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Synthesis of 8-azidooctyl glycoside derivatives of the O-chain repeating unit of *Escherichia coli* O9a lipopolysaccharide and a methylated analog

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Abstract—Described is the synthesis of 8-azidooctyl glycoside derivatives of the *Escherichia coli* serotype O9a O-chain tetrasaccharide repeating unit and the terminal tetrasaccharide motif in this polysaccharide, which contains a methyl group on O-3 of the distal mannopyranose residue. The assembly of these compounds involved the sequential addition of monosaccharide residues from the reducing to the nonreducing end of the molecule using glycosyl trichloroacetimidate donors. Both compounds were initially prepared as *p*-methoxyphenyl glycosides, which were converted to the corresponding 8-azidooctyl derivatives at a late stage in the synthesis.

Keywords: Lipopolysaccharide; Synthesis; Oligosaccharide; *Escherichia coli*; Neoglycoconjugate

1. Introduction

Gram-negative bacteria produce, as a component of their outer membrane lipopolysaccharide (LPS), a glycoconjugate containing three structural domains: Lipid A, a core oligosaccharide, and the O-chain.[1] LPS has potent endotoxic properties arising from the Lipid A domain.[1] The O-chain, which contains multiple copies of a repeating unit with typically 1–4 monosaccharide residues, is antigenic, and a number of these glycans have been studied as vaccine candidates.[2] In *Escherichia coli* serotype O9a, the O-chain repeating unit is a tetrasaccharide containing only mannopyranoside residues (**1**, Fig. 1). This system has been the focus of a number of biosynthetic investigations,[1] and a recent report[3] has established that the length of the O-chain is mediated by a methylation event, leading to structure **2**, which prevents further polymerization.

As part of a collaboration on the biosynthesis of the LPS O-chain in *E. coli* serotype O9a, we required milligram quantities of analogs of both **1** and **2**, which could be used as substrates and authentic standards in assays of the mannosyltransferase and methyltransferase enzymes. Although this tetrasaccharide repeating unit had been previously synthesized,[4] it was prepared as its methyl glycoside, which does not easily allow its conversion to neoglycoconjugates (e.g., fluorescently labeled analogs) that would facilitate these investigations. To the best of our knowledge, the synthesis of tetrasaccharide **2** has not been reported. We therefore describe here the synthesis of tetrasaccharides **3** and **4** (Fig. 2), both functionalized at the reducing end with a group (8-azidooctyl) that will allow for conjugation to other species either through classical methods (e.g., reduction to the amine and subsequent amidation) or through more recently developed approaches (e.g., an azide–alkyne 2+3 cycloaddition[5]).

2. Results and discussion

In designing a route to **3** and **4**, we envisioned that the former could be obtained from monosaccharides **5**–**7**,

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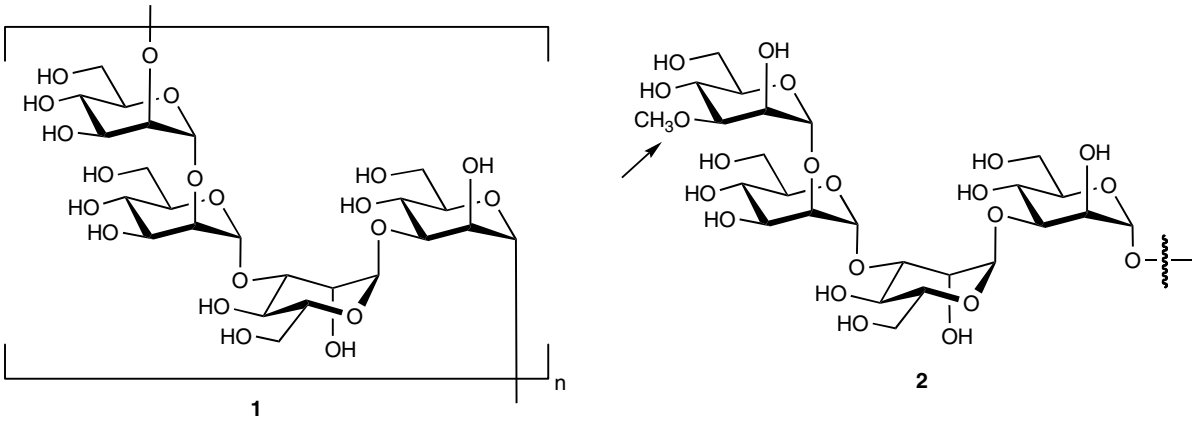


Figure 1. O-Chain repeating unit of LPS from *E. coli* serotype O9a (**1**) and the structure of the methylated repeating unit (**2**) that terminates the O-chain.

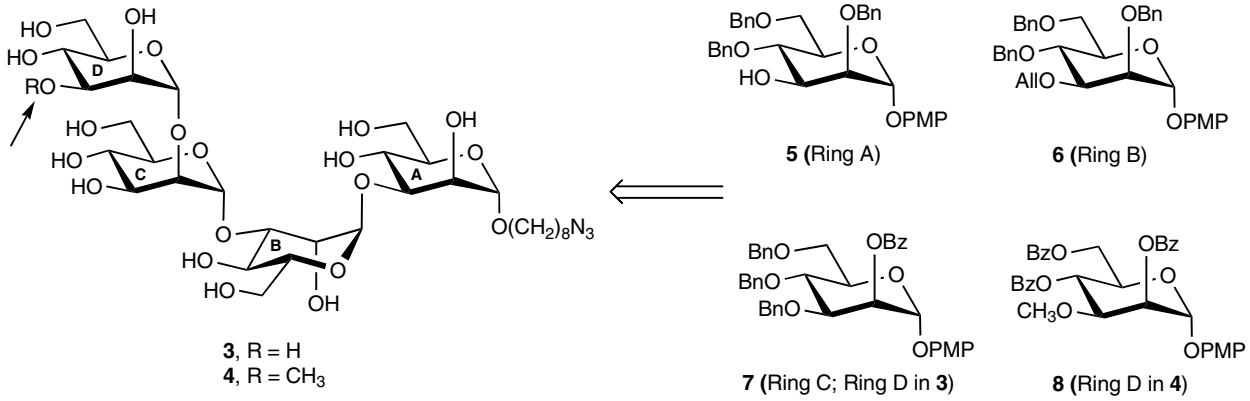
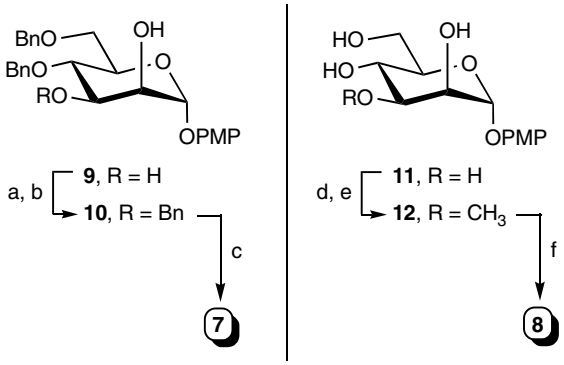


Figure 2. Target tetrasaccharides (**3** and **4**) and the building blocks (**5**–**8**) required for their synthesis.

while the preparation of the latter would require these compounds in addition to another building block, **8** (Fig. 2). The approach would involve the sequential assembly of the targets from the reducing to the nonreducing end via imidate donors derived by the *p*-methoxyphenyl glycosides shown in Figure 2. In a final sequence, the reducing-end *p*-methoxyphenyl aglycone would be exchanged for an 8-azidoctyl moiety. Of the building blocks chosen, **5** and **6** were prepared as described earlier,[6] and the preparation of **7** and **8** was accessed straightforwardly as described below. In the previous synthesis of the tetrasaccharide repeating unit of the *E. coli* serotype O9a O-chain by Kong and coworkers,[4] the molecule was obtained via a 2+2 coupling strategy in which the key glycosylation reaction proceeded in excellent yield. While this approach could have also been used to access **3** and **4**, as these two molecules differed in the identity of the terminal sugar residue, we viewed the step-wise approach as equally efficient in that the same trisaccharide (**18**, see below) could be used as the precursor to both molecules.

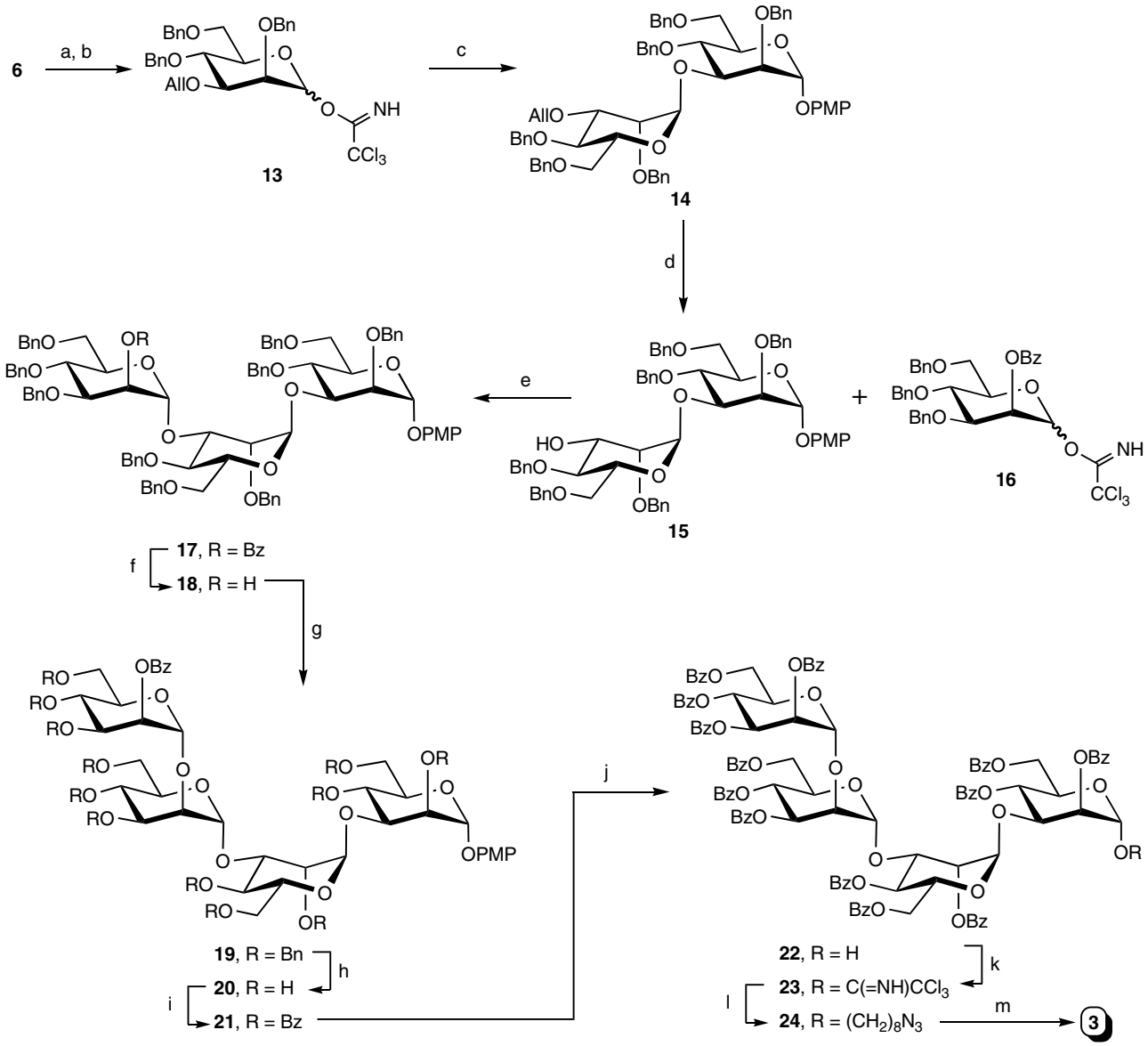
As illustrated in Scheme 1, the synthesis of **7** was achieved from the previously reported diol **9**[6] in three steps. Heating **9** with di-*n*-butyltin oxide in toluene gave the intermediate stannylidene acetal,[7] which was subsequently reacted with benzyl bromide and tetra *n*-butylammonium iodide to give alcohol **10** in 92% yield. The regioselectivity of the process was established



Scheme 1. Reagents and conditions: (a) *n*-Bu_2SnO, toluene, 105 °C; (b) BnBr, *n*-Bu_4NI, toluene, 105 °C, 92% over two steps; (c) BzCl, pyridine, DMAP, 0 °C→rt, 97%; (d) *n*-Bu_2SnO, toluene, 105 °C; (e) CH_3I, *n*-Bu_4NI, toluene, 105 °C, 83% over two steps; (f) BzCl, pyridine, DMAP, 0 °C→rt, 96%.

by ^{13}C NMR spectroscopy; as expected, the chemical shift of C-3 moved downfield upon alkylation ($\delta_{C3} = 71.6$ in **9** and $\delta_{C3} = 80.0$ in **10**). Benzoylation of **10** under standard conditions afforded building block **7** in 97% yield. A similar series of reactions was used to convert *p*-methoxyphenyl α-D-mannopyranoside (**11**)[8] to building block **8** in 80% overall yield in a three-step route that proceeded via intermediate **12**. Again, the regioselectivity of the methylation could be ascertained by comparing the C-3 chemical shift in the ^{13}C NMR spectrum of **11** ($\delta_{C3} = 72.5$) and **12** ($\delta_{C3} = 82.2$).

With the monosaccharide precursors in hand, tetrasaccharide **3** was assembled as shown in Scheme 2. First, the *p*-methoxyphenyl glycoside **6** was cleaved upon reaction with ceric ammonium nitrate (CAN) in wet CH_3CN to afford the corresponding reducing sugar, which was then converted to glycosyl trichloroacetimidate (**13**), in 84% overall yield. Glycosylation of **5** with **13** under the promotion of trimethylsilyl trifluoromethanesulfonate (TMSOTf) provided a 74% yield of the expected disaccharide **14**, together with 15% of the corresponding β-isomer, which could be separated by chromatography. The allyl group in **14** was then removed upon reaction with palladium chloride in methanol to give **15** in 86% yield. We observed none of the Wacker oxidation products. This disaccharide alcohol was the acceptor for a

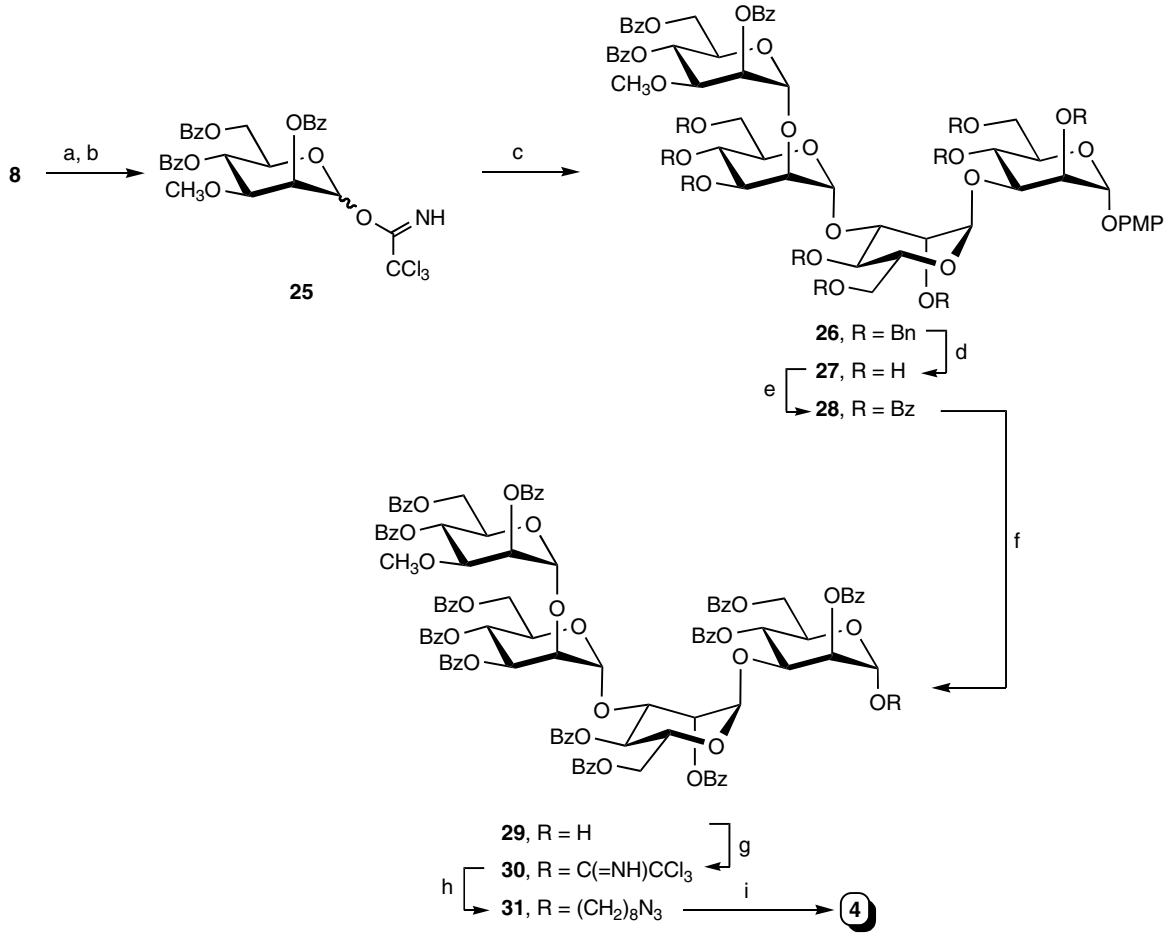


Scheme 2. Reagents and conditions: (a) CAN, H_2O, CH_3CN, rt; (b) DBU, CCl_3CN, CH_2Cl_2, rt, 84% over two steps from **6**; (c) **5**, TMSOTf, CH_2Cl_2, 0 °C, 74%; (d) $PdCl_2$, CH_3OH, rt, 86%; (e) TMSOTf, CH_2Cl_2, 0 °C, 87%; (f) $NaOCH_3$, CH_3OH, rt, 93%; (g) **16**, TMSOTf, CH_2Cl_2, 0 °C, 92%; (h) H_2, $Pd(OH)_2$–C, EtOAc/CH_3OH, rt, 100%; (i) BzCl, pyridine, DMAP, 50 °C, 96%; (j) CAN, H_2O, CH_3CN, rt, 97%; (k) DBU, CCl_3CN, CH_2Cl_2, rt, 100%; (l) $HO(CH_2)_8N_3$, TMSOTf, CH_2Cl_2, rt, 79%; (m) $NaOCH_3$, CH_3OH, rt, 85%.

second glycosylation reaction, this time with trichloroacetimidate donor **16**, which was prepared as previously described.[6] Upon reaction of **15** and **16** in the presence of TMSOTf, an 87% yield of trisaccharide **17** was obtained. Debenzoylation of **17** with sodium methoxide in methanol afforded trisaccharide alcohol **18** in 93% yield. The addition of the final monosaccharide residue was achieved by a TMSOTf-promoted glycosylation reaction between **18** and **16**, which gave a 92% yield of tetrasaccharide **19**.

Having assembled the tetrasaccharide, all that remained was the introduction of the azidooctyl aglycone. The inclusion of an azido group into the target necessitated a change in protecting groups, as the removal of benzyl protecting groups while leaving the azide group intact would be problematic, if not impossible. Therefore, the benzyl ethers in **19** were removed by hydrogenolysis over palladium hydroxide on carbon, and the resulting product, **20**, was benzoylated. This benzoylation proved sluggish, and the successful completion required that the reaction mixture be heated at 50 °C for 15 h. Nevertheless, desired product **21** was obtained in 96% yield over the two steps. Next, the *p*-methoxyphenyl glycoside in **21** was reacted with CAN in wet CH_3CN, which gave the reducing sugar **22** in 97% yield. Conversion of **22** into trichloroacetimidate **23** was carried out under standard conditions, and this donor was then reacted with 8-azido-1-octanol[9] and TMSOTf to give a 79% yield of the fully protected trisaccharide **24**. Removal of the benzoyl groups with sodium methoxide proceeded in excellent overall yield giving target **3** in 85% yield. In **3**, the stereochemistry of all mannopyranoside residues was established by the measurement of the $^1J_{C1,H1}$ for each glycosidic linkage. These values ranged from 168.0 to 172.2 Hz, thus clearly confirming the α-stereochemistry.[10]

An analogous series of transformations was used in the preparation of the methylated tetrasaccharide **4** (Scheme 3). First, *p*-methoxyphenyl glycoside **8** was converted to the corresponding imidate **25** in two steps. This donor was then used to glycosylate trisaccharide alcohol **19** in the presence of TMSOTf, which afforded tetrasac-



Scheme 3. Reagents and conditions: (a) CAN, H_2O, CH_3CN, rt; (b) DBU, CCl_3CN, CH_2Cl_2, rt, 78% over two steps from **8**; (c) **18**, TMSOTf, CH_2Cl_2, 0 °C, 79%; (d) H_2, $Pd(OH)_2$–C, EtOAc, CH_3OH, rt, 100%; (e) BzCl, pyridine, DMAP, 50 °C, 93%; (f) CAN, H_2O, CH_3CN, rt, 91%; (g) DBU, CCl_3CN, CH_2Cl_2, rt, 91%; (h) $HO(CH_2)_8N_3$, TMSOTf, CH_2Cl_2, rt, 72%; (i) $NaOCH_3$, CH_2Cl_2/CH_3OH, rt, 83%.

charide **26** in 79% yield. Replacement of the benzyl ethers in **26** with benzoate esters proceeded via **27** to give the expected product **28** in 93% yield over the two steps. CAN-mediated cleavage of the aglycone in **28** afforded a 91% yield of reducing sugar **29**, which was then converted to imidate **30**, also in 91% yield.

Glycosylation of 8-azido-1-octanol[9] with **30** was achieved in 72% yield upon treatment with TMSOTf. Reaction of the product of this reaction, **31**, with sodium methoxide provided, in 83% yield, target molecule **4**. The $^{1}J_{C1,H1}$ for each monosaccharide residue in **4** ranged from 168.2 to 172.3 Hz, which would be expected for a molecule containing four α-mannopyranoside residues.[10]

In conclusion, we have described the synthesis of 8-azidooctyl glycoside derivatives of the *E. coli* serotype O9a O-chain repeating unit, and the terminal tetrasaccharide motif in this polysaccharide, which contains a methyl group on O-3 of the distal mannopyranose residue. Both compounds were assembled by the addition of single monosaccharide units via glycosyl trichloroacetimidate donors, from the reducing to the nonreducing end of the molecule. The 8-azidooctyl aglycone will facilitate the preparation of neoglycoconjugates from these oligosaccharides, and their use in studying the biosynthesis of the O-chain in *E. coli* serotype O9a is in progress.

3. Experimental

3.1. General methods

Solvents used in the reactions were purified by successive passage through columns of alumina and copper under an argon atmosphere. All reagents used were purchased from commercial sources and used without further purification unless noted otherwise. ^{1}H NMR and ^{13}C NMR spectra were recorded at 500 MHz and 125 MHz, respectively. ^{1}H NMR chemical shifts are referenced to $(CH_3)_4Si$ (δ 0.0, $CDCl_3$) or CD_3OD (δ 3.30, CD_3OD). ^{13}C NMR chemical shifts were referenced to $CDCl_3$ (δ 77.23, $CDCl_3$) or CD_3OD (δ 48.90, CD_3OD). Optical rotations were measured at 21 ± 2 °C. Unless stated otherwise, all reactions were carried out at room temperature under a positive pressure of argon and monitored by TLC on Silica Gel 60 F_{254} (0.25 mm, E. Merck). Spots were detected under UV light and/or by charring with 10% H_2SO_4 in EtOH, anisaldehyde, or $CeSO_4$. Organic solutions of crude products were dried over anhyd Na_2SO_4. Solvents were evaporated under reduced pressure and below 40 °C. Column chromatography was performed on Silica Gel 60 (40–60 μm); the ratio between silica gel and crude product ranged from 100:1 to 20:1 (w/w). Electrospray-ionization mass spectra (ESIMS) were recorded on samples suspended in mixtures of THF with CH_3OH and added NaCl. Matrix-assisted laser-desportion ionization mass spectra (MALDI MS) were obtained on samples suspended in a DCTB (2-[(2*E*)-3-(4-*tert*-butylphenyl)-2-methylprop-2-enylidene]malononitrile) matrix using the delayed-extraction mode and positive-ion detection.

3.2. 8-Azidooctyl α-D-mannopyranosyl-(1→2)-α-D-mannopyranosyl-(1→3)-α-D-mannopyranosyl-(1→3)-α-D-mannopyranoside (3)

To a solution of compound **24** (49 mg, 0.02 mmol) in 1:1 CH_2Cl_2–CH_3OH (10 mL) was added M $NaOCH_3$ in CH_3OH (0.29 mL). After stirring for 16 h at rt, the reaction mixture was neutralized with Amberlite IR-120 (H^+) resin, filtered, and concentrated. The resulting oil was purified by chromatography in 2:1 CH_2Cl_2–CH_3OH to afford compound **3** (16 mg, 85%) as a white foam. R_f 0.38 (3:1, CH_2Cl_2–CH_3OH); $[\alpha]_D$ +77.6 (*c* 0.2, CH_3OH) ^{1}H NMR (500 MHz, CD_3OD, δ_H) 5.41 (d, 1H, $J = 1.5$ Hz, H-1), 5.02 (d, 1H, $J = 1.9$ Hz, H-1′), 4.98 (d, 1H, $J = 1.6$ Hz, H-1″), 4.71 (d, 1H, $J = 1.8$ Hz, H-1‴), 4.20–4.17 (dd, 1H, $J = 3.2$, 1.9 Hz, H-2′), 4.01 (dd, 1H, $J = 3.4$, 1.5 Hz, H-2), 3.99 (dd, 1H, $J = 2.9$, 1.8 Hz, H-2‴), 3.98–3.50 (m, 22H, H-2″, H-3, H-4, H-5, H-6_a, H-6_b, H-3′, H-4′, H-5′, H-$6'_a$, H-$6'_b$, H-3″, H-4″, H-5″, H-$6''_a$, H-$6''_b$, H-3‴, H-4‴, H-5‴, H-$6'''_a$, H-$6'''_b$, octyl OCH_2), 3.41 (ddd, 1H, $J = 9.6$, 6.4, 6.4 Hz, octyl OCH_2), 3.27 (dd, 2H, $J = 6.9$, 6.9 Hz, CH_2N_3), 1.63–1.54 (m, 4H, octyl CH_2), 1.42–1.31 (m, 8H, octyl CH_2); ^{13}C NMR (125 MHz, CD_3OD, δ_C) 104.2 (C-1″, $^{1}J_{CH} = 169.2$), 103.9 (C-1′, $^{1}J_{CH} = 169.8$), 101.8 (C-1, $^{1}J_{CH} = 172.2$), 101.6 (C-1‴, $^{1}J_{CH} = 168.0$), 80.8 (C-2″), 80.5 (C-2′), 80.2 (C-2), 75.2 (C-3′), 75.1 (C-2‴), 75.0 (C-4), 74.7 (C-3‴), 72.5 (C-4″), 72.1 (C-3), 71.9 (C-4‴), 71.5 (C-4′), 71.3 (C-3″), 69.4 (C-5), 68.8 (C-5′), 68.7 (octyl O*C*H$_2$), 67.7 (C-5‴), 67.6 (C-5″), 63.3 (2C, C-6′, C-6″), 62.9 (C-6‴), 62.8 (C-6), 52.5 (*C*H$_2$N$_3$), 30.6 (octyl *C*H$_2$), 30.4 (octyl *C*H$_2$), 30.2 (octyl *C*H$_2$), 29.9 (octyl *C*H$_2$), 27.8 (octyl *C*H$_2$), 27.3 (octyl *C*H$_2$). ESIMS: *m*/*z* calcd for $[C_{32}H_{57}O_{21}N_3]Na^+$: 842.3377. Found: 842.3375.

3.3. 8-Azidooctyl 3-*O*-methyl-α-D-mannopyranosyl-(1→2)-α-D-mannopyranosyl-(1→3)-α-D-mannopyranosyl-(1→3)-α-D-mannopyranoside (4)

To a solution of **31** (43 mg, 0.02 mmol) in 1:1 CH_2Cl_2–CH_3OH (10 mL) was added 1M $NaOCH_3$ in CH_3OH (0.25 mL). After stirring for 16 h at rt, the reaction mixture was neutralized with Amberlite IR-120 H^+ resin, filtered, and concentrated. The resulting oil was purified by chromatography in 2:1 CH_2Cl_2–CH_3OH to afford **4** (14 mg, 83%) as a white foam. R_f 0.41 (3:1, CH_2Cl_2–CH_3OH); $[\alpha]_D$ +73.9 (*c* 0.25, CH_3OH); ^{1}H NMR (500 MHz, CD_3OD, δ_H) 5.42 (d, 1H, $J = 1.6$ Hz, H-1), 5.03 (d, 1H, $J = 1.8$ Hz, H-1′), 5.01 (d, 1H, $J = 1.8$ Hz,

H-1″), 4.71 (d, 1H, $J = 1.8$ Hz, H-1‴), 4.21–4.26 (m, 2H, H-2′, H-2″), 4.07 (dd, 1H, $J = 3.4$, 1.6 Hz, H-2), 3.99 (dd, 1H, $J = 2.9$, 1.8 Hz, H-2‴), 3.95–3.51 (m, 21H, H-3, H-4, H-5, 2 × H-6, H-3′, H-4′, H-5′, 2 × H-6′, H-3″, H-4″, H-5″, 2 × H-6″, H-3‴, H-4‴, H-5‴, 2 × H-6‴, octyl OCH_2), 3.45 (s, 3H, OCH_3), 3.41 (ddd, 1H, $J = 9.7$, 6.3, 6.3 Hz, octyl OCH_2), 3.36 (dd, 1H, $J = 9.3$, 3.1 Hz, H-3″), 3.27 (t, 2H, $J = 6.9$ Hz, CH_2N$_3$), 1.63–1.55 (m, 4H, octyl CH_2), 1.43–1.31 (m, 8H, octyl CH_2); ^{13}C NMR (125 MHz, CD_3OD, δ_C) 104.2 (C-1″, $^1J_{CH} = 171.5$), 103.9 (C-1′, $^1J_{CH} = 170.4$), 101.8 (C-1, $^1J_{CH} = 172.3$), 101.6 (C-1‴, $^1J_{CH} = 168.2$), 82.1 (C-3″), 80.8 (C-2), 80.7 (C-2″), 80.3 (C-2‴), 75.2 (C-4), 75.0 (2C, C-4″, C-2′), 74.7 (C-3′), 72.0 (C-3‴), 71.5 (C-3), 71.3 (C-4′), 69.4 (C-4‴), 68.7 (octyl OCH_2), 67.9 (C-5″), 67.7 (2C, C-5, C-5′), 67.5 (C-5‴), 63.3 (2C, C-6′, C-6″), 62.9 (C-6‴), 62.8 (C-6), 57.4 (OCH_3), 52.5 (octyl CH_2N$_3$), 30.6 (octyl CH_2), 30.4 (octyl CH_2), 30.2 (octyl CH_2), 29.9 (octyl CH_2), 27.8 (octyl CH_2), 27.3 (octyl CH_2). ESIMS: m/z calcd for [$C_{33}H_{59}O_{21}N_3$]Na$^+$: 856.3533. Found: 856.3535.

3.4. *p*-Methoxyphenyl 2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (7)

Alcohol **10** (1.31 g, 2.35 mmol) was dissolved in CH_2Cl_2 (20 mL), pyridine (1.0 mL, 11.88 mmol), and benzoyl chloride (0.33 mL, 2.82 mmol) was added at 0 °C. The reaction mixture was stirred for 2 h at rt before being diluted with CH_2Cl_2 (50 mL) and sequentially washed with 1N HCl (2 × 50 mL), satd aq $NaHCO_3$ (50 mL), and H_2O (50 mL). The organic layer was dried and concentrated, and the crude product was purified by chromatography (6:1 hexane–EtOAc) to give **7** (1.51 g, 97%) as a colorless oil. R_f 0.54 (4:1 hexane–EtOAc); $[\alpha]_D$ +37.0 (c 0.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.12–8.08 (m, 2H, Ar), 7.59–7.55 (m, 1H, Ar), 7.40–7.21 (m, 17H, Ar), 7.04–7.02 (m, 2H, Ar), 6.83–6.80 (m, 2H, Ar), 5.80 (dd, 1H, $J = 3.2$, 1.9 Hz, H-2), 5.59 (d, 1H, $J = 1.9$ Hz, H-1), 4.91 (d, 1H, $J = 10.8$ Hz, PhCH_2), 4.86 (d, 1H, $J = 11.4$ Hz, PhCH_2), 4.71 (d, 1H, $J = 11.8$ Hz, PhCH_2), 4.66 (d, 1H, $J = 11.4$ Hz, PhCH_2), 4.58 (d, 1H, $J = 10.8$ Hz, PhCH_2), 4.50 (d, 1H, $J = 11.8$ Hz, PhCH_2), 4.32 (dd, 1H, $J = 3.2$, 9.7 Hz, H-3), 4.20 (dd, 1H, 9.7, 9.7 Hz, H-4), 4.03 (ddd, 1H, $J = 2.0$ Hz, $J = 9.7$, 3.9, 1.0 Hz, H-5), 3.90 (dd, 1H, $J = 3.9$, 10.9 Hz, H-6$_a$), 3.77–3.75 (m, 4H, OCH_3, H-6$_b$); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 165.7 (*C*=O), 155.1 (Ar), 150.0 (Ar), 138.41 (Ar), 138.36 (Ar), 138.0 (Ar), 133.2 (Ar), 130.0 (2 × Ar), 129.8 (Ar), 128.4 (2 × Ar), 128.33 (2 × Ar), 128.32 (2 × Ar), 128.30 (2 × Ar), 128.04 (2 × Ar), 127.96 (2 × Ar), 127.66 (Ar), 127.65 (Ar), 127.51 (2 × Ar), 127.47 (Ar), 117.8 (2 × Ar), 114.6 (2 × Ar), 97.0 (C-1), 78.1 (C-3), 75.3 (Ph*C*H$_2$), 74.2 (C-4), 73.4 (Ph*C*H$_2$), 72.1 (C-5), 71.8 (Ph*C*H$_2$), 68.9 (C-6), 68.8 (C-2), 55.6 (OCH_3). ESIMS: m/z calcd for [$C_{41}H_{40}O_8$]Na$^+$: 683.2615. Found: 683.2616.

3.5. *p*-Methoxyphenyl 2,4,6-tri-*O*-benzoyl-3-*O*-methyl-α-D-mannopyranoside (8)

To a solution of pyridine (10 mL), DMAP (11 mg, 0.09 mmol), and **12** (260 mg, 0.87 mmol) was added BzCl (0.36 mL, 3.13 mmol) dropwise. The reaction mixture was stirred at rt for 4 h before being diluted with CH_2Cl_2 (50 mL) and washed with N HCl (2 × 50 mL), satd aq $NaHCO_3$ (50 mL), and brine (50 mL). The organic layer was dried and concentrated, and the crude product was purified by chromatography (4:1 hexane–EtOAc) to give **8** (490 mg, 96%) as a colorless oil. R_f 0.71 (2:1, hexane–EtOAc); $[\alpha]_D$ +21.2 (c 0.4, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.12–8.06 (m, 4H, Ar), 8.02–7.98 (m, 2H, Ar), 7.59–7.54 (m, 3H, Ar), 7.47–7.36 (m, 6H, Ar), 7.12–7.07 (m, 2H, Ar), 6.80–6.75 (m, 2H, Ar), 5.87–5.81 (m, 2H, H-2, H-4), 5.62 (d, 1H, $J = 1.9$ Hz, H-1), 4.64–4.59 (m, 1H, H-6$_a$), 4.47–4.38 (m, 2H, H-5, H-6$_b$), 4.19 (dd, 1H, $J = 9.7$, 3.3 Hz, H-3), 3.75 (s, 3H, ArOCH_3), 3.46 (s, 3H, OCH_3); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 166.1 (*C*=O), 165.7 (*C*=O), 165.5 (*C*=O), 155.4 (Ar), 149.8 (Ar × 2), 133.4 (Ar), 133.3 (Ar), 133.0 (Ar), 130.0 (Ar × 2), 129.9 (Ar × 2), 129.8 (Ar × 2), 129.5 (Ar), 129.4 (Ar), 128.50 (Ar × 2), 128.48 (Ar × 2), 128.3 (Ar × 2), 118.0 (Ar × 2), 114.7 (Ar × 2), 97.0 (C-1), 77.2 (C-3), 69.4 (C-5), 68.45 (C-4), 68.42 (C-2), 63.2 (C-6), 58.1 (O*C*H$_3$), 55.6 (ArO*C*H$_3$). ESIMS: m/z calcd for [$C_{35}H_{32}O_{10}$]Na$^+$: 635.1888. Found: 635.1892.

3.6. *p*-Methoxyphenyl 3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (10)

Diol **9**[6] (1.20 g, 2.57 mmol) was dissolved in toluene (50 mL), and n-Bu_2SnO (0.92 g, 3.08 mmol) was added. The reaction mixture was heated to 105 °C and stirred for 2 h, then cooled for 30 min before n-Bu_4NI (1.14 g, 3.09 mmol) and benzyl bromide (3.06 mL, 25.7 mmol) were added. The reaction mixture was then heated to 105 °C again and stirred for 16 h. The reaction mixture was cooled and concentrated, and the crude product was purified by chromatography (4:1 hexane–EtOAc) to give **10** (1.31 g, 92%) as an oil. R_f 0.33 (2:1 hexane–EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.41–7.24 (m, 13H, Ar), 7.21–7.19 (m, 2H, Ar), 7.02–6.99 (m, 2H, Ar), 6.83–6.81 (m, 2H, Ar), 5.53 (d, 1H, $J = 1.7$ Hz, H-1), 4.88 (d, 1H, $J = 10.8$ Hz, PhCH_2), 4.76–4.81 (m, 2H, PhCH_2), 4.62 (d, 1H, $J = 11.9$ Hz, PhCH_2), 4.56 (d, 1H, $J = 10.8$ Hz, PhCH_2), 4.48 (d, 1H, $J = 11.9$ Hz, PhCH_2), 4.22 (br s, 1H, H-2), 4.09 (dd, 1H, $J = 3.3$, 8.4 Hz, H-3), 3.99–3.93 (m, 2H, H-4, H-5), 3.78–3.75 (m, 4H, H-6$_a$, OCH_3), 3.67 (dd, 1H, $J = 10.9$, 1.0 Hz, H-6$_b$), 2.56 (d, 1H, $J = 2.6$ Hz, 2-OH); ^{13}C NMR

(125 MHz, $CDCl_3$, δ_C) 155.0 (Ar), 150.1 (Ar), 138.3 (Ar), 138.2 (Ar), 137.9 (Ar), 128.6 (2 × Ar), 128.34 (2 × Ar), 128.26 (2 × Ar), 128.0 (Ar), 127.89 (2 × Ar), 127.86 (2 × Ar), 127.8 (2 × Ar), 127.7 (Ar), 127.5 (Ar), 117.8 (2 × Ar), 114.6 (2 × Ar), 98.2 (C-1), 80.0 (C-3), 75.2 (Ph*C*H_2), 74.2 (C-4), 73.4 (Ph*C*H_2), 72.2 (Ph*C*H_2), 71.6 (C-5), 68.8 (C-6), 68.4 (C-2), 55.6 (OCH_3). ESIMS: *m*/*z* calcd for $[C_{34}H_{36}O_7]Na^+$: 579.2353. Found: 579.2356.

3.7. *p*-Methoxyphenyl 3-*O*-methyl-α-D-mannopyranoside (12)

Compound **11**[8] (300 mg, 1.05 mmol) was dissolved in toluene (30 mL), and *n*-Bu_2SnO (380 mg, 1.27 mmol) was added. The reaction mixture was heated to 105 °C and stirred for 4 h, then cooled to room temperature before *n*-Bu_4NI (460 mg, 1.25 mmol) and iodomethane (0.65 mL, 10.5 mmol) were added. The reaction mixture was then heated to 105 °C again and stirred for 24 h. The reaction mixture was cooled and concentrated, and the crude product was purified by chromatography (10:1, CH_2Cl_2–CH_3OH) to give **12** (260 mg, 83%) as a colorless oil. R_f 0.39 (10:1, CH_2Cl_2–CH_3OH); $[\alpha]_D$ +105.3 (*c* 0.8, CH_3OH); ^1H NMR (500 MHz, CD_3OD, δ_H) 7.06–7.02 (m, 2H, Ar), 6.85–6.81 (m, 2H, Ar), 5.36 (d, 1H, $J = 2.0$ Hz, H-1), 4.20 (dd, 1H, $J = 3.3$, 2.0 Hz, H-2), 3.82–3.63 (m, 7H, ArOCH_3, H-4, H-5, H-6_a, H-6_b), 3.54 (dd, 1H, $J = 9.4$, 3.3 Hz, H-3), 3.50 (s, 3H, OCH_3); ^{13}C NMR (125 MHz, CD_3OD, δ_C) 156.7 (Ar), 152.0 (Ar), 119.2 (2 × Ar), 115.7 (2 × Ar), 101.1 (C-1), 82.2 (C-3), 75.2 (C-5), 68.1 (C-2), 67.3 (C-4), 62.7 (C-6), 57.6 (O*C*H_3), 56.1 (ArO*C*H_3). ESIMS: *m*/*z* calcd for $[C_{14}H_{20}O_7]Na^+$: 323.1101. Found: 323.1102.

3.8. 3-*O*-Allyl-2,4,6-tri-*O*-benzyl-D-mannopyranosyl trichloroacetimidate (13)

A solution of compound **6**[6] (560 mg, 0.94 mmol) and ceric ammonium nitrate (2.58 g, 4.7 mmol) in 4:1 CH_3CN–H_2O (25 mL) was stirred at rt for 1 h, diluted with EtOAc (40 mL), and washed with water (40 mL), satd aq $NaHCO_3$ (40 mL), and brine (40 mL). The organic layer was dried and concentrated, and the residue was purified by chromatography (3:1 hexane–EtOAc) to afford the expected monosaccharide (393 mg, 85%) as a colorless oil. The reducing monosaccharide (393 mg, 0.71 mmol) was then dissolved in dry CH_2Cl_2 (20 mL), and then CCl_3CN (0.85 mL, 8.52 mmol) and DBU (31.7 μL, 0.21 mmol) were sequentially added at 0 °C. The solution was stirred at rt for 2 h and then concentrated. The resulting oil was purified by chromatography (4:1 hexane–EtOAc and 1% Et_3N) to afford compound **13** (469 mg, 99%) as a colorless oil, which, following drying under vacuum overnight, was used immediately in the next step.

3.9. *p*-Methoxyphenyl 3-*O*-allyl-2,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-mannopyranoside (14)

Alcohol **5**[6] (380 mg, 0.68 mmol) and imidate **13** (621 mg, 0.89 mmol) were dissolved in dry CH_2Cl_2 (20 mL), and crushed molecular sieves (1 g) were added. The mixture was stirred at rt for 30 min before it was cooled to 0 °C. A solution of 10% TMSOTf in dry CH_2Cl_2 (124 μL, 0.07 mmol) was added dropwise. The reaction mixture was stirred for 1 h at 0 °C, it was then quenched by the addition of Et_3N. After filtration and concentration of the reaction mixture, the crude product was purified by chromatography (8:1 hexane–EtOAc) to give **14** (513 mg, 74%) as a colorless oil. R_f 0.32 (4:1 hexane–EtOAc); $[\alpha]_D$ +41.6 (*c* 0.5, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$, δ_H) 7.37–7.16 (m, 30H, Ar), 6.97–6.92 (m, 2H, Ar), 6.79–6.74 (m, 2H, Ar), 5.94–5.86 (m, 1H, CH_2=C*H*), 5.42 (d, 1H, $J = 1.8$ Hz, H-1), 5.32 (br s, 1H, H-1′), 5.30–5.24 (m, 1H, CH_2=CH), 5.15–5.10 (m, 1H, CH_2=CH), 4.90 (d, 1H, $J = 11.0$ Hz, PhCH_2), 4.75–4.48 (m, 10H, 10 × PhCH_2), 4.44 (dd, 1H, $J = 11.9$ Hz, PhCH_2), 4.35 (dd, 1H, $J = 9.5$, 3.0 Hz, H-3), 4.12–3.85 (m, 8H, H-2, H-4, 2 × CH_2=CHCH_2O, H-5, H-4′, H-5′, H-6_a), 3.82–3.62 (m, 8H, H-2′, ArOCH_3, H-3′, H-6_b, H-$6'_a$, H-$6'_b$); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 154.9 (Ar), 150.4 (Ar), 138.9 (Ar), 138.44 (2 × Ar), 138.43 (Ar), 138.37 (Ar), 138.2 (Ar), 135.1 (*C*H=CH_2), 128.40 (Ar), 128.38 (Ar), 128.31 (Ar), 128.24 (Ar), 128.22 (Ar), 128.19 (4 × Ar), 127.74 (2 × Ar), 127.69 (4 × Ar), 127.66 (4 × Ar), 127.56 (Ar), 127.5 (2 × Ar), 127.44 (2 × Ar), 127.42 (2 × Ar), 127.37 (2 × Ar), 127.0 (2 × Ar), 118.0 (2 × Ar), 116.6 (*C*H_2=CH), 114.5 (2 × Ar), 100.3 (C-1′), 96.6 (C-1), 79.7 (C-3), 77.6 (C-2′), 75.6 (C-2), 75.1 (C-5), 75.0 (C-5′), 74.8 (Ph*C*H_2), 74.6 (Ph*C*H_2), 73.5 (Ph*C*H_2), 73.3 (Ph*C*H_2), 72.7 (C-3'), 72.5 (C-4′), 72.42 (Ph*C*H_2), 72.39 (C-4), 72.36 (Ph*C*H_2), 71.1 (CH_2=CH*C*H_2O), 69.8 (C-6), 69.1 (C-6′), 55.7 (ArO*C*H_3). ESIMS: *m*/*z* calcd for $[C_{64}H_{68}O_{12}]Na^+$: 1051.4603. Found: 1051.4606.

3.10. *p*-Methoxyphenyl 2,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-mannopyranoside (15)

Compound **14** (634 mg, 0.63 mmol) was dissolved in 9:1 CH_3OH–CH_2Cl_2 (30 mL) and $PdCl_2$ (28 mg, 0.16 mmol) was added. The reaction mixture was stirred at rt for 2 h before it was filtered and concentrated. The crude product was purified by chromatography (4:1 hexane–EtOAc) to give **15** (524 mg, 86%) as a colorless oil. R_f 0.24 (4:1 hexane–EtOAc); $[\alpha]_D$ +50.4 (*c* 1.2, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$, δ_H) 7.38–7.15 (m, 30H, Ar), 6.98–6.94 (m, 2H, Ar), 6.82–6.76 (m, 2H, Ar), 5.44 (d, 1H, $J = 1.7$ Hz, H-1), 5.37 (br s, 1H, H-1′),

4.87 (d, 1H, $J = 11.3$ Hz, PhCH_2), 4.79–4.36 (m, 11H, 11 × PhCH_2), 4.17–4.04 (m, 4H, H-2, H-4, H-6_a, H-3′), 3.97–3.90 (m, 2H, H-3, H-5), 3.80–3.64 (m, 9H, ArOCH_3, H-6_b, H-2′, H-4′, H-5′, H-$6'_a$, H-$6'_b$), 2.31 (d, 1H, $J = 9.5$ Hz, 3′-OH); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 154.9 (Ar), 150.4 (Ar), 138.7 (Ar), 138.5 (Ar), 138.3 (2 × Ar), 138.1 (Ar), 137.8 (Ar), 128.4 (4 × Ar), 128.3 (4 × Ar), 128.2 (3 × Ar), 127.75 (Ar), 127.70 (2 × Ar), 127.67 (4 × Ar), 127.63 (4 × Ar), 127.59 (2 × Ar), 127.53 (2 × Ar), 127.4 (2 × Ar), 126.9 (2 × Ar), 117.8 (2 × Ar), 114.6 (2 × Ar), 99.2 (C-1), 96.6 (C-1′), 78.9 (C-2′), 78.7 (C-3′), 77.5 (C-2), 76.7 (C-4′), 75.1 (C-4), 74.5 (2 × PhCH_2), 73.5 (PhCH_2), 73.3 (PhCH_2), 72.6 (C-3), 72.37 (PhCH_2), 72.36 (PhCH_2), 71.8 (C-5′), 71.7 (C-5), 69.6 (C-6), 69.1 (C-6′), 55.7 (ArOCH_3). ESIMS: m/z calcd for $[C_{61}H_{64}O_{12}]Na^+$: 1011.4290. Found: 1011.4290.

3.11. 2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-D-mannopyranosyl trichloroacetimidate (16)

A solution of compound **7** (200 mg, 0.3 mmol) and ceric ammonium nitrate (830 mg, 1.5 mmol) in 4:1 CH_3CN–H_2O (25 mL) was stirred at rt for 1 h, diluted with EtOAc (40 mL), and washed with water (40 mL), satd aq $NaHCO_3$ (40 mL), and brine (40 mL). The organic layer was dried and concentrated, and the residue was purified by chromatography (3:1 hexane–EtOAc) to afford reducing monosaccharide (145 mg, 86%) as a colorless oil. A portion of this material (119 mg, 0.21 mmol) was then dissolved in dry CH_2Cl_2 (10 mL), and then CCl_3CN (0.27 mL, 2.57 mmoL) and DBU (9.9 μL, 0.06 mmol) were sequentially added at 0 °C. The solution was stirred at rt for 2 h and then concentrated. The resulting oil was purified by chromatography (5:1 hexane–EtOAc and 1% Et_3N) to afford **16** (132 mg, 88%) as a colorless oil, which, following drying under vacuum overnight, was used immediately in the next step.

3.12. *p*-Methoxyphenyl 2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-mannopyranoside (17)

Disaccharide **15** (524 mg, 0.52 mmol) and imidate **16** (562 mg, 0.80 mmol) were dissolved in dry CH_2Cl_2 (20 mL), and crushed molecular sieves (1 g) were added. The mixture was stirred at rt for 30 min and then it was cooled to 0 °C. A solution of 10% TMSOTf (98 μL, 0.05 mmol) in dry CH_2Cl_2 was added dropwise. The reaction mixture was stirred for 1 h at 0 °C, and then it was quenched by the addition of Et_3N. After filtration and concentration of the reaction mixture, the crude product was purified by chromatography (6:1 hexane–EtOAc) to give **17** (714 mg, 87%) as a colorless oil. R_f 0.31 (4:1 hexane–EtOAc); $[\alpha]_D$ +21.7 (c 0.7, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.06–8.03 (m, 2H, Ar), 7.57–7.54 (m, 1H, Ar), 7.38–7.12 (m, 47H, Ar), 6.98–6.94 (m, 2H, Ar), 6.79–6.76 (m, 2H, Ar), 5.74 (br s, 1H, H-2″), 5.46 (s, 1H, H-1), 5.35 (br s, 2H, H-1′, H-1″), 4.88 (d, 1H, $J = 11.1$ Hz, PhCH_2), 4.81 (d, 1H, $J = 11.0$ Hz, PhCH_2), 4.77–4.33 (m, 17H, 16 × PhCH_2, H-3), 4.28 (dd, 1H, $J = 8.7$, 2.8 Hz, H-3′), 4.15–3.86 (m, 9H, H-4, H-2, H-6_a, H-6_b, H-4′, H-2′, H-3″, H-4″, H-5), 3.78–3.60 (m, 8H, ArOCH_3, H-5′, H-$6'_a$, H-$6'_b$, H-$6''_a$, H-$6''_b$), 3.55–3.48 (m, 1H, H-5″); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 165.4 (C=O), 154.9 (Ar), 150.4 (Ar), 138.7 (Ar), 138.4 (Ar), 138.35 (Ar), 138.33 (Ar), 138.28 (Ar), 138.1 (Ar), 138.05 (Ar), 138.0 (2 × Ar), 133.0 (Ar), 130.0 (Ar), 128.42 (2 × Ar), 128.4 (4 × Ar), 128.32 (4 × Ar), 128.29 (4 × Ar), 128.28 (4 × Ar), 128.26 (4 × Ar), 128.24 (2 × Ar), 128.17 (2 × Ar), 128.0 (2 × Ar), 127.9 (2 × Ar), 127.73 (2 × Ar), 127.72 (2 × Ar), 127.68 (2 × Ar), 127.67 (2 × Ar), 127.58 (2 × Ar), 127.56 (2 × Ar), 127.45 (2 × Ar), 127.42 (2 × Ar), 127.2 (2 × Ar), 127.1 (Ar), 117.9 (2 × Ar), 114.5 (2 × Ar), 99.6 (2C, C-1′, C-1″), 96.6 (C-1), 78.1 (2C, C-2′, C-2), 78.0 (C-4), 77.6 (C-3″), 75.4 (C-4″), 75.0 (PhCH_2), 74.6 (2 × PhCH_2), 74.2 (2C, C-3′, C-5), 73.5 (PhCH_2), 73.4 (PhCH_2), 73.3 (PhCH_2), 72.5 (3C, C-4′, C-3, C-5″), 72.4 (PhCH_2), 72.0 (PhCH_2), 71.6 (PhCH_2), 69.5 (C-6″), 69.12 (2C, C-2″, C-5′), 69.07 (C-6′), 68.9 (C-6), 55.7 (ArOCH_3). ESIMS: m/z calcd for $[C_{95}H_{96}O_{18}]Na^+$: 1547.6489. Found: 1547.8496.

3.13. *p*-Methoxyphenyl 3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-mannopyranoside (18)

Compound **17** (714 mg, 0.47 mmol) was dissolved in 1:1 CH_3OH–CH_2Cl_2 (50 mL), and 1M $NaOCH_3$ (0.5 mL) was added. The reaction mixture was stirred at rt for 16 h. Amberlite IR-120 (H^+) resin was added, and the solution was filtered and concentrated. The crude product was purified by chromatography (3:1 hexane–EtOAc) to give **18** (618 mg, 93%) as a colorless oil. R_f 0.55 (2:1, hexane–EtOAc); $[\alpha]_D$ +50.3 (c 0.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.42–7.13 (m, 45H, Ar), 7.02–6.97 (m, 2H, Ar), 6.83–6.78 (m, 2H, Ar), 5.49 (br s, 1H, H-1), 5.36 (br s, 1H, H-1′), 5.30 (br s, 1H, H-1″), 4.85 (d, 1H, $J = 10.0$ Hz, PhCH_2), 4.74–4.58 (m, 8H, 8 × PhCH_2), 4.56–4.35 (m, 10H, 9 × PhCH_2, H-3), 4.26 (dd, 1H, $J = 5.4$, 2.3 Hz, H-3′), 4.11–3.86 (m, 10H, H-2, H-4, H-5, H-6_a, H-6_b, H-2′, H-2″, H-3″, H-4′, H-5′), 3.78 (s, 3H, ArOCH_3), 3.76–3.48 (m, 6H, H-$6''_a$, H-$6''_b$, H-5″, H-4″, H-$6'_a$, H-$6'_b$), 2.33 (br s, 1H, OH); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 154.9 (Ar), 150.4 (Ar), 138.7 (Ar), 138.4 (Ar), 138.32 (Ar), 138.30 (Ar), 138.27 (Ar), 138.24 (Ar), 138.16 (Ar), 138.1 (Ar), 138.0 (Ar), 128.50 (2 × Ar), 128.47 (2 × Ar), 128.4 (2 × Ar), 128.38 (2 × Ar), 128.32

(2 × Ar), 128.28 (2 × Ar), 128.25 (2 × Ar), 128.2 (4 × Ar), 127.9 (2 × Ar), 127.83 (2 × Ar), 127.79 (2 × Ar), 127.72 (2 × Ar), 127.70 (4 × Ar), 127.68 (4 × Ar), 127.50 (2 × Ar), 127.47 (Ar), 127.46 (Ar), 127.44 (Ar), 127.37 (Ar), 127.24 (2 × Ar), 127.20 (2 × Ar), 127.1 (Ar), 117.9 (2 × Ar), 114.6 (2 × Ar), 99.8 (C-1′), 96.6 (2C, C-1, C-1″), 80.0 (2C, C-3″, C-3′), 78.1 (C-3), 77.6 (C-5), 75.4 (2C, C-4′, C-5″), 75.0 (2C, C-4, C-4″), 74.8 (PhCH$_2$), 74.6 (PhCH$_2$), 74.2 (C-5′), 73.5 (PhCH$_2$), 73.4 (PhCH$_2$), 73.3 (2 × PhCH$_2$), 72.5 (C-2′), 72.3 (PhCH$_2$), 72.1 (PhCH$_2$), 72.0 (PhCH$_2$), 71.9 (C-2), 69.5 (C-6), 69.0 (C-6′), 68.9 (C-6″), 68.7 (C-2″), 55.6 (ArOCH$_3$). ESIMS: *m*/*z* calcd for [$C_{88}H_{92}O_{17}$]Na$^+$: 1442.6232. Found: 1443.6234.

3.14. *p*-Methoxyphenyl 2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→2)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-mannopyranoside (19)

To a solution of a mixture of trisaccharide **18** (618 mg, 0.43 mmol) and imidate **16** (497 mg, 0.71 mmol) in dry CH_2Cl_2 (20 mL) was added activated 4 Å molecular sieves (1 g), and the mixture was stirred at rt for 30 min. The mixture was then cooled to 0 °C and a solution of 10% TMSOTf in CH_2Cl_2 (78.7 μL, 0.04 mmol) was added. The reaction mixture was stirred for 1 h at 0 °C, and then it was neutralized by the addition of Et_3N, filtered, and concentrated to give a residue that was purified by chromatography (4:1 hexane–EtOAc) to afford **19** (782 mg, 92%) as a colorless oil. R_f 0.41 (3:1 hexane–EtOAc); $[\alpha]_D$ +25.6 (*c* 1.2, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.11–8.05 (m, 2H, Ar), 7.59–7.53 (m, 1H, Ar), 7.42–7.07 (m, 62H, Ar), 6.99–6.93 (m, 2H, Ar), 6.81–6.75 (m, 2H, Ar), 5.76 (dd, 1H, *J* = 2.3, 2.3 Hz, H-2‴), 5.44 (d, 1H, *J* = 1.4 Hz, H-1), 5.35 (d, 1H, *J* = 1.7 Hz, H-1′), 5.31 (br s, 1H, H-1″), 5.11 (br s, 1H, H-1‴), 4.88 (d, 1H, *J* = 11.1 Hz, PhCH_2), 4.83 (d, 1H, *J* = 10.9 Hz, PhCH_2), 4.78–4.34 (m, 23H, 21 × PhCH_2, H-3, H-3″), 4.30–4.24 (m, 2H, H-3′, PhCH_2), 4.17–3.87 (m, 13H, H-2, H-2′, H-2″, H-3‴, H-4″, H-6′$_a$, H-6$_a$, H-6$_b$, H-5, H-4, H-4′, H-4‴, H-5′), 3.77 (s, 3H, ArOCH_3), 3.75–3.50 (m, 6H, H-5″, H-6″$_a$, H-6″$_b$, H-6′$_b$, H-6‴$_a$, H-6‴$_b$), 3.44–3.36 (m, 1H, H-5‴); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 165.5 (*C*=O), 155.2 (Ar), 150.7 (Ar), 139.0 (Ar), 138.9 (Ar), 138.7 (Ar), 138.6 (2 × Ar), 138.44 (Ar), 138.35 (2 × Ar), 138.2 (2 × Ar), 133.0 (Ar), 130.1 (Ar), 130.0 (2 × Ar), 128.44 (Ar), 128.38 (4 × Ar), 128.36 (4 × Ar), 128.33 (2 × Ar), 128.31 (2 × Ar), 128.26 (4 × Ar), 128.23 (2 × Ar), 128.19 (4 × Ar), 128.1 (2 × Ar), 128.03 (2 × Ar), 128.01 (2 × Ar), 128.00 (2 × Ar), 127.93 (Ar), 127.87 (2 × Ar), 127.73 (2 × Ar), 127.71 (2 × Ar), 127.65 (2 × Ar), 127.60 (2 × Ar), 127.56 (2 × Ar), 127.5 (4 × Ar), 127.44 (2 × Ar), 127.41 (2 × Ar), 127.37 (2 × Ar), 127.31 (4 × Ar), 127.26 (4 × Ar), 127.1 (2 × Ar), 118.1 (2 × Ar), 114.7 (2 × Ar), 100.9 (C-1′), 99.8 (C-1″), 99.6 (C-1‴), 97.1 (C-1), 79.6 (C-2), 78.9 (C-2″), 78.6 (C-3‴), 77.9 (C-2′), 77.3 (C-4′), 76.1 (C-4), 75.6 (C-3″), 75.4 (C-3′), 75.2 (PhCH$_2$), 74.9 (C-3), 74.8 (PhCH$_2$), 74.7 (C-4″), 74.4 (C-4‴), 73.6 (PhCH$_2$), 73.5 (PhCH$_2$), 73.4 (PhCH$_2$), 73.3 (2 × PhCH$_2$), 73.0 (PhCH$_2$), 72.8 (C-5″), 72.7 (C-5′), 72.59 (C-5‴), 72.55 (2 × PhCH$_2$), 72.48 (C-5), 72.2 (PhCH$_2$), 71.7 (PhCH$_2$), 69.8 (C-6), 69.6 (C-6‴), 69.43 (C-6′), 69.36 (C-2‴), 68.9 (C-6″), 55.7 (ArOCH$_3$). MALDI MS: *m*/*z* calcd for [$C_{122}H_{124}O_{23}$]Na$^+$: 1979.8426. Found: 1979.8427.

3.15. *p*-Methoxyphenyl 2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl-(1→2)-3,4,6-tri-*O*-benzoyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-mannopyranoside (21)

To a solution of compound **19** (782 mg, 0.41 mmol) in CH_3OH–EtOAc 3:1 (24 mL) was added 20% Pd(OH)$_2$-on-carbon (100 mg), and the reaction mixture was stirred for 24 h under a hydrogen atmosphere. The reaction mixture was filtered through Celite and then concentrated; an ^{1}H NMR spectrum of the crude product revealed that all of the benzyl groups had been removed. The resulting oil (**20**) was dissolved in pyridine (10 mL). To this solution were added DMAP (5 mg) and benzoyl chloride (0.86 mL, 7.43 mmol) dropwise at rt. The reaction mixture was stirred at 50 °C for 15 h, and it was then diluted with CH_2Cl_2 (50 mL). The organic layer was washed by N HCl (2 × 50 mL), satd aq $NaHCO_3$ (50 mL), and brine (50 mL). After drying, the organic layer was concentrated, and the resulting residue was purified by chromatography (2:1 hexane–EtOAc) to afford **21** (815 mg, 96%) as a white foam. R_f 0.69 (1:1 hexane–EtOAc); $[\alpha]_D$ −23.4 (*c* 1.2, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.27–7.79 (m, 22H, Ar), 7.73–7.69 (m, 2H, Ar), 7.63–7.20 (m, 36H, Ar), 7.16–7.02 (m, 7H, Ar), 6.82–6.76 (m, 2H, Ar), 6.12 (dd, 1H, *J* = 10.1, 10.1 Hz H-4‴), 6.09 (dd, 1H, *J* = 9.8, 9.8 Hz, H-4), 6.01–5.90 (m, 4H, H-2, H-3‴, H-4′, H-4″), 5.73 (dd, 1H, *J* = 3.1, 1.8 Hz, H-2‴), 5.71 (d, 1H, *J* = 1.8 Hz, H-1), 5.62 (dd, 1H, *J* = 10.1, 3.1 Hz, H-3″), 5.49 (d, 1H, *J* = 2.3 Hz, H-1′), 5.41 (dd, 1H, *J* = 2.7, 2.3 Hz, H-2′), 5.27 (br s, 1H, H-1″), 4.87 (dd, 1H, *J* = 9.7, 3.3 Hz, H-3), 4.74 (d, 1H, *J* = 1.8 Hz, H-1‴), 4.66–4.42 (m, 6H, H-5, H-3′, H-5′, H-6$_a$, H-6$_b$, H-6′$_a$), 4.41–4.26 (m, 3H, H-5‴, H-6′$_b$, H-6‴$_a$), 4.23–4.04 (m, 4H, H-5″, H-6‴$_b$, H-6″$_a$, H-6″$_b$), 4.00 (dd, 1H, *J* = 3.1, 1.9 Hz, H-2″), 3.76 (s, 3H, ArOCH_3); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 166.12 (*C*=O), 166.08 (*C*=O), 166.0 (*C*=O), 165.9 (*C*=O), 165.8 (*C*=O), 165.7 (*C*=O), 165.4 (*C*=O), 165.3 (*C*=O), 165.0 (*C*=O), 164.9 (2 × *C*=O), 164.7 (*C*=O), 164.6 (*C*=O), 155.5 (Ar), 149.7 (Ar), 133.9 (Ar), 133.8 (Ar), 133.44 (Ar), 133.38 (Ar), 133.3 (2 × Ar), 133.08 (Ar), 133.06

(2 × Ar), 133.0 (2 × Ar), 132.94 (2 × Ar), 132.90 (Ar), 132.7 (Ar), 130.1 (Ar), 130.0 (2 × Ar), 129.9 (4 × Ar), 129.81 (4 × Ar), 129.79 (4 × Ar), 129.76 (4 × Ar), 129.7 (4 × Ar), 129.6 (2 × Ar), 129.3 (Ar), 129.24 (2 × Ar), 129.22 (2 × Ar), 129.1 (4 × Ar), 129.0 (Ar), 128.92 (2 × Ar), 128.87 (Ar), 128.8 (Ar), 128.74 (2 × Ar), 128.70 (2 × Ar), 128.66 (2 × Ar), 128.52 (4 × Ar), 128.46 (2 × Ar), 128.44 (2 × Ar), 128.38 (2 × Ar), 128.34 (4 × Ar), 128.31 (4 × Ar), 128.1 (2 × Ar), 118.0 (Ar), 114.7 (Ar), 100.5 (C-1″), 99.7 (C-1′), 99.4 (C-1‴), 96.5 (C-1), 77.0 (C-2″), 76.9 (C-3), 75.8 (C-3′), 71.8 (C-2), 71.6 (C-2′), 70.3 (C-2‴), 70.0 (C-3″), 69.9 (C-5′), 69.73 (C-5″), 69.70 (C-5‴), 69.4 (C-5), 69.2 (C-3‴), 68.2 (C-4′), 68.0 (C-4‴), 66.7 (C-4″), 66.2 (C-4), 63.0 (C-6), 62.9 (C-6‴), 62.5 (C-6′), 61.8 (C-6″), 55.6 (ArO*C*H$_3$). MALDI MS: *m*/*z* calcd for [$C_{122}H_{100}O_{35}$]Na$^+$: 2147.5937. Found: 2147.5951.

3.16. 8-Azidooctyl 2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl-(1→2)-3,4,6-tri-*O*-benzoyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-mannopyranoside (24)

A solution of compound **21** (196 mg, 0.09 mmol) and ceric ammonium nitrate (506 mg, 0.9 mmol) in 8:1 CH_3CN–H_2O (18 mL) was stirred at rt for 1 h, diluted with EtOAc (40 mL), and washed with water (40 mL), satd aq $NaHCO_3$ (40 mL), and brine (40 mL). The organic layer was then dried and concentrated, and the residue was purified by chromatography (1:1 hexane–EtOAc) to afford **22** (180 mg, 97%) as a colorless oil. Compound **22** (174 mg, 0.09 mmol) was then dissolved in dry CH_2Cl_2 (20 mL) and then CCl_3CN (0.18 mL, 1.7 mmol) and DBU (4 μL) were added in succession at 0 °C. The solution was stirred at rt for 2 h and then concentrated. The resulting oil was purified by chromatography (1:1 hexane–EtOAc and 1% Et_3N) to afford **23** (187 mg, 100%) as a colorless oil, which, following drying under vacuum overnight, was used immediately in the next step. To a solution of a mixture of 8-azido-1-octanol[9] (8 mg, 0.06 mmol) and **23** (35 mg, 0.02 mmol) in dry CH_2Cl_2 (10 mL) was added activated 4 Å molecular sieves (50 mg). After stirring at rt for 30 min, a solution of 10% TMSOTf in CH_2Cl_2 (8.7 μL) was added. The reaction mixture was then stirred for 16 h at rt, and then it was neutralized with Et_3N; concentration gave a residue that was purified by chromatography (4:1 toluene–EtOAc) to afford compound **24** (35 mg, 79%) as a colorless oil. R_f 0.79 (4:1 toluene–EtOAc); $[\alpha]_D$ −27.2 (*c* 1.8, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.20–7.75 (m, 24H, Ar), 7.69–7.65 (m, 2H, Ar), 7.60–7.20 (m, 35H, Ar), 7.12–7.00 (m, 4H, Ar), 6.08 (dd, 1H, *J* = 10.1, 10.1 Hz, H-4‴), 6.01 (dd, 1H, *J* = 10.0, 10.0 Hz, H-4′), 5.95–5.88 (m, 3H, H-4, H-4″, H-3‴), 5.70–5.65 (m, 2H, H-2‴, H-2′), 5.57 (dd, 1H, *J* = 10.0, 3.1 Hz, H-3″), 5.38 (d, 1H, *J* = 2.2 Hz, H-1), 5.32 (dd, 1H, *J* = 3.1, 2.2 Hz, H-2), 5.19 (br s, 1H, H-1″), 5.07 (d, 1H, *J* = 1.5 Hz, H-1′), 4.70 (d, 1H, *J* = 1.7 Hz, H-1‴), 4.65 (dd, 1H, *J* = 12.2, 2.6 Hz, H-6$_a^{‴}$), 4.60 (dd, 1H, *J* = 9.8, 3.1 Hz, H-3), 4.56 (dd, 1H, *J* = 12.5, 2.4 Hz, H-6$_a^{′}$), 4.51–4.44 (m, 2H, H-6$_b^{‴}$, H-3′), 4.37–4.27 (m, 5H, H-5′, H-5, H-5‴, H-6$_a$, H-6$_b$), 4.18 (dd, 1H, *J* = 12.5, 3.0 Hz, H-6$_b^{′}$), 4.15–4.09 (m, 2H, H-6$_a^{″}$, H-5″), 4.05–3.92 (m, 2H, H-6$_b^{″}$, H-2″), 3.79–3.72 (ddd, 1H, *J* = 9.7, 6.9, 6.9 Hz, octyl OCH_2), 3.54–3.46 (ddd, 1H, *J* = 9.7, 6.9, 6.9 Hz, octyl OCH_2), 3.25 (dd, 2H, *J* = 7.0, 7.0 Hz, CH_2N$_3$), 1.67–1.56 (m, 5H, octyl CH_2), 1.41–1.30 (m, 7H, octyl CH_2); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 166.07 (*C*=O), 166.05 (*C*=O), 166.0 (*C*=O), 165.9 (*C*=O), 165.8 (*C*=O), 165.7 (*C*=O), 165.34 (*C*=O), 165.31 (*C*=O), 164.93 (*C*=O), 164.87 (*C*=O), 164.8 (*C*=O), 164.64 (*C*=O), 164.57 (*C*=O), 133.7 (2 × Ar), 133.4 (Ar), 133.31 (Ar), 133.26 (2 × Ar), 133.01 (2 × Ar), 132.97 (Ar), 132.92 (Ar), 132.86 (Ar), 132.8 (Ar), 132.7 (Ar), 130.1 (Ar), 130.00 (Ar), 129.96 (Ar), 129.93 (Ar), 129.90 (2 × Ar), 129.86 (4 × Ar), 129.83 (4 × Ar), 129.78 (4 × Ar), 129.7 (4 × Ar), 129.64 (2 × Ar), 129.60 (2 × Ar), 129.3 (Ar), 129.22 (Ar), 129.21 (2 × Ar), 129.03 (Ar), 129.02 (Ar), 128.98 (2 × Ar), 128.9 (Ar), 128.85 (Ar), 128.78 (Ar), 128.7 (2 × Ar), 128.61 (2 × Ar), 128.56 (4 × Ar), 128.5 (4 × Ar), 128.38 (4 × Ar), 128.36 (4 × Ar), 128.33 (4 × Ar), 128.29 (Ar), 128.26 (Ar), 128.1 (2 × Ar), 100.5 (C-1′), 99.6 (C-1), 99.3 (C-1‴), 97.4 (C-1″), 77.6 (C-2″), 75.9 (C-2′), 72.0 (C-2), 71.6 (C-3′), 70.2 (C-2‴), 70.0 (C-4), 69.7 (2C, C-4″, C-3‴), 69.6 (2C, C-4‴, C-3), 69.2 (C-4′), 68.8 (C-3″), 68.7 (octyl O*C*H$_2$), 68.3 (C-5), 67.8 (C-5′), 66.7 (C-5‴), 66.2 (C-5″), 63.0 (C-6), 62.8 (C-6″), 62.2 (C-6′), 61.8 (C-6‴), 51.4 (*C*H$_2$N$_3$), 29.3 (octyl *C*H$_2$), 29.3 (octyl *C*H$_2$), 29.1 (octyl *C*H$_2$), 28.8 (octyl *C*H$_2$), 26.7 (octyl *C*H$_2$), 26.0 (octyl *C*H$_2$). MALDI MS: *m*/*z* calcd for [$C_{123}H_{109}O_{34}N_3$]Na$^+$: 2194.6785. Found: 2194.6800.

3.17. 2,4,6-tri-*O*-benzoyl-3-*O*-methyl-α-D-mannopyranosyl trichloroacetimidate (25)

A solution of compound **8** (187 mg, 0.31 mmol) and ceric ammonium nitrate (502 mg, 0.92 mmol) in 4:1 CH_3CN–H_2O (25 mL) was stirred at rt for 1 h, diluted with EtOAc (40 mL), and washed with water (40 mL), satd aq $NaHCO_3$ (40 mL), and brine (40 mL). The organic layer was dried and concentrated, and the residue was purified by chromatography (3:1 hexane–EtOAc) to afford reducing monosaccharide (154 mg, 100%) as a colorless oil. The resulting oil (154 mg, 0.30 mmol) was then dissolved in dry CH_2Cl_2 (20 mL), and then CCl_3CN (0.66 mL, 6.60 mmol) and DBU (13.7 μL, 0.09 mmol) were sequentially added at 0 °C. The solution was stirred at rt for 2 h and then concentrated. The resulting oil was purified by chromatography (5:1 hexane–EtOAc and 1% Et_3N) to afford **25**

(155 mg, 78%) as a colorless oil, which, following drying under vacuum overnight, was used immediately in the next step.

3.18. *p*-Methoxyphenyl 2,4,6-tri-*O*-benzoyl-3-*O*-methyl-α-D-mannopyranosyl-(1→2)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-mannopyranoside (26)

To a solution of a mixture of trisaccharide **18** (246 mg, 0.17 mmol) and imidate **25** (177 mg, 0.27 mmol) in dry CH_2Cl_2 (15 mL) was added activated 4 Å molecular sieves (500 mg). The reaction mixture was stirred at rt for 30 min and then cooled to 0 °C before a solution of 10% TMSOTf in CH_2Cl_2 (31.3 μL, 0.04 mmol) was added. The reaction mixture was stirred for 1 h at 0 °C, and then it was neutralized by the addition of Et_3N and concentrated to give a residue that was purified by chromatography (4:1 hexane–EtOAc) to afford **26** (262 mg, 79%) as a colorless oil. R_f 0.61 (2:1 hexane–EtOAc); $[\alpha]_D$ +25.7 (*c* 2.3, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.13–8.03 (m, 4H, Ar), 7.99–7.94 (m, 2H, Ar), 7.60–7.49 (m, 3H, Ar), 7.42–7.49 (m, 51H, Ar), 7.00–6.95 (m, 2H, Ar), 6.81–6.76 (m, 2H, Ar), 5.85 (dd, 1H, $J = 9.9$, 9.9 Hz, H-4‴), 5.77 (dd, 1H, $J = 2.5$, 2.5 Hz, H-2‴), 5.45 (d, 1H, $J = 1.5$ Hz, H-1), 5.37 (s, 2H, H-1′, H-1″), 5.16 (br s, 1H, H-1‴), 4.90 (d, 1H, $J = 11.2$ Hz, PhCH_2), 4.77–4.22 (m, 23H, 17 × PhCH_2, H-3, H-4, H-5, H-6$_a$, H-6$_b$, H-3‴), 4.14–3.86 (m, 11H, H-6‴$_a$, H-6′$_a$, H-2, H-2″, H-2′, H-3″, H-4″, H-5″, H-5‴, H-6″$_a$, H-6″$_b$), 3.77 (s, 3H, ArOCH_3), 3.76–3.49 (m, 5H, H-6‴$_b$, H-3′, H-4′, H-5′, H-6′$_b$), 3.30 (s, 3H, OCH_3); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 166.0 (*C*=O), 165.3 (2 × *C*=O), 154.9 (Ar), 150.4 (Ar), 138.7 (2 × Ar), 138.3 (2 × Ar), 138.2 (2 × Ar), 138.1 (2 × Ar), 138.0 (2 × Ar), 133.1 (2 × Ar), 132.8 (Ar), 130.2 (Ar), 129.95 (2 × Ar), 129.85 (2 × Ar), 129.8 (2 × Ar), 129.7 (4 × Ar), 128.50 (4 × Ar), 128.48 (2 × Ar), 128.40 (2 × Ar), 128.37 (2 × Ar), 128.35 (2 × Ar), 128.33 (2 × Ar), 128.24 (2 × Ar), 128.23 (2 × Ar), 128.18 (2 × Ar), 127.8 (2 × Ar), 127.72 (2 × Ar), 127.70 (2 × Ar), 127.66 (4 × Ar), 127.61 (Ar), 127.59 (Ar), 127.57 (2 × Ar), 127.54 (2 × Ar), 127.49 (Ar), 127.45 (2 × Ar), 127.4 (Ar), 127.33 (Ar), 127.29 (2 × Ar), 127.19 (2 × Ar), 127.16 (Ar), 127.1 (2 × Ar), 117.9 (2 × Ar), 114.5 (2 × Ar), 99.9 (2C, C-1′, C-1″), 99.1 (C-1‴), 96.5 (C-1), 79.5 (C-2″), 77.7 (C-3), 77.2 (C-2, C-2‴), 75.8 (C-3″), 75.4 (C-4), 74.9 (C-5, C-3‴), 74.8 (Ph*C*H$_2$), 74.7 (Ph*C*H$_2$), 74.3 (C-5″), 73.5 (Ph*C*H$_2$), 73.34 (Ph*C*H$_2$), 73.29 (2 × Ph*C*H$_2$), 72.6 (C-4′), 72.5 (Ph*C*H$_2$), 72.4 (C-4″, C-2′), 72.3 (Ph*C*H$_2$), 72.1 (Ph*C*H$_2$), 69.3 (C-3′), 69.1 (C-6′, C-6″), 68.9 (C-6), 68.4 (2C, C-5‴, C-5′), 68.1 (C-4‴), 62.5 (C-6‴), 57.8 (O*C*H$_3$), 55.6 (ArO*C*H$_3$). MALDI MS: *m*/*z* calcd for $[C_{116}H_{116}O_{25}]Na^+$: 1931.7698. Found: 1931.7699.

3.19. *p*-Methoxyphenyl 2,4,6-tri-*O*-benzoyl-3-*O*-methyl-α-D-mannopyranosyl-(1→2)-3,4,6-tri-*O*-benzoyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-mannopyranoside (28)

To a solution of compound **26** (229 mg, 0.12 mmol) in 3:1 CH_3OH–EtOAc (12 mL) was added 20% $Pd(OH)_2$-on-carbon (15 mg), and the reaction mixture was stirred for 24 h under a hydrogen atmosphere. The mixture was filtered through Celite and then concentrated; a ^{1}H NMR spectrum of the crude product revealed that all of the benzyl groups had been removed. The resulting oil (**27**) was dissolved in pyridine (8 mL), and to this solution were added DMAP (2 mg) and benzoyl chloride (0.15 mL, 1.32 mmol) dropwise at rt. The reaction mixture was stirred at 50 °C for 15 h, and it was then cooled to rt and diluted with CH_2Cl_2 (30 mL). The organic layer was washed with 1N HCl (2 × 30 mL), satd aq $NaHCO_3$ (30 mL), and brine (30 mL). After drying, the organic layer was concentrated and the residue was purified by chromatography (2:1 hexane–EtOAc) to afford **28** (227 mg, 93%) as an oil. R_f 0.65 (1:1 hexane–EtOAc); $[\alpha]_D$ −11.8 (*c* 0.1, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.22–7.91 (m, 22H, Ar), 7.87–7.78 (m, 4H, Ar), 7.72–7.66 (m, 2H, Ar), 7.63–7.24 (m, 28H, Ar), 7.11–7.00 (m, 6H, Ar), 6.80–6.74 (m, 2H, Ar), 6.05 (dd, 1H, $J = 9.8$, 9.8 Hz, H-4), 5.93–5.80 (m, 4H, H-2, H-4′, H-4″, H-4‴), 5.68 (d, 1H, $J = 1.8$ Hz, H-1), 5.56–5.50 (m, 2H, H-2‴, H-3″), 5.46 (d, 1H, $J = 2.2$ Hz, H-1′), 5.39 (dd, 1H, $J = 2.7$, 2.2 Hz, H-2′), 5.23 (br s, 1H, H-1″), 4.84 (dd, 1H, $J = 9.7$, 3.3 Hz, H-3), 4.64–4.41 (m, 7H, H-1‴, H-5, H-6$_a$, H-6$_b$, H-5′, H-6′$_a$, H-3′), 4.34–4.27 (m, 2H, H-6′$_b$, H-6″$_a$), 4.23–4.03 (m, 5H, H-5‴, H-6‴$_a$, H-6‴$_b$, H-5″, H-6″$_b$), 3.96–3.74 (m, 2H, H-3‴, H-2″), 3.75 (s, 3H, ArOCH_3), 3.24 (s, 3H, OCH_3); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 166.1 (*C*=O), 166.0 (*C*=O), 165.84 (*C*=O), 165.79 (2 × *C*=O), 165.7 (*C*=O), 165.30 (*C*=O), 165.27 (*C*=O), 164.99 (*C*=O), 164.96 (*C*=O), 164.9 (*C*=O), 164.8 (*C*=O), 155.4 (Ar), 149.6 (Ar), 134.5 (Ar), 133.8 (Ar), 133.6 (Ar), 133.54 (Ar), 133.53 (Ar), 133.49 (Ar), 133.43 (Ar), 133.37 (Ar), 133.20 (Ar), 133.18 (Ar), 133.1 (Ar), 133.0 (Ar), 132.9 (Ar), 130.6 (Ar), 130.2 (2 × Ar), 130.02 (Ar), 130.00 (Ar), 129.94 (4 × Ar), 129.91 (4 × Ar), 129.84 (4 × Ar), 129.76 (4 × Ar), 129.7 (Ar), 129.6 (Ar), 129.49 (Ar), 129.48 (Ar), 129.13 (2 × Ar), 129.09 (2 × Ar), 129.04 (2 × Ar), 129.00 (Ar), 128.96 (Ar), 128.9 (Ar), 128.84 (2 × Ar), 128.77 (Ar), 128.73 (Ar), 128.69 (Ar), 128.63 (2 × Ar), 128.61 (2 × Ar), 128.5 (4 × Ar), 128.44 (4 × Ar), 128.36 (4 × Ar), 128.3 (4 × Ar), 128.2 (2 × Ar), 117.9 (Ar), 114.7 (Ar), 100.5 (C-1″), 99.8 (C-1′), 99.7 (C-1‴), 96.4 (C-1), 77.1 (C-3‴), 76.8 (C-3), 75.7 (C-3′), 71.8 (C-2), 71.5 (C-2′), 70.4 (C-3″), 69.8 (C-5), 69.7 (C-5′), 69.5 (C-5″), 69.4 (C-5‴), 69.2 (C-2‴), 68.3 (C-4), 68.1 (C-4″), 67.8 (C-4‴), 67.6 (C-4′), 66.6 (C-2″), 63.0 (C-6),

62.6 (C-6′), 62.5 (C-6″), 62.0 (C-6‴), 57.7 (O*C*H$_3$), 55.6 (ArO*C*H$_3$). MALDI MS: *m*/*z* calcd for [$C_{116}H_{98}O_{34}$]-Na$^+$: 2057.5832. Found: 2057.5834.

3.20. 8-Azidooctyl 2,4,6-tri-*O*-benzoyl-3-*O*-methyl-α-D-mannopyranosyl-(1→2)-3,4,6-tri-*O*-benzoyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-mannopyranoside (31)

A solution of tetrasaccharide **28** (146 mg, 0.07 mmol) and ceric ammonium nitrate (393 mg, 0.7 mmol) in 8:1 CH_3CN–H_2O (18 mL) was stirred at rt for 1 h, diluted with EtOAc (40 mL), and washed with water (40 mL), satd aq $NaHCO_3$ (40 mL), and brine (40 mL). The organic layer was dried and concentrated, and the residue was purified by chromatography (1:1 hexane–EtOAc) to afford **29** (126 mg, 91%) as a colorless oil. Compound **29** (126 mg, 0.07 mmol) was then dissolved in dry CH_2Cl_2 (10 mL), and then CCl_3CN (0.13 mL, 1.31 mmoL) and DBU (2.9 μL) were sequentially added at 0 °C. The solution was stirred at rt for 2 h and then concentrated. The resulting oil was purified by chromatography (1:1 hexane–EtOAc and 1% Et_3N) to afford **30** (124 mg, 91%) as a colorless oil, which, following drying under vacuum overnight, was used immediately in the next step. To a solution of a 8-azido-1-octanol[9] (10 mg, 0.06 mmol) and **30** (41 mg, 0.02 mmol) in dry CH_2Cl_2 (5 mL) was added freshly activated 4 Å molecular sieves (50 mg), and the mixture was stirred at rt for 30 min. A 10% solution of TMSOTf in CH_2Cl_2 (11 μL) was added at rt. The reaction mixture was then stirred for 16 h, and it was then neutralized by adding Et_3N. The solution was then filtered and concentrated to a residue that was purified by chromatography (4:1 toluene–EtOAc) to afford **31** (30 mg, 72%) as a colorless oil. R_f 0.80 (4:1 toluene–EtOAc); $[\alpha]_D$ −9.7 (*c* 1.2, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.18–7.89 (m, 20H, Ar), 7.85–7.82 (m, 2H, Ar), 7.78–7.74 (m, 2H, Ar), 7.70–7.66 (m, 2H, Ar), 7.60–7.23 (m, 32H, Ar), 7.08–7.01 (m, 2H, Ar), 5.99 (dd, 1H, $J = 10.0$, 10.0 Hz, H-4′), 5.91 (dd, 1H, $J = 9.8$, 9.8 Hz, H-4), 5.84–5.77 (m, 2H, H-4‴, H-4″), 5.66 (dd, 1H, $J = 3.4$, 1.8 Hz, H-2′), 5.53 (dd, 1H, $J = 2.5$, 2.5 Hz, H-2‴), 5.49 (dd, 1H, $J = 10.1$, 3.1 Hz, H-3″), 5.37 (d, 1H, $J = 2.1$ Hz, H-1), 5.33 (dd, 1H, $J = 3.1$, 2.1 Hz, H-2), 5.18 (s, 1H, H-1″), 5.06 (d, 1H, $J = 1.8$ Hz, H-1′), 4.68–4.54 (m, 4H, H-1‴, H-3′, H-6′$_a$, H-6‴$_a$), 4.51–4.44 (m, 2H, H-6′$_b$, H-3), 4.36–4.26 (m, 3H, H-5′, H-5, H-6$_a$), 4.25–4.17 (m, 2H, H-5‴, H-6‴$_b$), 4.15–3.99 (m, 4H, H-5″, H-6″$_a$, H-6″$_b$, H-6$_b$), 3.92–3.86 (m, 2H, H-3‴, H-2″), 3.74 (ddd, 1H, $J = 9.6$, 6.7, 6.7 Hz, octyl OCH_2), 3.49 (ddd, 1H, $J = 9.6$, 6.7, 6.7 Hz, octyl OCH_2), 3.27–3.21 (m, 5H, OCH_3, CH_2N$_3$), 2.06–1.55 (m, 5H, octyl CH_2), 1.41–1.31 (m, 7H, octyl CH_2); ^{13}C NMR (125 MHz, CD_3Cl, δ_C) 166.1 (*C*=O), 166.0 (*C*=O), 165.9 (*C*=O), 165.8 (3 × *C*=O), 165.29 (*C*=O), 165.27 (*C*=O), 165.0 (*C*=O), 164.87 (*C*=O), 164.85 (*C*=O), 164.8 (*C*=O), 134.5 (Ar), 133.64 (Ar), 133.58 (Ar), 133.55 (Ar), 133.4 (Ar), 133.3 (Ar), 133.2 (Ar), 133.01 (Ar), 133.97 (Ar), 133.9 (Ar), 132.83 (Ar), 132.81 (Ar), 130.6 (Ar), 130.17 (Ar), 130.15 (Ar), 130.0 (Ar), 129.91 (2 × Ar), 129.88 (2 × Ar), 129.86 (2 × Ar), 129.82 (2 × Ar), 129.79 (4 × Ar), 129.74 (4 × Ar), 129.70 (4 × Ar), 129.68 (4 × Ar), 129.6 (Ar), 129.48 (2 × Ar), 129.46 (Ar), 129.2 (Ar), 129.14 (Ar), 129.11 (2 × Ar), 129.09 (2 × Ar), 129.0 (Ar), 128.9 (Ar), 128.8 (Ar), 128.7 (Ar), 128.61 (Ar), 128.58 (4 × Ar), 128.5 (4 × Ar), 128.43 (4 × Ar), 128.38 (2 × Ar), 128.36 (Ar), 128.33 (Ar), 128.30 (Ar), 128.1 (Ar), 100.5 (C-1′), 99.8 (C-1), 99.7 (C-1‴), 97.4 (C-1″), 77.4 (C-2), 77.1 (C-3‴), 75.8 (C-2″), 72.1 (C-2‴), 71.5 (C-4), 70.4 (C-2′), 69.7 (2C, C-3′, C-4″), 69.6 (C-3″), 69.1 (C-3), 68.8 (C-4′), 68.7 (octyl O*C*H$_2$), 68.4 (C-4‴), 67.9 (C-5″), 67.7 (C-5), 67.5 (C-5′), 66.6 (C-5‴), 63.1 (C-6), 62.5 (C-6″), 62.3 (C-6′), 62.0 (C-6‴), 57.6 (O*C*H$_3$), 51.4 (*C*H$_2$N$_3$), 29.3 (octyl *C*H$_2$), 29.2 (octyl *C*H$_2$), 29.0 (octyl *C*H$_2$), 28.8 (octyl *C*H$_2$), 26.6 (octyl *C*H$_2$), 26.0 (octyl *C*H$_2$). MALDI MS: *m*/*z* calcd for [$C_{117}H_{107}O_{33}N_3$]Na$^+$: 2104.6679. Found: 2104.6689.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.carres.2008.02.025.

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