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A Convergent Synthesis of 6-*O*-Branched β-Glucan Oligosaccharides

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β-Glucans are important carbohydrate antigens that are found on the surface of fungal cells, and they could be useful for the development of antifungal vaccines. This paper describes a highly convergent and efficient strategy for the synthesis of structurally defined branched β-glucan oligosaccharides that can be used for detailed studies of β-glucans and for the design of β-glucan-based vaccines. The strategy was highlighted by assembling three target compounds through preactivation-based glycosylation with thioglycosides as glycosyl donors. It was used to successfully prepare β-glucan oligosaccharides consisting of a β-1,3-linked nonaglucan backbone linked to a β-1,6-glucotetraose, a β-1,3-glucodiose, or a β-1,3-glucotetraose branch at the 6-*O*-position of the nonaglucan central sugar unit. The structure and size of the glycosyl donors and acceptors used in the syntheses did not significantly affect the efficiency of the glycosylation, which suggests that this strategy can be generally useful for the synthesis of more complex structures.

Introduction

With the drastic increase in fungal infections and antifungal-drug resistance in the past two decades,[1] antifungal vaccines are in urgent demand.[2] The unique polysaccharides,[3] especially β-1,3-linked glucans (known as β-glucans),[4] on the surface of fungal cells are attractive antigens for the development of antifungal vaccines.[5] Studies have shown that β-glucans are not only exposed, but are also consistently expressed and highly conserved on the cell surfaces of all pathogenic fungi.[6] It has also been shown that β-glucans can induce strong immune responses,[4] and that a vaccine composed of natural β-glucans can engender effective protection against *Candida albicans* and *Aspergillus fumigatus* infections in mouse.[7] In addition, CRM_{197} protein conjugates of β-glucan oligosaccharides have been shown to elicit immune responses comparable to that induced by conjugates of the natural β-glucans.[8] This demonstrates that oligosaccharide analogs of natural β-glucans are useful for the development of antifungal vaccines.

The structure of β-glucans has been well established.[3,6] Their main carbohydrate chain is composed of approximately 1500 β-1,3-linked glucose units, with ca. 40–50 additional short β-1,6- or β-1,3-glucans attached to the main-chain glucose 6-*O*-positions as branches.[9] However, the functions of the branches in β-glucans and their influence on the immunological properties of β-glucans have not been clarified. To study these issues, and to develop β-glucan-based vaccines, it is essential to have access to homogeneous and structurally defined β-glucan oligosaccharides. Although several linear β-glucan oligosaccharides, and an oligosaccharide with monosaccharide branches, have previously been prepared by the hydrolysis of natural β-glucans or by chemical synthesis,[8] current strategies have drawbacks that have limited their synthetic efficiency and applicability, especially in the synthesis of complex structures. There is a clear need for an efficient and generally applicable method for β-glucan oligosaccharide synthesis. Recently, we described the efficient synthesis of linear β-glucan oligosaccharides[10] through preactivation-based glycosylation.[11] In this paper, we report a highly convergent, efficient, and potentially generally applicable strategy for the synthesis of branched β-glucan oligosaccharides.

Results and Discussion

Our synthetic targets were **1**–**3** (Scheme 1). These molecules have a β-1,3-linked nonaglucan backbone with branches, including a β-1,6-glucotetraose (**1**), a β-1,3-glucodiose (**2**), and a β-1,3-glucotetraose (**3**), attached to the 6-*O*-position of the central sugar unit of the nona-β-glucan. These three compounds were supposed to span different structural properties and immunologically determinant epitopes of natural β-glucans.[12] Moreover, we planned to attach a free aminoethyl group to the reducing end of the oligosaccharides to facilitate their conjugation with various biomolecules and tags, such as carrier proteins, to be useful for biological studies and for the development of conjugate vaccines.

For the synthesis of target molecules **1**–**3**, we were interested in a strategy built on preactivation-based iterative one-pot glycosylation using thioglycosides as glycosyl do-

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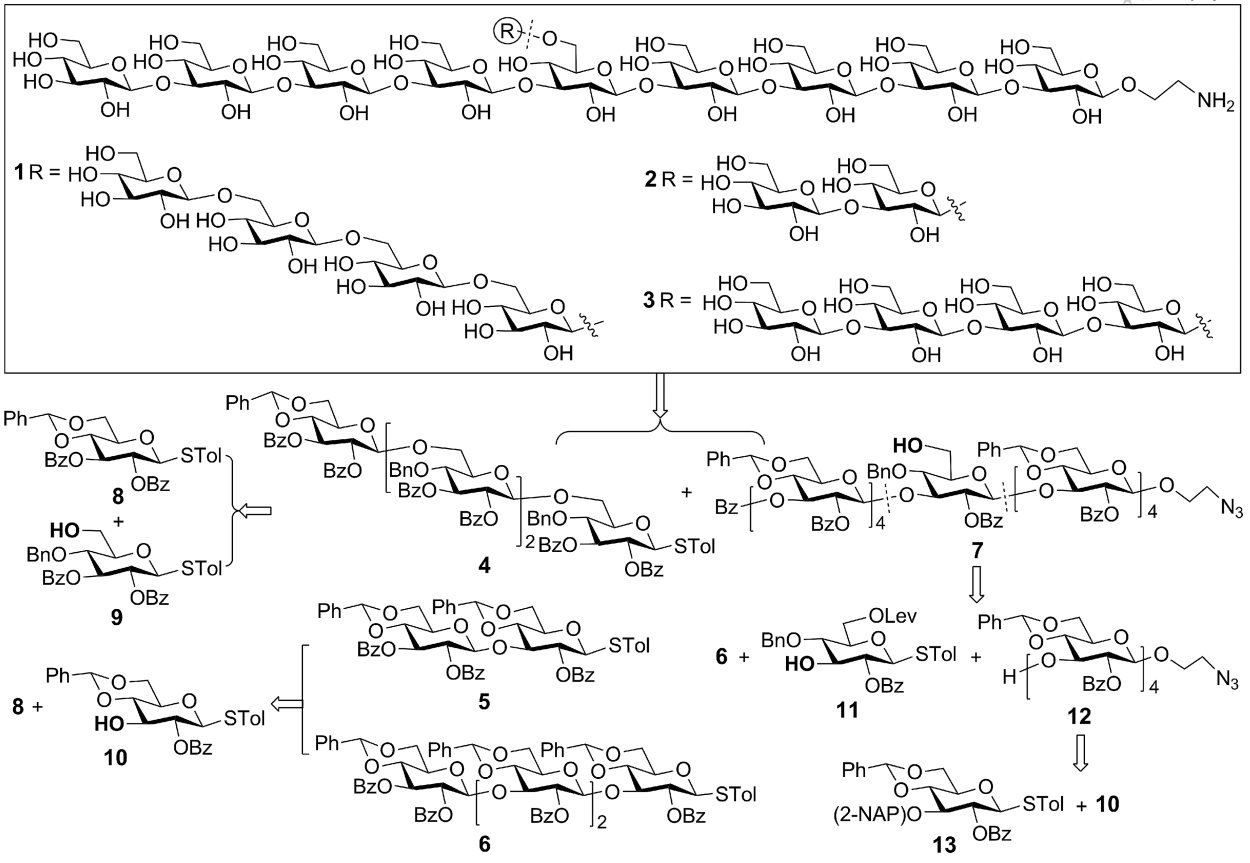
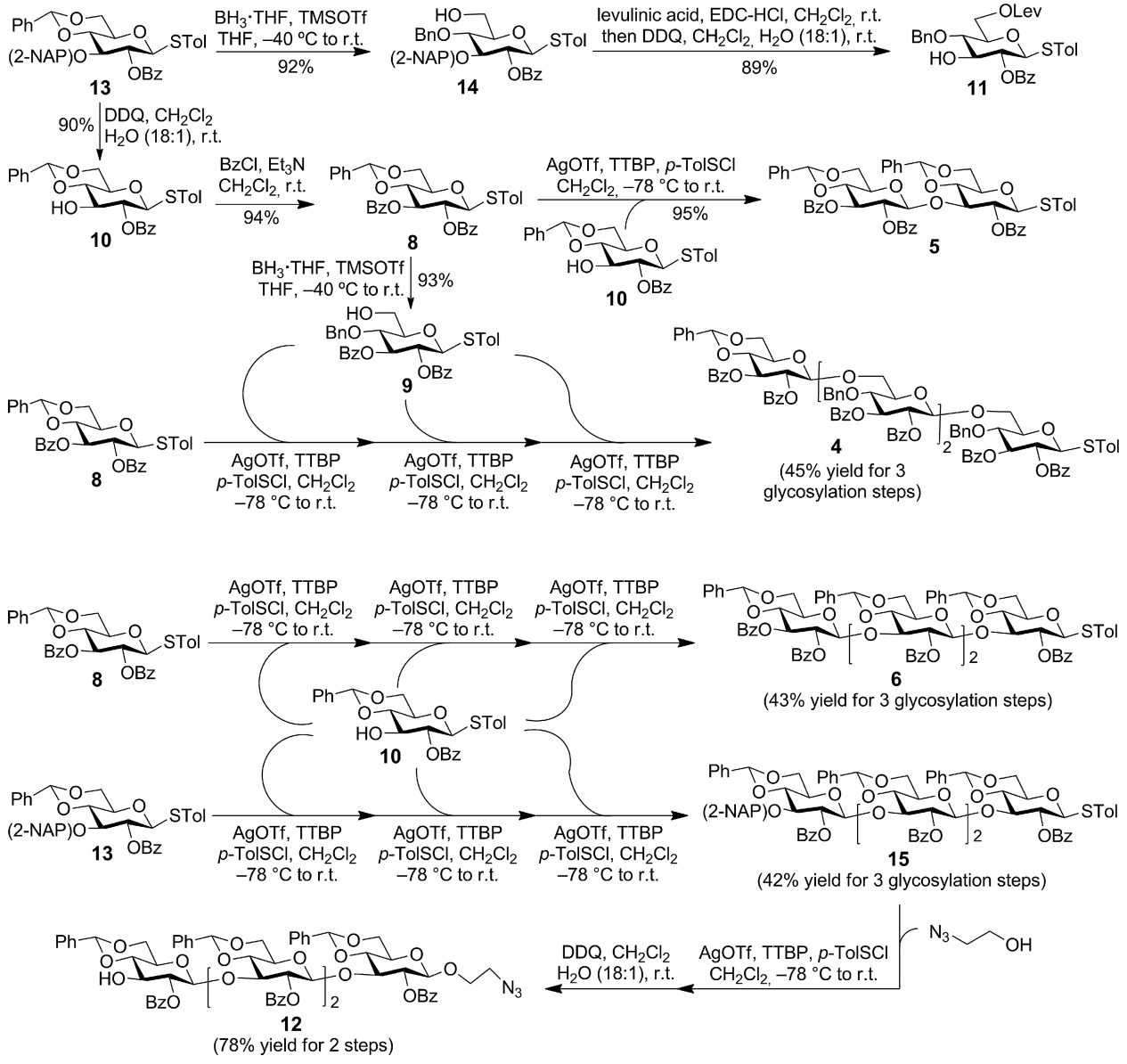


Scheme 1. Structures of target β-glucan oligosaccharides **1**–**3** with β-1,6-tetraglucose (**1**), β-1,3-diglucose (**2**), and β-1,3-tetraglucose (**3**) branches attached to the 6-*O*-position of the central glucose unit of a nonasaccharide; and retrosynthetic analysis of these molecules.

nors. This synthetic strategy has been shown to be simple and efficient as multiple intermediate conversion and separation steps can be avoided.[11] Accordingly, our synthetic plan (Scheme 1) was to separately prepare branches **4**–**6** as glycosyl donors and backbone nonasaccharide **7** as glycosyl acceptor, and then to stitch them together to give the fully protected oligosaccharides, which would finally be deprotected. Such a synthetic strategy could be applied more widely by using different donors to give different branches, and/or different backbone acceptors that could also have varied branching sites. In turn, oligosaccharides **4**–**6** could be prepared from monosaccharides **8**, **9**, and **10** through iterative one-pot glycosylation. Key intermediate **7** could be also constructed through one-pot glycosylation using **6**, **11**, and **12**. The synthesis of **12** would be similar to that of **6**, but using **13** and **10** as building blocks. In **13**, the 3-*O*-position would be temporarily protected with a 2-naphthylmethyl (NAP) group, which can be removed with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ),[13] but which is more acid-stable than the comparable *p*-methoxybenzyl group. As a result, this position would be selectively exposed for elongation of the sugar chain later on. In addition, the 2-*O*-positions of all of the glycosyl donors were protected with benzoyl (Bz) groups to ensure β-selective glycosylations as a result of neighboring-group participation.

Our synthesis began with the preparation of **13** according to a reported procedure.[14] Regioselective removal of the NAP group at the 3-*O*-position in **13** with DDQ, followed by 3-*O*-benzoylation, and then regioselective reductive ring opening of the benzylidene acetal in **8** using BH_3·THF and trimethylsilyl trifluoromethanesulfonate (TMSOTf) gave **9** (Scheme 2). On the other hand, reductive ring opening of the benzylidene acetal in **13**, followed by protection of the exposed 6-*O*-position with a levulinoyl (Lev) group through reaction with levulinic acid and *N*-(3-dimethylaminopropyl)-*N*′-ethylcarbodiimide hydrochloride (EDC·HCl), and then deprotection of the 3-*O*-position with DDQ produced **11**. Consequently, all of the required monosaccharide building blocks were readily synthesized from **13** in excellent overall yields.

For the synthesis of disaccharide building block **5**, we used the preactivation glycosylation protocol.[11a] First, glycosyl donor **8** was treated with the promoter *p*-toluenesulfenyl triflate (*p*TolSOTf; 1.0 equiv.), formed in situ by the reaction of *p*-toluenesulfenyl chloride (*p*TolSCl) with silver triflate (AgOTf), at –78 °C for 10 min, and then glycosyl acceptor **10** (0.9 equiv.) was added for the glycosylation. The reaction was β-specific, and **5** was formed in 95% yield. Starting from **8**, tetrasaccharide building blocks **4** and **6** were prepared through preactivation-based iterative one-pot glycosylation using **9** and **10** as glycosyl donors, respec-

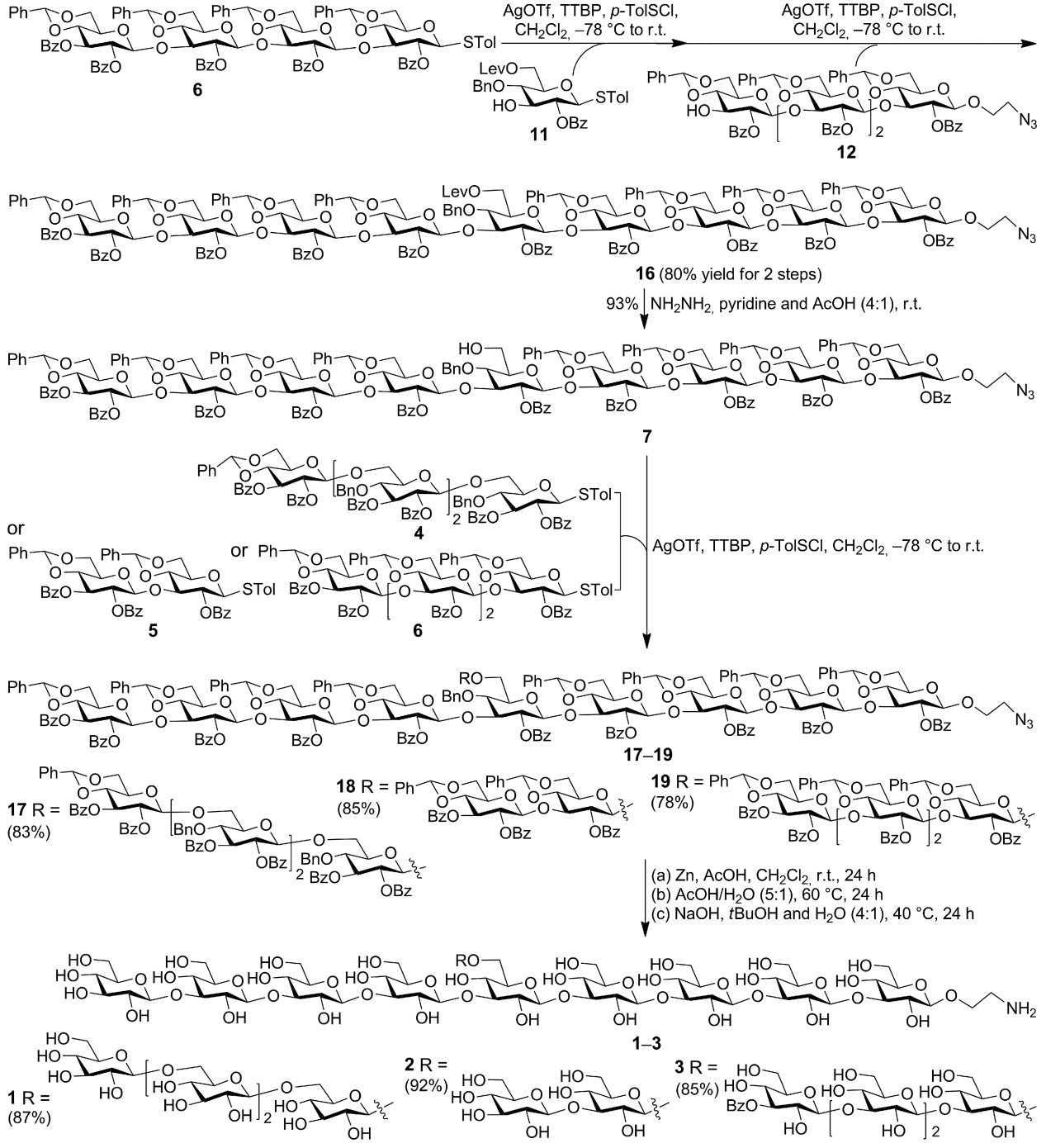


Scheme 2. Synthesis of the mono-, di-, and tetrasaccharide building blocks.

tively (Scheme 2).[11] Preactivation of the thioglycosyl donors with *p*TolSOTf was carried out at –78 °C for 10 min in a mixture of dichloromethane and acetonitrile. After the donor had been completely consumed (ca. 5 min at –78 °C, as shown by TLC), an acceptor (0.9 equiv.) was added, together with 2,4,6-tri-*tert*-butylpyrimidine (TTBP), which was used to neutralize the trifluoromethanesulfonic acid formed in the glycosylation reaction. The reaction was warmed to room temperature and stirred for ca. 20 min to guarantee complete consumption of the acceptor, as indicated by TLC. Then, the mixture was cooled to –78 °C for another round of preactivation and glycosylation by the same protocol. After the third round of glycosylation, and then work-up, **4** and **6** were obtained in 45% and 43% isolated yields, respectively. Similarly, tetrasaccharide **15** was prepared from **13** and **10** by iterative one-pot glycosylation in an overall yield of 42%. These results suggest that each glycosylation step gave an average of >75% yield, and that the overall yields were not significantly different for β-1,6- and β-1,3-linked tetrasaccharides. Tetrasaccharide **15** was then transformed into building block **12** by glycosylation with 2-azidoethanol in the presence of *p*TolSCl/AgOTf, and then removal of the 2-NAP protecting group with DDQ. All of the glycosylation reactions were β-specific, as confirmed by the ^{1}H NMR spectra of **4**, **5**, **6**, and **12**, which showed coupling constants in the range 6.2–10.1 Hz for all of the anomeric protons.

The preactivation-based one-pot glycosylation protocol was also used to prepare protected nonasaccharide **16** from **6**, **11**, and **12** (Scheme 3). We were pleased to find that these reactions gave an excellent overall yield (80%), despite the fact that they involved rather complex glycosyl donors and acceptors. Thereafter, the Lev group at the 6-*O*-position of the central sugar residue in **16** was selectively removed with

hydrazine to give **7**. Glycosylation of **7** with **4**, **5**, and **6** in the presence of *p*TolSCl/AgOTf to install the branches was smooth, and gave fully protected target molecules **17**, **18**, and **19**, respectively, in very good yields. Global deprotection of **17**–**19** was carried out by a stepwise protocol to deal with the solubility problems associated with the various partially deprotected reaction intermediates. Thus, **17**–**19** were first treated with Zn and acetic acid in dichloromethane to reduce the azide group. After filtration to remove solids and concentration to remove solvents, the crude product was dissolved in acetic acid and water (5:1), and the mixture was heated at 60 °C to remove all of the benzylidene groups. Finally, the benzoyl groups were removed by treatment with sodium hydroxide in *tert*-butanol and water (4:1) to give the desired products **1**, **2**, and **3**, which were purified with a Sephadex-G25 size-exclusion column, and fully characterized with 1D and 2D NMR spectroscopy, as well as HRMS. Although the intermediates in the global deprotection process were not purified, the reactions were carefully monitored by MS to make sure that each step was complete. This was critical for the successful and clean global deprotection, and for product purification.



Scheme 3. Synthesis of target oligosaccharides **1**–**3**.

Conclusions

Research towards β-glucan-based antifungal vaccines has made promising progress in recent decades, but access to complex, structurally well-defined β-glucan oligosaccharides that could be used for detailed structure–activity relationship studies and for the preparation of glycoconjugate vaccines is a significant hindrance in this area. In this paper, we have described a new, highly convergent, and efficient strategy for the synthesis of branched β-glucan oligosaccharides. The strategy was demonstrated by the application of preactivation-based iterative one-pot glycosylation to the efficient construction of the intermediate oligosaccharide fragments and the target molecules. This approach can remarkably decrease the number of synthetic and purification steps compared to reported methods.[8b,15] Three complex β-glucan oligosaccharides with β-1,3- and β-1,6-oligoglucose branches were efficiently assembled by the new strategy. We observed that the structure and the size of the glycosyl donors and acceptors used for the preactivation-based glycosylation had little influence on the efficiency of the reactions, which suggests that this synthetic strategy may be broadly applicable for the construction of more complex oligosaccharides in good yields. For example, oligosaccharides with significantly larger branches and backbones could be readily assembled by the procedures shown in Scheme 2, and used to construct larger oligosaccharides by the procedures shown in Scheme 3. The synthetic targets were designed to bear a free amino group at their reducing end, which will facilitate their conjugation with other molecules, such as carrier proteins, through bifunctional linkers. The resulting glycoconjugates could then be used to investigate the functions of branches in β-glucans, gain insights into structure–activity relationships, and so on.

Experimental Section

General Methods: Chemicals and materials were obtained from commercial suppliers, and were used as received without additional purification unless otherwise noted. Molecular sieves (4 Å) were flame-dried under high vacuum, and were used immediately, after cooling under a N_2 atmosphere. Analytical TLC was carried out on silica gel 60 Å F_{254} plates, with detection by UV light and/or by charring with H_2SO_4 (15% v/v in EtOH). NMR spectra were recorded with a 400, 500, or 600 MHz spectrometer. Chemical shifts are reported in ppm (δ) downfield from tetramethylsilane, which was used as an internal reference. Mass spectrometry (MS) was carried out with either a Bruker Daltonics Ultraflex MALDI TOF mass spectrometer or a Waters LCT Premier XE high-resolution ESI TOF mass spectrometer.

***p*-Tolyl 2-*O*-Benzoyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (10):**[13] DDQ (5.78 g, 25.47 mmol) was added to a stirred solution of **13** (7.88 g, 12.73 mmol) in CH_2Cl_2 (400 mL) and water (22 mL) at room temperature. The reaction was stirred at room temp. for 8 h, then saturated aq. $NaHCO_3$ solution was added, and the mixture was extracted with CH_2Cl_2. The combined organic extracts were washed with saturated aq. $NaHCO_3$ solution, and dried with Na_2SO_4, and the solvent was evaporated in vacuo. The residue was purified by silica gel column chromatography (toluene/ethyl acetate, 15:1 to 10:1) to give **10** (5.48 g, 90%) as a white solid. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.14–8.02 (m, 2 H), 7.60 (t, J = 7.4 Hz, 1 H), 7.52–7.42 (m, 4 H), 7.36 (m, 5 H), 7.28–7.06 (m, 3 H), 5.55 (s, 1 H), 5.17–5.05 (t, J = 9.12 Hz, 1 H), 4.83 (d, J = 10.0 Hz, 1 H, 1-H), 4.41 (dd, J = 10.6, 4.9 Hz, 1 H), 4.04 (m, 1 H), 3.81 (t, J = 10.2 Hz, 1 H), 3.66–3.50 (m, 2 H), 2.76 (d, J = 3.2 Hz, 1 H), 2.34 (d, J = 8.8 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 165.88, 138.72, 136.79, 133.76, 133.43, 130.03, 129.73, 129.50, 129.33, 128.46, 128.34, 127.83, 126.26, 101.91, 86.76 (C-1), 80.61, 77.21, 77.00, 76.79, 73.73, 73.24, 70.39, 68.50, 21.18 ppm. MS (ESI TOF): calcd. for $C_{27}H_{26}NaO_6S$ [M + Na]$^+$ 501.1; found 501.1.

***p*-Tolyl 2,3-Di-*O*-Benzoyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (8):**[16] Benzoyl chloride (3.7 mL, 31.37 mmol) was added to a solution of **10** (10.00 g, 20.09 mmol), Et_3N (17.9 mL, 127.27 mmol), and DMAP (catalytic amount) in anhydrous CH_2Cl_2 (160 mL) at 0 °C. The reaction mixture was stirred for 12 h, then the mixture was washed with saturated aq. $NaHCO_3$ solution and brine, dried with Na_2SO_4, and concentrated under vacuum. The residue was purified by silica gel column chromatography (ethyl acetate/toluene, 1:20) to give **8** (11.44 g, 94%) as a white solid. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.98 (d, J = 7.3 Hz, 2 H, Ph), 7.93 (d, J = 7.3 Hz, 2 H, Ph), 7.52 (t, J = 7.4 Hz, 1 H, Ph), 7.47 (t, J = 7.4 Hz, 1 H, Ph), 7.43–7.21 (m, 11 H, Ph), 7.12 (d, J = 7.9 Hz, 2 H, Ph), 5.78 (t, J = 9.5 Hz, 1 H, 3-H), 5.53 (s, 1 H, CHPh), 5.45 (t, J = 9.6 Hz, 1 H, 2-H), 4.96 (d, J = 10.0 Hz, 1 H, 1-H), 4.45 (dd, J = 10.6, 4.9 Hz, 1 H, 6-H), 3.94–3.82 (m, 2 H, 4-H, 5-H), 3.74 (dd, J = 9.6, 4.9 Hz, 1 H, 6-H), 2.35 (s, 3 H, CH_3) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 165.56, 165.15, 138.74, 136.71, 133.73, 133.27, 133.05, 129.86, 129.77, 129.76, 129.37, 129.25, 129.01, 128.37, 128.26, 128.16, 127.90, 126.10, 101.44, 87.25 (C-1), 78.57, 77.22, 77.01, 76.80, 73.34, 71.07, 70.91, 68.53, 21.19 ppm. HRMS (ESI TOF): calcd. for $C_{34}H_{31}O_7S$ [M + H]$^+$ 583.1790; found 583.1799.

***p*-Tolyl 2,3-Di-*O*-Benzoyl-4-*O*-benzyl-1-thio-β-D-glucopyranoside (9):** A mixture of **8** (3.50 g, 6.00 mmol) and molecular sieves (4 Å; 8 g) in anhydrous THF (120 mL) was stirred at room temp. for 1 h, and then it was cooled to –40 °C. BH_3·THF (1 M solution in THF; 29.7 mL, 30.00 mmol) was added. The mixture was stirred for 15 min, then TMSOTf (1.41 mL, 7.80 mmol) was added, and the mixture was stirred at –40 °C for a further 1 h. The reaction mixture was slowly warmed to room temp. and stirred for 24 h. Then, saturated aq. $NaHCO_3$ solution (50 mL) was added at 0 °C to quench the reaction, and the reaction mixture was diluted with CH_2Cl_2 (400 mL). The mixture was filtered to remove insoluble materials, and the two phases were separated. The organic layer was washed with saturated aq. $NaHCO_3$ solution and brine, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography (ethyl acetate/toluene, 1:25) to give **9** (3.26 g, 93%) as a white solid. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.95 (dd, J = 8.2, 1.0 Hz, 2 H, Ph), 7.90 (dd, J = 8.2, 1.0 Hz, 2 H, Ph), 7.53–7.46 (m, 2 H, Ph), 7.40–7.32 (m, 6 H, Ph), 7.20–7.07 (m, 7 H, Ph), 5.72 (t, J = 9.4 Hz, 1 H, 3-H), 5.33 (t, J = 9.8 Hz, 1 H, 2-H), 4.89 (d, J = 10.0 Hz, 1 H, 1-H), 4.57 (s, 2 H, CH_2Ph), 4.00–3.94 (m, 1 H, 6-H), 3.89 (t, J = 9.5 Hz, 1 H, 4-H), 3.79 (m, 1 H, 6-H), 3.65–3.56 (m, 1 H, 5-H), 2.33 (s, 3 H), 2.08–1.95 (br., 1 H, OH) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 165.65, 165.29, 138.61, 137.08, 133.41, 133.22, 133.17, 129.85, 129.78, 129.71, 129.33, 129.26, 128.35, 128.16, 127.96, 86.29 (C-1), 79.53, 76.23, 75.33, 74.84, 70.88, 61.73, 21.17 ppm. HRMS (ESI TOF): calcd. for $C_{34}H_{33}O_7S$ [M + H]$^+$ 585.1947; found 585.1941.

***p*-Tolyl 2-*O*-Benzoyl-4-*O*-benzyl-3-*O*-(naphthalen-2-ylmethyl)-1-thio-β-D-glucopyranoside (14):**[13] Compound **14** (1.84 g, 92%) was

prepared from **13** (2.00 g, 3.23 mmol) by the same procedure described for **9**. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.99 (d, J = 7.32 Hz, 2 H, Ph), 7.70–7.67 (m, 1 H, Ph), 7.63–7.60 (m, 1 H, Ph), 7.57–7.51 (m, 3 H, Ph), 7.42–7.29 (m, 11 H, Ph), 7.27–7.24 (m, 1 H, Ph), 7.10 (d, J = 7.63 Hz, 2 H, Ph), 5.28 (dd, J = 9.77, 8.55 Hz, 1 H, 2-H), 4.93 (d, J = 11.60 Hz, 1 H, 1/2 CH_2Ar), 4.90 (d, J = 11.29 Hz, 1 H, 1/2 CH_2Ar), 4.82 (d, J = 11.29 Hz, 1 H, 1/2 CH_2Ar), 4.76 (d, J = 10.07 Hz, 1 H, 1-H), 4.71 (d, J = 10.68 Hz, 1 H, 1/2 CH_2Ar), 3.96–3.90 (m, 2 H, 3-H, 6-H), 3.78–3.71 (m, 2 H, 4-H, 6-H), 3.53–3.49 (m, 1 H, 5-H), 2.33 (s, 3 H, CH_3), 1.93 (br. s, 1 H, OH) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.20, 138.43, 137.73, 135.10, 133.32, 133.21, 133.07, 132.90, 129.78, 129.73, 128.56, 128.49, 128.36, 128.16, 128.10, 128.04, 127.85, 127.64, 126.90, 126.07, 125.94, 125.81, 86.36 (C-1), 83.91, 79.54, 77.62, 75.39, 75.23, 72.42, 62.04, 21.17 ppm. HRMS (ESI TOF): calcd. for $C_{38}H_{36}NaO_6S$ [M + Na]$^+$ 643.2130; found 643.2139.

***p*-Tolyl 2-*O*-Benzoyl-4-*O*-benzyl-6-*O*-levulinoyl-1-thio-β-D-glucopyranoside (11):** A mixture of **14** (3.72 g, 6.00 mmol), levulinic acid (0.84 g, 7.23 mmol), and EDC·HCl (1.38 g, 7.20 mmol) in CH_2Cl_2 (50 mL) was stirred at room temp. for 4 h. The reaction mixture was washed with water and brine, dried with Na_2SO_4, and concentrated under vacuum.

The residue was dissolved in a mixture of CH_2Cl_2 (100 mL) and water (1.5 mL) at room temp., and then DDQ (2.72 g, 12.00 mmol) was added. The resulting mixture was stirred at room temp. for 6 h, then it was washed with saturated aq. $NaHCO_3$ solution and brine, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (ethyl acetate/toluene, 1:10) to give **11** (3.10 g, 89%) as a foamy solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.16–8.06 (m, 2 H, Ph), 7.66–7.56 (m, 1 H, Ph), 7.49 (t, J = 7.8 Hz, 2 H, Ph), 7.39–7.21 (m, 7 H, Ph), 7.10 (d, J = 7.9 Hz, 2 H, Ph), 4.98 (t, J = 9.5 Hz, 1 H, 3-H), 4.87 (d, J = 11.2 Hz, 1 H, 1-H), 4.72 (dd, J = 15.6, 10.6 Hz, 2 H, CH_2Ph), 4.46 (dd, J = 11.8, 2.0 Hz, 1 H, 6-H), 4.28 (dd, J = 11.8, 5.2 Hz, 1 H, 6-H), 3.96 (td, J = 8.9, 2.6 Hz, 1 H, 3-H), 3.61 (m, 1 H, 5-H), 3.56–3.48 (m, 1 H, 4-H), 2.88 (d, J = 3.4 Hz, 1 H, OH), 2.77 (t, J = 6.6 Hz, 2 H, CH_2CO_2), 2.69–2.56 (m, 2 H, CH_2CO), 2.34 (s, 3 H, CH_3), 2.21 (s, 3 H, CH_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 206.50, 172.43, 166.43, 138.44, 137.74, 133.53, 133.48, 130.05, 129.63, 129.45, 128.59, 128.51, 128.26, 128.08, 85.70, 77.69, 77.59, 76.86, 74.97, 73.34, 63.28, 37.91, 29.92, 27.88, 21.19 ppm. HRMS (ESI TOF): calcd. for $C_{32}H_{35}O_8S$ [M + H]$^+$ 579.2053; found 579.2051.

***p*-Tolyl [2,3-Di-*O*-Benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-2-*O*-benzoyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (5):** A mixture of glycosyl donor **8** (300.0 mg, 0.52 mmol) and molecular sieves (4 Å; 1.50 g) in anhydrous CH_2Cl_2 (10 mL) was stirred at room temp. for 1 h, and then it was cooled to –78 °C. A solution of AgOTf (397.0 mg, 1.55 mmol) in dry acetonitrile (3 mL) was added, and then after 10 min *p*-TolSCl (74 μL, 0.52 mmol) was added by microsyringe. The mixture was stirred at –78 °C for a further 15 min, after which time TLC showed that **8** had been completely consumed. A solution of acceptor **10** (221.8 mg, 0.46 mmol) and TTBP (127.9 mg, 0.52 mmol) in CH_2Cl_2 (3 mL) was added. The mixture was stirred at –78 °C for 20 min, and then it was warmed to room temp., followed by filtration to remove the molecular sieves (4 Å). The filtrate was washed with saturated aq. $NaHCO_3$ solution and brine, dried with Na_2SO_4, and concentrated under vacuum. The residue was purified by silica gel column chromatography (ethyl acetate/toluene, 1:30) to give **5** (411.4 mg, 95%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.89 (d, J = 7.6 Hz, 2 H), 7.81 (d, J = 7.6 Hz, 2 H), 7.58 (t, J = 6.5 Hz, 4 H), 7.48–7.19 (m, 19 H), 7.08 (d, J = 7.9 Hz, 2 H), 5.69–5.56 (m, 2 H), 5.44 (t, J = 7.9 Hz, 1 H), 5.34 (dd, J = 17.9, 8.7 Hz, 2 H), 5.05 (d, J = 7.2 Hz, 1 H, 1-H″), 4.82 (d, J = 10.0 Hz, 1 H, 1-H′), 4.44 (dd, J = 10.5, 4.7 Hz, 1 H), 4.33–4.22 (m, 2 H), 3.95 (t, J = 9.5 Hz, 1 H), 3.90–3.82 (m, 2 H), 3.78 (t, J = 10.2 Hz, 1 H), 3.68–3.53 (m, 2 H), 2.34 (s, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.54, 164.90, 164.64, 138.50, 137.12, 136.84, 133.37, 133.07, 132.75, 129.83, 129.72, 129.41, 129.33, 129.08, 128.99, 128.51, 128.40, 128.37, 128.25, 128.15, 128.11, 126.15, 126.11, 101.52, 101.30, 100.72, 87.63, 79.56, 79.32, 78.30, 72.90, 72.35, 72.07, 70.75, 68.68, 68.60, 66.27, 21.19 ppm. HRMS (ESI TOF): calcd. for $C_{54}H_{49}NO_{13}S$ [M + H]$^+$ 937.2894; found 937.2864.

***p*-Tolyl [2,3-Di-*O*-Benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→6)-[2,3-di-*O*-benzoyl-4-*O*-benzyl-β-D-glucopyranosyl]-(1→6)-[2,3-di-*O*-benzoyl-4-*O*-benzyl-β-D-glucopyranosyl]-(1→6)-2,3-di-*O*-benzoyl-4-*O*-benzyl-1-thio-β-D-glucopyranoside (4):** A mixture of donor **8** (349.8 mg, 0.60 mmol) and activated molecular sieves (4 Å) in CH_2Cl_2 (8 mL) was stirred at room temp. for 1 h, and then it was cooled to –78 °C. A solution of AgOTf (462.5 mg, 1.80 mmol) in dry acetonitrile (1.5 mL) was added, and then after 10 min *p*TolSCl (86 μL, 0.60 mmol) was added by microsyringe. The mixture was stirred for a further 15 min, after which time TLC showed that **8** had been completely consumed. Then, a solution of acceptor **9** (316.2 mg, 0.54 mmol) and TTBP (122.1 mg, 0.54 mmol) in CH_2Cl_2 (2 mL) was added. The mixture was warmed to room temp. slowly over 1 h, and stirred at room temp. for a further 20 min. The mixture was then cooled to –78 °C for another round of glycosylation with **9** (288.1 mg, 0.49 mmol) as the glycosyl acceptor by the same protocol. This was followed by a third round of glycosylation, also with **9** (262.3 mg, 0.45 mmol) as the glycosyl acceptor. Finally, the reaction mixture was warmed to room temp., stirred for 20 min, and then quenched with saturated aq. $NaHCO_3$ solution. The mixture was filtered to remove insoluble materials, and the organic layer was washed with saturated aq. $NaHCO_3$ solution and brine, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (ethyl acetate/toluene, 1:12) to give **4** (395.7 mg, 45%) as a white solid. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.03 (d, J = 7.9 Hz, 2 H), 8.01–7.89 (m, 11 H), 7.85 (d, J = 8.0 Hz, 2 H), 7.60–7.04 (m, 40 H), 7.01 (t, J = 7.4 Hz, 1 H), 6.99–6.91 (m, 4 H), 6.88 (t, J = 7.5 Hz, 2 H), 6.73 (d, J = 7.7 Hz, 2 H), 5.85 (t, J = 9.6 Hz, 1 H), 5.78 (t, J = 9.5 Hz, 1 H), 5.71–5.60 (m, 3 H), 5.47 (dd, J = 10.7, 7.0 Hz, 3 H), 5.30 (t, J = 9.7 Hz, 1 H), 4.98–4.87 (m, 3 H, anomeric), 4.58 (d, J = 7.9 Hz, 1 H, anomeric), 4.35 (dt, J = 10.5, 5.2 Hz, 4 H), 4.19 (m, 5 H), 4.06 (d, J = 11.3 Hz, 1 H), 3.91 (m, 5 H), 3.74 (m, 4 H), 3.63 (d, J = 9.5 Hz, 1 H), 3.54 (dd, J = 11.5, 6.3 Hz, 1 H), 2.39 (s, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 165.79, 165.68, 165.64, 165.60, 165.29, 165.23, 165.10, 164.81, 138.08, 137.14, 137.06, 136.92, 134.31, 133.30, 133.16, 133.09, 133.01, 132.97, 132.88, 132.77, 130.02, 129.89, 129.82, 129.78, 129.73, 129.67, 129.62, 129.56, 129.49, 129.46, 129.39, 129.33, 128.95, 128.93, 128.58, 128.50, 128.40, 128.29, 128.26, 128.22, 128.19, 128.14, 127.98, 127.92, 127.88, 127.80, 127.54, 126.08, 102.93, 101.70, 101.10, 101.06, 85.45, 79.17, 78.38, 77.83, 76.69, 76.62, 75.61, 75.15, 74.96, 74.89, 74.86, 74.77, 73.66, 72.94, 72.48, 72.15, 71.99, 70.75, 69.75, 69.39, 68.88, 68.36, 66.82, 21.30 ppm. HRMS (ESI TOF): calcd. for $C_{115}H_{106}NO_{28}S$ [M + NH_4]$^+$ 1980.6622; found 1980.6481.

***p*-Tolyl [2,3-Di-*O*-Benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-2-*O*-benzoyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (6):** Compound **6** (415.3 mg, 43%) was prepared from **8** (475.0 mg, 0.82 mmol) and **10** (1st glycosylation: 341.5 mg, 0.72 mmol; 2nd

glycosylation: 310.8 mg, 0.65 mmol; 3rd glycosylation: 282.8 mg, 0.59 mmol) after three rounds of glycosylation reactions by the protocol described for **4**, and was purified by silica gel column chromatography (ethyl acetate/toluene, 1:12). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.90 (t, J = 7.6 Hz, 4 H), 7.81 (d, J = 7.4 Hz, 2 H), 7.70 (d, J = 7.5 Hz, 2 H), 7.67 (d, J = 7.4 Hz, 2 H), 7.60 (t, J = 7.4 Hz, 1 H), 7.54 (d, J = 7.4 Hz, 2 H), 7.52–7.11 (m, 34 H), 7.07 (d, J = 8.0 Hz, 2 H), 5.67 (t, J = 9.2 Hz, 1 H), 5.48 (dd, J = 10.4, 5.8 Hz, 2 H), 5.39 (s, 1 H), 5.27 (t, J = 6.5 Hz, 1 H), 5.16 (s, 1 H), 5.12 (d, J = 7.5 Hz, 1 H, anomeric), 5.07 (d, J = 6.4 Hz, 1 H, anomeric), 4.89–4.81 (m, 2 H, anomeric), 4.76 (t, J = 9.3 Hz, 1 H), 4.66 (d, J = 10.1 Hz, 1 H, anomeric), 4.50 (s, 1 H), 4.34 (dd, J = 10.5, 4.9 Hz, 1 H), 4.27 (dd, J = 10.5, 4.9 Hz, 1 H), 4.22–4.15 (m, 2 H), 4.14–4.07 (m, 2 H), 3.94 (ddd, J = 18.8, 15.5, 9.3 Hz, 3 H), 3.76 (dt, J = 14.0, 9.6 Hz, 2 H), 3.71–3.57 (m, 4 H), 3.53–3.37 (m, 3 H), 3.12 (t, J = 9.5 Hz, 1 H), 2.32 (s, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 165.48, 165.08, 164.86, 164.57, 164.54, 138.23, 137.30, 137.09, 136.88, 133.60, 133.17, 132.98, 132.73, 130.16, 129.82, 129.76, 129.70, 129.66, 129.45, 129.39, 129.11, 129.08, 129.04, 129.01, 128.94, 128.77, 128.47, 128.39, 128.34, 128.27, 128.23, 128.18, 128.12, 127.92, 126.47, 126.18, 126.14, 126.05, 125.31, 101.99, 101.31, 101.00, 100.62, 99.74, 97.62, 97.11, 87.89, 78.81, 78.60, 78.45, 77.74, 77.19, 75.15, 74.71, 73.19, 72.87, 72.78, 72.63, 72.29, 70.68, 68.69, 68.49, 66.21, 65.86, 65.26, 21.13 ppm. HRMS (ESI TOF): calcd. for $C_{94}H_{88}NO_{25}S$ [M + NH_4] 1662.5366; found 1662.5244.

***p*-Tolyl [2-*O*-Benzoyl-4,6-*O*-benzylidene-3-*O*-(naphthalen-2-ylmethyl)-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-2-*O*-benzoyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (15):** Compound **15** (312.5 mg, 42%) was prepared from **13** (475.0 mg, 0.82 mmol) and **10** (1st glycosylation: 258.4 mg, 0.54 mmol; 2nd glycosylation: 235.2 mg, 0.49 mmol; 3rd glycosylation: 214.4 mg, 0.45 mmol) after three rounds of glycosylation reactions by the same protocol described for **4**, and was purified by silica gel column chromatography (ethyl acetate/toluene, 1:12). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.86 (d, J = 7.3 Hz, 2 H), 7.79 (d, J = 7.3 Hz, 2 H), 7.75 (d, J = 7.4 Hz, 2 H), 7.69 (d, J = 8.0 Hz, 1 H), 7.62 (d, J = 7.3 Hz, 2 H), 7.59–7.14 (m, 40 H), 7.06 (d, J = 8.0 Hz, 2 H), 5.53 (s, 1 H), 5.44 (s, 1 H), 5.32 (t, J = 7.8 Hz, 1 H), 5.17 (t, J = 5.8 Hz, 1 H), 5.00–4.94 (m, 3 H), 4.90 (d, J = 12.4 Hz, 1 H), 4.85–4.75 (m, 4 H), 4.66 (d, J = 10.1 Hz, 1 H, anomeric), 4.61 (s, 1 H), 4.35 (dd, J = 10.5, 4.9 Hz, 1 H), 4.20 (dd, J = 10.4, 5.0 Hz, 1 H), 4.16–4.04 (m, 4 H), 3.95 (t, J = 8.8 Hz, 1 H), 3.91–3.86 (m, 2 H), 3.83 (t, J = 8.7 Hz, 1 H), 3.72 (td, J = 10.2, 7.4 Hz, 2 H), 3.58 (t, J = 9.1 Hz, 3 H), 3.49–3.37 (m, 4 H), 3.24 (t, J = 9.4 Hz, 1 H), 2.32 (s, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 164.99, 164.82, 164.54 (2 C), 138.25, 137.33, 137.29, 137.24, 137.07, 135.38, 133.50, 133.26, 133.17, 133.10, 133.03, 132.83, 132.74, 129.81, 129.78, 129.75, 129.70, 129.63, 129.56, 129.44, 129.41, 129.37, 129.04, 129.01, 128.96, 128.87, 128.63, 128.49, 128.39, 128.36, 128.24, 128.07, 127.97, 127.90, 127.88, 127.56, 126.67, 126.42, 126.24, 126.09, 126.00, 125.77, 125.62, 125.30, 101.93, 101.14, 100.87, 100.84, 99.30, 97.99, 96.93, 87.93, 81.22, 78.57, 78.49, 78.17, 77.10, 75.69, 74.29, 73.72, 73.45, 73.20, 73.01, 72.66, 70.67, 68.72, 68.51, 66.01, 65.67, 65.38, 21.15 ppm. HRMS (ESI TOF): calcd. for $C_{98}H_{92}NO_{24}S$ [M + NH_4]$^+$ 1698.5730; found 1698.5598.

2-Azidoethyl [2-*O*-Benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranoside (12): Glycosylation of azidoethanol (15.8 mg, 0.18 mmol) with **15** (305.5 mg, 0.18 mmol) by the same protocol described for **5** gave a crude trisaccharide intermediate. This material was dissolved in CH_2Cl_2 (10 mL) and water (0.5 mL), and treated with DDQ (82.5 mg, 0.36 mmol). The reaction mixture was stirred at room temp. for 6 h, then it was washed with saturated aq. $NaHCO_3$ solution and brine, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (ethyl acetate/toluene, 1:8) to give **12** (213.6 mg, 78%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.95 (d, J = 7.8 Hz, 2 H), 7.90 (d, J = 7.9 Hz, 2 H), 7.82 (d, J = 7.8 Hz, 2 H), 7.70 (d, J = 7.9 Hz, 2 H), 7.62–7.16 (m, 32 H), 5.57 (s, 1 H), 5.44 (s, 1 H), 5.21 (dd, J = 9.3, 6.6 Hz, 2 H, anomeric), 5.08 (d, J = 7.4 Hz, 1 H, anomeric), 5.03 (d, J = 5.2 Hz, 1 H, anomeric), 4.97 (t, J = 8.1 Hz, 1 H), 4.91–4.85 (m, 2 H), 4.59 (d, J = 7.6 Hz, 1 H, anomeric), 4.37 (dd, J = 10.4, 4.8 Hz, 1 H), 4.23 (dd, J = 10.4, 4.9 Hz, 1 H), 4.14 (m, 3 H), 3.98 (m, 3 H), 3.89 (dd, J = 10.4, 4.8 Hz, 1 H), 3.80–3.38 (m, 11 H), 3.33–3.22 (m, 2 H), 2.71 (br. s, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.82, 164.68, 164.64, 164.60, 137.34, 137.26, 137.13, 137.06, 133.62, 133.41, 133.16, 133.11, 129.91, 129.77, 129.72, 129.68, 129.46, 129.41, 129.31, 129.25, 129.11, 129.07, 128.94, 128.66, 128.59, 128.40, 128.37, 128.33, 128.29, 128.26, 128.07, 126.42, 126.33, 126.11, 125.34, 101.88, 101.76, 101.28, 101.16, 100.79, 98.85, 98.42, 97.06, 80.81, 78.74, 78.30, 77.52, 76.94, 75.08, 74.88, 74.43, 73.78, 73.50, 72.65, 72.49, 68.71, 68.65, 67.89, 66.56, 66.04, 65.58, 50.68 ppm. HRMS (ESI TOF): calcd. for $C_{82}H_{81}N_4O_{25}$ [M + NH_4]$^+$ 1521.5190; found 1521.5090.

2-Azidoethyl [2,3-Di-*O*-Benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4-*O*-benzyl-6-*O*-levulinoyl-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranoside (16): A mixture of **6** (329.1 mg, 0.20 mmol) and activated molecular sieves (4 Å) in CH_2Cl_2 (4 mL) was stirred at room temp. for 1 h, and then it was cooled to –78 °C. A solution of AgOTf (154.2 mg, 0.60 mmol) in dry acetonitrile (1.5 mL) was added, and then after 10 min *p*TolSCl (29 μL, 0.20 mmol) was added by microsyringe. The mixture was stirred for a further 15 min, after which time TLC indicated that donor **6** had been completely consumed. A solution of **11** (104.2 mg, 0.18 mmol) and TTBP (44.7 mg, 0.18 mmol) in CH_2Cl_2 (1.5 mL) was added, and the mixture was slowly warmed to room temp. over 1 h. The mixture was stirred at room temp. for a further 20 min, then it was cooled to –78 °C for glycosylation with **12** (246.4 mg, 0.16 mmol) by the same protocol using AgOTf (138.7 mg, 0.54 mmol in 1 mL acetonitrile), *p*TolSCl (26 μL, 0.18 mmol), and TTBP (40.7 mg, 0.16 mmol). The reaction was finally quenched with saturated aq. $NaHCO_3$ solution, and filtered to remove insoluble materials. The organic layer was washed with saturated aq. $NaHCO_3$ solution and brine, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (ethyl acetate/toluene, 1:10) to give **16** (455.3 mg, 80%). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.89 (d, J = 8.2 Hz, 2 H), 7.86 (d, J = 8.1 Hz, 2 H), 7.74 (m, 10 H), 7.62 (m, 8 H), 7.55–7.13 (m, 73 H), 5.65 (t, J = 9.2 Hz, 1 H), 5.53 (s, 1 H), 5.46–5.42 (m, 1 H), 5.38 (s, 1 H), 5.30 (s, 1 H), 5.13 (dd, J = 9.7, 6.6 Hz, 2 H), 4.98–4.73 (m, 17 H), 4.73–4.68 (m, 2 H), 4.55 (d, J = 7.6 Hz, 1 H), 4.33 (dd, J = 10.3, 4.8 Hz, 1 H), 4.25 (td, J = 11.0, 4.6 Hz, 2 H), 4.20–4.01 (m, 11 H), 4.00–3.84 (m, 8 H), 3.78–3.67 (m, 3 H), 3.63–3.34 (m, 20 H), 3.26 (ddd, J = 13.9, 13.2, 7.1 Hz, 5 H), 2.59 (dd, J = 11.3, 6.3 Hz, 2 H), 2.44 (dd, J = 10.9, 6.3 Hz, 2 H), 2.10 (s, 3 H) ppm.

^{13}C NMR (150 MHz, $CDCl_3$): δ = 206.42, 172.46, 170.62, 165.47, 165.11, 164.69, 164.55, 164.48, 138.18, 137.86, 137.46, 137.30, 137.24, 137.18, 136.91, 133.67, 133.58, 133.48, 133.35, 133.18, 133.00, 129.88, 129.77, 129.72, 129.64, 129.54, 129.48, 129.42, 129.33, 129.17, 129.07, 128.96, 128.65, 128.53, 128.47, 128.42, 128.30, 128.26, 128.11, 127.73, 126.48, 126.41, 126.34, 126.15, 126.08, 125.34, 101.98, 101.50, 101.31, 101.25, 101.21, 101.16, 101.08, 100.80, 99.19, 99.11, 98.40, 98.01, 97.46, 97.11, 96.79, 96.70, 79.31, 78.78, 78.75, 78.67, 78.36, 77.94, 77.91, 77.58, 77.27, 75.26, 75.02, 74.96, 74.70, 74.60, 74.45, 74.15, 73.79, 73.64, 73.56, 73.23, 73.15, 73.02, 72.57, 72.49, 72.31, 72.05, 68.72, 68.65, 67.94, 66.49, 66.39, 66.27, 65.62, 65.53, 63.75, 50.66, 37.87, 29.85, 29.53, 27.90 ppm. HRMS (ESI TOF): calcd. for $C_{194}H_{181}N_3O_{58}$ $[M + 2H]^{2+}$ 1740.0653; found 1740.0428.

2-Azidoethyl [2,3-Di-*O*-Benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4-*O*-benzyl-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranoside (7): A mixture of **16** (420.0 mg, 120.7 μmol) and hydrazine [0.5 M solution in pyridine/acetic acid (4:1) buffer; 10 mL] was stirred under an Ar atmosphere at room temp. for 1 h. Then 2,4-pentanedione (1 mL) was added, and the stirring was continued for a further 20 min. The mixture was diluted with CH_2Cl_2, washed sequentially with saturated aq. $NaHCO_3$, $CuSO_4$, and NH_4Cl solutions, dried with Na_2SO_4, and concentrated under vacuum. The residue was purified by silica gel column chromatography (ethyl acetate/toluene, 1:8) to give **7** (380.6 mg, 93%) as a white foamy solid. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.90 (d, J = 7.6 Hz, 2 H), 7.86 (d, J = 7.6 Hz, 2 H), 7.77 (d, J = 7.7 Hz, 2 H), 7.73–7.57 (m, 16 H), 7.55–7.42 (m, 11 H), 7.42–7.19 (m, 62 H), 5.66 (t, J = 9.2 Hz, 1 H), 5.52 (s, 1 H), 5.48–5.43 (m, 1 H), 5.39 (s, 1 H), 5.27 (s, 1 H), 5.13 (dd, J = 9.5, 4.2 Hz, 2 H), 4.93–4.79 (m, 14 H), 4.78–4.70 (m, 5 H), 4.55 (d, J = 7.6 Hz, 1 H), 4.34 (dd, J = 10.4, 4.7 Hz, 1 H), 4.25 (dt, J = 10.7, 5.3 Hz, 2 H), 4.18–4.08 (m, 7 H), 4.06–4.01 (m, 2 H), 3.99–3.85 (m, 8 H), 3.76–3.68 (m, 2 H), 3.66–3.58 (m, 3 H), 3.57–3.36 (m, 20 H), 3.34–3.21 (m, 5 H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$): δ = 165.43, 165.07, 164.66, 164.62, 164.60, 164.57, 164.54, 164.52, 164.47, 164.40, 138.30, 137.29, 137.20, 137.17, 137.13, 136.87, 133.51, 133.44, 133.36, 133.32, 133.10, 132.96, 129.81, 129.75, 129.72, 129.62, 129.47, 129.39, 129.29, 129.24, 129.17, 129.08, 129.02, 128.95, 128.62, 128.57, 128.54, 128.47, 128.43, 128.38, 128.35, 128.29, 128.26, 128.21, 128.16, 128.11, 128.10, 128.07, 127.86, 127.69, 126.43, 126.34, 126.32, 126.29, 126.28, 126.26, 126.12, 126.04, 101.94, 101.44, 101.30, 101.24, 101.14, 101.11, 101.09, 100.78, 99.13, 99.06, 98.27, 98.23, 97.61, 97.44, 97.35, 96.87, 78.89, 78.69, 78.67, 78.34, 78.04, 77.95, 77.58, 77.46, 77.22, 75.50, 75.24, 75.02, 74.86, 74.83, 74.66, 74.34, 74.22, 73.78, 73.56, 73.53, 73.30, 73.26, 73.12, 72.94, 72.53, 72.45, 72.27, 68.69, 68.61, 67.91, 66.49, 66.29, 66.23, 65.62, 65.58, 65.54, 65.49, 62.13, 50.66 ppm. HRMS (ESI TOF): calcd. for $C_{189}H_{181}N_5O_{56}$ $[M + 2NH_4]^{2+}$ 1708.0734; found 1708.0634.

2-Azidoethyl [2,3-Di-*O*-Benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4-*O*-benzyl-6-*O*-{[2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→6)-[2,3-di-*O*-benzoyl-4-*O*-benzyl-β-D-glucopyranosyl]-(1→6)-[2,3-di-*O*-benzoyl-4-*O*-benzyl-β-D-glucopyranosyl]-(1→6)-2,3-di-*O*-benzoyl-4-*O*-benzyl-β-D-glucopyranosyl}-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranoside (17): Compound **17** (155.0 mg, 83%) was prepared from **4** (77.4 mg, 39.4 μmol) and **7** (120.0 mg, 35.5 μmol) by the same protocol described for **5**, and was purified by silica gel column chromatography (ethyl acetate/toluene, 1:12). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.37–6.69 (m, 155 H), 5.82 (d, J = 9.6 Hz, 1 H), 5.75 (m, 2 H), 5.69–5.64 (m, 2 H), 5.61–5.56 (m, 2 H), 5.49–5.46 (m, 1 H), 5.45–5.38 (m, 3 H), 5.31 (s, 1 H), 5.21 (d, J = 7.6 Hz, 1 H), 5.14 (m, 1 H), 5.09 (m, 1 H), 5.04–4.67 (m, 20 H), 4.65–4.57 (m, 4 H), 4.51 (m, 1 H), 4.41 (d, J = 10.8 Hz, 2 H), 4.36 (d, J = 6.2 Hz, 2 H), 4.31–4.24 (m, 4 H), 4.23–4.04 (m, 15 H), 4.03–3.74 (m, 19 H), 3.72–3.33 (m, 22 H), 3.32–3.22 (m, 5 H), 3.17 (d, J = 8.5 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 165.75, 165.72, 165.69, 165.40, 165.30, 165.07, 164.88, 164.81, 164.72, 164.62, 164.57, 164.50, 164.42, 163.91, 138.83, 137.74, 137.39, 137.35, 137.29, 137.21, 137.18, 137.12, 136.91, 134.45, 133.57, 133.22, 133.11, 133.07, 132.99, 132.93, 132.82, 132.64, 132.58, 130.08, 129.92, 129.74, 129.70, 129.52, 129.45, 129.40, 129.32, 129.22, 129.18, 129.10, 129.00, 128.92, 128.84, 128.77, 128.69, 128.48, 128.44, 128.36, 128.26, 128.21, 128.16, 128.12, 128.06, 127.99, 127.86, 127.80, 127.65, 127.49, 127.39, 126.87, 126.38, 126.35, 126.25, 126.17, 126.12, 126.07, 103.55, 102.49, 101.81, 101.63, 101.42, 101.30, 101.25, 101.15, 100.89, 100.80, 100.72, 100.66, 100.60, 98.73, 98.57, 97.91, 97.81, 97.57, 97.31, 96.68, 78.91, 78.83, 78.77, 78.22, 78.15, 78.03, 77.95, 77.53, 76.38, 75.89, 75.64, 75.53, 75.36, 75.11, 75.02, 74.87, 74.81, 74.63, 74.25, 73.98, 73.61, 73.30, 73.21, 73.10, 72.94, 72.64, 72.37, 72.33, 72.01, 68.65, 68.01, 67.84, 66.83, 66.51, 66.25, 65.63, 65.37, 60.03, 50.65 ppm. MS (MALDI TOF): calcd. for $C_{297}H_{267}KN_3O_{84}$ $[M + K]^+$ 5257.6; found 5257.9.

2-Azidoethyl [2,3-Di-*O*-Benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4-*O*-benzyl-6-*O*-{[2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl}-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranoside (18): Compound **18** (126.6 mg, 85%) was prepared from **5** (36.9 mg, 39.4 μmol) and **7** (120.0 mg, 35.5 μmol) by the protocol described for **5**, and was purified by silica gel column chromatography (ethyl acetate/toluene, 1:15). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.87 (m, 6 H), 7.76 (m, 3 H), 7.73–6.98 (m, 111 H), 5.67–5.63 (m, 1 H), 5.61–5.58 (m, 1 H), 5.55–5.49 (m, 2 H), 5.47–5.40 (m, 2 H), 5.37 (d, J = 7.5 Hz, 2 H), 5.21 (dd, J = 11.5, 5.1 Hz, 2 H), 5.15–5.09 (m, 2 H), 4.99–4.93 (m, 2 H), 4.91 (d, J = 5.3 Hz, 2 H), 4.87–4.69 (m, 13 H), 4.64 (d, J = 6.0 Hz, 2 H), 4.55 (dd, J = 14.0, 8.2 Hz, 2 H), 4.45 (d, J = 7.9 Hz, 1 H), 4.33 (s, 2 H), 4.24 (s, 2 H), 4.14 (d, J = 7.1 Hz, 3 H), 4.11–4.04 (m, 5 H), 4.00–3.81 (m, 11 H), 3.74 (dt, J = 18.7, 9.7 Hz, 5 H), 3.67–3.16 (m, 32 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 165.50, 165.43, 165.07, 164.86, 164.63, 164.59, 164.53, 164.20, 138.50, 137.57, 137.33, 137.28, 137.16, 136.87, 136.84, 133.42, 133.35, 133.29, 133.21, 133.14, 133.06, 132.98, 132.94, 132.68, 129.79, 129.70, 129.67, 129.61, 129.52, 129.48, 129.38, 129.36, 129.32, 129.21, 129.07, 129.01, 128.98, 128.93, 128.58, 128.48, 128.44, 128.39, 128.36, 128.25, 128.20, 128.14, 128.11, 128.06, 127.85, 127.68, 127.59, 127.43, 126.53, 126.43, 126.39, 126.29, 126.27, 126.11, 126.04, 101.90, 101.62, 101.43, 101.29, 101.22, 101.10, 100.91, 100.77, 100.66,

99.09, 98.54, 98.46, 98.20, 97.40, 96.93, 96.87, 96.64, 79.27, 78.78, 78.68, 78.41, 78.32, 78.12, 77.85, 77.56, 75.32, 75.26, 74.75, 74.66, 74.55, 73.87, 73.66, 73.55, 73.51, 73.43, 73.36, 72.99, 72.93, 72.81, 72.74, 72.57, 72.50, 72.44, 72.33, 72.28, 68.64, 68.60, 68.21, 67.87, 66.47, 66.31, 66.22, 66.16, 65.62, 65.55, 65.40, 60.03, 50.64 ppm. MS (MALDI TOF): calcd. for $C_{236}H_{213}KN_3O_{69}$ $[M + K]^+$ 4231.3; found 4231.5.

2-Azidoethyl [2,3-Di-*O*-Benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4-*O*-benzyl-6-*O*-{[2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl}-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-[2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl]-(1→3)-2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranoside (19): Compound **19** (135.8 mg, 78%) was prepared from **6** (64.8 mg, 39.4 μmol) and **7** (120.0 mg, 35.5 μmol) by the same protocol described for **5**, and was purified by silica gel column chromatography (ethyl acetate/toluene, 1:12). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.05–6.90 (m, 140 H), 5.64 (m, 2 H), 5.51 (s, 1 H), 5.44 (m, 3 H), 5.36 (d, J = 14.3 Hz, 3 H), 5.27 (m, 2 H), 5.18 (m, 1 H), 5.15–5.08 (m, 3 H), 5.00 (d, J = 5.5 Hz, 2 H), 4.94–4.64 (m, 22 H), 4.54 (d, J = 7.6 Hz, 1 H), 4.35–4.30 (m, 2 H), 4.22 (dd, J = 10.1, 4.6 Hz, 4 H), 4.16–4.06 (m, 8 H), 4.03 (d, J = 8.3 Hz, 1 H), 3.99–3.80 (m, 13 H), 3.70 (ddd, J = 33.2, 21.1, 11.0 Hz, 6 H), 3.62–3.21 (m, 33 H), 3.15 (d, J = 8.8 Hz, 1 H), 3.06–3.01 (m, 1 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 165.44, 165.05, 165.00, 164.95, 164.78, 164.65, 164.61, 164.55, 164.51, 164.48, 164.30, 164.19, 138.57, 137.60, 137.30, 137.19, 137.16, 136.88, 133.47, 133.39, 133.23, 133.15, 133.10, 132.96, 129.83, 129.75, 129.71, 129.67, 129.47, 129.43, 129.39, 129.29, 129.20, 129.06, 129.01, 128.92, 128.62, 128.56, 128.54, 128.50, 128.41, 128.37, 128.26, 128.21, 128.11, 128.07, 128.01, 127.65, 127.54, 126.64, 126.50, 126.42, 126.29, 126.12, 126.04, 101.95, 101.73, 101.55, 101.42, 101.30, 101.23, 101.15, 100.98, 100.91, 100.76, 100.65, 99.64, 99.27, 99.07, 98.93, 98.83, 98.42, 98.23, 97.47, 97.02, 96.79, 96.66, 78.74, 78.68, 78.53, 78.49, 78.30, 77.96, 77.88, 77.66, 77.60, 77.55, 77.40, 75.67, 75.36, 75.13, 74.91, 74.66, 74.50, 74.16, 74.02, 73.88, 73.73, 73.60, 73.49, 73.41, 73.18, 73.11, 73.06, 72.76, 72.66, 72.51, 72.44, 72.28, 68.65, 68.43, 68.24, 67.91, 66.47, 66.23, 65.65, 65.58, 65.53, 65.45, 60.39, 60.03, 50.65 ppm. MS (MALDI TOF): calcd. for $C_{276}H_{249}KN_3O_{81}$ $[M + K]^+$ 4939.5; found 4939.4.

2-Aminoethyl β-D-Glucopyranosyl-(1→3)-β-D-glucopyranosyl-(1→3)-β-D-glucopyranosyl-(1→3)-β-D-glucopyranosyl-(1→3)-{6-*O*-[β-D-glucopyranosyl-(1→6)-β-D-glucopyranosyl-(1→6)-β-D-glucopyranosyl-(1→6)-β-D-glucopyranosyl]-β-D-glucopyranosyl}-(1→3)-β-D-glucopyranosyl-(1→3)-β-D-glucopyranosyl-(1→3)-β-D-glucopyranosyl-(1→3)-β-D-glucopyranoside (1): Acetic acid (4 drops) and zinc powder (20 mg) were added to a solution of **17** (20.0 mg, 3.8 μmol) in CH_2Cl_2 (4 mL). The mixture was vigorously stirred at room temp. for 24 h, then it was filtered through a Celite pad, and concentrated under vacuum.

The residue was dissolved in AcOH and H_2O (5:1; 15 mL), and the solution was heated at 60 °C for 24 h. The solvents were removed in vacuo, and coevaporated with toluene (5×).

The resulting residue was dissolved in *t*BuOH and H_2O (4:1; 15 mL), and a solution of NaOH (15 mg) in H_2O (1.5 mL) was added in portions. The mixture was heated at 40 °C for 24 h, then the solvents were removed by lyophilization. The residue was dissolved in water, and the solution was neutralized with HCl (0.25 N), and then lyophilized. The crude product was purified on a Sephadex G-25 gel filtration column with water as the eluent. Lyophilization gave **1** (7.1 mg, 87%) as a white fluffy solid. ^{1}H NMR (600 MHz, D_2O): δ = 4.58 (m, 8 H), 4.39–4.33 (m, 5 H), 4.08–4.02 (m, 4 H), 3.97–3.94 (m, 1 H), 3.77 (m, 10 H), 3.69 (m, 5 H), 3.65–3.50 (m, 18 H), 3.50–3.26 (m, 34 H), 3.26–3.11 (m, 9 H), 3.10 (t, J = 4.8 Hz, 1 H) ppm. HRMS (ESI TOF): calcd. for $C_{80}H_{138}NNaO_{66}$ $[M + H + Na]^{2+}$ 1095.8686; found 1095.8658.

2-Aminoethyl β-D-Glucopyranosyl-(1→3)-β-D-glucopyranosyl-(1→3)-β-D-glucopyranosyl-(1→3)-β-D-glucopyranosyl-(1→3)-{6-*O*-[β-D-glucopyranosyl-(1→3)-β-D-glucopyranosyl]-β-D-glucopyranosyl}-(1→3)-β-D-glucopyranosyl-(1→3)-β-D-glucopyranosyl-(1→3)-β-D-glucopyranosyl-(1→3)-β-D-glucopyranoside (2): Compound **2** (5.8 mg, 92%) was prepared from **18** (15.0 mg, 3.6 μmol) by the same protocol described for **1**. ^{1}H NMR (600 MHz, D_2O): δ = 4.58 (m, 9 H), 4.40 (d, J = 8.2 Hz, 2 H), 4.06 (d, J = 10.7 Hz, 1 H), 4.00–3.95 (m, 1 H), 3.83–3.71 (m, 12 H), 3.58 (m, 20 H), 3.41 (m, 30 H), 3.26–3.23 (m, 2 H), 3.22–3.18 (m, 2 H), 3.12 (d, J = 4.7 Hz, 2 H) ppm. HRMS (ESI TOF): calcd. for $C_{68}H_{118}NO_{56}$ $[M + H]^+$ 1844.6416; found 1844.6464.

2-Aminoethyl β-D-Glucopyranosyl-(1→3)-β-D-glucopyranosyl-(1→3)-β-D-glucopyranosyl-(1→3)-β-D-glucopyranosyl-(1→3)-{6-*O*-[β-D-glucopyranosyl-(1→3)-β-D-glucopyranosyl-(1→3)-β-D-glucopyranosyl-(1→3)-β-D-glucopyranosyl]-β-D-glucopyranosyl}-(1→3)-β-D-glucopyranosyl-(1→3)-β-D-glucopyranosyl-(1→3)-β-D-glucopyranosyl-(1→3)-β-D-glucopyranoside (3): Compound **3** (6.0 mg, 85%) was prepared from **19** (15.0 mg, 3.1 μmol) by the same protocol described for **1**. ^{1}H NMR (600 MHz, D_2O): δ = 4.60 (m, 11 H), 4.39 (d, J = 7.8 Hz, 2 H), 4.06 (d, J = 12.1 Hz, 1 H), 3.98–3.93 (m, 1 H), 3.77 (m, 14 H), 3.58 (m, 25 H), 3.49–3.28 (m, 35 H), 3.25 (t, J = 8.0 Hz, 2 H), 3.20 (t, J = 8.6 Hz, 2 H), 3.09 (s, 2 H) ppm. HRMS (ESI TOF): calcd. for $C_{80}H_{138}NNaO_{66}$ $[M + H + Na]^{2+}$ 1095.8686; found 1095.8641.

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