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# Synthesis and Biological Evaluation of the Forssman Antigen Pentasaccharide and Derivatives by a One-Pot Glycosylation Procedure

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**Abstract:** The synthesis and biological evaluation of the Forssman antigen pentasaccharide and derivatives thereof by using a one-pot glycosylation and polymer-assisted deprotection is described. The Forssman antigen pentasaccharide, composed of GalNAcα-(1,3)GalNAcβ(1,3)Galα(1,4)Galβ-(1,4)Glc, was recently identified as a ligand of the lectin SLL-2 isolated from an octocoral Sinularia lochmodes. The chemo- and α-selective glycosylation of a thiogalactoside with a hemiacetal donor by using a mixture of $Tf_2O$, TTBP and $Ph_2SO$, followed by activation of the remaining thioglycoside, provided the trisaccharide at the reducing end in a one-pot procedure. The pentasaccharide was prepared by the α-selective glycosylation of the *N*-Troc-protected (Troc = 2,2,2-trichloroethoxycarbonyl) thioglycoside with a 2-azide-1-hydroxyl glycosyl donor, followed by glycosidation of the resulting disaccharide at the C3 hydroxyl group of the trisaccharide acceptor in a one-pot process. We next applied the one-pot glycosylation method to the synthesis of pentasaccharides in which the galactosamine units were partially and fully replaced by galactose units. Among the three possible pentasaccharides, Galα(1,3)GalNAc and Galα-(1,3)Gal derivatives were successfully prepared by the established method. An assay of the binding of the synthetic oligosaccharides to a fluorescent-labeled SLL-2 revealed that the NHAc substituents and the length of the oligosaccharide chain were both important for the binding of the oligosaccharide to SLL-2. The inhibition effect of the oligosaccharide relative to the morphological changes of *Symbiodinium* by SLL-2, was comparable to their binding affinity to SLL-2. In addition, we fortuitously found that the synthetic Forssman antigen pentasaccharide directly promotes a morphological change in *Symbiodinium*. These results strongly indicate that the Forssman antigen also functions as a chemical mediator of *Symbiodinium*.

**Keywords:** chemical biology · glycosylation · lectin · oligosaccharides · one-pot

## Introduction

Zooxanthellae symbiosis is nearly a standard relationship that corals depend on for energy and nutrients. Recent environmental changes have influenced these relationships and have resulted in the bleaching of coral and a subsequent deterioration in the extent of symbiosis.[1] A lectin SLL-2 isolated from an octocoral *Sinularia lochmodes* is an important mediator of the symbiotic relationship between corals and symbiotic microalgae (*Symbiodinium*).[2] Treatment of *Symbiodinium* cells with SLL-2 promotes their transformation into a non-flagellated coccoid form from a flagellated-swimming form. Frontal affinity chromatography analyses[3] of interactions between SLL-2 and various pyridylaminated oligosaccharides from various glycolipids and glycoproteins revealed that a pyridylaminated GalNAcα(1,3)GalNAcβ-(1,3)Galα(1,4)Galβ(1,4)Glc, namely the Forssman antigen[4] **1** acts as a high affinity ligand to SLL-2.[5] Therefore, the antigen and structurally related oligosaccharides would be expected to function as effective chemical probes for the elucidation, not only of the biological roles of SLL-2, but also the mechanism associated with the symbiotic relationship. However, oligosaccharides from natural sources are limited in terms of structural diversity and can be produced in only limited qualities. In addition, the effect of a glucose unit at the reducing end on their binding affinity is not clear because the pyridiylamination of oligosaccharides results in the formation of an acyclic form in the case of the sugar unit at the reducing end.[6] Therefore, the chemical synthesis of a Forssman antigen pentasaccharide and related oligosaccharides would be highly desirable in terms of structure–activity relationship studies. Several reports have appeared on the synthesis of the Forssman antigen oligosaccharide, based on a target-oriented strategy.[7] Therefore, an effective method for the synthesis of the Forssman antigen and relat-

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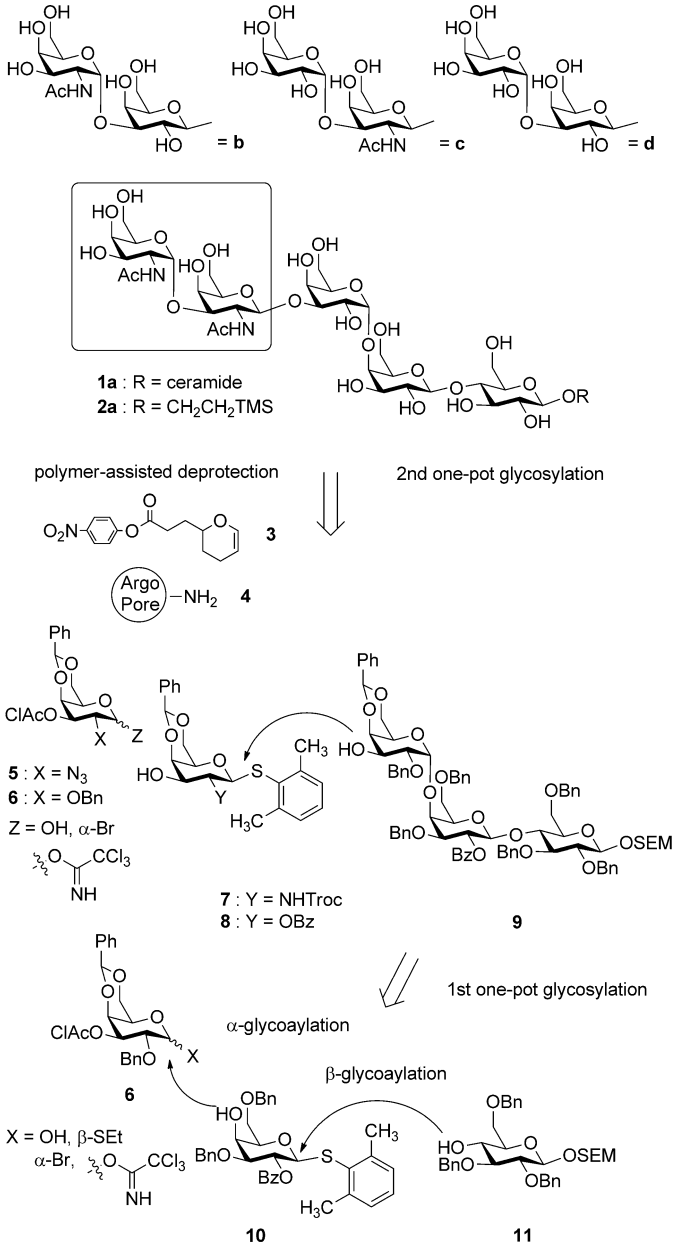
ed oligosaccharides based on a diverse-orientated strategy continues to remain highly desirable.

In a previous study, we reported on an efficient methodology for the synthesis of oligosaccharides based on a one-pot glycosylation procedure and polymer-assisted deprotection.[8] The one-pot glycosylation procedure involves the sequential chemo- and regioselective glycosylation to directly provide oligosaccharides from several simple building blocks without the need for purifying intermediates and is effective for the synthesis of a single target oligosaccharide as well as oligosaccharide libraries.[9] Polymer-assisted deprotection involves the deprotection of solid-supported oligosaccharides followed by their release from the solid. This procedure simplifies the manipulation of the highly polar, fully deprotected oligosaccharides and their synthetic intermediates.[10] Herein we report on the synthesis of the pentasaccharide **2** and derivatives that contain 2-trimethylsilylethyl group at the reducing end by two one-pot glycosylation reactions and polymer-assisted deprotection, and the biological evaluation of the final products.

## Results and Discussion

We first planned to prepare the Forssman antigen pentasaccharide **2a** with a 2-trimethysilylethyl group at the reducing end and derivatives **2b–d**, in which one and/or two galactosides are attached in place of the galactosamine units. The 2-trimethysilylethyl group at the non-reducing end is a lipophilic tag that allows for easy purification and can be chemoselectively removed by treatment with trifluoroacetic acid (TFA)[11] or $LiBF_4$[12] for further derivatization. Our strategy for the synthesis of the pentasaccharide derivatives **2a–d** involved two one-pot glycosylations combined with a polymer-assisted deprotection (Scheme 1). The first one-pot glycosylation involved the chemo- and α-stereoselective glycosylation of the thiogalactoside **10** with the galactoside **6** and the subsequent β-selective glycosyation of **11** with a disaccharide to prepare the common trisaccharide **9** at the reducing end. The methyl substituents on the phenyl group of **10** prevent the thiotransfer of the thioglycoside **10** in this chemoselective glycosylation.[13] The second one-pot glycosylation is initiated by the chemo- and α-stereoselective glycosylation of galacosamine **7** or galactoside **8** with galactosamine **5** or galactose **6**. A subsequent β-selective glycosidation of the resulting disaccharide donors at the C3 hydroxyl group of the trisaccharide acceptor **9** provides the protected Forssman pentasaccharides. Deprotection of the pentasaccharides involving modification of the *N*-Troc amino and azide groups to *N*-acetamides and the complete removal of all *O*-protecting groups was achieved by polymer-assisted deprotection by using the prelinker **3** and the amino functionalized ArgoPore resin **4** (Scheme 1).

Synthesis of the trisaccharide **9** at the reducing end is shown in Scheme 2. We first examined the chemo- and α-selective glycosylation of thioglycoside **10** with the 2*O*-benzyl-protected donors **6a–d**. Treatment of donors **6a–d** with a



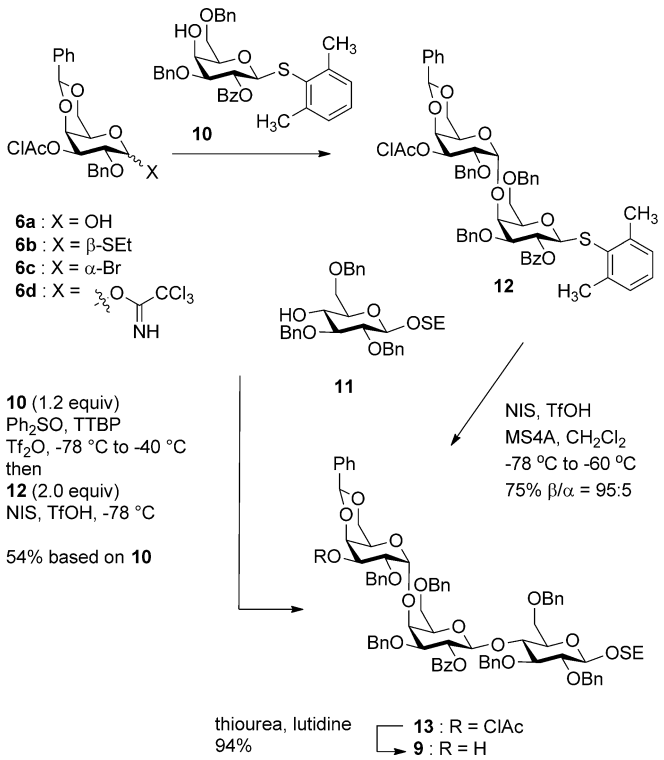

Scheme 1. Strategy for the synthesis of the pentasaccharides **2**.

different leaving group and 2,6-dimethylphenylthioglycoside **10** with the corresponding requisite activating reagents provided the disaccharide **12** with good α-selectivity (Table 1). Glycosidation of the activated hemiacetal **6a** with $Tf_2O$, 2,4,6-tri-*tert*-butylpyrimidine (TTBP), and $Ph_2SO$ resulted in

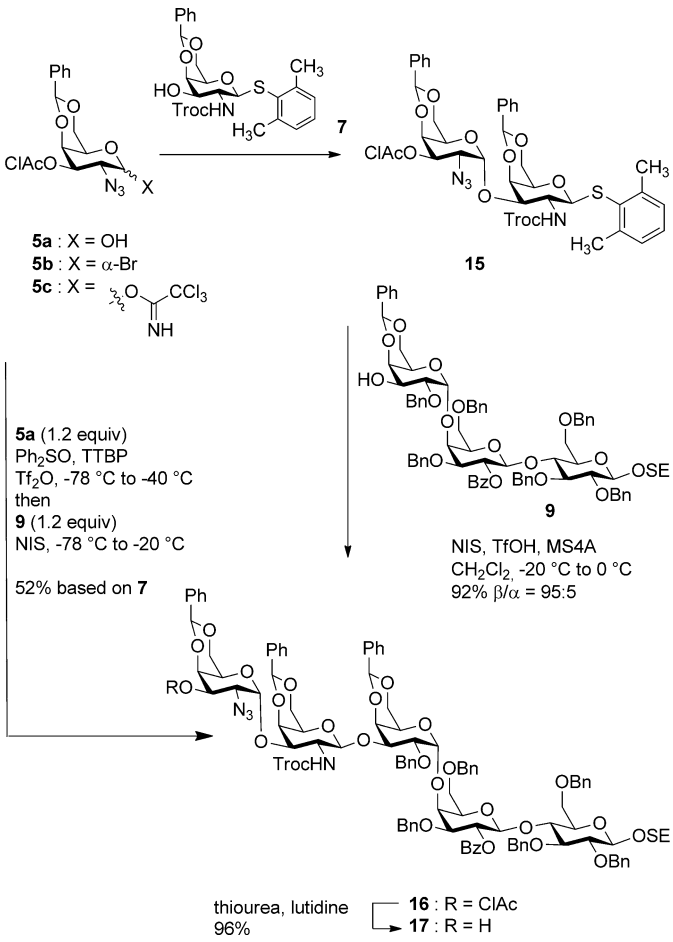
Table 1. α-Selective galactosylation at C4 position of glucose **10**.

| Entry | Donor | Conditions | Yield [%] | α/β[a] |
|---|---|---|---|---|
| 1 | **6a** | $Tf_2O$, TTBP, $Ph_2SO$ −78 to −30 °C, 4.0 h | 92 | 95:5 |
| 2 | **6b** | MeOTf, RT, 4.0 h | 85 | 95:5 |
| 3 | **6c** | AgOTf, −78 to −40 °C, 2.5 h | 43 | 95:5 |
| 4 | **6d** | TMSOTf, −78 °C, 2.0 h | 74 | 95:5 |

[a] The ratio was determined based on the $^1H$ NMR spectra.




Scheme 2. Stepwise, one-pot synthesis of trisaccharide **13**.




Scheme 3. Stepwise, one-pot synthesis of pentasaccharide **16**.

the highest yield of the disaccharide **12** among the compounds tested (Table 1, entry 1).[14] The resulting disaccharide **12** was activated with *N*-iodosuccinimide (NIS) and a catalytic amount of TfOH in the presence of 1.5 equivalents of acceptor **11** to give the trisaccharide **13** in 75% yield with good β-selectivity. The one-pot synthesis of trisaccharide **13** from the three building blocks **6a**, **10**, and **11** was next examined. Treatment of the hemiacetal **10a** and thioglycoside **11** with $Tf_2O$, TTBP, and $Ph_2SO$, followed by the addition of 2.0 equivalents of acceptor **11** and NIS resulted in the stereoselective formation of the trisaccharide **13** in 54% yield based on **10**. The chloroacetyl group of the trisaccharide **13** was removed by treatment with thiourea to give the alcohol **9** in 94% yield, which was used as the acceptor in the next one-pot glycosylation.

The synthesis of the pentasaccharide **17** was examined next (Scheme 3). We first examined the chemo- and α-selective glycosylation of thioglycoside **7**[15] with the 2-azido-glycosyl donors **5a–c** with a different leaving group (Table 2). Glycosylation of the thioglycoside **7** with glycosyl bromide and imidate **5b** or **5c** provided an anomeric mixture of the disaccharide **15** (Table 2, entries 2 and 3). On the other hand, activation of the hemiacetal **5a** with $Tf_2O$, $Ph_2SO$, and TTBP in the presence of thioglycoside **7** provided the disaccharide **15** in 92% yield with excellent α-selectivity (α/β = 92:8; Table 2, entry 1). The disaccharide **15** was activated by reaction with NIS and a catalytic amount of TfOH in the presence of trisaccharide **9** to give the pentasaccharide **16** in 92% yield. The one-pot synthesis of pentasaccharide **16** from the three building blocks **5a**, **7**, and **9** was then examined. Treatment of the hemiacetal **5a** and thioglycoside **7** with $Tf_2O$, TTBP, and $Ph_2SO$, followed by the addition of 1.2 equivalents of acceptor **9** and NIS resulted in the stereoselective formation of the trisaccharide **16** in 52% yield based on **7**. The chloroacetyl group of the trisaccharide was removed by treatment with thiourea to give the alcohol **17** in 96% yield.

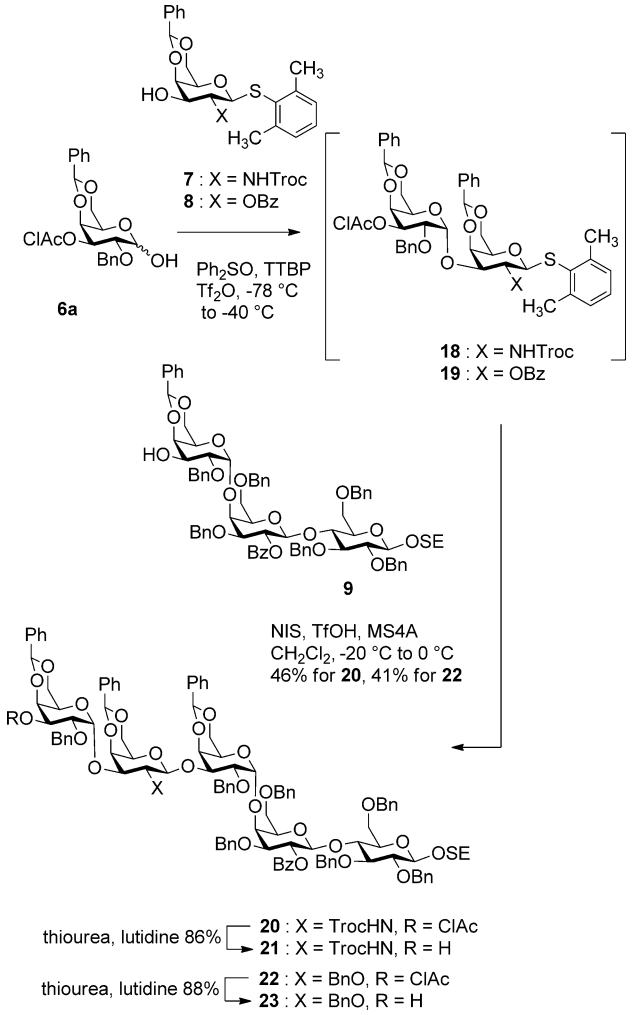
Table 2. α-Selective galactosylation at the C3 position of glucose **12**.

| Entry | Donor | Conditions | Yield [%] | α/β[a] |
|---|---|---|---|---|
| 1 | **5a** | $Tf_2O$, TTBP, $Ph_2SO$ −78 to −30 °C, 4.0 h | 77 | 92:8 |
| 2 | **5b** | AgOTf, −78 to −40 °C, 3.0 h | 57 | 63:37 |
| 3 | **5c** | TMSOTf, −78 °C, 2.0 h | 66 | 74:26 |

[a] The ratio was determined based on the $^1H$ NMR spectra.

The one-pot synthesis of pentasaccharides **2c–d** following the established method was examined (Scheme 4). Treatment of the hemiacetal **6a** and thioglycosides **7** and **8** with $Tf_2O$, TTBP, and $Ph_2SO$ provided the disaccharides **18** and **19**, respectively. The successive addition of 1.2 equivalents of acceptor **9** and NIS to the reaction mixture provided the trisaccharide **20** and **22** in 46 and 41% overall yields based

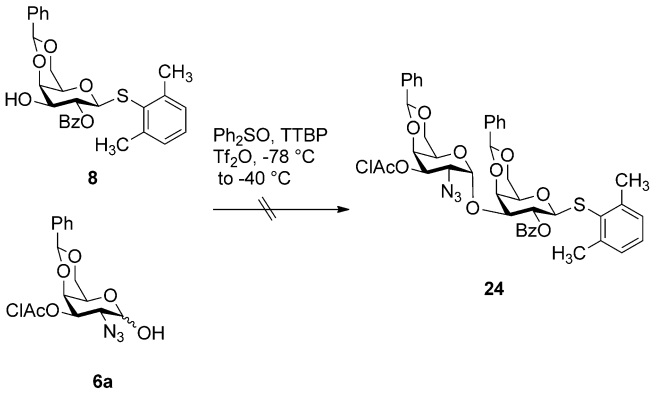
  




Scheme 4. One-pot synthesis of pentasaccharides **20** and **22**.

on **7** and **8**, respectively. The chloroacetyl group of the trisaccharides **20** and **22** was removed by treatment with thiourea to afford the alcohol **21** and **23** in 86 and 88% yields. However, the synthesis of pentasaccharide **2b** through a one-pot glycosylation failed because the glycosylation of the benzoate acceptor **8** with the azide donor **6a** did not proceed under these reaction conditions (Scheme 5). Increasing the reaction temperature and prolonging the reaction time resulted in the decomposition of the substrates **5a** and **8**.

The procedure used for the polymer-assisted deprotection of the protected oligosaccharides **17**, **21**, and **23** is shown in Scheme 6. Acetalization of pentasaccharides **17**, **21**, and **23** with the prelinker **3** under acidic conditions, followed by amidation of the remaining activated ester with amine **4** attached to an ArgoPore resin provided the solid-supported protected oligosaccharides **24**–**26**. The esters and carbamate were removal under basic conditions. The azide group was reduced to an amine by treatment with trimethylphosphine. The amino groups were converted into acetamides. The benzyl ethers and benzylidene acetals were removed under Birch reduction conditions. Finally, exposure of the solid-




Scheme 5. Chemo- and α-stereoselective glycosylation of **8** with hemiacetal **6a**.

supported pentasaccharides to a mixed solution (1 M HCl aq. $CH_2Cl_2$/MeOH) provided the fully deprotected pentasaccharides **2a**, **2c**, and **2d** in 43, 34 and 43% overall yields based on **17**, **21**, and **23**, respectively. Partial hydrolysis of the 2-trimethylsilylethyl glycosides occurred when TFA was used as an acid instead of HCl.

A biological evaluation of the pentasaccharides **2a**, **2c** and **2d**, and the related oligosaccharides **27**–**31** was carried out (Figure 1).[15] We first examined the use of a fluores-

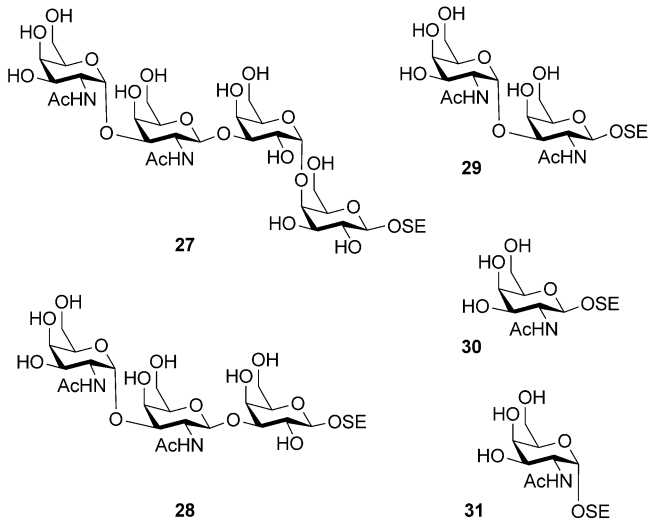
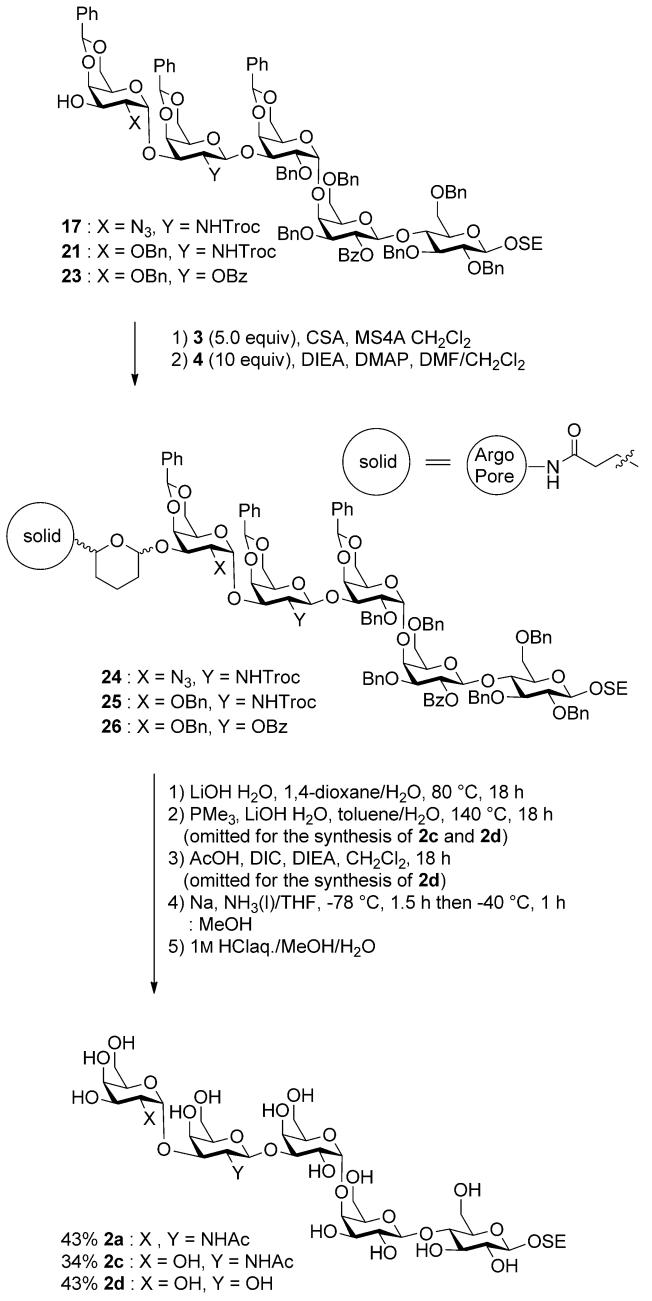



Figure 1. Structure of Forssman antigen-related oligosaccharides **27**–**31**.

cence enhancement assay to analyze the interaction between the synthetic oligosaccharides and FITC-labeled SLL-2. Figure 2 shows the relative fluorescent intensity of a mixture of FITC-labeled SLL-2 and the oligosaccharide based on the FITC-labeled SLL-2. The affinity of the oligosaccharides for SLL-2 was dependent on the number of sugar units in the oligosaccharide. The pentasaccharide **5** exhibited the strongest binding affinity. Modification of the GalNAc unit to a Gal unit reduced the binding affinity to SLL-2. These




Scheme 6. Polymer-assisted deprotection of **17**, **21**, and **23**.

results indicate that SLL-2 not only recognized the acetamide group at the non-reducing end of the Forsmann antigen, but also the sugar units at the reducing end. In addition, α-GalNAc **31** showed a stronger affinity than β-GalNAc **30**, comparable to that of tetrasaccharide **27**. A hydrophobic interaction of the 2-trimethysilylethyl group with the SLL-2 binding pocket might be responsible for the enhanced binding affinity of the monosaccharide unit.

We next examined the inhibition of the SLL-2-induced morphological change caused by oligosaccharides **2a**, **2c**, **2d**, and **27**–**31**. SLL-2 promotes a morphological change in symbiotic microalgae from the motile form to a coccoid

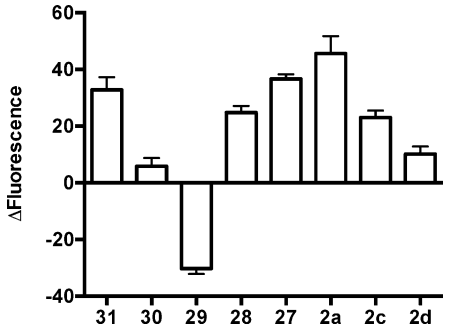



Figure 2. A fluorescence enhancement assay for analysis of the interaction between the synthetic oligosaccharides **2a**, **2c**, **2d**, and **27**–**31** and FITC-labeled SLL-2. The error bar indicates standard deviation ($n=3$).

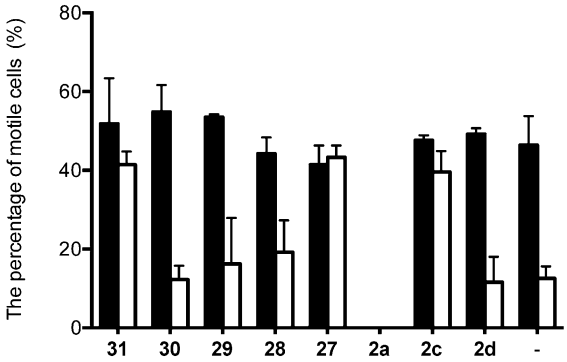



Figure 3. Inhibitory effect of the oligosaccharides on the SLL-2-induced morphological change of CS-156. The black bars and the white bars indicate CS-156 that was cultured with or without SLL-2, respectively. The error bar represents the standard deviation ($n>3$).

form. Figure 3 provides information on the inhibitory effect of the oligosaccharides on the SLL-2-induced morphological change in CS-156. The inhibitory effects of the oligosaccharides were dependent on their binding affinity for SLL-2, except for the original pentasaccharide **2a.** These results clearly indicate that the binding site of the oligosaccharides to SLL-2 is comparable to that of the native ligand on *Symbiodinium*. On the other hand, it should be noted that the Forssman pentasaccharide **2a** directly initiates a morphological change in CS-156. These unexpected results suggest that CS-156 might have receptors for the Forssman pentasaccharide, which promote this morphological change. However, the mechanism of this phenomenon is not currently clear. Additional biological studies are required to clarify this aspect of the process.

## Conclusion

We have described the synthesis of the Forssman antigen pentasaccharide **2a** and its derivatives **2c** and **2d** by two one-pot glycosylation reactions and polymer-assisted deprotection and their biological evaluation. The chemo-and α-stereoselective glycosylation of thioglycosides with the hemi-

acetal donors **6a** and **5a** by using a mixture of $Tf_2O$, TTBP, and $Ph_2SO$ was effective for formation of α-glycosidic linkage in one-pot glycosylation. However, the chemoselective and α-selective glycosylation of thioglycoside **8** containing a benzoate at the C2 position with the 2-azide glycoside **6a** did not proceed due to the low reactivity of the 2-azide glycosyl donor **6a**. An analysis of the interaction between the synthetic oligosaccharides **2a**, **2c**, **2d**, and **27–31** and the FITC-labeled SLL-2 by a fluorescence assay revealed that the NHAc substituents and the length of the oligosaccharide chains were important for the binding of the oligosaccharide to SLL-2. The inhibition effect of the oligosaccharide, relative to the morphological changes of *Symbiodinium* by SLL-2, was comparable to their binding affinity to SLL-2. In addition, we fortuitously discovered that the synthetic pentasaccharide **2a** directly promotes the morphological change in *Symbiodinium*. These results strongly indicate that the Forssman antigen also functions as a chemical mediator of *Symbiodinium*. A biological study to elucidate the mechanism of the morphological change derived from the pentasaccharide **2a** is currently in progress.

## Experimental Section

**General procedure**: NMR spectra were recorded on a JEOL Model EX-270 (270 MHz for $^1$H, 67.8 MHz for $^{13}$C) or a JEOL Model ECP-400 (400 MHz for $^1$H, 100 MHz for $^{13}$C) in the indicated solvent. Chemical shifts were reported in part per million (ppm) relative to the signal (0.00 ppm) for internal tetramethylsilane solutions in $CDCl_3$. $^1$H NMR spectral data are reported as follows: $CDCl_3$ (7.26 ppm), $CD_2Cl_2$ (5.32 ppm), [$D_6$]acetone (2.04 ppm), [$D_6$]DMSO (2.50 ppm), $CD_3OD$ (3.30 ppm) or $D_2O$ (HOD (4.7015 ppm at 303 K, 4.5977 ppm at 313 K, 4.5541 ppm at 318 K, 4.3168 ppm at 343 K)). $^{13}$C NMR spectral data are reported as follows: $CDCl_3$ (77.0 ppm), $CD_2Cl_2$ (53.8 ppm), [$D_6$]acetone (29.8 ppm), [$D_6$]DMSO (39.5 ppm), $CD_3OD$ (49.8 ppm) or $D_2O$ ([$D_6$]acetone (206.0 ppm) as an internal standard). Infrared spectra (IR) were recorded on a Perkin–Elmer Spectrum 1. Only the strongest and/or structurally important absorbances are reported as the IR data given in $cm^{-1}$. Optical rotations were measured on a JASCO model P-1020 polarimeter. All reactions were monitored by using thin layer chromatography carried out on Merck precoated TLC plates (60F-254) by using UV light and *p*-anisaldehyde $H_2SO_4$ ethanol solution or 10% ethanolic phosphomolybdic acid. Column chromatography separations were performed by using silica gel (Merck, silica gel). Flash column chromatography separations were performed by using silica gel (KANTO, silica gel 60N, spherical, neutral, 40–100 μm). ESI-TOF Mass spectra were measured with AppliedBioSystems Mariner TK-3500 Biospectrometry Workstation mass spectrometers and Waters LCT Premier XE. HRMS (ESI-TOF) were calibrated with angiotensin I (SIGMA), bradykinin (SIGMA), and neurotensin (SIGMA) as an internal standard. Gel permeation chromatography (GPC) for qualitative analysis were performed on Japan Analytical Industry Model LC908 (recycling preparative HPLC) by using a polystylene gel column (JAIGEL-1H, 20 mm × 600 mm). The detection of products was achieved by using a UV detector (Japan Analytical Industry Model 310) and refractive index detector (Japan Analytical Industry Model RI-5)

**2,6-Dimethylphenylthio (2-*O*-benzyl-4,6-*O*-benzylidene-3-*O*-chloroacetyl-α-D-galactopyranoyl)-(1→4)-2-*O*-benzoyl-3,6-di-*O*-benzyl-4-*O*-β-D-galactopyranoside (12)**: A mixture of **6a** (17.9 mg, 41.2 μmol), $Ph_2SO$ (13.3 mg, 66.0 μmol), TTBP (17.7 mg, 71.4 μmol; azeotroped twice with dry toluene), and pulverized activated MS 4 Å (200 mg) in dry $CH_2Cl_2$ (1.00 mL) was stirred at room temperature for 1 h under argon to remove a trace amount of $H_2O$. Then, the reaction mixture was cooled to −78 °C. After 5 min, $Tf_2O$ (8.30 μL, 49.5 μmol) was added to the reaction mixture at the same temperature. After being stirred at −40 °C for 1 h, a solution of **10** (16.7 mg, 27.5 μmol; azeotroped twice with dry toluene) in dry $CH_2Cl_2$ (1.00 mL) was added at the same temperature. After being stirred for 2 h, the reaction mixture was neutralized with $NEt_3$ and filtered through a pad of Celite. Then, the filtrate was concentrated in vacuo. The residue was purified by column chromatography on silica gel (elution with 99:1 $CHCl_3$/MeOH) and by using gel permeation chromatography (GPC) to give **12** (25.2 mg, 25.2 μmol, 92%). $[\alpha]_D^{26} = +129$ ($c$ = 1.22, $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 8.08 (d, 2H, $J$ = 7.3 Hz), 7.60 (dd, 1H, $J$ = 7.3, 7.7 Hz), 7.50–7.04 (m, 25H), 5.56 (dd, 1H, $J$ = 9.7, 10.2 Hz), 5.50 (dd, 1H, $J$ = 3.4, 10.6 Hz), 5.41 (s, 1H), 5.23 (d, 1H, $J$ = 3.9 Hz), 4.84 (d, 1H, $J$ = 12.1 Hz), 4.72 (d, 1H, $J$ = 12.1 Hz), 4.70 (d, 1H, $J$ = 12.1 Hz), 4.59 (br d, 1H, $J$ = 3.4 Hz), 4.53 (d, 1H, $J$ = 9.7 Hz), 4.46 (d, 1H, $J$ = 12.1 Hz), 4.34 (br s, 1H), 4.27 (br d, 1H, $J$ = 2.9 Hz), 4.26 (d, 1H, $J$ = 11.6 Hz), 4.24 (dd, 1H, $J$ = 3.9, 10.6 Hz), 4.18 (d, 1H, $J$ = 11.6 Hz), 4.03 (d, 1H, $J$ = 15.0 Hz), 4.02 (dd, 1H, $J$ = 7.7, 8.7 Hz), 3.95 (d, 1H, $J$ = 15.0 Hz), 3.63 (br s, 2H), 3.57 (dd, 1H, $J_{2,3}$ = 2.9, 10.2 Hz), 3.49 (dd, 1H, $J$ = 5.8, 8.7 Hz), 2.44 ppm (s, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 166.6, 165,2, 144.2, 138.4, 137.9, 137.8, 137.3, 133.1, 131.5, 130.0, 129.9, 129.8, 129.0, 128.4, 128.3, 128.0, 127.7, 127.6, 127.5, 127.4, 127.1, 126.1, 100.7, 100.4, 88.6, 80.4, 74.3, 74.2, 73.8, 73.7, 73.6, 73.2, 71.5, 70.4, 69.0, 67.5, 62.4, 40.8, 22.5 ppm; FTIR (KBr): $\tilde{\nu}$ = 3421, 2927, 1732, 1636, 1384, 1265, 1096, 756 $cm^{-1}$; HRMS (ESI-TOF): $m/z$ calcd for $C_{57}H_{61}NO_{12}SCl$ 1018.3603 $[M+NH_4]^+$; found: 1018.3598.

**2-(Trimethylsilyl)ethyl (2-*O*-benzyl-4,6-di-*O*-benzylidene-3-*O*-chloroacetyl-α-D-galactopyranosyl)-(1→4)-(2-*O*-benzoyl-3,6-di-*O*-benzyl-4-*O*-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (13)**: A mixture of **12** (45.0 mg, 44.9 μmol), compound **11** (37.1 mg, 67.4 μmol; azeotroped twice with dry toluene) and pulverized activated MS 4 Å (120 mg) in dry $CH_2Cl_2$ (1.20 mL) was stirred at room temperature for 1 h under argon to remove a trace amount of $H_2O$. Then, the reaction mixture was cooled to −78 °C. After 5 min, NIS (15.2 mg, 67.4 μmol) and a catalytic amount of TfOH (2.00 μL, 22.5 μmol) was added to the reaction mixture at the same temperature. After being stirred for 3.5 h, during which time the solution was allowed to warm to −60 °C, the reaction mixture was neutralized with $NEt_3$ and filtered through a pad of Celite. Then, the filtrate was concentrated in vacuo and the residue was purified by column chromatography on silica gel (elution with $CHCl_3$/MeOH = 99:1) and gel permeation chromatography (GPC) to give **13** (47.8 mg, 33.8 μmol, 75%). $[\alpha]_D^{25} = +88.3$ ($c$ = 0.890, $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 8.00 (d, 2H, $J$ = 8.2 Hz), 7.61–7.07 (m, 38H,), 5.46 (dd, 1H, $J$ = 8.2, 10.2 Hz), 5.41 (dd, 1H, $J$ = 3.4, 10.6 Hz), 5.38 (s, 1H), 5.20 (d, 1H, $J$ = 2.9 Hz), 5.05 (d, 1H, $J$ = 11.6 Hz), 4.87 (d, 1H, $J$ = 10.6 Hz), 4.84 (d, 1H, $J$ = 11.6 Hz), 4.82 (d, 1H, $J$ = 8.2 Hz), 4.74 (d, 1H, $J$ = 12.6 Hz), 4.68 (br s, 2H), 4.65 (d, 1H, $J$ = 10.6 Hz), 4.54 (br d, 1H, $J$ = 3.4 Hz), 4.52 (d, 1H, $J$ = 12.1 Hz), 4.38 (d, 1H, $J$ = 12.1 Hz), 4.33 (br s, 1H), 4.31 (d, 1H, $J$ = 8.2 Hz), 4.26 (d, 1H, $J$ = 12.1 Hz), 4.24 (d, 1H, $J$ = 12.1 Hz), 4.23 (br s, 1H), 4.22 (dd, 1H, $J$ = 2.9, 10.2 Hz), 4.21 (d, 1H, $J$ = 12.1 Hz), 4.18 (dd, 1H, $J$ = 7.3, 8.7 Hz), 3.93 (dt, 1H, $J$ = 7.3, 9.2 Hz), 3.88 (d, 1H, $J$ = 15.0 Hz), 3.86 (dd, 1H, $J$ = 9.2, 9.7 Hz), 3.80 (d, 1H, $J$ = 15.0 Hz), 3.66 (br d, 1H, $J$ = 12.6 Hz), 3.63 (dd, 1H, $J$ = 8.7, 9.2 Hz), 3.61 (dd, 1H, $J$ = 9.2, 9.7 Hz), 3.58 (br d, 1H, $J$ = 12.6 Hz), 3.54 (dd, 1H, $J$ = 6.8, 9.7 Hz), 3.53 (dt, 1H, $J$ = 7.3, 9.2 Hz), 3.44 (dd, 1H, $J$ = 2.9, 10.2 Hz), 3.43–3.31 (m, 4H), 0.99 (dt, 2H, $J$ = 7.3, 9.2 Hz), 0.00 ppm (s, 9H, Si-$(CH_3)_3$); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 166.4, 160.1, 139.5, 138.7, 138.4, 138.2, 138.1, 137.8, 137.4, 133.1, 130.0, 129.8, 128.7, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.7, 127.6, 127.5, 127.0, 126.9, 126.1, 102.9, 101.1, 101.0, 100.3, 83.1, 82.0, 79.3, 77.6, 76.5, 75.1, 74.7, 74.3, 73.9, 73.8, 73.5, 73.2, 73.1, 72.2, 71.2, 69.0, 68.5, 67.3, 67.1, 62.6, 60.3, 40.6, 18.4, 14.2, −1.49 ppm; FTIR (neat): $\tilde{\nu}$ = 2922, 1732, 1453, 1267, 1096, 736, 698 $cm^{-1}$; HRMS (ESI-TOF): $m/z$ calcd for $C_{81}H_{93}NO_{18}ClSi$: 1430.5851 $[M+NH_4]^+$; found 1430.5850.

**One-pot synthesis of 13**: A mixture of **6a** (17.5 mg, 40.3 μmol), $Ph_2SO$ (11.3 mg, 55.7 μmol), TTBP (16.1 mg, 65.0 μmol) was azeotroped twice with dry toluene and was diluted with dry $CH_2Cl_2$ (500 μL). The solution was stirred at room temperature for 1 h under argon in the presence of activated MS 4 Å (200 mg) to remove a trace amount of $H_2O$. Then, $Tf_2O$

(7.80 μL, 46.4 μmol) was added to the reaction mixture at −78 °C and stirred at −40 °C for 1 h. A solution of **10** (18.1 mg, 31.0 μmol) was azeotroped twice with dry toluene, diluted with dry $CH_2Cl_2$ (500 μL), and the solution was added to the reaction mixture at −78 °C. After additionally being stirred for 2.5 h at the same temperature, the reaction mixture was warmed to 0 °C. After being stirred for 30 min, the reaction mixture was cooled to −78 °C. After 5 min, a solution of **11** (34.1 mg, 61.9 μmol) in dry $CH_2Cl_2$ (800 μL), NIS (17.4 mg, 77.3 μmol, 2.50 equiv) and TfOH (2.80 μL, 30.1 μmol) was added to the reaction mixture. After being stirred for 2.5 h at the same temperature, the reaction mixture was neutralized with $NEt_3$ and filtered through a pad of Celite. Then, the filtrate was concentrated in vacuo. The residue was purified by column chromatography on silica gel (elution with $CHCl_3$/MeOH = 99:1) and further purified by gel permeation chromatography (GPC) to give **13** (23.8 mg, 15.7 μmol, 54 % based on **10**).

**2-(Trimethylsilyl)ethyl (2-*O*-benzyl-4,6-di-*O*-benzylidene-α-D-galactopyranosyl)-(1→4)-(2-*O*-benzoyl-3,6-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (5)**: Thiourea (11.4 mg, 149 μmol) and 2,6-lutidine (14.0 μL, 120 μmol) were added to a stirred solution of **13** (35.2 mg, 24.9 μmol) in dry DMF (600 μL) at room temperature. After being stirred at 50 °C for 14 h, the reaction mixture was poured into 1 M HCl with cooling. The aqueous layer was extracted with two portions of ethyl acetate. The combined extract was washed with 1 M HCl, saturated aq. $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by chromatography on silica gel (elution with toluene/acetone = 96:4) to give **5** (31.2 mg, 23.3 μmol, 94 %). $[\alpha]_D^{20} = +89.3$ ($c = 1.06$, $CHCl_3$); $^1$H NMR (400 MHz, [D$_6$]acetone): $\delta = 8.11$ (dd, 2H, $J = 1.0$, 7.7 Hz), 7.99–7.10 (m, 48H), 5.71 (s, 1H), 5.64 (s, 1H), 5.55 (dd, 1H, $J = 7.7$, 10.2 Hz), 5.47 (s, 1H), 5.30 (d, 1H, $J = 3.4$ Hz), 5.08 (d, 1H, $J = 3.4$ Hz), 5.04 (brs, 2H), 5.03 (d, 1H, $J = 7.7$ Hz), 4.92 (d, 1H, $J = 12.1$ Hz), 4.90 (d, 1H, $J = 11.1$ Hz), 4.77 (d, 1H, $J = 12.6$ Hz), 4.72 (d, 1H, $J = 8.7$ Hz), 4.67 (d, 1H, $J = 12.1$ Hz), 4.62 (brd, 1H, $J = 2.9$ Hz), 4.61 (d, 1H, $J = 11.1$ Hz), 4.52 (brs, 1H), 4.51 (d, 1H, $J = 12.6$ Hz), 4.43 (d, 1H, $J = 11.1$ Hz), 4.42 (d, 1H, $J = 8.2$ Hz), 4.34 (d, 1H, $J = 10.2$ Hz), 4.33 (dd, 1H, $J = 2.9$, 10.2 Hz), 4.32 (brd, 1H, $J = 2.9$ Hz), 4.31 (brd, 1H, $J = 10.2$ Hz), 4.30 (brs, 2H), 4.25 (d, 1H, $J = 12.1$ Hz), 4.23 (brd, 1H, $J = 12.1$ Hz), 4.18 (dd, 1H, $J = 6.3$, 8.7 Hz), 4.17 (d, 1H, $J = 10.2$ Hz), 4.15 (brd, 1H, $J = 10.2$ Hz), 4.11 (brdd, 1H, $J = 8.7$, 10.6 Hz), 4.10 (d, 1H, $J = 12.1$ Hz), 4.09 (dd, 1H, $J = 3.4$, 11.6 Hz), 4.09 (dd, 1H, $J = 1.4$, 12.1 Hz), 3.95 (dd, 1H, $J = 3.4$, 10.2 Hz), 3.94 (dd, 1H, $J = 3.4$, 10.6 Hz), 3.93 (brs, 1H), 3.90 (dd, 1H, $J = 8.7$, 9.7 Hz), 3.92 (dt, 1H, $J = 7.7$, 8.7 Hz), 3.80 (dd, 1H, $J = 2.9$, 10.2 Hz), 3.76 (d, 1H, $J = 12.1$ Hz), 3.68–3.62 (m, 6H), 3.57 (dd, 1H, $J = 4.8$, 9.2 Hz), 3.56 (dd, 1H, $J = 1.9$, 10.6 Hz), 3.45 (ddd, 1H, $J = 3.4$, 4.8, 9.7 Hz), 3.38 (dd, 1H, $J = 5.8$, 9.2 Hz), 3.31 (dd, 1H, $J = 8.2$, 9.2 Hz), 0.98 (t, 2H, $J = 7.7$ Hz), 0.00 ppm (s, 9H); $^{13}$C NMR (100 MHz, [D$_6$]acetone): $\delta = 165.6$, 155.4, 141.2, 140.8, 140.5, 140.3, 140.2, 140.1, 140.0, 139.7, 134.6, 131.7, 131.0, 130.0, 129.9, 129.6, 129.5, 129.4, 129.3, 129.1, 129.0, 128.9, 128.8, 128.7, 128.6, 128.5, 128.2, 127.8, 127.6, 104.2, 104.0, 102.7, 101.9×2, 101.6, 101.5, 97.4, 96.3, 83.7, 83.6, 80.8, 80.1, 79.1, 78.1, 77.8, 76.2, 75.7, 75.5, 75.4, 75.0, 74.8, 74.6, 74.3, 74.1, 74.0, 73.7, 72.3, 72.2, 70.6, 70.4, 70.3, 70.1, 68.7, 67.8. 67.6, 67.5, 64.8, 64.4, 61.2, 54.3, 19.4, −0.79 ppm; FTIR (KBr): $\tilde{\nu} = 3420$, 2923, 2111, 1730, 1453, 1268, 1219, 1097, 1023, 772 cm$^{-1}$; HRMS (ESI-TOF): *m/z* calcd for $C_{108}H_{121}N_5O_{27}SiCl_3$: 2052.7084 $[M+NH_4]^+$; found: 2052.7026.

**2,6-Dimethylphenylthio (2-azido-4,6-*O*-benzylidene-3-*O*-chloroacetyl-2-deoxy-α-D-galactopyranosyl)-(1→3)-4,6-*O*-benzylidene-2-deoxy-(2,2,2-trichloroethoxycarbonylamino)-β-D-galactopyranoside (15)**: A mixture of **6a** (84.0 mg, 227 μmol), $Ph_2SO$ (85.6 mg, 423 μmol), TTBP (113 mg, 454 μmol; azeotroped twice with dry toluene) and pulverized activated MS 4 Å (150 mg) in dry $CH_2Cl_2$ (1.00 mL) were stirred at room temperature for 1 h under argon to remove a trace amount of $H_2O$. Then, the reaction mixture was cooled to −78 °C. After 5 min, $Tf_2O$ (53.4 μL, 318 μmol) was added to the reaction mixture at the same temperature. After being stirred at −40 °C for 1 h, a solution of **7** (81.9 mg, 151 μmol; azeotroped twice with dry toluene) in dry $CH_2Cl_2$ (5.00 mL) was added at the same temperature. After being stirred for 1 h at the same temperature, the reaction mixture was neutralized with $NEt_3$ and filtered through a pad of Celite. Then, the filtrate was concentrated in vacuo and the residue was purified by column chromatography on silica gel (elution with $CHCl_3$/MeOH = 99:1) and gel permeation chromatography (GPC) to give **15** (102 mg, 116 μmol, 77 %, α/β = 92:8). The α/β ratio was determined by $^1$H NMR spectroscopic analysis. The α isomer was purified by an additional column chromatography on silica gel. $[\alpha]_D^{25} = +127$ ($c = 1.15$, $CH_2Cl_2$); $^1$H NMR (400 MHz, [D$_6$]acetone): $\delta = 7.61$ (dd, 2H, $J = 1.4$, 7.7 Hz), 7.61 (dd, 2H, $J = 5.3$, 7.7 Hz), 7.39–7.33 (m, 6H), 7.24 (brd, 1H, $J = 9.2$ Hz), 7.16–7.10 (m, 3H,), 5.71 (s, 1H), 5.63 (s, 1H), 5.48 (d, 1H, $J = 3.4$ Hz), 5.31 (dd, 1H, $J = 3.4$, 11.1 Hz), 4.96 (d, 1H, $J = 12.1$ Hz), 4.78 (d, 1H, $J = 12.1$ Hz), 4.72 (d, 1H, $J = 10.2$ Hz), 4.66 (brd, 1H, $J = 3.4$ Hz), 4.57 (brd, 1H, $J = 3.4$ Hz), 4.37 (d, 1H, $J = 15.0$ Hz), 4.31 (d, 1H, $J = 15.0$ Hz), 4.25 (brdd, 1H, $J = 3.4$, 10.6 Hz), 4.18 (dd, 1H, $J = 10.2$, 10.6 Hz), 4.16–4.12 (m, 4H), 4.05 (brs, 1H), 3.94 (dd, 1H, $J = 3.4$, 11.1 Hz), 3.53 (brs, 1H), 2.55 ppm (s, 6H); $^{13}$C NMR (67.8 MHz, [D$_6$]acetone): $\delta = 167.6$, 155.2, 147.6, 144.9, 140.0, 139.3, 132.3, 131.7, 130.2, 129.6, 129.5, 129.2, 128.8, 127.1, 127.0, 125.0, 101.1×2, 96.8, 96.2, 89.5, 76.4, 75.1, 74.0, 72.2, 71.5, 70.4, 69.5, 63.8, 57.9, 53.4, 41.4, 22.7 ppm; FTIR (KBr): $\tilde{\nu} = 2115$, 1763, 1708, 1443, 1090, 1044, 756, 537 cm$^{-1}$; HRMS (ESI-TOF): *m/z* calcd for $C_{39}H_{44}N_5O_{11}SiCl_4$: 930.1512 $[M+NH_4]^+$; found: 930.1531.

**2-(Trimethylsilyl)ethyl (2-azido-4,6-*O*-benzylidene-3-*O*-chloroacetyl-2-deoxy-α-D-galactopyranosyl)-(1→3)-[4,6-*O*-benzylidene-2-deoxy-(2,2,2-trichloroethoxycarbonylamino)-β-D-galactopyranosyl]-(1→3)-(2-*O*-benzyl-4,6-di-*O*-benzylidene-α-D-galactopyranosyl)-(1→4)-(2-*O*-benzoyl-3,6-di-*O*-benzyl-α-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (16)**: A mixture of **15** (45.5 mg, 45.6 μmol), compound **9** (30.5 mg, 22.8 μmol; azeotroped twice with dry toluene) and pulverized activated MS 4 Å (50.0 mg) in dry $CH_2Cl_2$ (1.20 mL) was stirred at room temperature for 1 h under argon to remove a trace amount of $H_2O$. Then, the reaction mixture was cooled to −20 °C. After 5 min, NIS (12.3 mg, 54.7 μmol) and a catalytic amount of TfOH (1.00 μL, 11.4 μmol) was added to the reaction mixture at the same temperature. After being stirred for 2 h, during which time the solution was allowed to warm to 0 °C, the reaction mixture was neutralized with $NEt_3$ and filtered through a pad of Celite. Then, the filtrate was concentrated in vacuo and the residue was purified by column chromatography on silica gel (elution with $CHCl_3$/MeOH = 99:1) and gel permeation chromatography (GPC) to give **16** (41.3 mg, 19.5 μmol, 92 %). $[\alpha]_D^{27} = +110$ ($c = 1.28$, $CHCl_3$); $^1$H NMR (400 MHz, [D$_6$]acetone): $\delta = 8.10$ (dd, 2H, $J = 1.0$, 7.3 Hz), 7.99–7.13 (m, 48H), 6.56 (brd, 1H, $J = 9.7$ Hz), 5.70 (s, 1H), 5.65 (s, 1H), 5.55 (dd, 1H, $J = 7.7$, 10.2 Hz), 5.47 (s, 1H), 5.46 (d, 1H, $J = 3.9$ Hz), 5.23 (brdd, 1H, $J = 3.4$, 11.1 Hz), 5.08 (d, 1H, $J = 3.4$ Hz), 5.04 (brs, 2H), 5.04 (d, 1H, $J = 7.7$ Hz), 4.92 (d, 1H, $J = 12.6$ Hz), 4.90 (d, 1H, $J = 11.6$ Hz), 4.77 (d, 1H, $J = 12.1$ Hz), 4.74 (d, 1H, $J = 7.7$ Hz), 4.68 (d, 1H, $J = 12.6$ Hz), 4.64 (d, 1H, $J = 11.6$ Hz), 4.63 (brs, 1H), 4.56 (brs, 1H), 4.52 (d, 1H, $J = 12.1$ Hz), 4.43 (d, 1H, $J = 7.7$ Hz), 4.42 (d, 1H, $J = 11.6$ Hz), 4.35–4.30 (m, 6H), 4.28 (d, 1H, $J = 13.1$ Hz), 4.24 (brd, 1H, $J = 12.1$ Hz), 4.21 (d, 1H, $J = 11.6$ Hz), 4.19 (dd, 1H, $J = 5.3$, 9.2 Hz), 4.17 (d, 1H, $J = 11.6$ Hz), 4.17 (brdd, 1H, $J = 7.7$, 10.6 Hz), 4.16 (d, 1H, $J = 12.1$ Hz), 4.16 (brd, 1H, $J = 11.1$ Hz), 4.15 (brs, 1H), 4.12 (d, 1H, $J = 12.1$ Hz), 4.12 (brd, 1H, $J = 12.1$ Hz), 4.02 (brs, 1H), 3.95 (dd, 1H, $J = 3.4$, 10.6 Hz), 3.94 (dt, 1H, $J = 7.7$, 9.7 Hz), 3.94 (dd, 1H, $J = 3.9$, 11.1 Hz), 3.90 (dd, 1H, $J = 9.2$ Hz, 9.7 Hz), 3.85 (d, 1H, $J = 12.6$ Hz), 3.81 (dd, 1H, $J = 2.4$, 10.6 Hz), 3.68 (dd, 1H, $J = 4.8$, 5.3 Hz), 3.66 (dd, 1H, $J = 9.7$, 9.7 Hz), 3.66 (dd, 1H, $J = 4.8$, 8.7 Hz), 3.62 (dt, 1H, $J = 7.7$, 9.7 Hz), 3.59 (dd, 1H, $J = 4.8$, 8.7 Hz), 3.58 (brd, 1H, $J = 11.6$ Hz), 3.56 (brd, 1H,, $J = 11.6$ Hz), 3.46 (brdt, 1H, $J = 4.8$, 9.7 Hz), 3.45 (brs, 1H), 3.38 (dd, 1H, $J = 4.8$, 9.2 Hz), 3.31 (dd, 1H, $J = 7.7$, 9.7 Hz), 0.98 (t, 2H, $J = 7.7$ Hz), 0.00 ppm (s, 9H); $^{13}$C NMR (67.8 MHz, [D$_6$]acetone): $\delta = 168.0$, 166.6, 155.5, 141.2, 140.8, 140.5, 140.4, 140.2, 139.9, 139.8, 139.6, 134.6, 131.2, 131.0, 130.0, 129.7, 129.6, 129.5, 129.4, 129.3, 129.1, 129.0, 128.9, 128.8, 128.7, 128.6, 128.5, 128.4, 128.2, 127.7, 127.6, 104.2, 103.9, 102.7, 101.9, 101.7, 101.6, 101.5, 97.2, 95.8), 83.4, 80.8, 80.2, 79.1, 78.1, 76.1, 75.7, 75.4, 75.0, 74.8, 74.5, 74.1, 74.0, 73.7, 72.3, 72.0, 71.8, 70.6, 70.3, 70.1, 68.7, 67.8, 67.5, 64.4, 64.1, 58.0, 54.1, 41.8, 19.4, −0.79 ppm; FTIR (KBr): $\tilde{\nu} = 2921$, 2112, 1731, 1454, 1268, 1219, 1095, 772, 698 cm$^{-1}$; HRMS (ESI-TOF): *m/z* calcd for $C_{110}H_{122}N_5O_{28}SiCl_4$: 2128.6800 $[M+NH_4]^+$; found: 2128.6799.

**One-pot synthesis of 16**: A mixture of **5a** (28.0 mg, 64.7 μmol), $Ph_2SO$ (20.1 mg, 99.6 μmol), TTBP (27.5 mg, 111 μmol) was azeotroped twice with dry toluene and was diluted with dry $CH_2Cl_2$ (1.00 mL) in the pres-

ence of pulverized activated MS 4 Å (110 mg). The mixture was stirred at room temperature for 1 h under argon to remove a trace amount of $H_2O$. $Tf_2O$ (13.0 μL, 77.5 μmol) was then added to the reaction mixture at −78 °C. The reaction mixture was warmed at −40 °C and then stirred at the same temperature for 1 h. Compound **7** (30.0 mg, 55.3 μmol) was then azeotroped twice with dry toluene and diluted with dry $CH_2Cl_2$ (2.50 mL). After being stirred for 1 h, the solution of **7** was added to the reaction mixture at the same temperature. After being stirred for 5 h at the same temperature the reaction mixture was warmed to 0 °C and stirred for 30 min. The reaction mixture was then cooled to −78 °C. A solution of **9** (88.8 mg, 66.4 μmol) in dry $CH_2Cl_2$ (1.00 mL) and NIS (14.9 mg, 66.4 μmol) was then added to the reaction mixture at the same temperature. After being stirred for 1 h, the reaction mixture was neutralized with $NEt_3$ at −20 °C and filtered through a pad of Celite. Then, the filtrate was concentrated in vacuo. The residue was purified by column chromatography on silica gel (elution with $CHCl_3$/MeOH = 99:1) and further purified by gel permeation chromatography (GPC) to give **16** (58.6 mg, 28.9 μmol, 52% based on **7**). $[\alpha]_D^{27} = +110$ ($c = 1.28$, $CHCl_3$); $^1$H NMR (400 MHz, [D$_6$]acetone): $\delta = 8.10$ (dd, 2H, $J = 1.0$, 7.3 Hz), 7.99–7.13 (m, 48H), 6.56 (brd, 1H, $J = 9.7$ Hz), 5.70 (s, 1H), 5.65 (s, 1H), 5.55 (dd, 1H, $J = 7.7$, 10.2 Hz), 5.47 (s, 1H), 5.46 (d, 1H, $J = 3.9$ Hz), 5.23 (brdd, 1H, $J_{2,3} = 3.4$, 11.1 Hz), 5.08 (d, 1H, $J = 3.4$ Hz), 5.04 (brs, 2H), 5.04 (d, 1H, $J = 7.7$ Hz), 4.92 (d, 1H, $J = 12.6$ Hz), 4.90 (d, 1H, $J = 11.6$ Hz), 4.77 (d, 1H, $J = 12.1$ Hz), 4.74 (d, 1H, $J = 7.7$ Hz), 4.68 (d, 1H, $J = 12.6$ Hz), 4.64 (d, 1H, $J = 11.6$ Hz), 4.63 (brs, C-4), 4.56 (brs, 1H), 4.52 (d, 1H, $J = 12.1$ Hz), 4.43 (d, 1H, $J = 7.7$ Hz), 4.42 (d, 1H, $J = 11.6$ Hz), 4.35–4.30 (m, 6H), 4.28 (d, 1H, $J = 13.1$ Hz), 4.24 (brd, 1H, $J = 12.1$ Hz), 4.21 (d, 1H, $J = 11.6$ Hz), 4.19 (dd, 1H, $J = 5.3$, 9.2 Hz), 4.17 (d, 1H, $J = 11.6$ Hz), 4.17 (brdd, 1H, $J = 7.7$, 10.6 Hz), 4.16 (d, 1H, $J = 12.1$ Hz), 4.16 (brd, 1H, $J = 11.1$ Hz), 4.15 (brs, 1H), 4.12 (d, 1H, $J = 12.1$ Hz), 4.12 (brd, 1H, $J = 12.1$ Hz), 4.02 (brs, 1H), 3.95 (dd, 1H, $J_{1,2} = 3.4$ Hz, 10.6 Hz), 3.94 (dt, 1H, $J = 7.7$, 9.7 Hz), 3.94 (dd, 1H, $J_{1,2} = 3.9$, 11.1 Hz), 3.90 (dd, 1H, $J = 9.2$, 9.7 Hz), 3.85 (d, 1H, $J = 12.6$ Hz), 3.81 (dd, 1H, $J = 2.4$, 10.6 Hz), 3.68 (dd, 1H, $J = 4.8$, 5.3 Hz), 3.66 (t, 1H, $J$ 9.7 Hz), 3.66 (dd, 1H, $J = 4.8$, 8.7 Hz), 3.62 (dt, 1H, $J = 7.7$, 9.7 Hz), 3.59 (dd, 1H, $J = 4.8$, 8.7 Hz), 3.58 (brd, 1H, $J = 11.6$ Hz), 3.56 (brd, 1H, $J = 11.6$ Hz), 3.46 (brdt, 1H, $J = 4.8$, 9.7 Hz), 3.45 (brs, 1H), 3.38 (dd, 1H, $J = 4.8$, 9.2 Hz), 3.31 (dd, 1H, $J = 7.7$, 9.7 Hz), 0.98 (t, 2H, $J = 7.7$ Hz), 0.00 ppm (s, 9H, Si(CH$_3$)$_3$); $^{13}$C NMR (67.8 MHz, [D$_6$]acetone): $\delta = 168.0$, 166.6, 155.5, 141.2, 140.8, 140.5, 140.4, 140.2, 139.9, 139.8, 139.6, 134.6, 131.2, 131.0, 130.0, 129.7, 129.6, 129.5, 129.4, 129.3, 129.1, 129.0, 128.9, 128.8, 128.7, 128.6, 128.5, 128.4, 128.2, 127.7, 127.6, 104.2, 103.9, 102.7, 101.9, 101.7, 101.6, 101.5, 97.2, 95.8, 83.4, 80.8, 80.2, 79.1, 78.1, 76.1, 75.7, 75.4, 75.0, 74.8, 74.5, 74.1, 74.0, 73.7, 72.3, 72.0, 71.8, 70.6, 70.3, 70.1, 68.7, 67.8, 67.5, 64.4, 64.1, 58.0, 54.1, 41.8, 19.4, −0.79 ppm; FTIR (KBr): $\tilde{\nu} =$ 2921, 2112, 1731, 1454, 1268, 1219, 1095, 772, 698 cm$^{-1}$; HRMS (ESI-TOF): $m/z$ calcd for $C_{110}H_{122}N_5O_{28}SiCl_4$: 2128.6800 $[M+NH_4]^+$; found: 2128.6799.

**2-(Trimethylsilyl)ethyl (2-azido-4,6-*O*-benzylidene-2-deoxy-α-D-galactopyranosyl)-(1→3)-[4,6-*O*-benzylidene-2-deoxy-(2,2,2-trichloroethoxycarbonylamino)-β-D-galactopyranosyl]-(1→3)-(2-*O*-benzyl-4,6-di-*O*-benzylidene-α-D-galactopyranosyl)-(1→4)-(2-*O*-benzoyl-3,6-di-*O*-benzyl-α-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (17)**: Thiourea (8.70 mg, 114 μmol) and 2,6-lutidine (10.0 μL, 91.5 μmol) were added to a stirred solution of **16** (35.2 mg, 24.9 μmol) in dry DMF (1.00 mL) at room temperature. After being stirred at the same temperature for 14 h, the reaction mixture was poured into 1 M HCl with cooling. The aqueous layer was extracted with two portions of ethyl acetate. The combined extracts were washed with 1 M HCl, saturated aq. $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by column chromatography on silica gel (elution with 92:8 toluene/acetone) to give **17** (37.1 mg, 18.4 μmol, 96%). $[\alpha]_D^{20} = +89.3$ ($c = 1.06$, $CHCl_3$); $^1$H NMR (400 MHz, [D$_6$]acetone): $\delta = 8.11$ (dd, 2H, $J = 1.0$, 7.7 Hz), 7.99–7.10 (m, 48H), 5.71 (s, 1H), 5.64 (s, 1H), 5.55 (dd, 1H, $J_1 = 7.7$, 10.2 Hz), 5.47 (s, 1H), 5.30 (d, 1H, $J = 3.4$ Hz), 5.08 (d, 1H, $J = 3.4$ Hz), 5.04 (brs, 2H), 5.03 (d, 1H, $J = 7.7$ Hz), 4.92 (d, 1H, $J = 12.1$ Hz), 4.90 (d, 1H, $J = 11.1$ Hz), 4.77 (d, 1H, $J = 12.6$ Hz), 4.72 (d, 1H, $J = 8.7$ Hz), 4.67 (d, 1H, $J = 12.1$ Hz), 4.62 (brd, 1H, $J = 2.9$ Hz), 4.61 (d, 1H, $J = 11.1$ Hz), 4.52 (brs, 1H), 4.51 (d, 1H, $J = 12.6$ Hz), 4.43 (d, 1H, $J = 11.1$ Hz), 4.42 (d, 1H, $J = 8.2$ Hz), 4.34 (d, 1H, $J = 10.2$ Hz), 4.33 (dd, 1H, $J = 2.9$, 10.2 Hz), 4.32 (brd, 1H, $J = 2.9$ Hz), 4.31 (brd, 1H, $J = 10.2$ Hz), 4.30 (brs, 2H), 4.25 (d, 1H, $J = 12.1$ Hz), 4.23 (brd, 1H, $J = 12.1$ Hz), 4.18 (dd, 1H, $J = 6.3$, 8.7 Hz), 4.17 (d, 1H, $J = 10.2$ Hz), 4.15 (brd, 1H, $J = 10.2$ Hz), 4.11 (brdd, 1H, $J = 8.7$, 10.6 Hz), 4.10 (d, 1H, $J = 12.1$ Hz), 4.09 (dd, 1H, $J = 3.4$, 11.6 Hz), 4.09 (dd, 1H, $J = 1.4$, 12.1 Hz), 3.95 (dd, 1H, $J = 3.4$, 10.2 Hz), 3.94 (dd, 1H, $J = 3.4$, 10.6 Hz), 3.93 (brs, 1H), 3.90 (dd, 1H, $J = 8.7$, 9.7 Hz), 3.92 (dt, 1H, $J = 7.7$, 8.7 Hz), 3.80 (dd, 1H, $J = 2.9$, 10.2 Hz), 3.76 (d, 1H, $J = 12.1$ Hz), 3.68–3.62 (m, 6H), 3.57 (dd, 1H, $J = 4.8$, 9.2 Hz), 3.56 (dd, 1H, $J_{5,6a} = 1.9$, 10.6 Hz), 3.45 (ddd, 1H, $J = 3.4$, 4.8, 9.7 Hz), 3.38 (dd, 1H, $J = 5.8$, 9.2 Hz), 3.31 (dd, 1H, $J = 8.2$, 9.2 Hz), 0.98 (t, 2H, $J = 7.7$ Hz), 0.00 ppm (s, 9H, Si(CH$_3$)$_3$); $^{13}$C NMR (100 MHz, [D$_6$]acetone): $\delta = 165.6$, 155.4, 141.2, 140.8, 140.5, 140.3, 140.2, 140.1, 140.0, 139.7, 134.6, 131.7, 131.0, 130.0, 129.9, 129.6, 129.5, 129.4, 129.3, 129.1, 129.0, 128.9, 128.8, 128.7, 128.6, 128.5, 128.2, 127.8, 127.6, 104.2, 104.0, 102.7, 101.9×2, 101.6, 101.5, 97.4, 96.3, 83.7, 83.6, 80.8, 80.1, 79.1, 78.1, 77.8, 76.2, 75.7, 75.5, 75.4, 75.0, 74.8, 74.6, 74.3, 74.1, 74.0, 73.7, 72.3, 72.2, 70.6, 70.4, 70.3, 70.1, 68.7, 67.8. 67.6, 67.5, 64.8, 64.4, 61.2, 54.3, 19.4, −0.79 ppm; FTIR (KBr): $\tilde{\nu} = 3420$, 2923, 2111, 1730, 1453, 1268, 1219, 1097, 1023, 772 cm$^{-1}$; HRMS (ESI-TOF): $m/z$ calcd for $C_{108}H_{121}N_5O_{27}SiCl_3$: 2052.7084 $[M+NH_4]^+$; found: 2052.7026.

**2-(Trimethylsilyl)ethyl (2-*O*-benzyl-4,6-*O*-benzylidene-3-*O*-chloroacetyl-α-D-galactopyranosyl)-(1→3)-[4,6-*O*-benzylidene-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-galactopyranosyl]-(1→3)-(2-*O*-benzyl-4,6-*O*-benzylidene-α-D-galactopyranosyl)-(1→4)-(2-*O*-benzoyl-3,6-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (20)**: A mixture of **6a** (15.5 mg, 35.7 μmol), $Ph_2SO$ (9.30 mg, 45.9 μmol), TTBP (12.7 mg, 51.0 μmol; azeotroped twice with dry toluene) and pulverized activated MS 4 Å (200 mg) in dry $CH_2Cl_2$ (1.00 mL) was stirred at room temperature for 1 h under argon to remove a trace amount of $H_2O$. Then, the reaction mixture was cooled to −78 °C. After 5 min, $Tf_2O$ (6.00 μL, 35.7 μmol) was added to the reaction mixture at the same temperature. After being stirred at −40 °C for 1 h, a solution of **7** (13.9 mg, 25.5 μmol; azeotroped twice with dry toluene) in dry $CH_2Cl_2$ (2.00 mL) was added at the same temperature. After being stirred for 1.5 h at the same temperature, the reaction mixture was warmed to 0 °C and stirred for 30 min. The reaction mixture was then cooled to −25 °C. After 5 min, a solution of **9** (40.9 mg, 30.5 μmol) in dry $CH_2Cl_2$ (750 μL) and NIS (8.60 mg, 38.3 μmol) was added to the reaction mixture. After being stirred for 2 h at the same temperature, the reaction mixture was neutralized with $NEt_3$ and filtered through a pad of Celite. Then, the filtrate was concentrated in vacuo and the residue was purified by column chromatography on silica gel (elution with $CHCl_3$/MeOH = 99:1) and gel permeation chromatography (GPC) to give **20** (22.3 mg, 10.5 μmol, 41% based on **7**). $[\alpha]_D^{23} = +106$ ($c = 0.885$, $CHCl_3$); $^1$H NMR (400 MHz, [D$_6$]acetone): $\delta = 8.11$ (dd, 2H, $J = 1.5$, 7.3 Hz), 7.68 (t, 1H, $J = 7.3$ Hz), 7.57–7.10 (m, 52H), 6.64 (brd, 1H, $J = 9.7$ Hz), 5.66 (s, 1H), 5.60 (s, 1H), 5.55 (dd, 1H, $J = 7.7$, 10.2 Hz), 5.48 (d, 1H, $J = 2.9$ Hz), 5.47 (s, 1H), 5.25 (dd, 1H, $J = 3.4$, 10.2 Hz), 5.08 (d, 1H, $J = 3.4$ Hz), 5.04 (d, 1H, $J = 7.7$ Hz), 5.03 (brs, 2H), 4.95 (d, 1H, $J = 13.1$ Hz), 4.90 (d, 1H, $J = 11.1$ Hz), 4.77 (d, 1H, $J = 12.1$ Hz), 4.76 (d, 1H, $J = 7.7$ Hz), 4.70 (d, 1H, $J = 13.1$ Hz), 4.65 (d, 1H, $J = 11.1$ Hz), 4.64 (d, 1H, $J = 11.1$ Hz), 4.63 (brd, 1H, $J = 2.4$ Hz), 4.62 (d, 1H, $J = 12.1$ Hz), 4.56 (brs, 1H), 4.53 (d, 1H, $J = 12.1$ Hz), 4.51 (d, 1H, $J = 12.1$ Hz), 4.48 (brd, 1H, $J = 3.4$ Hz), 4.44 (d, 1H, $J = 7.7$ Hz), 4.41 (d, 1H, $J = 11.6$ Hz), 4.33 (brd, 1H, $J = 2.9$ Hz), 4.32 (dd, 1H, $J = 2.4$, 9.7 Hz), 4.28 (d, 1H, $J = 12.1$ Hz), 4.28 (brd, 1H, $J = 11.1$ Hz), 4.25 (brs, 1H), 4.24 (d, 1H, $J = 12.6$ Hz), 4.23 (d, 1H, $J = 14.1$ Hz), 4.23 (brd, 1H, $J = 11.6$ Hz), 4.18 (dd, 1H, $J = 8.7$, 8.7 Hz), 4.16 (brdd, 1H, $J = 9.2$, 10.2 Hz), 4.13–4.07 (m, 6H), 4.02 (dd, 1H, $J = 2.4$, 10.2 Hz), 4.01 (brs, 1H), 3.96 (dd, 1H, $J = 3.4$, 9.7 Hz), 3.95 (dt, 1H, $J = 6.8$, 8.7 Hz), 3.89 (dd, 1H, $J = 8.7$, 9.2 Hz), 3.83 (d, 1H, $J = 12.1$ Hz), 3.81 (dd, 1H, $J = 2.9$, 10.2 Hz), 3.71–3.54 (m, 7H), 3.47 (dt, 1H, $J = 4.8$, 8.7 Hz), 3.41 (brs, 1H), 3.36 (dd, 1H, $J = 4.8$, 8.7 Hz), 3.12 (dd, 1H, $J = 7.7$, 8.7 Hz), 0.98 (t, 2H, $J = 8.7$ Hz), 0.00 ppm (s, 9H); $^{13}$C NMR (67.8 MHz, [D$_6$]acetone): $\delta = 167.5$, 166.0, 155.0, 140.6, 140.3, 139.9, 139.8, 139.6, 139.5, 139.4, 139.1, 134.0, 131.1, 130.5, 129.5, 129.4, 129.1, 129.0, 128.9, 128.8, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.6, 127.3, 127.0, 103.8, 103.4, 102.2, 101.4, 101.3, 101.0, 100.9, 96.7, 94.9, 83.1, 83.0, 79.6, 77.6, 75.5, 75.2, 74.8, 74.4, 74.3, 74.2, 74.1, 74.0,

73.7, 73.6, 73.5, 73.4, 73.1, 72.8, 72.0, 71.8, 71.7, 70.0, 69.9, 69.6, 68.1, 67.2, 67.1, 63.8, 63.3, 53.7, 51.5, 41.4, 18.8, −1.40 ppm; FTIR (KBr): $\tilde{\nu}$ = 2954, 1732, 1453, 1366, 1269, 1097, 753, 698 $cm^{-1}$; HRMS (ESI-TOF): *m/z* calcd for $C_{117}H_{129}N_2O_{29}SiCl_4$: 2193.7204 $[M+NH_4]^+$; found: 2193.7200.

**2-(Trimethylsilyl)ethyl (2-*O*-benzyl-4,6-*O*-benzylidene-α-D-galactopyranosyl)-(1→3)-[4,6-*O*-benzylidene-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-galactopyranosyl]-(1→3)-(2-*O*-benzyl-4,6-*O*-benzylidene-α-D-galactopyranosyl)-(1→4)-(2-*O*-benzoyl-3,6-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (21)**: Thiourea (5.80 mg, 76.3 μmol, 6.00 equiv) and 2,6-lutidine (6.80 μL, 61.0 μmol, 4.80 equiv) was added to a stirred solution of **20** (27.7 mg, 12.7 μmol) in dry DMF (1.00 mL) was added at room temperature. After being stirred at 50 °C for 14 h, the reaction mixture was poured into 1 M HCl with cooling. The aqueous layer was extracted with two portions of ethyl acetate. The combined extracts were washed with 1 M HCl, saturated $NaHCO_3$ (aq.) and brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (elution with 94:6 toluene/acetone) to give **21** (23.0 mg, 10.9 μmol, 86 %). $[\alpha]_D^{23}$ = +92.7 (*c* = 0.335, $CHCl_3$); $^1$H NMR (400 MHz, [D$_6$]acetone): δ = 8.12 (d, 2H, *J* = 7.3 Hz), 7.68 (dd, 1H, *J* = 7.3, 7.7 Hz), 7.57–7.11 (m, 52H), 6.57 (brd, 1H, *J* = 9.7 Hz), 5.68 (s, 1H), 5.59 (s, 1H), 5.55 (dd, 1H, *J* = 7.7, 10.2 Hz), 5.47 (s, 1H), 5.39 (d, 1H, *J* = 3.4 Hz), 5.09 (d, 1H, *J* = 3.4 Hz), 5.05 (d, 1H, *J* = 7.7 Hz), 5.03 (brs, 2H), 4.95 (d, 1H, *J* = 13.1 Hz), 4.90 (d, 1H, *J* = 11.6 Hz), 4.77 (d, 1H, *J* = 12.6 Hz), 4.75 (d, 1H, *J* = 7.7 Hz), 4.67 (d, 1H, *J* = 13.1 Hz), 4.66 (d, 1H, *J* = 11.6 Hz), 4.64 (d, 1H, *J* = 11.6 Hz), 4.64 (brs, 1H), 4.63 (d, 1H, *J* = 12.1 Hz), 4.59 (d, 1H, *J* = 12.6 Hz), 4.55 (brs, 1H), 4.51 (d, 1H, *J* = 12.6 Hz), 4.44 (d, 1H, *J* = 8.2 Hz), 4.41 (d, 1H, *J* = 12.1 Hz), 4.33 (brd, 1H, *J* = 2.4 Hz), 4.31 (dd, 1H, *J* = 3.4, 10.6 Hz), 4.30–4.26 (m, 2H), 4.24 (brs, 1H), 4.22 (d, 1H, *J* = 12.1 Hz), 4.21 (brd, 1H, *J* = 3.4 Hz), 4.20 (brd, 1H, *J* = 10.2 Hz), 4.19 (brd, 1H, *J* = 9.2 Hz), 4.16 (dd, 1H, *J* = 8.4, 9.2 Hz), 4.14 (brdd, 1H, *J* = 7.7, 10.2 Hz), 4.12 (brd, 1H, *J* = 10.2 Hz), 4.10 (d, 1H, *J* = 11.6 Hz), 4.07 (brd, 1H, *J* = 10.2 Hz), 4.06 (brdd, 1H, *J* = 3.4, 10.2 Hz), 3.98–3.83 (m, 6H), 3.81 (dd, 1H, *J* = 2.4, 10.2 Hz), 3.70–3.53 (m, 8H), 3.47 (ddd, 1H, *J* = 4.4, 4.8, 9.2 Hz), 3.42 (brs, 1H), 3.35 (dd, 1H, *J* = 5.8, 8.7 Hz), 3.31 (dd, 1H, *J* = 8.2, 8.7 Hz), 0.98 (t, 2H, *J* = 8.7 Hz), 0.00 ppm (s, 9H); $^{13}$C NMR (67.8 MHz, [D$_6$]acetone): δ = 166.0, 154.9, 140.6, 140.3, 139.9, 139.7, 139.5, 139.0, 134.0, 131.1, 130.5, 129.5, 129.0, 128.9, 128.7, 128.6, 128.5, 128.4, 128.2, 128.1, 128.0, 127.6, 127.3, 127.2, 103.4, 102.3, 101.3, 101.2, 101.1, 100.9, 96.8, 94.9, 94.8, 83.2, 83.1, 80.2, 79.8, 78.7, 77.8, 76.8, 76.2, 75.6, 74.8, 74.2, 73.8, 73.7, 73.4, 73.3, 71.8, 71.7, 69.4, 68.3, 68.1, 67.2, 67.0, 63.8, 53.6, 18.8, −1.37 ppm; FTIR (KBr): $\tilde{\nu}$ = 3569, 2869, 1730, 1454, 1366, 1269, 1097, 753, 698 $cm^{-1}$; HRMS (ESI-TOF): *m/z* calcd for $C_{115}H_{128}N_2O_{28}SiCl_3$: 2117.7488 $[M+NH_4]^+$; found: 2117.7485.

**2-(Trimethylsilyl)ethyl (2-*O*-benzyl-4,6-*O*-benzylidene-3-*O*-chloroacetyl-α-D-galactopyranosyl)-(1→3)-(2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-galactopyranosyl)-(1→3)-(2-*O*-benzyl-4,6-*O*-benzylidene-α-D-galactopyranosyl)-(1→4)-(2-*O*-benzoyl-3,6-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (22)**: A mixture of **6a** (21.4 mg, 49.3 μmol), $Ph_2SO$ (18.3 mg, 90.3 μmol), TTBP (26.9 mg, 108 μmol; azeotroped twice with dry toluene) and pulverized activated MS 4 Å (300 mg) in dry $CH_2Cl_2$ (1.20 mL) was stirred at room temperature for 1 h under argon to remove a trace amount of $H_2O$. Then, the reaction mixture was cooled to −78 °C. After 5 min, $Tf_2O$ (11.0 μL, 65.0 μmol) was added to the reaction mixture at the same temperature. After being stirred at −40 °C for 1 h, a solution of **8** (15.1 mg, 36.3 μmol; azeotroped twice with dry toluene) in dry $CH_2Cl_2$ (1.00 mL) was added at the same temperature. After being stirred for 3.5 h at the same temperature, the reaction mixture was warmed to 0 °C and stirred for 30 min. The reaction mixture was then cooled to −20 °C. After 5 min, a solution of **9** (58.0 mg, 43.4 μmol) in dry $CH_2Cl_2$ (1.00 mL) and NIS (12.2 mg, 54.1 μmol, 1.50 equiv) was added to the reaction mixture. After being stirred for 6 h at the same temperature, the reaction mixture was neutralized with $NEt_3$ and filtered through a pad of Celite. Then, the filtrate was concentrated in vacuo. The residue was purified by column chromatography on silica gel (elution with $CHCl_3$/MeOH = 99:10) and by gel permeation chromatography (GPC) to give **22** (29.7 mg, 16.6 μmol, 46 % based on **8**). $[\alpha]_D^{30}$ = +90.0 (*c* = 1.12, $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$): δ = 7.98 (dd, 2H, *J* = 1.5, 7.3 Hz), 7.90 (d, 2H, *J* = 7.3 Hz), 7.61 (dd, 1H, *J* = 7.3, 7.7 Hz), 7.51–7.03 (m, 55H), 5.68 (dd, 1H, *J* = 7.7, 9.7 Hz), 5.49 (dd, 1H, *J* = 7.7, 10.2 Hz), 5.45 (s, 1H), 5.26 (s, 2H), 5.19 (dd, 1H, *J* = 3.4, 10.2 Hz), 5.08 (d, 1H, *J* = 3.4 Hz), 5.08 (d, 1H, *J* = 3.4 Hz), 5.00 (d, 1H, *J* = 11.1 Hz), 4.90 (d, 1H, *J* = 11.1 Hz), 4.89 (d, 1H, *J* = 13.1 Hz), 4.86 (d, 1H, *J* = 7.7 Hz), 4.79 (d, 1H, *J* = 7.7 Hz), 4.73 (d, 1H, *J* = 12.6 Hz), 4.64 (d, 1H, *J* = 11.1 Hz), 4.62 (d, 1H, *J* = 11.1 Hz), 4.62 (d, 1H, *J* = 12.6 Hz), 4.54 (d, 1H, *J* = 12.1 Hz), 4.52 (d, 1H, *J* = 12.1 Hz), 4.50 (brs, 1H), 4.43 (d, 1H, *J* = 12.6 Hz), 4.37 (d, 2H, *J* = 12.6 Hz), 4.37 (dd, 1H, *J* = 3.4, 10.6 Hz), 4.36 (brd, 1H, *J* = 10.6 Hz), 4.32 (d, 1H, *J* = 7.7 Hz), 4.26 (d, 1H, *J* = 12.1 Hz), 4.22 (brs, 1H), 4.14 (brd, 1H, *J* = 2.4 Hz), 4.13 (dd, 1H, *J* = 8.2, 8.7 Hz), 4.10 (brd, 1H, *J* = 3.4 Hz), 4.08 (brd, 1H, *J* = 2.4 Hz), 4.07 (dd, 1H, *J* = 3.4, 10.2 Hz), 4.06 (d, 1H, *J* = 15.0 Hz), 4.02 (dd, 1H, *J* = 3.4, 10.6 Hz), 3.98 (d, 1H, *J* = 15.0 Hz), 3.96 (dt, 1H, *J* = 6.8, 9.2 Hz), 3.87 (dd, 1H, *J* = 9.2, 9.7 Hz), 3.87 (d, 1H, *J* = 12.1 Hz), 3.86 (brd, 1H, *J* = 10.6 Hz), 3.65 (dd, 1H, *J* = 2.4, 9.7 Hz), 3.61–3.41 (m, 9H), 3.39 (dd, 1H, *J* = 2.4, 10.2 Hz), 3.37 (dd, 1H, *J* = 7.7, 9.2 Hz), 3.33 (dd, 1H, *J* = 4.8, 8.2 Hz), 3.32 (dd, 1H, *J* = 4.8, 8.7 Hz), 3.30 (dt, 1H, *J* = 4.8, 9.2 Hz), 3.05 (brs, 1H), 1.02–0.98 (m, 2H), 0.01 ppm (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ = 166.4, 165.3, 164.9, 139.4, 138.7, 138.4, 138.3, 138.2, 138.1, 138.0, 137.8, 137.5, 137.4, 133.2, 132.9, 129.9, 129.8, 129.7, 129.6, 128.9, 128.7, 128.5, 128.3, 128.2, 128.1, 128.0, 127.8, 127.7, 127.6, 127.4, 127.3, 127.2, 126.9, 126.3, 126.2, 126.0, 103.0, 101.8, 101.4, 101.2, 100.7, 100.4, 100.2, 98.4, 82.5, 82.0, 79.2, 78.5, 76.2, 75.3, 74.8, 74.6, 74.4, 73.7, 73.5, 73.4, 73.3, 73.1, 72.9, 72.1, 71.1, 70.8, 69.0, 68.7, 68.5, 67.3, 67.0, 66.2, 63.3, 62.6, 40.7, 18.4, −1.50 ppm; FTIR (KBr): $\tilde{\nu}$ = 2861, 1734, 1267, 1097, 1000, 750, 698 $cm^{-1}$; HRMS (ESI-TOF): *m/z* calcd for $C_{121}H_{131}NO_{29}SiCl$: 2124.8265 $[M+NH_4]^+$; found: 2124.8240.

**2-(Trimethylsilyl)ethyl (2-*O*-benzyl-4,6-*O*-benzylidene-α-D-galactopyranosyl)-(1→3)-(2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-galactopyranosyl)-(1→3)-(2-*O*-benzyl-4,6-*O*-benzylidene-α-D-galactopyranosyl)-(1→4)-(2-*O*-benzoyl-3,6-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (23)**: Thiourea (8.70 mg, 114 μmol) and 2,6-lutidine (10.6 μL, 91.2 μmol) to a stirred solution of **22** (40.0 mg, 19.0 μmol) in dry DMF (1.00 mL) was added at room temperature. After being stirred at 50 °C for 12 h, the reaction mixture was poured into 1 M HCl with cooling. The aqueous layer was extracted with two portions of ethyl acetate. The combined extracts were washed with 1 M HCl, saturated $NaHCO_3$ (aq.) and brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by column chromatography on silica gel (elution with 95:5 toluene/acetone) to give **23** (33.9 mg, 16.7 μmol, 88 %). $[\alpha]_D^{22}$ = +80.2 (*c* = 0.935, $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$): δ = 7.98 (d, 2H, *J* = 7.3 Hz), 7.86 (d, 2H, *J* = 7.7 Hz), 7.60 (dd, 1H, *J* = 7.3 Hz, *J* = 7.7 Hz), 7.48–7.03 (m, 55H), 5.70 (dd, 1H, *J* = 8.2, 10.2 Hz), 5.49 (dd, 1H, *J* = 7.7, 10.2 Hz), 5.45 (s, 1H), 5.31 (s, 1H), 5.30 (s, 1H), 5.13 (d, 1H, *J* = 2.9 Hz), 5.03 (d, 1H, *J* = 3.4 Hz), 4.99 (d, 1H, *J* = 11.1 Hz), 4.90 (d, 2H, *J* = 11.1 Hz), 4.89 (d, 1H, *J* = 8.2 Hz), 4.78 (d, 1H, *J* = 7.7 Hz), 4.72 (d, 1H, *J* = 11.6 Hz), 4.65 (d, 1H, *J* = 11.1 Hz), 4.62 (d, 1H, *J* = 11.6 Hz), 4.53 (d, 1H, *J* = 13.1 Hz), 4.51 (brd, 1H, *J* = 3.9 Hz), 4.49 (d, 1H, *J* = 12.1 Hz), 4.42 (d, 1H, *J* = 12.6 Hz), 4.37 (d, 1H, *J* = 13.1 Hz), 4.36 (dd, 1H, *J* = 3.9, 10.2 Hz), 4.35 (d, 1H, *J* = 12.6 Hz), 4.31 (d, 1H, *J* = 7.7 Hz), 4.22 (brs, 1H), 4.25 (d, 2H, *J* = 12.1 Hz), 4.12 (brd, 1H, *J* = 3.4 Hz), 4.12 (brd, 1H, *J* = 3.4 Hz), 4.11 (dd, 1H, *J* = 7.7, 8.7 Hz), 4.03 (brd, 1H, *J* = 11.6 Hz), 4.02 (dd, 1H, *J* = 3.4, 10.2 Hz), 3.98–3.83 (m, 4H), 3.79 (dd, 1H, *J* = 2.9, 9.7 Hz), 3.78 (brs, 1H), 3.68 (dd, 1H, *J* = 3.4, 10.2 Hz, *J* = 3.4 Hz), 3.67 (brd, 1H, *J* = 9.7 Hz), 3.62–3.52 (m, 6H), 3.51 (brs, 1H), 3.40–3.29 (m, 7H,), 3.07 (brs, 1H), 2.33 (brd, 1H, *J* = 6.8 Hz), 0.99 (dt, 2H, *J* = 6.3, 10.2 Hz), 0.00 ppm (s, 9H); $^{13}$C NMR (67.8 MHz, $CDCl_3$): δ = 165.3, 164.8, 139.4, 138.6, 138.4, 138.3, 138.2, 138.1, 138.0, 137.8, 137.5, 137.4, 133.2, 133.0, 129.9, 129.7, 129.5, 129.0, 128.8, 128.5, 128.5, 128.3, 128.2, 128.1, 128.0, 127.8, 127.6, 127.5, 127.3, 127.2, 126.9, 126.4, 126.2, 126.1, 102.9, 101.9 x2, 101.4, 101.2, 100.9, 100.2, 97.0, 82.4, 82.0, 79.2, 76.3, 76.2, 75.8, 75.3, 74.8, 74.6, 74.4, 73.7, 73.5, 73.2, 72.8, 72.6, 72.2, 72.1, 71.1, 70.8, 69.1, 69.0, 68.9, 68.5, 67.9, 67.3, 67.0, 66.1, 62.9, 29.7, 18.5, −1.50 ppm; FTIR (KBr): $\tilde{\nu}$ = 3572, 2861, 1732, 1268, 1097, 752, 698 $cm^{-1}$; HRMS (ESI-TOF): *m/z* calcd for $C_{119}H_{130}NO_{28}Si$: 2048.8549 $[M+NH_4]^+$; found: 2048.8552.

**Polymer-assisted deprotection**

*2-(Trimethylsilyl)ethyl (2-acetamide-2-deoxy-α-D-galactopyranosyl)-(1→3)-(2-acetamide-2-deoxy-α-D-galactopyranosyl)-(1→3)-α-D-galactopyranosyl-(1→4)-α-D-galactopyranosyl-β-D-glucopyranoside (**2a**)*: A mixture of **17** (8.60 mg, 4.20 μmol), prelinker **3** (5.90 mg, 21.0 μmol; azeotroped twice with dry toluene) and pulverized activated MS 4 Å (100 mg) in dry $CH_2Cl_2$ (1.00 mL) was stirred at room temperature for 1 h under argon to remove a trace amount of $H_2O$. Then, CSA (1.00 mg, 4.20 μmol) was added to the reaction mixture at 0 °C. After being stirred at the same temperature for 4 h, the reaction mixture was filtered through a pad of Celite. Then, the filtrate was concentrated in vacuo. The residue was purified by column chromatography on silica gel (elution with $CHCl_3$) and further purified by gel permeation chromatography (GPC). To a solution of the above activated ester in dry $CH_2Cl_2$ (150 μL) and dry DMF (150 μL) was added ArgoPore-$NH_2$ resin (**4**) (56.3 mg, 42.0 μmol), a catalytic amount of DIEA and DMAP at room temperature. After being shaken at room temperature for 18 h, the reaction mixture was filtered and the resin was washed three times each with THF/$H_2O$ (1:1) (3.00 mL), MeOH (3.00 mL) and dry $CH_2Cl_2$ (3.00 mL), respectively. The resin was dried in vacuo to give **24** (FTIR (KBr): $\tilde{\nu}$ = 3327, 2924, 2116, 1717, 1665, 1493, 1219, 1095, 772 $cm^{-1}$). To a suspension of **24** packed into MacroKans microreactor in 1,4-dioxane (20.0 mL) and $H_2O$ (10.0 mL) was added LiOH·$H_2O$ (400 mg) at room temperature. After being stirred at 80 °C for 18 h, the reaction mixture was filtered and the resin was washed three times each with THF/$H_2O$ (1:1) (3.00 mL), MeOH (3.00 mL), and dry $CH_2Cl_2$ (3.00 mL). The resin was dried in vacuo (FTIR (KBr): $\tilde{\nu}$ = 3313, 2927, 1666, 1602, 1451, 1173 1026, 700 $cm^{-1}$). LiOH·$H_2O$ (100 mg) and $PMe_3$ (200 μL, 1.0 M in THF solution) was added to a suspension of the resultant resin packed into MacroKans microreactor in toluene (5.00 mL) and $H_2O$ (5.00 mL) was added at room temperature. After being stirred at 140 °C for 14 h, the reaction mixture was filtered and the resin was washed three times each with THF/$H_2O$ (1:1) (3.00 mL), MeOH (3.00 mL) and dry $CH_2Cl_2$ (3.00 mL), respectively. The resin was dried in vacuo (FTIR (KBr): $\tilde{\nu}$ = 3325, 2916, 1664, 1602, 1493, 1451, 984, 826 $cm^{-1}$). AcOH (70.0 μL), DIC (150 μL) and DIEA (330 μL) was added at room temperature to a suspension of the resultant resin packed into MacroKans microreactor in dry $CH_2Cl_2$ (10.0 mL). After being stirred at room temperature for 12 h, the reaction mixture was filtered and the resin was washed three times each with THF/$H_2O$ (1:1) (3.00 mL), MeOH (3.00 mL) and dry $CH_2Cl_2$ (3.00 mL), respectively. The resin was dried in vacuo. Liquid $NH_3$ (36.0 mL) was added to a suspension of the resultant resin packed into MacroKans microreactor in dry THF (4.00 mL). Sodium granules (40.0 mg) were subsequently added to the reaction mixture at −78 °C. After being stirred at the same temperature for 1.5 h, the reaction mixture was allowed to warm to −35 °C. After heating at reflux for 1 h, the reaction mixture was quenched with MeOH. The reaction mixture was filtered and the resin was washed three times each with THF/$H_2O$ (1:1) (3.00 mL), MeOH (3.00 mL) and dry $CH_2Cl_2$ (3.00 mL), respectively. Then, the resin was dried in vacuo. The resultant resin was treated with 1 M HCl (300 μL), dry $CH_2Cl_2$ (2.40 mL) and MeOH (200 μL) at room temperature for 20 min. Then, the reaction mixture was filtered and rinsed with dry $CH_2Cl_2$ (3.00 mL), MeOH (3.00 mL) and $H_2O$ (3.00 mL). The residue was dried in vacuo and purified by reverse-phase column chromatography (Bond Elut-C18) to give **2a** (1.70 mg, 1.50 μmol, 43% in 7 steps based on **17**). $[\alpha]_D^{23}$ = +97.8 (*c* 0.250, $H_2O$); $^1$H NMR (400 MHz, $D_2O$): δ = 5.05 (d, 1H, *J* = 3.9 Hz), 4.94 (d, 1H, *J* = 2.9 Hz), 4.72 (d, 1H, *J* = 8.2 Hz), 4.49 (d, 1H, *J* = 7.7 Hz), 4.45 (d, 1H, *J* = 7.7 Hz), 4.29 (dd, 1H, *J* = 6.3, 5.8 Hz), 4.23 (br s, 1H), 4.21 (dd, 1H, *J* = 3.9, 11.1 Hz), 4.09 (dd, 1H, *J* = 8.2, 11.1 Hz), 4.07 (br d, 1H, *J* = 3.4 Hz), 4.03 (br d, 1H, *J* = 3.4 Hz), 3.99 (br d, 1H, *J* = 2.9 Hz), 3.97 (dt, 1H, *J* = 6.3, 8.7 Hz), 3.96 (dd, 1H, *J* = 3.9, 10.2 Hz), 3.95 (br ddd, 1H, *J* = 3.9, 4.4, 9.7 Hz), 3.94 (dd, 1H, *J* = 2.9, 10.2 Hz), 3.91–3.74 (m, 13H), 3.71 (dd, 1H, *J* = 3.4, 10.2 Hz), 3.70 (br d, 1H, *J* = 5.3 Hz), 3.70 (br d, 1H, *J* = 5.3 Hz), 3.61 (dd, 1H, *J* = 5.3, 6.3 Hz), 3.61 (t, 1H, *J* = 8.7, 9.2 Hz), 3.56 (dd, 1H, *J* = 7.7, 10.2 Hz), 3.54 (dd, 1H, *J* = 8.7, 9.7 Hz), 3.28 (dd, 1H, *J* = 7.7, 9.2 Hz), 2.03 (s, 3H), 2.02 (s, 3H, 1.07–0.91 (m, 2H), 0.00 ppm (s, 9H); $^{13}$C NMR (67.8 MHz, $D_2O$, [$D_6$]acetone): δ = 165.4, 165.2, (94.1, 93.4, 92.2, 91.2, 84.4 anomeric), 69.7, 69.6, 68.1, 66.2, 65.6, 65.5, 65.4, 63.7, 63.0, 62.1, 61.7, 61.1, 59.7, 59.1, 58.9, 58.5, 58.4, 54.5, 51.8, 51.7, 51.2, 51.1, 41.7, 40.2, 13.1, 12.8, 8.37, −11.7 ppm; FTIR (KBr): $\tilde{\nu}$ = 3254, 1629, 1557, 1417, 1248, 1039, 713 $cm^{-1}$; HRMS (ESI-TOF): *m/z* calcd for $C_{39}H_{71}N_2O_{26}Si$: 1011.4064 $[M+H]^+$; found: 1011.4064.

*(α-D-Galactopyranosyl)-(1→3)-(2-acetamide-2-deoxy-α-D-galactopyranosyl)-(1→3)-α-D-galactopyranosyl-(1→4)-α-D-galactopyranosyl-β-D-glucopyranoside (**2c**)*: According to the polymer-assisted deprotection of **17**, compound **2c** was prepared from **21** (1.80 mg, 1.86 μmol, 34% in 6 steps based on **21**). $[\alpha]_D^{26}$ = +107 (*c* = 0.240, $H_2O$); $^1$H NMR (400 MHz, $D_2O$): δ = 5.08 (d, 1H, *J* = 3.4 Hz), 4.93 (d, 1H, *J* = 2.9 Hz), 4.72 (d, 1H, *J* = 8.2 Hz), 4.48 (d, 1H, *J* = 7.7 Hz), 4.44 (d, 1H, *J* = 7.7 Hz), 4.28 (t, 1H, C5, *J* = 6.3 Hz), 4.26 (br d, 1H, *J* = 2.9 Hz), 4.13 (br d, 1H, *J* = 1.9 Hz), 4.06 (dd, 1H, *J* = 8.2, 10.6 Hz), 4.02 (br d, 1H, *J* = 1.9 Hz), 3.97 (br d, 1H, *J* = 1.9 Hz), 3.95 (br dt, 1H, *J* = 4.8, 9.7 Hz), 3.94 (dt, 1H, *J* = 6.8, 10.2 Hz), 3.93 (dd, 1H, $J_{2,3}$ = 2.9, 11.6 Hz), 3.89 (dd, 1H, *J* = 2.9, 11.6 Hz), 3.85–3.68 (m, 17H), 3.64 (dd, 1H, $J_{5,6a}$ = 5.3, 5.8 Hz), 3.60 (dd, 1H, *J* = 8.7 Hz, 9.2 Hz), 3.55 (dd, 1H, *J* = 7.7, 10.6 Hz), 3.51 (dd, 1H, *J* = 9.2, 9.7 Hz), 3.27 (dd, 1H, *J* = 7.7, 8.7 Hz), 2.01 (s, 3H), 1.06–0.90 (m, 2H), −0.01 (s, 9H); $^{13}$C NMR (67.8 MHz, $D_2O$): δ = 162.8, 94.0, 93.2, 92.2, 91.1, 86.2, 69.9, 68.4, 66.5, 66.1, 65.5, 63.7, 63.2, 61.9, 61.8, 61.4, 60.2, 60.0, 59.9, 59.4, 58.8, 58.7, 58.4, 56.9, 54.9, 51.8, 51.7, 51.6, 51.5, 51.2, 51.1, 32.2, 13.1, 8.33, −11.8 ppm; FTIR (KBr): $\tilde{\nu}$ = 3371, 1642, 1437, 1250, 1035, 805, 591 $cm^{-1}$; HRMS (ESI-TOF): *m/z* calcd for $C_{37}H_{68}NO_{26}Si$: 970.3799 $[M+H]^+$; found: 970.3797.

*(α-D-Galactopyranosyl)-(1→3)-(α-D-galactopyranosyl)-(1→3)-α-D-galactopyranosyl-(1→4)-α-D-galactopyranosyl-β-D-glucopyranoside (**2d**)*: According to the polymer-assisted deprotection of **17**, compound **2d** was prepared from **21** (2.60 mg, 2.84 μmol, 43% in 5 steps based on **23**). $[\alpha]_D^{27}$ = +73.8 (*c* = 0.195, $H_2O$); $^1$H NMR (400 MHz, $D_2O$): δ = 5.12 (d, 1H, *J* = 3.9 Hz), 4.98 (d, 1H, *J* = 2.4 Hz), 4.66 (d, 1H, *J* = 7.3 Hz), 4.48 (d, 1H, *J* = 7.7 Hz), 4.44 (d, 1H, *J* = 7.7 Hz), 4.30 (t, 1H, *J* = 6.3 Hz), 4.24 (br s, 1H, C-4), 4.17 (t, 1H, *J* = 6.8 Hz), 4.13 (br d, 1H, *J* = 2.4 Hz), 4.02–3.83 (m, 8H), 3.81–3.68 (m, 15H), 3.66 (dd, 1H, *J* = 5.8, 6.3 Hz), 3.60 (dd, 1H, *J* = 8.7, 9.2 Hz), 3.56 (dd, 1H, *J* = 7.7, 10.2 Hz), 3.54 (dd, 1H, *J* = 8.7, 9.7 Hz), 3.28 (dd, 1H, *J* = 7.7, 9.2 Hz), 1.07–0.91 (m, 2H), 0.00 ppm (s, 9H); $^{13}$C NMR (67.8 MHz, $D_2O$): δ = 94.8, 94.1, 92.3, 91.1, 86.5, 70.1, 69.7, 68.5, 66.1, 65.6, 65.5, 63.8, 63.4, 62.0, 61.8, 61.6, 60.6, 60.3, 60.2, 59.8, 59.1, 58.8, 58.6, 56.0, 51.9, 51.8, 51.6, 51.3, 51.2, 8.45, −11.7 ppm; FTIR (KBr): $\tilde{\nu}$ = 3371, 1649, 1421, 1250, 1033, 804, 580 $cm^{-1}$; HRMS (ESI-TOF): *m/z* calcd for $C_{35}H_{65}O_{26}Si$: 923.3533 $[M+H]^+$; found: 929.3527.

**Biological evaluation**

*SLL-2 labeling*: SLL-2 (1 mg) was dissolved in $NaHCO_3$ (pH 9.0, 500 μL of 0.1 M). After the addition of fluorescein isothiocyanate (FITC; 100 μL of 10 mg $mL^{-1}$) in dimethylsulfoxide, the solution was mixed and incubated at room temperature for 1 h in the dark. The solution was dialyzed against 1 L of phosphate buffered saline at 4 °C overnight.

*Binding of the Forssman-antigen-related oligosaccharides to SLL-2*: The relative affinity of oligosaccharides to SLL-2 was tested by the change of fluorescence intensity using FP-715 (JASCO, Tokyo, Japan). Assay solution (400 μL of a solution of 150 mM NaCl, 0.1% Triton X-100, 20 mM Tris-HCl, pH 8.0) and FITC-labeled SLL-2 (3 μM) was added to a cuvette (ø = 7.0 mm). The fluorescence (excitation = 480 nm, emission = 530 nm) was measured every 15 s. After 1 min, an oligosaccharide was added and the fluorescence was measured after 5 min. The all measurement was carried out at 25.0 °C with stirring. The oligosaccharides used were Forssman-related saccharides. The specimens were analyzed in triplicate.

*Inhibition of SLL-2 activity by Forssman-related oligosaccharides*: The inhibition of SLL-2 effect to the morphology of CS-156 by the Forssman-related oligosaccharides was evaluated. The CS-156 was cultured to more than 10000 cells $mL^{-1}$. CS-156 (100 μL), adjusted to 3000 cells $mL^{-1}$ by IMK medium, was dispensed into a well of 96-well titer plate (Corning). The culture was incubated at 25 °C for 24 h. Forssman-related oligosaccharides (150 μL), at a concentration of 0.3 mM in IMK medium, were mixed with the filtrated SLL-2 (150 μL) at a concentration of 200 μg $mL^{-1}$ in IMK medium. This solution (100 μL) was added to each CS-156 (100 μL) culture, and incubated at 25 °C and cultured for 5 days. Photographs were taken at ten different fields for each well. A blurred

shape and a clear shape were identified as the motile form and a coccoid form, respectively. The motile cells and coccoid cells were counted, and then the motile percentage was determined. The specimens were analyzed in triplicate.

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[15] Details of the synthetic procedure for **27**–**31** are shown in the Supporting Information.

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