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# Synthesis of Oligosaccharide Fragments of Mannosylated Lipoarabinomannan from *Mycobacterium tuberculosis*

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Abstract. The synthesis of three mannosyl-arabinosides 4-6 found as terminal epitopes of mannosylated lipoarabinomannan (ManLAM) from *Mycobacterium tuberculosis* is reported. A key step in the synthesis of the required protected octyl  $\beta$ -D-arabinofuranoside derivative 7 involved glycosylation of octanol by 5-O-acetyl-2,3-di-O-benzyl- $\alpha$ -D-arabinofuranosyl chloride (12) in the absence of a promoter. The sequential addition of the mannopyranose residues to 7, using thioglycosides 8 and 9, provided the protected oligosaccharides 17, 19, and 21. Deprotection by deacylation and then hydrogenation afforded the targets. © 1999 Elsevier Science Ltd. All rights reserved.

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## Introduction

*Mycobacterium tuberculosis*, the causative agent of tuberculosis, claims nearly three million lives each year and a third of the world's population has been estimated to be infected by this pathogen.<sup>1,2</sup> Mycobacterial infections, including those leading to tuberculosis, have recently attracted renewed attention. This is due not only to their increasing incidence in both the industrialized and developing world,<sup>3</sup> but also to the emergence of strains of these organisms resistant to commonly used anti-mycobacterial drugs.<sup>4</sup> Historically, the treatment of these diseases has been difficult, requiring strict adherence to a regimen of three or more antibiotics that must be taken for several months.<sup>5</sup> Such treatments are required because the cell wall of this organism provides a formidable barrier to the passage of antibiotics into the organism.<sup>6</sup>

All mycobacteria possess a protective cell wall complex composed of polysaccharides, proteins, and lipids.<sup>7</sup> The major structural component of this cell wall is an arabinogalactan which is covalently bound to mycolic acids, lipids characteristic to mycobacteria. Interspersed throughout this glycolipid framework is another polysaccharide, lipoarabinomannan (LAM), the major antigenic component of the cell wall. LAM has been implicated in many immunomodulatory events occurring during progression of tuberculosis, including the inhibition of macrophage activation,<sup>8</sup> the induction of cytokines,<sup>9-11</sup> the neutralization of potentially cytotoxic oxygen free radicals,<sup>12</sup> the inhibition of protein kinase activities,<sup>13</sup> and inducing the expression of collegenases that destroy the extracellular matrix of the lung.<sup>14</sup>

The structure of LAM includes a phosphatidyl inositol moiety which is believed to be noncovalently associated with the plasma membrane of the organism through its lipid portion.<sup>15,16</sup> To this inositol residue is attached a polysaccharide composed of mannopyranose and arabinofuranose, the terminal ends of which are capped with the arabinofuranosyl hexasaccharide 1. Although in many mycobacterial strains this motif is found

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unsubstituted, in others 1 is further substituted with short mannopyranosyl oligosaccharides to provide a polymer known as ManLAM  $2.^{7,15,16}$ 

The terminal mannopyranosyl residues of ManLAM have been suggested to be involved in the initial stages of infection by adhering to human cells through their interaction with mannose binding proteins.<sup>17,18</sup> Consequently, drugs that act by inhibiting the enzymes that assemble these oligosaccharides are of possible use in the prevention and treatment of mycobacterial disease. The design of such inhibitors would be greatly facilitated by the isolation and characterization of these mannosyltransferases. This goal is in turn dependent upon the ready availability of potential oligosaccharide substrates which can be used for purification of these enzymes and in the development of assays for their activities. Although biosynthetic





studies of LAM have been carried out,<sup>16</sup> the assembly of the mannose caps has not been investigated. We describe here the first syntheses of a series of glycan fragments of ManLAM (3-6, Figure 2), which are potential substrates for the mannosyltransferases involved in its biosynthesis.



Figure 2. Synthetic Targets, R = (CH<sub>2</sub>)<sub>7</sub>CH<sub>3</sub>

## **Results and Discussion**

We envisioned that oligosaccharides 4-6 could be prepared straightforwardly from monosaccharide building blocks 7, 8, and 9, through a route involving the sequential addition of mannose residues to arabinofuranosyl-containing acceptors. Thioglycosides were chosen as the glycosyl donors due to their hydrolytic stability as well as the number of methods available for their activation.<sup>19</sup> We chose to prepare octyl glycosides because this hydrophobic group simplifies glycosyltransferase assays by allowing the use of reverse phase (C<sub>18</sub>) cartridges to separate and quantitate reaction products.<sup>20</sup> A critical issue to be addressed early in the synthetic sequence was the formation of the 1,2-*cis*-glycosidic bond on the arabinofuranose residue. This linkage is directly analogous to that of a  $\beta$ -mannopyranoside, which is notoriously difficult to prepare.<sup>21</sup>



Figure 3. Monosaccharide Building Blocks

Synthesis of monosaccharides. Thioglycosides  $8^{22}$  and  $9^{23}$  are known and were readily prepared from Dmannose as previously described. In contrast, there is considerably less precedence for the synthesis of 7. Relatively little work has been done on the synthesis of furanosidic oligosaccharides and, since Fletcher and Glaudemans reported the preparation of methyl  $\beta$ -D-arabinofuranoside over 30 years ago,<sup>24</sup> the stereoselective synthesis of linkages of this type has not been investigated. An intermolecular aglycone delivery route for the stereoselective synthesis of  $\beta$ -D-fructofuranosides has been recently reported<sup>25</sup> and, given the close structural similarities between these glycosides and 7, a similar approach is likely to succeed. However, the simplicity of the approach reported by Fletcher<sup>24</sup> prompted us to investigate this approach first as illustrated in Figure 4.

Commercially available 2,3,5-tri-O-benzyl-D-arabinofuranose (10) was treated under acetolysis conditions which resulted in the simultaneous cleavage of the O-5 benzyl ether and acetylation of the anomeric hydroxyl group. The product, 11, was obtained in 86% yield. Reaction of this diacetate with HCl in dichloroethane provided the labile chloride 12 which was not isolated. Instead, immediately after its formation, 12 was reacted with octanol in the absence of a promoter to give the  $\beta$ -glycoside 13. The product was contaminated with traces of the  $\alpha$ -isomer. However, separation could easily be achieved by first removing the acetyl group and then chromatography. The conversion of 11 to 7 proceeded in 35% overall yield. Despite this modest yield, the speed and ease with which 7 can be prepared by this route makes it a viable alternative to more elaborate methods (*e.g.*, the previously mentioned intramolecular aglycone delivery route<sup>25</sup>) that would possibly give the higher yields in the glycosylation step. Chloride 15, which was prepared in 2 steps from 10, was reacted with octanol in a manner identical to 12 to provide a 58% yield of the glycoside 16. In this case, the formation of the  $\alpha$ -anomer was not detected.<sup>26</sup> Hydrogenation of 16 gave arabinofuranoside 3 in 82% yield.



Figure 4. (a) Ac<sub>2</sub>O, H<sub>2</sub>SO<sub>4</sub>, 86%; (b) HCl, ClCH<sub>2</sub>CH<sub>2</sub>Cl; (c) CH<sub>3</sub>(CH<sub>2</sub>)<sub>7</sub>OH, CH<sub>2</sub>Cl<sub>2</sub>; (d) NaOCH<sub>3</sub>, CH<sub>3</sub>OH, 3 steps, 35%; (e) Ac<sub>2</sub>O, pyridine, reflux, 100%; (f) HCl, ClCH<sub>2</sub>CH<sub>2</sub>Cl; (g) CH<sub>3</sub>(CH<sub>2</sub>)<sub>7</sub>OH, CH<sub>2</sub>Cl<sub>2</sub>, 2 steps, 58%; (h) Pd/C, H<sub>2</sub>, CH<sub>3</sub>OH, 82%.

Determining the stereochemical outcome of these glycosylation reactions could be easily done by standard one-dimensional <sup>13</sup>C and <sup>1</sup>H NMR experiments.<sup>27</sup> The anomeric carbon of  $\alpha$ -D-arabinofuranosides resonate in the range of 107–110 ppm whereas the  $\beta$ -anomers appear between 97 and 104 ppm. Furthermore, <sup>3</sup>J<sub>H1,H2</sub> is small (0–2 Hz) for the  $\alpha$ -anomers and larger (3–5 Hz) for the  $\beta$ -anomers. It should also be mentioned that although <sup>1</sup>J<sub>C1,H1</sub> values are unambiguous determinants of anomeric stereochemistry in mannopyranosides,<sup>28</sup> they cannot be used here to make these assignments. In arabinofuranosides the magnitudes of these couplings have been shown to be insensitive to anomeric configuration.<sup>27</sup>

It is tempting to speculate that the formation of  $\beta$ -glycosides from 12 and 15 proceeds through a direct  $S_N^2$  displacement reaction. However, the methanolysis of 2-benzylated arabinofuranosyl chlorides has been previously studied<sup>24,29</sup> and it was shown that these reactions proceed through an ion-pair  $S_N^1$  mechanism. It should be noted that although the unpromoted glycosylation of these furanosyl halides proceeds efficiently with simple primary alcohols, attempts to react 15 with secondary carbohydrate alcohols produced no glycosides, only the hydrolysis product, 10.<sup>30</sup> Therefore, while this method is useful for the preparation of simple glycosides it appears to be of limited utility in oligosaccharide synthesis. Furthermore, it should also be mentioned that earlier work on the glycosylation of 12 in the presence of a promoter (Ag<sub>2</sub>O, AgCO<sub>3</sub>) results in the formation of the  $\alpha$ -glycoside.<sup>31</sup> This suggests that in the presence of a promoter, a naked carbocation forms and that the attack of the alcohol proceeds through the less sterically hindered face of the ring.

Synthesis of oligosaccharides. With the building blocks 7-9 in hand, the assembly of the oligosaccharides proceeded without serious difficulty. However, careful control of the temperature during the glycosylations was required in order to obtain good stereoselectivities. Despite the presence of a participating protecting group at C-2 in the donor, initiating the glycosylations at 0 °C or -10 °C resulted in the formation of significant amounts of the undesired  $\beta$ -anomers. For example, in the case of glycosylation of 7 with 9 to give 17 (Figure 5), at 0 °C a 3:2  $\alpha$ : $\beta$  ratio was obtained. When the same reaction was carried out at -10 °C the  $\alpha$ : $\beta$  ratio was 3:1.<sup>32</sup> In addition to lowering the overall yield, the formation of the  $\beta$ -glycosides greatly complicated purification as the two glycosides had very similar chromatographic mobilities in all solvent systems investigated. Best results were obtained by starting the reaction at -40 °C and allowing it to react as it warmed to 0 °C. Under these conditions, only trace amounts of the  $\beta$ -mannoside were formed, which could be separated from the desired compound by chromatography to give the product which was pure by <sup>1</sup>H NMR spectroscopy.



Figure 5. (a) 9, NIS, AgOTf, CH<sub>2</sub>Cl<sub>2</sub>, -40 ℃ → rt, 82%; (b) NaOCH<sub>3</sub>, CH<sub>3</sub>OH, 95%; (c) 9, NIS, AgOTf, CH<sub>2</sub>Cl<sub>2</sub>, -40 ℃ → rt, 87%; (d) NaOCH<sub>3</sub>, CH<sub>3</sub>OH, 96%; (e) Pd/C, H<sub>2</sub>, CH<sub>3</sub>OH, 90%; (f) Pd/C, H<sub>2</sub>, CH<sub>3</sub>OH, 93%.

The syntheses of disaccharide 4 and trisaccharide 5 are illustrated in Figure 5. Reaction of alcohol 7 with thioglycoside 9 promoted by *N*-iodosuccinimide and silver triflate afforded the protected disaccharide 17 in 82% yield. Deacetylation proceeded in 95% yield to give alcohol 18. A portion of this product was completely deprotected by hydrogenation providing 4 in 90% yield. The remainder of 18 was glycosylated, again with 9 under the same reaction conditions used for the synthesis of the disaccharide, to afford trisaccharide 19 in 87% yield. Treatment with sodium methoxide afforded a 96% yield of alcohol 20 which could then be converted, upon hydrogenation, to 5 (93%). Tetrasaccharide 6 was synthesized as shown in Figure 6. Its preparation involved first the reaction of trisaccharide 20 with the fully acylated mannose thioglycoside 8 to give 21 in 76% yield. Treatment with sodium methoxide followed by hydrogenation afforded 6 in 78% yield. Compouds 3-6 were all shown to be pure by 800 MHz <sup>1</sup>H NMR spectroscopy.



Figure 6. (a) 8, NIS, AgOTf, -40 °C → rt, 76%; (b) NaOCH<sub>3</sub>, CH<sub>3</sub>OH; (c) Pd/C, H<sub>2</sub>, CH<sub>3</sub>OH; 78%, two steps.

In conclusion, we have carried out the first syntheses of a series of mannosyl-arabinosides found as constituent parts of ManLAM from M. tuberculosis. The availability of these glycans will be important in elucidating the pathways by which this polysaccharide is assembled by the organism. The results of these biosynthetic investigations will be reported in due course.

#### Experimental

Optical rotations were measured at 22 ± 2 °C. Analytical TLC was perform ed on silica gel 60- $F_{254}$  (0.25 mm, Merck). Spots were detected under UV light or by charring with 10% H<sub>2</sub>SO<sub>4</sub> in ethanol. Unless otherwise indicated, all reactions were carried out at room temperature and under positive pressure of argon. Solvents were evaporated under reduced pressure and below 40 °C. Column chromatography was performed on silica gel or Iatrobeads. The ratio between silica gel and compound ranged from 100 to 50:1 (w/w). <sup>1</sup>H NMR spectra were recorded at 250 or 300 or 500 MHz, and first order proton chemical shifts  $\delta_{\rm H}$  are referenced to either to TMS ( $\delta_{\rm H}$  0.0, CDCl<sub>3</sub>) or HOD ( $\delta_{\rm H}$  4.78, D<sub>2</sub>O). <sup>13</sup>C NMR spectra were recorded at 75 or 125 MHz and <sup>13</sup>C chemical shifts  $\delta_{\rm C}$  are referenced to either to TMS ( $\delta_{\rm C}$  0.0, CDCl<sub>3</sub>) or dioxane ( $\delta_{\rm C}$  67.4, D<sub>2</sub>O). The assignment of resonances in **3–6** were made by two-dimensional homonuclear and heteronuclear shift correlation experiments. One-bond

carbon-hydrogen coupling constants involving the anomeric carbon of the mannose residues in 4–6 were measured to prove glycoside stereochemistry.<sup>28</sup> Elemental analyses were performed by Atlantic Microlab Inc., GA and the samples submitted for analyses were dried overnight under vacuum with phosphorus pentoxide at 56 °C (refluxing acetone). Fast atom bombardment mass spectra were recorded on samples suspended in thioglyceride matrix with a cesium gun. MALDI mass spectra were recorded on samples in an  $\alpha$ -cyano-4-hydroxycinnamic acid matrix.

*1,5-Di-O-acetyl-2,3-di-O-benzyl-D-arabinofuranose* (11). To a solution of 10<sup>33</sup> (2.5 g, 5.95 mmol) in acetic anhydride (15 mL) was added a solution containing 6 drops of conc. H<sub>2</sub>SO<sub>4</sub> in acetic anhydride (5 mL). The reaction was stirred for 2 h, and was then poured into ice (100 g) and stirred for 2 h, before being extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 30 mL). The organic layer was washed with water (30 mL) followed by a saturated NaHCO<sub>3</sub> solution (2 x 30 mL) and water (30 mL). The organic extract was dried (Na<sub>2</sub>SO<sub>4</sub>), filtered and concentrated to a light yellow syrup, which was purified by chromatography (4:1 toluene:EtOAc) to give 11 (2.1 g, 86%) as a colorless syrup in a 9:1 α:β ratio of anomers. R<sub>f</sub> 0.27 (4:1 toluene:EtOAc); [α]<sub>D</sub> -21.6° (*c* 0.8, CHCl<sub>3</sub>); <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>)  $\delta_{\rm H}$  7.25–7.40 (m, Ph), 6.30 (d,  $J_{1,2}$  = 4.2 Hz, H-1β), 6.23 (br. s, H-1α), 6.67 (d, J = 11.8 Hz, CH<sub>2</sub>Ph) 4.50–4.69 (m, CH<sub>2</sub>Ph), 4.37 (ddd,  $J_{4,5a}$  = 3.8,  $J_{3,4}$  = 5.8,  $J_{4,5b}$  = 6.0 Hz, H-4α), 4.27 (dd,  $J_{4,5a}$  = 3.8,  $J_{5a,5b}$  = 11.9 Hz, H-5aα), 4.13 (dd,  $J_{4,5b}$  = 6.0,  $J_{5a,5b}$  = 11.9 Hz, H-5bα), 4.08 (d,  $J_{2,3}$  = 2.3 Hz, H-2α), 3.89 (dd,  $J_{2,3}$  = 2.3,  $J_{3,4}$  = 5.8 Hz, H-3α), 2.08 (s, α-OCOCH<sub>3</sub>), 2.06 (s, β-OCOCH<sub>3</sub>), 2.04 (s, β-OCOCH<sub>3</sub>), 2.01 (s, α-OCOCH<sub>3</sub>); <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>)  $\delta_{\rm C}$  170.7, 169.9 (C=O), 137.7, 137.3, 137.1, 128.6, 128.2, 128.1, 128.0, 128.0 (Ph), 100.5 (C-1α), 94.5 (C-1β), 86.8, 84.1, 83.6, 81.8, 81.2, 72.7, 72.3, 72.2, 65.2, 63.7 (ring and benzylic C), 21.3, 21.2, 20.8 (OCOCH<sub>3</sub>). Anal. Calcd for C<sub>23</sub>H<sub>28</sub>O<sub>8</sub> (414.22): C, 66.64; H, 6.30.

Octyl 2,3-di-O-benzyl- $\beta$ -D-arabinofuranoside (7). HCl gas was bubbled through a solution of 11 (1.4 g, 3.38 mmol) in dry dichloroethane (10 mL) for 30 min. The reaction mixture was stirred for an additional 10 min and the solvent was concentrated to provide 5-O-acetyl-2,3-di-O-benzyl- $\alpha$ -D-arabinofuranosyl chloride 12 as a light yellow syrup. Without further purification, the crude product was dissolved in dry CH<sub>2</sub>Cl<sub>2</sub> (20 mL) and octanol (0.37 mL, 2.35 mmol) was added. After stirring for 90 min, the reaction mixture was diluted with CH<sub>2</sub>Cl<sub>2</sub> (40 mL) and then washed with water (30 mL) followed by a saturated NaHCO<sub>3</sub> solution (2 x 30 mL) and water (25 mL). The organic layer was dried ( $Na_2SO_4$ ), filtered and concentrated to give crude 13 as light yellow syrup. The product was dissolved in methanol (15 mL) and a few drops of 0.1 M NaOCH<sub>3</sub> was added and the reaction was stirred for 4 h. The reaction mixture was concentrated and the unreacted octanol was removed by azeotropic distillation with water (3 x 40 mL). The light yellow oil obtained was purified by chromatography (85:15 hexane: EtOAc) to obtain 7 (0.5 g, 35%) as a colorless oil. R<sub>f</sub> 0.31 (4:1 hexane:EtOAc);  $[\alpha]_{D}$  +14.5° (*c* 0.8, CHCl<sub>3</sub>); <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>)  $\delta_{H}$  7.25–7.39 (m, 15 H, Ph), 4.85 (d, 1 H,  $J_{1,2}$ = 4.4 Hz, H-1), 4.73 (d, 1 H, J = 11.7 Hz,  $CH_2Ph$ ), 4.60 (s, 2 H,  $CH_2Ph$ ), 4.58 (d, 1 H, J = 10.7 Hz,  $CH_2Ph$ ), 4.31 (dd, 1 H,  $J_{2,3} = 5.8$ ,  $J_{3,4} = 7.0$  Hz, H-3), 4.00-4.10 (m, 2 H, H-2, H-4), 3.50-3.80 (m, 3 H, H-5a, H-5a, H-5a) (m, 2 H, H-5a) 5b, octyl OCH<sub>2</sub>), 3.39 (dt, 1 H, J = 6.8, 9.6 Hz, octyl OCH<sub>2</sub>), 2.37 (dd, 1 H,  $J_{5a,5-OH} = 4.2$ ,  $J_{5b,5-OH} = 7.7$  Hz, 5-OH), 1.58–1.65 (m, 2 H, octyl CH<sub>2</sub>), 1.23–1.29 (m, 10 H, octyl CH<sub>2</sub>), 0.87 (t, 3 H, J = 6.1 Hz, octyl CH<sub>3</sub>); <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>) δ<sub>c</sub> 138.1, 137.7, 128.4, 128.1, 128.0, 127.8, 127.7 (Ph), 100.8 (C-1), 84.5, 82.2, 81.2, 72.5, 72.4, 69.2, 63.8 (ring and benzylic C, octyl OCH<sub>2</sub>), 31.8, 29.6, 29.5, 29.4, 26.1, 22.6 (octyl CH<sub>2</sub>), 14.1 (octyl CH<sub>3</sub>). Anal. Calcd for  $C_{27}H_{38}O_5$  (414.22): C, 73.27; H, 8.65. Found: C, 73.37; H, 8.59.

1-O-Acetyl-2,3,5-tri-O-benzyl-D-arabinofuranose (14). This compound was prepared as previously described.<sup>34</sup>

Octyl 2,3,5-tri-O-benzyl- $\beta$ -D-arabinofuranoside (16). HCl gas was bubbled through a solution of 14 (850 mg, 1.87 mmol) in dry dichloroethane (10 mL) for 30 min. After stirring for an additional 10 min the reaction mixture was concentrated to provide 2,3,5-tri-O-benzyl-α-D-arabinofuranosyl chloride 15 as a light yellow syrup. Without further purification, the crude product was dissolved in dry CH<sub>2</sub>Cl<sub>2</sub> (15 mL) and octanol (0.35 mL, 2.24 mmol) was added. The reaction mixture was stirred for 60 min and then diluted with CH<sub>2</sub>Cl<sub>2</sub> (40 mL), before being washed with water (30 mL), a saturated NaHCO<sub>3</sub> solution (2 x 30 mL) and water (25 mL). The organic layer was dried  $(Na_2SO_4)$ , filtered, and concentrated under vacuum to a light yellow syrup, which was purified by column chromatography (9:1 hexane:EtOAc) to give 16 (440 mg, 58%) as a colorless syrup.  $R_c$ 0.66 (4:1 hexane:EtOAc);  $[\alpha]_{D}$  -49.6° (c 1.4, CHCl<sub>3</sub>); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta_{H}$  7.26–7.40 (m, 15 H, Ph), 4.90 (d, 1 H,  $J_{1,2}$  = 4.0 Hz, H-1), 4.70 (d, 1 H, J = 11.7 Hz,  $CH_2Ph$ ), 4.60–4.66 (m, 3 H,  $CH_2Ph$ ), 4.70 (s, 2 H, CH, Ph), 4.05-4.22 (m, 3 H, H-2, H-3, H-4), 3.68 (dt, 1 H,  $J \approx 6.8$ , 9.2 Hz, octyl OCH<sub>2</sub>), 3.50-3.58(m, 2 H, H-5a, H-5b), 3.34 (dt, 1 H, J = 6.8, 9.2 Hz, octyl OCH<sub>2</sub>), 1.55–1.62 (m, 2 H, octyl CH<sub>2</sub>), 1.29– 1.35 (m, 10 H, octyl CH<sub>2</sub>), 0.91 (t, 3 H, J = 6.4 Hz, octyl CH<sub>3</sub>); <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>)  $\delta_{c}$  138.2, 138.1, 137.7, 128.3, 128.2, 128.2, 128.0, 127.8, 127.7, 127.6, 127.5, 127.5 (Ph), 100.5 (C-1), 84.2, 83.5, 80.1, 73.2, 72.7, 72.3, 72.2, 67.9 (ring and benzylic C, octyl OCH<sub>2</sub>), 31.8, 29.4, 29.3, 29.2, 26.2, 22.6 (octyl CH<sub>3</sub>), 14.0 (octyl CH<sub>3</sub>). Anal. Calcd for  $C_{34}H_{44}O_5$  (532.69): C, 76.66; H, 8.33. Found: C, 76.62; H, 8.36.

*Octyl* β-*D*-*arabinofuranoside* (**3**). To a solution of **16** (250 mg, 0.48 mmol) in methanol (10 mL) was added 10% Pd/C (70 mg). The reaction mixture was stirred under H<sub>2</sub> atmosphere for 6 h at room temperature, filtered, washed with methanol (2 x 5 mL) and CH<sub>2</sub>Cl<sub>2</sub> (5 mL) and then concentrated under vacuum to obtain a **3** as colorless syrup (100 mg, 82%). R<sub>f</sub> 0.38 (1:4 toluene:EtOAc);  $[\alpha]_D$  -29.3° (*c* 1.1, CHCl<sub>3</sub>); <sup>1</sup>H NMR (800 MHz, D<sub>2</sub>O)  $\delta_H$  4.90 (d, 1 H,  $J_{1,2}$  = 4.7 Hz, H-1), 4.02 (dd, 1 H,  $J_{1,2}$  = 4.7,  $J_{2,3}$  = 7.8 Hz, H-2), 3.93 (dd, 1 H,  $J_{2,3}$  = 7.8,  $J_{3,4}$  = 7.3 Hz, H-3), 3.79 (ddd, 1 H,  $J_{3,4}$  = 7.3,  $J_{4,5a}$  = 3.9,  $J_{4,5b}$  = 7.0 Hz, H-4), 3.65–3.70 (m, 2 H, H-5a, octyl OCH<sub>2</sub>), 3.55 (dd, 1 H,  $J_{4,5b}$  = 7.0,  $J_{5a,5b}$  = 11.9 Hz, H-5b), 3.42 (dt, 1 H, J = 6.6, 9.5 Hz, octyl OCH<sub>2</sub>), 1.50–1.52 (m, 2 H, octyl CH<sub>2</sub>), 1.20–1.26 (m, 10 H, octyl CH<sub>2</sub>), 0.79 (t, 3 H, J = 6.6 Hz, octyl CH<sub>3</sub>); <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>)  $\delta_C$  101.1 (C-1), 82.3 (C-4), 78.2 (C-2), 75.8 (C-3), 69.2 (C-5), 63.0 (octyl OCH<sub>2</sub>), 31.7, 29.5, 29.2, 29.1, 25.8, 22.5, (octyl CH<sub>2</sub>), 14.0 (octyl CH<sub>3</sub>). HR-FAB-MS calcd for C<sub>13</sub>H<sub>22</sub>O<sub>5</sub> [M + H]<sup>+</sup> 263.1859, found 263.1874.

Octyl 2-O-acetyl-3,4,6-tri-O-benzyl- $\alpha$ -D-mannopyranosyl- $(1 \rightarrow 5)$ -2,3-di-O-benzyl- $\beta$ -D-arabinofuranoside (17). Thioglycoside 9 (230 mg, 0.43 mmol), alcohol 7 (170 mg, 0.39 mmol), and powdered 4 Å molecular sieves (300 mg) were placed in a round-bottom flask and dried overnight in vacuo. Dry CH<sub>2</sub>Cl<sub>2</sub> (20 mL) was added and the mixture was cooled to -40 °C and stirred for 10 min. *N*-iodosuccinimide (115 mg, 0.51 mmol) was added and the reaction was stirred for 20 min before silver triflate (31 mg, 0.12 mmol) was added. The reaction mixture was allowed to gradually warm to 0 °C and was then quenched by addition of triethylamine (0.5 mL). The yellow solution was filtered, diluted with CH<sub>2</sub>Cl<sub>2</sub> (20 mL), washed with saturated Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> solution (2 x 20 mL) followed by brine (20 mL) and water (20 mL). After drying (Na<sub>2</sub>SO<sub>4</sub>), the organic layer was concentrated to a light yellow syrup, which was chromatographed (85:15 hexane:EtOAc) to give **17** (323 mg, 82%) as a colorless syrup. R<sub>f</sub> 0.33 (4:1 hexane:EtOAc);  $[\alpha]_D + 3.4^\circ$  (*c* 1.2, CHCl<sub>3</sub>); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta_H$  7.16–7.36 (m, 25 H, Ph), 5.38 (dd,  $J_{1',2'} = 1.8$ ,  $J_{2',3'} = 3.0$  Hz, H-2'), 4.41–4.90 (m, 12 H, H-1, H-1', 10 x CH<sub>2</sub>Ph), 3.60–4.10 (m, 10 H, H-2, H-3, H-4, H-5a, H-5b, H-3', H-4', H-5', H-6'a, octyl OCH<sub>2</sub>), 3.51 (dd, 1 H,  $J_{5',6'a} = 5.6$ ,  $J_{6'a,6'b} = 10.1$  Hz, H-6'b), 3.30 (dt, 1 H, J = 6.9, 9.7 Hz, octyl OCH<sub>2</sub>), 2.13 (s, 3 H, OCOCH<sub>3</sub>), 1.56–1.64 (m, 2 H, octyl CH<sub>2</sub>), 1.21–1.29 (m, 10 H, octyl CH<sub>2</sub>), 0.87 (t, 3 H, J = 6.7 Hz, octyl CH<sub>3</sub>); <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>)  $\delta_C$  170.3 (C=O), 138.5, 138.2, 138.1, 138.0, 137.9, 137.7, 128.4, 128.3, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.8, 127.8, 127.7, 127.5, 127.5 (Ph), 100.5 (C-1), 98.1 (C-1'), 84.2, 83.3, 79.5, 78.3, 75.1, 74.2, 73.5, 72.4, 71.8, 71.6, 71.5, 70.1, 68.6, 68.5, 68.0 (ring and benzylic C, octyl OCH<sub>2</sub>), 31.8, 29.5, 29.4, 29.3, 26.2, 22.6 (octyl CH<sub>2</sub>), 21.2 (OCOCH<sub>3</sub>), 14.1 (octyl CH<sub>3</sub>). Anal. Calcd for C<sub>56</sub>H<sub>68</sub>O<sub>11</sub> (917.15): C, 73.34; H, 7.47. Found: C, 73.62; H, 7.40.

Octyl α-D-mannopyranosyl- $(1\rightarrow 5)$ -β-D-arabinofuranoside (4). A solution of 17 (210 mg, 0.23 mmol) was dissolved in methanol (20 mL) and then 2 drops of 1M NaOMe was added. After stirring overnight, the solution was neutralized with a minimum amount of Amberlite118 H<sup>+</sup> resin and concentrated to a syrup, which was purified by chromatography (8:1 hexane:EtOAc) to give 18 (190 mg, 95%) as a colorless syrup. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta_{\rm H}$  7.18–7.44 (m, 25 H, Ph), 4.98 (d,  $J_{1'2'}$  = 1.4 Hz, H-1'), 4.91 (d, 1 H,  $J_{1,2}$  = 4.2 Hz, H-1), 4.87 (d, 1 H, J = 10.9 Hz, CH<sub>2</sub>Ph), 4.47–4.77 (m, 9 H, CH<sub>2</sub>Ph), 3.64–4.24 (m, 11 H, H-2, H-3, H-4, H-5a, H-5b, H-2', H-3', H-4', H-5', H-6'a, octyl OCH<sub>2</sub>), 3.59 (dd, 1 H,  $J_{5',6'b}$  = 5.7,  $J_{6'a,6'b}$  = 10.2 Hz, H-6'b), 3.36 (dt, 1 H, J = 6.9, 9.7 Hz, octyl OCH<sub>2</sub>), 2.53 (br. s, 1 H, OH), 1.56–1.64 (m, 2 H, octyl CH<sub>2</sub>), 1.26–1.33 (m, 10 H, octyl CH<sub>2</sub>), 0.94 (t, 3 H, J = 6.8 Hz, octyl CH<sub>3</sub>); <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>)  $\delta_{\rm c}$  138.5, 138.2, 138.0, 137.8, 128.6, 128.5, 128.4, 128.2, 128.0, 127.8, 127.7, 127.6 (Ph), 100.5 (C-1), 99.7 (C-1'), 84.3, 83.4, 80.3, 79.6, 75.2, 74.2, 73.5, 72.5, 72.1, 71.3, 69.7, 68.8, 68.3, 68.2 (ring and benzylic C, octyl OCH<sub>2</sub>), 31.9, 29.6, 29.5, 29.4, 26.3, 22.8 (octyl CH<sub>2</sub>), 14.2 (octyl CH<sub>3</sub>).

To a solution of **18** (100 mg, 0.11 mmol) in methanol (8 mL), was added 10% Pd/C (25 mg). The solution was stirred overnight under H<sub>2</sub> atmosphere and then the catalyst was separated by filtration and washed with CH<sub>3</sub>OH (10 mL). After concentrating, the product was purified by chromatography (4:1 CH<sub>2</sub>Cl<sub>2</sub>:CH<sub>3</sub>OH) on silica gel to give **4** (41 mg, 90%) as a foam. R<sub>f</sub> 0.53 (4:1 CH<sub>2</sub>Cl<sub>2</sub>:CH<sub>3</sub>OH);  $[\alpha]_D$  +2.9° (*c* 1.2, H<sub>2</sub>O); <sup>1</sup>H NMR (800 MHz, D<sub>2</sub>O)  $\delta_H$  4.91 (m, 1 H, H-1), 4.84 (d, 1 H,  $J_{1',2'}$  = 1.6 Hz, H-1'), 4.02–4.06 (m, 2 H, H-2, H-3), 3.91–3.94 (m, 1 H, H-4), 3.90 (dd, 1 H,  $J_{1',2'}$  = 1.6,  $J_{2',3'}$  = 3.3 Hz, H-2'), 3.70–3.81 (m, 4 H, H-5a, H-3', H-6'a, H-6'b), 3.61–3.68 (m, 3 H, H-4', H-5b, octyl OCH<sub>2</sub>), 3.57 (ddd, 1 H,  $J_{4',5'}$  = 9.7,  $J_{5',6'a}$  = 2.1,  $J_{5',6'b}$  = 5.0 Hz, H-5'), 3.42 (dt, 1 H, *J* = 6.8, 9.6 Hz, octyl OCH<sub>2</sub>), 1.58–1.65 (m, 2 H, octyl CH<sub>2</sub>), 1.23–1.29 (m, 10 H, octyl CH<sub>2</sub>), 0.87 (t, 3 H, *J* = 6.1 Hz, octyl CH<sub>3</sub>); <sup>13</sup>C NMR (125.8 MHz, D<sub>2</sub>O)  $\delta_C$  101.4 (C-1, <sup>1</sup> $J_{C,H}$  =171.8 Hz), 100.3 (C-1', <sup>1</sup> $J_{C,H}$  = 171.1 Hz), 80.0 (C-4), 76.8 (C-2), 75.3 (C-3), 73.3 (C-5'), 71.0 (C-3'), 70.1 (C-2'), 68.9 (octyl OCH<sub>2</sub>), 68.8 (C-5), 67.0 (C-4'), 61.2 (C-6'), 31.7, 29.5, 29.2, 29.1, 25.8, 22.5 (octyl CH<sub>2</sub>), 14.0 (octyl CH<sub>3</sub>). HR-FAB-MS calcd for C<sub>19</sub>H<sub>37</sub>O<sub>10</sub> [M + H]<sup>+</sup> 425.2387, found 425.2386.

Octyl 2-O-acetyl-3,4,6-tri-O-benzyl- $\alpha$ -D-mannopyranosyl- $(1 \rightarrow 2)$ -3,4,6-tri-O-benzyl- $\alpha$ -D-mannopyranosyl- $(1 \rightarrow 5)$ -2,3-di-O-benzyl- $\beta$ -D-arabinofuranoside (19). Thioglycoside 9 (120 mg, 0.22 mmol), disaccharide

18 (150 mg, 0.17 mmol), and powdered 4 Å molecular sieves (200 mg) were placed in a round-bottom flask and dried overnight in vacuo. Dry CH<sub>2</sub>Cl<sub>2</sub> (15 mL) was added and the mixture was cooled to -40 °C and stirred for 10 min. N-iodosuccinimide (52 mg, 0.23 mmol) was added and the reaction was stirred for 20 min before the addition of silver triflate (13 mg, 0.05 mmol). The reaction mixture was allowed to gradually warm to 0 °C and was then quenched by the addition of triethylamine (0.3 mL). The yellow solution was filtered, diluted with CH,Cl<sub>2</sub> (20 mL), washed with an saturated Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> solution (2 x 20 mL) followed by brine (20 mL) and water (20 mL). After drying (Na<sub>2</sub>SO<sub>4</sub>), it was filtered and concentrated under vacuum to a light yellow syrup, which was chromatographed (85:15 hexane:EtOAc) to give 19 (130 mg, 87%) as a colorless syrup. R<sub>f</sub> 0.32 (4:1 hexane:EtOAc);  $[\alpha]_{D}$  +4.7° (c 1.3, CHCl<sub>3</sub>); <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>)  $\delta_{H}$  7.13–7.37 (m, 40 H, Ph), 5.54 (dd, 1 H,  $J_{1'',2''} = 1.7$ ,  $J_{2'',3''} = 3.0$  Hz, H-2''), 5.11 (d, 1 H,  $J_{1'',2''} = 1.7$  Hz, H-1''), 4.79–4.92 (m, 5 H, H-1, H-1', 3 x CH,Ph), 4.41-4.71 (m, 12 H, CH,Ph), 4.38 (d, 1 H, J = 10.9 Hz, CH,Ph), 3.64-4.13 (m, 16 H, H-2, H-3, H-4, H-5a, H-5b, H-2', H-3', H-4', H-5', H-6'a, H-3", H-4", H-5", H-6"a, H-6"b, octyl OCH<sub>2</sub>), 3.47 (dd, 1 H,  $J_{5',6'b} = 5.6$ ,  $J_{6'a,6'b} = 10.0$  Hz, H-6'b), 3.30 (dt, 1 H, J = 6.9, 9.8 Hz, octyl OCH<sub>2</sub>), 2.13 (s, 3 H, OCOCH<sub>3</sub>) 1.56-1.64 (m, 2 H, octyl CH<sub>2</sub>), 1.21-1.29 (m, 10 H, octyl CH<sub>2</sub>), 0.88 (t, 3 H, J = 6.9 Hz, octyl CH<sub>3</sub>); <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>)  $\delta_{c}$  170.1 (C=O), 138.5, 138.4, 138.4, 138.3, 138.2, 138.1, 138.0, 137.7, 128.4, 128.3, 128.2, 128.2, 128.2, 128.1, 128.0, 127.9, 127.9, 127.8, 127.7, 127.7, 127.6, 127.6, 127.6, 127.5 127.4, 127.4, 127.4, 127.3, 127.3 (Ph), 100.4 (C-1), 99.5 (C-1'), 98.9 (C-1"), 84.3, 83.6, 79.9, 79.5, 78.2, 75.1, 74.5, 74.4, 74.2, 73.4, 72.4, 72.1, 72.0, 71.9, 71.8, 69.9, 69.0, 68.8, 68.7, 68.0 (ring and benzylic C, octyl OCH<sub>2</sub>), 31.8, 29.5, 29.4, 29.3, 26.2, 22.7 (octyl CH<sub>2</sub>), 21.2 (OCOCH<sub>3</sub>), 14.1 (octyl CH<sub>3</sub>). Anal. Calcd for C<sub>83</sub>H<sub>96</sub>O<sub>16</sub> (1349.66): C, 73.86; H, 7.17. Found: C, 73.73; H, 7.04. HR-MALDI-MS calcd for C<sub>83</sub>H<sub>96</sub>O<sub>16</sub> [M + Na]<sup>+</sup> 1371.6626, found 1371.6596.

Octyl α-D-mannopyranosyl- $(1\rightarrow 2)$ -α-D-mannopyranosyl- $(1\rightarrow 5)$ -β-D-arabinofuranoside (5). A solution of **19** (110 mg, 0.23 mmol) was dissolved in methanol (20 mL) and then 2 drops of 1M NaOMe was added. The mixture was allowed to stir overnight and then concentrated to a syrup, which was purified by chromatography (4:1 hexane:EtOAc) to give **20** (100 mg, 96%) as a syrup. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta_{\rm H}$ 7.19–7.33 (m, 40 H, Ph), 5.14 (d, 1 H,  $J_{1,",2"}$  = 1.6 Hz, H-1"), 4.94 (d, 1 H,  $J_{1',2'}$  = 1.6 Hz, H-1'), 4.41–4.86 (m 17 H, H-1, 16 x CH<sub>2</sub>Ph), 3.98–4.10 (m, 4 H), 3.60–4.15 (m, 17 H, H-2, H-3, H-4, H-5a, H-5b, H-2', H-3', H-4', H-5', H-6'a, H-2", H-3", H-4", H-5", H-6"a, H-6"b, octyl OCH<sub>2</sub>), 3.47 (dd, 1 H,  $J_{5',6b}$  = 5.6,  $J_{6a,6b}$ = 10.0 Hz, H-6'b), 3.29 (dt, 1 H, J = 6.9, 9.8 Hz, octyl OCH<sub>2</sub>), 1.56–1.64 (m, 2 H, octyl CH<sub>2</sub>), 1.21–1.29 (m, 10 H, octyl CH<sub>2</sub>), 0.88 (t, 3 H, J = 6.9 Hz, octyl CH<sub>3</sub>); <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>)  $\delta_{\rm c}$  170.1 (C=O), 138.5, 138.4, 138.2, 138.1, 138.0, 137.9, 137.7, 137.6, 128.3, 128.3, 128.2, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 127.6, 127.5, 127.4, 127.3, 127.2, 127.1 (Ph), 101.0 (C-1), 100.3 (C-1'), 98.9 (C-1"), 84.2, 83.5, 79.9, 79.8, 79.4, 74.9, 74.8, 74.7, 74.6, 74.5, 74.3, 74.2, 73.3, 72.2, 72.0, 71.5, 71.8, 69.9, 69.0, 68.4, 67.9 (ring and benzylic C, octyl OCH<sub>2</sub>), 31.7, 29.4, 29.3, 29.2, 26.0, 22.6 (octyl CH<sub>2</sub>), 14.0 (octyl CH<sub>3</sub>).

To a solution of **20** (100 mg, 0.11 mmol) in methanol (8 mL) was added 10% Pd/C (25 mg). The mixture was stirred overnight under an H<sub>2</sub> atmosphere and the catalyst was separated by filtration and washed with CH<sub>2</sub>Cl<sub>2</sub> (10 mL). After concentrating, the product was purified by chromatography (2:1 CH<sub>2</sub>Cl<sub>2</sub>:CH<sub>3</sub>OH) on Iatrobeads to obtain **5** (38 mg, 93%) as a foam. R<sub>f</sub> 0.29 (2:1 CH<sub>2</sub>Cl<sub>2</sub>:CH<sub>3</sub>OH);  $[\alpha]_D$  +5.2° (*c* 0.9, H<sub>2</sub>O); <sup>1</sup>H

NMR (800 MHz,  $D_2O$ )  $\delta_H 5.08$  (s, 1 H, H-1'), 4.96 (s, 1 H, H-1"), 4.93 (d, 1 H,  $J_{1,2} = 4.5$  Hz, H-1), 4.05 (dd, 1 H,  $J_{2,3} = 4.6$ ,  $J_{3,4} = 8.0$  Hz, H-3), 4.00–4.02 (m, 2 H, H-2, H-2"), 3.93 (ddd, 1 H,  $J_{3,4} = 8.0$ ,  $J_{4.5a} = 3.3$ ,  $J_{4.5b} = 6.9$  Hz, H-4), 3.88–3.91 (m, 2 H, H-2', H-3'), 3.80–3.83 (m, 2 H, H-6'a, H-6"a), 3.79 (dd, 1 H,  $J_{2",3"} = 3.3$ ,  $J_{3",4"} = 9.6$  Hz, H-3"), 3.63–3.75 (m, 5 H, H-5a, H-4', H-5", H-6'b, H-6"b), 3.54–3.61 (m, 4 H, H-5b, H-5', H-4", octyl OCH<sub>2</sub>), 3.44 (dt, 1 H, J = 7.0, 9.7 Hz, octyl OCH<sub>2</sub>), 1.58–1.65 (m, 2 H, octyl CH<sub>2</sub>), 1.23–1.29 (m, 10 H, octyl CH<sub>2</sub>), 0.87 (t, 3 H, J = 6.1 Hz, octyl CH<sub>3</sub>); <sup>13</sup>C NMR (125.8 MHz,  $D_2O$ )  $\delta_C$  102.8 (C-1',  ${}^{1}J_{C,H} = 170.7$  Hz), 101.4 (C-1,  ${}^{1}J_{C,H} = 174.4$  Hz), 98.7 (C-1",  ${}^{1}J_{C,H} = 171.8$  Hz), 80.0 (C-4), 79.2 (C-2'), 76.6 (C-3), 75.1 (C-2), 73.5 (C-5"), 73.3 (C-5'), 70.8 (C-3"), 70.6 (C-3'), 70.4 (C-2"), 69.1 (C-5), 69.0 (octyl OCH<sub>2</sub>), 67.3 (C-4'), 67.2 (C-4''), 61.6, 61.2 (C-6', C-6''), 31.6, 29.2, 29.0, 29.0, 25.8, 22.5 (octyl CH<sub>3</sub>), 13.9 (octyl CH<sub>4</sub>). HR-FAB-MS calcd for  $C_{25}H_{46}O_{15}$  [M + Na]\* 609.2734, found 609.2717.

2,3,4,6-Tetra-O-acetyl- $\alpha$ -D-mannopyranosyl- $(1\rightarrow 2)$ -3,4,6-tri-O-benzyl- $\alpha$ -D-mannopyranosyl-Octyl  $(1\rightarrow 2)$ -3,4,6-tri-O-benzyl- $\alpha$ -D-mannopyranosyl- $(1\rightarrow 5)$ -2,3-di-O-benzyl- $\beta$ -D-arabinofuranoside (21). Thioglycoside 8 (35 mg, 0.09 mmol), trisaccharide 20 (80 mg, 0.06 mmol), and powdered 4 Å molecular sieves (120 mg) were placed in a round-bottom flask and dried overnight in vacuo. The above mixture was dissolved in dry CH,Cl, (10 mL) and the mixture was cooled to -40 °C and stirred for 10 min. N-iodosuccinimide (20 mg, 0.09 mmol) was added and the reaction was stirred for 20 min before the addition of silver triflate (5 mg, 0.02 mmol). The reaction mixture was allowed to gradually warm to 0 °C and was then quenched by the addition of triethylamine (0.3 mL). The yellow solution was filtered, diluted with CH<sub>2</sub>Cl<sub>2</sub> (15 mL), washed with a saturated Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> solution (2 x 15 mL) followed by brine (20 mL) and water (20 mL). After drying (Na<sub>2</sub>SO<sub>4</sub>), it was filtered and concentrated under vacuum to a light yellow syrup, which was purified by chromatography (85:15 hexane:EtOAc) to give 21 (75 mg, 76%) as a syrup.  $R_f 0.37$  (2:1 hexane:EtOAc);  $[\alpha]_D + 11.4^\circ$  (c 0.9, CHCl<sub>3</sub>); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ<sub>H</sub> 7.19–7.34 (m, 40 H, Ph), 5.45–5.15 (m, 4 H, H-1", H-2", H-3", H-4""), 4.95-4.40 (m, 19 H, H-1, H-1", H-1", 16 x CH<sub>2</sub>Ph), 3.60-4.15 (m, 20 H, H-2, H-3, H-4, H-5a, H-5b, H-2', H-3', H-4', H-5', H-6'a, H-2", H-3", H-4", H-5", H-6"a, H-6"b, H-5", H-6"a, H-6"b, octyl OCH<sub>2</sub>), 3.47 (dd, 1 H,  $J_{5,6b} = 5.6$ ,  $J_{6a,6b} = 10.0$  Hz, H-6b), 3.31 (dt, 1 H, J = 6.9, 9.8 Hz, octyl OCH<sub>2</sub>), 2.11 (s, 3 H, OCOCH<sub>4</sub>), 1.99 (s, 3 H, OCOCH<sub>3</sub>), 1.98 (s, 3 H, OCOCH<sub>3</sub>), 1.95 (s, 3 H, OCOCH<sub>3</sub>), 1.50–1.57 (m, 2 H, octyl CH<sub>2</sub>), 1.23–1.33 (m, 10 H, octyl CH<sub>2</sub>), 0.87 (t, 3 H, J = 6.3 Hz, octyl CH<sub>3</sub>); <sup>13</sup>C NMR (75.5 MHz,  $CDCl_3$ )  $\delta_c$  170.1, 169.8, 169.7, 169.6 (C=O), 138.5, 138.4, 138.4, 138.3, 138.1, 137.8, 128.9, 128.4, 128.3, 128.2, 128.1, 128.1, 128.0, 128.0, 127.9, 127.9, 127.7, 127.6, 127.5, (Ph), 100.5 (C-1"), 100.3 (C-1"), 99.2 (C-1'), 98.9 (C-1), 84.3, 83.6, 79.8, 79.5, 79.3, 76.8, 75.2, 75.1, 75.0, 74.8, 74.7, 73.4, 73.3, 73.1, 72.5, 72.4, 72.3, 72.2, 72.1, 70.2, 69.6, 69.2, 69.1, 68.9, 68.0, 66.1 (ring and benzylic C, octyl OCH<sub>2</sub>), 31.9, 29.5, 29.5, 29.3, 26.2, 22.7 (octyl CH<sub>2</sub>), 20.9, 20.7, 20.6 (OCOCH<sub>3</sub>), 14.1 (octyl CH<sub>3</sub>). HR-MALDI-MS calcd for  $C_{95}H_{112}O_{24}[M + Na]^+$  1659.7441, found 1659.7504.

Octyl  $\alpha$ -D-mannopyranosyl- $(1\rightarrow 2)$ - $\alpha$ -D-mannopyranosyl- $(1\rightarrow 2)$ - $\alpha$ -D-mannopyranosyl- $(1\rightarrow 5)$ - $\beta$ -D-arabinofuranoside (6). A solution of **21** (75 mg, 0.05 mmol) was dissolved in methanol (10 mL) and then 3 drops of 1M NaOMe was added. The mixture was allowed to stir overnight and then concentrated to a syrup, which was purified by chromatography (19:1 CH<sub>2</sub>Cl<sub>2</sub>:CH<sub>3</sub>OH) to obtain **22** (66 mg, 90%). To a solution of **22** (66 mg, 0.045 mmol) in methanol (8 mL) was added 10% Pd/C (15 mg). The mixture was stirred overnight under an H<sub>2</sub> atmosphere and the catalyst was separated by filtration and washed with CH<sub>2</sub>Cl<sub>2</sub> (10 mL). After concentrating, the product was purified by chromatography (2:1 CH<sub>2</sub>Cl<sub>2</sub>:CH<sub>3</sub>OH) on Iatrobeads to obtain **6** (29 mg, 78% from **21**) as a foam. R<sub>f</sub> 0.25 (1:1 CH<sub>2</sub>Cl<sub>2</sub>:CH<sub>3</sub>OH);  $[\alpha]_{D}$  +15.4 ° (*c* 1.4, H<sub>2</sub>O); <sup>1</sup>H NMR (800 MHz, D<sub>2</sub>O)  $\delta_{H}$  5.22 (d, 1 H,  $J_{1",2"}$  = 1.8 Hz, H-1"), 5.06 (d, 1 H,  $J_{1',2"}$  = 1.2 Hz, H-1'), 4.98 (d, 1 H,  $J_{1",2"}$  = 1.8 Hz, H-1"), 4.93 (d, 1 H,  $J_{1,2}$  = 4.6 Hz, H-1), 4.03–4.07 (m, 2 H, H-2, H-2"), 3.99–4.02 (m, 2 H, H-3, H-2"), 3.93 (ddd, 1 H,  $J_{3,4}$  = 7.1,  $J_{4,5a}$  = 3.0,  $J_{4,5b}$  = 6.9 Hz, H-4), 3.87–3.90 (m, 3 H, H-2', H-3', H-3"), 3.81–3.84 (m, 3 H, H-6a", H-6a"), 3.79 (dd, 1 H,  $J_{2",3"}$  = 3.3,  $J_{3",4"}$  = 9.6 Hz, H-3"), 3.75-3.63 (m, 8 H, H-5a, H-4', H6b', H-4", H-6b", H-4", H-6b", octyl OCH<sub>2</sub>), 3.53-3.61 (m, 4 H, H-5b, H-5', H-5"), 3.42 (dt, 1 H, *J* = 6.6, 9.5 Hz, octyl OCH<sub>2</sub>), 1.58–1.64 (m, 2 H, octyl CH<sub>2</sub>), 1.22–1.29 (m, 10 H, octyl CH<sub>2</sub>), 0.86 (t, 3 H, *J* = 6.3 Hz, octyl CH<sub>3</sub>); <sup>13</sup>C NMR (125.8 MHz, D<sub>2</sub>O)  $\delta_{C}$  102.7 (C-1"", <sup>1</sup> $J_{C,H}$  = 169.3 Hz), 101.3 (C-1, <sup>1</sup> $J_{C,H}$  = 174.5 Hz), 101.1 (C-1", <sup>1</sup> $J_{C,H}$  = 167.8 Hz), 98.7 (C-1', <sup>1</sup> $J_{C,H}$  = 170.0 Hz), 80.0 (C-4), 79.3 (C-2'), 79.3 (C-2"), 76.5 (C-2), 75.0 (C-3), 73.6 (C-5"), 73.5 (C-5""), 73.3 (C-5'), 70.8 (C-3""), 70.6 (C-3"'), 70.5 (C-2""), 70.4 (C-3'), 69.1 (C-5), 69.0 (octyl OCH<sub>2</sub>), 67.5 (C-4""), 67.2 (C-4"), 61.6 (C-6""), 61.5 (C-6"'), 61.2 (C-6'), 31.5, 29.1, 28.9, 28.8, 25.7, 22.4 (octyl CH<sub>2</sub>), 13.8 (octyl CH<sub>3</sub>). HR-FAB-MS calcd for C<sub>31</sub>H<sub>37</sub>O<sub>20</sub> [M + Na]<sup>+</sup>749.3443, found 749.3470.

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