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Efficient Synthesis of Man_2, Man_3, and Man_5 Oligosaccharides, Using Mannosyl Iodide Donors[1]

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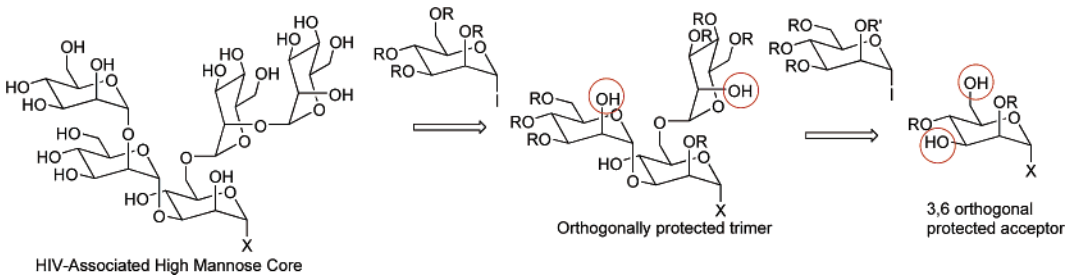

A highly efficient protocol for making Man_3 and Man_5 oligosaccharides with use of orthogonally protected glycosyl iodide donors has been developed. Glycosylation of a C-2-*O*-acetyl mannosyl iodide donor in the presence of silver triflate at −40 °C initially gave a mixture of the desired α-linked mannoside and an orthoacetate resulting from attack at the C-2 acetate. However, upon warming to room temperature the orthoacetate quantitatively rearranged to the desired oligosaccharide. Employing a 3,6-dihydroxy acceptor and subjecting it to double glycosidation quickly afforded high mannose sugars in nearly quantitative yields. Glycosyl iodide donors offer advantages over previously reported chloride donors as the reactions are faster, proceed in higher yields, and are not diminished in higher order constructs. These studies continue to dispel the notion that glycosyl iodides are too reactive to be of synthetic utility.

Introduction

The HIV-1 envelope is highly glycosylated with N-linked high-mannose oligosaccharides that play critical roles in the pathology of the disease.[2] For example, mannose undecasaccharide **1** (Man_9) and decasaccharide **2** (Man_8) are primary targets for cyanovirin-N (CVN), which is a multivalent anti-HIV lectin isolated from cyanobacterium *Nostoc ellipsosporum*.[3−6] CVN targets a disaccharide (**3**), which is triply and doubly displayed on **1** and **2**, respectively. Polyvalent presentation appears to be an important factor in this recognition process as the disaccharide alone is 100 times less effective in binding to CVN than either **1** or **2**. These same high mannose structures are required for recognition of 2G12, an HIV-associated neutralizing antibody.[7] Moreover, investigations in our own laboratory have led to the hypothesis that carbohydrate/carbohydrate interactions may mediate adhesion processes required for sexual transmission of the virus.[8] To probe this hypothesis, we have targeted the synthesis of high-mannose oligosaccharides. Here we disclose a highly efficient synthesis of Man_5 corresponding to the C-6 branch of Man_9 (Figure 1).

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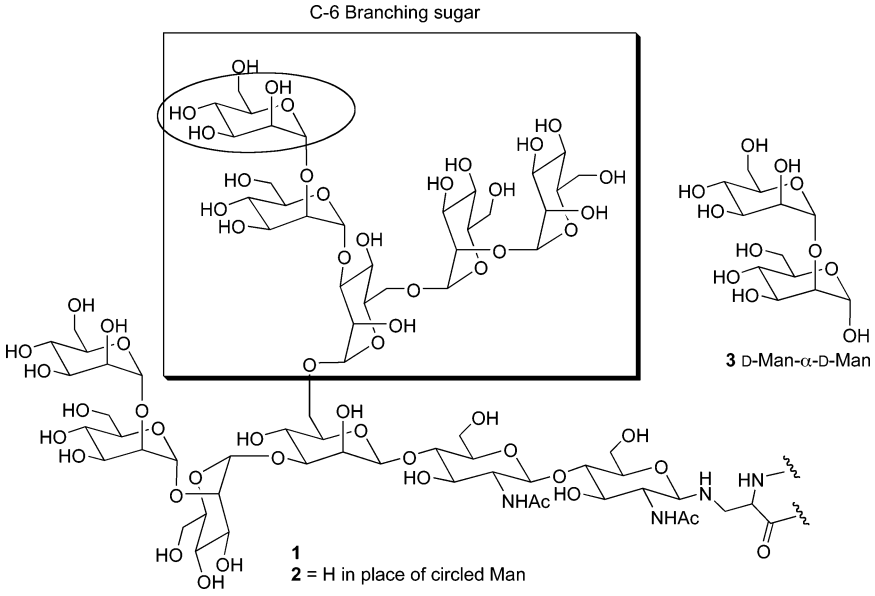

FIGURE 1. Representative high-mannose oligosaccharides of HIV-1 gp120.

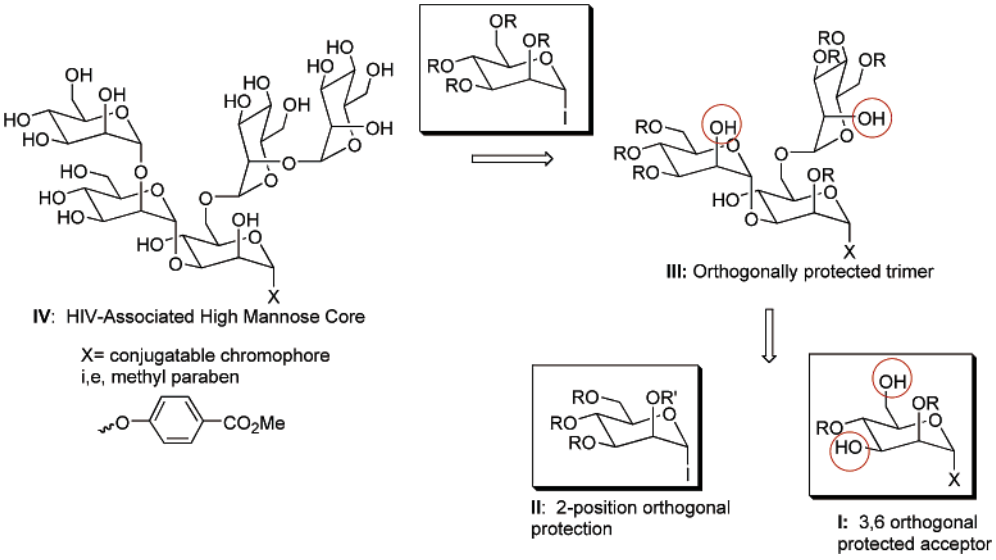

FIGURE 2. Retrosynthesis of Man_3 and Man_5 methyl paraben glycoconjugates.

We have recently demonstrated that mannosyl iodides efficiently undergo α glycosidation under in situ anomerization conditions.[9] The reaction is essentially quantitative, but purification is impeded by the formation of a glycal byproduct that coelutes with the product. We were able to scavenge the glycal by reacting it with dimethyl dioxirane to form the 1,2 anhydrosugar, which was trapped by norbornene-2-methanol and subjected to ROMP producing a polymer that could be filtered from the desired material. While we were happy to retrieve greater than 70% yield of the product, we decided to explore alternative methods for activation of the glycosyl iodide in hopes of avoiding glycal formation and improving upon the overall yields.

The retrosynthetic analysis shown in Figure 2 begins with a 3,6-orthogonally protected mannose derivative (**I**) serving as an acceptor for the selectively protected C-2 donor substrate (**II**) to yield trisaccharide **III**, which could be further extended to arrive at the target molecule **IV** (Figure 2). We chose to incorporate methyl paraben (X) at the reducing end of Man_5 to facilitate purification and provide a handle for conjugation to various supports for biological analyses. These studies led to a highly efficient synthesis of HIV-1 gp120 mannose di-, tri-, and pentasaccharides.

Results and Discussion

The synthesis of the core reducing sugar began with commercially available and readily synthesized[10] 3,4,6-tri-*O*-benzyl mannosyl ortho ester **4** (Scheme 1). HOAc mediated hydrolysis of the ortho ester quickly afforded 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-D-mannose **5**.[11] After acety-

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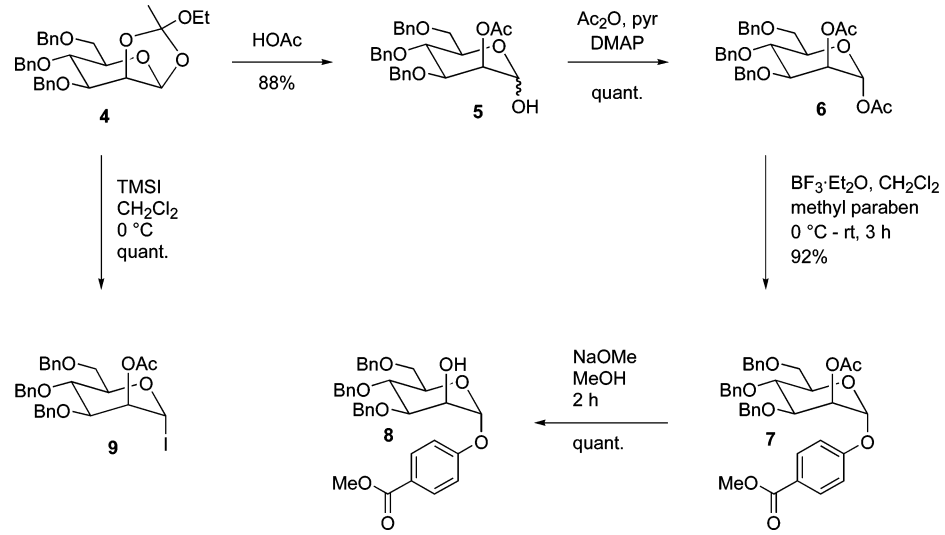
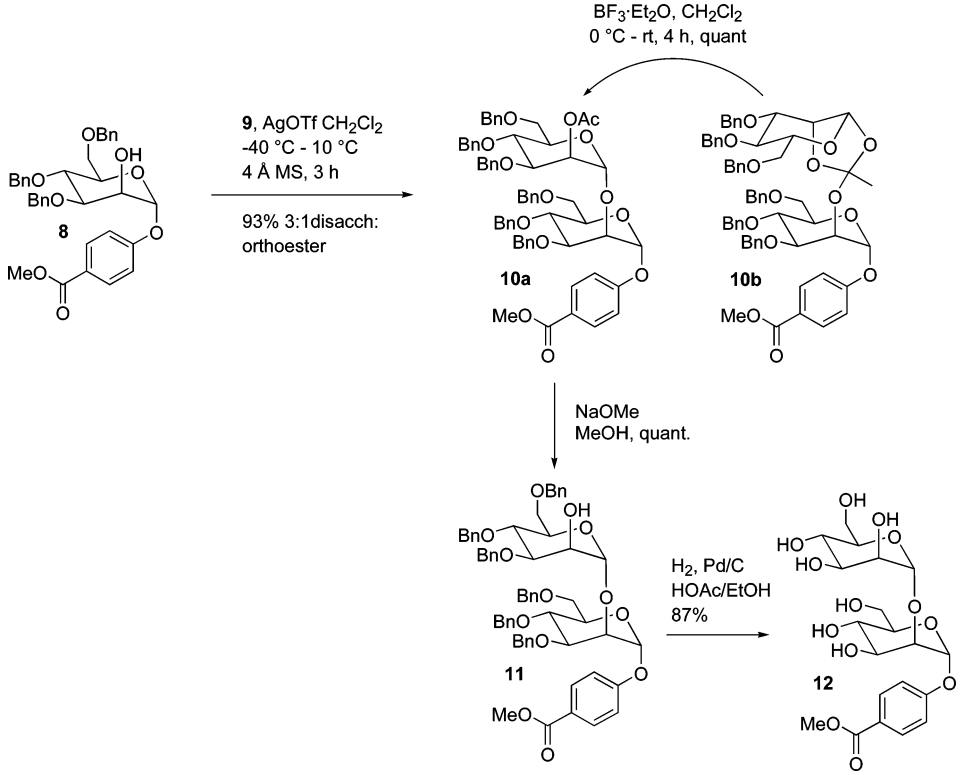
SCHEME 1. Synthesis of *p*-Methoxycarbonylphenyl Mannopyranoside



SCHEME 2. Synthesis of Man_2 (12)



lation, the 1,2-diacetate **6**[12] was used as a glycosyl donor via Lewis acid assisted *O*-arylation to provide the α-*O*-aryl mannopyranoside **7** in 92% isolated yield. Quantitative C-2 deacetylation of **7** with NaOMe in MeOH provided **8**. Compound **4** was also used for the formation of glycosyl iodide **9** in a one-pot procedure employing iodotrimethylsilane (TMSI).

In a model study, AgOTf activation of mannosyl iodide donor **9** at −40 °C and subsequent addition of acceptor **8** provided the α-(1→2)-linked disaccharide **10a** (Scheme 2) as confirmed by the ^1J coupling ($^1J_{H1,C1}$ = 175.8 Hz, $^1J_{H1',C1'}$ = 170.9 Hz). However, the 1,2-disaccharide ortho ester **10b** was also observed (a separable 3:1 mixture). This did not prove problematic as $BF_3{\cdot}Et_2O$ mediated rearrangement[13] of **10b** to **10a** proceeded quantitatively upon warming to 0 °C. C-2′ deacetylation gave **11** and catalytic hydrogenation at an elevated pressure supplied *p*-methoxycarbonylphenyl D-mannopyranosyl-α-(1→2)-α-D-mannopyranoside **12**. These preliminary studies demonstrated that AgOTf mediated glycosidations with **9** were identical with analogous reactions utilizing glycosyl chloride donors with respect to yields.[14] However, the

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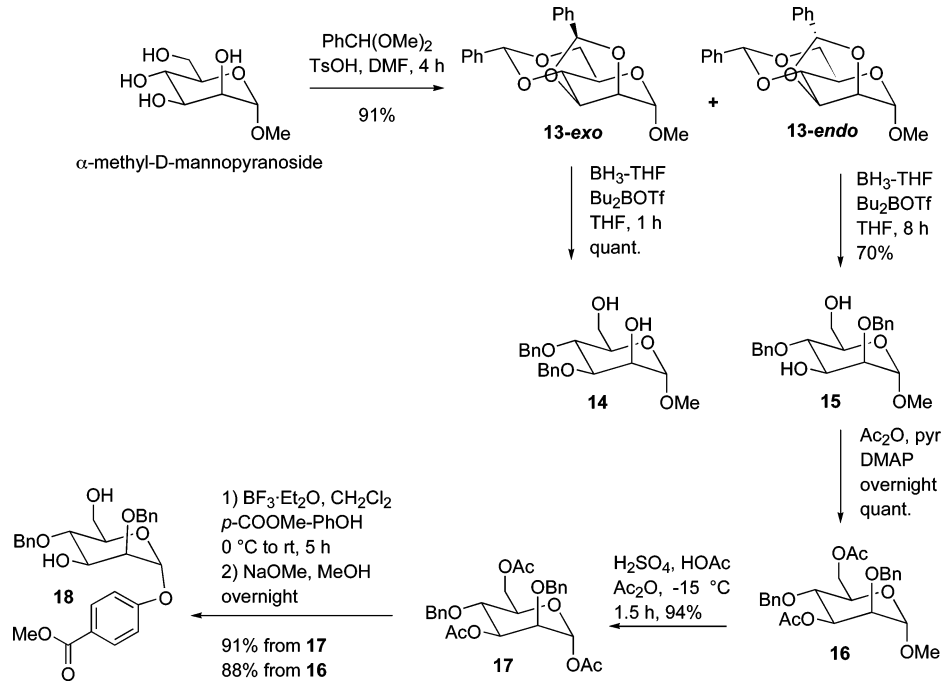
SCHEME 3. Synthesis of 3,6-Diol Core Acceptor 18



advantage of glycosyl iodides was clear as reaction times were significantly reduced, from >16 to 3 h. Acid catalysis also proved more efficient than in situ anomerization as no glycal was observed.[9]

Encouraged by these results, we set out to prepare a 3,6 orthogonally protected sugar to serve as the core acceptor **18** (Scheme 3). Acid-catalyzed acetal transfer to α-methyl-D-mannopyranoside afforded dibenzylidene mannose **13** as a mixture of isomers that could be separated by crystallization.[15] Numerous methods exist to regioselectively open the acetal giving orthogonally 4-*O*-benzyl[16−20] or 6-*O*-benzyl[20−23] sugars. When reacted with borane·tetrahydrofuran complex in the presence of dibutylborotriflate **13**-*exo* quantitatively afforded methyl 3,4-di-*O*-benzyl-α-D-mannopyranoside **14** while **13**-*endo* generated methyl 2,4-di-*O*-benzyl-α-D-mannopyranoside **15**.[24] In our hands, this reduction was conducted cleanly and smoothly within 1 h under strict anhydrous conditions. However, longer reaction times were required in situations where rigorous exclusion of water was not met. Upon completion of the reaction, the workup simply required quenching with methanol, removal of the methyl borates in vacuo, and flash chromatography. Satisfactory results (70% yield) were achieved on large scales (10 g of sugar) while quantitative transformations were achieved with small amounts (1 g of sugar). Through this two-step protocol, we prepared large quantities of **15**. Although only **13**-*endo* was needed in this situation to provide the desired 3,6-diol **6**, **13**-*exo* was not discarded as it is also an important building block for numerous other natural products and oligomers.[25−27] This protocol essentially bypasses the need for tin reagents and proved more attractive than alternative methods employed by Ogawa and co-workers.[28−30] The 3,6-diol **15** was quantitatively acetylated providing **16** and subsequent acetolysis presented 1,3,6-tri-*O*-acetyl-2,4-di-*O*-benzyl-D-mannopyranose **17**.[28] Treatment of **17** with $BF_3{\cdot}Et_2O$ in the presence of methyl paraben with concomitant deacetylation afforded **18**. The core diol acceptor was repeatedly prepared in high yields over multiple successive chromatography-free steps, 88% from **16** and 91% from **17**.

With the orthogonally protected diol acceptor (**18**) in hand, the double glycosidation was pursued. Reaction of **18** with **9** using AgOTf activation provided trisaccharide **19** in 91% yield after chromatography, Scheme 4. Instead of adding $BF_3{\cdot}OEt_2$ to effect the orthoacetate rearrangement, we simply let the reaction warm to room temperature from −40 °C over 3 h. After the usual workup, no ortho ester formation was detected as evidenced by NMR; $J_{C1,H1}$ coupling constants revealed only α-mannosyl linkages ($^1J_{H1''3,C1''3}$ = 172.0 Hz, $^1J_{H1''6,C1''6}$ = 171.0 Hz, $^1J_{H1',C1'}$ = 170.5 Hz). In comparison to double glycosidations in

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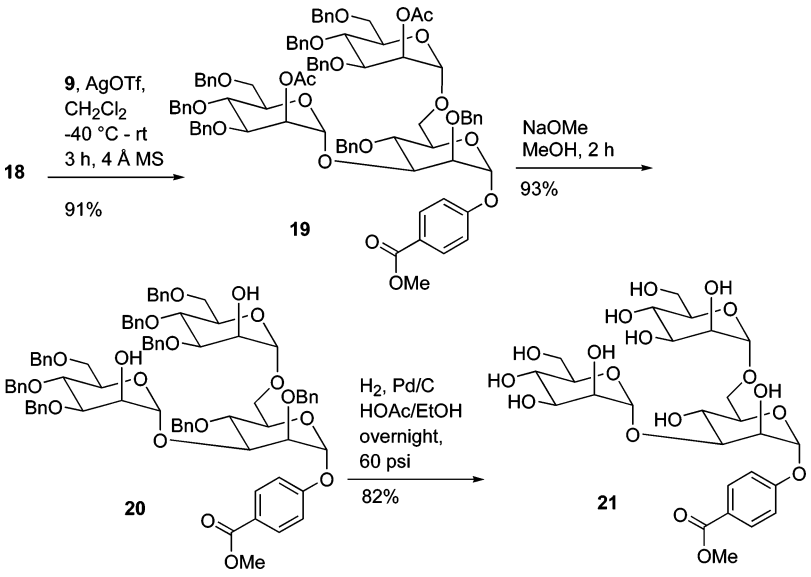
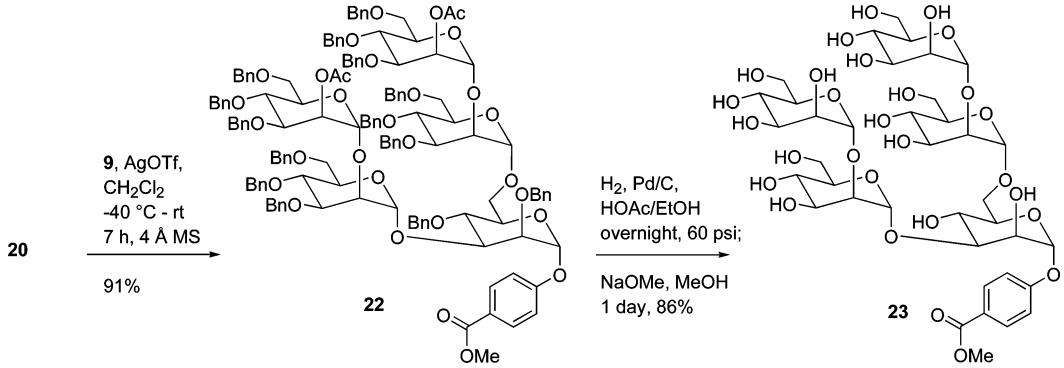
SCHEME 4. Syntheses of Man_3 (21) via Double Glycosidation



SCHEME 5. Synthesis of Man_5 (23) via Double Glycosidation



the glycosyl chloride work, this double glycosidation showed tremendous reduction in time (2 days to 3 h) and a slight enhancement of isolated yield (79 to 91%).[14] Global deprotection via deacetylation (to give **20**) and hydrogenation afforded trisaccharide **21** in 82% purified yield.

Further extension of this methodology led to the efficient synthesis of Man_5 (**23**) with similar savings in required time. In the event, action of **9** with AgOTf in the presence of acceptor **20** supplied pentasaccharide **22** ($^1J_{H1,C1}$ = 173.0 Hz, $^1J_{H1,C1}$ = 171.0 Hz, $^1J_{H1,C1}$ = 171.0 Hz, $^1J_{H1,C1}$ = 172.5 Hz, $^1J_{H1,C1}$ = 170.5 Hz) without complication in 91% purified yield, Scheme 5. Global deprotection yielded the pentasaccharide **23** in pure form, 86% yield. Contrary to what is generally accepted,[31] glycosyl acceptor size in these studies does not appear to affect the efficiency of mannosyl donor **9**. However, screening a larger array of higher ordered glycosyl acceptors is necessary before any conclusions as to the generality of **9** as a glycosyl donor for α-(1→2)-linked mannosides can be made.

Conclusion

In the course of these studies, we have clearly demonstrated the viability of C-2 *O*-acetyl mannosyl iodide donor **9** in the rapid construction of Man_2, Man_3, and Man_5 oligosaccharides. These represent the first cases where a C-2 participating group was employed in the formation of glycosidically linked oligosaccharides using glycosyl iodides. Although ortho ester formation posed a problem in initial glycosidations, simply allowing the reaction to warm to room temperature remedied the problem. AgOTf mediated glycosidations proved facile and efficient, as the transformations were often nearly quantitative. This process complements in situ anomerization glycosidations in demonstrating that a glycosyl iodide with a C-2 participating group is equally efficient and ameliorates problems associated with glycal formation. Glycosyl iodides were once thought too reactive to be of synthetic utility, these studies continue to dispel that notion. Overall, the use of glycosyl iodides toward oligosaccharide synthesis has proven extremely successful.

Experimental Section

Synthesis of 2-*O*-Acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl iodide (9). 3,4,6-Tri-*O*-benzyl-manno-ortho ester (**4**, 587 mg, 1.12 mmol) was dissolved in dry CH_2Cl_2 (12 mL) and cooled to 0 °C under an inert atmosphere. The stirring mixture was treated with TMSI (192 μL, 1.41 mmol) and allowed to stir at 0 °C for 50 min, after which time, TLC revealed complete conversion to **9** (R_f 0.54, 30% EtOAc/hexanes) and dry PhMe was added. The reaction was concen-

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trated in vacuo on a rotary evaporator. The evacuated system was purged with argon upon completion. The mixture was continuously azeotroped from dry PhMe until a clear distillate persisted. Mannosyl iodide **9** was redissolved in CH_2Cl_2 and used without further manipulation. ^{1}H NMR (C_6D_6, 500 MHz) δ 7.36−7.15 (15H, PhH), 6.83 (s, 1H, H-1), 5.84 (d, 1H, J = 1.8 Hz, H-2), 5.02 (d, 1H, J = 10.8 Hz, $PhCH_2$), 4.67 (m, 2H, H-3, $PhCH_2$), 4.62 (d, 1H, J = 11.4 Hz, $PhCH_2$), 4.65 (d, 1H, J = 12.0 Hz, $PhCH_2$), 4.40 (d, 1H, J = 11.4 Hz, $PhCH_2$), 4.36 (t, 1H, J = 9.6 Hz, H-4), 4.31 (d, 1H, J = 12.0 Hz, PhH), 3.88 (apparent d, 1H, J = 9.6 Hz, H-5), 3.80 (dd, 1H, J = 3.6 Hz, 11.4 Hz, H-6), 3.51 (d, 1H, J = 11.4 Hz, H-2), 1.71 (s, 3H, OAc). ^{13}C NMR (C_6D_6, 125 MHz) δ 169.2 (C=O), 139.0 (Ph-C), 138.6 (Ph-C), 138.1 (Ph-C), 128.61 (Ph-CH), 128.58 (Ph-CH), 128.52 (Ph-CH), 128.48 (Ph-CH), 128.44 (Ph-CH), 128.40 (Ph-CH), 128.3 (Ph-CH), 128.2 (Ph-CH), 128.09 (Ph-CH), 128.08 (Ph-CH), 128.06 (Ph-CH), 128.00 (Ph-CH), 127.94 (Ph-CH), 127.91 (Ph-CH), 127.87 (Ph-CH), 127.83, 127.78 (Ph-CH), 127.74 (Ph-CH), 127.69 (Ph-CH), 79.2 (C-5), 77.7 (C-3), 75.4 (OBn), 74.0 (C-4), 73.5 (OBn), 73.0 (C-2), 72.4 (C-1), 72.1 (OBn), 68.0 (C-6), 20.2 (OAc). HRFABMS m/z [M − I]$^+$ calcd for $C_{29}H_{31}O_6$ 475.2121, found 475.2123.

Preparation of *p*-Methoxycarbonylphenyl 2-*O*-Acetyl-3,4,6-tri-*O*-benzyl-D-mannopyranosyl-α-(1→2)-3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (10a). A mixture of acceptor (**8**, 264 mg, 0.46 mmol), AgOTf (434 mg, 1.69 mmol), and 4 Å MS (480 mg) was suspended in dry CH_2Cl_2 (3 mL) under argon, kept in the dark, and cooled to −40 °C. Glycosyl iodide (**9**, 1.12 mmol) was dissolved in CH_2Cl_2 (2 mL) and cooled to −60 °C. Into the stirring acceptor mixture was cannulated the donor solution. The reaction was allowed to gradually warm to −10 °C over 3 h, after which Et_3N (2 mL) was added and the mixture wasstirred for 5 min. The heterogeneous mixture was filtered over a pad of Celite. The solid mass was washed with copious amounts of EtOAc. The filtrate was extracted with saturated aq $NaHCO_3$ (2 × 75 mL) and brine. The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The crude material was chromatographed via a flash silica gel column with use of 25% EtOAc/hexanes as the eluent to provide 341 mg of **10a**, 70% yield. Data for **10a**: $[\alpha]^{25}_D$ +57 (c 1.0, $CHCl_3$). ^{1}H NMR (C_6D_6, 500 MHz) δ 8.20 (d, 2H, J = 8.5 Hz, PhH), 7.54 (d, 2H, J = 7.5 Hz, PhH), 7.42−7.35 (m, 9H, PhH), 7.31−7.11 (m, 21H, PhH), 6.35 (s, 1H, H-1′), 6.00 (s, 1H, H-2″), 5.31 (s, 1H, H-1″), 5.09 (t, 2H, J = 10.5 Hz, $PhCH_2$, $PhCH_2$), 4.79 (d, 1H, J = 11.0 Hz, $PhCH_2$), 4.68−4.44 (m, 8H, $PhCH_2$, $PhCH_2$, $PhCH_2$, $PhCH_2$, H-5′, $PhCH_2$, H-4″, $PhCH_2$), 4.42−4.34 (m, 4H, $PhCH_2$, $PhCH_2$, H-3′, H-3″), 4.30 (d, 1H, J = 11.0 Hz, $PhCH_2$), 4.26 (s, 1H, H-2′), 4.07 (t, 1H, J = 9.5 Hz, H-4′), 4.03 (m, 1H, H-5″), 3.91 (apparent d, 1H, J = 10.5 Hz, H-6′), 3.87 (dd, 1H, J = 4.0 Hz, 11.5 Hz, H-6″), 3.81 (dd, 1H, J = 6.5 Hz, 10.5 Hz, H-6′), 3.62 (apparent d, 1H, J = 11.5 Hz, H-6″), 3.59 (s, 3H, OMe), 1.78 (s, 3H, OAc). HSQC (C_6D_6, 500 MHz) without ^{1}H-decoupling: $J_{H1,C1}$ = 175.8 Hz, $J_{H1',C1'}$ = 170.9 Hz. ^{13}C NMR (C_6D_6, 500 MHz) δ 169.8 (C=O), 166.2 (Ph-C), 160.1 (Ph-C), 139.4 (Ph-C), 139.2 (Ph-C), 139.04 (Ph-C), 138.95 (Ph-C), 138.7 (Ph-C), 138.7 (Ph-C), 131.9 (Ph-CH), 129.2 (Ph-CH), 128.8 (Ph-CH), 128.6 (Ph-CH), 128.49 (Ph-CH), 128.47 (Ph-CH), 128.4 (Ph-CH), 128.34 (Ph-CH), 128.29 (Ph-CH), 128.2 (Ph-CH), 128.1 (Ph-CH), 128.0 (Ph-CH), 127.81 (Ph-CH), 127.75 (Ph-CH), 127.7 (Ph-CH), 127.63 (Ph-CH), 127.60 (Ph-CH), 127.5 (Ph-CH), 124.9 (Ph-CH), 116.5 (Ph-CH), 101.0 (C-1′), 97.0 (C-1), 79.6 (C-3′), 78.8 (C-3), 76.7 (C-2), 75.5 (OBn), 75.4 (OBn), 75.3 (C-4), 74.5 (C-4′), 73.5 (OBn), 73.43 (OBn), 73.42 (C-5′), 72.8 (C-5), 72.4 (OBn), 71.9 (OBn), 70.2 (C-6), 69.3 (C-2′), 69.1 (C-6′), 51.4 (OMe), 20.5 (OAc). MALDI-HRMS m/z [M + Na]$^+$ calcd for $C_{64}H_{66}NaO_{14}$ 1081.4350, found 1081.4391.

Preparation of *p*-Methoxycarbonylphenyl 3,4,6-Tri-*O*-benzyl-D-mannopyranosyl-α-(1→2)-3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (11). 2-Acetoxy-disaccharide (**10a**, 383 mg, 0.36 mmol) was dissolved in dry MeOH (25 mL) and CH_2Cl_2 (5 mL) under argon. The solution was treated with 30 wt % NaOMe/MeOH (100 μL) for 1.5 h. A new spot with R_f 0.27 was revealed through TLC analyses (40% EtOAc/hexanes). The reaction was quenched with Dowex H$^+$ resin until neutral and the resin was filtered off. The resin was washed with copious amounts of MeOH/CH_2Cl_2 and the mother liquor was concentrated in vacuo to provide 318 mg of **11**. $[\alpha]^{25}_D$ +41 (c 1.0, $CHCl_3$). ^{1}H NMR (C_6D_6, 600 MHz) δ 8.18 (d, 2H, J = 8.5 Hz, PhH), 7.41 (t, 4H, J = 8.4 Hz, PhH), 7.36 (d, 2H, J = 7.2 Hz, PhH), 7.33−7.10 (m, 28H, PhH), 6.38 (s, 1H, H-1), 5.42 (s, 1H, H-1′), 5.11 (d, 1H, J = 11.4 Hz, $PhCH_2$), 4.93 (d, 1H, J = 11.4 Hz, $PhCH_2$), 4.80 (d, 1H, J = 11.4 Hz, $PhCH_2$), 4.65 (d, 1H, J = 11.4 Hz, $PhCH_2$), 4.62−4.52 (m, 4H, $PhCH_2$, $PhCH_2$, $PhCH_2$, H-5′), 4.49−4.46 (m, 3H, $PhCH_2$, $PhCH_2$, H-4), 4.39 (apparent d, 2H, H-2′, $PhCH_2$), 4.36−4.29 (m, 4H, $PhCH_2$, H-3, $PhCH_2$, H-2), 4.14 (dd, 1H, J = 3.6 Hz, 9.0 Hz, H-3′), 4.00 (apparent dd, 1H, J = 2.4 Hz, 9.6 Hz, H-5), 3.94 (t, 1H, J = 9.6 Hz, H-4′), 3.91 (apparent d, 1H, J = 11.4 Hz, H-6′), 3.89 (dd, 1H, J = 3.6 Hz, 11.4 Hz, H-6), 3.78 (dd, 1H, J = 7.2 Hz, 11.4 Hz, H-6′), 3.61 (m, 1H, H-6), 3.59 (s, 3H, OMe), 2.50 (br, 1H, OH). HSQC (C_6D_6, 500 MHz) without ^{1}H-decoupling: $J_{H1,C1}$ = 175.8 Hz, $J_{H1',C1'}$ = 169.8. ^{13}C NMR (C_6D_6, 125 MHz) δ 166.3 (C=O), 160.1 (Ph-C), 139.4 (Ph-C), 139.2 (Ph-C), 139.0 (Ph-C), 138.9 (Ph-C), 138.67 (Ph-C), 138.65 (Ph-C), 131.9 (Ph-CH), 128.7 (Ph-CH), 128.6 (Ph-CH), 128.52 (Ph-CH), 128.50 (Ph-CH), 128.4 (Ph-CH), 128.3 (Ph-CH), 128.19 (Ph-CH), 128.15 (Ph-CH), 128.1 (Ph-CH), 128.0 (Ph-CH), 127.9 (Ph-CH), 127.8 (Ph-CH), 127.72 (Ph-CH), 127.68 (Ph-CH), 127.62 (Ph-CH), 127.60 (Ph-CH), 127.5 (Ph-CH), 124.8 (Ph-CH), 116.5 (Ph-CH), 102.6 (C-1′), 97.1 (C-1), 80.8 (C-3′), 79.6 (C-3), 76.3 (C-2), 75.3 (OBn, OBn, C-4′), 74.7 (C-4), 73.5 (OBn, OBn, C-5), 72.6 (C-5′), 72.4 (OBn), 71.9 (OBn), 70.3 (C-6′), 69.2 (C-6), 68.9 (C-2′), 51.4 (OMe). MALDI-HRMS m/z [M + Na]$^+$ calcd for $C_{62}H_{64}NaO_{13}$ 1039.4244, found 1039.4248.

Preparation of *p*-Methoxycarbonylphenyl d-Mannopyranosyl-α-(1→2)-α-D-mannopyranoside (12). Benzylated disaccharide (**11**, 287 mg, 0.28 mmol) was dissolved in 10% HOAc/EtOH (10 mL). To the solution was added 10% Pd/C dry (162 mg). The mixture was degassed under vacuum to −10 mmHg and repressurized to 60 psi of H_2. This routine was repeated twice more and the mixture was shaken overnight at 60 psi of H_2. The heterogeneous mixture was filtered over a pad of Celite and the solid mass was washed with copious amounts of MeOH. Following concentration of the mother liquor in vacuo, the mass was redissolved in H_2O and passed through a C8 plug. The mother liquor was lyophilized to yield a white foamy solid, 122 mg. $[\alpha]^{25}_D$ +27 (c 1.0, $CHCl_3$). ^{1}H NMR (D_2O, 500 MHz) δ 7.76 (d, 2H, J = 9.0 Hz, PhH), 7.02 (d, 2H, J = 9.0 Hz, PhH), 5.89 (s, 1H, H-1′), 4.97 (s, 1H, H-1″), 4.06−4.01 (m, 3H, H-5′, H-2′, H-2″), 3.83−3.77 (m, 3H, H-6″, H-3′, H-3″), 3.74 (s, 3H, OMe), 3.70 (t, 1H, J = 10.0 Hz, H-4″), 3.65−3.60 (m, 4H, H-5″, H-6′, H-6′, H-6″), 3.54−3.50 (m, 2H, H-4′, H-5″). HSQC (D_2O, 500 MHz) without ^{1}H-decoupling: $J_{H1,C1}$ = 175.8 Hz, $J_{H1',C1'}$ = 169.8. ^{13}C NMR (D_2O, 125 MHz) δ 169.0 (C=O), 159.9 (Ph-C), 131.7 (Ph-CH), 123.7 (Ph-C), 116.6 (Ph-CH), 116.5 (Ph-CH), 102.8 (C-1″), 96.3 (C-1′), 79.2 (C-2′), 73.8 (C-5″), 73.7 (C-3″), 70.6 (C-3′), 70.21 (C-2″), 70.16 (C-5′), 67.2 (C-4″), 66.9 (C-4′), 61.5 (C-6″), 60.8 (C-6′), 52.7 (OMe). MALDI-HRMS m/z [M + Na]$^+$ calcd for $C_{20}H_{28}NaO_{13}$ 499.1428, found 499.1455.

Preparation of *p*-Methoxycarbonylphenyl 2,4-Di-*O*-benzyl-α-D-mannopyranoside (18). A solution of 1,3,6-tri-*O*-acetyl mannose[14] (**17**, 473 mg, 0.97 mmol) and methyl *p*-hydroxybenzoate (765 mg, 4.87 mmol) was dissolved in dry CH_2Cl_2 (10 mL) and cooled to 0 °C under an inert atmosphere. The solution was treated with $BF_3{\cdot}Et_2O$ (247 μL, 2.75 mmol) and stirred for 10 min at 0 °C. The reaction was then removed from the bath and allowed to warm to room temperature over 4 h, after which, TLC (30% EtOAc/hexanes) revealed the complete consumption of the starting material and the presence of a major spot (R_f 0.49). The reaction was then diluted with CH_2Cl_2 (50 mL) and washed with saturated aq K_2CO_3 (3 × 50 mL). The organic layer was dried over $MgSO_4$ and concentrated in vacuo. ^{1}H NMR revealed only the presence of

the α-linked product. As the acceptor could not be separated from the desired product, the crude mixture was redissolved in dry MeOH (20 mL) and treated with 30 wt % NaOMe/MeOH (1 mL) for 40 min. TLC (30% EtOAc/Hexanes) revealed complete deacetylation to afford **18** (R_f 0.08). The mixture was neutralized with Dowex 50WX8 H^+ resin. After removal of the resin, the mother liquor was concentrated in vacuo and purified via silica gel column chromatography (30% EtOAc/hexanes) to provide 435 mg of the desired diol **18**, 91% over 2 steps. $[\alpha]^{25}_D$ +59 (*c* 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.97 (d, 2H, *J* = 8.5 Hz, PhH), 7.41−7.29 (m, 10H, PhH), 7.00 (d, 1H, *J* = 8.4 Hz, PhH), 5.63 (s, 1H, H-1), 4.91 (d, 1H, *J* = 11.0 Hz, $PhCH_2$), 4.78 (d, 1H, *J* = 11.0 Hz, $PhCH_2$), 4.70 (d, 2H, *J* = 11.0 Hz, $PhCH_2$, $PhCH_2$), 4.20 (dt, 1H, *J* = 5.0 Hz, 9.5 Hz, H-3), 3.95 (m, 1H, H-2), 3.88 (s, 3H, OMe), 3.84 (t, 1H, *J* = 9.5 Hz, H-4), 3.76 (m, 2H, H-6, H-6), 3.64 (m, 1H, H-5), 2.39 (d, 1H, *J* = 9.5 Hz, C3-OH), 1.85 (t, 1H, *J* = 6.5 Hz, C6-OH). HSQC ($CDCl_3$, 500 MHz) without ^{1}H-decoupling: $J_{H1,C1}$ = 175.8 Hz, $J_{H1',C1'}$ = 169.8. ^{13}C NMR ($CDCl_3$, 125 MHz) δ 166.6 (C=O), 159.5 (Ph-C), 138.1 (Ph-C), 137.4 (Ph-C), 131.6 (Ph-CH), 128.7 (Ph-CH), 128.5 (Ph-CH), 128.3 (Ph-CH), 128.0 (Ph-CH), 127.9 (Ph-CH), 124.3 (Ph-CH), 125.7 (Ph-CH), 95.2 (C-1), 77.8 (C-2), 75.7 (C-4), 75.0 (OBn), 73.5 (OBn), 72.5 (C-5), 71.5 (C-3), 61.8 (C-6), 52.0 (OMe). MALDI-HRMS *m/z* [M + Na]$^+$ calcd for $C_{28}H_{30}NaO_8$ 517.1838, found 517.1813.

Preparation of *p*-Methoxycarbonylphenyl (2-*O*-Acetyl-3,4,6-tri-*O*-benzyl-D-mannopyranosyl-α-(1→3))-(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-D-mannopyranosyl-α-(1→6))-2,4-di-*O*-benzyl-α-D-mannopyranoside (19). A mixture of diol monosaccharide acceptor (**18**, 110 mg, 0.22 mmol), AgOTf (429 mg, 1.67 mmol), and 4 Å MS (464 mg) was suspended in dry CH_2Cl_2 (3 mL) under argon, kept in the dark, and cooled to −40 °C. Mannosyl iodide (**9**, 1.11 mmol) was dissolved in CH_2Cl_2 (2 mL) and cooled to −60 °C. Into the stirring acceptor mixture was cannulated the donor solution. The reaction was allowed to gradually warm to room temperature over 3 h, after which Et_3N (2 mL) was added and the mixture was stirred for 5 min. TLC analyses (40% EtOAc/hexanes) showed the presence of a new spot, R_f 0.37. The heterogeneous mixture was filtered over a pad of Celite. The solid mass was washed with copious amounts of EtOAc (100 mL). The filtrate was extracted with saturated aq $NaHCO_3$ (2 × 50 mL) and brine. The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The crude material was chromatographed via a flash silica gel column, using 25% EtOAc/hexanes as the eluent to provide **19**, 293 mg (91% yield). $[\alpha]^{25}_D$ +31 (*c* 1.0, $CHCl_3$). ^{1}H NMR (C_6D_6, 500 MHz) δ 8.29 (d, 2H, *J* = 8.5 Hz, PhH), 7.52−7.07 (m, 42H, PhH), 5.98 (s, 1H, H-2‴^{3}), 5.78 (s, 1H, H-2‴^{6}), 5.67 (s, 1H, H-1′), 5.61 (s, 1H, H-1‴^{3}), 5.23 (d, 1H, *J* = 11.0 Hz, $PhCH_2$), 5.12 (d, 1H, *J* = 11.0 Hz, $PhCH_2$), 5.11 (s, 1H, H-1‴^{6}), 5.06 (d, 1H, *J* = 11.0 Hz, $PhCH_2$), 4.80−4.61 (m, 10H, 10 $PhCH_2$, H-3′), 4.53−4.50 (m, 5H, 4 $PhCH_2$, H-5‴^{3}), 4.47−4.31 (m, 4H, H-3″,^{3} H-5″,^{6} H-4″,^{6} H-4′), 4.26−4.25 (m, 2H, H-2′, H-3‴^{6}), 4.15 (t, 1H, *J* = 9.5 Hz, H-4‴^{3}), 4.00 (apparent d, 2H, *J* = 9.0 Hz, H-6″,^{6} H-5′), 3.94 (apparent d, 2H, *J* = 11.0 Hz, H-6′, H-6‴^{3}), 3.87 (dd, 1H, *J* = 6.0 Hz, 11.0 Hz, H-6′), 3.80 (d, 1H, *J* = 11.0 Hz, H-6‴^{3}), 3.67 (d, 1H, *J* = 9.0 Hz, H-6‴^{6}), 3.56 (s, 3H, OMe), 1.81 (s, 6H, 2 OAc). HSQC (C_6D_6, 500 MHz) without ^{1}H-decoupling: $J_{H1''3,C1''3}$ = 172.0 Hz, $J_{H1''6,C1''6}$ = 171.0 Hz, $J_{H1',C1'}$ = 170.5 Hz. ^{13}C NMR (C_6D_6, 125 MHz) δ 169.8 (2 C=O), 166.3 (C=O), 160.2 (Ph-C), 139.5 (Ph-C), 139.2 (Ph-C), 138.9 (Ph-C), 138.8 (Ph-C), 138.6 (Ph-C), 138.5 (Ph-C), 132.1 (Ph-CH), 128.9 (Ph-CH), 128.7 (Ph-CH), 128.6 (Ph-CH), 128.54 (Ph-CH), 128.48 (Ph-CH), 128.4 (Ph-CH), 128.2 (Ph-CH), 128.1 (Ph-CH), 127.8 (Ph-CH), 127.6 (Ph-CH), 124.9 (Ph-CH), 116.5 (Ph-CH), 100.6 (C-1‴^{3}), 98.4 (C-1‴^{6}), 95.6 (C-1′), 78.9 (C-3′), 78.6 (C-3‴^{3}), 78.4 (C-3‴^{6}), 77.9 (C-4‴^{6}), 75.5 (OBn), 75.34 (OBn), 75.27 (OBn, C-5‴^{6}), 75.2 (C-4‴^{3}), 75.0 (C-4′), 73.7 (OBn), 73.5 (OBn), 73.2 (C-5‴^{3}), 73.0 (C-5′), 72.8 (OBn), 72.4 (C-2′), 72.0 (OBn), 71.7 (OBn), 70.3 (C-6′), 69.6 (C-6‴^{3}), 69.2 (C-2‴^{3}), 68.7 (C-2‴^{6}), 66.3 (C-6‴^{6}), 51.5 (OMe), 20.6 (OAc), 20.5 (OAc). MALDI-HRMS *m/z* [M + Na]$^+$ calcd for $C_{86}H_{90}NaO_{20}$ 1465.5922, found 1465.5843.

Preparation of *p*-Methoxycarbonylphenyl (3,4,6-Tri-*O*-benzyl-D-mannopyranosyl-α-(1→3))-(3,4,6-tri-*O*-benzyl-D-mannopyranosyl-α-(1→6))-2,4-di-*O*-benzyl-α-D-mannopyranoside (20). The trisaccharide **19** was dissolved in dry MeOH (25 mL) and dry CH_2Cl_2 (5 mL) under argon at room temperature and treated with 30 wt % NaOMe/MeOH (100 μL) for 1 h. TLC (40% EtOAc/hexanes) revealed complete deacetylation of **19** to afford **20** (R_f 0.12) and Dowex 50WX8 H^+ resin was added to neutralize the mixture. Following removal of the resin, the mother liquor was concentrated in vacuo, and flash silica gel column chromatography with 40% EtOAc/hexanes provided the trisaccharide diol, 220 mg, 93% yield. $[\alpha]^{25}_D$ +61 (*c* 1.0, $CHCl_3$). ^{1}H NMR (C_6D_6, 500 MHz) δ 8.29 (d, 2H, *J* = 8.5 Hz, PhH), 7.50 (d, 2H, *J* = 8.5 Hz), 7.46−7.35 (m, 14H, PhH), 7.30−7.05 (m, 26H, PhH), 5.63 (s, 1H, H-1‴^{3}), 5.61 (s, 1H, H-1′), 5.22 (s, 1H, H-1‴^{6}), 5.10 (d, 1H, *J* = 11.0 Hz, $PhCH_2$), 4.98 (d, 1H, *J* = 11.0 Hz, $PhCH_2$), 4.89 (d, 1H, *J* = 11.0 Hz, $PhCH_2$), 4.73 (d, 2H, *J* = 11.0 Hz, $PhCH_2$, $PhCH_2$), 4.68 (d, 1H, *J* = 11.0 Hz, $PhCH_2$), 4.65−4.52 (m, 8H, $PhCH_2$, $PhCH_2$, $PhCH_2$, $PhCH_2$, $PhCH_2$, C-3′, $PhCH_2$, $PhCH_2$), 4.48−4.43 (m, 5H, $PhCH_2$, $PhCH_2$, $PhCH_2$, H-2′, H-4‴^{6}), 4.27−4.13 (m, 6H, H-4′, H-2‴^{3}, H-5″,^{6} H-5‴^{3}, H-3‴^{3}, H-2‴^{6}), 4.04−3.91 (m, 6H, H-4‴^{3}, H-3″,^{6} H-6″,^{6} H-5′, H-6‴^{3}, H-6′), 3.85−3.81 (m, H-6‴^{3}, H-6′), 3.55 (s, 3H, OMe), 2.48 (br, 2H, OH, OH). HSQC (C_6D_6, 500 MHz) without ^{1}H-decoupling: $J_{H1''3,C1''3}$ = 171.5 Hz, $J_{H1''6,C1''6}$ = 170.0 Hz, $J_{H1',C1'}$ = 171.0 Hz. ^{13}C NMR (C_6D_6, 125 MHz) δ 166.4 (C=O), 160.3 (Ph-C), 139.5 (Ph-C), 139.3 (Ph-C), 139.2 (Ph-C), 138.9 (Ph-C), 138.82 (Ph-C), 138.75 (Ph-C), 138.7 (Ph-C), 138.6 (Ph-C), 132.0 (Ph-CH), 128.74 (Ph-CH), 128.70 (Ph-CH), 128.64 (Ph-CH), 128.60 (Ph-CH), 128.54 (Ph-CH), 128.52 (Ph-CH), 128.50 (Ph-CH), 128.4 (Ph-CH), 128.3 (Ph-CH), 128.2 (Ph-CH), 128.1 (Ph-CH), 128.0 (Ph-CH), 127.9 (Ph-CH), 127.8 (Ph-CH), 127.7 (Ph-CH), 127.62 (Ph-CH), 127.56 (Ph-CH), 127.5 (Ph-CH), 124.8 (Ph-CH), 116.5 (Ph-CH), 102.0 (C-1‴^{3}), 99.8 (C-1‴^{6}), 95.7 (C-1′), 80.7 (C-3‴^{3}), 80.6 (C-3‴^{6}),78.1 (C-4‴^{6}), 75.4 (OBn, C-4′), 75.2 (OBn, C-4‴^{3}), 75.0 (OBn, C-3′, C-5‴^{6}), 73.8 (OBn), 73.53 (OBn), 72.95 (C-2′), 72.23 (C-5′), 72.7 (OBn), 72.1 (C-5‴^{3}), 72.0 (OBn), 71.7 (OBn), 70.5 (C-6′), 69.7 (C-6‴^{3}), 69.1 (C-2‴^{3}), 68.4 (C-2‴^{6}), 66.0 (C-6‴^{6}), 51.5 (OMe). MALDI-HRMS *m/z* [M + Na]$^+$ calcd for $C_{82}H_{86}NaO_{18}$ 1381.5712, found 1381.5735.

Preparation of *p*-Methoxycarbonylphenyl (D-Mannopyranosyl-α-(1→3))-(D-mannopyranosyl-α-(1→6))-α-D-mannopyranoside (21). Benzylated trisaccharide (**20**, 94 mg, 0.07 mmol) was dissolved in 10% HOAc/EtOH (10 mL). To the solution was added 10% Pd/C dry (102 mg). The mixture was degassed under vacuum to −10 in Hg and repressurized to 60 psi of H_2. This routine was repeated twice more and the mixture was shaken overnight at 60 psi of H_2. The heterogeneous mixture was filtered over a pad of Celite and the solid mass was washed with copious amounts of MeOH. Following concentration of the mother liquor in vacuo, the mass was redissolved in H_2O and passed through a C8 plug. The mother liquor was lyophilized to yield a white foamy solid. HPLC purification was performed with a C18 Vydac prep column at a flow rate of 5 mL/min with a linear gradient from 100% H_2O to 100% over 60 min. Fully deprotected trisaccharide **21** was provided in 82% isolated yield (37 mg) after lyophilization. $[\alpha]^{25}_D$ +48 (*c* 1.0, $CHCl_3$). ^{1}H NMR (D_2O, 500 MHz) δ 7.92 (d, 2H, *J* = 9.0 Hz, PhH), 7.12 (d, 2H, *J* = 9.0 Hz), 5.62 (s, 1H, H-1′), 5.09 (s, 1H, H-1‴^{3}), 4.63 (s, 1H, H-1‴^{6}), 4.25 (s, 1H, H-2′), 4.08 (dd, 1H, *J* = 4.5 Hz, 9.5 Hz, H-3′), 4.00 (s, 1H, H-2‴^{3}), 3.84−3.52 (m, 18H). Estimated ^{1}H chemical shifts from HSQC (D_2O, 500 MHz) data of 3.84−3.52 region: 3.85 (H-4′), 3.84 (H-6‴^{3}, H-3‴^{3}), 3.83 (OMe), 3.80 (H-6′), 3.78 (H-6‴^{3}), 3.75 (H-3‴^{6}), 3.74 (H-4‴^{6}), 3.71 (H-6‴^{6}), 3.65 (H-6‴^{6}), 3.63 (H-5‴^{3}), 3.61 (H-2‴^{6}), 3.60 (H-6′, H-4‴^{3}), 3.55 (H-5‴^{6}), 3.54 (H-5′). HSQC (D_2O, 500 MHz) without ^{1}H-decoupling: $J_{H1''3,C1''3}$ = 172.0 Hz, $J_{H1''6,C1''6}$ = 171.0 Hz, $J_{H1',C1'}$ = 174.5 Hz. ^{13}C NMR (D_2O, 125 MHz) δ 169.2 (C=O), 159.5 (Ph-C), 131.8 (Ph-CH, Ph-CH),

124.0 (Ph-C), 116.6 (Ph-CH, Ph-CH), 102.7 (C-1‴^{3}), 99.1 (C-1‴^{6}), 97.5 (C-1′), 78.3 (C-3′), 73.7 (C-4‴6), 72.9 (C-5‴6), 71.8 (C-3‴6), 70.8 (C-2‴6), 70.6 (C-3‴3), 70.3 (C-2‴3), 70.1 (C-5‴3), 69.5 (C-2′), 67.0 (C-4‴3), 66.9 (C-5′), 66.0 (C-4′), 65.3 (C-6′), 61.23 (C-6‴6), 61.16 (C-6‴3), 52.8 (OMe). MALDI-HRMS *m/z* $[M + Na]^+$ calcd for $C_{26}H_{38}NaO_{18}$ 661.1956, found 661.1954.

Preparation of *p*-Methoxycarbonylphenyl (2-*O*-Acetyl-3,4,6-tri-*O*-benzyl-D-mannopyranosyl-α-(1→2)-3,4,6-tri-*O*-benzyl-D-mannopyranosyl-α-(1→3))-(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-D-mannopyranosyl-α-(1→2)-3,4,6-tri-*O*-benzyl-D-mannopyranosyl-α-(1→6))-2,4-di-*O*-benzyl-α-D-mannopyranoside (22). A mixture of diol trisaccharide acceptor (**20**, 113 mg, 0.08 mmol), AgOTf (116 mg, 0.23 mmol), and 4 Å MS (356 mg) was suspended in dry CH_2Cl_2 (2 mL) under argon, kept in the dark, and cooled to −40 °C. Mannosyl iodide (**9**, 0.42 mmol) was dissolved in CH_2Cl_2 (1.5 mL) and cooled to −60 °C. The donor solution was cannulated into the stirring acceptor mixture. The reaction was allowed to gradually warm to room temperature over 7 h, after which TLC (40% EtOAc/hexanes) analyses revealed a major spot (R_f 0.40). After stirring with Et_3N (2 mL) for 5 min, the heterogeneous mixture was filtered over a pad of Celite. The solid mass was washed with copious amounts of EtOAc (50 mL). The filtrate was extracted with saturated aq $NaHCO_3$ (2 × 25 mL) and brine. The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The crude material was chromatographed via a flash silica gel column with 25% EtOAc/hexanes as the eluent to provide 175 mg (91% yield) of pentasaccharide **22**. $[\alpha]^{25}_D$ +29 (*c* 0.8, $CHCl_3$). ^{1}H NMR (C_6D_6, 500 MHz) δ 8.28 (d, 2H, *J* = 8.5 Hz, PhH), 7.59 (m, 4H, PhH), 7.47 (m, 9H, PhH), 7.41 (m, 16H, PhH), 7.34−7.04 (m, 111H, PhH), 6.02 (s, 1H, C-2‴^{3}), 5.99 (s, 1H, C-2‴^{6}), 5.95 (s, 1H, H-1), 5.70 (s, 1H, H-1), 5.49 (s, 1H, H-1), 5.31 (s, 1H, H-1), 5.28 (S, 1H, H-1), 5.23 (d, 1H, *J* = 11.0 Hz, $PhCH_2$), 5.14 (d, 1H, *J* = 11.0 Hz, $PhCH_2$), 5.11 (d, 1H, *J* = 11.0 Hz, $PhCH_2$), 5.10 (d, 1H, *J* = 11.0 Hz, $PhCH_2$), 5.09 (d, 1H, *J* = 11.0 Hz, $PhCH_2$), 5.02 (d, 1H, *J* = 11.0 Hz, $PhCH_2$), 4.84 (d, 1H, *J* = 11.0 Hz, $PhCH_2$), 4.80 − 4.73 (m, 4H, $PhCH_2$, $PhCH_2$, $PhCH_2$, $PhCH_2$), 4.70−4.64 (m, 8H), 4.63−4.47 (m, 12H), 4.45−4.51 (m, 4H), 3.36−3.34 (m, 2H), 4.31−4.19 (m, 9H), 4.09 (dd, 1H, *J* = 5.0, 10.5 Hz, H-6), 4.04−3.98 (m, 2H, H-6, H-6), 3.96−3.90 (m, 3H, H-6, H-6, H-6), 3.86−3.79 (m, 4H), 3.68 (d, 1H, *J* = 10.0 Hz, H-6), 3.57 (OMe), 1.83 (s, 3H, OAc), 1.82 (s, 3H, OAc). HSQC (C_6D_6, 500 MHz) without ^{1}H-decoupling: $J_{H1,C1}$ = 173.0 Hz, $J_{H1,C1}$ = 171.0 Hz, $J_{H1,C1}$ = 171.0 Hz, $J_{H1,C1}$ = 172.5 Hz, $J_{H1',C1'}$ = 170.5 Hz. ^{13}C NMR (C_6D_6, 125 MHz) δ 169.8 (C=O), 169.7 (C=O), 166.3 (C=O), 160.4 (Ph-C), 139.6 (Ph-C), 139.4 (Ph-C), 139.3 (Ph-C), 139.2 (Ph-C), 139.12 (Ph-C), 139.07 (Ph-C), 139.05 (Ph-C), 139.0 (Ph-C), 138.92 (Ph-C), 138.89 (Ph-C), 138.87 (Ph-C), 138.8 (Ph-C), 138.6 (Ph-C), 132.1 (Ph-CH), 128.81 (Ph-CH), 128.77 (Ph-CH), 128.7 (Ph-CH), 128.60 (Ph-CH), 128.58 (Ph-CH), 128.55 (Ph-CH), 128.53 (Ph-CH), 128.50 (Ph-CH), 128.48 (Ph-CH), 128.44 (Ph-CH), 128.42 (Ph-CH), 128.38 (Ph-CH), 128.36 (Ph-CH), 128.3 (Ph-CH), $PhCH_2$, 128.2 (Ph-CH), 128.01 (Ph-CH), 127.94 (Ph-CH), 127.9 (Ph-CH), 127.8 (Ph-CH), 127.70 (Ph-CH), 127.67 (Ph-CH), 127.64 (Ph-CH), 127.61 (Ph-CH), 127.56 (Ph-CH), 127.5 (Ph-CH), 127.4 (Ph-CH), 124.9 (Ph-CH), 116.6 (Ph-CH), 102.2 (C-1), 100.7 (C-1), 99.3 (C-1), 95.7 (C-1), 80.2 (C-3), 79.9 (C-3), 78.8 (C-3), 78.8 (C-3), 78.4 (C-3), 77.0, 76.4, 75.6, 75.42, 75.36, 75.24, 75.17, 75.1, 73.7, 73.5, 73.4, 73.1, 72.8, 72.71, 72.66, 72.6, 72.4, 71.9, 71.8, 70.5, 69.9 (C-6), 69.6 (C-6), 69.5 (C-6), 69.30 (C-6), 69.28 (C-6), 66.8 (C-6), 51.5 (OMe), 30.2 (OAc), 20.6 (OAc). MALDI-HRMS *m/z* $[M + Na]^+$ calcd for $C_{140}H_{146}NaO_{30}$ 2329.9796, found 2329.9753.

Preparation of *p*-Methoxycarbonylphenyl (D-Mannopyranosyl-α-(1→2)-D-mannopyranosyl-α-(1→3))-(D-mannopyranosyl-α-(1→2)-D-mannopyranosyl-α-(1→6))-α-D-mannopyranoside (23). Benzylated pentasaccharide (**22**, 175 mg, 0.08 mmol) was dissolved in 10% HOAc/EtOH (10 mL). To the solution was added 10% Pd/C dry (112 mg). The mixture was degassed under vacuum to −10 in Hg and repressurized to 60 psi of H_2 (g). This routine was repeated twice more and the mixture was shaken overnight at 60 psi of H_2 (g). The heterogeneous mixture was filtered over a pad of Celite and the solid mass was washed with copious amounts of MeOH. The mother liquor was concentrated, redissolved in H_2O, and lyophilized to yield a yellowish-white foamy solid. The debenzylated pentasaccharide was redissolved in MeOH (50 mL) and treated with 5 mL of 30 wt % NaOMe/MeOH for 1 day. Following concentration of the mother liquor in vacuo, the mass was redissolved in H_2O and passed through a C8 plug. The concentrated fully deprotected pentasaccharide was purified with HPLC under conditions reported for **21**. After concentration of fractions 22 and 23, **23** was isolated in 86% yield (66 mg) over 2 steps. $[\alpha]^{25}_D$ +37 (*c* 0.8, $CHCl_3$). ^{1}H NMR (D_2O, 500 MHz) δ 7.88 (d, 2H, *J* = 8.5 Hz, PhH), 7.09 (d, 2H, *J* = 8.5 Hz, PhH), 5.59 (s, 1H, H-1′), 5.35 (s, 1H, H-1), 4.96 (s, 1H, H-1), 4.88 (s, 1H, H-1), 4.65 (s, 1H, H-1), 4.23 (s, 1H, H-2′), 4.03 (s, 2H, *J* = 9.5 Hz, H-3′, H-2), 3.98 (s, 1H, H-2‴^{3}), 3.92 (d, 1 H, *J* = 9.5 Hz, H-3), 3.89 (s, 1H, H-2), 3.85−3.45 (m, 24H). HSQC (D_2O, 500 MHz) without ^{1}H-decoupling: $J_{H1,C1}$ = 171.5 Hz, $J_{H1,C1}$ = 170.0 Hz, $J_{H1,C1}$ = 172.0 Hz, $J_{H1,C1}$ = 171.0 Hz, $J_{H1,C1}$ = 174.5 Hz. ^{13}C NMR (D_2O, 125 MHz) δ 169.2 (C=O), 159.5 (Ph-C), 131.9 (Ph-CH, Ph-CH), 124.0 (Ph-C), 116.7 (Ph-CH, Ph-CH), 102.6 (C-1), 102.5 (C-1), 101.1 (C-1), 98.0 (C-1), 97.5 (C-1), 79.0 (C-3), 78.8 (C-3), 78.7 (C-3), 73.7, 73.6, 73.4, 73.04, 73.01, 72.7, 72.2, 71.0, 70.7, 70.59, 70.55, 70.44, 70.37, 70.3, 70.24, 70.20, 69.6, 67.30, 67.27, 67.2, 67.14, 67.10, 67.02, 66.98, 66.1, 66.0, 61.44 (C-6), 61.39 (C-6), 61.36 (C-6), 61.30 (C-6), 61.25 (C-6), 52.8 (OMe). MALDI-HRMS *m/z* $[M + Na]^+$ calcd for $C_{38}H_{58}NaO_{28}$ 985.3012, found 985.3038.

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Supporting Information Available: General experimental details, experimental data for **7** and **8**, and ^{1}H NMR and ^{13}C NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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