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Synthetic Study and Structural Analysis of the Antifreeze Agent Xylomannan from *Upis ceramboides*

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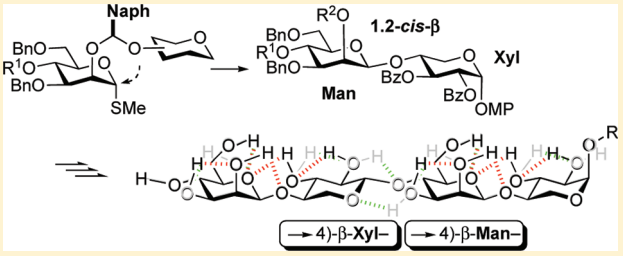
Supporting Information

ABSTRACT: The novel antifreeze factor, xylomannan, first isolated from the freeze-tolerant Alaskan beetle *Upis ceramboides*, demonstrates a high degree of thermal hysteresis, comparable to that of the most active insect antifreeze proteins. Although the presence of a lipid component in this factor has not yet been verified, it has been proposed that the glycan backbone consists of a β-D-mannopyranosyl-(1→4)-β-D-xylopyranose-disaccharide-repeating structure according to MS and NMR analyses. In this contribution, we report the stereoselective synthesis of the tetrasaccharide β-D-mannopyranosyl-(1→4)-β-D-xylopyranosyl-(1→4)-β-D-mannopyranosyl-(1→4)-D-xylopyranoside, a structural component of xylomannan. Our synthesis features the use of 2-naphthylmethyl (NAP)-ether-mediated intramolecular aglycon delivery (IAD) as the key reaction in obtaining β-mannopyranoside stereoselectively. Various donors for NAP-IAD were tested to determine the most suitable for the purposes of this synthesis. Fragment coupling between a disaccharyl fluoride and a disaccharide acceptor obtained from a common β-D-mannopyranosyl-(1→4)-β-D-xylopyranoside derivative was successfully carried out to afford the desired tetrasaccharide in the presence of Cp_2HfCl_2−$AgClO_4$. Structural analysis of the resulting synthetic tetrasaccharide using NMR techniques and molecular modeling was performed in order to demonstrate the presence of the proposed xylomannan linkages in this molecule.



INTRODUCTION

Antifreeze substances such as antifreeze proteins (AFPs) and glycoproteins (AFGPs) are vitally important for the survival of plants, insects, collembola, bacteria, and fungi, especially in the Arctic and Antarctic and their subregions.[1,2] Both AFP and AFGP are capable of inducing thermal hysteresis (TH) and thus protect the cell membranes of cold-tolerant organisms from damage due to extracellular ice-crystal formation at low temperatures. Such TH factors (THF) have not been precisely characterized structurally, although it has been suggested that they function by binding to the surface of ice crystals to prevent further ice formation,[3] for which an anchored clathrate mechanism[4] has been recently proposed. Synthetic studies on various artificial antifreeze substances, especially those having a glycoprotein moiety, have also been reported.[5]

In 2009, Walters et al. reported the isolation of the novel antifreeze xylomannan from the freeze-tolerant Alaskan beetle *Upis ceramboides*.[6] This substance was subsequently also identified in other diverse taxa.[7] This THF shows 3.7 ± 0.3 °C of TH at a concentration of 5 mg/mL, which is comparable to that of the most active insect AFP, although it has been suggested that it contains little or no protein. The presence of lipid components in this THF has not been verified, but its glycan backbone is considered to consist of a β-D-mannopyranosyl-(1→4)-β-D-xylopyranose-disaccharide-repeating unit, according to MS and NMR analyses (Figure 1).

In this study, we achieved the stereoselective synthesis of a structural portion of xylomannan; the tetrasaccharide, β-D-mannopyranosyl-(1→4)-β-D-xylopyranosyl-(1→4)-β-D-mannopyranosyl-(1→4)-D-xylopyranoside (Man_2Xyl_2). Our synthesis features the use of 2-naphthylmethyl (NAP)-ether-mediated intramolecular aglycon delivery (IAD)[8] as the key reaction to produce β-mannopyranoside stereoselectively (Figure 2). Various mannopyranose donors for NAP-IAD were examined to determine their suitability for this purpose. Detailed structural analysis of the resulting tetrasaccharide has been carried out to support the presence of the proposed xylomannan linkages.[6]

RESULTS AND DISCUSSION

The stereoselective synthesis of 1,2-*cis*-glycosides such as β-mannopyranoside is potentially problematic,[9] and a number of strategies to accomplish this type of synthesis have been explored.[10] Among these, approaches based on intramolecular

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aglycon delivery (IAD)[11] are especially promising, since they are predicted to result in the exclusive formation of 1,2-*cis*-glycosides. The concept of IAD was first proposed by Baressi and Hindsgaul,[12] who employed isopropylidene mixed acetals as a tether to make a temporary linkage between donor and acceptor as a mixed acetal. Subsequent work by Stork et al.[13] explored the use of silaketal for similar purposes. Following these pioneering reports, newer versions of IAD have been developed using various tethers including the *p*-methoxybenzylidene acetal utilized in our work.[14] Efficiency of the *p*-methoxybenzyl-ether-assisted β-mannopyranosylation was optimized by the introduction of a 4,6-*O*-cyclic protective group[15] especially in reactions with challenging acceptors such as chitobiose derivatives. We recently found that 2-naphthylidene acetal is highly effective as a tether for IAD and that NAP ether-mediated IAD could be applied to the formation of various types of 1,2-*cis*-glycosides[8] such as β-D-mannopyranosides, β-D-arabinofuranosides,[8c] α-D-glucopyranosides, and β-L-rhamnopyranosides,[8b] resulting in high yields with complete selectivity. The NAP-protected donor was cleanly converted to the mixed acetal upon oxidative activation with DDQ. This was followed by the subsequent activation of the thioglycosidic linkage to initiate rearrangement of an aglycon from the 2-naphthylidene acetal moiety, affording 1,2-*cis*-glycosides (Figure 2).

Our synthetic scheme for xylomannan is depicted in Figure 1. It employs a disaccharide $(ManXyl)_1$ donor and acceptor obtained from a common mannopyranosylxylopyranoside $(ManXyl)_1$ fragment, allowing fragment couplings to produce a xylosyl-mannoside linkage with a 1,2-*trans*-β-configuration. For the fragment coupling, fluoride was chosen as the leaving group, due to its high reactivity[16] and its use in standardized synthetic procedures involving the application of 4-methoxyphenyl glycoside.[17] Synthesis of a common $(ManXyl)_1$ fragment was to be achieved by the stereoselective introduction of β-mannopyranose residues by using our NAP-protected mannopyranose donors with xylopyranose acceptor via IAD.

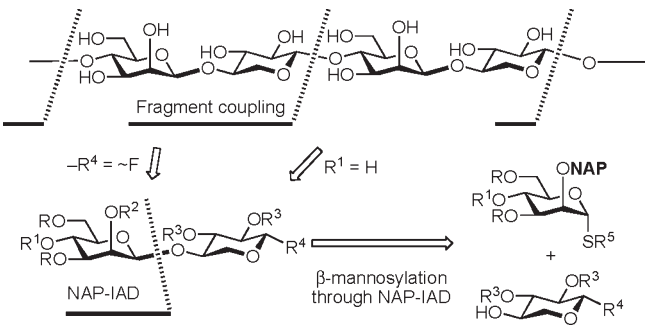
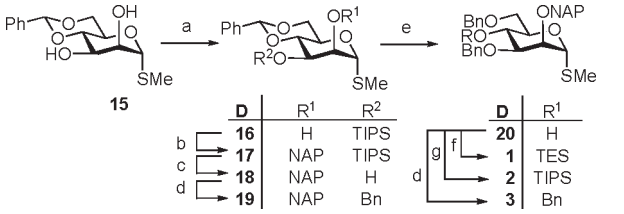


Figure 1. Retrosynthetic analysis of xylomannan.

Synthesis of Monosaccharide Fragments. NAP-protected mannopyranosyl donors for the synthesis of xylomannan fragment were prepared from methyl 4,6-*O*-benzylidene-1-thio-α-D-mannopyranoside **15**[18] (Figure 2, Scheme 1). Regioselective protection of diol **15** gave the 3-*O*-triisopropylsilyl (TIPS) ether **16**, which was then equipped with a 2-*O*-NAP group to give **17**. The TIPS ether was then converted to a benzyl ether through **18**. Reductive ring-opening of the resultant **19** with trifluoroacetic acid (TFA) and triethylsilane (TESH)[19] gave 3,6-di-*O*-benzyl derivative **20** in good yield. A triethylsilyl (TES) group was introduced to **20** by treatment with TESCl to give **1**, while conversion to the TIPS ether **2** required more vigorous reaction conditions and the use of 5 equiv of TIPSOTf. Tri-*O*-benzyl-protected methyl thioglycoside **3** was also synthesized from **20**.

Scheme 1. Synthesis of 2-*O*-NAP-Ether-Protected Mannose donors[a]



[a] Reagents and conditions: (a) TIPSCl, imidazole, DMF, 70%; (b) NAPBr, NaH, DMF, 95%; (c) TBAF, 90%; (d) BnBr, NaH, DMF, 92% (**19**), 96% (**3**); (e) TESH, TFA, CH_2Cl_2, 86%; (f) TESCl, imidazole, DMF, 87%; (g) TIPSOTf, 2,6-lutidine, 85%.

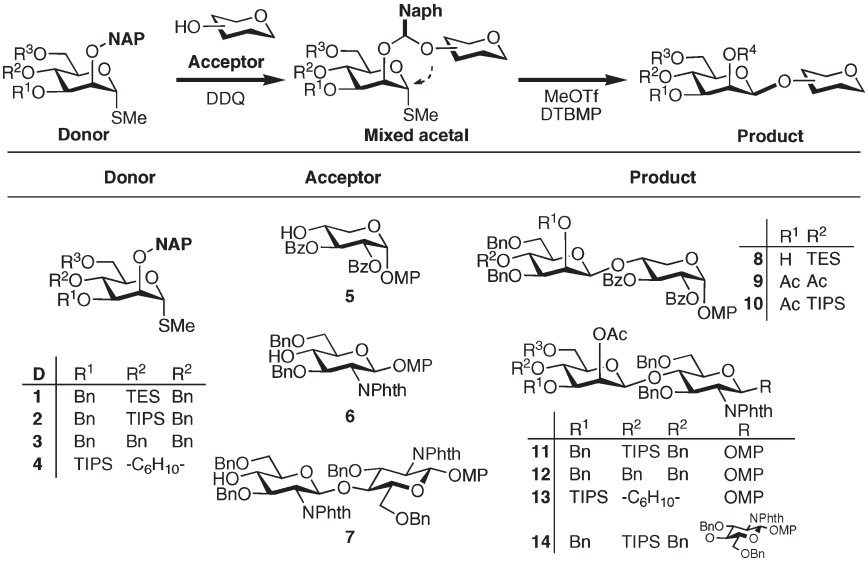


Figure 2. NAP-ether-mediated intramolecular aglycon delivery.

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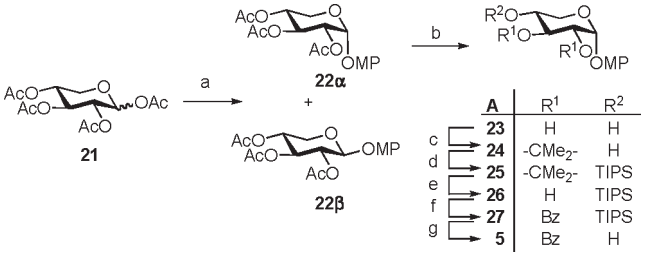
Xylopyranose acceptor **5** was synthesized from peracetylated xylopyranose **21**[20] as depicted in Scheme 2. Reaction of **21** with 4-methoxyphenol in the presence of TMSOTf unexpectedly gave the α-glycoside **22α** ($J_{H1,H2}$ = 3.7 Hz) exclusively. The same reaction at lower temperature in the presence of triethylamine (TEA)[21] resulted in β-selective glycoside formation, albeit in low yield. Since β-glycoside **22β** ($J_{H1,H2}$ = 6.4 Hz) was observed to isomerize readily to **22α**, we decided to use α-glycoside to avoid any complications caused by isomerization at a later stage in the synthesis. Deprotection of the acetate followed by regioselective acetonide formation of the triol **23** with 2-methoxypropene[22] gave **24**. Temporary TIPS protection of **24** followed by deprotection of the acetonide of **25**, benzoylation of resultant diol **26** and deprotection of the TIPS ether of **27** gave a xylose acceptor **5**, whose regioselective formation was confirmed by ^{1}H NMR of **5** (d 5.31 ppm for 2-H and 5.76 ppm for 3-H).

Scheme 2. Synthesis of Xylose Acceptor 5[a]



[a] Reagents and conditions: (a) 4-methoxyphenol, TMSOTf, CH_2Cl_2, 90% (α); (b) MeONa, MeOH, 95%; (c) 2-methoxypropene, CSA, 74%; (d) TIPSCl, imidazole, DMF; (e) THF−AcOH−H_2O; (f) BzCl, DMAP, pyridine, 79% in three steps; (g) TBAF−AcOH, 72%.

Table 1. β-Mannosylation Using Various Mannopyranose Donors through NAP-IAD[a]

entry	D[b]	A[b]	MA[b] (%)	product (%)	$J_{C1,H1}$ (Hz)
1	**1**	**5**	**93**	**8** (55, β)	–
2	**1**	**5**	–	**9** (93, β)	161.2
3	**2**	**5**	95	**10** (93, β)	157.4
4	**2**	**6**	96	**11** (90, β)	160.2
5	**2**	**7**	92	**14** (90, β)	163.1
6	**3**	**6**	92	**12** (85, β)	161.2
7	**4**	**6**	quant.	**13** (90, β)	161.7

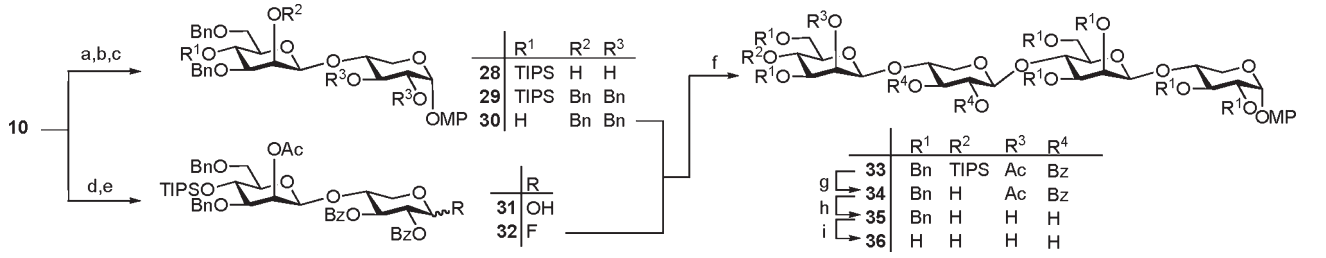
[a] Reagents and conditions: (a) DDQ, MS4A, CH_2Cl_2; (b) i) MeOTf, DTBMP, MS4A, $(CH_2Cl)_2$; ii) for entries 2−7: TFA, CH_2Cl_2, then Ac_2O, pyridine. [b] D: donor, A: acceptor, MA: mixed acetals.

***β*-Mannnopyranosylation through NAP-Ether-Mediated IAD.** In order to achieve the synthesis of xylomannan disaccharide fragments, we examined the use of β-mannopyranosylation through NAP-ether-mediated intramolecular aglycon delivery (IAD).[8] Although the importance of 4,6-*O*-cyclic protection in achieving the highest possible efficiency in IAD has been reported,[15,23] we experimented with the use of the 3,6-di-*O*-benzyl-protected flexible donors **1** and **2**. While IAD of **1** with **5** under standardized conditions gave 53% yield of the desired β-mannopyranoside **8** (Table 1, entry 1),[24] concomitant formation of dimeric 2-naphthaldehyde bis(disaccharyl)-acetal was evident by MALDI TOF MS analysis ($[M + Na]^+$ calcd for $C_{115}H_{126}O_{26}Si_2Na_1$, 2001.80, found 2001.99). Accordingly, we carried out acidic workup of the crude IAD mixture followed by acetylation to give diacetate **9** in 93% yield (entry 2). In order to preserve a silyl group at the 4-position, the TIPS protected donor **2** was employed, which gave mannopyranosylxylopyranoside $(ManXyl)_1$ as the 2-*O*-acetate **10** in good yield (entry 3), which was then used as the key intermediate in subsequent work.

Application of the 3,6-di-*O*-benzyl-protected donors **2** and **3** in the context of the synthesis of the core structures of *N*-glycan was also examined using acceptors **6**[25] and **7**.[26] With the glucosamine acceptor **6**, both **2** and **3** gave the desired β-mannopyranosides (**11**, **12**) cleanly (entries 4 and 6), with little or no reduction of yield compared to the previously reported 4,6-*O*-cyclohexylidene-protected donor **4**[8a] which gave **13**[8a] (entry 7). Even reaction with a chitobiose acceptor **7** (entry 5), which has been a challenging acceptor for IAD without the use of a cyclic acetal-protected donor,[15] proceeded without difficulty, giving the desired core trisaccharide derivative ($Man_1GlcNAc_2$, **14**) in a highly satisfactory yield of 83%.[27]

Synthesis of the Tetrasaccharide and Structural Analysis. The common disaccharide fragment **10** was diverged to a disaccharide acceptor **30** and a disaccharide donor **32** as shown in Scheme 3. After conversion of acetate and benzoate groups to benzyl ethers through triol **28**, the TIPS ether of **29** was deprotected to give **30** in good yield.[28] Deprotection of the 4-methoxyphenyl glycoside of **10** with CAN followed by fluorination of **31** with DAST gave the fluoride **32** in good yield. The fragment coupling of **30** with **32** was carried out under Suzuki's Cp_2HfCl_2−$AgClO_4$ conditions[29] in benzene[16b] to afford the tetrasaccharide $(ManXyl)_2$ derivative **33** in good yield. Configuration of the newly generated β-xyloside moiety was assigned by ^{1}H NMR ($J_{H1,H2}$ = 6.4 Hz). Conventional three-step

Scheme 3. Synthesis of Xylomannan Tetrasaccharide Fragment 36[a]



[a] Reagents and conditions: (a) MeONa, MeOH−THF (1:1); (b) NaH, BnBr, DMF; (c) TBAF, THF (85% in three steps); (d) CAN, CH_3CN−H_2O; (e) DAST, CH_2Cl_2, 67% in two steps (α:β = 84:16); (f) Cp_2HfCl_2, $AgClO_4$, PhH, 88% (β); (g) TBAF, THF; (h) MeONa, MeOH; (i) $Pd(OH)_2$, H_2, MeOH−H_2O (2:1), 70% in three steps.

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Table 2. ^{13}C and ^{1}H NMR Chemical Shifts and $^{1}H-^{1}H$ and $^{13}C-^{1}H$ Spin-Couplings of Saccharide Signals for Reported Xylomannan and Synthetic Man_2Xyl_2, **36**, and Standard β-Glycosides

	chemical shifts (ppm)						
	C1 (H1)	C2 (H2)	C3 (H3)	C4 (H4)	C5 (H5, H5′)	C6 (H6, H6′)	*J*-coupling (Hz)
Man:							$^{1}J_{C1,H1}$
xylomannan[a]	100.2 (4.92)	70.1 (4.30)	71.6 (3.93)	76.6 (3.96)	75.1 (3.74)	60.6 (4.09, 3.93)	~160
β-Man²-[b]	98.5 (4.94)	71.0 (4.15)	73.1 (3.81)	67.0 (3.75)	76.6 (3.56)	61.3 (4.12, 3.91)	162.1
4)-**β-Man¹-**[b]	98.6 (4.97)	70.2 (4.20)	71.7 (3.90)	76.6 (3.95)	75.4 (3.70)	60.6 (4.18, 4.00)	163.9
Δδ (ppm)[c]	−1.6 (+0.05)	+0.1 (−0.10)	+0.1 (−0.03)	±0.0 (−0.01)	+0.3 (−0.04)	± 0.0 (+0.09, +0.07)	
β-D-Man-OMe[d]	101.3 (4.66)	70.6 (4.07)	73.3 (3.72)	67.1 (3.63)	76.6 (3.46)	61.4 (4.02, 3.83)	159.5
Xyl:							$^{3}J_{H1,H2}$
xylomannan[a]	101.7 (4.66)	72.8 (3.48)	73.8 (3.73)	76.6 (4.00)	63.0 (4.28, 3.55)		7.8
4)-**β-Xyl²-**[b]	103.5 (4.60)	73.1 (3.51)	74.1 (3.79)	76.5 (4.05)	63.2 (4.30, 3.56)		8.0
Δδ (ppm)[c]	+1.8 (−0.06)	+0.3 (+0.03)	+0.3 (+0.06)	−0.1 (+0.05)	+0.2 (+0.02, +0.01)		
4)-**α-Xyl¹**-OMP[b]	98.6 (5.68)	71.8 (3.93)	77.0 (4.17)	72.2 (4.10)	59.8 (4.03, 3.89)		4.0
β-D-Xyl-OMe[d]	105.1 (4.42)	74.0 (3.35)	76.9 (3.53)	70.4 (3.71)	66.3 (4.06, 3.42)		7.8

[a] Data from ref 6. [b] Data of residues from synthetic **36** measured in pH 7.5 phosphate buffer at 40 °C. [c] The differences from reported xylomannan. [d] Data from ref 32.

deprotection afforded $(ManXyl)_2$ derivative **36**. The synthetic tetrasaccharide derivative exhibited neither TH nor recrystallization inhibition activities.[6,7,30,31] These results are not unexpected, because suppression of TH activity after degradation of xylomannan by β-(1→4)xylosidase has been reported.[6]

NMR analysis of synthetic $(ManXyl)_2$ **36** was carried out at 40 °C to allow comparison with reported ^{13}C and ^{1}H chemical shifts and $^{1}H-^{1}H$ and $^{13}C-^{1}H$ spin-couplings of xylomannan (Table 2).[32] Both chemical shifts and spin-couplings of the internal β-mannopyranoside (**Man¹**) and β-xylopyranoside (**Xyl²**) of **36** were in good agreement with those of the core $(ManXyl)_n$ structure of xylomannan, especially for carbon resonance of the 4-position of the pyranoside. Although the ^{13}C signal at 103.5 ppm assignable to C1 of **Xyl²** appeared was discernibly different from that reported for xylomannan (101.7 ppm), our results generally support the proposed xylomannan structure as consisting of repeating →4)-β-Man and →4)-β-Xyl linkages.

All 1-H−4-H′ cross peaks related to both Man-(1→4)-β-Xyl and Xyl-(1→4)-β-Man linkages (linkage A and linkage B, respectively) were detected during ROESY analysis of **36** (Figure 3a). Molecular modeling of $(ManXyl)_n$ (n = 2, 10^{33}) using *Macro-Model*, ver 8.1,[34] supported the ROESY results concerning both the 1,4-linkages (Figure 3b). Both NMR and modeling studies suggested that the 1,4-linkages result in the formation of intra- and inter-residual hydrogen bonding, the stabilizing effects of which cause slight conformational differences between these two linkages. Specifically, Man-(1→4)-β-Xyl (A) forms the inter-residual ring C5−O···H−O−C3′ as well as intra-residual C5−O···H−O−C6 hydrogen bonds, as has previously been proposed for cellulose, the most common β-(1→4)-glycan which has a planar structure in the solid state.[35] Since xylose, unlike glucose, lacks the HO-C6H_2 group, only the presence of the inter-residual ring C5−O···H−O−C3′ contributes to the formation of a three-dimensional hydrogen-bond network, resulting in a smaller degree of conformational turn as compared to the Man-(1→4)-β-Xyl linkage. The angles between two mannoside units is on the order of 70°, causing $(ManXyl)_5$ to form a single helix (Figure 3c).[33,36] In addition, calculations were performed on the basis of the planar model structure of cellulose,[35] which has two constrained torsion angles (~98° and 140° for O5−C1−O1−C4′ and C1−O1−C4′−C5′, respectively) (Figure 3d). The analysis suggested that, due to the absence of HO-C6H_2 and HO-C2 in the xylose and mannose residues, respectively, the interaction between each planar structure of xylomannan chains via intermolecular hydrogen bonding[35] is likely far less significant than in the cellulose three-dimensional planar structure. In the planar structure of xylomannan, all the axial HO-C2 groups of mannoside direct to the same phase, resulting in a difference in hydrophobicity between the two phases of the xylomannan chain. The repeat spacing of the oxygen atoms of water molecules in an ice lattice on the primary prism plane (7.35, 4.52 Å) and the basal plane (7.83, 4.52 Å),[37] however, did not correlate well with the distance between the axial HO-C2 groups of mannose residues (10.7 Å).[33]

■ CONCLUSION

In this study we achieved the stereoselective synthesis of the tetrasaccharide β-D-mannopyranosyl-(1→4)-β-D-xylopyranosyl-(1→4)-β-D-mannopyranosyl-(1→4)-D-xylopyranoside, proposed as a structural component of the novel natural antifreeze xylomannan. As the key step, we employed the use of 3,6-di-*O*-benzyl-protected open-type mannopyranose donors for NAP-ether-mediated intramolecular aglycon delivery. This procedure was applied to the synthesis of various β-mannopyranoside-containing oligosaccharides including the xylomannan fragment and core trisaccharide of *N*-glycans. Structural analysis via NMR and molecular modeling of the tetrasaccharide obtained through fragment coupling of a disaccharyl fluoride and a disaccharide acceptor supported the proposed structure. Although some details of the structure of xylomannan are still unknown (including its molecular weight and the regularity of the repeating disaccharide) and its mode of action is not entirely clear, the proposed helical and/or biphasic nature of this molecule might account for its utility in preventing the growth of ice crystals.[38]

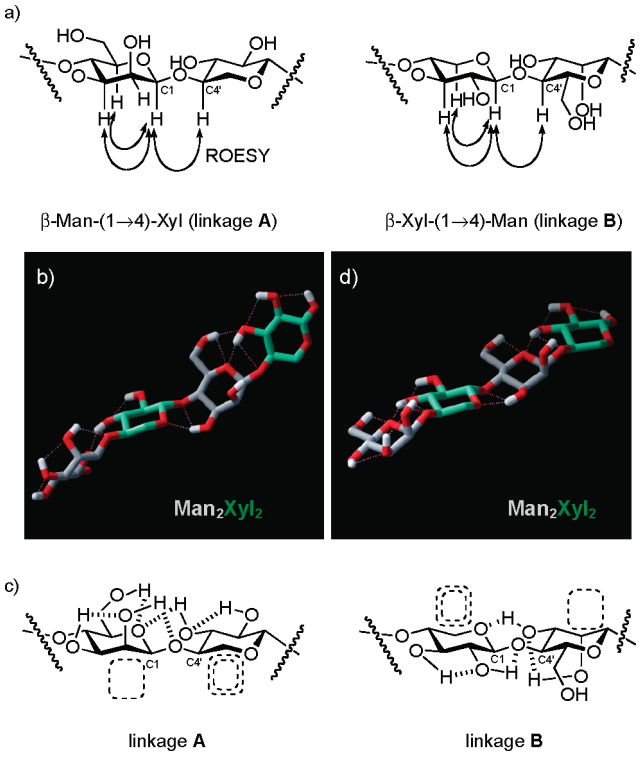

Figure 3. Analysis of β-1,4-glycan structure of xylomannan. (a) ROESY correlation of two linkages (linkage A: β-Man-(1→4)-Xyl and linkage B: β-Xyl-(1→4)-Man) using tetrasaccharide **36**. (b) Global minimum structure of tetrasaccharide β-Man-(1→4)-β-Xyl-(1→4)-β-Man-(1→4)-β-Xyl in H_2O. Manno- and xylopyranosides are colored gray and green, respectively. Dotted lines indicate possible hydrogen bondings. (c) Possible hydrogen-bond network of the two linkages calculated by *MacroModel*, ver 8.1. The single- and double-dotted squares indicate the absence of functionality in mannoside and xyloside from cellulose, respectively. (d) Global minimum structure of the planar model structure of tetrasaccharide β-Man-(1→4)-β-Xyl-(1→4)-β-Man-(1→4)-β-Xyl in H_2O using the parameter for that of cellulose which has two constrained torsion angles (~98° and 140° for O5−C1−O1−C4′ and C1−O1−C4′ −C5′, respectively) with force constants of 300 kJ/mol·Å^2.

The results of antifreeze activity measurements of the resulting tetrasaccharide indicate that a longer repeating motif of xylomannan should be required for these activities. Further synthetic and structural studies are underway to clarify these intriguing issues.

EXPERIMENTAL SECTION

General Procedure. All reactions sensitive to air and/or moisture were carried out under nitrogen or argon atmosphere with anhydrous solvents. Substrates of glycosylations were dried by azeotropic removal with toluene. Column chromatography was performed on silica gel 60N, 100−210 mesh (Kanto Kagaku Co., Ltd.). Preparative thin layer chromatography (PTLC) was performed on silica gel 60 F_{254}, 0.5 mm (E. Merck). Gel filtration was performed on Sephadex LH-20 (Pharmacia). All other reagents were purchased from Wako Pure Chemical Industries Ltd., Kanto Chemicals Co. Inc., Tokyo Kasei Kogyo Co., Ltd. and Aldrich Chemical Co.. Optical rotations were measured with a JASCO DIP 370 polarimeter. The melting point was determined with a Büchi 510 melting point apparatus. ^{1}H NMR spectra were recorded at 400 MHz on a JEOL JNM-AL 400 or ECX 400 spectrometer, and chemical shifts are referred to internal tetramethylsilane (0 ppm), $CDCl_3$ (7.24 ppm), HOD (4.80), or CD_3OD (3.30 ppm). ^{13}C NMR spectra were recorded at 100 MHz on the same instrument, and chemical shifts are referred to internal $CDCl_3$ (77.0 ppm), C_6D_6 (128.0 ppm), CD_3OD (49.0 ppm), $(CD_3)_2CO$ (34.1 ppm), or native scale. MALDI-TOF mass spectra were recorded on a SHIMADZU Kompact MALDI AXIMA-CFR spectrometer with 2,5-dihydroxybenzoic acid as the matrix. ESI-TOF mass spectra were recorded on a JEOL AccuTOF JMS-T700LCK (RIKEN Advanced Science Institute) with CF_3CO_2Na as the internal standard.

*Methyl 3,6-Di-O-benzyl-2-O-(2-naphthylmethyl)-1-thio-4-O-triethylsilyl-α-D-mannopyranoside (**1**).* To a solution of **20** (500.0 mg, 0.95 mmol) and 2,6-lutidine (0.335 mL, 2.85 mmol) in CH_2Cl_2 (5.0 mL) was added dropwise TESOTf (0.474 mL, 2.09 mmol) at 0 °C under Ar atmosphere, and the mixture was stirred for 4 d at room temperature. The reaction was quenched with triethylamine, extracted with $CHCl_3$, washed with sat. $NaHCO_3$ aq and brine, dried over Na_2SO_4, and evaporated in vacuo. The residue was purified by silica gel column chromatography using a gradient solvent system (toluene/ethyl acetate = 100/1 to 50/1 to 20/1 to 10/1) to give the title compound **1** (534.4 mg, 87%). **1**: $[\alpha]^{25}_D$ 46.9° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.43−0.60 (m, TES, 6H), 0.82−0.88 (m, TES, 9H), 2.10 (s, SMe, 3H), 3.63 (dd, *J* = 8.7, 2.8 Hz, 3-H, 1H), 3.70−3.76 (m, 6a-H, 6b-H, 2H), 3.81 (dd, *J* = 2.8, 1.8 Hz, 2-H, 1H), 3.96−4.01 (m, 5-H, 1H), 4.05 (t, *J* = 9.2 Hz, 4-H, 1H), 4.52 (s, CH_2Ph, 2H), 4.59 (s, CH_2Ph, 2H), 4.66 (d, *J* = 12.8 Hz, CH_2Ph, 1H), 4.77 (d, *J* = 12.8 Hz, CH_2Ph, 1H), 5.29 (d, *J* = 1.8 Hz, 1-H, 1H), 7.17−7.79 (m, Ar, 17H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 5.08, 6.93, 13.6, 68.4, 69.7, 71.6, 72.1, 73.3, 73.5, 75.9, 80.6, 83.2, 125.68, 125.73, 126.0, 126.2, 127.3, 127.4, 127.59, 127.63, 127.9, 128.0, 128.2, 132.9, 133.2, 125.8, 138.35, 138.44; MALDI-TOF MS: $[M + Na]^+$ calcd for $C_{38}H_{48}O_5S_1Si_1Na_1$, 667.29, found 667.77. ESI-TOF MS: $[M + Na]^+$ calcd for $C_{38}H_{48}O_5S_1Si_1Na_1$, 667.29, found 667.21; HRMS ESI-TOF: $[M + Na]^+$ calcd for $C_{38}H_{48}O_5S_1Si_1Na_1$, 667.2889, found 667.2871.

*Methyl 3,6-Di-O-benzyl-2-O-(2-naphthylmethyl)-1-thio-4-O-triisopropylsilyl-α-D-mannopyranoside (**2**).* To a solution of **20** (1.6023 g, 3.02 mmol) and 2,6-lutidine (2.665 mL, 22.65 mmol) in CH_2Cl_2 (30 mL) was added dropwise TIPSOTf (4.1 mL, 15.1 mmol) at 0 °C under Ar atmosphere, and the mixture was stirred for 24 h at room temperature. The reaction was quenched with triethylamine, extracted with $CHCl_3$, washed with sat. $NaHCO_3$ aq and brine, dried over Na_2SO_4, and evaporated in vacuo. The residue was purified by silica gel column chromatography using a gradient solvent system (toluene/ethyl acetate = 100/1 to 50/1 to 20/1 to 10/1) to give the title compound **2** (1.7587 g, 85%). **2**: $[\alpha]^{25}_D$ 39.8° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.02−1.04 (m, TIPS, 21H), 1.97 (s, SMe, 3H), 3.89−4.00 (m, 2-H, 3-H, 6a-H, 6b-H, 4H), 4.18 (d, *J* = 11.5 Hz, CH_2Ph, 1H), 4.37−4.43 (m, 5-H, CH_2Ph × 2, 3H), 4.57−4.63 (m, 4-H, CH_2Ph × 3, 4H), 5.43 (s, 1-H, 1H), 7.04−7.35 (m, Ar, 12H), 7.44 (d, *J* = 8.7 Hz, Ar, 1H), 7.58−7.61 (m, Ar, 2H), 7.65 (d, *J* = 7.3 Hz, Ar, 1H), 7.78 (s, Ar, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.9, 13.5, 18.1, 18.2, 68.8, 69.8, 71.1, 71.9, 73.2, 74.0, 75.3, 80.6, 82.4, 125.5, 125.7, 125.9, 126.1, 127.3, 127.4, 127.5, 127.6, 127.8, 127.9, 128.1, 128.2, 132.9, 133.6, 135.7, 137.2, 138.3; MALDI-TOF MS: $[M + Na]^+$ calcd for $C_{41}H_{54}O_5S_1Si_1Na_1$, 709.34, found 709.14. ESI-TOF MS: $[M + Na]^+$ calcd for $C_{41}H_{54}O_5S_1Si_1Na_1$, 709.34, found 709.25; HRMS ESI-TOF: $[M + Na]^+$ calcd for $C_{41}H_{54}O_5S_1Si_1Na_1$, 709.3359, found 709.3386.

*Methyl 3,4,6-Tri-O-benzyl-2-O-(2-naphthylmethyl)-1-thio-α-D-mannopyranoside (**3**).* **3** was synthesized according to the procedure for the synthesis of **19** except using **20** instead of **18** as starting material (96%). **3**: $[\alpha]^{27}_D$ 51.8° (*c* 1.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.08 (s, SMe, 3H), 3.72 (dd, *J* = 11.2, 2.0 Hz, 6-H, 1H), 3.81 (dd, *J* = 11.2, 4.8 Hz, 6-H, 1H), 3.38−3.87 (m, 2-H, 3-H, 2H), 4.04 (dd, *J* = 10.0, 8.4 Hz, 4-H, 1H), 4.07−4.18 (m, 5-H, 1H), 4.50 (d, *J* = 10.8 Hz, CH_2Ar, 1H), 4.52 (d, *J* = 12.4 Hz, CH_2Ar, 1H), 4.53 (d, *J* = 11.8 Hz, CH_2Ar, 1H), 4.58 (d, *J* = 11.8 Hz, CH_2Ar, 1H), 4.65(d, *J* = 12.4 Hz, CH_2Ar, 1H), 4.79 (d, *J* = 12.8 Hz, CH_2Ar, 1H), 4.87 (d, *J* = 12.8 Hz, CH_2Ar, 1H), 4.87

(d, J = 10.8 Hz, CH_2Ar, 1H), 5.32 (s, 1-H, 1H), 7.15−7.81 (m, Ar, 22H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.7 (q), 69.0 (t, C6), 71.8 (d, C5), 71.9 (t), 72.1 (t), 73.2 (t), 74.9 (d, C4), 75.0 (t), 76.0 (d, C2), 80.2 (d, C3), 83.1 (C1, $J_{C,H}$ = 168.81 Hz), 125.8, 125.9, 126.0, 126.5, 127.41, 127.49, 127.54, 127.58, 127.66, 127.8, 128.1, 128.2, 128.3, 132.9, 133.1, 135.4, 138.1, 138.2, 138.3. ESI-TOF MS: $[M + Na]^+$ calcd for $C_{39}H_{40}O_5S_1Na_1$, 643.25, found 643.24; HRMS ESI-TOF: $[M + Na]^+$ calcd for $C_{39}H_{40}O_5S_1Na_1$, 643.2494, found 643.2469.

*4-Methoxyphenyl 3,6-Di-O-benzyl-4-O-triethylsilyl-β-D-mannopyranosyl-(1→4)-2,3-di-O-benzoyl-α-D-xylopyranoside (**8**). General Procedure for the Synthesis of Mixed Acetal (MA).* To a mixture of acceptor **5** (46.4 mg, 100 μmol), donor 1 (67.7 mg, 105 μmol), and dried powdered MS4A (100 mg) in dry CH_2Cl_2 (1.0 mL) was added DDQ (27.8 mg, 120 μmol) at 0 °C under Ar atmosphere. The mixture was stirred for 4 h at room temperature, quenched with aqueous ascorbate buffer (L-ascorbic acid (0.7 g), citric acid monohydrate (1.2 g), and NaOH (0.92 g) in H_2O (100 mL)), and then was filtered through Celite. The filtrate was extracted with $CHCl_3$ and washed with sat. $NaHCO_3$ aq and brine. The combined organic layers were dried over Na_2SO_4 and evaporated in vacuo. The crude product was purified by gel filtration chromatography (SX-3, ethyl acetate/toluene = 1/1) to give the mixed acetal (103.2 mg, 93%). Mixed acetal (**1**+**5**): ^{1}H NMR (400 MHz, C_6D_6): δ 0.56−0.65 (m, TES, 6H), 0.90−0.94 (m, TES, 9H), 2.11 (s, SMe, 3H), 3.19 (s, OMe, 3H), 3.73 (dd, J = 11.0, 1.4 Hz, 6a-H^{Man}, 1H), 3.77 (dd, J = 9.6, 3.2 Hz, 3-H^{Man}, 1H), 3.90 (dd, J = 11.0, 5.0 Hz, 6b-H^{Man}, 1H), 4.10−4.33 (m, 2-H^{Man}, 5-H^{Man}, 4-H^{Xyl}, 5a-H^{Xyl}, 5b-H^{Xyl}, CH_2Ph × 2, 7H), 4.44−4.52 (m, 4-H^{Man}, CH_2Ph, 2H), 4.60 (d, J = 12.4 Hz, CH_2Ph, 1H), 5.32 (dd, J = 10.5, 3.6 Hz, 2-H^{Xyl}, 1H), 5.72 (d, J = 1.4 Hz, 1-H^{Man}, 1H), 5.81 (d, J = 2.3 Hz, 1-H^{Xyl}, 1H), 5.82 (s, >CHNaph, 1H), 6.50−6.52 (m, Ar, 2H), 6.71 (dd, J = 10.1, 9.6 Hz, 3-H^{Xyl}, 1H), 6.82−6.93 (m, Ar, 5H), 6.98−7.20 (m, Ar, 11H), 7.26−7.30 (m, Ar, 2H), 7.35−7.37 (m, Ar, 2H), 7.50−7.66 (m, Ar, 4H), 8.10−8.17 (m, Ar, 5H); MALDI-TOF MS: $[M + Na]^+$ calcd for $C_{64}H_{70}O_{13}S_1Si_1Na_1$, 1129.42, found 1129.71. ESI-TOF MS: $[M + Na]^+$ calcd for $C_{64}H_{70}O_{13}S_1Si_1Na_1$, 1129.42, found 1129.31; HRMS ESI-TOF: $[M + Na]^+$ calcd for $C_{64}H_{70}O_{13}S_1Si_1Na_1$, 1129.4204, found 1129.4240.

General Procedure for Intramolecular Aglycon Delivery 1. To the mixed acetal (**1**+**5**) (103.2 mg, 93.0 μmol) were added DTBMP (116.9 mg, 558 μmol) and MS4A in dry $(CH_2Cl)_2$ (10 mL) at room temperature under Ar atmosphere Then MeOTf (47.4 μL, 419 μmol) was added to the mixture, and the mixture was stirred for 48 h at 40 °C. After the mixture was cooled down, the reaction mixture was quenched with triethylamine, diluted with ethyl acetate, and filtered through Celite. The filtrate was washed with sat. $NaHCO_3$ aq and brine. The washed organic layer was dried over Na_2SO_4 and evaporated in vacuo. The crude product was purified by gel filtration chromatography (SX-3, ethyl acetate/toluene = 1/1) to give the product (46.9 mg, 55%, β). **8**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.40−0.51 (m, TES, 6H), 0.86−0.84 (m, TES, 9H), 2.52 (br s, OH, 1H), 2.87 (dd, J = 10.5, 7.3 Hz, 6a-H^{Man}, 1H), 3.20 (dd, J = 9.2, 3.2 Hz, 3-H^{Man}, 1H), 3.27 (ddd, J = 9.2, 7.3, 1.8 Hz, 5-H^{Man}, 1H), 3.51 (dd, J = 10.5, 1.8 Hz, 6b-H^{Man}, 1H), 3.58 (t, J = 9.2 Hz, 4-H^{Man}, 1H), 3.72 (s, OMe, 3H), 3.86 (dd, J = 11.4, 6.0 Hz, 5a-H^{Xyl}, 1H), 3.90−4.00 (m, 2-H^{Man}, 5b-H^{Xyl}, 2H), 4.24 (d, J = 12.4 Hz, CH_2Ph, 1H), 4.30−4. Twenty-four (m, 4-H^{Xyl}, CH_2Ph, 2H), 4.48−4.55 (m, 1-H^{Man}, CH_2Ph, 2H), 4.63 (d, J = 11.9 Hz, CH_2Ph, 1H), 5.37 (dd, J = 10.1, 3.7 Hz, 2-H^{Xyl}, 1H), 5.71 (d, J = 3.7 Hz, 1-H^{Xyl}, 1H), 6.03 (dd, J = 10.1, 9.6 Hz, 3-H^{Xyl}, 1H), 6.76−8.02 (m, Ar, 24H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 5.0, 6.8, 55.6, 59.9, 67.4, 67.6, 69.8, 70.8, 71.1 (×2), 76.8, 81.4, 95.6, 97.0, 114.6, 118.1, 127.5, 127.9, 128.2, 128.3, 128.4, 129.0, 129.9, 130.2, 132.9, 133.3, 137.8, 138.4, 150.4, 155.3, 165.9, 167.0; MALDI-TOF MS: $[M + Na]^+$ calcd for $C_{52}H_{60}O_{13}Si_1Na_1$, 943.37, found 943.56.

*4-Methoxyphenyl 2,4-Di-O-acetyl-3,6-di-O-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-O-benzoyl-α-D-xylopyranoside (**9**). General Procedure for Intramolecular Aglycon Delivery 2.* To the mixed acetal (**1**+**5**) (92.0 mg, 83.1 mmol) were added DTBMP (104.3 mg, 497 μmol) and MS4A (100 mg/mL) in dry $(CH_2Cl)_2$ (8.5 mL) at room temperature under Ar atmosphere Then MeOTf (42.3 μL, 374 μmol) was added to the mixture, and the mixture was stirred for 20 h at 40 °C. The reaction mixture was quenched with triethylamine, diluted with ethyl acetate, and filtered through Celite. The filtrate was washed with sat. $NaHCO_3$ aq and brine. The washed organic layer was dried over Na_2SO_4 and evaporated in vacuo. To the mixture in CH_2Cl_2 (10.0 mL) was added TFA (1.0 mL) at 0 °C, and the mixture was stirred for 30 min at the same temperature. After evaporation, to the mixture in pyridine (0.5 mL) was added Ac_2O (0.1 mL), and the mixture was stirred for 1 h at room temperature. After evaporation, the residue was diluted with ethyl acetate, washed with sat. $NaHCO_3$ aq and brine, dried over Na_2SO_4, and evaporated in vacuo. The crude product was purified by gel filtration chromatography (SX-3, ethyl acetate/toluene = 1/1) to give the product (68.6 mg, 93%, β) as acetate. **9**: $[\alpha]^{29}_D$ 27.6° (c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ 1.65 (s, Ac, 3H), 1.72 (s, Ac, 3H), 3.23 (s, OMe, 3H), 3.28−3.46 (m, 3-H^{Man}, 5-H^{Man}, 6-H$_2^{Man}$, 4H), 3.75 (dd, J = 11.4, 5.9 Hz, 5a-H^{Xyl}, 1H), 4.03 (dd, J = 11.5, 11.4 Hz, 5b-H^{Xyl}, 1H), 4.20 (s, 1-H^{Man}, 1H), 4.20−4.32 (m, 4-H^{Xyl}, 1H), 4.29 (s, CH_2Ph, 2H), 4.38 (d, J = 12.4 Hz, CH_2Ph, 1H), 4.70 (d, J = 12.4 Hz, CH_2Ph, 1H), 5.39 (dd, J = 10.1, 9.6 Hz, 4-H^{Man}, 1H), 5.60 (dd, J = 10.6, 3.6 Hz, 2-H^{Xyl}, 1H), 5.63 (d, J = 2.8 Hz, 2-H^{Man}, 1H), 5.94 (d, J = 3.7 Hz, 1-H^{Xyl}, 1H), 6.55 (t, J = 10.1 Hz, 3-H^{Xyl}, 1H), 6.58−6.61 (m, Ar, 2H), 6.85−7.42 (m, Ar, 17H), 8.18−8.20 (m, Ar, 5H); ^{13}C NMR (100 MHz, C_6D_6): 20.1 (Ac), 20.6 (Ac), 55.0 (OMe), 60.2 (C5^{Xyl}), 67.4 (C2^{Man}), 69.2 (C4^{Man}), 70.7 (C6^{Man}), 70.96 (Bn), 70.99 (C3^{Xyl}), 72.2 (C2^{Xyl}), 73.6 (Bn), 73.8 (C4^{Xyl}), 73.9 (C5^{Man}), 76.8 (C3^{Man}), 96.3 (C1^{Xyl}, $J_{C,H}$ = 177.4 Hz), 96.8 (C1^{Man}, $J_{C,H}$ = 161.2 Hz), 114.9, 118.7, 127.7−128.7 (Ar, overlapped with C_6D_6), 129.5, 130.06, 130.13, 130.85, 132.9, 133.4, 138.3, 138.7, 150.8, 155.9, 166.1, 166.2, 169.3, 170.3; MALDI-TOF MS: $[M + Na]^+$ calcd for $C_{50}H_{50}O_{15}Na_1$, 913.30, found 913.88. ESI-TOF MS: $[M + Na]^+$ calcd for $C_{50}H_{50}O_{15}Na_1$, 913.30, found 913.20; HRMS ESI-TOF: $[M + Na]^+$ calcd for $C_{50}H_{50}O_{15}Na_1$, 913.3047, found 913.3013.

*4-Methoxyphenyl 2-O-Acetyl-3,6-di-O-benzyl-4-O-triisopropylsilyl-β-D-mannopyranosyl-(1→4)-2,3-di-O-benzoyl-α-D-xylopyranoside (**10**).* The title compound was synthesized from **2** and **5** according to the procedure for the synthesis of the mixed acetal (**1**+**5**) (95%) followed by the procedure for the synthesis of **9** (93%, β). Mixed acetal (**2**+**5**): ^{1}H NMR (400 MHz, C_6D_6): δ 1.02−1.06 (m, TIPS, 21H), 1.95 (s, SMe, 3H), 3.18 (s, OMe, 3H), 3.78 (dd, J = 9.2, 2.3 Hz, 3-H^{Man}, 1H), 3.83 (dd, J = 10.6, 1.8 Hz, 6a-H^{Man}, 1H), 3.92 (dd, J = 10.6, 5.5 Hz, 6b-H^{Man}, 1H), 4.00−4.03 (m, 5-H^{Man}, 1H), 4.16−4.19 (m, 4-H^{Man}, CH$_2$Ph, 2H), 4.26−4.37 (m, 2-H^{Man}, 5-H^{Man}, 5-H^{Xyl}, CH$_2$Ph, 4H), 4.49−4.59 (m, 4-H^{Man}, CH$_2$Ph, 3H), 5.31 (d, J = 10.6, 3.7 Hz, 2-H^{Xyl}, 1H), 5.74 (s, >CHNaph, 1H), 5.80 (s, 1-H^{Man}, 1H), 5.82 (d, J = 3.6 Hz, 1-H^{Xyl}, 1H) 6.51−6.53 (m, Ar, 2H), 6.72 (dd, J = 10.1, 9.6 Hz, 3-H^{Xyl}, 1H), 6.82−7.20 (m, Ar, 16H), 7.28−7.31 (m, Ar, 2H), 7.35−7.37 (m, Ar, 2H), 7.53−7.62 (m, Ar, 3H), 7.69−7.72 (m, Ar, 1H), 8.11−8.15 (m, Ar, 5H); MALDI-TOF MS: $[M + Na]^+$ calcd for $C_{68}H_{80}O_{13}S_1Si_1Na_1$, 1187.50, found 1187.77. **10**: $[\alpha]^{29}_D$ 36.9° (c 2.0, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ 0.99−1.05 (m, TIPS, 21H), 1.84 (s, Ac, 3H), 3.15 (dd, J = 9.2, 3.2 Hz, 3-H^{Man}, 1H), 3.25 (s, OMe, 3H), 3.25−3.30 (m, 5-H^{Man}, 1H), 3.59 (dd, J = 11.0, 6.4 Hz, 6a-H^{Man}, 1H), 3.77−3.80 (m, 6b-H^{Man}, 1H), 3.87−3.91 (m, 5-H^{Xyl}, 1H), 3.98 (dd, J = 9.7, 9.2 Hz, 4-H^{Man}, 1H), 4.03−4.14 (m, 5-H^{Xyl}, CH$_2$Ph, 2H), 4.36 (s, 1-H^{Man}, 1H), 4.40 (ddd, J = 11.0, 6.0, 5.0 Hz, 4-H^{Xyl}, 1H), 4.46−4.56 (m, CH$_2$Ph, 2H), 4.85 (d, J = 10.1 Hz, CH$_2$Ph, 1H), 5.62 (dd, J = 10.5, 3.7 Hz, 2-H^{Xyl}, 1H), 5.65 (d, J = 3.2 Hz, 2-H^{Man}, 1H), 5.96 (d, J = 3.6 Hz, 1-H^{Xyl}, 1H), 6.57−6.63 (m, 3-H^{Xyl}, Ar, 3H), 6.87−7.20 (m, Ar, 11H), 7.25−7.29 (m, Ar, 2H), 7.33−7.39 (m, Ar, 4H), 8.18−8.23 (m, Ar, 4H); ^{13}C NMR (100 MHz, C_6D_6): δ 13.3, 18.4, 18.5, 20.3, 55.1, 60.3, 67.2, 68.8, 69.9, 70.9, 71.2, 72.4, 72.5, 73.7, 77.7, 81.0, 96.4 (C1^{Xyl}, $J_{C,H}$ = 176.4 Hz), 96.6 (C1^{Man}, $J_{C,H}$ = 157.4 Hz), 115.0, 118.8, 127.8−128.7 (Ar, overlapped with C_6D_6), 129.7, 130.15, 130.17, 130.9, 132.8, 133.3, 138.0, 139.1, 150.9,

155.9, 166.11, 166.19, 170.1; MALDI-TOF MS: $[M + Na]^+$ calcd for $C_{57}H_{68}O_{14}Si_1Na_1$, 1027.43, found 1027.59. ESI-TOF MS: $[M + Na]^+$ calcd for $C_{57}H_{68}O_{14}Si_1Na_1$, 1027.43, found 1027.33; HRMS ESI-TOF: $[M + Na]^+$ calcd for $C_{57}H_{68}O_{14}Si_1Na_1$, 1027.4276, found 1027.4232.

*4-Methoxyphenyl 2-O-Acetyl-3,6-di-O-benzyl-4-O-triisopropylsilyl-β-D-mannopyranosyl-(1→4)-3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (**11**).* The title compound was synthesized from **2** and **6** according to the procedure for the synthesis of the mixed acetal (**1**+**5**) (96%) followed by the procedure for the synthesis of **9** (90%, β). Mixed acetal (**2**+**6**): MALDI-TOF MS: $[M + Na]^+$ calcd for $C_{76}H_{85}N_1O_{13}Si_1Na_1$, 1302.54, found 1303.01. ESI-TOF MS: $[M + Na]^+$ calcd for $C_{76}H_{85}N_1O_{13}Si_1Na_1$, 1302.54, found 1302.43; HRMS ESI-TOF: $[M + Na]^+$ calcd for $C_{76}H_{85}N_1O_{13}Si_1Na_1$, 1302.5409, found 1302.5371. **11**: $[\alpha]^{24}_D$ 33.6° (c 1.0, $CHCl_3$); ^1H NMR (400 MHz, C_6D_6): δ 1.01−1.11 (m, TIPS, 21H), 1.91 (s, Ac, 3H), 3.12 (dd, *J* = 9.2, 3.2 Hz, 3-H^{Man}, 1H), 3.19 (s, OMe, 3H), 3.24 (ddd, *J* = 9.6, 5.5, 3.6 Hz, 5-H^{Man}, 1H), 3.41 (m, 5-H^{GlcNAc}, 1H), 3.57 (dd, *J* = 11.9, 1.8 Hz, 6a-H^{GlcNAc}, 1H), 3.72−3.80 (m, 6a-H^{Man}, 6b-H^{GlcNAc}, 2H), 3.85−3.88 (m, 6b-H^{Man}, 1H), 3.93 (d, *J* = 10.1 Hz, CH_2Ph, 1H), 4.22 (dd, *J* = 9.6, 9.2 Hz, 4-H^{Man}, 1H), 4.32 (d, *J* = 11.9 Hz, CH_2Ph, 1H), 4.45 (dd, *J* = 9.6, 9.2 Hz, 4-H^{GlcNAc}, 1H), 4.50−4.55 (m, CH_2Ph, 2H), 4.72 (dd, *J* = 10.6, 9.2 Hz, 3-H^{GlcNAc}, 1H), 4.80−4.88 (m, 1-H^{Man}, CH_2Ph, 3H), 5.03 (dd, *J* = 11.0, 8.7 Hz, 2-H^{GlcNAc}, 1H), 5.32 (d, *J* = 12.8 Hz, CH_2Ph, 1H), 5.78 (d, *J* = 2.7 Hz, 2-H^{Man}, 1H), 6.06 (d, *J* = 8.7 Hz, 1-H^{GlcNAc}, 1H), 6.55−6.59 (m, Ar, 2H), 6.67−6.85 (m, Ar, 5H), 6.97−7.00 (m, Ar, 2H), 7.10−7.31 (m, Ar, 14H), 7.38−7.45 (m, Ar, 5H); ^{13}C NMR (100 MHz, C_6D_6): δ 13.4, 18.4, 18.6, 20.7, 55.0, 56.5, 67.9, 68.5, 68.9, 69.5, 70.9, 73.5, 73.6, 75.1, 77.9, 78.0, 79.6, 81.7, 98.3 ($C1^{GlcNAc}$, $J_{C,H}$ = 169.77 Hz), 99.6 ($C1^{Man}$, $J_{C,H}$ = 160.23 Hz), 114.8, 119.0, 123.2, 125.6, 127.2, 127.5−128.7 (Ar, overlapped with C_6D_6), 132.2, 133.4, 138.2, 138.6, 139.2, 139.5, 151.5, 156.0, 168.0, 168.2, 170.1. MALDI-TOF MS: $[M + Na]^+$ calcd for $C_{66}H_{77}N_1O_{14}Si_1Na_1$, 1158.50, found 1158.82. ESI-TOF MS: $[M + Na]^+$ calcd for $C_{66}H_{77}N_1O_{14}Si_1Na_1$, 1158.50, found 1158.39; HRMS ESI-TOF: $[M + Na]^+$ calcd for $C_{66}H_{77}N_1O_{14}Si_1Na_1$, 1158.5011, found 1158.5016.

*4-Methoxyphenyl 2-O-Acetyl-3,4,6-tri-O-benzyl-β-D-mannopyranosyl-(1→4)-3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (**12**).* The title compound was synthesized from **3** and **6** according to the procedure for the synthesis of the mixed acetal (**1**+**5**) (92%) followed by the procedure for the synthesis of **9** (85%, β). **12**: $[\alpha]^{25}_D$ 39.7° (*c* 0.59, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 2.09 (s, Ac, 3H), 3.28 (ddd, *J* = 10.4, 4.8, 2.0 Hz, 5-H^{Man}, 1H), 3.38 (dd, *J* = 9.2, 3.2 Hz, 3-H^{Man}, 1H), 3.58 (dd, *J* = 11.6, 4.8 Hz, 6-H^{Man}, 1H), 3.62−3.71 (m, 4-H^{Man}, 6-H^{Man}, 5-H^{GlcNAc}, 6-H^{GlcNAc}, 4H), 3.63 (s, OMe, 3H), 3.75 (dd, *J* = 11.2, 3.6 Hz, 6-H^{GlcNAc}, 1H), 4.13 (dd, *J* = 9.6, 8.4 Hz, 4-H^{GlcNAc}, 1H), 4.27 (dd, *J* = 11.6, 8.4 Hz, 3-H^{GlcNAc}, 1H), 4.29 (dd, *J* = 11.6 Hz, CH_2Ph, 1H), 4.34 (dd, *J* = 11.6, 8.0 Hz, 2-H^{GlcNAc}, 1H), 4.34−4.47 (m, CH_2Ph, 5H), 4.56 (dd, *J* = 11.6 Hz, CH_2Ph, 1H), 4.63 (s, 1-H^{Man}, 1H), 4.64 (dd, *J* = 12.8 Hz, CH_2Ph, 1H), 4.76 (dd, *J* = 11.6 Hz, CH_2Ph, 1H), 4.89 (dd, *J* = 12.8 Hz, CH_2Ph, 1H), 5.42 (d, *J* = 3.2 Hz, 2-H^{Man}, 1H), 5.53 (d, *J* = 8.0 Hz, 1-H^{GlcNAc}, 1H), 6.59−7.59 (m, Ar, 33H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.2 (q, Ac), 55.6 (q, OMe), 55.7 (d, $C2^{GlcNAc}$), 68.4 (d, $C2^{Man}$), 68.6 (t, $C6^{GlcNAc}$), 68.9 (t, $C6^{Man}$), 71.5 (t, Bn), 73.3 (t, Bn), 73.4 (t, Bn), 74.1 (d, $C4^{Man}$), 74.5 (d, $C5^{GlcNAc}$), 74.8 (t, Bn), 75.0 (t, Bn), 75.7 (d, $C5^{Man}$), 77.3 (d, $C3^{GlcNAc}$), 78.7 (d, $C4^{GlcNAc}$), 80.5 (d, $C3^{Man}$), 97.6 (d, $C1^{GlcNAc}$, $J_{C,H}$ = 174.5 Hz), 99.1 (d, $C1^{Man}$, $J_{C,H}$ = 161.2 Hz), 114.3, 118.6, 123.3, 127.0, 127.3, 127.5, 127.6, 127.6, 127.72, 127.75, 127.79, 127.82, 127.9, 128.0, 128.1, 128.27, 128.31, 128.4, 128.5, 133.7, 137.7, 137.9, 138.4, 138.7, 150.8, 155.3, 167.9, 170.5. ESI-TOF MS: $[M + Na]^+$ calcd for $C_{64}H_{63}N_1O_{14}Na_1$, 1092.41, found 1092.42; HRMS ESI-TOF: $[M + Na]^+$ calcd for $C_{64}H_{63}N_1O_{14}Na_1$, 1092.4146, found 1092.4102.

*4-Methoxyphenyl 2-O-Acetyl-3,6-di-O-benzyl-4-O-triisopropylsilyl-β-D-mannopyranosyl-(1→4)-3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→4)-3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (**14**).* The title compound was synthesized from **2** and **7** according to the procedure for the synthesis of the mixed acetal (**1**+**5**) (92%) followed by the procedure for the synthesis of **9** (90%, β). Mixed acetal (**2**+**7**): MALDI-TOF MS: $[M + Na]^+$ calcd for $C_{104}H_{110}N_2O_{19}Si_1Na_1$, 1773.71, found 1774.25. ESI-TOF MS: $[M + Na]^+$ calcd for $C_{104}H_{110}N_2O_{19}Si_1Na_1$, 1773.71, found 1774.63; HRMS ESI-TOF: $[M + Na]^+$ calcd for $C_{104}H_{110}N_2O_{19}Si_1Na_1$, 1773.7090, found 1773.7060. 14: $[\alpha]^{24}_D$ 12.0° (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, C_6D_6): δ 1.04−1.09 (m, TIPS, 21H), 1.90 (s, Ac, 3H), 3.15−3.17 (m, 3-H^{Man}, OMe, 4H), 3.27−3.29 (m, 5-$H^{GlcNAc2}$, 1H), 3.41− 3.45 (m, 6-$H^{GlcNAc2}$, 5-H^{Man}, 2H), 3.50 (dd, *J* = 11.5, 3.7 Hz, 6-$H^{GlcNAc2}$, 1H), 3.56−3.59 (m, 6-$H^{GlcNAc1}$, 1H), 3.65 (dd, *J* = 12.4, 2.8 Hz, 6-$H^{GlcNAc1}$, 1H), 3.74 (dd, *J* = 11.0, 5.0 Hz, 6a-H^{Man}, 1H), 3.87− 3.93 (m, 6b-H^{Man}, 1H), 4.22 (dd, *J* = 9.6, 9.2 Hz, 4-H^{Man}, 1H), 4.40−4.63 (m, 4-$H^{GlcNAc1}$, 3-$H^{GlcNAc2}$, 4-$H^{GlcNAc2}$, CH_2Ph, 7H), 4.67−4.95 (m, 2-$H^{GlcNAc1}$, 3-$H^{GlcNAc1}$, 2-$H^{GlcNAc2}$, CH_2Ph, 10H), 4.97 (s, 1-H^{Man}, 1H), 5.10 (d, *J* = 13.3 Hz, CH_2Ph, 1H), 5.36 (d, *J* = 12.8 Hz, CH_2Ph, 1H), 5.62 (d, *J* = 8.2 Hz, 1-$H^{GlcNAc1}$, 1H), 5.79 (d, *J* = 3.2 Hz, 2-H^{Man}, 1H), 5.83 (d, *J* = 8.7 Hz, 1-$H^{GlcNAc2}$, 1H), 6.50−7.60 (m, Ar, 42H); ^{13}C NMR (100 MHz, C_6D_6): δ 13.4, 18.4, 18.6, 20.7, 54.9, 56.4, 57.3, 67.8, 67.9, 68.4, 68.6, 69.5, 70.9, 73.1, 73.2, 73.6, 74.9, 75.1, 76.1, 77.0, 77.6, 78.1, 79.3, 81.8, 97.5 ($C1^{GlcNAc1}$, $J_{C,H}$ = 166.6 Hz), 98.0 ($C1^{GlcNAc2}$, $J_{C,H}$ = 175.5 Hz), 99.2 ($C1^{Man}$, $J_{C,H}$ = 163.1 Hz), 114.6, 119.2, 123.1, 123.5, 127.5−128.7 (Ar, overlapped with C_6D_6), 132.2, 133.3, 133.5, 133.9, 138.2, 138.7, 138.9, 139.2, 139.3, 139.7, 151.5, 155.8, 167.8, 168.5, 170.0; MALDI-TOF MS: $[M + Na]^+$ calcd for $C_{94}H_{102}N_2O_{20}Si_1Na_1$, 1629.67, found 1629.87. ESI-TOF MS: $[M + Na]^+$ calcd for $C_{94}H_{102}N_2O_{20}Si_1Na_1$, 1629.67, found 1629.59; HRMS ESI-TOF: $[M + Na]^+$ calcd for $C_{94}H_{102}N_2O_{20}Si_1Na_1$, 1629.6693, found 1629.6723.

*Methyl 4,6-O-Benzylidene-1-thio-3-O-triisopropylsilyl-α-D-mannopyranoside (**16**).* To a solution of **15** (15.8 g, 0.053 mol) and imidazole (9.02 g, 0.133 mol) in DMF (50 mL) was added dropwise TIPSCl (12.5 mL, 0.058 mol) at 0 °C under Ar atmosphere, and the mixture was stirred for 18 h at room temperature. The reaction was quenched with sat. $NaHCO_3$ aq, extracted with $CHCl_3$, washed with brine, dried over Na_2SO_4, and evaporated in vacuo. The residue was purified by silica gel column chromatography using a gradient solvent system (hexane/ethyl acetate = 50/1 to 20/1 to 10/1 to 5/1) to give the title compound **16** (17.04 g, 70%). **16**: $[\alpha]^{25}_D$ 90.4° (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 1.01−1.14 (m, TIPS, 21H), 2.13 (s, SMe, 3H), 3.00 (br s, OH, 1H), 3.84 (t, *J* = 9.6 Hz, 6a-H, 1H), 3.90 (t, *J* = 9.6 Hz, 4-H, 1H), 4.01 (d, *J* = 3.7 Hz, 2-H, 1H), 4.12−4.24 (m, 3-H, 5-H, 6b-H, 3H), 5.27 (s, 1-H, 1H), 5.50 (s, >C*H*Ph, 1H), 7.30−7.46 (m, Ar, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.2, 13.5, 17.88, 17.92, 63.7, 68.7, 70.2, 73.2, 79.5, 85.3, 102.3, 126.3, 128.0, 129.0, 137.3; MALDI-TOF MS: $[M + Na]^+$ calcd for $C_{23}H_{38}O_5S_1Na_1$, 477.21, found 477.55. ESI-TOF MS: $[M + Na]^+$ calcd for $C_{23}H_{38}O_5S_1Si_1Na_1$, 477.21, found 477.14; HRMS ESI-TOF: $[M + Na]^+$ calcd for $C_{23}H_{38}O_5S_1Si_1Na_1$, 477.2107, found 477.2123.

*Methyl 4,6-O-Benzylidene-2-O-(2-naphthylmethyl)-1-thio-3-O-triisopropylsilyl-α-D-mannopyranoside (**17**).* After azeotropic removal of water by toluene, to a solution of **16** (1.20 g, 2.64 mmol) in DMF (50 mL) was added NaH (60%, 95.04 mg, 3.96 mmol) and 2-NAPBr (668.8 mg, 2.90 mmol) at 0 °C under Ar atmosphere, and the mixture was stirred for 3 h at room temperature. The reaction was quenched with triethylamine and brine, extracted with $CHCl_3$, washed with sat. $NaHCO_3$ aq and brine, dried over Na_2SO_4, and evaporated in vacuo. The residue was purified by silica gel column chromatography using a gradient solvent system (hexane/ethyl acetate = 50/1 to 25/1 to 10/1 to 5/1 to 3/1) to give the title compound **17** (1.492 g, 95%). **17**: $[\alpha]^{25}_D$ 44.6° (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 0.92−1.11 (m, TIPS, 21H), 2.10 (s, SMe, 3H), 3.87 (t, *J* = 10.1 Hz, 6a-H, 1H), 3.92 (dd, *J* = 3.2, 1.6 Hz, 2-H, 1H), 4.09−4.21 (m, 4-H, 5-H, 6b-H, 3H), 4.30 (dd, *J* = 9.2, 3.2 Hz, 3-H, 1H), 4.84 (d, *J* = 12.4, C*H*$_2$Ph, 1H), 4.99 (d, *J* = 12.4, C*H*$_2$Ph, 1H), 5.23 (d, *J* = 1.6 Hz, 1-H, 1H), 5.54 (s, >C*H*Ph, 1H),

7.27−7.39 (m, Ar, 3H), 7.47−7.57 (m, Ar, 5H), 7.84−7.86 (m, Ar, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.5, 13.9, 18.0, 18.1, 64.9 (C5), 68.7 (C6), 70.9 (C3), 73.9 (Bn), 79.5 (C4), 81.4 (C2), 85.3 (C1), 102.4, 125.9, 126.1, 126.4, 126.5, 127.7, 127.9, 128.0, 128.1, 128.9, 133.0, 133.2, 135.7, 137.5; MALDI-TOF MS: $[M + Na]^+$ calcd for $C_{34}H_{46}O_5S_1Si_1Na_1$, 617.27, found 617.11. ESI-TOF MS: $[M + Na]^+$ calcd for $C_{34}H_{46}O_5S_1Si_1Na_1$, 617.27, found 617.18; HRMS ESI-TOF: $[M + Na]^+$ calcd for $C_{34}H_{46}O_5S_1Si_1Na_1$, 617.2733, found 617.2758.

*Methyl 4,6-O-Benzylidene-2-O-(2-naphthylmethyl)-1-thio-α-D-mannopyranoside (**18**).* After azeotropic removal of water by toluene, to a solution of **17** (10.01 g, 16.8 mmol) in THF (20 mL) was added 1.0 M solution of TBAF in THF (25.2 mL, 25.2 mmol) at 0 °C under Ar atmosphere, and the mixture was stirred for 18 h at room temperature. The reaction was quenched with sat. $NaHCO_3$ aq, extracted with ethyl acetate, washed with brine, dried over Na_2SO_4, and evaporated in vacuo. The residue was purified by silica gel column chromatography using a gradient solvent system (hexane/ethyl acetate = 50/1 to 25/1 to 5/1 to 3/1) to give the title compound **18** (6.636 g, 90%). **18**: $[\alpha]^{25}_D$ 64.6° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.10 (s, SMe, 3H), 2.43 (d, *J* = 8.2, OH, 1H), 3.97 (dd, *J* = 10.1, 9.6 Hz, 6a-H, 1H), 3.98 (d, *J* = 3.6 Hz, 2-H, 1H), 4.07 (ddd, *J* = 10.1, 8.2, 3.6 Hz, 3-H, 1H), 4.15 (d, *J* = 10.1, 5.0 Hz, 6b-H, 1H), 4.33 (ddd, *J* = 11.4, 10.1, 5.0 Hz, 5-H, 1H), 4.78 (d, *J* = 12.4, C*H*$_2$Ph, 1H), 4.91 (d, *J* = 11.9, C*H*$_2$Ph, 1H), 5.31 (s, 1-H, 1H), 5.57 (s, >C*H*Ph, 1H), 7.32−7.36 (m, Ar, 3H), 7.47−7.50 (m, Ar, 5H), 7.81−7.86 (m, Ar, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.7, 63.9, 68.6, 69.0, 73.2, 79.7, 79.8, 83.9, 102.2, 125.7, 126.2, 126.3, 126.9, 127.7, 127.9, 128.3, 128.5, 129.1, 133.1, 133.2, 134.7, 137.2; MALDI-TOF MS: $[M + Na]^+$ calcd for $C_{25}H_{26}O_5S_1Na_1$, 461.14, found 462.34. ESI-TOF MS: $[M + Na]^+$ calcd for $C_{25}H_{26}O_5S_1Na_1$, 461.14, found 461.07; HRMS ESI-TOF: $[M + Na]^+$ calcd for $C_{25}H_{26}O_5S_1Na_1$, 461.1399, found 461.1393.

*Methyl 3-O-Benzyl-4,6-O-benzylidene-2-O-(2-naphthylmethyl)-1-thio-α-D-mannopyranoside (**19**).* After azeotropic removal of water by toluene, to a solution of **18** (6.636 g, 15.1 mmol) in DMF (10 mL) was added NaH (60%, 846 mg, 21.1 mmol) and BnBr (2.21 mL, 18.12 mmol) at 0 °C under Ar atmosphere, and the mixture was stirred for 3 h at room temperature. The reaction was quenched with triethylamine and brine, extracted with $CHCl_3$, washed with sat. $NaHCO_3$ aq and brine, dried over Na_2SO_4, and evaporated in vacuo. The residue was purified by silica gel column chromatography using a gradient solvent system (hexane/ethyl acetate = 50/1 to 25/1 to 10/1 to 5/1) to give the title compound **19** (7.10 g, 92%). **19**: $[\alpha]^{25}_D$ 73.8° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.07 (s, SMe, 3H), 3.89−3.95 (m, 2-H, 3-H, 6a-H, 3H), 4.13−4.19 (m, 5-H, 1H), 4.23 (dd, *J* = 10.1, 5.0 Hz, 6b-H, 1H), 4.31 (td, *J* = 9.6, 1.2 Hz, 4-H, 1H), 4.60 (d, *J* = 12.4 Hz, C*H*$_2$Ph, 1H), 4.79 (d, *J* = 12.4 Hz, C*H*$_2$Ph, 1H), 4.86 (d, *J* = 13.2 Hz, C*H*$_2$Ph, 1H), 4.91 (d, *J* = 13.2 Hz, C*H*$_2$Ph, 1H), 5.23 (s, 1-H, 1H), 5.64 (s, >C*H*Ph, 1H), 7.25−7.84 (m, Ar, 17H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.8, 64.6, 68.7, 73.0, 73.2, 76.4, 77.8, 79.2, 84.9, 101.5, 126.0, 126.1, 126.9, 127.56, 127.63, 127.93, 128.16, 128.22, 128.29, 128.84, 133.0, 133.2, 135.2, 137.6, 138.4; MALDI-TOF MS: $[M + Na]^+$ calcd for $C_{32}H_{32}O_5S_1Na_1$, 551.19, found 551.33. ESI-TOF MS: $[M + Na]^+$ calcd for $C_{32}H_{32}O_5S_1Na_1$, 551.19, found 551.11; HRMS ESI-TOF: $[M + Na]^+$ calcd for $C_{32}H_{32}O_5S_1Na_1$, 551.1868, found 551.1880.

*Methyl 3,6-Di-O-benzyl-2-O-(2-naphthylmethyl)-1-thio-α-D-mannopyranoside (**20**).* After azeotropic removal of water by toluene, to a solution of **19** (4.073 g, 7.94 mmol) in CH_2Cl_2 (5.0 mL) was added TESH (6.34 mL, 39.7 mmol) at 0 °C under Ar atmosphere, and TFA (2.95 mL, 39.7 mmol) was added dropwise to the mixture at the same temperature. The mixture was stirred for 20 h at room temperature, and then the reaction was quenched with triethylamine, extracted with ethyl acetate, washed with sat. $NaHCO_3$ aq and brine, dried over Na_2SO_4, and evaporated in vacuo. The residue was purified by silica gel column chromatography using a gradient solvent system (hexane/ethyl acetate = 50/1 to 25/1 to 10/1 to 5/1) to give the title compound **20** (3.61 g, 86%). **20**: $[\alpha]^{28}_D$ 21.4° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.14 (s, SMe, 3H), 2.66 (s, OH, 1H), 3.72 (dd, *J* = 8.7, 3.2 Hz, 3-H, 1H), 3.80−3.86 (m, 6a-H, 6b-H, 2H), 3.91 (dd, *J* = 3.2, 1.8 Hz, 2-H, 1H), 4.10−4.19 (m, 4-H, 5-H, 2H), 4.47−4.67 (m, C*H*$_2$Ph, 4H), 4.72 (d, *J* = 12.8 Hz, C*H*$_2$Ph, 1H), 4.87 (d, *J* = 12.4 Hz, C*H*$_2$Ph, 1H), 5.38 (s, 1-H, 1H), 7.24−7.36 (m, Ar, 10H), 7.46−7.53 (m, Ar, 3H), 7.75−7.85 (m, Ar, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.7, 67.7, 70.0, 71.6, 71.7, 72.0, 73.4, 75.3, 77.2, 79.7, 83.2, 125.9, 126.0, 126.6, 127.4, 127.5, 127.6, 127.8, 127.9, 128.1, 128.2, 128.4, 132.4, 132.9, 133.1, 135.3, 137.8, 138.2; MALDI-TOF MS: $[M + Na]^+$ calcd for $C_{32}H_{34}O_5S_1Na_1$, 553.20, found 552.90. ESI-TOF MS: $[M + Na]^+$ calcd for $C_{32}H_{34}O_5S_1Na_1$, 553.20, found 553.12; HRMS ESI-TOF: $[M + Na]^+$ calcd for $C_{32}H_{34}O_5S_1Na_1$, 553.2025, found 553.2003.

*4-Methoxyphenyl 2,3,4-Tri-O-acetyl-D-xylopyranoside (**22α**).* After azeotropic removal of H_2O with toluene, to a solution of **21** (synthesized from xylose (100 g 0.67 mol) treated with Ac_2O in pyridine), 4-methoxyphenol (91.49 g, 737 mmol) and MS4A in CH_2Cl_2 was added TMSOTf (12.31 mL, 67 mmol) at 0 °C. After stirring for 12 h at room temperature, further TMSOTf (12.31 mL, 67 mmol) was added to the mixture at 0 °C. After stirring for 12 h at room temperature, the reaction mixture was quenched with sat. $NaHCO_3$ aq and extracted with $CHCl_3$. The combined organic layers were washed with brine, dried over Na_2SO_4, and evaporated in vacuo to give unexpected α-isomer (230.6 g, 90%, α). **22α**: $[\alpha]^{27}_D$ 125.6° (*c* 1.0, CH_3OH); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.02 (s, Ac, 3H), 2.05 (s, Ac, 6H), 3.74 (dd, *J* = 11.0, 9.6 Hz, 5a-H, 1H), 3.75 (s, OMe, 3H), 3.83 (dd, *J* = 11.4, 6.4 Hz, 5b-H, 1H), 4.92 (dd, *J* = 10.6, 3.7 Hz, 2-H, 1H), 5.03 (ddd, *J* = 10.1, 9.6, 6.4 Hz, 4-H, 1H), 5.50 (d, *J* = 3.7 Hz, 1-H, 1H), 5.66 (t, *J* = 10.1 Hz, 3-H, 1H), 6.78−6.83 (m, Ar, 2H), 6.93−7.00 (m, Ar, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.7, 20.8, 55.7, 58.9, 69.2, 69.5, 70.8, 95.1, 114.6, 117.8, 150.2, 150.2, 170.0, 170.1, 170.3; MALDI-TOF MS: $[M + Na]^+$ calcd for $C_{18}H_{22}O_9Na_1$, 405.12, found 405.62. ESI-TOF MS: $[M + Na]^+$ calcd for $C_{18}H_{22}O_9Na_1$, 405.12, found 405.06; HRMS ESI-TOF: $[M + Na]^+$ calcd for $C_{18}H_{22}O_9Na_1$, 405.1162, found 405.1181.

*4-Methoxyphenyl 2,3,4-Tri-O-acetyl-β-D-xylopyranoside (**22β**).* **22β** was obtained according to the procedure for **22α** except 2.4 equiv of $BF_3 \cdot OEt$ was used instead of TMSOTf in the presence of 0.7 equiv of triethylamine (20%, β as the major product). **22β** was isomerized completely to **22α** in the presence of 0.1 equiv of TMSOTf in $CDCl_3$ within 26 h. **22β**: $[\alpha]^{26}_D$ −33.6° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.06 (s, Ac, 3H), 2.07 (s, Ac, 3H), 2.09 (s, Ac, 3H), 3.46 (dd, *J* = 12.4, 8.7 Hz, 5a-H, 1H), 3.76 (s, OMe, 3H), 4.20 (dd, *J* = 11.9, 5.0 Hz, 5b-H, 1H), 4.98−5.05 (m, 4-H, 1H), 5.02 (d, *J* = 6.4 Hz, 1-H, 1H), 5.14 (dd, *J* = 8.2, 6.4 Hz, 2-H, 1H), 5.22 (t, *J* = 8.2 Hz, 3-H, 1H), 6.79−6.84 (m, Ar, 2H), 6.92−7.00 (m, Ar, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.7, 55.6, 61.9, 68.5, 70.3, 70.9, 99.7, 114.5, 114.7, 115.9, 117.8, 118.4, 150.6, 155.2, 169.4, 169.8, 170.0; MALDI-TOF MS: $[M + Na]^+$ calcd for $C_{18}H_{22}O_9Na_1$, 405.12, found 405.33.

*4-Methoxyphenyl α-D-Xylopyranoside (**23**).* To a solution of **22α** (230.56 g, 0.603 mol) in dry methanol (500 mL) was added NaOMe to justify to alkaline pH, indicated by phenolphthalein, at room temperature under Ar atmosphere, and the mixture was stirred for 16 h at the same temperature. Amberlist 15H$^+$ was added to the mixture to quench excess NaOMe. The resin was filtered off, and the mixture was concentrated. The residue was purified by recrystallization in hexane/ethyl acetate to give the title compound **23** (146.79 g, 95%). **23**: $[\alpha]^{25}_D$ 172.4° (*c* 1.0, CH_3OH); mp 152−154 °C; ^{1}H NMR (400 MHz, CD_3OD): δ 3.49 (dd, *J* = 9.3, 3.7 Hz, 2-H, 1H), 3.51−3.60 (m, 4-H, 5a-H, 5b-H, 3H), 3.71 (s, OMe, 3H), 3.74 (dd, *J* = 10.1, 8.2 Hz, 3-H, 1H), 5.28 (d, *J* = 3.7 Hz, 1-H, 1H), 6.79−6.83 (m, Ar, 2H), 6.99−7.03 (m, Ar, 2H); ^{13}C NMR (100 MHz, CD_3OD): δ 56.0, 63.5, 71.4, 73.4, 75.1, 100.1, 115.5, 119.3, 152.4, 156.7; MALDI-TOF MS: $[M + Na]^+$ calcd for $C_{12}H_{16}O_6Na_1$, 279.08, found 279.14. ESI-TOF MS: $[M + Na]^+$

calcd for $C_{12}H_{16}O_6Na_1$, 279.08, found 279.04; HRMS ESI-TOF: $[M + Na]^+$ calcd for $C_{12}H_{16}O_6Na_1$, 279.0845, found 279.0836.

*4-Methoxyphenyl 2,3-O-Isopropylidene-α-D-xylopyranoside (**24**).* To a mixture of **23** (1.0027 g, 3.90 mmol) and 2-methoxypropene (0.41 mL, 4.29 mmol) in dry DMF was added CSA (90.6 mg, 0.39 mmol) at room temperature, and the mixture was stirred for 18 h at room temperature. The reaction was quenched by sat. $NaHCO_3$ aq and extracted with $CHCl_3$. Combined solutions were washed with brine and dried over Na_2SO_4. After concentration, the residue was purified by silica gel column chromatography using a gradient solvent system (hexane/ethyl acetate = 40/0 to 20/1 to 10/1 to 5/1) to give the title compound (855.2 mg, 74%). **24**: $[\alpha]^{25}_D$ 170.6° (*c* 1.0, CH_3OH); ^{1}H NMR (400 MHz, C_6D_6): δ 1.41 (s, CH_3, 3H), 1.49 (s, CH_3, 3H), 2.05 (d, *J* = 4.6 Hz, OH, 1H), 3.26 (s, OMe, 3H), 3.43 (dd, *J* = 9.6, 3.2 Hz, 2-H, 1H), 3.52 (t, *J* = 11.0 Hz, 5a-H, 1H), 3.66 (dd, *J* = 11.4, 5.5 Hz, 5b-H, 1H), 3.80 (ddd, *J* = 11.0, 10.1, 5.5, 4-H, 1H), 4.29 (dd, *J* = 10.1, 9.6 Hz, 3-H, 1H), 5.54 (d, *J* = 3.2 Hz, 1-H, 1H), 6.66−6.71 (m, Ar, 2H), 7.03−7.07 (m, Ar, 2H); ^{13}C NMR (100 MHz, C_6D_6): δ 26.7, 27.1, 55.1, 63.6, 70.3, 76.2, 77.7, 97.0, 110.7, 114.9, 118.9, 151.3, 155.9; MALDI-TOF MS: $[M + Na]^+$ calcd for $C_{15}H_{20}O_6Na_1$, 319.12, found 319.56. ESI-TOF MS: $[M + Na]^+$ calcd for $C_{15}H_{20}O_6Na_1$, 319.12, found 319.07; HRMS ESI-TOF: $[M + Na]^+$ calcd for $C_{15}H_{20}O_6Na_1$, 319.1158, found 319.1133.

*4-Methoxyphenyl 2,3-Di-O-benzoyl-α-D-xylopyranoside (**27**).* To a solution of **24** (7.74 g, 26.13 mmol) and imidazole (6.60 g, 96.9 mmol) in DMF (50 mL) was added dropwise TIPSCl (9.2 mL, 43.0 mmol) at 0 °C under Ar atmosphere, and the mixture was stirred for 18 h at room temperature. The reaction was quenched with sat. $NaHCO_3$ aq, extracted with $CHCl_3$, washed with brine, dried over Na_2SO_4, and evaporated in vacuo to give crude 4-methoxyphenyl 2,3-*O*-isopropylidene-4-*O*-triisopropyl-silyl-α-D-xylopyranoside (**25**) which was used in the next reaction without further purifications. To a solution of **25** in isopropanol (20 mL) was added PPTS (667 mg, 2.6 mmol) at room temperature under Ar atmosphere, and the mixture was stirred for 3 d at the same temperature. The reaction was quenched with triethylamine, diluted with ethylacetate, washed with sat. $NaHCO_3$ aq and brine, dried over Na_2SO_4, and evaporated in vacuo to give crude 4-methoxyphenyl 4-*O*-triisopropylsilyl-α-D-xylopyranoside (**26**) which was used in the next reaction without further purifications. To a solution of **26** in pyridine (10 mL) were added BzCl (6.64 mL, 57.2 mmol) and DMAP (318 mg, 2.6 mmol) at 0 °C under Ar atmosphere, and the mixture was stirred for 1.5 h at room temperature. The reaction was quenched with MeOH and evaporated in vacuo. The residue was diluted with CH_2Cl_2 and washed with 1 N HCl aq, water, sat. $NaHCO_3$ aq, water, and brine, dried over $MgSO_4$, and evaporated in vacuo. The residue was purified by silica gel column chromatography using a gradient solvent system (hexane/ethyl acetate = 50/1 to 20/1 to 10/1 to 5/1) to give 4-methoxyphenyl 2,3-di-*O*-benzoyl-4-*O*-triisopropylsilyl-α-D-xylo-pyranoside (**27**) (13.04 g, 79%). **27**: MALDI-TOF MS: $[M + Na]^+$ calcd for $C_{35}H_{44}O_8Si_1Na_1$, 643.27, found 643.85. ESI-TOF MS: $[M + Na]^+$ calcd for $C_{35}H_{44}O_8Si_1Na_1$, 643.27, found 643.27; HRMS ESI-TOF: $[M + Na]^+$ calcd for $C_{35}H_{44}O_8Si_1Na_1$, 643.2703, found 643.2686. After azeotropic removal of water by toluene, to a solution of **27** (8.91 g, 14.36 mmol) in THF (100 mL) were added acetic acid (1.972 mL, 34.46 mmol) and 1.0 M solution of TBAF in THF (34.46 mL, 34.46 mmol) at 0 °C under Ar atmosphere, and the mixture was stirred for 18 h at room temperature. The reaction was quenched with sat. $NaHCO_3$ aq, extracted with ethyl acetate, washed with brine, dried over Na_2SO_4, and evaporated in vacuo. The residue was purified by silica gel column chromatography using a gradient solvent system (hexane/ethyl acetate = 50/1 to 25/1 to 5/1 to 3/1) to give the title compound **5** (4.80 g, 72%). **5**: $[\alpha]^{26}_D$ 163.4° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.99 (br s, OH, 1H), 3.73 (s, OMe, 3H), 3.86−3.96 (m, 5a-H, 5b-H, 2H), 4.10 (td, *J* = 9.2, 6.8 Hz, 4-H, 1H), 5.37 (dd, *J* = 10.1, 4.1 Hz, 2-H, 1H), 5.69 (d, *J* = 4.1 Hz, 2-H, 1H), 5.81 (dd, *J* = 10.1, 9.2 Hz, 3-H, 1H), 6.78−8.02 (m, Ar, 14H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.6, 55.7, 62.3, 69.6, 70.8, 74.9, 95.9, 114.7, 118.2, 128.5, 128.99, 129.03, 129.8, 129.9, 133.4, 133.6, 150.5, 155.3, 165.9, 167.8; MALDI-TOF MS: $[M + Na]^+$ calcd for $C_{26}H_{24}O_8Na_1$, 487.14, found 487.67. ESI-TOF MS: $[M + Na]^+$ calcd for $C_{26}H_{24}O_8Na_1$, 487.14, found 487.06; HRMS ESI-TOF: $[M + Na]^+$ calcd for $C_{26}H_{24}O_8Na_1$, 487.1369, found 487.1372.

*4-Methoxyphenyl 2,3,6-Tri-O-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-O-benzyl-α-D-xylopyranoside (**30**).* To a solution of **10** (35.0 mg, 34.8 μmol) in MeOH−THF (1:1, 2.0 mL) was added 1 M solution of NaOMe in MeOH (10.0 μL) at 0 °C. After stirring for 4 h at room temperature, the reaction was quenched by Amberlyst H^+ resin, filtered, and concentrated in vacuo to give a crude, deacylated compound **28** (MALDI-TOF MS: $[M + Na]^+$ calcd for $C_{41}H_{58}O_{11}Si_1Na_1$, 777.36, found 777.62). To a solution of crude **28** in dry DMF (1.0 mL) were added NaH (60%, 6.3 mg, 157.5 μmol) and BnBr (13.7 μL, 115.2 μmol) at 0 °C, and the mixture was stirred for 2 h at the same temperature. The reaction was quenched by triethylamine and brine, extracted with $CHCl_3$, dried over Na_2SO_4, and evaporated in vacuo to give crude **29** (MALDI-TOF MS: $[M + Na]^+$ calcd for $C_{62}H_{76}O_{11}Si_1Na_1$, 1047.51, found 1047.51). To a solution of the crude **29** in THF (1.0 mL) was added 1.0 M THF solution of TBAF (0.1 mL, 100 μmol), and the mixture was stirred for 3 h at room temperature. After evaporation the residue was purified by PTLC (hexane/ethyl acetate = 1/1) to give the title compound **30** (25.6 mg, 85% in three steps). **30**: $[\alpha]^{27}_D$ −2.4° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.70 (br s, OH, 1H), 3.24 (dd, *J* = 10.0, 2.8 Hz, 3-H^{Man}, 1H), 3.32 (dt, *J* = 10.0, 4.8 Hz, 5-H^{Man}, 1H), 3.49 (dd, *J* = 9.2, 3.6 Hz, 2-H^{Xyl}, 1H), 3.47−3.65 (m, 6-H^{Man}, 5-H_2^{Xyl}, 3H), 3.70−3.73 (m, 6-H^{Man}, 1H), 3.71 (s, OMe, 3H), 3.76 (d, *J* = 2.8 Hz, 2-H^{Man}, 1H), 3.91−4.02 (m, 4-H^{Man}, 3-H^{Xyl}, 4-H^{Xyl}, 3H), 4.37 (d, *J* = 12.4 Hz, CH_2Ph, 1H), 4.42 (d, *J* = 12.4 Hz, CH_2Ph, 1H), 4.46 (s, 1-H^{Man}, 1H), 4.47 (d, *J* = 12.0 Hz, CH_2Ph, 1H), 4.48 (d, *J* = 12.4 Hz, CH_2Ph, 1H), 4.60 (d, *J* = 12.4 Hz, CH_2Ph, 1H), 4.70 (d, *J* = 12.4 Hz, CH_2Ph, 1H), 4.73 (d, *J* = 10.8 Hz, CH_2Ph, 1H), 4.75 (d, *J* = 12.0 Hz, CH_2Ph, 1H), 4.82 (d, *J* = 12.4 Hz, CH_2Ph, 1H), 5.03 (d, *J* = 10.8 Hz, CH_2Ph, 1H), 5.18 (d, *J* = 3.6 Hz, 1-H^{Xyl}, 1H), 6.75−7.30 (m, Ar, 24H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.6 (q, OMe), 59.8 (t, C5^{Xyl}), 68.5 (d, C4^{Man}), 70.9 (t, C6^{Man}), 71.4 (t, Bn), 73.6 (t, Bn), 73.7 (t, Bn), 74.2 (t, Bn), 74.3 (d, C2^{Man}), 75.2 (d, C5^{Man} and t, Bn), 75.9 (d, C4^{Xyl}), 78.8 (d, C2^{Xyl}), 80.0 (d, C3^{Xyl}), 81.4 (d, C3^{Man}), 96.8 (d, C1^{Xyl}), 99.6 (d, C1^{Man}), 114.5, 118.3, 127.2, 127.4, 127.5, 127.6, 127.7, 127.8, 127.8, 128.0, 128.1, 128.3, 128.4, 128.5, 137.9, 138.0, 138.1, 138.5, 139.1, 150.8, 155.1; MALDI-TOF MS: $[M + Na]^+$ calcd for $C_{53}H_{56}O_{11}Na_1$, 891.37, found 891.21; ESI-TOF MS: $[M + Na]^+$ calcd for $C_{53}H_{56}O_{11}Na_1$, 891.37, found 891.45; HRMS ESI-TOF: $[M + Na]^+$ calcd for $C_{53}H_{56}O_{11}Na_1$, 891.3720, found 891.3741.

*2-O-Acetyl-3,6-di-O-benzyl-4-O-triisopropylsilyl-β-D-mannopyranosyl-(1→4)-2,3-di-O-benzoyl-D-xylopyranosyl Fluoride (**32**).* To a solution of **10** (41.8 mg, 41.6 μmol) in CH_3CN (2.0 mL) and H_2O (0.2 mL) was added CAN (68.4 mg, 125 μmol) at 0 °C under Ar atmosphere. The reaction mixture was stirred for 18 h at room temperature, diluted with ethyl acetate and washed with sat. $NaHCO_3$ aq and brine, dried over Na_2SO_4, and evaporated in vacuo. The crude product was purified by florisil column chromatography using a gradient solvent system (hexane/ethyl acetate =20/1 to 10/1 to 5/1 to 2/1 to 1/1) to give 2-*O*-acetyl-3,6-di-*O*-benzyl-4-*O*-triisopropylsilyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-D-xylopyranose (**31**). **31**: MALDI-TOF MS: $[M + Na]^+$ calcd for $C_{50}H_{62}O_{13}Si_1Na_1$, 921.39, found 921.32. To a solution of a mixture of **31** (27.1 mg, 29.4 μmol) in dry CH_2Cl_2 (1.0 mL) was added DAST (7.8 μL, 58.8 μmol) at −40 °C under Ar atmosphere. The reaction mixture was stirred for 2 h at the same temperature and then quenched with MeOH and sat. $NaHCO_3$ aq. The reaction mixture was extracted with $CHCl_3$, and the combined organic layers were washed with sat. $NaHCO_3$ aq and brine, dried over Na_2SO_4, and evaporated in vacuo.

The crude product was purified by silica gel flash column chromatography using a gradient solvent system (hexane/ethyl acetate = 50/1 to 20/1 to 10/1 to 5/1 to 3/1 to 1/1) to give **32** (25.8 mg, 67% in two steps, α:β = 84:16). **32**: α-isomer (major): ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.70−1.00 (m, TIPS, 21H), 1.95 (s, Ac, 21H), 3.29 (dd, J = 10.4, 7.2 Hz, 6a-H^{Man}, 1H), 3.38 (dd, J = 9.2, 2.8 Hz, 3-H^{Man}, 1H), 3.44 (ddd, J = 9.0, 7.2, 1.2 Hz, 5-H^{Man}, 1H), 3.67 (dd, J = 10.4, 1.2 Hz, 6b-H^{Man}, 1H), 3.77 (t, J = 9.2 Hz, 4-H^{Man}, 1H), 3.87 (dd, J = 13.2, 2.4 Hz, 5a-H^{Xyl}, 1H), 4.02 (dd, J = 5.2, 2.4 Hz, 4-H^{Xyl}, 1H), 4.11 (d, J = 10.0 Hz, CH_2Ph, 1H), 4.02 (dd, J = 13.2, 2.4 Hz, 5b-H^{Xyl}, 1H), 4.30 (d, J = 12.0 Hz, CH_2Ph, 1H), 4.75 (d, J = 10.0 Hz, CH_2Ph, 1H), 4.80 (s, 1-H^{Man}, 1H), 5.18−5.23 (m, 2-H^{Xyl}, 1H), 5.58 (d, J = 56.4 Hz, 1-H^{Xyl}, 1H), 5.60−5.66 (m, 3-H^{Xyl}, 1H), 5.67 (d, J = 2.8 Hz, 2-H^{Man}, 1H), 7.00−8.12 (m, Ar, 20H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.9, 18.0, 18.1, 20.8, 59.7 (C5^{Xyl}), 66.7 (C2^{Xyl}C1^{Xyl}−F), 67.1 (C2^{Xyl}C1^{Xyl}−F), 67.3 (C3^{Xyl}), 67.6 (C2^{Man}), 68.4 (C4^{Man}), 69.7 (C6^{Man}), 70.8 (C4^{Xyl}, Bn), 73.3 (Bn), 77.2 (C5^{Man}), 81.1 (C3^{Man}), 97.4 (C1^{Man}), 103.9 (C1^{Xyl}−F), 106.2 (C1^{Xyl}−F), 127.4, 127.5, 127.6, 127.8, 128.0, 128.1, 128.4, 128.5, 129.0, 129.3, 129.9, 130.4, 129.9, 130.4, 133.5, 137.4, 138.1, 164.8, 165.2, 170.4; MALDI-TOF MS: $[M + Na]^+$ calcd for $C_{50}H_{61}F_1O_{12}Si_1Na_1$, 923.38, found 923.72; ESI-TOF MS: $[M + Na]^+$ calcd for $C_{50}H_{61}F_1O_{12}Si_1Na_1$, 923.38, found 923.36; HRMS ESI-TOF: $[M + Na]^+$ calcd for $C_{50}H_{61}F_1O_{12}Si_1Na_1$, 923.3814, found 923.3827.

*4-Methoxyphenyl 2-O-Acetyl-3,6-di-O-benzyl-4-O-triisopropylsilyl-β-D-mannopyranosyl-(1→4)-2,3-di-O-benzoyl-β-D-xylopyranosyl-(1→4)-2,3,6-tri-O-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-O-benzyl-α-D-xylopyranoside (**33**).* A mixture of $AgClO_4$ (14.4 mg, 69.2 μmol), Cp_2HfCl_2 (13.8 mg, 34.6 μmol), and dried powdered MS 4A (250 mg) in dry benzene (1.0 mL) was stirred for 30 min at room temperature under Ar atmosphere. To the mixture was added through a cannula a solution of **32** (16.0 mg, 17.3 μmol) and **30** (11.7 mg, 13.5 μmol) in dry benzene (1.0 mL + 0.5 mL for rinsing) at the same temperature, and the mixture was stirred for 3 h at the same temperature under Ar atmosphere. The reaction mixture was diluted with ethyl acetate, quenched with sat. $NaHCO_3$ aq, and filtered through Celite. The filtrate was extracted with ethyl acetate, and the combined organic layers were washed with brine. The washed organic layer was dried over Na_2SO_4 and evaporated in vacuo. The crude product was purified by gel filtration chromatography (Biobeads, SX-3, ethyl acetate/toluene, 1/1) followed by PTLC (hexane/ethyl acetate = 3/1) to give **33** (20.7 mg, 88%). **33**: $[\alpha]^{25}_D$ 7.4° (c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.80−0.97 (m, TIPS, 21H), 1.95 (s, Ac, 3H), 3.16 (ddd, J = 9.6, 4.0, 1.6 Hz, 5-H^{Man1}, 1H), 3.22 (dd, J = 12.0, 10.4 Hz, 5-H^{Xyl2}, 1H), 3.28−3.34 (m, 6-H^{Man2}, 5-H^{Man2}, 2H), 3.36 (dd, J = 9.2, 3.2 Hz, 3-H^{Man1}, 1H), 3.39 (dd, J = 9.2, 2.4 Hz, 3-H^{Man2}, 1H), 3.50−3.77 (m, 4-H^{Man2}, 6-H^{Man2}, 2-H^{Man1}, 6-H$_2$^{Man1}, 2-H^{Xyl1}, 5-H$_2$^{Xyl1}, 8H), 3.78 (s, OMe, 3H), 3.91 (ddd, J = 10.0, 9.2, 6.4 Hz, 4-H^{Xyl1}, 1H), 3.98−4.04 (m, 5-H^{Xyl2}, 3-H^{Xyl1}, 2H), 4.13−4.20 (m, 4-H^{Xyl2}, CH$_2$Ph, 2H), 4.24 (d, J = 12.0 Hz, CH$_2$Ph, 1H), 4.28 (t, J = 9.6 Hz, 4-H^{Man1}, 1H), 4.37 (d, J = 11.2 Hz, CH$_2$Ph, 1H), 4.38 (s, 1-H^{Man1}, 1H), 4.47 (d, J = 11.2 Hz, CH$_2$Ph, 1H), 4.51 (d, J = 12.4 Hz, CH$_2$Ph, 1H), 4.58 (s, 1-H^{Man2}, 1H), 4.61 (d, J = 12.4 Hz, CH$_2$Ph, 1H), 4.64 (d, J = 12.0 Hz, CH$_2$Ph, 1H), 4.71−4.77 (m, 1-H^{Xyl2}, CH$_2$Ph, 4H), 4.80 (d, J = 12.4 Hz, CH$_2$Ph, 1H), 4.85 (s, CH$_2$Ph, 2H), 5.06 (d, J = 11.6 Hz, CH$_2$Ph, 1H), 5.22 (d, J = 3.6 Hz, 1-H^{Xyl1}, 1H), 5.30 (dd, J = 9.2, 6.4 Hz, 2-H^{Xyl2}, 1H), 5.42 (dd, J = 9.6, 9.6 Hz, 3-H^{Xyl2}, 1H), 5.55 (d, J = 3.2 Hz, 2-H^{Man2}, 1H), 6.80−7.98 (m, Ar, 49H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.9, 17.9, 18.1, 20.5, 55.6, 59.7 (C6^{Man1}), 62.8 (C5^{Xyl2}), 66.8 (C2^{Man2}), 68.2 (C5^{Xyl1}), 68.3 (C4^{Man2}), 69.7 (C6^{Man2}), 70.6 (Bn), 72.1 (C4^{Xyl2}), 72.47 (C2^{Xyl2}), 72.54 (C3^{Xyl2}), 72.9 (C4^{Man1}), 73.3 (Bn), 73.4 (Bn), 73.5 (Bn), 74.1 (Bn), 75.1 (Bn), 75.3 (C2^{Man1}), 75.5 (Bn), 75.9 (C5^{Man1}), 76.0 (C4^{Xyl1}), 77.2 (C5^{Man2}), 78.8 (C2^{Xyl1}), 79.9 (C3^{Man1}), 80.1 (C3^{Xyl1}), 80.6 (C3^{Man2}), 95.9 (C1^{Man2}, $J_{C,H}$ = 157.4 Hz), 96.7 (C1^{Xyl1}, $J_{C,H}$ = 176.4 Hz), 99.5 (C1^{Man1}, $J_{C,H}$ = 155.5 Hz), 100.8 (C1^{Xyl2}, $J_{C,H}$ = 168.8 Hz), 114.5, 118.3, 127.1, 127.2, 127.4, 127.47, 127.50, 127.6, 127.7, 127.77, 127.83, 127.95, 127.98, 128.1, 128.27, 128.33, 128.36, 128.40, 129.3, 120.8, 130.1, 132.7, 133.2, 137.4, 138.1, 138.29, 138.34, 138.6, 138.7, 139.1, 150.8, 155.1, 165.2, 165.7, 170.3. MALDI-TOF MS: $[M + Na]^+$ calcd for $C_{103}H_{116}O_{23}Si_1Na_1$, 1771.76, found 1772.12; ESI-TOF MS: $[M + Na]^+$ calcd for $C_{103}H_{116}O_{23}Si_1Na_1$, 1771.76, found 1771.91; HRMS ESI-TOF: $[M + Na]^+$ calcd for $C_{103}H_{116}O_{23}Si_1Na_1$, 1771.7574, found 1771.7557.

*4-Methoxyphenyl β-D-Mannopyranosyl-(1→4)-β-D-xylopyranosyl-(1→4)-β-D-mannopyranosyl-(1→4)-α-D-xylopyranoside (**36**).* To a solution of protected **33** (15.1 mg, 8.63 μmol) in dry THF (1 mL) was added TBAF (86 μL, 86 μmol) at room temperature. After the mixture stirred for 18 h at the same temperature, the solvent was evaporated in vacuo to give 4-methoxyphenyl 2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-xylopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzyl-α-D-xylopyranoside (**34**) (MALDI-TOF MS: $[M + Na]^+$ calcd for $C_{94}H_{96}O_{23}Na_1$, 1615.62, found 1615.57; ESI-TOF MS: $[M + Na]^+$ calcd for $C_{94}H_{96}O_{23}Na_1$, 1615.62, found 1615.70; HRMS ESI-TOF: $[M + Na]^+$ calcd for $C_{94}H_{96}O_{23}Na_1$, 1615.6240, found 1615.6224.). To the crude mixture in MeOH (2.0 mL) was added 1 M MeOH solution of NaOMe (39 μL) and stirred for 24 h at room temperature. After stirring for 4 h at room temperature, the reaction was quenched by Amberlyst 15H$^+$ resin, filtered, and concentrated in vacuo. Then the residue was purified by PTLC (hexane/ethyl acetate = 3:1) to give 4-methoxyphenyl 3,6-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-D-xylopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-β-D-mannopyranosyl-(1→4)-2,3-di-*O*-benzyl-α-D-xylopyranoside (**35**) (MALDI-TOF MS: $[M + Na]^+$ calcd for $C_{78}H_{86}O_{20}Na_1$, 1365.56, found 1365.92; ESI-TOF MS: $[M + Na]^+$ calcd for $C_{78}H_{86}O_{20}Na_1$, 1365.56, found 1365.64; HRMS ESI-TOF: $[M + Na]^+$ calcd for $C_{78}H_{86}O_{20}Na_1$, 1365.5610, found 1365.5586). Hydrogenolysis of the resulting residue **35** was carried out in the presence of $Pd(OH)_2$ (15.0 mg) in MeOH−H_2O (2:1, 3 mL) for 24 h at room temperature. The mixture was filtered through Celite under Ar atmosphere, and the filtrate was concentrated in vacuo to give the title compound **36** (4.3 mg, 70% in three steps). **36**: ^{1}H NMR (400 MHz, D_2O): δ 3.31 (dd, J = 9.2, 7.8 Hz, 2-H ^{Xyl2}, 1H), 3.32−3.40 (m, 5-H^{Man2}, 5-H^{Xyl2}, 2H), 3.48−3.63 (m, 5-H^{Man1}, 3-H^{Man2}, 4-H^{Man2}, 3-H^{Xyl2}, 5-H^{Xyl1}, 5H), 3.66−3.76 (m, 3-H^{Man1}, 4-H^{Man1}, 6-H^{Man2}, 2-H^{Xyl1}, 4H), 3.77−3.87 (m, 6-H^{Man1}, 5-H^{Xyl1}, 4-H^{Xyl2}, 3H), 3.79 (s, OMe, 3H), 3.88−4.02 (m, 2-H^{Man1}, 6-H^{Man1}, 2-H^{Man2}, 6-H^{Man2}, 3-H^{Xyl1}, 4-H^{Xyl1}, 6H), 4.10 (dd, J = 11.6, 5.2 Hz, 5-H^{Xyl2}, 1H), 4.44 (d, J = 7.8 Hz, 1-H^{Xyl2}, 1H), 4.74 (s, 1-H^{Man2}, 1H), 4.77 (s, 1-H^{Man1}, 1H), 5.49 (d, J = 3.2 Hz, 1-H^{Xyl1}, 1H), 6.95−7.11 (m, Ar, 4H); ^{13}C NMR (100 MHz, D_2O): δ 56.6 (OMe), 60.4 (C5^{Xyl1}), 61.2 (C6^{Man1}), 61.9 (C6^{Man2}), 63.8 (C5^{Xyl2}), 67.6 (C4^{Man2}), 71.3 (C2^{Man1}), 71.6 (C2^{Man2}), 71.8 (C2^{Xyl1}), 72.2 (C4^{Xyl1}), 72.4 (C3^{Man1}), 73.7 (C2^{Xyl2}, C3^{Man2}), 74.7 (C3^{Xyl2}), 76.0 (C5^{Man1}), 77.0 (C3^{Xyl1}, C4^{Xyl2}), 77.2 (C4^{Man1}, C5^{Man2}), 98.6 (C1^{Xyl1}, $J_{C,H}$ = 175.5 Hz), 98.9 (C1^{Man1}, $J_{C,H}$ = 165.0 Hz), 99.2 (C1^{Man2}, $J_{C,H}$ = 165.5 Hz), 104.2 (C1^{Xyl2}, $J_{C,H}$ = 174.5 Hz), 116.0, 119.6, 151.0, 155.5; MALDI-TOF MS: $[M + Na]^+$ calcd for $C_{29}H_{44}O_{20}Na_1$, 735.23, found 735.31; ESI-TOF MS: $[M + Na]^+$ calcd for $C_{29}H_{44}O_{20}Na_1$, 735.23, found 735.28; HRMS ESI-TOF: $[M + Na]^+$ calcd for $C_{29}H_{44}O_{20}Na_1$, 735.2324, found 735.2335. ^{1}H NMR (400 MHz, D_2O, pH 7.5 phosphate buffer at 40 °C): δ 3.51 (dd, J = 9.2, 8.0 Hz, 2-H ^{Xyl2}, 1H), 3.52−3.60 (m, 5-H^{Man2}, 5-H^{Xyl2}, 2H), 3.48−3.63 (m, 5-H^{Man1}, 3-H^{Man2}, 4-H^{Man2}, 3-H^{Xyl2}, 4H), 3.86−3.96 (m, 3-H^{Man1}, 4-H^{Man1}, 6-H^{Man2}, 2-H^{Xyl1}, 5-H^{Xyl1}, 5H), 3.87−4.07 (m, 6-H^{Man1}, 5-H^{Xyl1}, 4-H^{Xyl2}, 3H), 3.99 (s, OMe, 3H), 4.08−4.21 (m, 2-H^{Man1}, 6-H^{Man1}, 2-H^{Man2}, 6-H^{Man2}, 3-H^{Xyl1}, 4-H^{Xyl1}, 6H), 4.29 (dd, J = 12.0, 5.2 Hz, 5-H^{Xyl2}, 1H), 4.60 (d, J = 8.0 Hz, 1-H^{Xyl2}, 1H), 4.94 (s, 1-H^{Man2}, 1H), 4.97 (s, 1-H^{Man1}, 1H), 5.49 (d, J = 4.0 Hz, 1-H^{Xyl1}, 1H), 7.14−7.32 (m, Ar, 4H); ^{13}C NMR (100 MHz, D_2O, pH 7.5 phosphate buffer at 40 °C, processed using native scale): δ 56.2 (OMe), 59.8 (C5^{Xyl1}), 60.6 (C6^{Man1}), 61.3 (C6^{Man2}), 63.2 (C5^{Xyl2}), 67.0 (C4^{Man2}), 70.7 (C2^{Man1}), 71.0 (C2^{Man2}), 71.2 (C2^{Xyl1}), 71.6 (C4^{Xyl1}), 71.7 (C3^{Man1}),

73.1 ($C2^{Xyl2}$, $C3^{Man2}$), 74.1 ($C3^{Xyl2}$), 75.4 ($C5^{Man1}$), 76.5 ($C3^{Xyl1}$, $C4^{Xyl2}$), 76.5 ($C4^{Man1}$, $C5^{Man2}$), 98.0 ($C1^{Xyl1}$, $J_{C,H}$ = 175.5 Hz), 98.4 ($C1^{Man1}$, $J_{C,H}$ = 162.1 Hz), 98.6 ($C1^{Man2}$, $J_{C,H}$ = 163.9 Hz), 103.5 ($C1^{Xyl2}$, $J_{C,H}$ = 170.7 Hz), 115.5, 119.1, 150.4, 155.0 (also see Table 2).

Molecular Modeling Experiment. The modelings were performed on *MacroModel*, ver. 8.1,[34a] through a conformational search program. Conformational profiles were generated by 1000 step Monte Carlo (MCMM)[34b] searches with Amber*[39] force fields in water using the GB/SA continuum solvation model,[40] and then reminimized by multiple minimization program with the force fields in order to give a sufficient global minimum when the structure did not reach a gradient to <0.05 kJ/Å·mol by C-search.

■ ASSOCIATED CONTENT

Supporting Information. Experimental procedures and results of antifreeze activity of **36**; results of molecular modeling of $(ManXyl)_{10}$ and $(ManXyl)_2$ in H_2O calculated by *MacroModel*, ver 8.1; ^1H and ^{13}C NMR spectra of **1**, **2**, **5**, **8**−**12**, **14**, **16**−**20**, **22**−**24**, **30**, **32**, **33**, **36**. This material is available free of charge via the Internet at http://pubs.acs.org.

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