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Efficient Synthesis of Man₂, Man₃ and Man₅ Oligosaccharides Using Mannosyl Iodide Donors¹

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Abstract

A highly efficient protocol for making Man $_3$ and Man $_5$ oligosaccharides using 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 $-40\,^{\circ}$ 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

HIV-1 envelope is highly glycosylated with N-linked high-mannose oligosaccharides that play critical roles in the pathology of the disease. For example, mannose undecasaccharide 1 (Man₉) and decasaccharide 2 (Man₈) are primary targets for cyanovirin-N (CVN), which is a multivalent anti-HIV lectin isolated from cyanobacterium *Nostoc ellipsosporum*. ³,4,5,6 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. 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. To probe this hypothesis, we have targeted the synthesis of highmannose oligosaccharides. Here we disclose a highly efficient synthesis of Man₅ corresponding to the C-6 branch of Man₉ (Figure 1).

We have recently demonstrated that mannosyl iodides efficiently undergo alpha glycosidation under in situ anomerization conditions. ⁹ The reaction is essentially quantitative, but purification is impeded by the formation of a glycal byproduct that co-elutes 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

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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 orthoester 4 (Scheme 1). HOAc mediated hydrolysis of the orthoester quickly afforded 2- O -acetyl-3,4,6-tri- O -benzyl- D -mannose 5. 11 After acetylation, the 1,2-diacetate 612 was used as a glycosyl donor via Lewis acid assisted O -arylation to provide the O -aryl mannopyranoside 7 in 92% isolated yield. Quantitative C-2 deacetylation of 7 using 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 $\bf 9$ at -40 °C and subsequent addition of acceptor $\bf 8$ provided the α - $(1\rightarrow 2)$ -linked disaccharide $\bf 10a$ (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 orthoester $\bf 10b$ was also observed (a separable 3:1 mixture). This did not prove problematic as BF₃·Et₂O mediated rearrangement 13 of $\bf 10b$ to $\bf 10a$ proceeded quantitatively upon warming to 0 °C. C-2' deacetylation gave $\bf 11$ and catalytic hydrogenation at an elevated pressure supplied p-methoxycarbonylphenyl $_{\rm D}$ -mannopyranosyl- α -($1\rightarrow 2$)- α - $_{\rm D}$ -mannopyranoside $\bf 12$. These preliminary studies demonstrated that AgOTf mediated glycosidations using $\bf 9$ were identical to analogous reactions utilizing glycosyl chloride donors with respect to yields. 14 However, the advantage of glycosyl iodides was clear as reaction times were significantly reduced, from >16 h 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-Dmannopyranoside afforded di-benzylidene mannose 13 as a mixture of isomers that could be separated by crystallization. Numerous methods exist to regioselectively open the acetal giving orthogonally 4-*O*-benzyl 16,17,18,19,20 or 6-*O*-benzyl 20,21,22,23 sugars. When reacted with borane tetrahydrofuran complex in the presence dibutylborotriflate 13-exo quantitatively afforded methyl 3,4-di-O-benzyl-α-p-mannopyranoside 14 while 13-endo generated methyl 2,4-di-O-benzyl-α-p-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 using 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, 13exo was not discarded as it is also an important building block for numerous other natural products and oligomers. 25,26,27 This protocol essentially bypasses the need for tin reagents and proved more attractive than alternative methods employed by Ogawa and co-workers. 28, ^{29,30} 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 BF₃·Et₂O 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 BF₃•OEt₂ to effect the orthoacetate rearrangement, we simply let the reaction warm to rt from -40 °C over 3 h. After the usual work up, no orthoester formation was detected as evidenced by NMR; $J_{C1,H1}$ coupling constants revealed only α -mannosyl linkages (${}^{1}J_{H1"3, C1"3} = 172.0$ Hz, ${}^{1}J_{H1"6, C1"6} = 171.0$ Hz, ${}^{1}J_{H1",C1'} = 170.5$ Hz). In comparison to double glycosidations in 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 Man₅ (23) with similar savings in required time. In the event, action of 9 with AgOTf in the presence of acceptor 20 supplied pentasaccharide 22 (${}^{1}J_{H1, C1} = 173.0 \text{ Hz}$, ${}^{1}J_{H1, C1} = 171.0 \text{ Hz}$, ${}^{1}J_{H1, C1} = 171.0 \text{ Hz}$, ${}^{1}J_{H1, C1} = 172.5 \text{ Hz}$, ${}^{1}J_{H1, C1} = 170.5 \text{ Hz}$) 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 - $(1\rightarrow 2)$ -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 Man₂, Man₃ and Man₅ 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 orthoester 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

Synthesis of 2-O-acetyl-3,4,6-tri-O-benzyl-α-p-mannopyranosyl iodide (9)

3,4,6-Tri-O-benzylmanno-orthoester (**4**, 587 mg, 1.12 mmol) was dissolved in dry CH₂Cl₂ (12 mL) and cooled to 0 °C under an inert atmosphere. The stirring mixture was treated with TMSI (192 μ L, 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 concentrated 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 CH₂Cl₂ and used without further manipulation. 1 H-NMR (C₆D₆, 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, PhCH₂), 4.67 (m, 2H, H-3, PhCH₂), 4.62

(d, 1H, J 11.4 Hz, PhCH₂), 4.65 (d, 1H, J 12.0 Hz, PhCH₂), 4.40 (d, 1H, J 11.4 Hz, PhCH₂), 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). ¹³C-NMR (C₆D₆, 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), 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 C₂₉H₃₁O₆: 475.2121, found: 475.2123.

Preparation of p-Methoxycarbonylphenyl 2-O-acetyl-3,4,6-tri-O-benzyl- $_{\text{D}}$ -mannopyranosyl- $_{\text{C}}$ -mannopyranosyl- $_{\text{D}}$ -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 CH₂Cl₂ (3 mL) under argon, kept in the dark and cooled to -40 ° C. Glycosyl iodide (9, 1.12 mmol) was dissolved in CH₂Cl₂ (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 3h, after which Et₃N (2 mL) was added and stirred 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 sat'd aq. NaHCO₃ (2 × 75 mL) and brine. The organic layer was dried over MgSO₄ and concentrated in vacuo. The crude material was chromatographed via a flash silica gel column using 25% EtOAc/Hexanes as the eluent to provide 341 mg of **10a**, 70% yield. Data for 10a: $[\alpha]_D^{25}$: +57° (c 1.0, CHCl₃). ¹H-NMR 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, PhCH₂), 4.79 (d, 1H, J 11.0 Hz, PhCH₂), 4.68 – 4.44 (m, 8H, PhCH₂, PhCH₂, PhCH₂, PhCH₂, H-5', PhCH₂, H-4", PhCH₂), 4.42 – 4.34 (m, 4H, PhCH₂, PhCH₂, H-3', H-3'', 4.30 (d, 1H, *J* 11.0 Hz, PhCH₂), 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 ¹H-decoupling: $J_{H1, C1}$ = 175.8 Hz, $J_{\text{H1}',\text{C1}'} = 170.9$ Hz. ¹³C-NMR (C₆D₆, 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) 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 C₆₄H₆₆NaO₁₄: 1081.4350, found: 1081.4391.

Preparation of p-Methoxycarbonylphenyl 3,4,6-tri-O-benzyl- $_{D}$ -mannopyranosyl- $_{C}$ -mannopyranoside (11)

2-Acetoxy-disaccharide (**10a**, 383 mg, 0.36 mmol) was dissolved in dry MeOH (25 mL) and CH₂Cl₂ (5 mL) under argon. The solution was treated with 30% wt NaOMe/MeOH (100 μ L) 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/CH₂Cl₂ and the mother liquor was concentrated in vacuo to provide 318 mg of **11**. [α]_D²⁵: +41° (c 1.0, CHCl₃). ¹H-NMR (C₆D₆, 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, PhCH₂), 4.93 (d, 1H, J 11.4 Hz, PhCH₂), 4.80 (d, 1H, J 11.4 Hz, PhCH₂), 4.65 (d, 1H, J 11.4 Hz, PhCH₂), 4.62 – 4.52 (m, 4H, PhCH₂, PhCH₂, PhCH₂, H-5'), 4.49 – 4.46 (m, 3H, PhCH₂, PhCH₂, H-4), 4.39 (apparent d, 2H, H-2', PhCH₂), 4.36 – 4.29 (m, 4H, PhCH₂, H-3, PhCH₂, 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 ¹H-decoupling: $J_{H1, C1} = 175.8$ Hz, $J_{\text{H1'},\text{C1'}} = 169.8$. ¹³C-NMR (C₆D₆, 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) 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 C₆₂H₆₄NaO₁₃: 1039.4244, found: 1039.4248.

Preparation of p-Methoxycarbonylphenyl _□-mannopyranosyl-α-(1→2)-α-_□-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 mm Hg and repressurized to 60 psi of H₂. This routine was repeated twice more and the mixture was shaken overnight at 60 psi of H₂. 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 H₂O and passed through a C8 plug. The mother liquor was lyophilized to yield a white foamy solid 122 mg. $[\alpha]_D^{25}$: +27° (c 1.0, CHCl₃). ¹H-NMR (D₂O, 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 (D₂O, 500 MHz) without ¹H-decoupling: $J_{\text{H1,C1}} = 175.8 \text{ Hz}$, $J_{\text{H1,C1}} = 169.8$. ¹³C-NMR (D₂O, 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) 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 C₂₀H₂₈NaO₁₃: 499.1428, found: 499.1455.

Preparation of p-Methoxycarbonylphenyl 2,4-di-O-benzyl-α-p-mannopyranoside (18)

A solution of 1,3,6-tri-O-acetyl mannose 14 (17, 473 mg, 0.97 mmol) and methyl phydroxybenzoate (765 mg, 4.87 mmol) was dissolved in dry CH_2Cl_2 (10 mL) was 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 rt 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 sat'd aq. K_2CO_3 (3 × 50 mL). The organic layer was dried over MgSO₄ and concentrated in vacuo. 1H -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. [α] $_D^{25}$: +59° (c 1.0, CHCl₃). 1 H-NMR (CDCl₃, 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, PhCH₂), 4.78 (d, 1H, J 11.0 Hz, PhCH₂), 4.70 (d, 2H, J 11.0 Hz, PhCH₂, PhCH₂), 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 (CDCl₃, 500 MHz) without ¹H-decoupling: $J_{\text{H1, C1}} = 175.8 \text{ Hz}$, $J_{\text{H1', C1'}} = 169.8$. ¹³C-NMR (CDCl₃, 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 C₂₈H₃₀NaO₈: 517.1838, found: 517.1813.

Preparation of p-Methoxycarbonylphenyl (2-O-acetyl-3,4,6-tri-O-benzyl- $_{\text{D}}$ -mannopyranosyl- $_{\text{C}}(1\rightarrow 3)$)-(2-O-acetyl-3,4,6-tri-O-benzyl- $_{\text{D}}$ -mannopyranosyl- $_{\text{C}}(1\rightarrow 6)$)-2,4-di-O-benzyl- $_{\text{D}}$ -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 CH₂Cl₂ (3 mL) under argon, kept in the dark and cooled to -40 °C. Mannosyl iodide (9, 1.11 mmol) was dissolved in CH₂Cl₂ (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 rt over 3h, after which Et₃N (2 mL) was added and 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 sat'd aq. NaHCO₃ (2×50 mL) and brine. The organic layer was dried over MgSO₄ 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). $[\alpha]_D^{25}$: +31° (c 1.0, CHCl₃) ¹H-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, PhCH₂), 5.12 (d, 1H, J 11.0 Hz, PhCH₂), 5.11 (s, 1H, H-1"⁶), 5.06 (d, 1H, J 11.0 Hz, PhCH₂), 4.80 – 4.61 (m, 10H, 10 PhCH₂, H-3'), 4.53 – 4.50 (m, 5H, 4 PhCH₂, 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 (C₆D₆, 500 MHz) without ¹H-decoupling: $J_{\text{H1}"3, \text{C1}"3} = 172.0 \text{ Hz}$, $J_{\text{H1}"6, \text{C1}"6} = 171.0 \text{ Hz}$, $J_{\text{H1}', \text{C1}'} = 170.5$ Hz. ¹³C-NMR (C₆D₆, 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) 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- $_{\text{D}}$ -mannopyranosyl- $_{\text{C}}$ -(1 \rightarrow 3))- (3,4,6-tri-O-benzyl- $_{\text{D}}$ -mannopyranosyl- $_{\text{C}}$ -(1 \rightarrow 6))-2,4-di-O-benzyl- $_{\text{D}}$ -mannopyranoside (20)

The trisaccharide **19** was dissolved in dry MeOH (25 mL) and dry CH₂Cl₂ (5 mL) under argon at rt and treated with 30% wt NaOMe/MeOH (100 μ L) for 1h. 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 using 40% EtOAc/hexanes provided the trisaccharide diol 220 mg, 93% yield. [α]_D²⁵: +61° (c 1.0, CHCl₃). ¹H-NMR

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, PhCH₂), 4.98 (d, 1H, J 11.0 Hz, PhCH₂), 4.89 (d, 1H, J 11.0 Hz, PhCH₂), 4.73 (d, 2H, J 11.0 Hz, PhCH₂), PhCH₂), 4.68 (d, 1H, J 11.0 Hz, PhCH₂), 4.65 – 4.52 (m, 8H, PhCH₂, PhCH₂, PhCH₂, PhCH₂, PhCH₂, C-3', PhCH₂, PhCH₂), 4.48 – 4.43 (m, 5H, PhCH₂, PhCH₂, PhCH₂, H-2', H-4"6), 4.27 – 4.13 (m, 6H, H-4', H-2"³, H-5"⁶, H-5"³, $H-3^{\circ}{}^{3}$, $H-2^{\circ}{}^{6}$), 4.04-3.91 (m, 6H, $H-4^{\circ}{}^{3}$, $H-3^{\circ}{}^{6}$, $H-6^{\circ}{}^{6}$, $H-5^{\circ}{}^{7}$, $H-6^{\circ}{}^{3}$, $H-6^{\circ}{}^{7}$), 3.85-3.81 (m, H-6", H-6', 3.55 (s, 3H, OMe), 2.48 (br, 2H, OH, OH). HSQC (C₆D₆, 500 MHz) without ¹H-decoupling: $J_{\text{H1"3, C1"3}} = 171.5 \text{ Hz}$, $J_{\text{H1"6, C1"6}} = 170.0 \text{ Hz}$, $J_{\text{H1', C1'}} = 171.0$ Hz. 13 C-NMR ($^{C}_{6}$ D₆, 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) 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 $(C-2^{\circ}), 66.0 (C-6^{\circ}), 51.5 (OMe)$. MALDI-HRMS $m/z [M+Na]^+$ calcd for $C_{82}H_{86}NaO_{18}$: 1381.5712, found: 1381.5735.

Preparation of p-Methoxycarbonylphenyl (p-mannopyranosyl- α -(1 \rightarrow 3))-(p-mannopyranosyl- α -(1 \rightarrow 6))- α -p-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 H₂. 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 H₂O and passed through a C8 plug. The mother liquor was lyophilized to yield a white foamy solid. HPLC purification was performed using a C18 Vydac prep column at a flow rate of 5 ml/min with a linear gradient from 100% H₂O to 100% over 60 min. Fully deprotected trisaccharide 21 was provided in 82% isolated yield (37 mg) after lyophilization. [α]_D²⁵: +48° (c 1.0, CHCl₃). ¹H-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 ¹H chemical shifts from HSQC $(D_2O, 500 \text{ MHz})$ 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 (D₂O, 500 MHz) without ¹H-decoupling: $J_{\text{H1"3, C1"3}} = 172.0 \text{ Hz}$, $J_{\text{H1"6, C1"6}} = 171.0 \text{ Hz}$, $J_{\text{H1', C1'}} = 174.5$ Hz. ¹³C-NMR (D₂O, 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 C₂₆H₃₈NaO₁₈: 661.1956, found: 661.1954.

Preparation of p-Methoxycarbonylphenyl (2-O-acetyl-3,4,6-tri-O-benzyl- $_{\text{D}}$ -mannopyranosyl- $_{\text{C}}$ (1 \rightarrow 2)-3,4,6-tri-O-benzyl- $_{\text{D}}$ -mannopyranosyl- $_{\text{C}}$ (1 \rightarrow 3))-(2-O-acetyl-3,4,6-tri-O-benzyl- $_{\text{D}}$ -

mannopyranosyl- α -(1 \rightarrow 2)-3,4,6-tri-O-benzyl- $_{\text{D}}$ -mannopyranosyl- α -(1 \rightarrow 6))-2,4-di-O-benzyl- α -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 CH₂Cl₂ (2 mL) under argon, kept in the dark and cooled to -40 °C. Mannosyl iodide (9, 0.42 mmol) was dissolved in CH₂Cl₂ (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 rt over 7h, after which TLC (40% EtOAc/hexanes) analyses revealed a major spot ($R_f = 0.40$). After stirring with Et₃N (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 sat'd aq. NaHCO₃ (2 × 25 mL) and brine. The organic layer was dried over MgSO₄ and concentrated in vacuo. The crude material was chromatographed via a flash silica gel column using 25% EtOAc/Hexanes as the eluent to provide 175 mg (91% yield) of pentasaccharide 22. [α]_D²⁵: +29° (c 0.8, CHCl₃). ¹H-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, PhCH₂), 5.14 (d, 1H, J 11.0 Hz, PhCH₂), 5.11 (d, 1H, J 11.0 Hz, PhCH₂), 5.10 (d, 1H, J 11.0 Hz, PhCH₂), 5.09 (d, 1H, J 11.0 Hz, PhCH₂), 5.02 (d, 1H, J 11.0 Hz, PhCH₂), 4.84 (d, 1H, J 11.0 Hz, PhCH₂), 4.80 – 4.73 (m, 4H, PhCH₂, PhCH₂, PhCH₂, $PhCH_2$, 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 Hz, 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 (C₆D₆, 500 MHz) without ¹H-decoupling: $J_{\text{H1, C1}} = 173.0 \text{ Hz}, J_{\text{H1, C1}} = 171.0 \text{ Hz}, J_{\text{H1, C1}} = 171.0 \text{ Hz}, J_{\text{H1, C1}} = 172.5 \text{ Hz}, J_{\text{H1', C1'}} = 172.5 \text{ Hz}$ 170.5 Hz. 13 C-NMR (C 6D₆, 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) 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), PhCH₂, 128.2 (Ph-CH), 128.01 (Ph-CH), 127.94 (Ph-CH), 127.9 (Ph-CH), 127.8 (Ph-CH), 127.70 (Ph-CH) 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 C₁₄₀H₁₄₆NaO₃₀: 2329.9796, found: 2329.9753.

Preparation of p-Methoxycarbonylphenyl ($_{D}$ -mannopyranosyl- α -(1 \rightarrow 2)- $_{D}$ -mannopyranosyl- α -(1 \rightarrow 3))-($_{D}$ -mannopyranosyl- α -(1 \rightarrow 2)- $_{D}$ -mannopyranosyl- α -(1 \rightarrow 6))- α - $_{D}$ -mannopyranosyl- α -(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 H₂ (g). This routine was repeated twice more and the mixture was shaken overnight at 60 psi of H₂ (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 H₂O, 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 H₂O and passed through a C8 plug. The concentrated fully deprotected pentasaccharide was purified using HPLC under conditions reported for **21**. After concentration of fractions 22 and 23, **23** was isolated in 86% yield (66

mg) over 2 steps. [α]_D²⁵: +37° (c 0.8, CHCl₃). ¹H-NMR (D₂O, 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, , 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 (D₂O, 500 MHz) without ¹H-decoupling: $J_{\rm HI, C1}$ = 171.5 Hz, $J_{\rm HI, C1}$ = 170.0 Hz, $J_{\rm HI, C1}$ = 172.0 Hz, $J_{\rm HI, C1}$ = 174.5 Hz. ¹³C-NMR (D₂O, 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 C₃₈H₅₈NaO₂₈: 985.3012, found: 985.3038.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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

Figure 2. Retrosynthesis of Man₃ and Man₅ methyl paraben glycoconjugates.

Scheme 1. Synthesis of *p*-methoxycarbonylphenyl mannopyranoside

Scheme 2. Synthesis of Man₂ (12).

Scheme 3. Synthesis of 3,6-diol core acceptor **18**.

Scheme 4. Syntheses of Man₃ (**21**) via double glycosidation.

Scheme 5. Synthesis of Man₅ (**23**) via double glycosidation