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Synthesis of Oligosaccharides Related to a Biodynamic Saponin from *Calamus Insignis* as Their Propargyl Glycosides

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The total synthesis of the carbohydrate portion (penta- and tetrasaccharides) of steroidal saponins, isolated from *Calamus insignis*, is reported. A simple route is followed, starting from commercially available D-glucose and L-rhamnose, through high-yielding protecting group manipulation strategies. Sulfuric acid immobilized on silica (H_2SO_4/silica) was used as an effective Brönsted acid source in conjunction with *N*-iodosuccinimide for activation of thioglycosides or alone for trichloroacetimidate donors in key glycosylation steps.

Introduction

With the growing interest in carbohydrate-based drug design, carbohydrate-containing natural products such as saponins or flavonoids have gained a great deal of importance in recent times. Even though numerous plants are used as folk medicines for various illnesses, the active constituents have been largely uncharacterized until recently. Steroidal saponins are glycosylated plant secondary metabolites that are found in many major food crops,[1] synthesized by plants as part of their normal programme of growth and development. Examples include plants that are exploited as sources of drugs, such as ginseng and liquorice, and also crop plants, such as legumes and oats.[2] It is assumed that they act as preformed chemical barriers against fungal attack as many saponins have potent antifungal properties and are present in healthy plants in high concentration.[3] Apart from their role in the plant kingdom, saponins often show promising bioactivities such as cell-growth inhibition or cell-cycle inhibition, which in turn, opens up a new dimension in drug discovery.[4] One common feature of all saponins is the presence of a sugar chain attached to the aglycon at the C-3 hydroxy position. The sugar chains differ substantially between saponins but are often branched and may consist of up to five sugar units (usually selected from glucose, arabinose, glucuronic acid, xylose or rhamnose).[5] An understanding of the glycosylation process, which is believed to be the terminal stage in the saponin biosynthesis, is important since the presence of the C-3 sugar chain is critical for saponin biological activity.[6] As the isolation of these saponins from natural sources is not easy, in order to establish the order of events in saponin biosynthesis and evaluate the medicinal properties associated with the saponins, synthetic saccharide fragments are needed.[7] Smart synthetic strategies will provide a large-scale source of these oligosaccharides so that they can be used as therapeutics,[8] if they are found suitable for those purposes.

Calamus insignis, a kind of rattan that grows widely in tropical regions of Southeast Asia, southern China and the western Pacific, is used as a medicinal agent. During the search for biodynamic natural products having cell-growth inhibitory or cell-cycle inhibitory activities, Ishibashi et al.[9] isolated a group of spirostanol (**A**–**D**) saponins and a furostanol (**E**) saponin from *Calamus insignis* (Figure 1). The spirostanols (**A**–**D**) showed growth-inhibitory activity against HeLa cells at low concentrations ($IC_{50} < 10\ \mu\text{M}$). Moreover, spirostanol **A** showed cell-cycle inhibitory activity by arresting the G2/M phase HeLa cell-cycle progression at concentrations of 1.5 μM and 2.9 μM. Recently, Yu et al.[10] clearly demonstrated the importance of the sugar chain on the haemolytic and cytotoxic properties of a saponin. In the continuation of our constant effort toward the synthesis of carbohydrate-containing natural products,[11] herein we report a simple route for the synthesis of the tetrasaccharide (**1**) and pentasaccharide (**2**) parts of these natural products as their propargyl glycosides (Figure 2).

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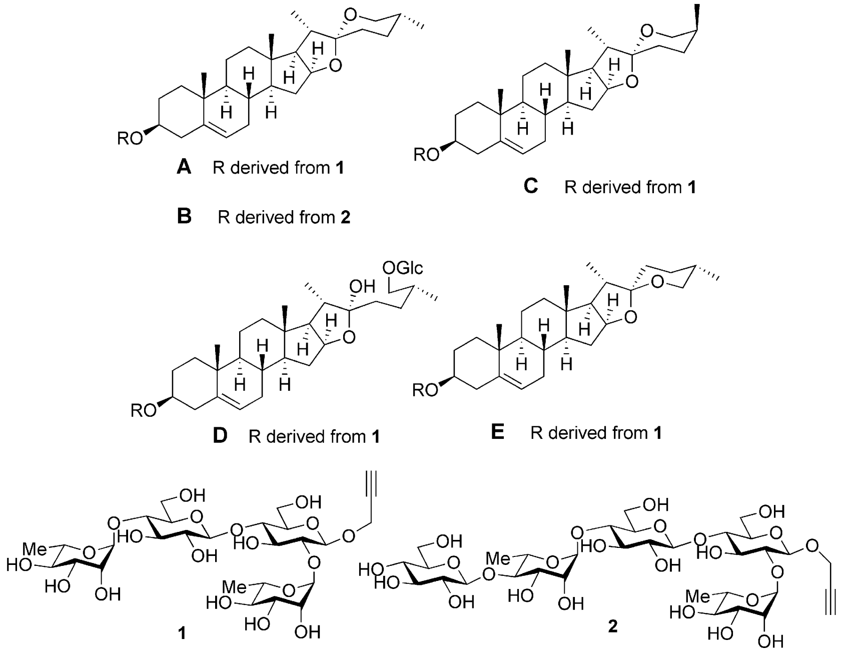


Figure 1. Structures of the saponins isolated from *Calamus insignis.*

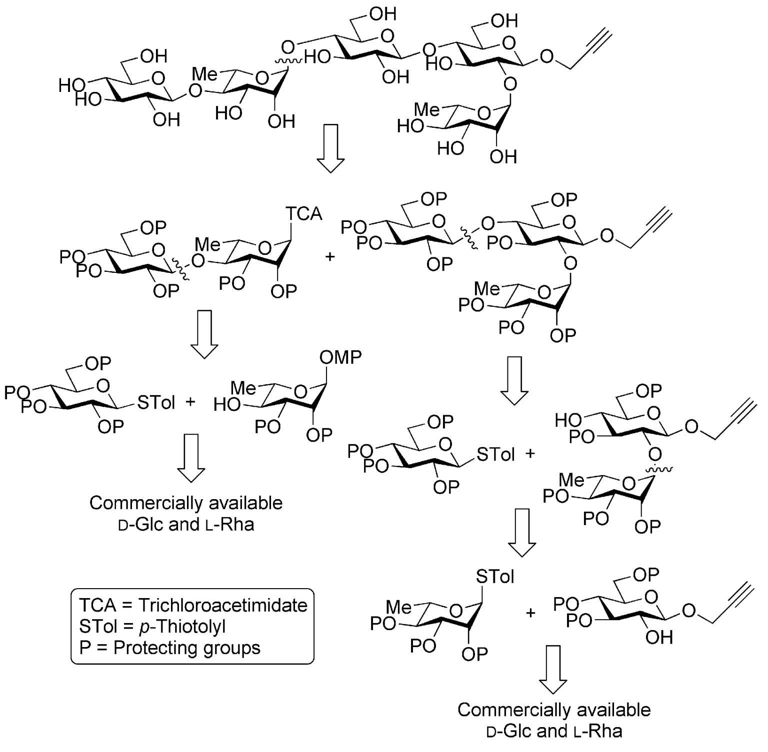
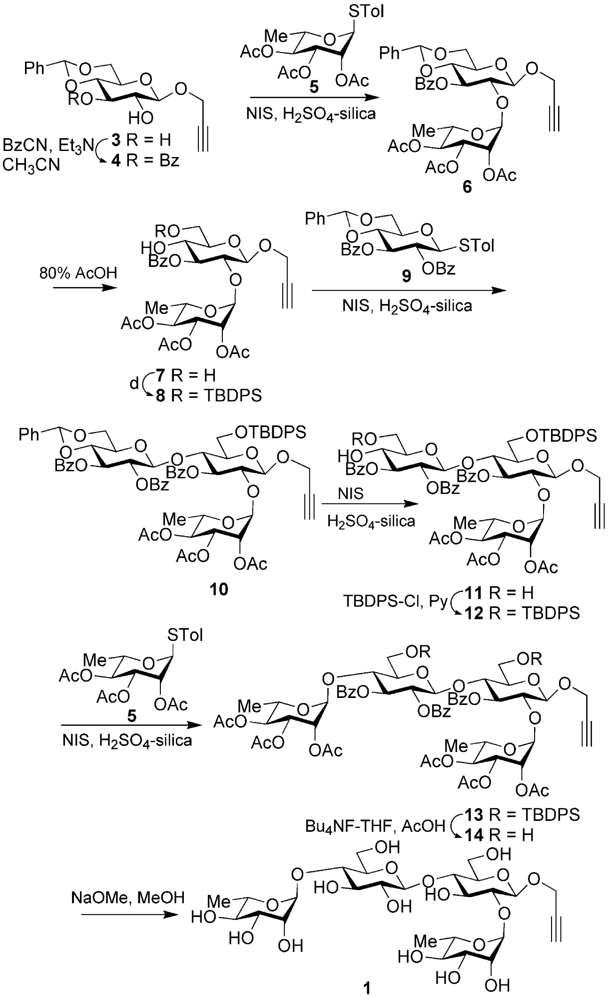


Figure 2. Retrosynthetic analysis for the synthesis of the pentasaccharide. D-Glc = D-glucose, L-Rha = L-rhamnose and MP = *p*-methoxyphenyl.

As we desired to evaluate the synthetic oligosaccharides for their biological activities in the form of suitable glycoconjugates,[12] the choice of the reducing end appendage was very important. We opted for the propargyl glycoside since it is suitable for various types of multicomponent reactions[13] and cycloadditions with the azido functionality[14] to make different types of conjugates as needed. Interestingly, many of these reactions can be performed in aqueous media, and therefore, can be exercised after global deprotection of the oligosaccharide. Moreover, the propargyl glycoside can be cleaved to form the corresponding hemiacetal derivative, if necessary[15] (Figure 1).

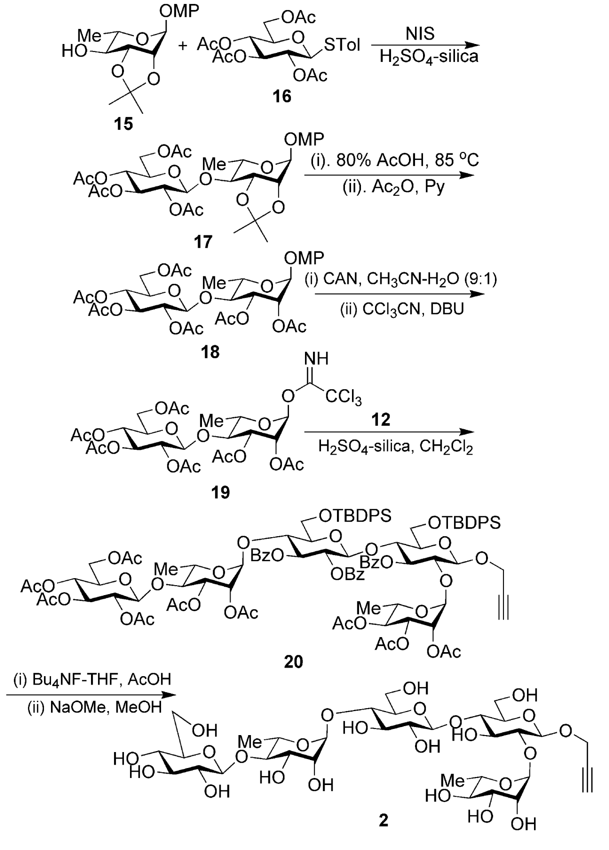
Results and Discussion

Our synthesis commenced with the known propargyl β-D-glucopyranoside. The formation of the 4,6-*O*-benzylidene acetal derivative (**3**) with benzaldehyde dimethyl acetal in the presence of 10-camphorsulfonic acid followed by selective 3-*O*-benzoylation with benzoyl cyanide in the presence of triethylamine[16] afforded the acceptor **4** in 78% yield over two steps. The acceptor was then glycosylated with the known rhamnosyl donor **5**[17] using *N*-iodosuccinimide (NIS) in the presence of H_2SO_4/silica[18] to furnish the disaccharide **6** in 89% yield. To judge the efficiency of H_2SO_4/silica,[19] we performed parallel glycosylation reactions with TfOH[20] and TMSOTf[21] in conjunction with *N*-iodosuccinimide, and the yield of the glycosylations were 83% and 86%, respectively. The results showed that H_2SO_4/silica was comparable or even better than TfOH or TMSOTf for NIS-mediated glycosylation. It is important to note that the propargyl glycoside was unaffected during the H_2SO_4/silica-catalyzed glycosylation reactions. Therefore, we opted for the H_2SO_4/silica-promoted reaction. The complete removal of the benzylidene acetal with 80% AcOH at 80 °C[22] followed by the selective protection of the primary hydroxy with the *tert*-butyldiphenylsilyl group afforded the disaccharide acceptor **8** in 84% yield. The glycosylation of disaccharide acceptor **8** with the known glucosyl donor **9**[23] using NIS in the presence of H_2SO_4/silica afforded the protected trisaccharide **10** in 91% yield. Following the same path as before, the complete hydrolysis of the benzylidene acetal followed by selective primary protection with TBDPS provided the trisaccharide acceptor **12**. We found that the TBDPS group was the most effective choice for selective protection of the primary hydroxy group and provided better reactivity of the adjacent OH group, which served as the acceptor site for glycosylation. The regioselective opening of the benzylidene acetal to produce the required 4-OH derivative was low-yielding, and the selective protection of the primary OH group with benzoyl cyanide was unsuccessful due to migration. Therefore, TBDPS was used as the protecting group, although it is arguably not the best option with respect to atom economy. Once the acceptor trisaccharide was in hand, glycosylation with the known rhamnosyl donor **5** with NIS and H_2SO_4/silica resulted in the formation of the protected tetrasaccharide **13**. However, the complete purification of tetrasaccharide **13** was unsuccessful at this stage even after repeated flash chromatography. Therefore, we proceeded to the next step. The removal of the TBDPS groups with tetrabutylammonium fluoride in THF[24] afforded the corresponding tetrasaccharide diol **14** in 82% yield over two steps. Finally, global deprotection was achieved by NaOMe in methanol to afford the target tetrasaccharide **1** in 88% yield (Scheme 1).



Scheme 1. Synthesis of the tetrasaccharide **2**.

For the synthesis of the pentasaccharide fragment, a sequential approach from the tetrasaccharide could have reached the target. However, to achieve that, a further protecting group manipulation was required in the terminal rhamnose moiety, which was not a wise choice for a large tetrasaccharide molecule. Instead, we took a “3+2“ strategy to construct the target pentasaccharide. The trisaccharide acceptor **12** required no modifications. For the disaccharide part, the known *p*-methoxyphenyl 2,3-*O*-isopropylidene-α-L-rhamnopyranoside (**15**)[25] was glycosylated with the known thioglucoside **16**[26] to afford the disaccharide **17** in 86% yield. In order to convert disaccharide **17** into a donor for the pentasaccharide formation, the oxidative removal of the *p*-methoxyphenyl group was necessary. From our previous experience, it was evident that isopropylidene acetals do not withstand CAN-mediated oxidative cleavage.[27] Therefore, the complete removal of the isopropylidene group and the subsequent protection of the resulting hydroxyls with acetate groups were performed to afford the acetylated disaccharide **18** in 86% yield over two steps. The CAN-mediated oxidative cleavage[28] of the OMP group then proceeded smoothly to form the corresponding hemiacetal, which was subsequently reacted with trichloroacetonitrile in the presence of DBU[29] to afford the required disaccharide donor **19** in 83% yield over two steps. Due to the instability of trichloroacetimidate derivatives, **19** was used for the glycosylation without further characterization. The glycosylation between trisaccharide acceptor **12** and disaccharide donor **19** was successfully achieved by activation with H_2SO_4/silica to furnish the protected pentasaccharide **20** in 87% yield. Similar to the NIS-mediated glycosylations, H_2SO_4/silica proved to be a better promoter than traditional promoters like TMSOTf. The usual global deprotection afforded the target pentasaccharide **2** in 77% yield (Scheme 2).



Scheme 2. Synthesis of the pentasaccharide **2**.

Conclusions

In conclusion, we have accomplished the total synthesis of a tetra- and a pentasaccharide related to the biologically significant saponin isolated from *Calamus insignis*. The target oligosaccharides were prepared as their propargyl glycosides, which allows for further glycoconjugate formation with cycloaddition or many other multicomponent strategies. Since these reactions are feasible in aqueous media, the deprotected oligosaccharides will be used for making various glycoconjugates. Presently, we are engaged in synthesizing such glycoconjugates, which will, in turn, help us to evaluate the biological activity of these oligosaccharides and their potential applications.

Experimental Section

General Methods: All reagents and solvents were dried prior to use according to standard methods.[30]Commercially available reagents were used without further purification unless otherwise stated. Analytical TLC was performed with silica gel 60-F_{254} (Merck or Whatman) with detection by fluorescence and/or by charring following immersion in a 10% ethanolic solution of sulfuric acid. An orcinol dip, prepared by the careful addition of concentrated sulfuric acid (20 mL) to an ice-cold solution of 3,5-dihydroxytoluene (360 mg) in EtOH (150 mL) and H_2O (10 mL), was used to detect deprotected compounds by charring. Flash chromatography was performed with silica gel 230–400 mesh (Qualigens, India). Optical rotations were measured at the sodium D-line at ambient temperature with a Perkin–Elmer 141 polarimeter. ^{1}H NMR and ^{13}C NMR spectra were recorded with a Bruker Avance spectrometer at 300 and 75 MHz, respectively, with Me_4Si or CH_3OH as internal standards, as appropriate.

Propargyl 3-*O*-benzoyl-4,6-benzylidene-β-D-glucopyranoside (4): To a suspension of propargyl β-D-glucopyranoside (3 g, 9.8 mmol) in dry CH_3CN (40 mL) was added benzaldehyde dimethyl acetal (2.2 mL, 14.7 mmol) followed by 10-CSA (50 mg), and the mixture was allowed to stir at room temperature for 4 h, at which time the solution became clear, and TLC (*n*-hexane/EtOAc, 1:1) showed the complete conversion of the starting material to a faster-moving spot. The solution was neutralized with Et_3N, and the solvents were evaporated in vacuo. The semi-solid mass thus obtained was purified by flash chromatography with a gradient of *n*-hexane/EtOAc (2:1 to 1:1) as the eluent. The purified benzylidene acetal was suspended in dry CH_3CN (40 mL), and BzCN (1.2 mL, 9.8 mmol) was added followed by Et_3N (20 μL). The solution became clear within 15 min, at which time TLC (*n*-hexane/EtOAc, 2:1) showed the complete consumption of the starting benzylidene acetal. MeOH (2 mL) was added to quench the reaction. The solvents were evaporated in vacuo, and the residue was purified by flash chromatography with 2:1 *n*-hexane/EtOAc to afford pure propargyl 2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranoside (**4**, 4.2 g, 78%) as a white foam. $[\alpha]_{\mathrm{D}}^{25}$ = +106 (*c* 1.1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.12–7.32 (m, 10 H), 5.55 (t, *J* = 8.7 Hz, 1 H), 5.53 (s, 1 H), 4.80 (d, *J* = 7.8 Hz, 1 H), 4.46 (m, 2 H), 4.40 (dd, *J* = 5.1, 10.5 Hz, 1 H), 3.88–3.79 (m, 3 H), 3.66 (m, 1 H), 2.88 (br. s, 1 H), 2.55 (t, *J* = 2.4 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 166.5, 136.8, 133.2, 129.9 (2), 129.6, 129.0, 128.3 (2), 128.2 (2), 126.1 (2), 101.5, 101.3, 78.5, 78.2, 75.8, 74.2, 73.3, 68.6, 66.6, 56.5 ppm. HRMS calcd. for $C_{23}H_{22}O_7Na$ [M + Na]$^+$ 433.1263; found 433.1261.

Propargyl 2,3,4-Tri-*O*-acetyl-α-L-rhamnopyranosyl(1→2)-3-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranoside (6): A mixture of **4** (2.0 g, 4.9 mmol), **5** (2.3 g, 5.9 mmol) and 4 Å MS (3.0 g) in dry CH_2Cl_2 (30 mL) was stirred under nitrogen for 30 min at ambient temperature. NIS (1.7 g, 7.7 mmol) was added followed by H_2SO_4/silica (150 mg), and stirring was continued for another 45 min, at which time TLC (*n*-hexane/EtOAc, 2:1) showed the complete consumption of the starting material. The mixture was filtered through a pad of celite, and the filtrate was washed successively with aqueous $Na_2S_2O_3$ (2 × 40 mL), aqueous $NaHCO_3$ (2 × 40 mL) and H_2O (40 mL). The organic phase was separated, dried (Na_2SO_4), filtered and concentrated to a syrup in vacuo. The crude product thus obtained was purified by flash chromatography with *n*-hexane/EtOAc (3:1) as the eluent to afford pure disaccharide **6** (3.0 g, 89%) as a colourless foam. $[\alpha]_{\mathrm{D}}^{25}$ = +113 (*c* 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.03–7.25 (m, 10 H), 5.64 (t, *J* = 9.3 Hz, 1 H), 5.45 (s, 1 H), 5.20 (dd, *J* = 3.3, 9.6 Hz, 1 H), 4.98 (dd, *J* = 1.8, 3.3 Hz, 1 H), 4.89 (t, *J* = 9.6 Hz, 1 H), 4.84 (d, *J* = 8.7 Hz, 1 H), 4.82 (s, 1 H), 4.41 (m, 2 H), 4.37 (dd, *J* = 4.5, 10.5 Hz, 1 H), 4.28 (m, 1 H), 3.82 (dd, *J* = 8.7, 9.3 Hz, 1 H), 3.76 (t, *J* = 9.3 Hz, 1 H), 3.74 (dd, *J* = 1.8, 10.5 Hz, 1 H), 3.64 (m, 1 H), 2.54 (t, *J* = 2.1 Hz, 1 H), 2.00 (s, 3 H), 1.90 (s, 3 H), 1.81 (s, 3 H), 1.17 (d, *J* = 6.0 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 169.4, 169.1, 168.5, 164.7, 136.7, 132.8, 129.9 (2), 129.3, 128.8, 128.1 (2), 128.0 (2), 126.1 (2), 101.3, 99.7, 98.2, 78.4, 78.1, 76.5, 75.9, 74.1, 71.0, 69.5, 68.5, 68.4, 66.7, 66.2, 56.3, 20.6, 20.4, 20.2, 17.1 ppm. HRMS calcd. for $C_{35}H_{38}O_{14}Na$ [M + Na]$^+$ 705.2159; found 705.2156.

Propargyl 2,3,4-Tri-*O*-acetyl-α-L-rhamnopyranosyl(1→2)-3-*O*-benzoyl-β-D-glucopyranoside (7): A solution of **6** (2.5 g, 3.7 mmol) in 80% AcOH (30 mL) was stirred at 80 °C for 2 h, at which time TLC (*n*-hexane/EtOAc, 1:1) showed the complete conversion of the starting material to a slower-moving spot. The solvents were evaporated in vacuo, and the residue thus obtained was purified by flash chromatography with a gradient of *n*-hexane/EtOAc (2:1 to 1:1) to afford pure **7** (2.0 g, 91%) as a white amorphous solid. $[\alpha]_D^{25}$ = +121 (*c* 1.2, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ = 8.00–7.98 (m, 5 H), 5.35 (t, *J* = 9.3 Hz, 1 H), 5.21 (dd, *J* = 3.6, 10.2 Hz, 1 H), 4.98 (m, 1 H), 4.95 (t, *J* = 10.2 Hz, 1 H), 4.85 (s, 1 H), 4.75 (d, *J* = 7.8 Hz, 1 H), 4.42 (m, 2 H), 4.31 (m, 1 H), 3.88 (dd, *J* = 2.7, 10.5 Hz, 1 H), 3.86–3.76 (m, 4 H), 3.53 (m, 1 H), 2.63 (br. s, 1 H), 2.56 (t, *J* = 2.4 Hz, 1 H), 2.01 (s, 3 H), 1.88 (s, 3 H), 1.81 (s, 3 H), 1.18 (d, *J* = 6.0 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 170.0, 169.9, 169.1, 166.7, 133.4, 129.8 (2), 128.9, 128.3 (2), 99.4 (C-1), 98.3, 78.7, 78.4, 76.5, 75.7, 75.5, 70.9, 69.4, 69.3, 68.8, 66.7, 61.9, 56.4, 20.7, 20.5, 20.3, 17.0 ppm. HRMS calcd. for $C_{28}H_{34}O_{14}Na$ [M + Na]$^+$ 617.1846; found 617.1843.

Propargyl 2,3,4-Tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→2)-3-*O*-benzoyl-6-*O*-(*tert*-butyldiphenylsilyl)-β-D-glucopyranoside (8): To a solution of **7** (1.8 g, 3.0 mmol) in dry pyridine (20 mL) was added TBDPS-Cl (1.0 mL, 3.9 mmol), and the resulting solution was stirred at ambient temperature for 6 h, at which time TLC (2:1, *n*-hexane/EtOAc) showed the complete conversion of the starting material. The solvents were evaporated in vacuo and co-evaporated with toluene to remove residual pyridine. The syrupy mass thus obtained was dissolved in CH_2Cl_2 (30 mL) and washed successively with H_2O (30 mL). The organic layer was collected, dried (Na_2SO_4), filtered and concentrated in vacuo. The crude product was purified by flash chromatography with *n*-hexane/EtOAc (3:1) to yield pure **8** (2.1 g, 84%) as a colourless syrup. $[\alpha]_D^{25}$ = +102 (*c* 1.0, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ = 8.02–7.21 (m, 15 H), 5.32 (t, *J* = 9.3 Hz, 1 H), 5.17 (dd, *J* = 3.6, 10.2 Hz, 1 H), 4.93 (m, 1 H), 4.90 (t, *J* = 10.2 Hz, 1 H), 4.83 (s, 1 H), 4.69 (d, *J* = 7.8 Hz, 1 H), 4.35 (dd, *J* = 2.7, 10.8 Hz, 1 H), 4.31 (dd, *J* = 1.8, 10.8 Hz, 1 H), 4.28 (m, 1 H), 3.95 (m, 2 H), 3.77 (m, 2 H), 3.48 (m, 1 H), 2.48 (t, *J* = 2.1 Hz, 1 H), 2.00 (s, 3 H), 1.87 (s, 3 H), 1.83 (s, 3 H), 1.17 (d, *J* = 6.0 Hz, 1 H), 1.06 (s, 9 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 169.4, 169.2, 168.3, 166.3, 135.8 (2), 135.7 (2), 133.3, 133.1, 133.0, 130.0 (2), 129.7 (2), 128.9, 128.2 (2), 127.7 (2), 123.6 (2), 99.1, 98.2, 79.2, 78.5, 76.2, 75.4, 71.1, 69.6, 69.5, 68.7, 66.6, 63.6, 55.9, 26.9 (3), 20.7, 20.5, 20.3, 19.3, 17.7 ppm. HRMS calcd. for $C_{44}H_{52}O_{14}SiNa$ [M + Na]$^+$ 855.3024; found 855.3026.

***p*-Tolyl 2,3-Di-*O*-benzoyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (9):** To a mixture of *p*-tolyl 4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (2 g, 5.3 mmol) in dry pyridine (20 mL), BzCl (1.9 mL, 16 mmol) was added dropwise at 0 °C. After complete addition, the temperature was allowed to rise to room temperature. After 2 h, TLC (*n*-hexane/EtOAc, 4:1) showed the complete conversion of the starting material. The solvents were evaporated, and the residue was diluted with CH_2Cl_2 (20 mL) and washed with brine (2 × 20 mL). The organic layer was collected, dried (Na_2SO_4) and concentrated in vacuo. The crude product thus obtained was purified by flash chromatography with 4:1 *n*-hexane/EtOAc to afford pure **9** (2.8 g, 91%). ^1H NMR ($CDCl_3$, 300 MHz): δ = 7.96–7.07 (m, 19 H), 5.72 (t, *J* = 9.3 Hz, 1 H), 5.49 (s, 1 H), 5.37 (t, *J* = 9.3 Hz, 1 H), 4.90 (d, *J* = 9.3 Hz, 1 H), 4.42 (dd, *J* = 4.5, 10.2 Hz, 1 H), 3.83 (m, 2 H), 3.71 (m, 1 H), 2.35 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 165.4, 164.9, 138.6, 136.8, 134.2 (2), 133.2, 133.0, 130.0 (2), 129.7 (2), 129.6 (2), 129.5, 129.0, 128.4 (2), 128.3 (2), 128.1 (2), 127.9 (2), 126.2 (2), 101.6, 87.1, 78.7, 73.4, 71.1, 71.0, 68.6, 21.3 ppm. HRMS calcd. for $C_{34}H_{30}O_7SNa$ [M + Na]$^+$ 605.1610; found 605.1608.

Propargyl 2,3,4-Tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→2)-4-*O*-(2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl)-3-*O*-benzoyl-6-*O*-(*tert*-butyldiphenylsilyl)-β-D-glucopyranoside (10): A mixture of disaccharide acceptor **8** (1.8 g, 2.2 mmol), donor **9** (1.7 g, 2.9 mmol) and 4 Å MS (2.0 g) in dry CH_2Cl_2 (30 mL) was stirred under nitrogen for 30 min at ambient temperature. NIS (850 mg, 3.8 mmol) was added followed by H_2SO_4/silica (50 mg), and the mixture was allowed to stir at ambient temperature for 45 min, at which time TLC (*n*-hexane/EtOAc, 2:1) showed the complete consumption of the starting materials. The mixture was filtered through a pad of celite and washed with CH_2Cl_2 (10 mL). The entire filtrate was washed successively with aqueous $Na_2S_2O_3$ (2 × 40 mL), saturated aqueous $NaHCO_3$ (2 × 40 mL) and H_2O (40 mL). The organic layer was collected, dried (Na_2SO_4), filtered and concentrated in vacuo. The crude thus obtained was purified by flash chromatography with *n*-hexane/EtOAc (2:1) as the eluent to afford pure trisaccharide **10** (2.5 g, 91%) as a colourless foam. $[\alpha]_D^{25}$ = +136 (*c* 1.3, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ = 8.13–7.15 (m, 30 H), 5.62 (t, *J* = 9.3 Hz, 1 H), 5.52 (t, *J* = 9.3 Hz, 1 H), 5.37 (dd, *J* = 7.8, 9.3 Hz, 1 H), 5.23 (s, 1 H), 5.22 (dd, *J* = 3.6, 9.9 Hz, 1 H), 5.08 (d, *J* = 7.8 Hz, 1 H), 5.01 (dd, *J* = 1.8, 3.6 Hz, 1 H), 4.96 (t, *J* = 9.9 Hz, 1 H), 4.83 (d, *J* = 1.8 Hz, 1 H), 4.61 (d, *J* = 7.5 Hz, 1 H), 4.39–4.18 (m, 4 H), 3.95 (dd, *J* = 4.8, 10.5 Hz, 1 H), 3.80 (m, 3 H), 3.62 (t, *J* = 9.3 Hz, 1 H), 3.42 (m, 1 H), 3.25 (bd, 1 H), 2.45 (t, *J* = 2.1 Hz, 1 H), 2.01 (s, 3 H), 1.90 (s, 3 H), 1.87 (s, 3 H), 1.19 (d, *J* = 6.6 Hz, 3 H), 1.13 (s, 9 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 169.6, 169.2, 168.7, 165.2, 164.8, 164.3, 136.6, 136.0 (2), 135.5 (2), 134.1, 133.3, 132.9 (2), 132.4, 130.4, 130.1 (2), 129.7 (2), 129.6 (2), 129.4, 128.9, 128.3, 128.2 (3), 128.1, 128.0 (2), 127.7 (2), 126.2 (2), 101.2, 100.5, 98.8, 98.2, 78.4, 78.3, 77.2, 75.5 (2), 75.3, 74.9, 74.0, 72.3, 72.0, 71.2, 69.8, 68.7, 68.0, 66.6, 66.5, 61.0, 55.7, 26.9 (3), 20.8, 20.6, 20.5, 19.6, 17.2 ppm. ESIMS: *m*/*z* = 1313.3 [M + Na]$^+$.

Propargyl 2,3,4-Tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→2)-4-*O*-(2,3-di-*O*-benzoyl-β-D-glucopyranosyl)-3-*O*-benzoyl-6-*O*-(*tert*-butyldiphenylsilyl)-β-D-glucopyranoside (11): Trisaccharide **10** (2.0 g, 1.6 mmol) was suspended in 80% AcOH (20 mL), and the mixture was allowed to stir at 80 °C for 2 h, at which time TLC (*n*-hexane/EtOAc, 1:1) showed the complete conversion of the starting material to a slower-running spot. The solvents were evaporated in vacuo, and the residue thus obtained was purified by flash chromatography with a gradient of *n*-hexane/EtOAc (2:1 to 1:1) to afford pure trisaccharide diol **11** (1.6 g, 87%) as a white amorphous solid. $[\alpha]_D^{25}$ = +127 (*c* 1.1, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ = 8.12–7.17 (m, 25 H), 5.48 (t, *J* = 9.3 Hz, 1 H), 5.30 (m, 2 H), 5.21 (dd, 1 H), 5.05 (d, 1 H), 4.98 (m, 1 H), 4.96 (t, *J* = 10.2 Hz, 1 H), 4.85 (br. s, 1 H), 4.61 (d, *J* = 8.1 Hz, 1 H), 4.41–4.19 (m, 5 H), 3.89–3.68 (m, 4 H), 3.51 (bd, 1 H), 3.37–3.24 (m, 4 H), 2.46 (t, *J* = 1.8 Hz, 1 H), 2.00 (s, 3 H), 1.89 (s, 3 H), 1.82 (s, 3 H), 1.20 (d, *J* = 6.0 Hz, 3 H), 1.13 (s, 9 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 170.1, 169.7, 169.1, 167.0, 164.8, 164.6, 135.8 (2), 135.4 (3), 133.4, 133.3, 133.2, 133.0, 132.4, 130.2, 129.9 (3), 129.7, 129.5 (3), 128.9, 128.8, 128.5 (2), 128.4 (2), 128.3 (2), 128.1 (2), 127.7 (2), 99.9, 98.7, 98.3, 78.3, 77.1, 75.8, 75.5, 75.3 (2), 74.9, 73.6, 71.4, 71.1, 69.6, 69.0, 68.6, 66.6, 61.5, 60.9, 55.6, 26.9 (3), 20.7, 20.6, 20.4, 19.4, 17.1 ppm. ESIMS: *m*/*z* = 1225.3 [M + Na]$^+$.

Propargyl 2,3,4-Tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→2)-4-*O*-[2,3-di-*O*-benzoyl-6-*O*-(*tert*-butyldiphenylsilyl)-β-D-glucopyranosyl]-3-*O*-benzoyl-6-*O*-(*tert*-butyldiphenylsilyl)-β-D-glucopyranoside (12): To solution of **11** (1.3 g, 1.1 mmol) in dry pyridine (20 mL) was added TBDPS-Cl (360 μL, 1.4 mmol) and the resulting solution was stirred at ambient temperature for 6 h, , at which time TLC (*n*-hexane/EtOAc, 2:1) showed the complete conversion of the starting material. The solvents were evaporated in vacuo and co-evaporated with toluene to remove residual pyridine. The crude product thus obtained was purified by flash chromatography with 2:1 *n*-hexane/EtOAc as the eluent to afford trisaccharide acceptor **12** (1.3 g, 82%). $[\alpha]_D^{25}$ = +127 (*c* 1.1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.95–6.82 (m, 35 H), 5.49 (t, *J* = 9.6 Hz, 1 H), 5.42 (t, *J* = 9.9 Hz, 1 H), 5.24 (t, *J* = 9.9 Hz, 1 H), 5.13 (dd, *J* = 3.3, 10.2 Hz, 1 H), 5.04 (d, *J* = 7.8 Hz, 1 H), 4.89 (m, 1 H), 4.85 (t, *J* = 10.2 Hz, 1 H), 4.67 (s, 1 H), 4.55 (d, *J* = 7.5 Hz, 1 H), 4.32 (dd, *J* = 2.1, 15.6 Hz, 1 H), 4.19 (m, 3 H), 3.87–3.67 (m, 6 H), 3.55 (m, 1 H), 3.28 (t, 1 H), 3.19 (bd, 1 H), 2.43 (t, *J* = 1.8 Hz, 1 H), 1.98 (s, 3 H), 1.87 (s, 3 H), 1.76 (s, 3 H), 1.17 (d, *J* = 6.0 Hz, 3 H), 1.14 (s, 9 H), 0.99 (s, 9 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 169.6, 169.2, 168.5, 165.9, 164.7, 164.3, 136.0 (2), 135.5 (8), 132.9, 132.6, 132.5, 132.3, 132.2, 132.1, 132.0, 130.3 (2)130.1, 130.0 (2), 129.9, 129.7 (4), 129.0, 128.3 (3), 128.2 (3), 128.19 (4), 127.7 (4), 99.8, 98.9, 98.1, 78.4, 77.2, 75.5 (2), 75.4, 75.0 (2), 73.6, 73.4 (2), 71.5, 71.2, 69.7, 68.7, 66.6, 66.2, 61.0, 55.7, 27.1 (3), 26.8 (3), 20.7, 20.6, 20.4, 19.5, 19.1, 17.2 ppm. ESIMS: *m*/*z* = 1463.4 [M + Na]$^+$.

Propargyl 2,3,4-Tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→4)-2,3-di-*O*-benzoyl-β-D-glucopyranosyl-(1→4)-2-*O*-(2,3,4-tri-*O*-acetyl-*α*-L-rhamnopyranosyl)-3-*O*-benzoyl-β-D-glucopyranoside (14): A mixture of trisaccharide acceptor **12** (1.1 g, 0.8 mmol), known rhamnosyl donor **5** (396 mg, 1.0 mmol) and 4 Å MS (1.0 g) in dry CH_2Cl_2 (15 mL) was stirred under nitrogen for 30 min at ambient temperature. NIS (290 g, 1.3 mmol) was added followed by H_2SO_4/silica (50 mg), and the mixture was stirred at ambient temperature for 1 h, at which time TLC (*n*-hexane/EtOAc, 2:1) showed the complete consumption of the acceptor trisaccharide **12**. The mixture was filtered through a pad of celite, and the filtrate was washed successively with aqueous $Na_2S_2O_3$ (2 × 30 mL), saturated aqueous $NaHCO_3$ (2 × 30 mL) and H_2O (30 mL). The organic layer was collected, dried (Na_2SO_4), filtered and concentrated in vacuo. The crude product thus obtained was purified by flash chromatography with *n*-hexane/EtOAc (2:1) as the eluent. The residue was dissolved in dry THF (20 mL), AcOH (0.25 mL) was added, followed by Bu_4NF/THF (1.5 mL, 1.6 mmol), and the solution was stirred at ambient temperature for 6 h, at which time TLC (*n*-hexane/EtOAc, 2:1) showed the complete conversion of the starting material to a slower-running spot. The solvents were evaporated in vacuo, and the residue was purified by flash chromatography with a gradient of *n*-hexane/EtOAc (2:1 to 1:1) to yield pure tetrasaccharide diol **14** (775 mg, 82%) as a colourless foam. $[\alpha]_D^{25}$ = +74 (*c* 1.1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.12–7.28 (m, 15 H), 5.61 (t, *J* = 9.3 Hz, 1 H), 5.52 (t, *J* = 9.3 Hz, 1 H), 5.25 (dd, *J* = 8.1, 9.3 Hz, 1 H), 5.19 (dd, *J* = 3.3, 9.9 Hz, 1 H), 5.03 (m, 1 H), 4.97 (dd, *J* = 3.3, 9.9 Hz, 1 H), 4.95 (m, 1 H), 4.93 (t, *J* = 9.9 Hz, 1 H), 4.84 (d, *J* = 8.1 Hz, 1 H), 4.80 (t, *J* = 9.9 Hz, 1 H), 4.79 (s, 1 H), 4.76 (s, 1 H), 4.67 (d, *J* = 7.5 Hz, 1 H), 4.37 (m, 2 H), 4.25 (dd, *J* = 6.3, 9.9 Hz, 1 H), 4.02 (m, 2 H), 3.77 (m, 2 H), 3.67 (br. s, 2 H), 3.52 (dd, *J* = 6.3, 9.9 Hz, 1 H), 3.37 (m, 3 H), 3.04 (m, 1 H), 2.50 (t, *J* = 2.1 Hz, 1 H), 2.04 (s, 3 H), 2.00 (s, 3 H), 1.92 (s, 3 H), 1.90 (s, 3 H), 1.86 (s, 3 H), 1.79 (s, 3 H), 1.16 (d, *J* = 6.3 Hz, 3 H), 0.54 (d, *J* = 6.3 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 170.1, 170.0, 169.9, 169.7, 169.6, 168.9, 165.8, 164.8, 164.5, 133.6, 133.2, 133.1, 129.8 (2), 129.6 (2), 129.5 (2), 129.4, 129.3, 128.9, 128.7 (2), 128.4 (2), 128.2 (2), 100.8, 99.2, 98.4, 97.8, 78.2, 75.6 (2), 75.4, 75.3, 75.2, 74.8, 73.9, 73.6, 72.3, 71.1, 70.4, 69.6, 69.5, 68.7, 68.6, 67.0, 66.7, 60.4, 60.0, 56.4, 20.8, 20.7, 20.6 (2), 20.5, 20.3, 17.0, 16.7 ppm. ESIMS: *m*/*z* = 1259.3 [M + Na]$^+$.

Propargyl α-L-Rhamnopyranosyl-(1→4)-β-D-glucopyranosyl-(1→4)-2-*O*-(α-L-rhamnopyranosyl)-β-D-glucopyranoside (1): To a solution of **14** (700 mg, 0.5 mmol) in dry MeOH (10 mL) was added NaOMe in MeOH (1 mL, 0.5 M), and the solution was allowed to stir for 12 h for the complete removal of the *O*-acetyl and *O*-benzoyl groups. The solution was then neutralized with DOWEX 50W H$^+$, filtered through a cotton plug, and the filtrate was concentrated in vacuo to afford pure tetrasaccharide **1** (335 mg, 88%) as a white amorphous solid. $[\alpha]_D^{25}$ = +58 (*c* 1.4, H_2O). ^{1}H NMR (D_2O, 300 MHz): δ = 5.08 (s, 1 H), 4.74 (s, 1 H), 4.49 (d, *J* = 6.3 Hz, 1 H), 4.47 (d, *J* = 6.0 Hz, 1 H), 3.98 (m, 5 H), 3.84–3.51 (m, 13 H), 3.45 (m, 3 H), 3.34 (t, *J* = 9.6 Hz, 1 H), 2.94 (t, *J* = 1.8 Hz, 1 H), 1.28 (d, 3 H), 1.26 (d, 3 H) ppm. ^{13}C NMR (D_2O, 75 MHz): δ = 102.6, 101.4, 100.9, 99.2, 79.2, 78.8, 78.2, 77.2, 76.5, 76.4, 75.2, 74.9, 74.7, 74.2, 72.7, 72.0, 71.9, 70.4, 70.2, 70.1, 69.1, 69.0, 60.2, 60.0, 56.6, 16.6, 16.5 ppm. HRMS calcd. for $C_{27}H_{44}O_{19}Na$ [M + Na]$^+$ 695.2375; found 695.2373.

***p*-Methoxyphenyl 2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl-(1→4)-2,3-isopropylidene-α-L-rhamnopyranoside (17):** A solution of **15** (2.0 g, 6.4 mmol), **16** (3.5 g, 7.7 mmol) and 4 Å MS (3.0 g) in dry CH_2Cl_2 (40 mL) was stirred under nitrogen for 30 min at ambient temperature. NIS (2.25 g, 10 mmol) was then added, followed by H_2SO_4/silica (100 mg), and the mixture was allowed to stir for another 1 h, at which time TLC (*n*-hexane/EtOAc, 3:1) showed the complete consumption of the starting material. The mixture was filtered through a pad of celite, and the filtrate was washed successively with aqueous $Na_2S_2O_3$ (2 × 30 mL), aqueous saturated $NaHCO_3$ (2 × 30 mL) and H_2O (30 mL). The organic layer was separated, dried (Na_2SO_4), filtered and concentrated in vacuo. The crude product thus obtained was purified by flash chromatography with a gradient of *n*-hexane/EtOAc (4:1 to 2:1) to yield the pure disaccharide **17** (3.6 g, 86%). $[\alpha]_D^{25}$ = +56 (*c* 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 6.93 (d, 2 H), 6.77 (d, 2 H), 5.52 (s, 1 H), 5.19 (t, *J* = 9.3 Hz, 1 H), 5.02 (t, *J* = 9.3 Hz, 1 H), 4.95 (d, *J* = 9.0 Hz, 1 H), 4.91 (dd, *J* = 9.0, 9.3 Hz, 1 H), 4.28–4.17 (m, 3 H), 4.09 (dd, *J* = 2.1, 12.3 Hz, 1 H), 3.75 (s, 3 H), 3.73 (t, *J* = 9.9 Hz, 1 H), 3.66 (m, 1 H), 3.57 (dd, *J* = 7.5, 9.9 Hz, 1 H), 2.07 (s, 3 H), 2.06 (s, 3 H), 2.01 (s, 3 H), 2.00 (s, 3 H), 1.54 (s, 3 H), 1.38 (s, 3 H), 1.19 (d, *J* = 6.3 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 170.0, 169.8, 169.0 (2), 155.0, 150.2, 117.7 (2), 114.6 (2), 109.4, 99.52, 96.1, 79.4, 78.1, 76.2, 73.0, 71.9, 71.6, 68.7, 64.8, 62.1, 55.4, 28.0, 26.5, 20.7, 20.6, 20.5 (2), 17.5 ppm. HRMS calcd. for $C_{30}H_{40}O_{15}Na$ [M + Na]$^+$ 663.2265; found 663.2263.

***p*-Methoxyphenyl 2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-acetyl-α-L-rhamnopyranoside (18):** A solution of **17** (3.0 g, 4.7 mmol) in 80% AcOH (30 mL) was stirred at 80 °C for 2 h, at which time TLC (*n*-hexane/EtOAc, 2:1) showed the complete conversion of the starting material to a slower-moving spot. The solvents were evaporated and co-evaporated with toluene to remove residual AcOH. The semi-solid mass thus obtained was dissolved in dry pyridine (12 mL) followed by Ac_2O (10 mL), and the solution was stirred at ambient temperature for 3 h until the reaction was complete (by TLC). The solvents were evaporated in vacuo and co-evaporated with toluene to remove residual pyridine. The crude acetate derivative thus obtained was purified by flash chromatography with *n*-hexane/EtOAc (3:1) to yield pure disaccharide **18** (2.7 g, 86%) as a white foam. $[\alpha]_D^{25}$ = +73 (*c* 1.2, $CHCl_3$).

^{1}H NMR (CDCl$_3$, 300 MHz): δ = 6.97 (d, J = 9.0 Hz, 2 H), 6.77 (d, J = 9.0 Hz, 2 H), 5.39 (dd, J = 3.3, 9.6 Hz, 1 H), 5.27 (dd, J = 1.2, 3.6 Hz, 1 H), 5.22 (d, J = 1.2 Hz, 1 H), 5.11 (t, J = 9.3 Hz, 1 H), 5.03 (t, J = 9.3 Hz, 1 H), 4.90 (dd, J = 8.1, 9.3 Hz, 1 H), 4.69 (d, J = 8.1 Hz, 1 H), 4.25 (dd, J = 4.5, 12.0 Hz, 1 H), 4.15 (dd, J = 2.4, 12.0 Hz, 1 H), 3.91 (m, 1 H), 3.75 (s, 3 H), 3.62 (t, J = 9.6 Hz, 1 H), 2.17 (s, 3 H), 2.11 (s, 3 H), 2.08 (s, 3 H), 2.01 (s, 3 H), 2.00 (s, 3 H), 1.98 (s, 3 H), 1.27 (d, J = 6.0 Hz, 3 H) ppm. ^{13}C NMR (CDCl$_3$, 75 MHz): δ = 170.0, 169.9, 169.4, 169.2, 168.9 (2), 155.3, 150.0, 117.9 (2), 114.6 (2), 100.8, 96.6, 77.1, 73.0, 71.7, 71.3, 71.1, 70.2, 68.6, 67.4, 61.8, 55.4, 21.0, 20.9, 20.6, 20.5 (2), 20.3, 17.7 ppm. HRMS calcd. for $C_{31}H_{40}O_{16}Na$ [M + Na]$^+$ 691.2214; found 691.2216.

Propargyl 2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl-(1→4)-2,3-di-*O*-acetyl-α-L-rhamnopyranosyl-(1→4)-2,3-di-*O*-benzoyl-6-*O*-(*tert*-butyldiphenylsilyl)-β-D-glucopyranosyl-(1→4)-2-*O*-(2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl)-3-*O*-benzoyl-6-*O*-(*tert*-butyldiphenylsilyl)-β-D-glucopyranoside (20): To a solution of **18** (2.5 g, 3.65 mmol) in CH$_3$CN/H$_2$O (9:1, 40 mL) was added CAN (4 g, 7.3 mmol), and the mixture was stirred at ambient temperature for 45 min, at which time TLC (*n*-hexane/EtOAc, 2:1) showed the complete conversion of the starting material. The solvents were evaporated in vacuo, and the residue was dissolved in CH$_2$Cl$_2$ (40 mL) and washed with H$_2$O (2 × 30 mL). The organic layer was separated, dried (Na$_2$SO$_4$), filtered and the solvents were evaporated. The crude disaccharide hemiacetal thus obtained was purified by flash chromatography with *n*-hexane/EtOAc (2:1). The syrupy compound obtained after chromatographic purification was dissolved in dry CH$_2$Cl$_2$ (15 mL), and CCl$_3$CN (1.1 mL, 11 mmol) and DBU (600 µL, 3.65 mmol) were added. The resulting solution was stirred at ambient temperature for 1 h, until a complete reaction was confirmed by TLC. The solvents were evaporated in vacuo, and the residue thus obtained was purified by flash chromatography with *n*-hexane/EtOAc (2:1) to afford pure disaccharide trichloroacetimidate (**19**, 2.2 g, 83%). A mixture of **19** (1 g, 1.4 mmol), trisaccharide acceptor **12** (1.5 g, 1.1 mmol) and molecular sieves (4 Å) in dry CH$_2$Cl$_2$ (15 mL) was then stirred under nitrogen for 30 min. H$_2$SO$_4$/silica (50 mg) was added, and the mixture was allowed to stir at ambient temperature for 1 h, at which time TLC (*n*-hexane/EtOAc, 2:1) showed the complete consumption of the starting materials. The mixture was filtered through a pad of celite and washed with CH$_2$Cl$_2$ (10 mL). The complete filtrate was washed with aqueous saturated NaHCO$_3$ (2 × 20 mL) and brine (20 mL). The organic layer was collected, dried (Na$_2$SO$_4$), filtered and concentrated in vacuo. The residue was purified by flash chromatography with a gradient of *n*-hexane and EtOAc (2:1 to 1:1) to afford pure pentasaccharide **20** (1.8 g, 87%) as a white foam. $[\alpha]_D^{25}$ = +101 (c 1.0, CHCl$_3$). ^{1}H NMR (CDCl$_3$, 300 MHz): δ = 7.72–7.10 (m, 35 H, Ar*H*), 5.49 (t, J = 9.6 Hz, 1 H), 5.47 (t, J = 9.6 Hz, 1 H), 5.19 (m, 2 H), 5.07 (t, J = 9.3 Hz, 1 H), 5.04–4.91 (m, 7 H), 4.76 (s, 1 H), 4.72 (s, 1 H), 4.54 (m, 2 H), 4.38–4.06 (m, 6 H), 3.87–3.58 (m, 6 H), 3.49–3.31 (m, 4 H), 3.29 (m, 1 H), 2.48 (t, J = 1.8 Hz, 1 H), 2.03 (2s, 6 H), 2.01 (2s, 6 H), 2.00 (s, 3 H), 1.98 (s, 3 H), 1.97 (s, 3 H), 1.93 (s, 3 H), 1.89 (s, 3 H), 1.20 (d, J = 6.3 Hz, 3 H), 1.03 (s, 9 H), 1.01 (s, 9 H), 0.70 (d, J = 6.0 Hz, 3 H) ppm. ^{13}C NMR (CDCl$_3$, 75 MHz): δ = 170.4, 170.2, 170.0, 169.5, 169.3, 169.2, 169.1, 169.0, 168.8, 165.6, 164.8, 164.6, 135.8 (2), 135.7 (2), 135.6 (2), 135.5 (2), 133.6, 133.2, 133.0, 132.9, 132.8, 132.7 (2), 129.9, 129.8 (4), 129.7 (2), 129.6, 129.5 (2), 129.4, 129.1, 128.9, 128.2 (2), 128.1 (2), 128.0 (2), 127.9 (2), 127.7 (2), 127.6 (4), 100.1, 99.2, 98.9, 98.3, 97.8, 78.4, 77.2, 76.8, 76.2, 75.5, 75.3, 75.2 (2), 74.9, 73.8, 73.7, 72.9, 72.6, 71.2 (2), 71.1, 71.0, 70.6, 70.0, 69.4, 68.8, 68.5, 67.3, 66.5, 63.2, 62.1, 61.9 (2), 55.7, 29.6, 26.9, 20.8, 20.7, 20.6, 20.5 (4), 20.3, 20.2, 19.3, 19.2, 17.1, 16.9 ppm. MALDI-TOF-MS: m/z = 2023.6 [M + Na]$^+$.

Propargyl β-D-Glucopyranosyl-(1→4)-α-L-rhamnopyranosyl-(1→4)-β-D-glucopyranosyl-(1→4)-2-*O*-(α-L-rhamnopyranosyl)-β-D-glucopyranoside (2): Compound **20** (1.5 g, 1.6 mmol) was dissolved in dry THF (20 mL), AcOH (1 mL) and Bu$_4$NF/THF (1.1 mL, 3.7 mmol) were added, and the solution was stirred at ambient temperature for 12 h, at which time TLC (*n*-hexane/EtOAc, 2:1) showed the complete conversion of the starting material to a slower-running spot. The solvents were evaporated in vacuo, and the residue was purified by flash chromatography with *n*-hexane/EtOAc (1:1). The purified product was dissolved in dry MeOH (20 mL). NaOMe in MeOH (2 mL, 0.5 M) was added, and the solution was stirred overnight at ambient temperature. The solution was then neutralized with DOWEX H$^+$ resin, filtered and concentrated to afford pure pentasaccharide target **2** (320 mg, 77%) as a white amorphous mass. $[\alpha]_D^{25}$ = +149 (c 0.8, H$_2$O). ^{1}H NMR (D$_2$O, 300 MHz): δ = 5.09 (s, 1 H), 4.72 (d, J = 7.8 Hz, 1 H), 4.68 (d, J = 7.5 Hz, 1 H), 4.46 (d, J = 7.8 Hz, 1 H), 4.44 (s, 1 H), 2.91 (t, J = 1.8 Hz, 1 H), 1.30 (d, J = 6.0 Hz, 3 H), 1.25 (d, J = 6.0 Hz, 3 H) ppm. ^{13}C NMR (D$_2$O, 75 MHz): δ = 104.4, 103.6, 102.6, 101.9, 100.3, 82.3, 80.4, 79.9, 79.4, 78.4, 77.6, 77.2, 77.0, 76.3, 76.1, 75.9, 75.4, 75.1, 74.8, 73.2, 71.5, 71.4 (3), 70.7, 70.2, 68.8, 61.8, 61.3, 61.1, 57.8, 50.1, 17.9, 17.8 ppm. HRMS calcd. for $C_{33}H_{54}O_{24}Na$ [M + Na]$^+$ 857.2903; found 857.2901.

Supporting Information (see also the footnote on the first page of this article): Copies of ^{1}H NMR and ^{13}C spectra of all compounds.

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