °C, 24 h (y. 98%).

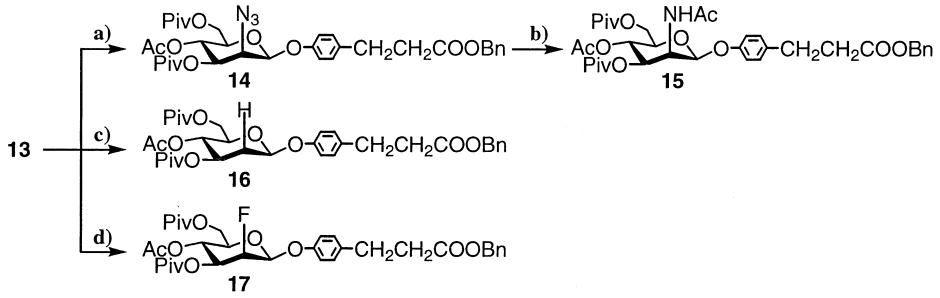
Scheme 1.



a) $SnCl_4$, HO-C_6H_4-CH_2CH_2COOBn (34) / CH_2Cl_2, -19 °C (y. 59%); b) NaOBn / CH_2Cl_2, rt (y.74%); c) $(Bu_3Sn)_2O$ / Benzene, reflux, 2 h then PivCl / Benzene, rt (y. 66%); d) Tf_2O, Py. / CH_2Cl_2, 0 °C (y. quant.); e) CsOAc, 18-crown-6 / Toluene, Ultrasonication, rt (y. 87%); f) CsOAc (1.2 mol equiv), 18-crown-6 (1.2 mol equiv) / Toluene, rt (y. 92%).

Scheme 2.

spacer-armed β-D-mannopyranoside derivative **12**, the 2-acetamido-2-deoxy-β-D-mannopyranoside derivative **15**, the 2-deoxy-β-D-*arabino*-hexopyranoside derivative **16**, and the 2-deoxy-2-fluoro-β-D-mannopyranoside derivative **17** starting from the β-D-galactopyranoside derivative **10** (Schemes 2 and 3). Compound **10** was synthesized as follows. Glycosylation of 1,2,3,4,6-penta-*O*-acetyl-β-D-galactopyranose **7** with benzyl 3-(*p*-hydroxyphenyl)propionate in the presence of tin(IV) chloride gave the corresponding β-D-galactopyranoside **8** in 59% yield, which was then treated with NaOBn/BnOH in dichloromethane to give *p*-[2-(ben-



a) *n*-Bu_4NN_3 / Toluene, Ultrasonication, rt (y. 87%); b) 5% Pd-C, H_2 / Toluene, rt, then Ac_2O. (y. 53%); c) *n*-Bu_4NBH_4 / Toluene, Ultrasonication, rt (y. 52%); d) *n*-Bu_4NF, Benzene, rt (y. 37%).

Scheme 3.

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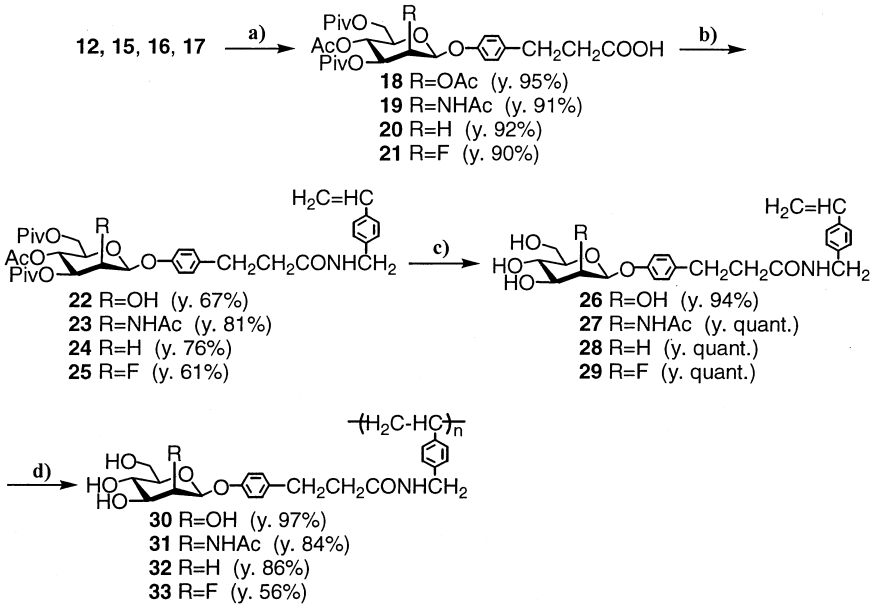
zyloxycarbonyl)ethyl]phenyl β-D-galactopyranoside **9** in 74% yield. Selective stannylation of **9** with bis(tributyltin) oxide and subsequent pivaloylation were performed in 66% yield (2 steps). The resulting pivaloate **10** was then treated with trifluoromethanesulfonic anhydride in pyridine at −19°C to give the 2,4-bistriflate derivative **11** in quantitative yield. Simultaneous nucleophilic substitution reactions at the *C*-2 and *C*-4 positions of **11** with cesium acetate (3.0 mol equiv) afforded the β-D-mannopyranoside derivative **12** in 87% yield. The structure of **12** was identified by ^{1}H NMR ($J_{3,4}$ = 9.7 Hz, $J_{4,5}$ = 9.7 Hz, $J_{1,2}$ = 1.2 Hz and $J_{2,3}$ = 3.0 Hz). When a small amount of cesium acetate (1.2 mol equiv) was used, the reaction afforded the 4-*O*-acetyl glucopyranoside **13** exclusively (92%) (Scheme 2). This β-D-glucopyranoside derivative (2-triflate) **13** was treated with *n*-Bu_4NN_3, *n*-Bu_4NBH_4,[20,21] or *n*-Bu_4NF,[20,22] under ultrasonication conditions to afford the corresponding manno-type 2-azido **14**, 2-deoxy **16**, and 2-fluoro **17** derivatives, respectively, in moderate yields (Scheme 3). Catalytic reduction of the azido group of **14** and subsequent acetylation gave the desired 2-acetamido-β-D-mannopyranoside derivative **15** in 53% yield as well as unreacted **14** (42%). β-D-Mannopyranosyl derivatives **12**, **15**, **16**, and **17** thus obtained were then hydrogenolyzed to give the corresponding carboxylic acid derivatives **18** (95%), **19** (91%), **20** (92%), and **21** (90%), respectively. Condensation of **18**, **19**, **20**, and **21** with *p*-vinylbenzylamine[16] led to the corresponding amide derivatives **22**, **23**, **24**, and **25** in 67, 81, 76, and 61% yields, respectively. *O*-Deacylation of **22**, **23**, **24**, and **25** with NaOMe/MeOH, was performed in near quantitative yield to afford the desired *p*-[3-(*N*-*p*-vinylbenzyl)carbamoyl]ethyl]phenyl glycomonomers of β-D-mannopyranoside **26**, 2-deoxy-2-acetamido-β-D-mannopyranoside **27**, 2-deoxy-β-D-*arabino*-hexopyranoside **28**, and 2-deoxy-2-fluoro-β-D-mannopyranoside **29**, respectively. A polymerization reaction with 2,2′-azobisisobutyronitrile (AIBN) in dimethylsulfoxide was performed to give the corresponding glycopolymers **30**, **31**, **32** and **33** containing β-D-mannopyranoside (97% yield), 2-acetamido-2-deoxy-β-D-mannopyranoside (84% yield), 2-deoxy-2-fluoro-β-D-mannopyranoside (86% yield), 2-deoxy-β-D-*arabino*-hexopyranoside (56% yield) residues, respectively (Scheme 4). The averaged molecular weights and reduced viscosities were analyzed by gel permeation chromatography (GPC). The physical properties of the synthesized glycopolymers are shown in Table 1.

Con A Binding Assay

Binding assays of the synthetic glycopolymers toward Con A was performed using the enzyme linked lectin assay (ELLA)[23–25] method, which is a standard assay in the field. Soybean lectin with high mannose-type sugar chains was coated on a 96-well test plate and then used for the ELLA. The results are shown in Table 2.

The inhibition abilities of methyl α-D-mannopyranoside **35** and methyl α-D-glucopyranoside **36** show the same relative binding abilities in our assay system as in the published data.[24] The binding affinity of methyl α-D-glucopyranoside **36**



a) 10% Pd-C, H_2 / MeOH, rt; b) H_2N-CH_2-C_6H_4-CH=CH_2, WSC / CH_2Cl_2, 0 °C; c) NaOMe / MeOH, rt; d) AIBN / DMSO, 65 °C, 24 h.

Scheme 4.

Table 1. Physical Properties of Glycopolymers

Polymers	$Mn^a \times 10^{-4}$	Mw / Mn^a	η_{red} [dL/g][b]
6	6.3	1.90	0.47
30	5.1	1.45	0.12
31	2.3	1.65	0.10
32	5.3	1.63	0.18
33	7.6	1.53	0.33

[a] Determined by GPC based on polystyrene;
[b] Measured at 30 °C in DMSO.

Table 2. Inhibition Ability of Glycopolymers

Polymers	Number of Monomer	IC_{50} [M]	Monovalency-IC_{50} [mM]	Relative Potency
6	1.51×10^2	2.0×10^{-2}	3.0	5.6×10^2
30	1.22×10^2	3.1×10^{-1}	37	45
31	50.1	—	—	—
32	1.32×10^2	6.0	8.0×10^2	2.1
33	1.81×10^2	4.0×10^{-2}	7.2	2.4×10^2
35[a]	1.00	1.7×10^3	1.7×10^3	1.0
36[b]	1.00	2.5×10^3	2.5×10^3	6.9×10^{-1}

[a] Methyl α-D-mannopyranoside: **35**; [b]Methyl α-D-glucopyranoside: **36**.

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was measured to be 70% of that of α-D-mannopyranoside **35**. In polymers, the inhibition ability of 2-deoxy-β-D-mannosyl polymer **32** is shown to be only 2.1 times stronger than that of α-D-mannopyranoside **35** despite the multivalency. Also, 2-deoxy-2-acetamido-β-D-mannosyl polymer **31** showed no inhibitory activity. For a natural-type mannopyranosyl polymer, α-D-mannopyranosyl polymer **6** displayed potent inhibition activity (3.0 μM/residue). The binding affinity of the β-D-mannopyranosyl polymer **30** was one-twelfth of that of the α-D-mannopyranosyl polymer **6** due to the multivalency effect. Further, the inhibition potency was dramatically improved by the fluoro substituent of **33** resulting in a level comparable to that of the α-D-mannopyranosyl polymer **6**.

Con A recognizes α-D-mannopyranoside in strong preference to other monocarbohydrate ligands. When β-D-mannopyranoside is used as a ligand, the binding affinity is one-fortieth of that of α-D-mannopyranoside.[1] This tendency was also observed with the carbohydrate polymers **6** and **30**. The binding ability of the β-D-mannopyranosyl polymer **30** is one-twelfth of that of the corresponding α-D-mannopyranosyl polymer **6**, but the binding ability of β-D-mannopyranosyl polymer **30** is 45 times larger than that of methyl α-D-mannopyranoside **36**. These enhanced binding affinities almost certainly result from the multivalency effect. The hydrogen (deoxy) and acetamide groups at *C*-2 did not result in a notable enhancement in binding affinity. In contrast, the fluorine atom at *C*-2 enhanced the binding affinity of the β-D-mannopyranosyl polymer to the same level as that of the α-D-mannopyranosyl polymer. From this result we speculate that the fluorine atom at *C*-2 forms a hydrogen bond with an amino acid at the entrance of the Con A binding site, resulting in enhanced binding affinity. Recently, H. Tanaka and co-workers synthesized a glycoconjugate polymer carrying a 3,6-branched α-D-mannopyranosyl trisaccharide[26] on its scaffold.[27] Although it would seem that using a natural-type branched oligosaccharide residue would be most effective for increasing the binding ability, it is also important to consider the special properties of synthetic derivatives as inhibitors for use with *in vivo* assays, both for binding affinity and for resistance to *exo*-glycosidase digestion.

In conclusion, we have succeeded in the synthesis of new styryl polymers containing β-D-mannopyranose derivatives and found them to be potent inhibitors of *exo*-α-mannosidase digestion. We believe this to be the first report of such polymers. The results of Con A binding affinity studies show that some of these novel glycopolymers display impressive properties. We feel that the new approach described herein, which combines the multivalency effect and enhancer techniques, constitutes an exciting advance for the synthesis of highly potent inhibitors resistant to *exo*-glycosidase digestion.

EXPERIMENTAL

General Methods. All melting points were uncorrected. The solutions were concentrated under reduced pressure at a bath temperature not exceeding 45°C. The optical rotations were measured in a 0.5 dm tube with JASCO DIP-140

polarimeter in chloroform unless otherwise stated. ^{1}H NMR spectra were recorded with a JEOL EX-90, JEOL FX-200, JEOL EX-270, or JEOL A-500 spectrometer. IR spectra were recorded with a Hitachi 270-30 spectrometer. Elemental analyses were performed on a Perkin-Elmer 2400 II elemental analyzer. The chemical shifts, coupling constants, and IR frequencies were recorded in δ, Hz, and cm^{-1} units, respectively. Column chromatography was performed on silica gel (Silica gel 60, 70-230 mesh, Merck). Thin-layer chromatography (TLC) on silica gel (Silica gel 60 F_{254}, Merck) was used to monitor the reactions and to certify the reaction products. The molecular weights of the glycopolymers were estimated by gel permeation chromatography (GPC) with the use of a TOSO Model HLC-8020 GPC equipped with a refractive index detector using TSK gel columns (Tosoh Co. Ltd.) (eluent: *N,N*-dimethylformamide, calibrated with narrow molecular weight polystyrene standards).

***p*-[2-(Benzyloxycarbonyl)ethyl]phenyl 2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranoside (2).** To a solution of 1,2,3,4,6-penta-*O*-acetyl-α,β-D-mannnopyranose (**1**) (558 mg, 1.6 mmol), benzyl 3-(*p*-hydroxyphenyl)propionate (**34**) (665 mg, 2.6 mmol), and molecular sieves 4A in dry dichloromethane (20 mL), trimethylsilyl trifluoromethanesulfonate (0.31 mL, 1.6 mmol) was added dropwise under argon at 0°C. The reaction mixture was stirred at room temperature for 12 h until the disappearance of **1** on TLC with hexane/ethyl acetate (3/1 v/v). Triethylamine (1 mL) was added to the reaction mixture at 0°C, then molecular sieves were filtered off. The filtrate was poured into a saturated aq $NaHCO_3$ solution, extracted with ethyl acetate, washed with brine and water, dried over anhydrous magnesium sulfate, filtered, and concentrated to give a residue. The remaining residue was purified on a column of silica gel with hexane/ethyl acetate (3/1 v/v) to give **2** (692 mg, 83%): $[\alpha]_D^{25}$ +58.2° (*c* 2.1, $CHCl_3$); IR (cm^{-1}) 1743 (C=O); ^{1}H NMR (FX-200, $CDCl_3$) δ 7.37–7.29 (m, 5H, -CH_2*Ph*, J = 8.8 Hz), 7.12, 6.99 (each d, 4H, phenylene), 5.56 (dd, 1H, H-3, $J_{3,4}$ = 9.9 Hz), 5.47 (dd, 1H, H-1, $J_{1,2}$ = 1.8 Hz), 5.43 (dd, 1H, H-2, $J_{2,3}$ = 3.6 Hz), 5.37 (t, 1H, H-4, $J_{4,5}$ = 10.1 Hz), 5.10 (s, 2H, -C*H*$_2$Ph), 4.27 (dd, 1H, H-6′, $J_{5,6'}$ = 5.1 Hz), 4.10 (ddd, 1H, H-5, $J_{5,6}$ = 2.4 Hz), 4.05 (dd, 1H, H-6, $J_{6,6'}$ = 12.2 Hz), 2.93 (t, 2H, -CH_2C*H*$_2$CO-, J = 8.0 Hz), 2.65 (t, 2H, -C*H*$_2$$CH_2$CO-), 2.19, 2.05, 2.03, 2.02 (each s, 3H × 4, OAc).

Anal. Calcd for $C_{30}H_{34}O_{12}$: C, 61.43; H, 5.84. Found: C, 61.41; H, 5.88.

***p*-(2-Carboxyethyl)phenyl 2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranoside (3).** *p*-[2-(Benzyloxycarbonyl)ethyl]phenyl glycoside **2** (1.60 g, 2.7 mmol) was hydrogenolyzed in ethanol (25 mL) in the presence of a catalytic amount of 10% $Pd(OH)_2$-C/H_2 for 2 h until the disappearance of **2** on TLC with hexane/ethyl acetate (3/1 v/v). The solution was then filtered through a pad of celite and concentrated to afford **3** (1.34 g, 97% yield): $[\alpha]_D^{25}$ +67.4° (*c* 0.8, $CHCl_3$); IR (cm^{-1}) 3192 (OH), 1748 (C=O); ^{1}H NMR (FX-200, $CDCl_3$) δ 7.13, 7.00 (each d, 4H, phenylene, J = 8.1 Hz), 6.78 (br s, 1H, COOH), 5.55 (dd, 1H, H-3, $J_{3,4}$ = 10.0 Hz), 5.48 (dd, 1H, H-1, $J_{1,2}$ = 1.9 Hz), 5.43 (dd, 1H, H-2, $J_{2,3}$ = 3,4 Hz), 5.36 (dd, 1H,

H-4, $J_{4,5}$ = 10.0 Hz), 4.28 (dd, 1H, H-6′, $J_{5,6'}$ = 5.1 Hz, $J_{6,6'}$ = 12.0 Hz), 4.13–4.04 (m, 2H, H-5 and H-6), 2.89 (t, 2H, -CH_2CH_2CO-, J = 7.8 Hz), 2.61 (t, 2H, -CH_2CH_2CO-), 2.20, 2.05, 2.03, 2.03 (each s, 3H × 4, OAc).

Anal. Calcd for $C_{23}H_{28}O_{12}$: C, 55.65; H, 5.68. Found: C, 55.45; H, 5.72.

***p*-[2-[*N*-(*p*-Vinylbenzyl)carbamoyl]ethyl]phenyl 2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranoside (4).** To a solution of *p*-(2-carboxyethyl)phenyl glycoside **3** (1.27 g, 2.50 mmol) and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (WSC) (585 mg, 3.05 mmol) in dichloromethane (100 mL), a solution of *p*-vinylbenzylamine[16] (378 mg, 2.82 mmol) in dichloromethane (40 mL) was added dropwise at 0°C, and stirred for 1 h until the disappearance of **3** on TLC with hexane/ethyl acetate (1/1 v/v). The reaction mixture was diluted with dichloromethane, washed with 10 % aq citric acid solution, brine and water, dried over anhydrous magnesium sulfate, filtered, and concentrated to give a residue. The remaining residue was purified on a column of silica gel with hexane/ethyl acetate (3/5 v/v) to afford **4** (1.14 g, 73% yield): $[\alpha]_D^{25}$ +66.0° (*c* 0.7, $CHCl_3$); IR (cm^{-1}) 1758 (C=O), 1650 (C=C); ^{1}H NMR (A-500, $CDCl_3$) δ 7.34, 7.12 (each d, 4H, styryl phenylene, J = 7.9 Hz), 7.12, 6.99 (each d, 4H, phenylene, J = 8.5 Hz), 6.69 (dd, 1H, -Ph-C*H*=CHaHb, J_{trans} = 17.6 Hz, J_{cis} = 11.2 Hz), 5.73 (dd, 1H, Ha, J_{gem} = 0.7 Hz), 5.71 (t, 1H, -CONH-), 5.56 (dd, 1H, H-3, $J_{3,4}$ = 9.9 Hz), 5.47 (dd, 1H, H-1, $J_{1,2}$ = 1.8 Hz), 5.43 (1H, dd, H-2, $J_{2,3}$ = 3.6 Hz), 5.37 (1H, dd, H-4, $J_{4,5}$ = 10.1 Hz), 5.23 (1H, dd, Hb), 4.37 (2H, d, -NHCH_2-, $J_{NH,CH2}$ = 5.8 Hz), 4.27 (1H, dd, H-6′, $J_{5,6'}$ = 5.1 Hz), 4.10 (1H, ddd, H-5, $J_{5,6}$ = 2.4 Hz), 4.05 (dd, 1H, H-6, $J_{6,6'}$ = 12.2 Hz), 2.94 (t, 2H, -CH_2CH_2CO-, J = 7.8 Hz), 2.47 (t, 2H, -CH_2CH_2CO-), 2.19, 2.05, 2.03, 2.02 (each s, 3H × 4, OAc).

Anal. Calcd for $C_{32}H_{37}O_{11}N$: C, 62.84; H, 6.10; N, 2.15. Found: C, 62.42; H, 6.55; N, 2.26.

***p*-[2-[*N*-(*p*-Vinylbenzyl)carbamoyl]ethyl]phenyl α-D-Mannopyranoside (5).** To a solution of *p*-[2-[*N*-(*p*-vinylbenzyl)carbamoyl]ethyl]phenyl glycoside **4** (1.14 g, 1.86 mmol) in methanol (25 mL), sodium methoxide (1.9M methanol solution) was carefully added at pH 10, stirred for 2 h until the disappearance of **4** on TLC with hexane/ethyl acetate (1/2 v/v). The reaction mixture was neutralized with Dowex 50W-X8 (H^+ form) ion-exchange resin, filtered, and concentrated to give pure styryl monomer containing carbohydrate residue **5** (756 mg, 97% yield): mp 171–174°C (methanol); $[\alpha]_D^{25}$ +83.6° (*c* 0.7, $CHCl_3$); IR (cm^{-1}) 3284 (OH), 1640 (C=O, C=C); ^{1}H NMR (A-500, d_6-DMSO) δ 8.35 (t, 1H, NH), 7.33, 6.98 (each d, 4H, styryl phenylene, J = 8.2 Hz), 7.12, 7.11 (each d, 4H, phenylene, J = 8.6 Hz), 6.68 (dd, 1H, -Ph-C*H*=CHaHb, J_{trans} = 17.4 Hz, J_{cis} = 10.8 Hz), 5.76, 5.73 (dd, 1H, Ha, J_{gem} = 0.9 Hz), 5.35 (d, 1H, H-1, $J_{1,2}$ = 1.9 Hz), 5.21 (dd, 1H, Hb), 4.26 (d, 2H, -NHCH_2-, $J_{NH,CH2}$ = 5.5 Hz), 3.89 (d, 1H, H-2, $J_{2,3}$ = 3.3 Hz), 3.75 (dd, 1H, H-3, $J_{3,4}$ = 9.2 Hz), 3.63–3.57 (m, 3H, H-4, H-6, and H-6′), 3.49 (ddd, 1H, H-5, $J_{4,5}$ = 9.5 Hz, $J_{5,6}$ = 2.7 Hz, $J_{5,6'}$ = 5.2 Hz), 3.39 (s, 4H, OH), 2.83 (t, 2H, -CH_2CH_2CO-, J = 7.8 Hz), 2.45 (t, 2H, -CH_2CH_2CO-); ^{13}C NMR (A-500, d_6-DMSO) δ 171.32 (C=O), 138.87, 135.54, 134.46, 128.95, 127.20, 125.71 (Ph),

136.12 (*C*H=CH_2), 113.33 (CH=*C*H_2), 98.95 (C-1), 74.14 (C-2), 70.61 (C-3), 69.96 (C-4), 66.67 (C-5), 60.90 (C-6), 41.69, 37.11, 30.29 (CH_2).

Anal. Calcd for $C_{24}H_{29}O_{76}N$: C, 65.00; H, 6.59; N, 3.16. Found: C, 64.82; H, 6.30; N, 2.70.

Poly[*p*-[2-[*N*-(*p*-vinylbenzyl)carbamoyl]ethyl]phenyl α-D-mannopyranoside] (6). To a solution of **5** (726 mg, 1.64 mmol) in DMSO (2.0 mL), 2,2′-azobisisobutyronitrile (4.0 mg, 0.02 mmol) was added. The mixture was set in a sealed tube, degassed with argon, and kept at 65°C in oil bath for 24 h. The reaction mixture was poured into stirred acetone, and the precipitate was filtered using a glass filter to give **6** (710 mg, 98% yield): IR (cm^{-1}) 3408 (OH), 1646 (C=O); ^{13}C NMR (A-500, d_6-DMSO) δ 171.32 (C=O), 128.99, 116.65 (Ph), 126.52 (-*C*H-CH_2-), 99.00 (C-1), 74.58 (C-2), 70.66 (C-3), 70.09 (C-4), 66.69 (C-5), 60.99 (C-6), 41.72, 40.41, 37.19, 30.33 (CH_2).

***p*-[2-(Benzyloxycarbonyl)ethyl]phenyl 2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranoside (8).** To a mixture of **7** (15.0 g, 384 mmol) and **34** (10.8 g, 422 mmol) in dry CH_2Cl_2 (300 mL), anhydrous tin(IV) chloride (5.0 mL, 422 mmol) was added dropwise under argon at −19°C. The reaction mixture was kept with stirring for 1 h until the disappearance of **7** on TLC with hexane/ethyl acetate (3/1 v/v). The reaction mixture was poured into a saturated aq $NaHCO_3$ solution with activated potassium fluoride (5.0 g), and stirred for 12 h. The above mixture was filtered and extracted with $CHCl_3$. The combined organic solution was washed with brine and water, dried over anhydrous magnesium sulfate, filtered, and concentrated to give a residue. The remaining residue was purified on a column of silica gel with hexane/ethyl acetate (3/1 v/v) to afford **8** (13.8 g, 59% yield): mp 108–109°C (ethanol-hexane); $[\alpha]_D^{25}$ −13.4° (*c* 0.9, $CHCl_3$); IR (cm^{-1}) 1752 (C=O); ^1H NMR (FX-200, $CDCl_3$) δ 7.37–7.26 (m, 4H, -CH_2*Ph*), 7.11, 6.99 (each d, 4H, phenylene, J = 8.8 Hz), 5.48 (dd, 1H, H-2, $J_{2,3}$ = 10.5 Hz), 5.45 (dd, 1H, H-4, $J_{4,5}$ = 0.9 Hz), 5.10 (dd, 1H, H-3, $J_{3,4}$ = 3.4 Hz), 5.10 (s, 2H, -C*H*$_2$Ph), 5.00 (d, 1H, H-1, $J_{1,2}$ = 7.8 Hz), 4.25–4.04 (m, 3H, H-5, H-6, and H-6′), 2.93 (t, 2H, -CH_2C*H*$_2$CO-, J = 7.8 Hz), 2.65 (t, 2H, -C*H*$_2$$CH_2$CO-), 2.18, 2.07, 2.06, 2.01 (each s, 3H × 4, OAc).

Anal. Calcd for $C_{30}H_{34}O_{12}$: C, 61.43; H, 5.84. Found: C, 61.41; H, 5.88.

***p*-[2-(Benzyloxycarbonyl)ethyl]phenyl β-D-Galactopyranoside (9).** To a solution of **8** (200 mg, 0.34 mmol) in CH_2Cl_2 (50 mL), 1M NaOBn in BnOH was carefully added at pH 11 at 0°C, and stirred for 1 h until the disappearance of **9** on TLC with hexane/ethyl acetate (3/1 v/v). The reaction mixture was neutralized with Dowex 50W-X8 (H^+ form) ion-exchange resin, filtered, and concentrated to give a residue. The remaining residue was purified on a column of silica gel with $CHCl_3$/MeOH (8/1 v/v) to afford **9** (120 mg, 74% yield): $[\alpha]_D^{25}$ −25.4° (*c* 0.9, MeOH); mp 86–87.5°C (methanol-ether); IR (cm^{-1}) 3369 (OH), 1730 (C=O); ^1H NMR (A-500, CD_3OD) δ 7.24–7.14 (m, 5H, -CH_2*Ph*), 7.11, 7.02 (each d, 4H, phenylene, J = 8.8 Hz), 5.10 (s, 2H, -C*H*$_2$Ph), 4.84 (d, 1H, H-1, $J_{1,2}$ = 7.6 Hz),

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3.93 (dd, 1H, H-4, $J_{4,5}$ = 1.0 Hz), 3.82 (dd, 1H, H-2, $J_{2,3}$ = 9.8 Hz), 3.81 (dd, 1H, H-6′. $J_{6,6'}$ = 11.3 Hz), 3.77 (dd, 1H, $J_{5,6}$ = 6.7 Hz), 3.69 (ddd, 1H, H-5, $J_{5,6'}$ = 5.2 Hz), 3.60 (dd, 1H, H-3, $J_{3,4}$ = 3.7 Hz), 2.90 (t, 2H, -CH_2CH_2CO-, J = 7.6 Hz), 2.66 (t, 2H, -CH_2CH_2CO-).

Anal. Calcd for $C_{22}H_{26}O_8$: C, 63.15; H, 6.26. Found: C, 63.35; H, 6.26.

***p*-[2-(Benzyloxycarbonyl)ethyl]phenyl 3,6-Di-*O*-pivaloyl-β-D-galactopyranoside (10).** A solution of **9** (300 mg, 0.72 mmol) and bis(tributyltin) oxide (1.31 g, 2.2 mmol) in toluene was refluxed for 2 h with a Dean-Stark apparatus, then pivaloyl chloride (2.5 mL, 2.09 mmol) was added at 0°C and stirred for 72 h at rt until the disappearance of **9** on TLC with chloroform/methanol (8/1 v/v). The mixture was diluted with ethyl acetate (50 mL), treated with a saturated aq $NaHCO_3$ solution and activated potassium fluoride, filtered, and separated. The aqueous solution was extracted with ethyl acetate. The combined organic solution was washed with brine and water, dried over anhydrous magnesium sulfate, filtered, and concentrated to give a residue. The remaining residue was purified on a column of silica gel with hexane/ethyl acetate (2/1 v/v) to afford **10** (278 mg, 66% yield): mp 104–105°C (ethanol-hexane); $[\alpha]_D^{25}$ +17.4° (*c* 0.5, $CHCl_3$); IR (cm^{-1}) 3548 (OH), 1724 (C=O); ^{1}H NMR (A-500, $CDCl_3$) δ 7.37–7.28 (m, 5H, -CH_2Ph), 7.08, 6.97 (each d, 4H, phenylene, J = 8.5 Hz), 5.10 (s, 2H, -CH_2Ph), 4.93 (dd, 1H, H-3, $J_{3,4}$ = 10.1 Hz), 4.88 (d, 1H, H-1, $J_{1,2}$ = 7.7 Hz), 4.36 (dd, 1H, H-6, $J_{6,6'}$ = 11.6 Hz), 4.29 (dd, 1H, H-6′), 4.12 (ddd, 1H, H-2, $J_{2,3}$ = 3.4 Hz), 4.04 (dd, 1H, H-4), 3.89 (dd, 1H, H-5, $J_{5,6}$ = 5.2 Hz, $J_{5,6'}$ = 7.4 Hz), 2.91 (t, 2H, -CH_2CH_2CO, J = 7.7 Hz), 2.64 (t, 2H, -CH_2CH_2CO-), 2.46 (d, 1H, OH, $J_{2,OH}$ = 3.3 Hz), 2.21 (d, 1H, OH, $J_{4,OH}$ = 4.9 Hz), 1.27, 1.20 (each s, 9H × 2, OPiv).

Anal. Calcd for $C_{32}H_{42}O_{10}$: C, 65.26; H, 7.22. Found: C, 65.26; H, 7.22.

***p*-[2-(Benzyloxycarbonyl)ethyl]phenyl 3,6-Di-*O*-pivaloyl-2,4-bis(*O*-trifluoromethylsulfonyl)-β-D-galactopyranoside (11).** To a solution of **10** (100 mg, 0.17 mmol) in pyridine (10 mL), trifluoromethanesulfonic anhydride (0.1 mL, 0.59 mmol) was added under argon at −19°C. The reaction mixture was stirred at room temperature for 4 h until the disappearance of **10** on TLC with hexane/ethyl acetate (2/1 v/v). The reaction mixture was poured into a saturated aq $NaHCO_3$ solution and extracted with $CHCl_3$. The combined organic layer was washed with brine and water, dried over anhydrous magnesium sulfate, and concentrated to give a residue. The remaining residue was purified on a short column of silica gel with hexane/ethyl acetate (3/1 v/v) to afford **10** (145 mg, quantitatively): IR (cm^{-1}) 2974 (OH), 1740 (C=O); ^{1}H NMR (FX-200, $CDCl_3$) δ 7.40–7.28 (m, 5H, -CH_2 *Ph*), 7.12, 6.94 (each d, 4H, phenylene, J = 8.8 Hz), 5.36 (d, 1H, H-4, $J_{3,4}$ = 2.7 Hz), 5.23 (dd, 1H, H-2, $J_{2,3}$ = 9.3 Hz), 5.22 (dd, 1H, H-3), 5.20 (d, 1H, H-1, $J_{1,2}$ = 6.8 Hz), 5.11 (s, 2H, -CH_2Ph), 4.37 (dd, 1H, H-6, $J_{6,6'}$ = 10.5 Hz), 4.19 (dd, 1H, H-5, $J_{5,6'}$ = 6.1 Hz), 4.08 (dd, 1H, H-6, $J_{5,6}$ = 6.1 Hz), 2.94 (t, 2H, -CH_2CH_2CO-, J = 7.8 Hz), 2.65 (t, 2H, -CH_2CH_2CO-), 1.31, 1.21 (each s, 9H × 2, OPiv).

***p*-[2-(Benzyloxycarbonyl)ethyl]phenyl 2,4-Di-*O*-acetyl-3,6-di-*O*-pivaloyl-β-D-mannopyranoside (12).** The reaction mixture of **11** (145 mg, 0.17 mmol), cesium acetate (98 mg, 0.51 mmol, 3.0 mol equiv) and 18-crown-6 ether (135 mg, 0.51 mmol) in dry benzene (30 mL) was stirred overnight under ultrasonication for 12 h until the disappearance of **11** on TLC with hexane/ethyl acetate (3/1 v/v). The reaction mixture was diluted with ethyl acetate, washed with brine and water, dried over anhydrous magnesium sulfate, filtered, and concentrated to give a residue. The remaining residue was purified on a column of silica gel with hexane/ethyl acetate (3/1 v/v) to afford **12** (99 mg, 87% yield): $[\alpha]_D^{25}$ −36.1° (*c* 0.7, $CHCl_3$); IR (cm^{-1}) 1740 (C=O); ^1H NMR (FX-200, $CDCl_3$) δ 7.33–7.26 (m, 5H, -CH_2*Ph*), 7.08, 6.92 (each d, 4H, phenylene, J = 8.7 Hz), 5.69 (dd, 1H, H-2, $J_{2,3}$ = 3.0 Hz), 5.34 (t, 1H, H-4, $J_{4,5}$ = 9.7 Hz), 5.17 (d, 1H, H-1, $J_{1,2}$ = 1.2 Hz), 5.10 (s, 2H, -CH_2Ph), 5.10 (dd, 1H, H-3, $J_{3,4}$ = 9.7 Hz), 4.30 (dd, 1H, H-6′, $J_{6,6'}$ = 12.2 Hz), 4.17 (dd, 1H, H6, $J_{5,6}$ = 6.7 Hz), 3.86 (ddd, 1H, H-5, $J_{5,6'}$ = 2.4 Hz), 2.91 (t, 2H, -CH_2CH_2CO-, J = 7.8 Hz), 2.62 (t, 2H, -C$H_2$$CH_2$CO-), 2.20, 2.05 (each s, 3H × 2, OAc), 1.22, 1.15 (each s, 9H × 2, OPiv).

Anal. Calcd for $C_{36}H_{46}O_{12}$: C, 50.98; H, 5.76. Found: C, 64.03; H, 7.25.

***p*-[2-(Benzyloxycarbonyl)ethyl]phenyl 4-*O*-Acetyl-3,6-di-*O*-pivaloyl-2-*O*-trifluoromethylsulfonyl-β-D-glucopyranoside (13).** To a solution of **11** (1.27 g, 1.5 mmol) in dry toluene (55 mL), cesium acetate (344 mg, 1.79 mmol) and 18-crown-6 ether (474 mg, 1.79 mmol, 2.0 mol equiv) were added and stirred for 4 h at rt until the disappearance of **11** on TLC with hexane/ethyl acetate (3/1 v/v). The reaction mixture was diluted with ethyl acetate, washed with brine and water, dried over anhydrous magnesium sulfate, filtered, and concentrated to give a residue. The remaining residue was purified on a column of silica gel with hexane/ethyl acetate (3/1 v/v) to afford **17** (1.04 g, 92% yield): $[\alpha]_D^{25}$ −14.6° (*c* 0.9, $CHCl_3$); IR (cm^{-1}) 1743 (C=O); ^1H NMR (FX-200, $CDCl_3$) δ 7.37–7.29 (m, 5H, -CH_2*Ph*), 7.10, 6.70 (each d, 4H, phenylene, J = 8.5 Hz), 5.50 (dd, 1H, H-3, $J_{3,4}$ = 9.4 Hz), 5.14 (d, 1H, H-1, $J_{1,2}$ = 7.9 Hz), 5.13 (dd, 1H, H-4, $J_{4,5}$ = 9.4 Hz), 5.10 (s, 2H, -CH_2Ph), 4.97 (dd, 1H, H-2, $J_{2,3}$ = 9.5 Hz), 4.23 (dd, 1H, H-6′, $J_{5,6'}$ = 2.1 Hz), 4.12 (dd, 1H, H-6, $J_{6,6'}$ = 12.2 Hz), 3.89 (ddd, 1H, H-5, $J_{5,6}$ = 6.4 Hz), 2.93 (t, 2H, -CH_2CH_2CO-, J = 7.8 Hz), 2.65 (t, 2H, -C$H_2$$CH_2$CO-), 2.04 (s, 3H, OAc), 1.22, 1.21 (each s, 9H × 2, OPiv).

Anal. Calcd for $C_{35}H_{43}F_3O_{12}S$: C, 56.44; H, 5.82. Found: C, 56.35; H, 6.15.

***p*-[2-(Benzyloxycarbonyl)ethyl]phenyl 4-*O*-Acetyl-2-azido-2-deoxy-3,6-di-*O*-pivaloyl-β-D-mannopyranoside (14).** To a solution of **13** (839 mg, 1.10 mmol) in dry benzene (30 mL), tetrabutylammonium azide (627 mg, 2.20 mmol) was added and stirred for 12 h in a water bath under ultrasonication until the disappearance of **13** on TLC with hexane/ethyl acetate (3/1 v/v). The reaction mixture was diluted with ethyl acetate, washed with brine and water, dried over anhydrous magnesium sulfate, and concentrated to give a residue. The remaining residue was purified on a column of silica gel with hexane/ethyl acetate (3/1 v/v) to afford **14** (691 mg, 96% yield): mp 61.5–64°C (ether-hexane); $[\alpha]_D^{25}$ +45.0° (*c* 0.9, $CHCl_3$);

IR (cm^{-1}) 2112 (N_3), 1732 (C=O); ^{1}H NMR (A-500, $CDCl_3$) δ 7.38–7.29 (m, 5H, -CH_2*Ph*), 7.02, 6.94 (each d, 4H, phenylene, J = 8.5 Hz), 5.31 (dd, 1H, H-4, $J_{4,5}$ = 9.7 Hz), 5.20 (d, 1H, H-1, $J_{1,2}$ = 1.2 Hz), 5.10 (s, 2H, -CH_2Ph), 5.02 (dd, 1H, H-3, $J_{3,4}$ = 9.7 Hz), 4.27 (dd, 1H, H-2, $J_{2,3}$ = 3.6 Hz), 4.26 (dd, 1H, H-6, $J_{6,6'}$ = 11.9 Hz), 4.13 (dd, 1H, H-6′, $J_{5,6'}$ = 6.7 Hz), 3.77 (1H, ddd, H-5, $J_{5,6}$ = 2.4 Hz), 2.92 (t, 2H, -CH_2CH_2CO-, J = 7.8 Hz), 2.64 (t, 2H, -C$H_2$$CH_2$CO-), 2.04 (s, 3H, OAc), 1.23, 1.21 (each s, 9H × 2, OPiv).

Anal. Calcd for $C_{34}H_{43}N_3O_{10}$: C, 62.47; H, 6.63; N, 6.43. Found: C, 62.75; H, 6.88; N, 6.34.

***p*-(Benzyloxycarbonylethyl)phenyl 2-Acetamido-4-*O*-acetyl-2-deoxy-3,6-di-*O*-pivaloyl-β-D-mannopyranoside (15).** Compound **14** (733 mg, 1.12 mmol) was hydrogenolyzed in the presence of a catalytic amount of 5% Pd-C/H_2 in benzene (25 mL) for 1 h. The reaction mixture was then filtered through a pad of celite. The filtrate was treated with acetic anhydride (0.5 mL) at rt for 30 min, and concentrated to give a residue. The remaining residue was purified on a column of silica gel with hexane/ethyl acetate (2/1 v/v) to afford **15** (400 mg, 53% yield) and recovered **14** (311 mg, 42% yield): mp 116–117°C (dec.) (ethanol-hexane); $[\alpha]_D^{25}$ −5.6° (*c* 0.7, $CHCl_3$); IR (cm^{-1}) 1737 and 1680 (C=O); ^{1}H NMR (EX-270, $CDCl_3$) δ 7.37–7.30 (m, 5H, -CH_2*Ph*), 7.08, 6.91 (each d, 4H, phenylene, J = 8.5 Hz), 5.82 (d, 1H, NHAc, $J_{NH,2}$ = 9.5 Hz), 5.26 (d, 1H, H-1, $J_{1,2}$ = 2.1 Hz), 5.15 (t, 1H, H-4, $J_{4,5}$ = 8.5 Hz), 5.10 (s, 2H, -CH_2Ph), 5.07 (dd, 1H, H-3, $J_{3,4}$ = 8.5 Hz), 4.94 (ddd, 1H, H-2, $J_{2,3}$ = 3.9 Hz), 4.25 (dd, 1H, H-6, $J_{6,6'}$ = 12.2 Hz), 4.02 (dd, 1H, H-6′, $J_{5,6'}$ = 6.7 Hz), 3.89 (ddd, 1H, H-5, $J_{5,6}$ = 3.7 Hz), 2.91 (t, 2H, -CH_2CH_2CO-, J = 7.3 Hz), 2.63 (t, 2H, -C$H_2$$CH_2$CO-), 2.07, 2.06 (each s, 6H, OAc), 1.19, 1.19 (each s, 9H × 2, OPiv).

Anal. Calcd for $C_{36}H_{47}NO_{11}$: C, 64.56; H, 7.07; N, 2.09. Found: C, 64.72; H, 7.14; N, 1.97.

***p*-[2-(Benzyloxycarbonyl)ethyl]phenyl 4-*O*-Acetyl-2-deoxy-3,6-di-*O*-pivaloyl-β-D-*arabino*-hexopyranoside (16).** To a solution of **13** (1.01 g, 1.64 mmol) in dry benzene (30 mL), tetrabutylammonium tetrahydroborate (680 mg, 2.70 mmol) was added, and kept for 29 h in a water bath under ultrasonication until the disappearance of **13** on TLC with hexane/1ethyl acetate (3/1 v/v). The reaction mixture was poured into a saturated aq $NaHCO_3$ solution, extracted with ethyl acetate, washed with brine and water, dried over anhydrous magnesium sulfate, and concentrated to give a residue. The remaining residue was purified on a column of silica gel with hexane/ethyl acetate (3/1 v/v) to afford **16** (784 mg, 52% yield): mp 70–71°C (ethanol-hexane); $[\alpha]_D^{25}$ −30.1° (*c* 1.0, $CHCl_3$); IR (cm^{-1}) 1737 (C=O); ^{1}H NMR (A-500, $CDCl_3$) δ 7.37–7.29 (m, 5H, -CH_2*Ph*), 7.09, 6.93 (each d, 4H, phenylene, J = 8.5 Hz), 5.16 (dd, 1H, H-1, $J_{1,2eq}$ = 2.0 Hz, $J_{1,2ax}$ = 9.4 Hz), 5.10 (s, 2H, -CH_2Ph), 5.06 (ddd, 1H, H-3, $J_{3,4}$ = 9.5 Hz, $J_{2eq,3}$ = 4.6 Hz), 5.04 (dd, 1H, H-4, $J_{4,5}$ = 9.5 Hz), 4.24 (dd, 1H, H-6, $J_{5,6}$ = 2.4 Hz, $J_{6,6'}$ = 12.1 Hz), 4.13 (dd, 1H, H-6′, $J_{5,6'}$ = 6.9 Hz), 3.78 (ddd, 1H, H-5), 2.91 (t, 2H, -CH_2CH_2CO-, J = 7.8 Hz), 2.64 (t, 2H, -C$H_2$$CH_2$CO-), 2.50 (ddd, 1H, H-2eq,

$J_{2eq,2ax}$ = 12.2 Hz), 2.05 (3H, s, OAc), 1.98 (1H, ddd, H-2ax), 1.21, 1.18 (each s, 9H × 2, OPiv).

Anal. Calcd for $C_{34}H_{44}O_{10}$: C, 66.65; H, 7.24. Found: C, 66.55; H, 7.24.

***p*-[2-(Benzyloxycarbonyl)ethyl]phenyl 4-*O*-Acetyl-2-deoxy-2-fluoro-3,6-di-*O*-pivaloyl-β-D-mannopyranoside (17).** To a solution of **13** (844 mg, 1.11 mmol) in dry benzene (50 mL), tetrabutylammonium fluoride (1M solution in tetrahydrofuran, 5.6 mL, 0.55 mmol) was added dropwise at 0°C, and the reaction mixture was stirred for 24 h at rt under argon until the disappearance of **13** on TLC with hexane/ethyl acetate (3/1 v/v). The reaction mixture was poured into a saturated aq $NaHCO_3$ solution, extracted with ethyl acetate, washed with brine and water, dried over anhydrous magnesium sulfate, filtered, and concentrated to give a residue. The remaining residue was purified on a column of silica gel with hexane/ethyl acetate (3/1 v/v) to afford **17** (258 mg, 37% yield): $[\alpha]_D^{25}$ −39.0° (*c* 0.8, $CHCl_3$); IR (cm_{-1}) 1737 (C=O); ^{1}H NMR (A-500, $CDCl_3$) δ 7.37–7.29 (m, 5H, -CH_2*Ph*), 7.08, 6.91 (each d, 4H, styryl phenylene, *J* = 8.6 Hz), 5.41 (dd, 1H, H-4, $J_{3,4} = J_{4,5}$ = 9.8 Hz), 5.12 (dd, 1H, H-1, $J_{1,2}$ = 0.3 Hz, $J_{1,F}$ = 15.2 Hz), 5.10 (s, 2H, -C*H*$_2$Ph), 5.02 (ddd, 1H, H-3, $J_{2,3}$ = 2.4 Hz, $J_{3,F}$ = 23.8 Hz), 5.00 (ddd, 1H, H-2, $J_{2,F}$ = 51.8 Hz), 4.30 (dd, 1H, H-6, $J_{5,6}$ = 2.5 Hz, $J_{6,6'}$ = 12.2 Hz), 4.16 (dd, 1H, H-6, $J_{5,6'}$ = 6.7 Hz), 3.83 (ddd, 1H, H-5), 2.92 (t, 2H, -CH_2C*H*$_2$CO-, *J* = 7.9 Hz), 2.64 (t, 2H, -C*H*$_2$$CH_2$CO-), 2.07 (s, 3H, OAc), 1.22, 1.21 (each s, 9H × 2, OPiv).

Anal. Calcd for $C_{34}H_{43}FO_{10}$; C, 64.75; H, 6.87. Found: C, 65.22; H, 7.01.

***p*-(2-Carboxyethyl)phenyl 2,4-Di-*O*-acetyl-3,6-di-*O*-pivaloyl-β-D-mannopyranoside (18).** *p*-[2-(Benzyloxycarbonyl)ethyl]phenyl glycoside **12** (754 mg, 1.12 mmol) was hydrogenolyzed in ethanol (25 mL) in the presence of a catalytic amount of 10% $Pd(OH)_2$-C/H_2 for 2 h until the disappearance of **12** on TLC with hexane/ethyl acetate (3/1 v/v). The reaction mixture was filtered through a pad of celite and concentrated to afford **18** (617 mg, 95% yield): $[\alpha]_D^{25}$ −44.4° (*c* 0.8, $CHCl_3$); IR (cm^{-1}) 3240 (OH), 1746 (C=O); ^{1}H NMR (FX-200, $CDCl_3$) δ 7.07, 6.92 (each d, 4H, phenylene, *J* = 7.6 Hz), 5.67 (dd, 1H, H-2, $J_{2,3}$ = 3.2 Hz), 5.34 (t, 1H, H-4, $J_{4,5}$ = 9.8 Hz), 5.19 (s, 1H, H-1), 5.10 (dd, 1H, H-3, $J_{3,4}$ = 9.8 Hz), 4.30 (dd, 1H, H-6′, $J_{6,6'}$ = 12.0 Hz), 4.19 (dd, 1H, H-6), 3.84 (ddd, 1H, H-5, $J_{5,6}$ = 6.6 Hz), 2.85 (t, 2H, -CH_2C*H*$_2$CO-, *J* = 7.8 Hz), 2.58 (t, 2H, -C*H*$_2$$CH_2$ CO-), 2.20, 2.05 (each s, 6H, OAc), 1.22, 1.15 (each s, 9H × 2, OPiv).

Anal. Calcd for $C_{28}H_{40}O_{12}$: C, 59.14; H, 7.09. Found: C, 59.64; H, 7.08.

***p*-(2-Carboxyethyl)phenyl 2-Acetamido-4-*O*-acetyl-2-deoxy-3,6-di-*O*-pivaloyl-β-D-mannopyranoside (19).** *p*-[2-(Benzyloxycarbonyl)ethyl]phenyl glycoside **15** (80 mg, 0.12 mmol) was hydrogenolyzed in ethanol (10 mL) in the presence of a catalytic amount of 10% $Pd(OH)_2$-C/H_2 for 1 h until the disappearance of **15** on TLC with hexane/ethyl acetate (2/1 v/v). The reaction mixture was then filtered through a pad of celite and concentrated to afford **19** (63 mg, 91% yield): mp 88–91°C (ethanol-hexane); $[\alpha]_D^{25}$ −55.6° (*c* 0.6, $CHCl_3$); IR (cm^{-1}) 3388 (OH), 1728 and 1644 (C=O); ^{1}H NMR (A-500, $CDCl_3$) δ 7.10, 6.93 (each d,

4H, phenylene, J = 8.5 Hz), 6.80 (br s, 1H, COOH), 5.89 (d, 1H, NHAc, $J_{NH,2}$ = 9.1 Hz), 5.27 (d, 1H, H-1, $J_{1,2}$ = 1.9 Hz), 5.15 (t, 1H, H-4, $J_{4,5}$ = 8.6 Hz), 5.08 (dd, 1H, H-3, $J_{3,4}$ = 8.6 Hz), 4.95 (ddd, 1H, H-2, $J_{2,3}$ = 4.0 Hz), 4.24 (dd, 1H, H-6, $J_{6,6'}$ = 12.2 Hz), 4.20 (dd, 1H, H-6′, $J_{6',5}$ = 6.4 Hz), 3.90 (ddd, 1H, H-5, $J_{5,6}$ = 3.6 Hz), 2.89 (t, 2H, -CH_2CH_2CO-, J = 7.7 Hz), 2.62 (t, 2H, -CH_2CH_2CO-), 2.07, 2.06 (each s, 3H × 2, OAc), 1.19, 1.19 (each s, 9H × 2, OPiv).

Anal. Calcd for $C_{29}H_{41}NO_{11}$: C, 60.09; H, 7.13; N, 2.42. Found: C, 59.80; H, 6.64; N, 2.47.

***p*-(2-Carboxyethyl)phenyl 4-*O*-Acetyl-2-deoxy-3,6-di-*O*-pivaloyl-β-D-*arabino*-hexopyranoside (20).** *p*-[2-(Benzyloxycarbonyl)ethyl]phenyl glycoside **16** (610 mg, 1.00 mmol) was hydrogenolyzed in ethanol (50 mL) in the presence of a catalytic amount of 10% $Pd(OH)_2$-C/H_2 for 1 h until the disappearance of **16** on TLC with hexane/ethyl acetate (3/1 v/v). The reaction mixture was then filtered through a pad of celite and concentrated to afford **20** (476 mg, 92% yield): mp 147–148°C (ethanol-hexane); $[\alpha]_D^{25}$ −35.0° (*c* 1.0, $CHCl_3$); IR (cm^{-1}) 3460 (OH), 1734 (C=O); ^{1}H NMR (A-500, $CDCl_3$) δ 8.58 (br s, 1H, COOH), 7.09, 6.95 (each d, 4H, -CH_2Ph, J = 8.9 Hz), 5.17 (dd, 1H, H-1, $J_{1,2eq}$ = 2.2 Hz, $J_{1,2ax}$ = 9.3 Hz), 5.06 (ddd, 1H, H-3, $J_{3,4}$ = 9.4 Hz, $J_{2eq,3}$ = 4.6 Hz, $J_{2ax,3}$ = 11.2 Hz), 5.04 (dd, 1H, H-4, $J_{4,5}$ = 9.5 Hz), 4.24 (dd, 1H, H-6, $J_{5,6}$ = 2.4 Hz, $J_{6,6'}$ = 12.1 Hz), 4.13 (dd, 1H, H-6′, $J_{5,6'}$ = 6.9 Hz), 3.79 (ddd, 1H, H-5), 2.89 (t, 2H, -CH_2CH_2CO-, J = 7.8 Hz), 2.62 (t, 2H, -CH_2CH_2CO-), 2.50 (ddd, 1H, H-2eq, $J_{2eq,2ax}$ = 12.2 Hz), 2.05 (s, 3H, OAc), 1.98 (ddd, 1H, H-2ax), 1.21, 1.18 (each s, 9H × 2, OPiv).

Anal. Calcd for $C_{27}H_{38}O_{10}$: C, 62.05; H, 7.33. Found: C, 62.26; H, 7.33.

***p*-(2-Carboxyethyl)phenyl 4-*O*-Acetyl-2-deoxy-2-fluoro-3,6-di-*O*-pivaloyl-β-D-mannopyranoside (21).** *p*-[2-(Benzyloxycarbonyl)ethyl]phenyl glycoside **17** (224 mg, 0.36 mmol) was hydrogenolyzed in ethanol (50 mL) in the presence of a catalytic amount of 10% $Pd(OH)_2$-C/H_2 for 1 h until the disappearance of **17** on TLC with hexane/ethyl acetate (2/1 v/v). The reaction mixture was then filtered through a pad of celite and concentrated to afford **21** (173 mg, 90%): mp 168–169°C (ethanol-hexane); $[\alpha]_D^{25}$ −40.3° (*c* 1.0, $CHCl_3$); IR (cm^{-1}) 3358 (OH), 1740 (C=O); ^{1}H NMR (A-500, $CDCl_3$) δ 9.25 (br s, 1H, COOH), 7.12, 6.99 (each d, 4H, phenylene, J = 8.5 Hz), 5.41 (dd, 1H, H-4, $J_{3,4} = J_{4,5}$ = 9.8 Hz), 5.15 (dd, 1H, H-1, $J_{1,2}$ = 0.3 Hz, $J_{1,F}$ = 17.1 Hz), 5.03 (ddd, 1H, H-3, $J_{2,3}$ = 2.5 Hz, $J_{3,F}$ = 26.8 Hz), 5.01 (ddd, 1H, H-2, $J_{2,F}$ = 51.9 Hz), 4.30 (dd, 1H, H-6, $J_{5,6}$ = 2.4 Hz, $J_{6,6'}$ = 12.2 Hz), 4.17 (dd, 1H, H-6′, $J_{5,6'}$ = 6.7 Hz), 3.85 (ddd, 1H, H-5), 2.90 (t, 2H, -CH_2CH_2CO-, J = 7.7 Hz), 2.63 (t, 2H, -CH_2CH_2CO-), 2.06 (s, 3H, OAc), 1.22 (each s, 9H × 2, OPiv).

Anal. Calcd for $C_{27}H_{37}FO_{10}$: C, 60.00; H, 6.90. Found: C, 60.07; H, 7.13.

***p*-[2-(*N*-*p*-Vinylbenzyl)carbamoyl]ethyl]phenyl 2,4-Di-*O*-acetyl-3,6-di-*O*-pivaloyl-β-D-mannopyranoside (22).** To a solution of *p*-(2-carboxyethyl) phenyl glycoside **18** (617 mg, 1.06 mmol) and 1-ethyl-3-(3-dimethylamino-

propyl)carbodiimide (WSC) (275 mg, 1.43 mmol) in dichloromethane (50 mL), a solution of *p*-vinylbenzylamine[16] (200 mg, 1.52 mmol) in dichloromethane (20 mL) was added dropwise at 0°C, and the reaction mixture was stirred for 1 h until the disappearance of **18** on TLC with hexane/ethyl acetate (3/1 v/v). The reaction mixture was diluted with dichloromethane, washed with 10% aq citric acid solution, brine and water, dried over anhydrous magnesium sulfate, filtered, and concentrated to give a residue. The remaining residue was purified on a column of silica gel with hexane/ethyl acetate (3/5 v/v) to afford **22** (496 mg, 67% yield): mp 125–129°C (ethanol-hexane); $[\alpha]_D^{25}$ −33.0° (*c* 0.8, $CHCl_3$); IR (cm^{-1}) 1736 (C=O), 1648 (C=C); ^{1}H NMR (FX-200, $CDCl_3$) δ 7.34, 7.07 (each d, 4H, styryl phenylene, J = 8.3 Hz), 7.11, 6.92 (each d, 4H, phenylene, J = 8.5 Hz), 6.69 (dd, 1H, -Ph-C*H*=CHaHb, J_{trans} = 17.6 Hz, J_{cis} = 11.0 Hz), 5.74 (dd, 1H, Ha, J_{gem} = 0.9 Hz), 5.68 (dd, 1H, H-2, $J_{2,3}$ = 3.2 Hz), 5.60 (t, 1H, -CONH-), 5.34 (t, 1H, H-4, $J_{4,5}$ = 9.8 Hz), 5.25 (dd, 1H, Hb), 5.17 (d, 1H, H-1, $J_{1,2}$ = 1.0 Hz), 5.10 (dd, 1H, H-3, $J_{3,4}$ = 9.8 Hz), 4.36 (d, 2H, -NHC*H*$_2$-, $J_{NH,CH2}$ = 5.6 Hz), 4.30 (dd, 1H, H-6′, $J_{5,6'}$ = 7.1 Hz, $J_{6,6'}$ = 12.0 Hz), 4.16 (dd, 1H, H-6), 3.84 (ddd, 1H, H-5, $J_{5,6}$ = 2.4 Hz), 2.93 (t, 2H, -CH$_2$C*H*$_2$CO-, J = 7.8 Hz), 2.46 (t, 2H, -C*H*$_2$CH$_2$CO-), 2.20, 2.05 (each s, 3H × 2, OAc), 1.21, 1.15 (each s, 9H × 2, OPiv).

Anal. Calcd for $C_{38}H_{49}O_{11}N$: C, 59.14; H, 7.09, N, 2.39. Found: C, 65.82; H, 7.26, N, 2.01.

***p*-[2-[*N*-(*p*-Vinylbenzyl)carbamoyl]ethyl]phenyl 2-Acetamido-4-*O*-acetyl-2-deoxy-3,6-di-*O*-pivaloyl-β-D-mannopyranoside (23).** To a solution of *p*-(2-carboxyethyl)phenyl glycoside **19** (170 mg, 0.29 mmol) and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (WSC) (67 mg, 0.35 mmol) in dichloromethane (25 mL), a solution of *p*-vinylbenzylamine[16] (5 mg, 0.38 mmol) in dichloromethane (10 mL) was added dropwise at 0°C, and the reaction mixture was stirred for 1 h until the disappearance of **19** on TLC with hexane/ethyl acetate (1/3 v/v). The reaction mixture was diluted with dichloromethane, washed with 10% aq citric acid solution, brine and water, dried over anhydrous magnesium sulfate, filtered, and concentrated to give a residue. The remaining residue was purified on a column of silica gel with hexane/ethyl acetate/pyridine (25/75/3 v/v/v) to afford **23** (124 mg, 81% yield): mp 88–91°C (hexane-ethanol): $[\alpha]_D^{25}$ −44.3° (*c* 0.9, $CHCl_3$); IR (cm^{-1}) 1737 (C=O), 1653 (C=C); ^{1}H NMR (A-500, $CDCl_3$) δ 7.34, 7.11 (each d, 4H, styryl phenylene, J = 8.3 Hz), 7.09, 6.90 (each d, 4H, phenylene, J = 8.5 Hz), 6.70 (dd, 1H, -Ph-C*H*=CHaHb, J_{trans} = 17.4 Hz, J_{cis} = 10.9 Hz), 5.84 (d, 1H, NHAc, $J_{NH,2}$ = 9.2 Hz), 5.73 (dd, 1H, Ha, J_{gem} = 0.9 Hz), 5.65 (t, 1H, -CONH-), 5.25 (dd, 1H, Hb), 5.24 (d, 1H, H-1, $J_{1,2}$ = 1.8 Hz), 5.15 (t, 1H, H-4, $J_{4,5}$ = 8.8 Hz), 5.07 (dd, 1H, H-3, $J_{3,4}$ = 8.9 Hz), 4.94 (ddd, 1H, H-2, $J_{2,3}$ = 3.9 Hz), 4.38 (1H, d, -NHC*H*$_2$-, $J_{NH,CH2}$ = 5.6 Hz), 4.25 (dd, 1H, H-6, $J_{6,6'}$ = 11.9 Hz), 4.19 (dd, 1H, H-6′, $J_{5,6'}$ = 6.7 Hz), 3.88 (ddd, 1H, H-5, $J_{5,6}$ = 3.4 Hz), 2.94 (t, 2H, -CH$_2$C*H*$_2$CO-, J = 7.9 Hz), 2.64 (t, 2H, -C*H*$_2$CH$_2$CO-), 2.07, 2.06 (each s, 3H × 2, OAc), 1.19, 1.19 (each s, 9H × 2, OPiv); ^{13}C NMR (A-500, $CDCl_3$) δ 177.91, 177.29, 171.71, 170.21, 169.51 (C=O), 135.66 (*C*H=CH$_2$), 129.51, 128.34,

128.04, 126.50, 116.80 (Ph), 114.09 (CH=CH$_2$), 97.00 (C-1), 72.75 (C-5), 70.77 (C-3), 66.18 (C-4), 62.72 (C-6), 49.66 (C-2), 43.34, 38.81, 30.88 (CH$_2$).

Anal. Calcd for $C_{38}H_{50}N_2O_{10}$: C, 65.68; H, 7.24; N, 4.03. Found: C, 65.18; H, 7.36; N, 3.86.

***p*-[2-[*N*-(*p*-Vinylbenzyl)carbamoyl]ethyl]phenyl 4-*O*-Acetyl-2-deoxy-3,6-di-*O*-pivaloyl-β-D-*arabino*-hexopyranoside (24).** To a solution of *p*-(carboxyethyl)phenyl glycoside **20** (60 mg, 0.11 mmol) and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (WSC) (24 mg, 0.12 mmol) in dichloromethane (10 mL), a solution of *p*-vinylbenzylamine[16] (5 mg, 0.15 mmol) in dichloromethane (3 mL) was added dropwise at 0°C, and the reaction mixture was stirred for 1 h until the disappearance of **20** on TLC with hexane/ethyl acetate (1/2 v/v). The reaction mixture was diluted with dichloromethane, washed with 10% aq citric acid solution, brine and water, dried over anhydrous magnesium sulfate, filtered, and concentrated to give a residue. The remaining residue was purified on a column of silica gel with hexane/ethyl acetate (1/1 v/v) to afford **24** (56 mg, 76% yield): mp 131–132°C (ethanol-hexane); $[\alpha]_D^{25}$ −24.4° (*c* 1.0, $CHCl_3$); IR (cm^{-1}) 1734 (C=O), 1644 (C=C); ^{1}H NMR (A-500, $CDCl_3$) δ 7.34, 7.11 (each d, 4H, styryl phenylene, J = 8.0 Hz), 7.08, 6.92 (each d, 4H, phenylene, J = 8.6 Hz), 6.69 (dd, 1H, -Ph-CH=CHaHb, J_{trans} = 17.4 Hz, J_{cis} = 10.7 Hz) 5.73 (dd, 1H, Ha, J_{gem} = 0.6 Hz), 5.66 (t, 1H, -CONH-), 5.25 (dd, 1H, Hb), 5.14 (dd, 1H, H-1, $J_{1,2eq}$ = 2.1 Hz, $J_{1,2ax}$ = 9.4 Hz), 5.05 (ddd, 1H, H-3, $J_{2eq,3}$ = 4.9 Hz, $J_{2ax,3}$ = 11.6 Hz, $J_{3,4}$ = 9.1 Hz), 5.04 (dd, 1H, H-4, $J_{4,5}$ = 9.1 Hz), 4.37 (d, 2H, -NHCH_2-, $J_{NH,CH2}$ = 5.6 Hz), 4.24 (dd, 1H, H-6, $J_{5,6}$ = 2.2 Hz, $J_{6,6'}$ = 11.9 Hz), 4.12 (dd, 1H, H-6′, $J_{5,6'}$ = 6.7 Hz), 3.78 (ddd, 1H, H-5), 2.93 (t, 2H, -CH_2CH$_2$CO-, J = 7.8 Hz), 2.50 (ddd, 1H, H-2, $J_{2eq,2ax}$ = 11.3 Hz), 2.46 (t, 2H, -CH$_2$CH_2CO-), 2.05 (s, 3H, OAc), 1.98 (ddd, 1H, H-2ax), 1.20, 1.18 (each s, 9H × 2, OPiv); ^{13}C NMR (A-500, $CDCl_3$) δ 178.26, 177.69, 171.78, 169.53 (C=O), 136.36 (*C*H=CH$_2$), 129.36, 116.83, 127.99, 126.50 (Ph), 114.06 (CH=*C*H$_2$), 97.42 (C-1), 72.49 (C-5), 70.12 (C-3), 68.92 (C-4), 63.01 (C-6), 35.90 (C-2), 43.32, 38.73, 30.93 (CH$_2$).

Anal. Calcd for $C_{36}H_{47}O_9N$: C, 67.80; H, 7.43; N, 2.20. Found: C, 68.24; H, 7.72; N, 2.00.

***p*-[2-[*N*-(*p*-Vinylbenzyl)carbamoyl]ethyl]phenyl 4-*O*-Acetyl-2-deoxy-2-fluoro-3,6-di-*O*-pivaloyl-β-D-mannopyranoside (25).** To a solution of *p*-(propionic acid)phenyl glycoside **21** (83 mg, 0.15 mmol) and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (WSC) (32 mg, 0.16 mmol) in dichloromethane (5 mL), a solution of *p*-vinylbenzylamine[16] (25 mg, 0.19 mmol) in dichloromethane (5 mL) was added dropwise at 0°C, and the reaction mixture was stirred for 20 min until the disappearance of **21** on TLC with hexane/ethyl acetate (1/3 v/v). The reaction mixture was diluted with dichloromethane, washed with 10% aq citric acid solution, brine and water, dried over anhydrous magnesium sulfate, filtered, and concentrated to give a residue. The remaining residue was purified on a column of silica gel with hexane/ethyl acetate (1/2 v/v) to afford **25** (62 mg, 61%): mp

86–89°C (ether-hexane); $[\alpha]_D^{25}$ −35.2° (*c* 0.9, $CHCl_3$); IR (cm^{-1}) 1737 (C=O) and 1646 (C=C); ^{1}H NMR (A-500, $CDCl_3$) δ 7.34, 7.11 (each d, 4H, styryl phenylene, J = 7.9 Hz), 7.09, 6.96 (each d, 4H, phenylene, J = 9.2 Hz), 6.69 (dd, 1H, -Ph-C*H*=CHaHb, J_{trans} = 17.7 Hz, J_{cis} = 11.0 Hz), 5.74 (dd, 1H, Ha, J_{gem} = 0.6 Hz), 5.61 (t, 1H, -CONH-), 5.41 (d, 1H, H-4, $J_{3,4} = J_{4,5}$ = 9.8 Hz), 5.25 (dd, 1H, Hb), 5.10 (dd, 1H, H-1, $J_{1,2}$ = 0.3 Hz, $J_{1,F}$ = 17.1 Hz), 5.02 (dd, 1H, H-3, $J_{2,3}$ = 2.4 Hz, $J_{3,F}$ = 26.9 Hz), 5.00 (ddd, 1H, H-2, $J_{2,F}$ = 52.3 Hz), 4.37 (d, 1H, -NHC*H*$_2$-, $J_{NH,CH2}$ = 5.6 Hz), 4.29 (dd, 1H, H-6, $J_{5,6}$ = 2.3 Hz, $J_{6,6'}$ = 11.9 Hz), 4.15 (dd, 1H, H-6′, $J_{5,6'}$ = 6.8 Hz), 3.83 (ddd, 1H, H-5), 2.94 (t, 2H, -CH_2C*H*$_2$CO-, J = 7.4 Hz), 2.46 (t, 2H, -C*H*$_2$$CH_2$CO-), 2.06 (s, 3H, OAc), 1.22, 1.20 (each s, 9H × 2, OPiv); ^{13}C NMR (A-500, $CDCl_3$) δ 178.17, 177.61, 171.69, 169.54 (C=O), 136.33 (*C*H=CH_2), 129.47, 127.97, 126.50, 116.82 (Ph), 114.09 (CH=*C*H_2), 96.84 (C-1, $J_{1,F}$ = 15.5 Hz), 87.01 (C-2, $J_{2,F}$ = 191.4 Hz), 72.77 (C-5), 71.40 (C-3, $J_{3,F}$ = 16.6 Hz), 65.63 (C-4), 62.56 (C-6), 43.30, 38.65, 30.90 (CH_2).

Anal. Calcd for $C_{37}H_{45}FO_9N_1$: C, 66.65; H, 6.80; N, 2.10. Found: C, 66.50; H, 6.70; N, 1.95.

***p*-[2-[*N*-(*p*-Vinylbenzyl)carbamoyl]ethyl]phenyl β-D-Mannopyranoside (26).** To a solution of *p*-[2-[*N*-(*p*-vinylbenzyl)carbamoyl]ethyl]phenyl glycoside **22** (484 mg, 0.69 mmol) in methanol (10 mL), sodium methoxide (1.9M in methanol solution) was carefully added at pH 10, and the reaction mixture was stirred for 2 h until the disappearance of **22** on TLC with hexane/ethyl acetate (1/2 v/v). The reaction mixture was neutralized with Dowex 50W-X8 (H^+ form) ion-exchange resin, filtered, and concentrated to afford **26** (289 mg, 94% yield): mp 123–126°C (methanol); $[\alpha]_D^{25}$ −26.8° (*c* 0.7, MeOH); IR (cm^{-1}) 3322 (OH), 1644 (C=C); ^{1}H NMR (A-500, d_6-DMSO) δ 8.23 (t, 1H, NH), 7.36, 7.12 (each d, 4H, styryl phenylene, Hb, J_{trans} = 17.7 Hz, J_{cis} = 11.0 Hz), 5.75 (dd, 1H, Ha, J_{gem} = 0.9 Hz), 5.22 (dd, 1H, Hb), 5.22 (s, 1H, H-1), 4.24 (d, 2H, -NHC*H*$_2$-, $J_{NH,CH2}$ = 5.1 Hz), 3.88 (d, 1H, H-2, $J_{2,3}$ = 3.3 Hz), 3.73 (dd, 1H, H-3, $J_{3,4}$ = 11.3 Hz), 3.51–3.41 (m, 3H, H-4, H-6, and H-6′), 3.32 (br s, 4H, OH), 3.24 (ddd, 1H, H-5, $J_{4,5}$ = 8.8 Hz, $J_{5,6}$ = 2.1 Hz, $J_{5,6'}$ = 6.1 Hz), 2.81 (t, 2H, -CH_2C*H*$_2$CO-, J = 7.8 Hz), 2.42 (t, 2H, -C*H*$_2$$CH_2$CO-); ^{13}C NMR (A-500, d_6-DMSO) δ 171.24 (C=O), 136.46, 135.52, 134.20, 128.94, 127.25, 125.79 (Ph), 136.22 (*C*H=CH_2), 113.46 (CH=*C*H_2), 97.84 (C-1), 77.43 (C-2), 73.42 (C-3), 70.54 (C-4), 66.78 (C-5), 60.99 (C-6), 41.70, 37.16, 30.22 (CH_2).

Anal. Calcd for $C_{24}H_{29}O_7N$: C, 65.00; H, 6.59; N, 3.16. Found: C, 64.94; H, 6.48; N, 2.99.

***p*-[2-[*N*-(*p*-Vinylbenzyl)carbamoyl]ethyl]phenyl 2-Acetamido-2-deoxy-β-D-mannopyranoside (27).** To a solution of *p*-[2-[*N*-(*p*-vinylbenzyl)carbamoyl]ethyl]phenyl glycoside **23** (478 mg, 0.69 mmol) in methanol (30 mL), sodium methoxide (1.9M in methanol solution) was carefully added at pH 10, and the reaction mixture was stirred for 2 h until the disappearance of **23** on TLC with hexane/ethyl acetate (1/4 v/v). The reaction mixture was neutralized with Dowex

50W-X8 (H^+ form) ion-exchange resin, filtered, and concentrated to afford **27** (333 mg, quantitatively): mp 99–102°C (methanol); $[\alpha]_D^{25}$ −67.8° (*c* 0.8, MeOH); IR (cm^{-1}) 3304 (OH), 1656 (C=C); ^{1}H NMR (A-500, d_6-DMSO) δ 8.29 (t, 1H, -CONH-), 7.42 (d, 1H, NHAc, $J_{NH,2}$ = 9.8 Hz), 7.37, 7.12 (each d, 4H, styryl phenylene, J = 8.3 Hz), 7.09, 6.86 (each d, 4H, phenylene, J = 8.5 Hz), 6.70 (dd, 1H, -Ph-C*H*=CHaHb, J_{trans} = 17.4 Hz, J_{cis} = 10.9 Hz), 5.78 (dd, 1H, Ha, J_{gem} = 0.6 Hz), 5.21 (dd, 1H, Hb,), 5.19 (d, 1H, H-1, $J_{1,2}$ = 1.5 Hz), 4.47 (ddd, 1H, H-2, $J_{2,3}$ = 1.8 Hz), 4.22 (d, 2H, -NHCH_2-, $J_{NH,CH2}$ = 5.1 Hz), 3.74 (dd, 1H, H-3, $J_{3,4}$ = 11.6 Hz), 3.57 (dd, 1H, H-6, $J_{6,6'}$ = 9.2 Hz), 3.54 (dd, 1H, H-6′, $J_{6',5}$ = 6.4 Hz), 3.34 (t, 1H, H-4, $J_{4,5}$ = 9.7 Hz), 3.29 (ddd, 1H, H-5, $J_{5,6}$ = 4.6 Hz), 3.29 (br s, 4H, OH), 2.77 (t, 2H, -CH_2CH_2CO-, J = 7.9 Hz), 2.40 (t, 2H, -CH_2CH_2CO-), 1.93 (s, 3H, NHAc); ^{13}C NMR (A-500, d_6-DMSO) δ 171.27, 169.97 (C=O), 129.07, 127.37, 125.95, 116.06 (Ph), 134.51 (*C*H=CH_2), 113.75 (CH=*C*H_2), 96.94 (C-1), 77.87 (C-5), 73.97 (C-3), 66.97 (C-4), 61.04 (C-6), 52.35 (C-2), 41.70, 37.11, 30.22 (CH_2), 22.94 (CH_3).

Anal. Calcd for $C_{26}H_{32}N_2O_7$: C, 64.45; H, 6.66; N, 5.78. Found: C, 64.34; H, 6.53; N, 5.84.

***p*-[2-[*N*-(*p*-Vinylbenzyl)carbamoyl]ethyl]phenyl β-D-*Arabino*-hexopyranoside (28).** To a solution of *p*-[2-[*N*-(*p*-vinylbenzyl)carbamoyl]ethyl]phenyl glycoside **24** (416 mg, 0.65 mmol) in methanol (18 mL), sodium methoxide (1.9M in methanol solution) was carefully added at pH 10, and the reaction mixture was stirred for 2 h until the disappearance of **24** on TLC with hexane/ethyl acetate (1/1 v/v). The reaction mixture was neutralized with Dowex 50W-X8 (H^+ form) ion-exchange resin, filtered, and concentrated to afford **28** (279 mg, quantitatively): mp 171–172°C (ethanol-hexane); $[\alpha]_D^{25}$ −28.6° (*c* 0.6, DMSO); IR (cm^{-1}) 3298 (OH), 1644 (C=C); ^{1}H NMR (A-500, d_6-DMSO) δ 8.28 (t, 1H, -CONH-), 7.37, 7.09 (each d, 4H, styryl phenylene, J = 8.3 Hz), 7.11, 6.90 (each d, 4H, phenylene, J = 8.5 Hz), 6.69 (dd, 1H, -Ph-C*H*=CHaHb, J_{trans} = 17.7 Hz, J_{cis} = 11.0 Hz), 5.78 (dd, 1H, Ha, J_{gem} = 0.9 Hz), 5.21 (dd, 1H, Hb), 5.16 (dd, 1H, H-1, $J_{1,2eq}$ = 2.2 Hz, $J_{1,2ax}$ = 9.7 Hz), 4.22 (d, 2H, -NHCH_2-, $J_{NH,CH2}$ = 5.8 Hz), 3.68 (ddd, 1H, H-6, $J_{5,6}$ = 2.1 Hz, $J_{6,6'}$ = 11.9 Hz), 3.50 (ddd, 1H, H-6′, $J_{5,6}$ = 6.0 Hz), 3.48 (dd, 1H, H-4, $J_{5,4}$ = $J_{5,6}$ = 9.5 Hz), 3.54 (dd, 1H, H-6 ′, $J_{5,6'}$ = 6.4 Hz), 3.34 (t, 1H, H-4, $J_{4,5}$ = 9.7 Hz), 3.31 (br s, 3H, OH), 3.23 (ddd, 1H, H-5), 3.05 (ddd, 1H, H-3, $J_{2eq,3}$ = 5.2 Hz, $J_{2ax,3}$ = 11.6 Hz), 2.77 (t, 2H, -CH_2CH_2CO-, J = 7.8 Hz), 2.40 (t, 2H, -CH_2CH_2CO-), 2.14 (ddd, 1H, H-2ax, $J_{2ax,2eq}$ = 12.3 Hz), 1.55 (ddd, 1H, H-2eq); ^{13}C NMR (A-500, d_6-DMSO) δ 171.25 (C=O), 136.35 (*C*H=CH_2), 129.05, 127.34, 125.93, 115.87 (Ph), 113.72 (CH=*C*H_2), 96.73 (C-1), 77.18 (C-5), 71.21 (C-3), 70.38 (C-4), 60.82 (C-6), 41.67 ($NHCH_2$), 39.50 (C-2), 37.15, 30.2 (CH_2).

Anal. Calcd for $C_{24}H_{29}O_6N$: C, 67.80; H, 6.84; N, 3.28. Found: C, 67.17; H, 7.03; N, 3.31.

***p*-[2-[*N*-(*p*-Vinylbenzyl)carbamoyl]ethyl]phenyl 2-Deoxy-2-fluoro-β-D-mannopyranoside (29).** To a solution of *p*-[2-[*N*-(*p*-vinylbenzyl)carbamoyl]-ethyl]phenyl glycoside **25** (37 mg, 0.06 mmol) in methanol (1 mL), sodium

methoxide (1.9M in methanol solution, 1 mL) was carefully added at pH 10, and the reaction mixture was stirred for 2 h until the disappearance of **25** on TLC with hexane/ethyl acetate (1/2 v/v). The reaction mixture was neutralized with Dowex 50W-X8 (H^+ form) ion-exchange resin, filtered, and concentrated to afford **29** (25 mg, quantitatively): mp 185–186°C (ether-hexane); $[\alpha]_D^{25}$ −35.2° (*c* 0.2, DMSO); IR (cm^{-1}) 3280 (OH), 1641 (C=C); ^{1}H NMR (A-500, d_6-DMSO) δ 8.30 (t, 1H, -CONH-), 7.38, 7.12 (each d, 4H, styryl phenylene, J = 7.9 Hz), 7.12, 6.92 (each d, 4H, phenylene, J = 8.6 Hz), 6.69 (dd, 1H, -Ph-C*H*=CHaHb, J_{trans} = 17.8 Hz, J_{cis} = 11.0 Hz), 5.78 (dd, 1H, Ha, J_{gem} = 0.6 Hz), 5.28 (dd, 1H, H-1, $J_{1,2}$ = 0.3 Hz, $J_{1,F}$ = 19.5 Hz), 5.21 (dd, 1H, Hb), 4.72 (ddd, 1H, H-2, $J_{2,F}$ = 52.5 Hz), 4.22 (d, 2H, -NHCH_2-, $J_{NH,CH2}$ = 4.9 Hz), 3.70 (dd, 1H, H-6, $J_{6,6'}$ = 11.7 Hz), 3.57 (ddd, 1H, H-3, $J_{2,3}$ = 2.4 Hz, $J_{3,F}$ = 31.1 Hz), 3.47 (dd, 1H, H-6′, $J_{6',5}$ = 5.7 Hz), 3.40 (dd, 1H, H-4, $J_{3,4}$ = $J_{4,5}$ = 9.3 Hz), 3.29 (ddd, 1H, H-5, $J_{5,6}$ = 1.2 Hz), 3.29 (br s, 3H, OH), 2.78 (t, 2H, -CH_2CH_2CO-, J = 7.8 Hz), 2.40 (t, 1H, -C$H_2$$CH_2$CO-); ^{13}C NMR (A-500, d_6-DMSO) δ 171.24 (C=O), 136.34 (*C*H=CH_2), 129.13, 127.35, 125.95, 115.70 (Ph), 113.73 (CH=*C*H_2), 95.75 (C-1, $J_{1,F}$ = 14.4 Hz), 90.53 (C-2, $J_{2,F}$ = 185.2 Hz), 77.47 (C-5), 71.70 (C-3, $J_{3,F}$ = 17.6 Hz), 66.69 (C-4), 60.57 (C-6), 41.69, 37.13, 30.21 (CH_2).

Anal. Calcd for $C_{24}H_{28}FO_6N$: C, 64.70; H, 6.34; N, 3.14. Found: C, 64.59; H, 6.37; N, 2.86.

Poly[*p*-[2-[*N*-(*p*-vinylbenzyl)carbamoyl]ethyl]phenyl β-D-mannopyranoside] (30). To a solution of **26** (269 mg, 0.61 mmol) in DMSO (1.0 mL), 2,2′-azobisisobutyronitrile (4.0 mg, 0.02 mmol) was added. The reaction mixture was set in a sealed tube, degassed with argon, and kept at 65°C in an oil bath for 24 h. The reaction mixture was poured into stirred acetone, and the precipitate separated using a glass filter to give **30** (260 mg, 97% yield): IR (cm^{-1}) 3340 (OH), 1644 (C=O); ^{13}C NMR (A-500, d_6-DMSO) δ 171.24 (C=O), 128.58, 115.76 (Ph), 126.58 (-*C*H-CH_2-), 97.78 (C-1), 77.35 (C-2), 73.41 (C-3), 70.45 (C-4), 66.77 (C-5), 60.99 (C-6), 41.70, 40.40, 37.24, 30.51 (CH_2).

Poly[*p*-[2-[*N*-(*p*-vinylbenzyl)carbamoyl]ethyl]phenyl 2-acetamido-2-deoxy-β-D-mannopyranoside] (31). To a solution of **27** (204 mg, 0.42 mmol) in DMSO (1.0 mL), 2,2′-azobisisobutyronitrile (4.0 mg, 0.02 mmol) was added. The reaction mixture was set in a sealed tube, degassed with argon, and kept at 65°C in an oil bath for 24 h. The reaction mixture was poured into stirred acetone, and the precipitate separated using a glass filter to give **31** (171 mg, 84% yield): IR (cm^{-1}) 3430 (OH), 1644 (C=O); ^{13}C NMR (A-500, d_6-DMSO) δ 170.19 (C=O), 128.95, 116.06 (Ph), 126.58 (-*C*H-CH_2-), 96.85 (C-1), 77.75 (C-5), 71.97 (C-3), 66.91 (C-4), 61.02 (C-6), 52.38 (C-2), 37.22, 30.63, 30.33, 26.77 (CH_2), 22.92 (CH_3).

Poly[*p*-[2-(*N*-(*p*-vinylbenzyl)carbamoyl)ethyl]phenyl β-D-*arabino*-hexopyranoside] (32). To a solution of **28** (234 mg, 0.55 mmol) in DMSO (2.0 mL), 2,2′-azobisisobutyronitrile (3.0 mg, 0.015 mmol) was added. The reaction mixture was set in a sealed tube, degassed with argon, and kept at 65°C in an oil bath for

24 h. The reaction mixture was poured into stirred acetone, and the precipitate separated using a glass filter to give **32** (202 mg, 86% yield): IR (cm^{-1}) 3412 (OH), 1647 (C=O); ^{13}C NMR (A-500, d_6-DMSO) δ 171.48 (C=O), 128.95, 115.87 (Ph), 126.36 (-*C*H-CH_2-), 96.73 (C-1), 77.10 (C-5), 71.18 (C-), 70.39 (C-4), 60.80 (C-6), 39.34 (C-2), 37.27, 30.63, 30.33 (CH_2).

Poly[*p*-[2-[*N*-(*p*-vinylbenzyl)carbamoyl]ethyl]phenyl 2-deoxy-2-fluoro-β-D-mannopyranoside] (33). To a solution of **29** (229 mg, 0.514 mmol) in DMSO (1.0 mL), 2,2′-azobisisobutyronitrile (4.0 mg, 0.02 mmol) was added. The reaction mixture was set in a sealed tube, degassed with argon, and kept at 65°C in an oil bath for 24 h. The reaction mixture was poured into stirred acetone, and the precipitate separated using a glass filter to give **33** (128 mg, 56% yield): IR (cm^{-1}) 3448 (OH), 1638 (C=O); ^{13}C NMR (A-500, d_6-DMSO) δ 171.37 (C=O), 129.03, 115.72 (Ph), 127.76 (-*C*H-CH_2-), 95.71 (C-1, $J_{1,F}$ = 14.5 Hz), 90.51 (C-2, $J_{2,F}$ = 184.1 Hz), 77.40 (C-5), 71.76 (C-3, $J_{3,F}$ = 18.6 Hz), 66.68 (C-4), 60.58 (C-6), 40.09, 37.25, 30.65, 30.30 (CH_2).

Benzyl 3-(*p*-hydroxyphenyl)propionate (34). To a solution of 3-(*p*-hydroxyphenyl)propionic acid (500 mg, 3.0 mmol) and potassium hydrogencarbonate (600 mg, 6.0 mmol) in *N,N*-dimethylformamide (10 mL), benzyl bromide (0.4 mL, 3.39 mmol) was added dropwise at 0°C and the reaction mixture was stirred for 12 h at rt until the disappearance of starting compound on TLC with hexane/ethyl acetate (4/1 v/v). The reaction mixture was poured into a saturated aq $NaHCO_3$ solution, extracted with ethyl acetate, washed with brine and water, dried over anhydrous magnesium sulfate, filtered, and concentrated to give a residue. The remaining residue was purified on a column of silica gel with hexane/ethyl acetate (4/1 v/v). The yield of **34** was quantitative (765 mg): IR (cm^{-1}) 3406 (OH), 1713 (C=O); ^1H NMR (EX-90, $CDCl_3$) δ 7.34–7.32 (m, 5H, -CH_2*Ph*), 7.04, 6.73 (each d, 4H, phenylene, J = 8.6 Hz), 5.33 (m, 1H, OH), 5.10 (s, 2H, -C*H*$_2$Ph), 2.85 (t, 2H, -CH_2C*H*$_2$CO-, J = 7.8 Hz), 2.68 (t, 2H, -C*H*$_2$$CH_2$CO-).

Anal. Calcd for $C_{16}H_{16}O_3$: C, 74.98%; H, 6.29%. Found: C, 74.49%; H, 6.44%.

Enzyme-linked lectin assay (ELLA)[23–25] using Concanavaline A and the synthetic glycopolymers as inhibitors. Nunclon microtiter plates (Nuc439454) were coated with soybean lectin (SBA) (Honen Co. Ltd.: 03907) at 100 μL/well of 2-fold serial dilution in 50 μg/L Tris-HCl buffer (pH 7.3), containing 0.15 M NaCl, and 0.1% (v/v) Tween 20 (PBST) and incubated overnight at 4°C. The plates were then washed with 50 mM Tris-HCl buffer, containing 0.15M NaCl, and 0.1% Tween 20, and blocked with 400 μL of 1% (v/v) BSA in PBS for 1 h at rt and then the plate was washed three times. Each inhibitor, methyl α-D-mannopyranoside, methyl α-D-glucopyranoside, and synthesized glycopolymers (**6**, **30**, **31**, **32**, **33**) (50% (v/v) DMSO/H_2O), was added to biotin labeled-Con A (Honen Co. Ltd.: 90408) (10 ng/mL in washing solution containing 0.25% (v/v) gelatine). After storing for 60 min at rt, 100 μL of the above inhibitor solutions were transferred to the

SBA-coated plates and incubated for 60 min at rt. After washing three times as mentioned above, 100 μL of horseradish peroxidase labeled-streptavidin (Funakoshi Co. Ltd.: Vector SA-5004) (1 μg/mL in washing solution) was added, and then incubated for 30 min at rt. After washing three times as mentioned above, 100 μL of color-producing reagent (Funakoshi Co. Ltd.: 50507600) was added. After 30 min at rt, the reaction was stopped with 100 μL of 2 mM NaN_3 solution, and the adsorbance of each well at 450 relative to 600 nm was determined on a micro plate reader (Tosho Co. Ltd.: MPR-A4i).

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