A Linear Synthesis of Branched High-Mannose Oligosaccharides from the HIV-1 Viral Surface Envelope Glycoprotein gp120

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Keywords: High-Mannose / Nonasaccharide / Cyanovirin / Oligosaccharides / HIV

Described is a linear solution-phase synthesis of the HIV-1 viral surface envelope glycoprotein gp120 high-mannose nonasaccharide pentyl glycoside. Envisioning the automated solid-phase assembly of complex carbohydrates, the synthesis of the nonasaccharide and the related tri- and hexamannosides demonstrates the facile assembly of highly branched structures in a stepwise fashion incorporating monosaccharide building blocks. A differentially protected core trisaccharide was prepared and further elongated in two high-yielding tri-mannosylations to furnish the triantennary structure. The tri-, hexa-, and nonamannoside *n*-pentyl glycosides obtained via the described synthesis are currently being used for detailed study of the carbohydrate protein interactions responsible for binding of the anti-HIV protein cyanovirin-*N* to the glycoprotein gp120.

Introduction

Carbohydrates play a vital role in HIV retroviral pathogenesis. The function of HIV-1 surface envelope glycoprotein gp120 in helper T lymphocyte (T_h) infection has been understood by biologists for some time.[1,2] Glycoprotein gp120 is highly glycosylated, containing up to 24 *N*-linked high-mannose carbohydrates, which compose 50% of the molecular mass of the glycoprotein.[3] Gp120 mediates viral fusion with the CD4 receptor on the surface of T_h cells. HIV fusion and subsequent lymphocyte infection occur upon binding of the glycoprotein and the CD4 receptor.

A novel protein has been recently discovered that exhibits potent anti-HIV activity. Isolated from the blue-green algae *Nostoc ellipsosporum*, cyanovirin-N (CVN) was found to bind gp120, inactivating HIV, and preventing lymphocyte infection.[2,4–7] CVN is a novel, monomeric, 11-kDa virucidal protein. Both natural and recombinant forms of the protein have been shown to irreversibly inactivate a wide variety of HIV strains while exhibiting minimal toxicity to host cells. The mode of HIV inactivation by CVN has been studied and the protein's affinity for the gp120 high-mannose structure Man_9 **1** was established (Figure 1).[8] This affinity appears to be the mechanism through which CVN prevents gp120 from interacting with the CD4 receptor of the host lymphocyte. A detailed understanding of the specific interaction between CVN and Man_9 **1** could lead to the development of potential HIV preventatives and possibly even therapeutics. Access to synthetically derived mannosides as synthetic tools has therefore become particularly important in order to probe CVN-gp120 binding.

The total synthesis of high-mannose type cell surface glycans, that are found throughout nature as *N*-linked glycoconjugates, has been explored for the past two decades.[9–12] A synthesis of the high-mannose core structures of Man_9, isolated from calf thyroglobul, was reported by Ogawa in 1981; a decade before the role of such structures in HIV pathogenesis was discovered.[9] Two successful and highly convergent syntheses of the HIV-1 nonamannoside structure by Fraser-Reid[13] and Ley[14–16] were recently completed. However, the convergent nature of these solution-phase syntheses does not allow for their application to automated solid-phase synthesis.

Herein we describe a linear synthesis of the pentyl nonamannoside **2** and the related hexamannoside **3** and trimannoside **4** structures (Figure 1). The synthetic strategy was planned and executed with automated solid-phase synthesis in mind. Using three monomer building blocks the nonamannoside was assembled in four glycosylation events. Two sequential tri-mannosylation reactions, with a single mannosyl donor, allowed for access to the completed structure in a minimal number of steps. The target structures currently serve as tools in biophysical studies focusing on the elucidation of cyanovirin-*N*-binding to branched high-mannose structures.

Results and Discussion

Our retrosynthetic analysis of Man_9 analog **2** (Scheme 1) was guided by our long-term goal of developing a synthetic

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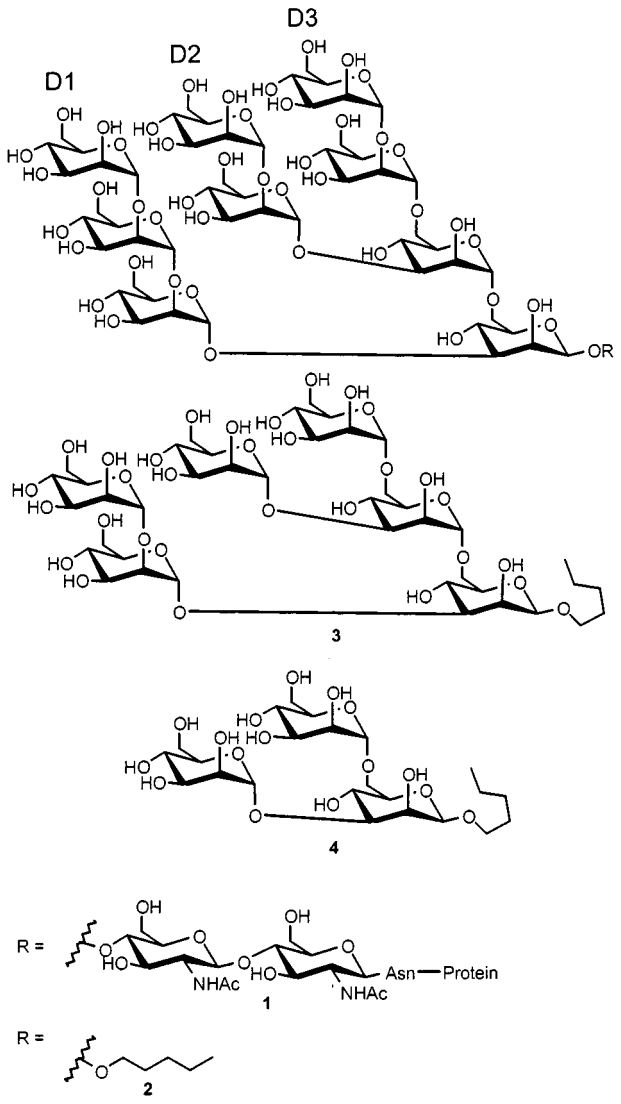
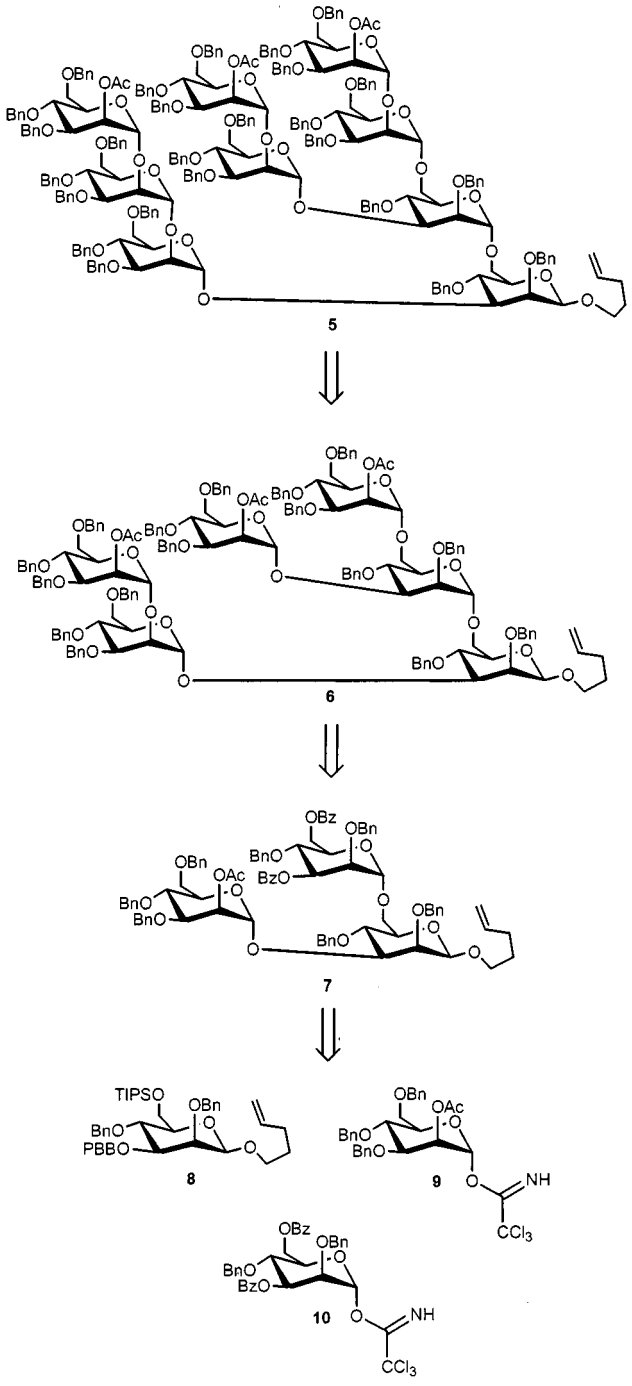


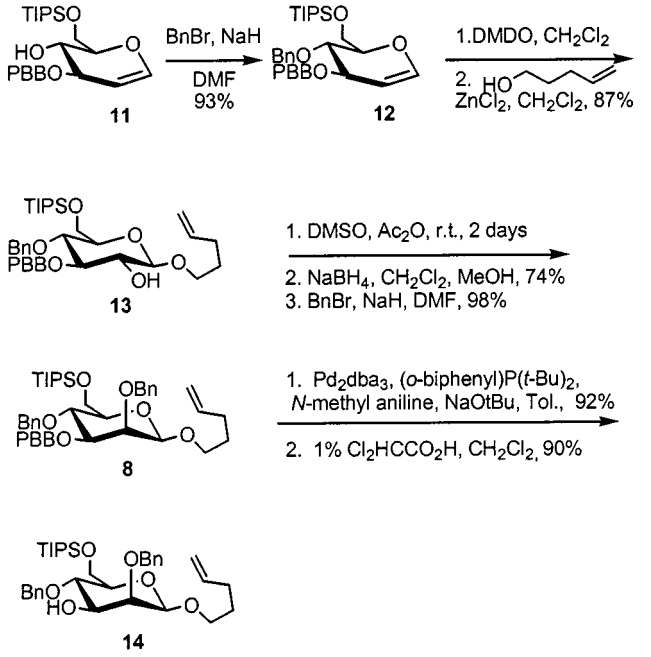
Figure 1. High-mannose oligosaccharide targets



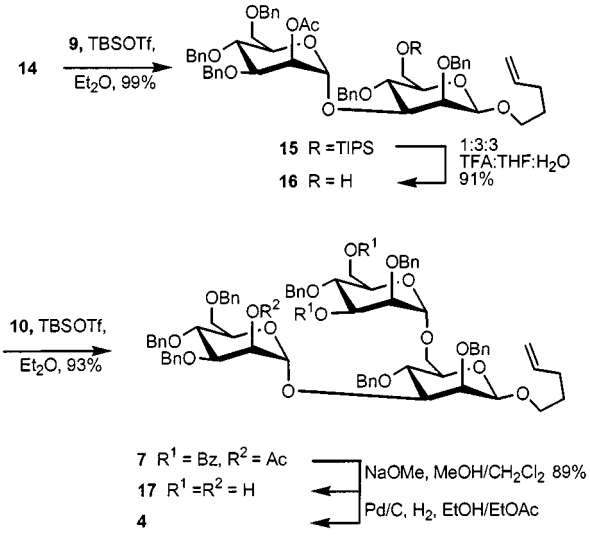
Scheme 1. Retrosynthesis of nonamannoside **5**

strategy that could be applied to the solid support and eventually automated. We planned to obtain the fully protected nonamannoside **5** via simultaneous tri-mannosylation of a hexasaccharide triol derived from **6**. This hexasaccharide would in turn be prepared by the tri-mannosylation of a trisaccharide core triol ensuing from **7**. The differentially protected trisaccharide **7** would be constructed from three protected monosaccharide building blocks **8**, **9**, and **10**. The stepwise nature of this strategy would facilitate access to a triply branched nonasaccharide using just four glycosylations. A solution-phase synthesis of the β-pentenyl glycoside analog of the natural structure was selected for our studies, based on our strategy for solid phase oligosaccharide synthesis that furnishes the pentenyl glycoside upon cleavage from the solid-support.[17] In addition to functioning as glycosyl donors, *n*-pentenyl glycosides are versatile handles, that can be converted into a range of functional groups by transformation of the terminal olefin to a carboxylic acid, aldehyde, ester, thioether, thioester, or hydroxyl group.[18–20] In this fashion the *n*-pentenyl moiety may allow for attachment of the products of our synthetic studies to a linker, fluorescent tag, or biomarker.

Initially, reliable synthetic access to the monosaccharide building blocks had to be established. The core 3,6-differentially protected β-mannoside **8** was the most synthetically challenging building block to be procured. Since glycals have proven to be useful intermediates in oligosaccharide assembly[21–22] we utilized glycals for the preparation of β-mannoside **8**. The synthesis of **8** commenced with benzylation of known glycal **11**[23] to yield differentially protected



Scheme 2. Synthesis of the core β-mannoside **8**



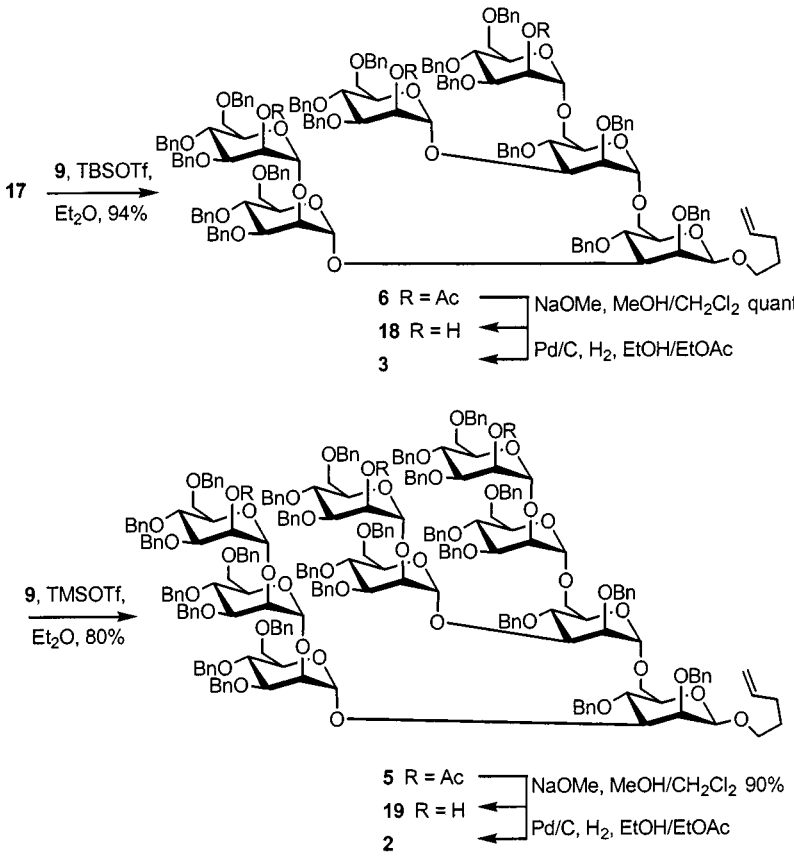
Scheme 3. Assembly of core trimannoside **7**

glucal **12** (Scheme 2). Stereospecific epoxidation of glycal **12** by treatment with dimethyldioxirane, followed by opening of the 1,2-anhydrosugar with 4-penten-1-ol in the presence of zinc chloride yielded β-glucoside **13** containing an unprotected C2 hydroxyl group. Inversion of the C2 stereocenter was achieved via an oxidation-reduction sequence. Oxidation of the C2 hydroxyl under Pfitzner–Moffatt conditions (Ac_2O/DMSO) was followed by stereoselective reduction with sodium borohydride and benzylation to furnish the fully protected β-mannoside **8**. Selective removal of the halobenzyl ether was accomplished by palladium-catalyzed amination with *N*-methyl aniline followed by treatment with dichloroacetic acid to afford monosaccharide acceptor **14**.[23]

At this stage only two other mannosyl monosaccharide building blocks were required for the completion of the nonamannoside; one with a temporary protecting group on C2 (**9**), and the other incorporating temporary protecting groups on C3 and C6 (**10**). The C3 hydroxyl of the reducing end mannose is the point of attachment of a linear strand of α-(1→2) linked mannoses (branch D1). The C6 hydroxyl of the core *n*-pentenyl-β-mannoside is the origin of a 3,6-differentiated α-mannose that serves as the core for two branches (D2 and D3) of the triantennary structure (Figure 1). Differentially protected mannopyranosyl trichloroacetimidate **9**[24] as well as mannosyl donor **10**[25] were prepared using known procedures. Synthesized on multi gram scale, **9** was about to serve as the source of seven of the nine mannoses in the final Man_9 structure.

With the three monosaccharide building blocks **8**, **9**, and **10** in hand the assembly of larger structures began. We first focused on the preparation of core trimannoside **7**. The α-selective mannosylation of the C3 hydroxyl of **14** with donor **9** afforded disaccharide **15** (Scheme 3). Removal of the C6 silyl ether was accomplished in high yield using aqueous trifluoroacetic acid in THF to furnish disaccharide acceptor **16**. Installation of the second mannose building block on C6 that will serve as root for branches D2 and D3 required the use of a mannose donor that did not utilize a C2 participating ester group but rather a permanently blocked benzyl ether. Nevertheless, complete α-selectivity was achieved in the TBDMSOTf catalyzed glycosylation of disaccharide acceptor **16** with mannosyl donor **10** to yield the fully-protected core trisaccharide **7**. Precedence for α-selectivity has been established previously in the case of similar mannosyl donors containing non-participating protecting groups on C2.[26–27] Treatment of trisaccharide **7** with sodium methoxide accomplished the simultaneous cleavage of one C2 acetate and two benzoates to provide trisaccharide triol **17** in good yield (89%).

Simultaneous extension of the D1, D2, and D3 branches from the core trisaccharide was accomplished via two sequential tri-mannosylations with donor **9** (Scheme 4). Mannosylation of **17** with donor **9** (4.5 equivalents) yielded hexasaccharide **6** in a single step in 94% yield. Deprotection with sodium methoxide produced hexasaccharide triol **18**. Trimannosylation of **18** using **9** furnished the fully protected high-mannose nonasaccharide **5** in 80% yield. In just three steps the initial trisaccharide **7** tripled in size to nonasaccharide **5** with 75% overall yield. Liberation of **5** from all protecting groups in two steps by treatment with sodium methoxide to afford triol **19**, followed by Pd-catalyzed hydrogenation yielded the desired high-mannose pentyl glycoside **2** (Man_9). Fully deprotected hexasaccharide **3** and core trisaccharide **4** pentyl glycosides were prepared in similar fashion from **17** and **18** (Scheme 4). The three high-mannose oligosaccharides **2**, **3**, and **4** are currently used in biophysical studies to better understand the carbohydrate protein interactions between cyanovirin-*N* and gp120. Results of these studies are expected to elucidate the formation of very tight carbohydrate-protein interactions that form



Scheme 4. Assembly of nonasaccharide **6**

the basis for novel HIV preventatives and possibly constitute a general principle for protein-carbohydrate interactions.

Conclusion

In summary, we have completed a linear synthesis of the high-mannose nonasaccharide pentyl glycoside **2**, and the trimannoside **4** and hexamannoside **3** structures, using just three monomeric glycosyl building blocks. Construction of triantennary nonasaccharide **2** was achieved in four high-yielding glycosidation events; construction of a differentiated core trisaccharide followed by two sequential trimannosylations. Access to these synthetic structures has permitted further study of the anti-HIV micobicide activity exhibited by cyanovirin-N. The strategy described here for the solution phase assembly of three large oligosaccharides constitutes the basis for the solid phase and eventually the automated synthesis of branched high-mannose motifs.

Experimental Section

All commercial materials were used without further purification, unless otherwise noted. Dichloromethane (CH_2Cl_2) and diethyl ether (Et_2O) were purchased from J. T. Baker (Cycletainer™) and passed through neutral alumina columns prior to use. Toluene was purchased from J. T. Baker (Cycletainer™) and passed through neutral alumina and copper(II) oxide columns prior to use. Analytical thin-layer chromatography was performed on E. Merck silica gel 60 F_{254} plates (0.25 mm). Compounds were visualized by dipping the plates in a cerium sulfate-ammonium molybdate solution, followed by heating. Liquid chromatography was performed using forced flow of the indicated solvent on Silicycle Inc. silica gel (230−400 mesh). ^{1}H NMR spectra were obtained on either a Bruker Avance 400 (400 MHz) or Varian VXR-500 (500 MHz) and are reported in parts per million (δ) relative to chloroform (δ = 7.26). Coupling constants (*J*) are reported in Hz. ^{13}C NMR spectra were recorded on either a Bruker Avance 400 (100 MHz) or a Varian VXR-500 (125 MHz) and are reported in δ relative to $CDCl_3$ (δ = 77.23) as an internal reference. IR spectra were obtained on a Perkin−Elmer 1600 series FTIR spectrometer. ESI Mass spectrometry was performed on a Bruker Daltonics Apex 3 Tesla Fourier Transform Mass Spectrometer. MALDI-TOF mass spectra were obtained on a PerSpective Biosystems Voyager Elite DE Spectrometer using 2,5-dihydroxybenzoic acid or α-cyano-4-hydroxycinnamic acid as the matrix.

1,5-Anhydro-4-*O*-benzyl-3-*O*-(4-bromobenzyl)-2-deoxy-6-*O*-triisopropylsilyl-D-*arabino*-hex-1-enitol (12): 1,5-anhydro-3-*O*-(4-bromobenzyl)-2-deoxy-6-*O*-triisopropylsilyl-D-*arabino*-hex-1-enitol **11** (7.80 g, 16.5 mmol) was dissolved in DMF (125 mL) and cooled on an ice-bath to 0 °C. Sodium hydride (0.80 g, 60% in mineral oil, 20 mmol) was carefully added to the solution, and stirred for 20 min at 0 °C. Benzyl bromide (3.39 g, 19.9 mmol) was added to the reaction mixture and slowly warmed to room temperature for 2 h. Methanol (3 mL) was slowly added to quench the reaction, which was further diluted in 150 mL water. The solution was extracted with diethyl ether (3 × 300 mL). After concentration in

vacuo the resulting residue was purified by flash column chromatography on silica gel (2→5% EtOAc/hexanes) to afford 8.60 g (93%) of **12** as a clear oil. $[\alpha]_D^{24} = -19.6$ (c = 1.1, CH_2Cl_2). IR (thin film): $\tilde{\nu}$ = 942, 2865, 1647, 1240, 1101, 682 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 1.07−1.10 (m, 21 H), 3.93−4.07 (m, 4 H), 4.18−4.20 (m, 1 H), 4.52 (d, J = 12.2 Hz, 1 H), 4.59 (d, J = 11.9 Hz, 1 H), 4.78−4.85 (m, 3 H), 6.41 (dd, J = 1.5, 6.1 Hz, 1 H), 7.20−7.22 (d, J = 8.2 Hz, 2 H), 7.30−7.36 (m, 5 H), 7.44−7.46 (d, J = 8.2 Hz, 2 H). ^{13}C NMR ($CDCl_3$): δ = 12.2, 18.2, 18.2, 62.0, 70.0, 74.1, 74.2, 76.0, 78.3, 99.5, 121.6, 128.0, 128.1, 128.6, 129.5, 137.7, 138.6, 145.1. ESI MS m/z ($M + Na^+$) calcd. 583.1849, found 583.1838.

4-Pentenyl 4-*O*-Benzyl-3-*O*-(4-bromobenzyl)-6-*O*-triisopropylsilyl-β-D-glucopyranoside (13): Glucal **12** (1.82 g, 3.23 mmol) was dissolved in CH_2Cl_2 (6 mL) and cooled to 0 °C. A 0.08 M solution of dimethyldioxirane in acetone (48.5 mL, 3.88 mmol) was added and the reaction was stirred for 15 min. After the solvent was removed the remaining residue was dried in vacuo for 1.5 h and subsequently dissolved in CH_2Cl_2 (10 mL). The solution was cooled to −78 °C followed by the addition of 4-penten-1-ol (1.61 mL, 16.15 mmol). A 1.0 M solution of $ZnCl_2$ in diethyl ether (3.55 mL, 3.55 mmol) was added and the reaction was warmed slowly to room temperature and stirred over 16 h. The reaction was diluted with EtOAc (200 mL) and washed with sat. aqueous $NaHCO_3$ (2 × 100 mL), water (2 × 100 mL), and brine (2 × 100 mL) and dried (Na_2SO_4). The organic phase was concentrated in vacuo and the resulting residue purified by flash column chromatography on silica gel (15% EtOAc/hexanes) to afford 1.86 g (87%) of **13** as a clear oil. $[\alpha]_D^{24} = -20.8$ (c = 1.3, CH_2Cl_2). IR (thin film): $\tilde{\nu}$ = 456, 2941, 2865, 1115, 1069, 689 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.89−1.07 (m, 21 H), 1.61−1.68 (m, 2 H), 2.02−2.08 (m, 2 H), 2.27−2.28 (m, 1 H), 3.21−3.25 (m, 1 H), 3.51−3.60 (m, 4 H), 3.76−3.92 (m, 3 H), 4.15 (d, J = 7.5, 1 H), 4.63 (d, J = 11.6, 1 H), 4.79 (d, J = 12.5, 1 H), 4.82 (d, J = 11.6, 1 H), 4.81 (d, J = 11.4, 1 H), 4.89−4.98 (m, 2 H), 5.69−5.79 (m, 1 H), 7.16−7.26 (m, 7 H), 7.36 (d, J = 6.5 Hz, 2 H). ^{13}C NMR ($CDCl_3$): δ = 12.2, 18.2, 29.0, 30.5, 62.6, 69.2, 74.4, 75.1, 75.3, 76.4, 77.4, 84.6, 102.6, 115.1, 121.7, 128.0, 128.1, 128.7, 129.8, 131.7, 138.0, 138.3, 138.5. ESI MS m/z ($M + Na^+$) calcd. 685.2530, found 685.2532.

4-Pentenyl 2,4-Di-*O*-benzyl-3-*O*-(4-bromobenzyl)-6-*O*-triisopropylsilyl-β-D-mannopyranoside (8): Glucoside **13** (0.56 g, 0.85 mmol) was azeotropically dried with toluene (3 × 3 mL) and dissolved in dimethyl sulfoxide (3.5 mL). Acetic anhydride (1.75 mL) was added and the reaction was allowed to stir 24 h at room temperature. After the solvent was removed in vacuo, addition of CH_2Cl_2 (20 mL) was followed by washing with water (2 × 20 mL) and drying of the organic phase (Na_2SO_4). After concentration in vacuo the residue was dissolved in 1:1 CH_2Cl_2/MeOH (10 mL) and cooled to 0 °C. $NaBH_4$ (0.161 g, 4.25 mmol) was slowly added and the reaction was stirred 16 h at room temperature. CH_2Cl_2 (100 mL) was added and the organic phase was washed with water (100 mL), 1% aqueous citric acid (2 × 100 mL), sat. aqueous $NaHCO_3$ (100 mL), brine (100 mL), and dried (Na_2SO_4). The organic phase was dried in vacuo to give a clear oil and purified by flash column chromatography on silica gel (6→7% EtOAc/hexanes) to afford 0.42 g (74%) of the desired 4-pentenyl 4-*O*-benzyl-3-*O*-(4-bromobenzyl)-6-*O*-triisopropylsilyl-β-D-mannopyranoside. $[\alpha]_D^{24} = -32.0$ (c = 1.3, CH_2Cl_2). IR (thin film): $\tilde{\nu}$ = 3439, 2940, 2864, 1638, 1105, 1069, 683 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.97−1.05 (m, 2 H), 1.60−1.67 (m, 21 H), 2.04 (m, 2 H), 2.26 (d, J = 2.9 Hz, 1 H), 3.15−3.19 (m, 1 H), 3.40−3.46 (m, 2 H), 3.78−3.92 (m, 4 H), 3.98 (m, 1 H), 4.32 (d, J = 0.9 Hz, 1 H), 4.53- 4.68 (m, 3 H), 4.80 (d, J = 10.9 Hz, 1 H), 4.87−4.97 (m, 2 H), 5.68−5.78 (m, 1 H), 7.17−7.29 (m, 7 H), 7.36 (d, J = 8.4 Hz, 2 H). ^{13}C NMR ($CDCl_3$): δ = 12.4, 18.4, 29.1, 30.7, 63.0, 68.9, 69.1, 71.0, 74.3, 75.6, 76.8, 82.0, 99.8, 115.2, 122.0, 128.2, 128.5, 128.9, 129.9, 131.9, 137.5, 138.5, 138.8. ESI MS m/z ($M + Na^+$) calcd. 685.2530, found 685.2539. 4-Pentenyl 4-*O*-benzyl-3-*O*-(4-bromobenzyl)-6-*O*-triisopropylsilyl-β-D-mannopyranoside (1.0 g, 1.5 mmol) was azeotropically dried with toluene (3 × 3 mL) and dissolved in DMF (15 mL). The solution was cooled to 0 °C and sodium hydride (90 mg, 60% in mineral oil, 1.81 mmol) was carefully added and the mixture was warmed to room temperature. Benzyl bromide (214 μL, 1.81 mmol) was added to the solution, and stirred for 2 h. The reaction was diluted with diethyl ether (100 mL), washed with water (100 mL), followed by extraction of the combined aqueous phase with diethyl ether (50 mL). The combined organic phase was washed with sat. aqueous $NaHCO_3$ (100 mL), water (100 mL), brine (100 mL), dried (Na_2SO_4), and concentrated to give a thick oil in vacuo. The residue was purified by flash column chromatography on silica gel (5 → 20% EtOAc/hexanes) to afford 1.17 g (98%) of **8**. $[\alpha]_D^{24} = -54.0°$ (c = 1.2, CH_2Cl_2). IR (thin film): $\tilde{\nu}$ = 2940, 2865, 1454, 1361, 1107, 1070, 696 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 1.04−1.16 (m, 21 H), 1.72−1.79 (m, 1 H), 2.18 (m, 2 H), 3.28−3.32 (m, 1 H), 3.43−3.51 (m, 2 H), 3.89−4.05 (m, 5 H), 4.68 (d, J = 11.0 Hz, 1 H), 4.85−5.08 (m, 5 H), 5.82−5.92 (m, 1 H), 7.17 (d, J = 8.4 Hz, 2 H), 7.28−7.49 (m, 12 H). ^{13}C NMR ($CDCl_3$): δ = 12.2, 18.2, 29.2, 30.6, 63.3, 69.1, 70.7, 73.7, 74.0, 75.0, 75.4, 77.4, 82.6, 102.0, 115.1, 121.7, 127.5, 127.9, 128.2, 128.4, 128.6, 129.4, 131.6, 137.6, 138.5, 138.7, 139.1. ESI MS m/z ($M + Na^+$) calcd. 775.3000, found 775.3020.

4-Pentenyl 2,4-Di-*O*-benzyl-6-*O*-triisopropylsilyl-β-D-mannopyranoside (14): Mannoside **8** (0.51 g, 0.67 mmol) was azeotropically dried with toluene (3 × 3 mL) then for 1 h in vacuo. The residue was dissolved in toluene (2 mL) followed by the addition of *N*-methyl aniline (86 mg, 0.805 mmol). An oven-dried Schlenk flask was evacuated and backfilled with argon (5 ×). The flask was charged with $Pd_2(dba)_3$ (12.3 mg, 2 mol %), (*o*-biphenyl)P(*t*Bu)$_2$ (4 mol %), and NaO*t*Bu (0.090 g, 0.94 mmol), evacuated and backfilled with argon (5 ×). A rubber septum was installed and the aryl bromide/amine solution was added via cannula. The flask was sealed using a Teflon screwcap and the reaction mixture was heated to 80 °C with stirring. After 18 h, the reaction was cooled to room temperature, diluted with diethyl ether (20 mL), filtered through a pad of celite, and concentrated in vacuo. The crude product was purified by flash column chromatography on silica gel (2 → 5% EtOAc/hexanes) to yield 0.483 g (92%) of 4-pentenyl 4-*O*-benzyl-3-*O*-[4-(*N*-methyl-*N*-phenylamino)benzyl]-6-*O*-triisopropylsilyl-β-D-mannopyranoside. $[\alpha]_D^{24} = -52.6$ (c = 1.5, CH_2Cl_2). IR (thin film): $\tilde{\nu}$ = 2940, 2865, 1595, 1497, 1105, 1067, 696 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 1.10−1.16 (m, 21 H), 1.71−1.79 (m, 2 H), 2.15−2.21 (m, 2 H), 3.29−3.35 (m, 4 H), 3.43−3.49 (m, 1 H), 3.55 (dd, J = 3.0, 9.4 Hz, 1 H), 3.90−4.06 (m, 5 H), 4.40 (s, 1 H), 4.47 (d, J = 11.5 Hz, 1 H), 4.54 (d, J = 11.5 Hz, 1 H), 4.67 (d, J = 10.9 Hz, 1 H), 4.89−5.09 (m, 5 H), 5.82−5.93 (m, 1 H), 6.97−7.08 (m, 4 H), 7.23−7.37 (m, 13 H), 7.51 (d, J = 6.9 Hz, 2 H). ^{13}C NMR ($CDCl_3$): δ = 12.2, 18.2, 29.2, 30.6, 40.5, 63.4, 69.0, 71.5, 73.7, 74.1, 75.0, 75.4, 82.6, 102.0, 115.1, 120.6, 120.9, 121.6, 127.4, 127.8, 128.2, 128.4, 128.5, 129.2, 129.4, 131.0, 138.5, 138.9, 139.3, 148.9, 149.3. ESI MS m/z ($M + Na^+$) calcd. 802.4479, found 802.4473. The aminated product (68 mg, 0.088 mmol) was dissolved in CH_2Cl_2 (3 mL) followed by the addition of dichloroacetic acid (72 μL, 0.88 mmol), resulting in a transparent blue color. The reaction was stirred for 30 min at room temperature then diluted with CH_2Cl_2 (20 mL). Washing with sat. aqueous $NaHCO_3$ (2 × 30 mL), brine (30 mL), was followed by drying (Na_2SO_4) and concentration in

vacuo. The crude product was purified by flash column chromatography on silica gel (2 → 5% EtOAc/ toluene) to afford 46 mg (90%) of **14**. $[\alpha]_D^{24} = -31.4°$ (c = 1.3, CH_2Cl_2). IR (thin film): $\tilde{\nu}$ = 446, 2940, 2865, 1734, 1455, 1249, 1085, 695 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.94−1.07 (m, 21 H), 1.62−1.67 (m, 2 H), 2.03−2.08 (m, 2 H), 2.48 (d, J = 9.7 Hz, 1 H), 3.17−3.20 (m, 1 H), 3.35−3.41 (m, 1 H), 3.53−3.64 (m, 2 H), 3.73 (d, J = 3.1 Hz, 1 H), 3.83−3.96 (m, 3 H), 4.39 (d, J = 0.4 Hz, 1 H), 4.53−4.56 (m, 2 H), 4.80 (d, J = 11.1 Hz, 1 H), 4.87−5.00 (m, 3 H), 5.69−5.80 (m, 1 H), 7.17−7.32 (m, 10 H). ^{13}C NMR ($CDCl_3$): δ = 12.5, 18.2, 29.2, 30.6, 63.2, 69.1, 74.1, 74.6, 75.0, 76.7, 76.9, 77.9, 101.7, 115.0, 127.9, 128.2, 128.5, 138.4, 138.7, 138.8. ESI MS m/z ($M + Na^+$) calcd. 607.3425, found 607.3440.

4-Pentenyl 2-*O*-Acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→3)-2,4-di-*O*-benzyl-6-*O*-triisopropylsilyl-β-D-mannopyranoside (15): Mannosyl trichloroacetimidate **9** (65 mg, 0.10 mmol) and glycosyl acceptor **14** (30 mg, 0.051 mmol) were azeotropically dried with toluene (3 × 3 mL) and dissolved in CH_2Cl_2 (1 mL). The solution was cooled to −20 °C for 15 min, followed by the addition TBDMSOTf (2.4 μL, 0.010 mmol), and stirred for 30 min at −20 °C. The reaction was quenched by addition of Et_3N (50 μL), and dried in vacuo. The crude product was purified by flash column chromatography on silica gel (2 → 5% EtOAc/toluene) to afford 54 mg (99%) disaccharide **15**. $[\alpha]_D^{24} = -15.6$ (c = 1.4, CH_2Cl_2). IR (thin film): $\tilde{\nu}$ = 940, 2865, 1745, 1235, 1078, 697 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.93−1.04 (m, 21 H), 1.57−1.64 (m, 2 H), 1.99−2.06 (m, 5 H), 3.13−3.17 (m, 1 H), 3.27−3.33 (m, 1 H), 3.51−3.52 (m, 2 H), 3.54−3.93 (m, 9 H), 4.29 (s, 1 H), 4.35−4.70 (m, 8 H), 4.79 (d, J = 11.1 Hz, 1 H), 4.87−4.95 (m, 3 H), 5.12 (d, J = 1.2 Hz, 1 H), 5.43−5.44 (m, 1 H), 5.69−5.79 (m, 1 H), 7.04−7.32 (m, 25 H). ^{13}C NMR ($CDCl_3$): δ = 12.5, 18.2, 21.2, 29.2, 30.6, 63.0, 69.0, 69.1, 69.2, 72.1, 72.2, 73.6, 73.8, 73.9, 74.5, 75.0, 75.3, 77.2, 77.7, 78.3, 80.6, 99.9, 101.7, 114.9, 127.2, 127.6, 127.7, 127.8, 127.9, 127.9, 128.2, 128.3, 128.4, 128.4 128.5, 128.6, 138.1, 138.3, 138.4, 138.4, 138.8, 139.2, 170.5. ESI MS m/z ($M + Na^+$) calcd. 1081.5468, found 1081.5428.

4-Pentenyl 2-*O*-Acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→3)-2,4-di-*O*-benzyl-β-D-mannopyranoside (16): To a solution of disaccharide **15** (0.108 g, 0.103 mmol) in THF (2 mL), water (2 mL) and trifluoroacetic acid (0.8 mL) were added. The turbid white solution was stirred for 2 h at room temperature. The reaction was diluted with diethyl ether (30 mL) and washed with sat. aqueous $NaHCO_3$ (2 × 20 mL), brine (20 mL), dried (Na_2SO_4), and concentrated. The residue was purified by flash column chromatography on silica gel (10 → 30% EtOAc/hexanes) to afford 84 mg (91%) of disaccharide **16**. $[\alpha]_D^{24} = -24.0$ (c = 0.5, CH_2Cl_2). IR (thin film): $\tilde{\nu}$ = 443, 2089, 1639, 1234, 698 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 1.70−1.78 (m, 2 H), 2.12−2.22 (m, 6 H), 3.31−3.39 (m, 1 H), 3.41−3.44 (m, 1 H), 3.63−3.69 (m, 2 H), 4.75−3.43 (m, 9 H), 4.43−4.73 (m, 8 H), 4.78−4.84 (m, 2 H), 4.91 (d, J = 11.0 Hz, 1 H), 4.97−5.09 (m, 3 H), 5.26 (d, J = 1.5 Hz, 1 H), 5.54−5.55 (m, 1 H), 5.80−5.90 (m, 1 H), 7.17−7.42 (m, 25 H). ^{13}C NMR ($CDCl_3$): δ = 21.2, 29.0, 30.4, 62.3, 68.9, 69.2, 69.7, 72.1, 72.3, 74.4, 74.4, 75.0, 75.4, 76.0, 77.5, 78.1, 80.0, 99.8, 101.8, 115.4, 127.6, 127.7, 127.8, 127.8, 127.8, 128.0, 128.0, 128.1, 128.3, 128.4, 128.2, 128.6, 128.6, 137.9, 137.9, 138.2, 138.3, 138.6, 138.7, 170.5. ESI MS m/z ($M + Na^+$) calcd. 925.4133, found 925.4141.

4-Pentenyl 2-*O*-Acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→3)-[2,4-di-*O*-benzyl-3,6-di-*O*-benzoyl-α-D-mannopyranosyl-(1→6)]-2,4-di-*O*-benzyl-β-D-mannopyranoside (7): Mannosyl trichloroacetimidate **10** (94 mg, 0.15 mmol) and disaccharide **15** (80 mg, 0.088 mmol) were combined, azeotropically dried with toluene (3 × 3 mL) and dissolved in diethyl ether (2 mL). The solution was cooled to −20 °C for 15 min, followed by the addition of TBDMSOTf (4 μL, 0.018 mmol), and stirred for 30 min at −20 °C. The reaction was quenched by the addition of Et_3N (50 μL), and dried in vacuo. The crude product was purified by flash column chromatography on silica gel (5 → 10% EtOAc/toluene) to afford 120 mg (93%) of trisaccharide **7**. $[\alpha]_D^{24} = +9.1$ (c = 1.0, CH_2Cl_2). IR (thin film): $\tilde{\nu}$ = 917, 1721, 1452, 1270, 1097, 1070, 698 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 1.42−1.51 (m, 2 H), 1.88−1.94 (m, 2 H), 1.97 (s, 3 H), 3.21−3.27 (m, 2 H), 3.46−3.53 (m, 2 H), 3.65−4.03 (m, 12 H), 4.16−4.35 (m, 5 H), 4.40−4.62 (m, 10 H), 4.73−4.85 (m, 5 H), 5.11 (s, 1 H), 5.40−5.42 (m, 1 H), 5.55−5.64 (m, 2 H), 6.83−6.86 (m, 1 H), 6.95−7.25 (m, 36 H), 7.31−7.49 (m, 4 H), 7.92−7.98 (m, 4 H). ^{13}C NMR ($CDCl_3$): δ = 21.5, 29.3, 30.6, 64.0, 66.5, 69.3, 69.4, 69.6, 70.4, 72.5, 72.5, 72.5, 73.6, 73.8, 74.4, 74.6, 74.8, 75.2, 75.4, 75.5, 75.7, 76.1, 77.1, 77.8, 78.4, 80.7, 98.6, 100.1, 101.9, 115.2, 127.6, 127.7, 127.8, 128.0, 128.1, 128.2, 128.2, 128.4, 128.5, 128.6, 128.7, 128.7, 128.8, 128.8, 128.9, 128.9, 130.2, 130.5, 130.5, 133.3, 133.5, 137.9, 138.3, 138.3, 138.6, 138.8, 139.0, 139.0, 166.0, 166.8, 170.4. ESI MS m/z ($M + Na^+$) calcd. 1475.6130, found 1475.6141.

4-Pentenyl 3,4,6-Tri-*O*-benzyl-α-D-mannopyranosyl-(1→3)-[2,4-di-*O*-benzyl-α-D-mannopyranosyl-(1→6)]-2,4-di-*O*-benzyl-β-D-mannopyranoside (17): Trisaccharide **7** (100 mg, 0.0687 mmol) was dissolved in CH_2Cl_2/MeOH (4 mL, 1:1). A solution of sodium methoxide in MeOH (450 μL, 25% w/v, 2 mmol) was added and the reaction was heated on an oil-bath to 45 °C for 1.5 h. The reaction was quenched with DOWEX-50 W-hydrogen strongly acidic ion-exchange resin, filtered, and dried in vacuo. The resulting crude product was purified by flash column chromatography on silica gel (10 → 40% EtOAC/toluene) to afford 73 mg (89%) of trisaccharide **17**. $[\alpha]_D^{24} = 11.0$ (c = 1.3, CH_2Cl_2). IR (thin film): $\tilde{\nu}$ = 470, 2922, 1453, 1364, 1072, 697 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 1.50−1.56 (m, 2 H), 1.84 (br. s, 1 H), 1.94−2.00 (m, 2 H), 2.23 (br. s, 2 H), 3.20−3.29 (m, 2 H), 3.49−3.54 (m, 2 H), 3.55−3.83 (m, 13 H), 3.86−3.92 (m, 3 H), 4.25−4.58 (m, 10 H), 4.64−4.76 (m, 3 H), 4.83−4.91 (m, 4 H), 5.11 (d, J = 0.97 Hz, 1 H), 5.18 (d, J = 1.2 Hz, 1 H), 5.61−5.72 (m, 1 H), 7.05−7.30 (m, 35 H). ^{13}C NMR ($CDCl_3$): δ = 29.3, 30.6, 62.7, 66.5, 69.1, 69.4, 69.7, 71.7, 72.2, 72.2, 72.6, 73.0, 73.7, 75.2, 75.4, 75.7, 76.1, 76.9, 77.6, 77.9, 79.1, 80.3, 80.6, 98.0, 101.7, 102.1, 115.3, 127.8, 127.9, 127.9, 128.0, 128.1, 128.1, 128.1, 128.1, 128.3, 128.3, 128.4, 128.6, 128.7, 128.7, 128.8, 128.9, 129.0, 129.0, 138.2, 138.2, 138.4, 138.4, 138.4, 138.6, 138.9, 138.9, 139.0. ESI MS m/z ($M + Na^+$) calcd. 1225.5500, found 1225.5497.

4-Pentenyl 2-*O*-Acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→2)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→3)-[2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→3)-[2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→6)]-2,4-di-*O*-benzyl-α-D-mannopyranosyl-(1→6)]-2,4-di-*O*-benzyl-β-D-mannopyranoside (6): Trisaccharide acceptor **17** (25 mg, 0.021 mmol) and mannosyl trichloroacetimidate **9** (60 mg, 0.093 mmol, 4.5equiv.) were combined, azeotropically dried with toluene (3 × 3 mL) and dissolved in CH_2Cl_2 (2 mL). The solution was cooled to −20 °C for 15 min, followed by the addition of TMSOTf (2.2 μL, 0.012 mmol). The reaction mixture was stirred and warmed to room temperature over 40 min. The reaction was quenched by the addition of Et_3N (100 μL), and dried in vacuo. The crude product was purified by flash column chromatography on silica gel (2 → 20% EtOAc/toluene) to afford 51 mg (94%) of hexasaccharide **6**. $[\alpha]_D^{24} = +34.9$ (c = 1.3, CH_2Cl_2). IR (thin film): $\tilde{\nu}$ = 029, 2916, 1744, 1235, 1076, 736, 697 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 1.56−1.60 (m, 2 H), 2.01−2.04 (m, 2 H), 2.09

(s, 3 H), 2.13 (s, 3 H), 2.16 (s, 3 H), 3.19−3.22 (m, 1 H), 3.30−3.36 (m, 2 H), 3.54−3.62 (m, 7 H), 3.67−3.72 (m, 6 H), 3.78−3.87 (m, 6 H), 3.89−3.99 (m, 10 H), 4.00−4.07 (m, 2 H), 4.09−4.13 (m, 1 H), 4.23−4.28 (m, 2 H), 4.34−4.37 (m, 1 H), 4.39−4.50 (m, 10 H), 4.53−4.59 (m, 6 H), 4.61−4.68 (m, 6 H), 4.73 (app. s, 1 H), 4.76 (d, J = 2.3 Hz, 1 H), 4.81−4.89 (m, 5 H), 4.90−4.94 (m, 3 H), 4.98−5.03 (m, 3 H), 5.20−5.24 (m, 2 H), 5.52−5.53 (m, 3 H), 5.70−5.77 (m, 1 H), 7.10−7.40 (m, 80 H). ^{13}C NMR ($CDCl_3$): δ = 21.8, 21.9, 29.6, 31.0, 66.1, 66.3, 68.4, 68.7, 68.8, 69.0 69.4, 69.5, 71.0, 71.4, 71.7, 72.0, 72.0, 72.0, 72.1, 72.3, 72.4, 72.6, 73.4, 73.4, 73.5, 73.6, 74.1, 74.2, 74.7, 74.9, 75.0, 75.2, 75.2, 75.3, 75.4, 77.5, 77.6, 77.8, 78.2, 78.4, 79.8, 81.7, 97.0, 98.4, 99.6, 100.0, 101.2, 101.7, 114.9, 127.4, 127.4, 127.5, 127.5, 127.6, 127.6, 127.6, 127.6, 127.7, 127.7, 127.7, 127.7, 127.8, 127.8, 127.9, 127.9, 127.9, 128.0, 128.0, 128.1 128.2, 128.3, 128.3, 128.4, 128.4, 128.4, 128.4, 128.5, 128.5, 128.5, 128.6, 128.6, 128.7, 128.7, 129.2, 138.0, 138.0, 138.2, 138.3, 138.4, 138.4, 138.5, 138.5, 138.5, 138.7, 138.8, 138.9, 139.0, 170.3, 170.3, 170.4; HSQC anomeric cross-peaks ($CDCl_3$) δ (4.23 × 101.8), (4.93 × 97.0), (5.02 × 98.4), (5.06 × 99.5), (5.21 × 99.9), (5.22 × 101.1). ESI MS m/z (M + Na^+) calcd. 2648.1622, found 2648.1530.

4-Pentenyl 3,4,6-Tri-*O*-benzyl-α-D-mannopyranosyl-(1→2)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→3)-[3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→3)-[3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→6)]-2,4-di-*O*-benzyl-α-D-mannopyranosyl-(1→6)]-2,4-di-*O*-benzyl-β-D-mannopyranoside (18): Hexasaccharide **6** (46 mg, 0.018 mmol) was azeotropically dried with toluene (3 × 3 mL) and dissolved in CH_2Cl_2 (1.5 mL). MeOH (5 mL) was added followed by a solution of sodium methoxide in MeOH (120 μL, 25% w/v, 0.525 mmol). The reaction was stirred for 1 h, quenched with DOWEX-50 W-hydrogen strongly acidic ion-exchange resin, filtered, and dried in vacuo. The resulting residue was purified by flash column chromatography on silica gel (5 → 20% EtOAc/toluene) to afford 46 mg (quant.) of hexasaccharide triol **18**. $[\alpha]_D^{24}$ = +34.3 (c = 1.0, CH_2Cl_2). IR (thin film): $\tilde{\nu}$ = 448, 3029, 2916, 1453, 1053, 697 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 1.43−1.53 (m, 2 H), 1.89−1.95 (m, 2 H), 2.07−2.28 (br. s, 3 H), 3.10−3.13 (m, 1 H), 3.19−3.24 (m, 1 H), 3.33−3.36 (m, 1 H), 3.43−3.62 (m, 13 H), 3.64−3.81 (m, 14 H), 3.82−3.92 (m, 3 H), 3.99−4.02 (m, 4 H), 4.13 (app. s, 1 H), 4.22−4.30 (m, 3 H), 4.35−4.40 (m, 8 H), 4.45−4.51 (m, 12 H), 4.53−4.65 (m, 4 H), 4.69−4.75 (m, 5 H), 4.78−4.83 (m, 3 H), 4.86−4.97 (m, 2 H), 5.02 (app. s, 1 H), 5.11 (app. s, 1 H), 5.16 (app. s, 1 H), 5.57−5.67 (m, 1 H), 6.81−7.48 (m, 80 H). ^{13}C NMR ($CDCl_3$): δ = 14.9, 21.8, 22.2, 69.4, 69.5, 69.7, 69.9, 70.1, 71.9, 72.0, 72.0, 72.3, 72.5, 72.6, 72.7, 72.8, 73.0, 73.2, 73.9, 74.0, 74.1, 74.2, 74.6, 74.9, 74.9, 75.2, 75.4, 75.5, 75.7, 75.8, 75.9, 76.2, 77.9, 78.4, 78.5, 80.3, 80.5, 80.8, 82.5, 97.5, 100.5, 101.8, 101.8, 102.1, 102.1, 115.4, 127.9, 128.0, 128.1, 128.1, 128.2, 128.3, 128.3, 128.4, 128.4, 128.4, 128.5, 128.5, 128.6, 128.6, 128.8, 128.9, 128.9, 129.0, 129.0, 129.0, 129.1, 129.1, 129.1, 129.2, 129.3, 138.6, 138.7, 138.7, 138.8, 138.8, 138.9, 139.0, 139.0, 139.1, 139.3, 139.4, 139.5. ESI MS m/z (M + Na^+) calcd. 2522.1305, found 2522.1307.

4-Pentenyl 2-*O*-Acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→2)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→2)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→3)-[2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→2)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→3)-[2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→2)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→6)]-2,4-di-*O*-benzyl-α-D-mannopyranosyl-(1→6)]-2,4-di-*O*-benzyl-β-D-mannopyranoside 5. Hexasaccharide **18** (19 mg, 0.0075 mmol) and mannosyl trichloroacetimidate **9** (36 mg, 0.056 mmol, 7.5equiv.) were azeotropically dried with toluene (3 × 3 mL), dried an additional 1.5 h in vacuo and dissolved in diethyl ether (2 mL). The solution was cooled to −20 °C for 15 min, followed by the addition of TMSOTf (1 μL, 0.005 mmol), and stirred for 30 min. The reaction was quenched by the addition of Et_3N (50 μL), and dried in vacuo. The crude product was purified by flash column chromatography on silica gel (2 → 18% EtOAc/toluene) affording 24 mg (80%) of nonasaccharide **5**. $[\alpha]_D^{24}$ = +24.7 (c = 0.9, CH_2Cl_2). IR (thin film): $\tilde{\nu}$ = 029, 2864, 1744, 1453, 1137, 1056, 736, 697 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 1.48−1.55 (m, 2 H) 1.94−1.98 (m, 2 H), 2.08 (s, 3 H), 2.12 (s, 3 H), 2.13 (s, 3 H), 3.13−3.18 (m, 2 H), 3.26−3.30 (m, 1 H), 3.35−3.46 (m, 5 H), 3.50−3.52 (m, 3 H), 3.55−3.67 (m, 10 H), 3.73−3.78 (m, 4 H), 3.82−3.94 (m, 21 H), 3.97−4.06 (m, 5 H), 4.08−4.13 (m, 4 H), 4.16−4.22 (m, 3 H), 4.30−4.43 (m, 12 H), 4.45−4.51 (m, 9 H), 4.54−4.55 (m, 6 H), 4.56−4.58 (m, 4 H), 4.60−4.61 (m, 2 H), 4.63−4.68 (m, 4 H), 4.71−4.73 (m, 1 H), 4.74−4.77 (m, 2 H), 4.80−4.89 (m, 7 H), 4.95−5.00 (m, 2 H), 5.08−5.11 (m, 3 H), 5.14 (m, 1 H), 5.17 (m, 1 H), 5.23−5.24 (m, 1 H), 5.52−5.55 (m, 4 H), 5.60−5.69 (m, 1 H), 7.00−7.02 (m, 1 H), 7.07−7.34 (m, 124 H). ^{13}C NMR ($CDCl_3$): δ = 20.5, 21.0, 21.3, 22.0, 29.1, 30.3, 66.6, 66.6, 66.6, 66.7, 68.2, 68.2, 68.8, 68.8, 68.8, m68.9, 69.0, 69.2, 69.2, 69.2, 69.4, 70.5, 70.8, 70.9, 71.4, 71.4, 71.9, 72.0, 72.0, 72.1, 72.2, 72.3, 72.7, 72.8, 73.3, 73.3, 73.4, 73.5, 73.5, 74.2, 74.9, 74.9, 75.2, 75.2, 75.2, 75.4, 75.4, 75.5, 77.4, 78.3, 78.4, 79.1, 79.2, 79.5, 79.9, 80.1, 82.2, 97.0, 99.3, 99.5, 99.5, 99.7, 100.7, 101.1, 101.4, 101.4, 115.0, 125.7, 126.2, 126.7, 126.6, 127.3, 128.0, 128.0, 128.3, 128.7, 129.3, 129.8, 130.3, 131.3, 132.5, 171.0, 171.0, 171.1; HSQC anomeric cross-peaks ($CDCl_3$) δ (4.16 × 102.0), (4.86 × 97.0), (5.00 × 99.6), three (5.10 × 99.6), (5.12 × 100.7), (5.18 × 101.2), (5.21 × 101.3). ESI MS m/z (M + Na^+) calcd. 3944.7437, found 3944.7440.

4-Pentenyl 3,4,6-Tri-*O*-benzyl-α-D-mannopyranosyl-(1→2)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→2)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→3)-[3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→2)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→3)-[3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→2)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→6)]-2,4-di-*O*-benzyl-α-D-mannopyranosyl-(1→6)]-2,4-di-*O*-benzyl-β-D-mannopyranoside (19): Nonasaccharide **5** (14 mg, 0.0035 mmol) was dissolved in a mixture of CH_2Cl_2/MeOH (3 mL, 1:2) and cooled to 0 °C. A solution of sodium methoxide in MeOH (35 μL, 25% w/v) was added and the reaction was slowly warmed to room temperature over 1 h, quenched with DOWEX-50 W-hydrogen strongly acidic ion-exchange resin, filtered, and dried in vacuo. The resulting residue was purified by flash column chromatography on silica gel (5 → 30% EtOAc/toluene) affording 12 mg (90%) of nonasaccharide triol **19**. ^{1}H NMR ($CDCl_3$): δ = 1.37−1.43 (m, 2 H), 1.85−1.88 (m, 2 H), 2.23 (br. s, 1 H), 2.29 (br. s, 2 H), 3.07−3.27 (m, 3 H), 3.30−4.27 (m, 56 H), 4.28−4.66 (m, 41 H), 4.70−4.77 (m, 9 H), 4.79 (d, J = 10.5 Hz, 1 H), 4.94 (app. s, 1 H), 5.02 (app. s, 1 H), 5.08−5.09 (m, 3 H), 5.13 (m, 2 H), 5.51−5.60 (m, 1 H), 6.92−7.44 (m, 125 H).

***n*-Pentyl α-D-Mannopyranosyl-(1→3)-[α-D-mannopyranosyl-(1→6)]-β-D-mannopyranoside (4):** Activated palladium on carbon (100 mg, 10%) was suspended in ethanol (10 mL) and exposed to an atmosphere of hydrogen gas (balloon). After 30 min, trisaccharide triol **17** (70 mg, 0.058 mmol) in EtOAc (5 mL) was added by cannula and stirred for 48 h under an atmosphere of hydrogen. The product was filtered through celite, dried in vacuo, to afford 6 mg (79%) trisaccharide **4**. $[\alpha]_D^{24}$ = +35.0 (c = 0.4, H_2O/EtOH 1:1). ^{1}H NMR (D_2O): δ = 0.70−0.73 (m, 3 H), 1.15−1.17 (m, 4 H), 1.43−1.46 (m, 2 H), 3.37−3.40 (m, 1 H), 3.47−3.83 (m, 19 H), 3.90−3.91 (m, 1 H), 3.98 (d, J = 1.6 Hz, 1 H), 4.52 (app. s, 1 H), 4.75 (app. s, 1 H), 4.94 (app. s, 1 H). ^{13}C NMR (D_2O): δ = 13.6, 22.1, 27.2, 28.7,

61.2, 65.8, 66.1, 67.0, 67.1, 70.2, 70.3, 70.4, 70.6, 70.7, 72.9, 73.6, 74.4, 81.1, 99.7, 100.0, 102.7. MALDI-TOF *m*/*z* (M + Na^+) calcd. 595.22, found 596.77.

***n*-Pentyl α-D-Mannopyranosyl-(1→2)-α-D-mannopyranosyl-(1→3)-[α-D-mannopyranosyl-(1→3)-[α-D-mannopyranosyl-(1→6)]-α-D-mannopyranosyl-(1→6)]-β-D-mannopyranoside (3):** Activated palladium on carbon (50 mg, 10%) was suspended in ethanol (5 mL) and exposed to an atmosphere of hydrogen gas (balloon). After 30 min, hexasaccharide triol **18** (35 mg, 0.014 mmol) in EtOAc (2 mL) was added by cannula and stirred for 48 h under an atmosphere of hydrogen. The product was filtered through celite, dried in vacuo, to afford 12 mg (81%) hexasaccharide **3**. $[\alpha]_D^{24}$ = +54.5 (*c* = 0.5, H_2O/EtOH 1:1). ^1H NMR (D_2O): δ = 0.70−0.74 (m, 3 H), 1.15−1.17 (m, 4 H), 1.43−1.46 (m, 2 H), 3.38−3.43 (m, 1 H), 3.46−3.89 (m, 33 H), 3.89−3.92 (m, 2 H), 3.96−3.97 (m, 2 H), 4.00 (app. s, 1 H), 4.51 (app. s, 1 H), 4.72 (app. s, 1 H), 4.75 (app. s, 1 H), 4.89 (app. s, 1 H), 4.98 (app. S, 1 H), 5.19 (app. s, 1 H),. MALDI-TOF *m*/*z* (M + Na^+) calcd. 1081.38, found 1082.54.

***n*-Pentyl α-D-Mannopyranosyl-(1→2)-α-D-mannopyranosyl-(1→2)-α-D-mannopyranosyl-(1→3)-[α-D-mannopyranosyl-(1→2)-α-D-mannopyranosyl-(1→3)-[α-D-mannopyranosyl-(1→2)-α-D-mannopyranosyl-(1→6)]-α-D-mannopyranosyl-(1→6)]-β-D-mannopyranoside (2):** Activated palladium on carbon (50 mg, 10%) was suspended in ethanol (5 mL) and exposed to an atmosphere of hydrogen gas (balloon). After 30 min, nonasaccharide triol **19** (12 g, 0.0031 mmol) in EtOAc (2 mL) was added by cannula and stirred for 48 h under an atmosphere of hydrogen. The product was separated by filtration through celite and dried in vacuo to yield 4 mg (88%) of fully deprotected nonasaccharide **2**. $[\alpha]_D^{24}$ = +38.0 (*c* = 0.05, H_2O/EtOH 1:1). ^1H NMR (D_2O): δ = 0.71−0.74 (m, 3 H), 1.16−1.18 (m, 5 H), 1.44−1.46 (m, 2 H), 3.38−3.40 (m, 1 H), 3.46−3.52 (m, 5 H), 3.52−3.57 (m, 5 H), 3.58−3.66 (m, 12 H), 3.68−3.72 (m, 6 H), 3.73−3.76 (m, 6 H), 3.79−3.82 (m, 3 H), 3.84−3.87 (m, 4 H), 3.91−3.99 (m, 7 H), 4.00 (app. s, 1 H), 4.51 (app. s, 1 H), 4.72 (app. s, 1 H), 4.89 (app. s, 3 H), 5.00 (app. s, 1 H), 5.16 (app. s, 1 H), 5.19 (app. s, 1 H), 5.26 (app. s, 1 H). ^{13}C NMR ($CDCl_3$): δ = 13.4, 21.9, 23.3, 27.5, 28.4, 61.1, 61.1, 61.2, 61.2, 65.6, 65.6, 65.7, 65.7, 65.7, 65.9, 66.9, 67.1, 69.7, 70.1, 70.3, 70.3, 70.3, 70.3, 70.3, 70.5, 71.2, 72.8, 73.3, 73.3, 74.2, 78.6, 78.8, 78.8, 79.1, 98.2, 99.7, 99.9, 100.8, 100.8, 100.9, 102.4, 102.4, 102.4; HSQC anomeric cross-peaks ($CDCl_3$) δ (4.51 × 99.9), (4.72 × 99.8), three (4.89 × 102.4), (5.00 × 98.1), (5.16 × 100.8), (5.19 × 100.8), (5.26 × 100.9). MALDI-TOF *m*/*z* (M + Na^+) calcd. 1567.54, found 1569.09.

Acknowledgments

Financial support from: the donors of the Petroleum ether Research Fund, administered by the ACS (ACS-PRF 34649-G1) for partial support of this research; the Mizutani Foundation for Glycoscience; the Kenneth M. Gordon Scholarship Fund (Fellowship for O.J.P.); the NIH (Biotechnology Training Grant for O.J.P. and D.M.R.); and Pfizer (ACS Division of Organic Chemistry-Pfizer Fellowship for O.J.P.) is gratefully acknowledged. Funding for the MIT-DCIF Inova 500 was provided by NSF (Award# CHE-9808061). Funding for the MIT-DCIF Avance (DPX) 400 was provided by NIH (Award# 1S10RR13886−01). Funding for the MIT-DCIF Mercury 300 was provided by NSF (Award# CHE-9808061) and NSF (Award# DBI-9729592).

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Received October 22, 2001
[O01511]