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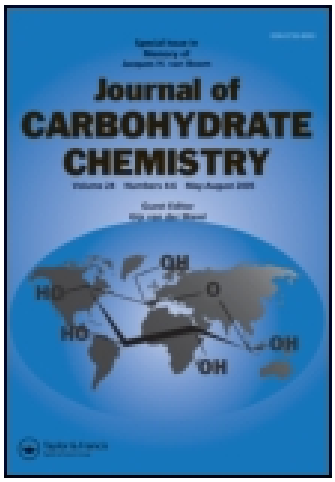

Journal of Carbohydrate Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lcar20

Synthesis of Oligosaccharide Fragments of Mannosylated Lipoarabinomannan Appropriately Functionalized for Neoglycoconjugate Preparation

Rajendrakumar Reddy Gadikota [a], Christopher S. Callam [a], Ben J. Appelmelk [b] & Todd L. Lowary [a]

[a] Department of Chemistry, Ohio State University, 100 West 18th Avenue, Columbus, Ohio, 43210, USA

[b] Department of Medical Microbiology, Vrije University, Medical School, Amsterdam, The Netherlands

Published online: 23 Aug 2006.

To cite this article: Rajendrakumar Reddy Gadikota, Christopher S. Callam, Ben J. Appelmelk & Todd L. Lowary (2003) Synthesis of Oligosaccharide Fragments of Mannosylated Lipoarabinomannan Appropriately Functionalized for Neoglycoconjugate Preparation, Journal of Carbohydrate Chemistry, 22:6, 459-480, DOI: 10.1081/CAR-120025322

To link to this article: http://dx.doi.org/10.1081/CAR-120025322

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JOURNAL OF CARBOHYDRATE CHEMISTRY
Vol. 22, No. 6, pp. 459–480, 2003

Synthesis of Oligosaccharide Fragments of Mannosylated Lipoarabinomannan Appropriately Functionalized for Neoglycoconjugate Preparation[#]

Rajendrakumar Reddy Gadikota,[1] Christopher S. Callam,[1] Ben J. Appelmelk,[2] and Todd L. Lowary[1,*]

[1]Department of Chemistry, Ohio State University, Columbus, Ohio, USA
[2]Department of Medical Microbiology, Vrije University, Medical School, Amsterdam, The Netherlands

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ABSTRACT

The synthesis of a panel of oligosaccharides that are fragments of mannosylated lipoarabinomannan from *Mycobacterium tuberculosis* is reported. The compounds were prepared as their 8-aminooctyl glycosides to enable their easy incorporation into neoglycoconjugates.

Key Words: Immunology; Mycobacteria; Lipoarabinomannan; LAM; ManLAM.

[#]This article appeared in the *Journal of Carbohydrate Chemistry*, Volume 22, Issues 3 & 4, pp. 149–170, 2003 and is being reprinted due to errors in the original version.

[*]Correspondence: Todd L. Lowary, Department of Chemistry, Ohio State University, 100 West 18th Ave., Columbus, OH 43210, USA; E-mail: lowary.2@osu.edu.

DOI: 10.1081/CAR-120025322
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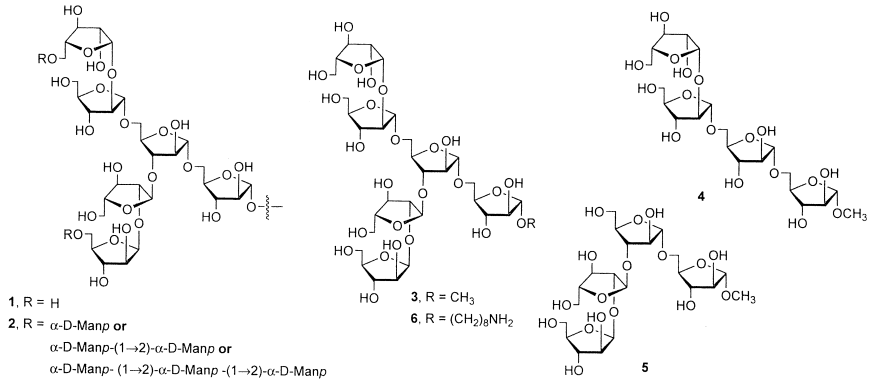
INTRODUCTION

All mycobacteria, including the human pathogen *Mycobacterium tuberculosis*, synthesize a complex cell wall structure that is composed in large part of two polysaccharides, an arabinogalactan (AG) and a lipoarabinomannan (LAM).[1,2] The AG is covalently bound to branched chain lipids, the mycolic acids, to form the mycolyl–arabinogalactan complex, which is the major structural component of the cell wall. Within this glycolipid complex is interspersed the major antigenic component of the cell wall, the LAM.[3] A number of immunomodulatory events are known to involve LAM, including the inhibition of protein kinase activities,[4] the inhibition of macrophage activation,[5] the neutralization of potentially cytotoxic oxygen free radicals,[6] the induction of cytokines,[7–9] and the induction of collagenases that destroy the extracellular matrix of the lung.[10] It is also known that T-cells recognize LAM via major histocompatibility complex (MHC)-independent presentation pathways.[11,12]

The structure of LAM consists of a phosphatidylinositol moiety that is non-covalently attached to the cytoplasmic membrane of the organism through its lipid portion.[3,13] A polysaccharide comprised of mannopyranosyl and arabinofuranosyl residues is attached to the inositol moiety and this glycan chain is terminated at the non-reducing end with the hexasaccharide **1** (Scheme 1). In some mycobacterial strains, hexasaccharide **1** is found unsubstituted, while in others this motif is further glycosylated with short mannopyranosyl oligosaccharides to provide mannosylated-lipoarabinomannan or ManLAM, **2**.[3,13] It has been suggested that the terminal mannopyranosyl residues of ManLAM (the mannose ''caps'') are involved in the initial stages of infection by adhering to human cells through their interaction with mannose binding proteins.[14,15]

It was recently shown that one of the major antibodies generated against mycobacterial LAM (CS-35) binds hexasaccharide **3** and, to a lesser degree, tetrasaccharide **4** (Scheme 1).[16] Interestingly, this antibody did not recognize another oligosaccharide fragment of **3**, tetrasaccharide **5**. These investigations not only clarified the epitope bound by this antibody, but also demonstrated that the glycan portion of hexasaccharide **3** is a potential hapten for the generation of an anti-tuberculosis



Scheme 1.

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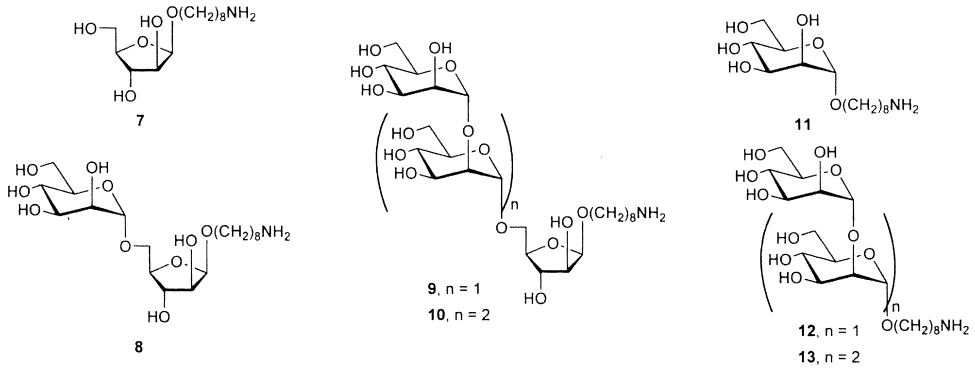

Scheme 2.

vaccine.[17] These findings prompted our interest in determining the oligosaccharide structures preferentially recognized by other antibodies generated against mycobacterial LAM. In particular, we were curious as to if any of these antibodies recognized ManLAM structural motifs.

In order to efficiently complete these investigations, it was necessary to have access to oligosaccharide fragments of LAM and ManLAM containing a functional group that could be used for the conjugation of these compounds either to an ELISA plate (for immunoassays) or to a protein carrier (for vaccine generation). We describe here the synthesis of a panel of oligosaccharides, (**6**–**13**, Schemes 1 and 2) that contain an 8-aminooctyl aglycone. This aglycone was chosen because the amino group in the products can be readily used as a reactive functionality for the generation of neoglycoconjugates.[18–20] The potential of hexasaccharide **1** in vaccine development (see above) prompted us to synthesize **6**. Compounds **7**–**13** were of interest as they represent structures that are expressed at the periphery of ManLAM and thus are likely to be the motifs that are recognized by antibodies other than CS-35.

RESULTS AND DISCUSSION

We envisioned that the oligosaccharide targets could all be synthesized from eight monosaccharide building blocks **14**–**21** (Scheme 3). Thioglycoside donors **17**–**21** are known and were synthesized as previously reported from either D-arabinose or D-mannose.[21–25] The preparation of the acceptors **14**–**16** is detailed below. In designing these syntheses, we chose to use an azido functional group as the precursor to the amino group present in the targets.

Synthesis of Monosaccharides 14 and 15

The synthesis of the arabinofuranoside acceptors **14** and **15** commenced from glycosyl bromide **22**[26] (Figure 1). Glycosylation of 8-azidooctanol[27] with **22** was achieved upon reaction with iodine[28] in acetonitrile, which produced a 3:1 α:β mixture of glycosides **23** in 75% combined yield. The isomers were not separated but were

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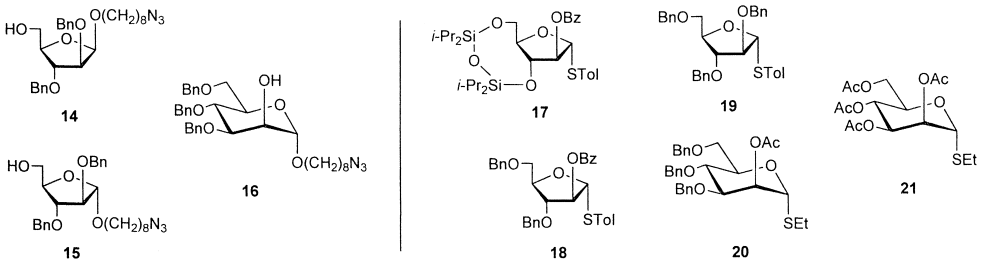

Scheme 3.

instead debenzoylated to give an inseparable α:β mixture of deprotected glycosides **24**. Treatment of **24** with *t*-butyldiphenylchlorosilane in pyridine afforded the corresponding 5-*O*-*t*-butyldimethylsilyl ethers **25** and **26**, which were separated by chromatography and isolated in 67% and 21% yield, respectively. Differentiation of **25** and **26** was readily done by ^{1}H and ^{13}C NMR spectroscopy.[29] In the ^{1}H NMR spectrum of α-glycoside **25** the anomeric hydrogen appeared as a singlet, while in the spectrum of β-glycoside **26** this hydrogen appeared as a doublet with $^{3}J_{H1,H2} = 4.3$ Hz. The values are consistent with the assigned structures as are the chemical shifts of the anomeric carbons in the ^{13}C NMR spectrum (108.6 ppm for **25**, 101.1 ppm in **26**). Benzylation of **25** gave **27** and then the silyl ether was removed to give **15** in 89% yield over two steps. Identical transformations were used to convert diol **26** into **14** in 85% overall yield.

Synthesis of 7–10

With these building blocks in hand, we were able to proceed with the synthesis of the targets. Monosaccharide **7** was obtained in two steps from **26** as illustrated in

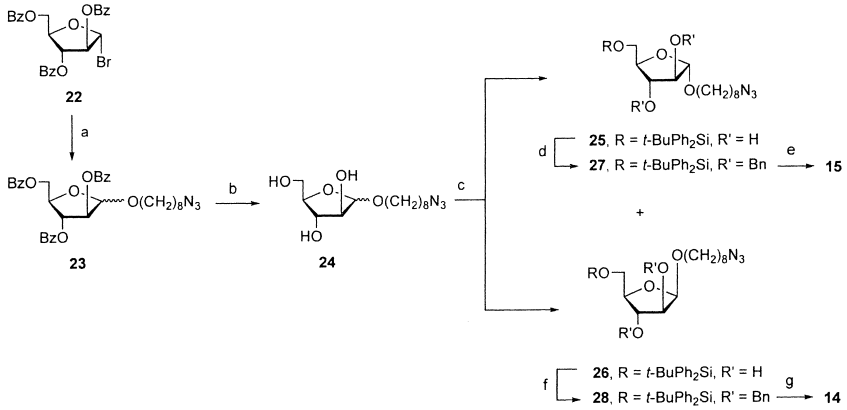

Figure 1. (a) $HO(CH_2)_8N_3$, I_2, CH_3CN, rt, 75%. (b) $NaOCH_3$, CH_3OH, CH_2Cl_2, rt, 97%, (c) *t*-$BuPh_2SiCl$, pyridine, 0°C to rt, 67% **25**, 21% **26**. (d) BnBr, NaH, DMF, 0°C to rt, 96%. (e) *n*-Bu_4NF, THF, 93%. (f) BnBr, NaH, DMF, 0°C to rt. (g) *n*-Bu_4NF, THF, 85% (2 steps from **26**).

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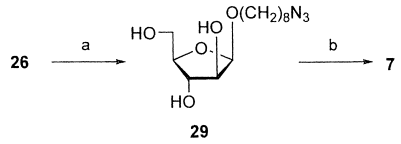

Figure 2. (a) *n*-Bu_4NF, THF, rt, 88%. (b) Ph_3P, H_2O, THF, 0°C to rt, 77%.

Figure 2. First, the silyl ether in **26** was cleaved by treatment with *n*-Bu_4NF, which afforded **29** in 88% yield. Reduction of the azido group with triphenylphosphine and water provided a 77% yield of **7**.

The preparation of oligosaccharides **8**–**10** is illustrated in Figure 3.[30] All glycosylation reactions with the thioglycoside donors were carried out in dichloromethane using activation by *N*-iodosuccinimide and silver triflate. Glycosylation of **14** with thioglycoside **20** provided a 79% yield of disaccharide **30**, which was subsequently deacetylated upon treatment with sodium methoxide to give alcohol **31** (96% yield). A portion of **31** was converted to target **8**, in 76% yield, by hydrogenolysis of the benzyl ethers and simultaneous reduction of the azido group. The remainder of **31** was glycosylated, again with **20**, to give trisaccharide **32** in 79% yield; the acetate ester

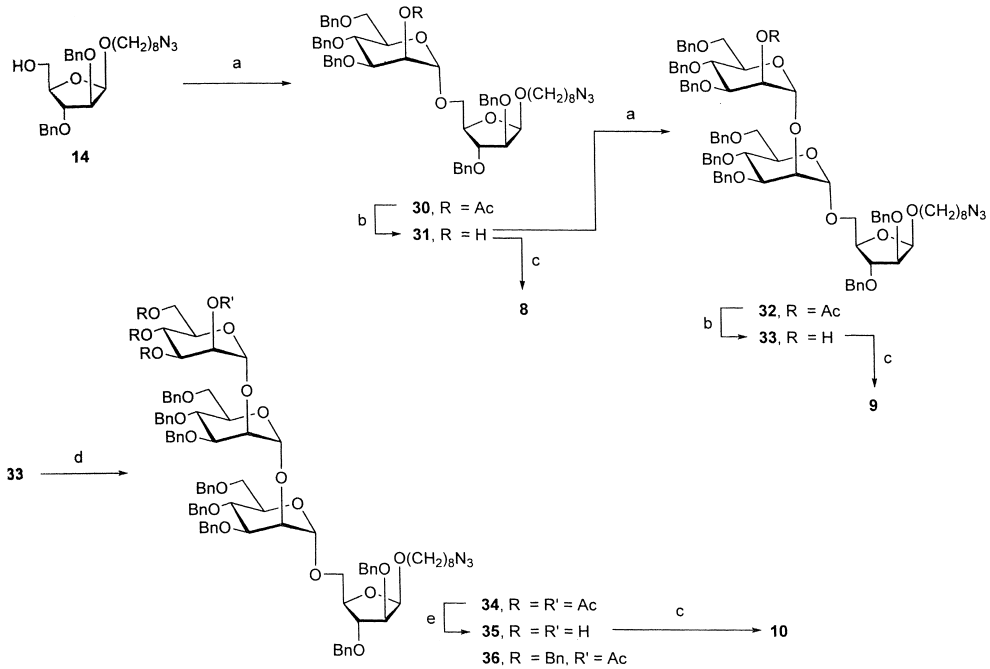

Figure 3. (a) **20**, *N*-iodosuccinimide, AgOTf, CH_2Cl_2, 0°C, 79% (for **14**), 79% (for **31**). (b) $NaOCH_3$, CH_3OH, CH_2Cl_2, rt, 96% (for **30**), 93% (for **32**). (c) H_2, Pd/C, CH_3OH, rt, 76% (for **31**), 65% (for **33**), 66% (for **35**). (d) **21**, *N*-iodosuccinimide, AgOTf, CH_2Cl_2, 0°C. (e) $NaOCH_3$, CH_3OH, CH_2Cl_2, rt, 82% (over 2 steps from **33**).

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was then cleaved providing a 93% yield of **33**. Reaction of **33** with hydrogen and Pd/C gave target **9** in 65% yield. Alternatively, coupling of **33** with thioglycoside **21** gave an impure tetrasaccharide (**34**) that was deacetylated to give **35** in 82% overall yield. Reduction of the azide and removal of the benzyl ethers in **35** was achieved in a single step (H_2, Pd/C) giving tetrasaccharide **10** (66% yield). In the course of our investigations, we also prepared an alternate protected tetrasaccharide derivative (**36**), through the coupling of **33** with thioglycoside **20**. However, although the product could be synthesized without difficulty, removal of the benzyl groups in the product was extremely sluggish and complete cleavage of all the benzyl ethers was never possible, even under forcing conditions. Fortunately, we found that this problem could be avoided through the use of **21** as the reagent for the introduction of the terminal mannose residue into the tetrasaccharide. The anomeric stereochemistry in the mannose residues was confirmed through measurement of the $^{1}J_{C1,H1}$ magnitudes in oligosaccharides **8**–**10**, which were in the range of 167.3–172.0 Hz, consistent with the α-mannopyranose stereochemistry.[31]

Synthesis of Oligosaccharides 11–13

Oligosaccharides **11**–**13** were synthesized (Figure 4) via routes analogous to those used for the preparation of **8**–**10**. Thus, 8-azidooctanol was glycosylated with **20** to give the α-mannoside **37**, which was then converted to **16** by reaction with sodium methoxide. This alcohol was then either deprotected and the azide reduced (affording **11** in 82% yield) or converted to disaccharide **38** (in 86% yield) upon reaction with **20** and *N*-iodosuccinimide and silver triflate. Removal of the acetate ester in **38** yielded an 98% yield of **39**, which was converted (in 83% yield) to trisaccharide **40** by glycosylation with **21**. Disaccharide **39** was also the precursor to **12**, which was obtained in 80% yield upon treatment with hydrogen and palladium on

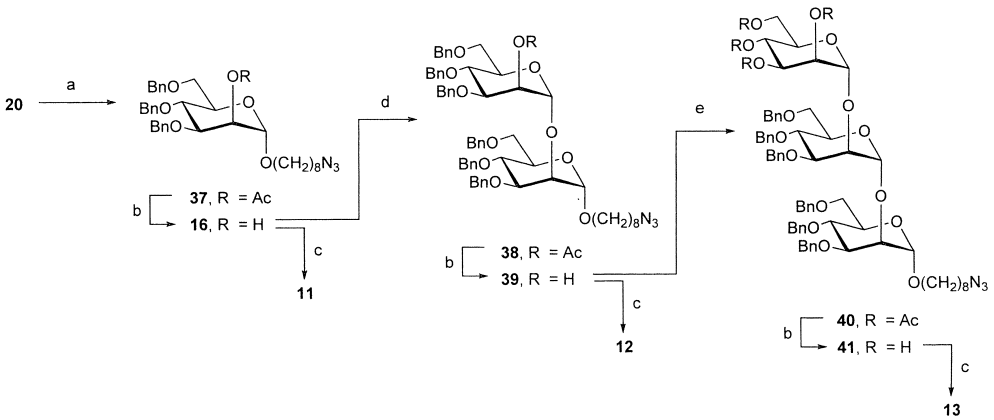

Figure 4. (a) $HO(CH_2)_8N_3$, *N*-iodosuccinimide, AgOTf, CH_2Cl_2, 0°C, 90%. (b) $NaOCH_3$, CH_3OH, CH_2Cl_2, rt, 99% (for **37**), 98% (for **38**), 98% (for **40**). (c) H_2, Pd/C, CH_3OH, rt, 82% (for **16**), 80% (for **39**), 70% (for **41**). (d) **20**, *N*-iodosuccinimide, AgOTf, CH_2Cl_2, 0°C, 86%. (e) **21**, *N*-iodosuccinimide, AgOTf, CH_2Cl_2, 0°C, 83%.

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carbon. Conversion of trisaccharide **40** into **13** was achieved in two steps by standard means, providing the product in 68% yield. As was done for **8**–**10**, the stereochemistry of the mannopyranose residues in **11**–**13** was established by measurement of the $^{1}J_{C1,H1}$ magnitudes.

Synthesis of Hexasaccharide 6

For the synthesis of hexasaccharide **6**, we used a modification of the approach[32] we have previously used to prepare its methyl glycoside counterpart, **3** (Figure 5). Alcohol **15** was glycosylated with thioglycoside **17** to give a siloxane-protected disaccharide, which was immediately debenzoylated affording **42** in 72% yield over the two steps. Conversion of **42** into diol **43** was achieved in two steps and 62% overall yield by benzylation and then cleavage of the siloxane protecting group with *n*-Bu_4NF. Coupling of **43** with an excess of **18** afforded tetrasaccharide **44** (81% yield), which was subsequently reacted with sodium methoxide to give **45** (85% yield). The introduction of the β-arabinofuranoside residues was achieved in a highly stereoselective manner by reaction of **45** at low temperature with thioglycoside **19** using *N*-iodosuccinimide and silver triflate promotion.[32] The product, **46**, was produced in 81% yield. We first attempted to convert **46** directly into target **6**, by reaction with H_2

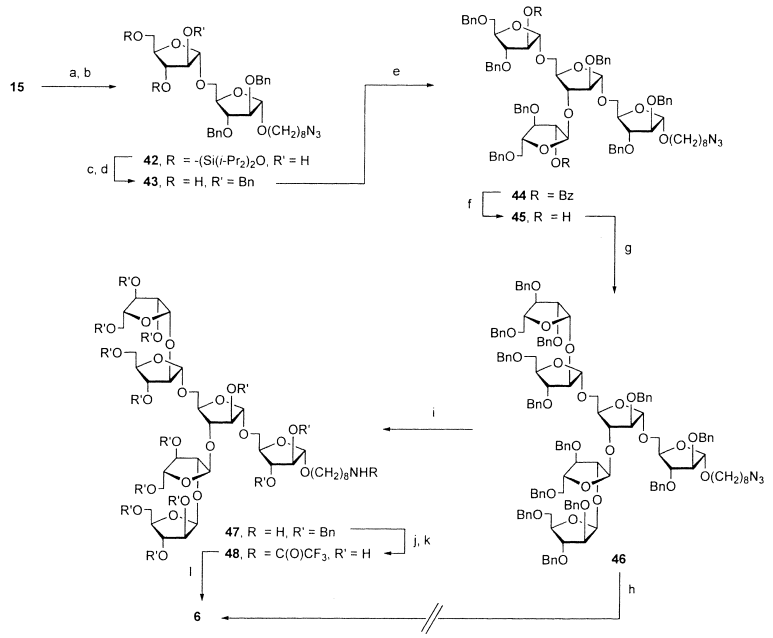

Figure 5. (a) **17**, *N*-iodosuccinimide, AgOTf, CH_2Cl_2, 0°C. (b) $NaOCH_3$,CH_3OH, CH_2Cl_2, rt, 72% (2 steps). (c) BnBr, NaH, DMF, rt. (d) *n*-Bu_4NF, THF, rt, 62% (2 steps). (e) **18**, *N*-iodosuccinimide, AgOTf, CH_2Cl_2, 0°C, 81%. (f) $NaOCH_3$, CH_3OH, rt, 85%. (g) **19**, *N*-iodosuccinimide, AgOTf, CH_2Cl_2, − 78°C, 81%. (h) H_2, Pd/C, CH_3OH, rt, 0%. (i) Ph_3P, H_2O, THF, 0°C to rt, 78%. (j) Trifluoroacetic anhydride, pyridine, rt. (k) H_2, Pd/C, CH_3OH, rt, 65% (2 steps). (l) NH_3, CH_3OH.

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and Pd/C, but were unsuccessful. The products produced, even at long reaction times, had one or more benzyl groups still in place. We were therefore forced to take a more circuitous route, as illustrated in Figure 5. First the azido group was reduced (in 78% yield) to the amine via a Staudinger reaction. The amino group in the product (**47**) was protected as an *N*-trifluoroacetamide and the benzyl groups were removed by hydrogenolysis to give hexasaccharide **48** in 65% overall yield. Treatment of **48** with ammonia in methanol afforded the target **6** in 53% yield.

CONCLUSION

In summary, we describe here the synthesis of a number of oligosaccharide fragments of mycobacterial LAM and ManLAM functionalized with an amino group that will allow for their ready incorporation into neoglycoconjugates. These compounds were prepared, for the most part, without incident. However, in the synthesis of **6** and **10**, the removal of all of the benzyl ether protecting groups at the end of the synthesis was problematic and slight modification of the synthetic routes was required. The use of these glycans in probing the selectivity of antibodies directed against mycobacterial LAM and in vaccine generation is currently in progress (a preliminary report of these investigations has appeared in Ref. [33]).

EXPERIMENTAL

Optical rotations were measured at 22 ± 2°C. Analytical TLC was performed on silica gel 60-F_{254} (0.25 mm, Merck). Spots were detected under UV light or by charring with 10% H_2SO_4 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. Iatrobeads refers to a beaded silica gel 6RS-8060, which is manufactured by Iatron Laboratories (Tokyo). The ratio between silica gel and compound ranged from 100 to 50:1 (w/w). ^{1}H NMR spectra were recorded at 400 or 500 MHz, and first order proton chemical shifts δ_H are referenced either to TMS (δ_H 0.0, $CDCl_3$) or HOD (δ_H 4.78, D_2O). ^{13}C NMR spectra were recorded at 100 or 125 MHz and ^{13}C chemical shifts δ_C are referenced either to TMS (δ_C 0.0, $CDCl_3$) or dioxane (δ_C 67.4, D_2O). One-bond carbon–hydrogen coupling constants involving the anomeric carbon of the mannose residues were measured where appropriate to prove glycoside stereochemistry. Electrospray mass spectra were recorded on samples suspended in mixtures of THF and CH_3OH with added NaCl.

8-Aminooctyl 5-*O*-{3,5-di-*O*-[2-*O*-(β-D-arabinofuranosyl)-α-D-arabinofuranosyl]-α-D-arabinofuranosyl}-α-D-arabinofuranoside (6). A solution of **48** (65 mg, 0.062 mmol) dissolved in NH_3-saturated CH_3OH (5 mL) was stirred for 36 h and then concentrated. Purification of the product on Iatrobeads (H_2O/CH_3OH, 1:1) gave **6** (31 mg, 53%) as an oil: R_f 0.11 (CH_2Cl_2/CH_3OH, 1:2); $[\alpha]_D$ + 22.3° (*c* 1.0, H_2O); ^{1}H NMR (400 MHz, D_2O, δ) 5.29 (s, 1 H), 5.19 (s, 1 H), 5.18 (s, 1 H), 5.14–5.12 (m, 2 H), 4.95 (s, 1 H), 4.23–3.63 (m, 32 H), 2.66 (dd, 2 H, *J* = 6.8, 6.8 Hz), 1.61–1.53 (m, 4 H),

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1.14–1.02 (m, 8 H); ^{13}C NMR (100 MHz, D_2O, δ) 107.7, 107.5, 106.0 (2), 101.1, 101.0, 87.4, 87.1, 83.2, 82.4, 81.9, 81.2, 76.6, 75.2, 74.5, 69.0, 63.3, 60.9, 39.9, 28.9, 28.5, 28.4, 27.0, 25.8, 25.4. HRMS (ESI) Calcd for $[C_{38}H_{67}NO_{25}]Na^+$: 960.3894. Found: 960.3819.

8-Aminooctyl β-D-arabinofuranoside (7). To a solution of **29** (300 mg, 0.99 mmol), in THF:water (10 mL, 10:1) cooled to 0°C was added Ph_3P (1.03 g, 3.9 mmol). The reaction mixture was stirred for 10 h while warming to rt and then concentrated to an oil, which was purified by chromatography (CH_2Cl_2/CH_3OH, 10:1) to give **7** (212 mg, 77%) an oil: R_f 0.1 (CH_2Cl_2/CH_3OH, 10:1); $[\alpha]_D$ − 32.1° (*c* 0.8, H_2O); ^{1}H NMR (400 MHz, D_2O, δ) 4.85 (d, 1 H, *J* = 4.8 Hz), 3.97 (dd, 1 H, *J* = 4.6, 7.8 Hz), 3.73–3.71 (m, 1 H), 3.65–3.59 (m, 2 H), 3.49 (dd, 1 H, *J* = 7.2, 10.1 Hz), 3.46–3.35 (m, 1 H), 2.64 (dd, 2 H, *J* = 6.8, 6.8 Hz), 1.48–1.38 (m, 4 H), 1.20–1.18 (m, 8 H); ^{13}C NMR (100 MHz, D_2O, δ) 101.4, 82.2, 76.7, 75.2, 68.8, 63.7, 40.4, 29.7, 28.8, 28.7, 26.4, 26.1, 25.6. HRMS (ESI) Calcd for $[C_{13}H_{27}NO_5]Na^+$: 300.1781. Found: 300.1767.

8-Aminooctyl 5-*O*-(α-D-mannopyranosyl)-β-D-arabinofuranoside (8). To a solution of **31** (210 mg, 0.22 mmol) in CH_3OH (20 mL), was added 10% Pd/C (50 mg). The solution was stirred overnight under a H_2 atmosphere and then the catalyst was filtered. The filtrate was concentrated to a residue that was purified by chromatography on Iatrobeads (CH_2Cl_2/CH_3OH, 1:1) to give **8** (76 mg, 76%) as an oil: R_f 0.2 (CH_2Cl_2/CH_3OH, 1:1); $[\alpha]_D$ + 6.3° (*c* 1.1, H_2O); ^{1}H NMR (400 MHz, D_2O, δ) 4.90 (d, 1 H, *J* = 4.3 Hz), 4.81 (d, 1 H, *J* = 0.8 Hz), 4.03–3.87 (m, 2 H), 3.86–3.76 (m, 2 H), 3.74–3.47 (m, 8 H), 3.27 (ddd, 1 H, *J* = 6.8, 6.8, 1.6 Hz), 2.91 (d, 2 H, *J* = 6.8, 6.8 Hz), 1.58–1.49 (m, 4 H), 1.30–1.21 (m, 8 H); ^{13}C NMR (100 MHz, D_2O, δ) 101.2, 100.1 ($^1J_{C1\text{-}H1}$ = 168.1 Hz), 81.3, 76.3, 74.7, 73.1, 70.8, 70.4, 68.9, 68.6, 66.9, 61.2, 39.8, 29.0, 28.6, 27.0, 25.8, 25.5, 25.4. HRMS (ESI) Calcd for $[C_{19}H_{37}NO_{10}]Na^+$: 462.2309. Found: 462.2311.

8-Aminooctyl 5-*O*-[2-*O*-(α-D-mannopyranosyl)-α-D-mannopyranosyl]-β-D-arabinofuranoside (9). Debenzylation of trisaccharide **33** (220 mg, 0.163 mmol) was carried out in CH_3OH (20 mL) with 10% Pd/C (50 mg) as described for the synthesis of **8**. The product was purified by chromatography on Iatrobeads (CH_2Cl_2/CH_3OH, 1:1) to give **9** (66 mg, 65%) as an oil: R_f 0.15 (CH_2Cl_2/CH_3OH, 1:1); $[\alpha]_D$ + 8.1° (*c* 1.0, H_2O); ^{1}H NMR (400 MHz, D_2O, δ) 5.09 (s, 1 H), 4.98 (d, 1 H, *J* = 1.1 Hz), 4.95(d, 1 H, *J* = 4.3 Hz), 4.08–4.02 (m, 3 H), 3.95–3.79 (m, 6 H), 3.76–3.56 (m, 9 H), 3.46 (ddd, 1 H, *J* = 5.5, 5.5, 1.6 Hz), 2.96 (dd, 2 H, *J* = 6.1, 6.1 Hz), 1.63–1.56 (m, 4 H), 1.39–1.30 (m, 8 H); ^{13}C NMR (100 MHz, D_2O, δ) 102.7, 101.3 ($^1J_{C1\text{-}H1}$ = 169.0 Hz), 99.9 ($^1J_{C1\text{-}H1}$ = 170.1 Hz), 80.0, 77.1, 76.4, 74.8, 73.6, 73.2, 70.7, 70.5, 70.3, 68.9, 68.8, 67.3, 67.2, 61.5, 61.2, 39.9, 29.1, 28.6, 28.5, 27.0, 25.9, 25.5. HRMS (ESI) Calcd for $[C_{25}H_{47}NO_{15}]Na^+$: 624.2837. Found: 624.2809.

8-Aminooctyl 5-*O*-{2-*O*-[2-*O*-(α-D-mannopyranosyl)-α-D-mannopyranosyl]-α-D-mannopyranosyl}-β-D-arabinofuranoside (10). Debenzylation of tetrasaccharide **35** (150 mg, 0.99 mmol) was carried out in CH_3OH (20 mL) with 10% Pd/C (40 mg) as described for the synthesis of **8**. The product was purified by chromatography on Iatrobeads (CH_2Cl_2/CH_3OH, 1:2) to give **10** (50 mg, 66%) as an oil: R_f 0.12 (CH_2Cl_2/

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CH_3OH, 1:2); $[\alpha]_D$ + 21.3° (*c* 1.0, H_2O); ^1H NMR (400 MHz, D_2O, δ) 5.22 (d, 1 H, *J* = 0.7 Hz), 5.07 (s, 1 H), 4.99 (d, 1 H, *J* = 0.8 Hz), 4.96 (d, 1 H, *J* = 4.3 Hz), 4.05–3.29 (m, 24 H), 2.95 (dd, 2 H, *J* = 6.8, 6.8 Hz), 1.58–1.52 (m, 4 H), 1.29–1.22 (m, 8 H); ^{13}C NMR (100 MHz, D_2O, δ) 102.6, 101.3 ($^1J_{C1\text{-}H1}$ = 167.9 Hz), 101.0 ($^1J_{C1\text{-}H1}$ = 170.1 Hz), 98.5 ($^1J_{C1\text{-}H1}$ = 168.9 Hz), 80.0, 79.3, 78.9, 76.4, 74.9, 73.6, 73.2, 70.7, 70.5, 70.3, 69.0, 68.8, 67.4, 67.1, 62.9, 61.5, 61.4, 61.2, 39.9, 29.0, 28.6, 28.4, 27.0, 25.9, 25.5. HRMS (ESI) Calcd for $[C_{31}H_{57}NO_{20}]Na^+$: 786.3366. Found: 786.3368.

8-Aminooctyl α-D-mannopyranoside (11). To a solution of **16** (150 mg, 0.23 mmol) dissolved in CH_3OH (10 mL) was added 10% Pd/C (40 mg). The resulting mixture was placed under a H_2 atmosphere and allowed to stir at rt for 10 h. The mixture was subsequently filtered through Celite and concentrated under reduced pressure. The product was purified by chromatography on Iatrobeads ($CHCl_3/CH_3OH$, 1:3) to give **11** (60 mg, 82%) as an oil: R_f 0.11 ($CHCl_3/CH_3OH$, 1:3); $[\alpha]_D$ + 6.3° (*c* 1.0, H_2O); ^1H NMR (500 MHz, D_2O, δ) 5.06 (s, 1 H), 4.05–3.29 (m, 8 H), 2.95 (dd, 2 H, *J* = 6.7, 6.7 Hz), 1.58–1.53 (m, 4 H), 1.29–1.22 (m, 8 H); ^{13}C NMR (125 MHz, D_2O, δ) 100.2, 82.3, 76.8, 75.3, 70.7, 68.9, 63.7, 40.3, 29.7, 28.8, 28.6, 26.4, 26.1, 25.6. HRMS (ESI) Calcd for $[C_{14}H_{29}NO_6]Na^+$: 330.1893. Found: 330.1880.

8-Aminooctyl 2-*O*-(α-D-mannopyranosyl)-α-D-mannopyranoside (12). Debenzylation and reduction of disaccharide **39** (150 mg, 0.14 mmol) was carried out in CH_3OH (10 mL) with 10% Pd/C as described for the synthesis of **11**. The product was purified by chromatography on Iatrobeads ($CHCl_3/CH_3OH$, 1:3) to give **12** (52 mg, 80%) as an oil: R_f 0.09 ($CHCl_3/CH_3OH$, 1:3); $[\alpha]_D$ + 7.1° (*c* 1.0, H_2O); ^1H NMR (500 MHz, D_2O, δ) 5.09 (s, 1 H), 5.01 (s, 1 H), 4.08–4.02 (m, 3 H), 3.95–3.78 (m, 6 H), 3.76–3.56 (m, 3 H), 2.96 (dd, 2 H, *J* = 6.7, 6.7 Hz), 1.58–1.52 (m, 4 H), 1.29–1.20 (m, 8 H); ^{13}C NMR (125 MHz, D_2O, δ) 101.3, 100.1, 80.1, 76.8, 76.1, 73.6, 73.2, 70.7, 70.3, 68.8, 67.2, 67.1, 61.3, 39.3, 29.1, 28.6, 28.5, 27.1, 26.1, 25.5. HRMS (ESI) Calcd for $[C_{19}H_{37}N_{11}]Na^+$: 478.2264. Found: 478.2271.

8-Aminooctyl 2-*O*-[2-*O*-(α-D-mannopyranosyl)-α-D-mannopyranosyl]-α-D-mannopyranoside (13). Debenzylation and reduction of trisaccharide **41** (160 mg, 0.13 mmol) was carried out in CH_3OH (10 mL) with 10% Pd/C as described for the synthesis of **11**. The product was purified by chromatography on Iatrobeads ($CHCl_3/CH_3OH$, 1:3) to give **13** (56 mg, 70%) as an oil: R_f 0.10 ($CHCl_3/CH_3OH$, 1:3); $[\alpha]_D$ + 8.9° (*c* 1.0, H_2O); ^1H NMR (500 MHz, D_2O, δ) 5.13 (d, 1 H, *J* = 0.7 Hz), 5.09 (s, 1 H), 5.01 (s, 1 H), 4.08–4.02 (m, 6 H), 3.98–3.73 (m, 8 H), 3.76–3.53 (m, 4 H), 2.98 (dd, 2 H, *J* = 6.7, 6.7 Hz), 1.58–1.51 (m, 4 H), 1.29–1.22 (m, 8 H); ^{13}C NMR (125 MHz, D_2O, δ) 101.3, 101.0, 99.8, 80.1, 79.3, 78.8, 76.8, 76.4, 74.8, 73.6, 73.2, 70.7, 70.5, 70.3, 69.0, 68.8, 67.4, 67.1, 63.8, 40.4, 29.8, 28.7, 28.6, 26.4, 26.1, 25.6. HRMS (ESI) Calcd for $[C_{25}H_{47}NO_{16}]Na^+$: 640.2793. Found: 640.2781.

8-Azidooctyl 2,3-di-*O*-benzyl-β-D-arabinofuranoside (14). Diol **26** (1.4 g, 2.58 mmol) was benzylated with benzyl bromide (920 mg, 5.4 mmol) and NaH (155 mg, 6.46 mmol) in DMF (15 mL) as described for the preparation of **27**. Following workup, the crude dibenzyl ether (**28**) was dissolved in THF, the solution cooled to 0°C under argon atmosphere and *n*-Bu_4NF (3.1 mL of a 1.0 M solution in THF, 3.1 mmol) was

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added. The reaction mixture was stirred for 2 h and then concentrated to an oil that was purified by chromatography (hexane/EtOAc, 6:1) to give **14** (1.05 g, 85%) as an oil: R_f 0.35 (hexanes/EtOAc, 2:1); $[\alpha]_D$ + 17.6° (*c* 0.9, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, δ) 7.36–7.17 (m, 10 H), 4.85 (d, 1 H, *J* = 4.8 Hz), 1.70 (d, 1 H, *J* = 11.9 Hz), 4.62–4.55 (m, 3 H), 4.28 (dd, 1 H, *J* = 6.9, 5.9 Hz), 4.08–4.03 (m, 3 H), 3.75–3.67 (m, 2 H), 3.56 (dd, 1 H, *J* = 4.7, 5.9 Hz), 3.36 (ddd, 1 H, *J* = 6.8, 6.8, 1.6 Hz), 3.22 (dd, 2 H, *J* = 6.8, 6.8 Hz), 1.64–1.53 (m, 4 H), 1.35–1.25 (m, 8 H); ^{13}C NMR (100 MHz, $CDCl_3$, δ) 138.5, 138.1, 129.4, 129.3, 128.8, 128.4, 128.3, 128.2, 128.1, 101.2, 84.9, 82.6, 81.6, 73.0, 72.9, 69.4, 64.3, 51.8, 29.9, 29.6, 29.4, 29.2, 27.0, 26.4. HRMS (ESI) Calcd for $[C_{27}H_{37}N_3O_5]Na^+$: 506.2625. Found: 506.2624.

8-Azidooctyl 2,3-di-*O*-benzyl-α-D-arabinofuranoside (15). To a solution of **27** (4.8 g, 6.6 mmol) in THF (50 mL) cooled to 0°C, was added *n*-Bu_4NF (8.0 mL of a 1.0 M solution in THF, 8.0 mmol) under an argon atmosphere. The reaction mixture was stirred for 1 h and then concentrated to an oil, which was purified by chromatography (hexane/EtOAc, 6:1) to give **15** (2.99 g, 93%) as an oil: R_f 0.4 (hexanes/EtOAc, 2:1); $[\alpha]_D$ + 33.2° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, δ) 7.37–7.25 (m, 10 H), 5.08 (s, 1 H), 4.61–4.49 (m, 4 H), 4.14–4.10 (m, 1 H), 4.03–3.97 (m, 2 H), 3.84–3.82 (m, 1 H), 3.72–3.61 (m, 2 H), 3.39 (ddd, 1 H, *J* = 6.8, 6.8, 1.6 Hz), 3.24 (dd, 2 H, *J* = 6.8, 6.8 Hz), 1.62–1.55 (m, 4 H), 1.37–1.32 (m, 8 H); ^{13}C NMR (100 MHz, $CDCl_3$, δ) 138.8, 137.8, 135.2, 128.9, 128.8, 128.3, 128.2, 128.1(2), 106.6, 88.5, 83.1, 82.2, 72.7, 72.3, 68.0, 62.6, 51.8, 29.9, 29.6, 29.5, 29.2, 27.0, 26.4. HRMS (ESI) Calcd for $[C_{27}H_{37}N_3O_5:]Na^+$506.2625. Found: 506.2624.

8-Azidooctyl 3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (16). To a solution of **37** (2.3 g, 3.6 mmol) in CH_3OH (10 mL) and CH_2Cl_2 (10 mL) was added $NaOCH_3$ (1 mL, 1M solution in CH_3OH). The solution was stirred at rt for 2 h, then neutralized with acetic acid and concentrated. The product was purified by chromatography (hexanes/EtOAc 10:1) to yield **16** (2.2 g, 99%) as an oil: R_f 0.21 (hexanes/EtOAc 4:1); $[\alpha]_D$ + 39.9° (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ) 7.42–7.23 (m, 15 H), 4.96 (d, 1 H, *J* = 0.8 Hz), 4.89 (d, 1 H, *J* = 10.6 Hz), 4.79–4.70 (m, 3 H), 4.60 (d, 1 H, *J* = 10.6 Hz), 4.57 (d, 1 H, *J* = 10.7 Hz), 4.09 (dd, 1 H, *J* = 3.0, 1.8 Hz), 3.97–3.72 (m, 6 H), 3.48 (ddd, 1 H, *J* = 6.6, 6.6, 9.6 Hz), 3.29 (dd, 2 H, *J* = 6.9, 6.9 Hz), 1.67–1.59 (m, 4 H), 1.41–1.33 (m, 8 H); ^{13}C NMR (125 MHz, $CDCl_3$, δ) 138.7, 138.6, 128.9, 128.8, 128.7, 128.4, 128.3, 128.2 (2), 128.1, 128.0, 99.6, 80.9, 75.6, 74.8, 73.9, 72.4, 71.5, 69.5, 68.9, 68.1, 51.9, 29.8, 29.7, 29.5, 29.3, 27.1, 26.5. HRMS (ESI) Calcd for $[C_{35}H_{45}N_3O_6]Na^+$: 626.3200. Found: 626.3201.

8-Azidooctyl 2,3,5-tri-*O*-benzoyl-α/β-D-arabinofuranoside (23). To a solution of freshly prepared glycosyl bromide **22** (11.0 g, 20.9 mol) and 8-azidooctanol (4.3 g, 25.1 mmol) in CH_3CN (75 mL) was added I_2 (8.0 g, 63.0 mmol). After stirring for 3 h, the reaction mixture was diluted with a saturated aq. $Na_2S_2O_3$ solution and CH_2Cl_2. The organic layer was washed with water, dried, concentrated to an oil and purified by chromatography (hexane/EtOAc, 8:1) to give **23** (10.2 g, 75%) as an oil: R_f 0.35 (hexanes/EtOAc, 10:1); ^{1}H NMR (400 MHz, $CDCl_3$, δ) 8.10–8.00 (m, 6 H), 7.56–7.29 (m, 9 H), 6.00–5.98 (m, 0.25 H), 5.58 (d, 0.75 H, *J* = 4.8 Hz), 5.30 (s, 0.75 H), 5.47–5.46 (m, 0.5 H), 5.29 (s, 0.75 H), 4.88–4.57 (m, 3 H), 3.81–3.78 (m, 1 H), 3.56–3.15

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(m, 3 H), 1.67–1.10 (m, 12 H); ^{13}C NMR (100 MHz, $CDCl_3$, δ) 166.6, 166.5, 166.3 (2), 166.1, 165.8, 133.9 (2), 133.8, 133.4 (2), 130.3 (2), 130.2 (2), 130.1, 129.6 (2), 129.5, 128.9, 128.8, 128.7, 106.1, 101.1, 82.4, 81.4, 79.2, 78.8, 78.2, 77.2, 69.0, 67.9, 66.4, 64.2, 51.8, 29.9, 29.6, 29.5, 29.4, 29.3, 29.2, 29.1, 27.0, 26.9, 26.4, 26.2. HRMS (ESI) Calcd for $[C_{34}H_{37}N_3O_8]Na^+$: 638.2478. Found: 638.2463.

8-Azidooctyl α/β-D-arabinofuranoside (24). To a solution of **23** (9.5 g, 14.7 mmol) in CH_3OH (75 mL) and CH_2Cl_2 (25 mL) was added 1.0 M CH_3ONa in CH_3OH (2 mL). After stirring for 4 h, the reaction mixture was neutralized with pre-washed Amberlite IR-120(H^+) resin, filtered, and concentrated. The residue was purified by chromatography (CH_2Cl_2/CH_3OH 15:1) to give **24** (4.31 g, 97%) as an oil: R_f 0.25 (hexanes/EtOAc, 1:2); ^{1}H NMR (400 MHz, $CDCl_3$, δ) 4.98 (s, 0.7 H), 4.90 (d, 0.3 H, J = 4.3 Hz), 4.11–3.68 (m, 7 H), 3.44–3.24 (m, 4 H), 1.63–1.56 (m, 4 H), 1.38–1.32 (m, 8 H); ^{13}C NMR (100 MHz, $CDCl_3$, δ) 108.2, 101.6, 86.5, 82.6, 79.7, 78.4, 77.1, 69.6, 68.1, 63.3, 61.8, 51.8, 29.9, 29.8, 29.5, 29.4, 29.1, 27.0, 26.3, 26.2. HRMS (ESI) Calcd for $[C_{13}H_{25}N_3O_5]Na^+$: 326.1686. Found: 326.1691.

8-Azidooctyl 5-*O*-tert-butyldiphenylsilyl-α-D-arabinofuranoside (25) and 8-azidooctyl 5-*O*-tert-butyldiphenylsilyl-β-D-arabinofuranoside (26). To a solution of **24** (4.0 g, 13.2 mmol) in pyridine (30 mL) cooled to 0°C was added *tert*-butylchlorodiphenylsilane (4.2 g, 15.3 mmol). The reaction mixture was allowed to stir for 10 h while warming to rt. The solution was then diluted with CH_2Cl_2 and washed successively with 2% aq. HCl, a saturated aq. solution of $NaHCO_3$, and water. The organic layer was dried, concentrated, and the resulting residue was purified by chromatography (hexane/EtOAc, 4:1) to give **25** (4.77 g, 67%) and **26** (1.48 g, 21%) as an oil. **25**: R_f 0.5 (hexanes/EtOAc, 2:1); $[\alpha]_D$ + 19.2° (*c* 1.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, δ) 7.70–7.65 (m, 4 H), 7.45–7.25 (m, 6 H), 5.08 (s, 1 H), 4.20–4.10 (m, 3 H), 4.02 (d, 1 H, J = 11.8 Hz), 3.82 (dd, 1 H, J = 2.2, 11.4 Hz), 3.77–3.71 (m, 3 H), 3.46 (ddd, 1 H, J = 6.8, 6.8, 1.6 Hz), 3.24 (dd, 2 H, J = 6.8, 6.8 Hz), 1.65–1.54 (m, 4 H), 1.36–1.10 (m, 8 H) 1.09–1.05 (m, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$, δ) 136.0 (2), 132.2, 132.1, 130.6, 130.4, 128.4, 128.3, 108.6, 87.9, 78.6, 78.4, 67.9, 64.4, 51.8, 29.8, 29.5, 29.4, 29.2, 27.0 (2), 26.4, 19.4. HRMS (ESI) Calcd for $[C_{29}H_{43}N_3O_5Si]Na^+$: 564.2864. Found: 564.2837. **26**: R_f 0.35 (hexanes/EtOAc, 2:1); $[\alpha]_D$ + 14.7° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, δ) 7.69–7.66 (m, 4 H), 7.42–7.25 (m, 6 H), 4.90 (d, 1 H, J = 4.3 Hz), 4.11–4.02 (m, 2 H), 3.90 (dd, 1 H, J = 5.8, 11.6 Hz), 3.79–3.67 (m, 5 H), 3.38 (ddd, 1 H, J = 6.8, 6.8, 1.6 Hz), 3.23 (dd, 2 H, J = 6.8, 6.8 Hz), 1.58–1.47 (m, 4 H), 1.34–1.24 (m, 8 H) 1.09–1.06 (m, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$, δ) 135.9, 133.6, 130.2, 130.1, 128.1, 101.1, 82.3, 78.4, 78.2, 68.7, 65.9, 51.8, 29.8, 29.6, 29.4, 29.2 (2), 27.2, 27.0, 26.3, 19.6. HRMS (ESI) Calcd for $[C_{29}H_{43}N_3O_5Si]Na^+$: 564.2864. Found: 564.2831.

8-Azidooctyl 5-*O*-tert-butyldiphenylsilyl-2,3-di-*O*-benzyl-α-D-arabinofuranoside (27). To a slurry of hexane-washed NaH (711 mg, 29.5 mmol) in DMF (10 mL) cooled to 0°C, was added a solution of **25** (4.0 g, 7.3 mmol) in DMF (10 mL). Benzyl bromide (3.14 g, 18.4 mmol) was added dropwise to this solution and the mixture was stirred for 1 h while warming to rt before CH_3OH (2 mL) was added. The reaction mixture was poured into ice water and was extracted into diethyl ether. The combined

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ethereal extracts were dried, filtered, and concentrated to a residue, which was purified by chromatography (hexane/EtOAc, 10:1) to give **27** (5.11 g, 96%) as an oil: R_f 0.45 (hexanes/EtOAc, 10:1); $[\alpha]_D$ + 42.1° (*c* 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, δ) 7.69–7.65 (m, 4 H), 7.40–7.24 (m, 16 H), 5.03 (s, 1 H), 4.58–4.48 (m, 4 H), 4.17–4.13 (m, 1 H), 4.05–4.03 (m, 2 H), 3.84–3.67 (m, 3 H), 3.41 (ddd, 1 H, *J* = 6.8, 6.8, 1.6 Hz), 3.20 (dd, 2 H, *J* = 6.8, 6.8 Hz), 1.63–1.53 (m, 4 H), 1.36–1.32 (m, 8 H), 1.04–1.00 (m, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$, δ) 138.5, 138.5, 138.2, 136.1 (2), 133.9, 130.0 (2), 128.8, 128.7, 128.2 (2), 128.1, 128.0 (3), 106.6, 88.9, 83.6, 82.5, 72.4, 72.2, 68.0, 64.0, 51.8, 30.0, 29.7, 29.5, 29.2, 27.3, 27.1, 26.5, 19.7. HRMS (ESI) Calcd for $[C_{43}H_{55}N_3O_5Si]Na^+$: 744.3803. Found: 744.3747.

8-Azidooctyl β-D-arabinofuranoside (29). Glycoside **26** (800 mg, 1.47 mmol) was desilylated with *n*-Bu_4NF (1.8 mL of a 1.0 M solution in THF, 1.8 mmol) as described for the synthesis of **15**. The product was purified by chromatography (hexane/EtOAc, 1:2) to give **29** (390 mg, 88%) as an oil: R_f 0.23 (hexanes/EtOAc, 1:2); $[\alpha]_D$ − 14.7° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, δ) 4.92 (d, 1 H, *J* = 4.8 Hz), 4.16 (dd, 1 H, *J* = 6.9, 7.0 Hz), 4.15–3.92 (m, 2 H), 3.91–3.89 (m, 1 H), 3.80–3.64 (m, 3 H), 3.50 (ddd, 1 H, *J* = 6.8, 6.8, 1.6 Hz), 3.26 (dd, 2 H, *J* = 6.8, 6.8 Hz), 3.16 (br. d, 1 H, *J* = 1.0 Hz), 2.74 (br. s, 1 H), 1.62–1.56 (m, 4 H), 1.40–1.32 (m, 8 H); ^{13}C NMR (100 MHz, $CDCl_3$, δ) 101.6, 82.7, 78.7, 76.2, 69.6, 63.4, 51.8, 29.9, 29.6, 29.4, 29.1, 27.0, 26.2. HRMS (ESI) Calcd $[C_{13}H_{25}N_3O_5]Na^+$: 326.1700. Found: 326.1701.

8-Azidooctyl 5-*O*-(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-2,3-di-*O*-benzyl-β-D-arabinofuranoside (30). Thioglycoside **20** (1.31 g, 2.19 mmol), alcohol **14** (800 mg, 1.82 mmol), and powdered 4 Å molecular sieves (1.0 g) were dried overnight in vacuo and then CH_2Cl_2 (40 mL) was added. The suspension was cooled to 0°C and stirred for 10 min. *N*-iodosuccinimide (490 mg, 2.18 mmol) was added and the reaction was stirred for 20 min before silver triflate (99 mg, 0.38 mmol) was added. The reaction mixture was stirred for 1 h and then Et_3N (1 mL) was added. The resulting yellow solution was filtered, diluted with CH_2Cl_2, washed with a saturated aq. $Na_2S_2O_3$ solution and then brine and water. After drying, the organic layer was concentrated to an oil, which was purified by chromatography (hexanes/EtOAc, 10:1) to give **30** (1.37 g, 79%) as an oil; R_f 0.43 (hexanes/EtOAc, 4:1); $[\alpha]_D$ + 22.6° (*c* 1.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, δ) 7.34–7.15 (m, 25 H), 5.39 (d, 1 H, *J* = 0.8 Hz), 4.86–4.82 (m, 3 H), 4.69–4.44 (m, 9 H), 4.12 (dd, 1 H, *J* = 5.7, 5.9 Hz), 4.05–4.38 (m, 4 H), 3.83–3.64 (m, 6 H), 3.51 (ddd, 1 H, *J* = 6.8, 6.8, 1.6 Hz), 3.31 (d, 2 H, *J* = 6.8, 6.8 Hz), 2.13 (s, 3 H), 1.68–1.51 (m, 4 H), 1.33–1.26 (m, 8 H); ^{13}C NMR (100 MHz, $CDCl_3$, δ) 170.8, 138.9, 138.6, 138.5, 138.3, 138.1, 128.8 (2), 128.7 (2), 128.5, 128.4, 128.3(2), 128.2, 128.1, 128.0(2), 100.9, 98.5, 84.6, 83.7, 79.9, 78.7, 75.6, 74.6, 73.9, 72.8 (2), 72.2, 72.0, 70.5, 69.1, 69.0, 68.5, 51.8, 29.9, 29.7, 29.5, 29.2, 27.1, 26.5, 21.5. HRMS (ESI) Calcd for $[C_{56}H_{67}N_3O_{11}]Na^+$: 980.4667. Found: 980.4695.

8-Azidooctyl 5-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-2,3-di-*O*-benzyl-β-D-arabinofuranoside (31). Disaccharide **30** (1.2 g, 1.25 mmol) was deacetylated as described for the preparation of **24** using 1.0 M $NaOCH_3$ in CH_3OH (1 mL) and CH_3OH (10 mL). The product was purified by chromatography (hexanes/EtOAc, 6:1) to give **31** (1.1 g, 96%) as an oil: R_f 0.3 (hexanes/EtOAc, 4:1); $[\alpha]_D$ + 36.1° (*c* 1.3,

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$CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$, δ) 7.35–7.16 (m, 25 H), 4.92 (d, 1 H, J = 4.3Hz), 4.80 (d, 1 H, J = 11.3 Hz), 4.68–4.48 (m, 9 H), 4.13 (dd, 1 H, J = 5.9, 6.0 Hz), 4.05–4.00 (m, 3 H), 3.88–3.86 (m, 3 H), 3.70–3.64 (m, 5 H), 3.52 (dd, 1 H, J = 6.8, 6.8), 3.30 (ddd, 1 H, J = 6.8, 6.8, 1.6 Hz), 3.21 (dd, 2 H, J = 6.8, 6.8 Hz), 1.68–1.52 (m, 4 H), 1.32–1.24 (m, 8 H); ^{13}C NMR (100 MHz, $CDCl_3$, δ) 138.3, 138.1, 137.8, 137.7, 128.5, 128.3 (2), 128.0, 127.8 (2), 127.7 (2), 127.6 (2), 127.5, 100.4, 99.5, 84.2, 83.3, 80.2, 79.5, 75.0, 74.1, 73.4, 72.4 (2), 72.0, 71.2, 69.6, 68.7, 68.2, 68.1, 51.4, 29.4, 29.3, 29.1, 28.8, 26.6, 26.0. HRMS (ESI) Calcd for $[C_{54}H_{65}N_3O_{10}]Na^+$: 938.4562. Found: 938.4597.

8-Azidooctyl 2,3-di-*O*-benzyl-5-*O*-[2-O-(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl]-β-D-arabinofuranoside (32). Disaccharide **31** (300 mg, 0.32 mmol) was glycosylated with thioglycoside **20** (250 mg, 0.42 mmol) as described for the preparation of **30** using powdered 4 Å molecular sieves (400 mg), *N*-iodosuccinimide (88 mg, 0.39 mmol) and silver triflate (25 mg, 0.09 mmol) in CH_2Cl_2 (20 mL). The product was purified by chromatography (hexanes: EtOAc, 10: 1) to give **32** (360 mg, 79%) as an oil: R_f 0.4 (hexanes/EtOAc, 6:1); $[\alpha]_D$ + 22.8° (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$, δ) 7.34–7.19 (m, 40 H), 5.53 (dd, 1 H, J = 1.8, 2.9 Hz), 5.09 (d, 1 H, J = 0.8 Hz), 4.90 (d, 1 H, J = 0.8 Hz), 4.86–4.80 (m, 3 H), 4.68–4.35 (m, 14 H), 4.08–3.88 (m, 9 H), 3.79–3.64 (m, 7 H), 3.45 (dd, 1 H, J = 6.8, 6.8 Hz), 3.28 (ddd, 1 H, J = 6.8, 6.8, 1.6 Hz), 3.18 (dd, 2 H, J = 6.8, 6.8 Hz), 2.10 (s, 3 H), 1.57–1.50 (m, 4 H), 1.31–1.26 (m, 8 H); ^{13}C NMR (100 MHz, $CDCl_3$, δ) 170.5, 138.9, 138.7, 138.6, 128.8, 128.7 (2), 128.6 (2), 128.4 (2), 128.3, 128.2 (2), 128.1, 128.0(2), 127.9, 127.7, 100.9, 100.8, 99.9, 84.7, 79.9, 78.6, 75.5, 75.4, 74.9, 74.6, 73.8 (2), 72.5, 72.3, 69.1, 68.4, 51.8, 30.1, 29.9, 29.7, 29.5, 27.1, 26.5, 21.5. HRMS (ESI) Calcd for $[C_{83}H_{95}N_3O_{16}]Na^+$: 1412.6604. Found: 1412.6630.

8-Azidooctyl 2,3-di-*O*-benzyl-5-*O*-[2-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl]-β-D-arabinofuranoside (33). Trisaccharide **32** (300 mg, 0.21 mmol) was deacetylated as described for the preparation of **24** using 1.0 M $NaOCH_3$ in CH_3OH (0.5 mL) and CH_3OH (10 mL). The product was purified by chromatography (hexanes/EtOAc, 4:1) to give **33** (271 mg, 93%) as an oil: R_f 0.31 (hexanes/EtOAc, 3:1); $[\alpha]_D$ + 31.1° (*c* 1.2, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$, δ) 7.50–7.07 (m, 40 H), 5.14 (d, 1 H, J = 1.7 Hz), 4.85 (d, 1 H, J = 1.6 Hz), 4.83–4.46 (m, 18 H), 4.11–4.01 (m, 5 H), 3.93–3.64 (m, 12 H), 3.45 (dd, 1 H, J = 1.5, 1.9 Hz), 3.29 (ddd, 1 H, J = 6.8, 6.8, 1.6 Hz), 3.17 (dd, 2 H, J = 6.8, 6.8 Hz), 1.72–1.26 (m, 12 H); ^{13}C NMR (100 MHz, $CDCl_3$, δ) 139.0 (2), 138.8, 138.7, 138.6, 138.5, 138.4, 128.9, 128.8 (2), 128.7 (2), 128.4, 128.3 (3), 128.1, 128.0, 127.8 (2), 101.5, 100.9, 99.4, 84.7, 84.0, 80.4, 80.3, 80.0, 75.5, 75.4, 75.2, 75.1, 74.7, 73.8, 72.8 (2), 72.7, 72.6, 72.1, 69.4, 69.0, 68.4, 51.8, 29.9, 29.7, 29.5, 29.2, 27.1, 26.5. HRMS (ESI) Calcd for $[C_{81}H_{93}N_3O_{15}]Na^+$: 1370.6498. Found: 1370.6403.

8-Azidooctyl 5-*O*-[3,4,6-tri-*O*-benzyl-2-*O*-[3,4,6-tri-*O*-benzyl-2-*O*-(α-D-mannopyranosyl)-α-D-mannopyranosyl]-α-D-mannopyranosyl]-2,3-di-*O*-benzyl-β-D-arabinofuranoside (35). Trisaccharide **33** (200 mg, 0.15 mmol) was glycosylated with thioglycoside **21** (100 mg, 0.22 mmol), as described for the preparation of **30** using powdered 4 Å molecular sieves (500 mg), *N*-iodosuccinimide (49 mg, 0.22 mmol) and

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silver triflate (10 mg, 0.03 mmol) in CH_2Cl_2 (15 mL). The product was purified by chromatography (hexanes/EtOAc, 9:1) to give a tetrasaccharide (**34**), which was contaminated with succinimide. The crude trisaccharide was therefore dissolved in CH_3OH (30 mL) and 1.0 M $NaOCH_3$ in CH_3OH (0.5 mL) was added dropwise. After stirring for 4 h, the reaction mixture was neutralized with Amberlite IR-120 (H^+) resin, filtered, and concentrated. The residue was purified by chromatography (hexanes/EtOAc, 4:1) to give **35** (180 mg, 82%) as an oil: R_f 0.25 (hexanes/EtOAc, 3:1); $[\alpha]_D$ + 22.9° (*c* 1.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, δ) 7.32–7.12 (m, 40 H), 5.13 (s, 1 H), 5.06 (s, 1 H), 4.93 (s, 1 H), 4.84 (d, 1 H, *J* = 4.3 Hz), 4.83–4.39 (m, 20 H), 4.09–4.35 (m, 24 H), 3.28 (ddd, 1 H, *J* = 6.8, 6.8, 1.6 Hz), 3.17 (dd, 2 H, *J* = 6.8, 6.8 Hz), 1.54–1.48 (m, 4 H), 1.28–1.25 (m, 8 H); ^{13}C NMR (100 MHz, $CDCl_3$, δ) 139.0, 138.6, 138.5, 138.2, 129.0, 128.8(2), 128.7(2), 128.4, 128.3 (2), 128.2 (2), 128.0, 127.9, 127.8, 101.9, 101.1, 100.9, 99.4, 84.7, 84.0, 80.0, 79.9, 75.6, 75.4, 75.3, 73.8, 73.6, 73.3, 72.8 (2), 72.5, 72.1, 71.5, 70.6, 69.6 (2), 68.4, 66.8, 61.3, 51.8, 29.9, 29.7, 29.5, 29.2, 27.1, 26.5. HRMS (ESI) Calcd for $[C_{87}H_{103}N_3O_{20}]Na^+$: 1532.7027. Found: 1532.7156.

8-Azidooctyl 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (37). 8-azidooctanol (0.59 g, 3.6 mmol) was glycosylated with **20** (2.5 g, 4.2 mmol) as described for the preparation of **30** using powdered 4 Å molecular sieves (1.0 g), *N*-iodosuccinimide (0.9 g, 4.2 mmol) and silver triflate (100 mg, 0.42 mmol) in CH_2Cl_2 (50 mL). The product was purified by chromatography (hexanes/EtOAc 10:1) to yield **37** (2.3 g, 90%) as an oil: R_f 0.46 (hexanes/EtOAc 4:1); $[\alpha]_D$ + 58.1° (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ) 7.41–7.23 (m, 15 H), 5.43 (dd, 1 H, *J* = 3.2, 1.8 Hz), 4.92 (d, 1 H, *J* = 10.6 Hz), 4.88 (d, 1 H, *J* = 1.6 Hz), 4.77 (d, 1 H, *J* = 10.6 Hz), 4.76 (d, 1 H, *J* = 10.6 Hz), 4.61–4.53 (m, 3 H), 4.05 (dd, 1 H *J* = 9.3, 3.4 Hz), 9.94 (dd, 1 H, *J* = 3.9, 3.9 Hz), 3.88–3.85 (m, 2 H), 3.79–3.70 (m, 2 H), 3.47 (ddd, 1 H, *J* = 6.6, 6.6, 9.6 Hz), 3.29 (dd, 2 H, *J* = 6.9, 6.9 Hz), 2.21 (s, 3 H), 1.67–1.59 (m, 4 H), 1.41–1.32 (m, 8 H); ^{13}C NMR (125 MHz, $CDCl_3$, δ) 170.9, 138.8, 138.7, 138.4, 128.8, 128.7, 128.6, 128.5, 128.4, 128.2, 128.1, 128.0 (2), 98.2, 78.8, 75.7, 74.8, 73.8, 72.2, 71.8, 69.4, 69.3, 68.4, 51.9, 29.8, 29.7, 29.5, 29.3, 27.1, 26.5, 21.6. HRMS (ESI) Calcd for $[C_{37}H_{47}N_3O_7]Na^+$: 668.3306. Found: 668.3317.

8-Azidooctyl 3,4,6-tri-*O*-benzyl-2-*O*-(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-α-D-mannopyranoside (38). Alcohol **16** (1.3 g, 2.2 mmol) was glycosylated with **20** (1.5 g, 2.6 mmol) as described for the preparation of **30** using powdered 4 Å molecular sieves (1.0 g), *N*-iodosuccinimide (0.58 g, 2.6 mmol) and silver triflate (70 mg, 0.26 mmol) in CH_2Cl_2 (50 mL). The product was purified by chromatography (hexanes/EtOAc 10:1) to yield **38** (1.9 g, 86%) as an oil: R_f 0.26 (hexanes/EtOAc 3:1); $[\alpha]_D$ + 18.9° (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ) 7.42–7.29 (m, 30 H), 5.63 (dd, 1 H, *J* = 3.2, 1.8 Hz), 5.17 (d, 1 H, *J* = 0.8 Hz), 4.96–4.92 (m, 3 H), 4.79–4.72 (m, 5 H), 4.65–4.48 (m, 5 H), 4.09–4.04 (m, 4 H), 4.01–3.77 (m, 7 H), 3.68 (ddd, 1 H, *J* = 3.6, 3.6, 6.6 Hz), 3.37–3.29 (m, 3 H), 2.20 (s, 3 H), 1.68–1.56 (m, 4 H), 1.42–1.34 (m, 8 H); ^{13}C NMR (125 MHz, $CDCl_3$, δ) 170.6, 139.0, 138.9, 138.8, 138.4, 128.8 (2), 128.7 (3), 128.6, 128.5, 128.2, 128.1, 128.0 (2), 127.9 (3), 127.8, 100.0, 99.1, 80.3, 78.6, 75.6, 75.5, 75.4, 74.8, 73.8, 73.7, 72.4, 72.3, 72.2, 69.8, 69.6, 69.2, 68.1, 51.8, 29.8, 29.7, 29.5, 29.3, 27.1, 26.5, 21.6. HRMS (ESI) Calcd for $[C_{64}H_{75}N_3O_{12}]Na^+$: 1100.5242. Found: 1100.5243.

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8-Azidooctyl 3,4,6-tri-*O*-benzyl-2-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-α-D-mannopyranoside (39). Disaccharide **38** (1.2 g, 1.1 mmol) was deacetylated as described for the preparation of **16** using 1.0 M $NaOCH_3$ in CH_3OH (1 mL) and CH_3OH (10 mL). The product was purified by chromatography (hexanes/EtOAc 10:1) to yield **39** (1.1 g, 98%) as an oil: R_f 0.41 (hexanes/EtOAc 2:1); $[\alpha]_D$ + 61.4° (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ) 7.39–7.24 (m, 30 H), 5.21 (d, 1 H, *J* = 0.9 Hz), 4.97 (d, 1 H, *J* = 0.8 Hz), 4.91 (d, 1 H, *J* = 10.6 Hz), 4.86 (d, 1 H, *J* = 10.6 Hz), 4.77–4.55 (m, 11 H), 4.19 (dd, 1 H, *J* = 2.3, 1.8 Hz), 4.09–3.76 (m, 10 H), 3.64 (ddd, 1 H, *J* = 3.6, 3.6, 6.6 Hz), 3.34–3.27 (m, 3 H), 1.67–1.59 (m, 4 H), 1.41–1.33 (m, 8 H); ^{13}C NMR (125 MHz, $CDCl_3$, δ) 138.9, 138.7, 138.4, 128.9, 128.8 (2), 128.7 (3), 128.4, 128.3, 128.2 (2), 128.1, (3), 127.8, 127.7, 101.5, 99.2, 80.5, 80.3, 75.6, 75.5, 75.4, 75.3, 74.9, 73.8, 73.7, 72.7, 72.5, 72.2, 71.9, 69.8, 69.6, 69.0, 68.1, 51.9, 29.8, 29.7, 29.5, 29.3, 27.1, 26.5. HRMS (ESI) Calcd for $[C_{62}H_{73}N_3O_{11}]Na^+$: 1058.5137. Found: 1058.5099.

8-Azidooctyl 3,4,6-tri-*O*-benzyl-2-*O*-[3,4,6-tri-*O*-benzyl-2-*O*-(2-3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl)-α-D-mannopyranosyl]-α-D-mannopyranoside (40). Alcohol **39** (0.80 g, 0.77 mmol) was glycosylated with **21** (0.42 g, 0.93 mmol) as described for the preparation of **30** using powdered 4 Å molecular sieves (1.0 g), *N*-iodosuccinimide (0.22 g, 0.93 mmol) and silver triflate (100 mg, 0.01 mmol) in CH_2Cl_2 (50 mL). The product was purified by chromatography (hexanes/EtOAc 10:1) to yield **40** (0.88 g, 83%) as an oil: R_f 0.13 (hexanes/EtOAc 1:1); $[\alpha]_D$ + 98.5°(*c* 0.9, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ) 7.41–7.23 (m, 30 H), 5.49–5.44 (m, 2 H), 5.34–5.24 (m, 2 H), 4.96 (dd, 1 H, *J* = 1.6, 2.8 Hz), 4.90–4.87 (m, 3 H), 4.76–4.54 (m 10 H), 4.19–4.16 (m, 2 H), 4.06–3.75 (m, 13 H), 3.61 (ddd, 1 H, *J* = 3.6, 3.6, 6.6 Hz), 3.30–3.26 (m, 3 H), 2.17 (s, 3 H), 2.07 (s, 3 H), 2.05 (s, 3 H), 2.03 (s, 3 H), 1.67–1.59 (m, 4 H), 1.41–1.32 (m, 8 H); ^{13}C NMR (125 MHz, $CDCl_3$, δ) 170.9, 170.2, 170.1, 170.0, 169.9, 139.0, 138.8 (2), 138.7, 128.9, 128.8 (2), 128.7 (2), 128.5, 128.4, 128.3, 128.1, 128.0 (2), 127.9 (2), 127.8, 127.7, 100.8, 99.6, 99.1, 80.1, 79.6, 76.1, 75.6, 75.4, 75.3, 73.7, 73.5, 72.8, 72.7, 72.6, 72.2, 70.0, 69.9, 69.6, 69.3, 68.1, 66.5, 62.7, 51.9, 29.8, 29.7, 29.5, 29.2, 27.1, 26.5, 21.3, 21.1, 21.0. HRMS (ESI) Calcd for $[C_{76}H_{91}N_3O_{20}]Na^+$: 1388.6088. Found: 1388.6099.

8-Azidooctyl 3,4,6-tri-*O*-benzyl-2-*O*-[3,4,6-tri-*O*-benzyl-2-*O*-(α-D-mannopyranosyl)-α-D-mannopyranosyl]-α-D-mannopyranoside (41). Trisaccharide **40** (500 mg, 0.36 mmol) was deacetylated as described for the preparation of **16** using 1.0 M $NaOCH_3$ in CH_3OH (1 mL) and CH_3OH (10 mL) and CH_2Cl_2 (10 mL). Theproduct was purified by chromatography (hexanes/EtOAc 10:1) to yield **41** (430 mg, 98%) as an oil: R_f 0.21 (hexanes/EtOAc 4:1); $[\alpha]_D$ + 39.9° (*c* 1.0, $CHCl_3$);^{1}H NMR (500 MHz, $CDCl_3$, δ) 7.37–7.23 (m, 30 H), 5.17 (s, 1 H), 5.09 (s, 1 H), 4.92 (d, 1 H, *J* = 0.7 Hz), 4.86 (d, 1 H, *J* = 10.7 Hz), 4.83 (d, 1 H, *J* = 10.7 Hz), 4.72 (d, 1 H, *J* = 10.7 Hz), 4.68–4.48 (m, 8 H), 4.11–4.09 (m, 2 H), 3.99–3.92 (m, 6 H), 3.84–3.52 (m, 14 H), 3.29–3.25 (m, 3 H), 1.64–1.58 (m, 2 H), 1.52–1.50 (m, 2 H), 1.37–1.29 (m, 10 H); ^{13}C NMR (125 MHz, $CDCl_3$, δ) 139.0, 138.8, 138.7, 138.6, 128.9, 128.8, 128.7 (3), 128.4, 128.2, 128.1 (2), 127.9 (2), 127.8 (2), 101.8, 101.1, 99.1, 80.0, 78.9, 75.8, 75.5, 75.4 (4), 73.7, 73.6, 73.1, 72.8, 72.7, 72.5, 72.2, 72.1, 69.8, 69.7, 68.1, 67.3, 61.6, 51.8, 29.8, 29.6, 29.4, 29.3, 27.1, 26.4. HRMS (ESI) Calcd for $[C_{68}H_{83}N_3O_{16}]Na^+$: 1220.5665. Found: 1220.5618.

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8-Azidooctyl 5-*O*-[3,5-*O*-(1,1,3,3-tetraisopropylsiloxane-1,3-diyl)-α-D-arabinofuranosyl]-2,3-di-*O*-benzyl-α-D-arabinofuranoside (42). Alcohol **15** (1.5 g, 3.1 mmol) was glycosylated with thioglycoside **17** (2.5 g, 3.91 mmol), as described for the preparation of **30** using powdered 4 Å molecular sieves (1.0 g), *N*-iodosuccinimide (1.04 g, 4.6 mmol) and silver triflate (150 mg, 0.58 mmol) in CH_2Cl_2 (30 mL). The product was purified by chromatography (hexanes/EtOAc, 15:1) to yield the product as an oil, which was contaminated with a *p*-thiocresol-based impurity. Therefore, a solution of the crude product in CH_2Cl_2 (25 mL) and CH_3OH (75 mL) was treated with 0.1 M $NaOCH_3$ in CH_3OH (2 mL). After stirring for 4 h, the reaction mixture was neutralized with prewashed Amberlite IR-120 (H^+) resin, filtered, and concentrated. The resulting residue was purified by chromatography (hexanes/EtOAc, 6:1) to give **42** (1.99 g, 72%) as an oil: R_f 0.28 (hexanes/EtOAc, 6:1); $[\alpha]_D$ + 31.2°(*c* 1.1, $CHCl_3$; ^1H NMR (400 MHz, $CDCl_3$, δ) 7.36–7.23 (m, 10 H), 5.01 (s, 1 H), 4.95 (d, 1 H, *J* = 0.8 Hz), 4.14–3.68 (m, 16 H), 3.25 (ddd, 1 H, *J* = 6.8, 6.8, 1.6 Hz), 3.20 (dd, 2 H, *J* = 6.8, 6.8 Hz), 1.59–1.55 (m, 4 H), 1.31–1.28 (m, 8 H) 1.10–1.00 (m, 28 H); ^{13}C NMR (100 MHz, $CDCl_3$, δ) 138.8, 137.7, 129.4, 128.9, 128.8, 128.6, 128.5, 128.4, 128.1 (2), 125.7, 108.4, 106.4, 88.6, 83.3, 82.5, 81.6, 80.9, 76.4, 72.5, 72.4, 67.8, 67.4, 61.7, 51.8, 31.0, 29.8, 29.5, 29.2, 27.0, 26.4, 18.4 (2), 17.8, 17.7, 17.5 (2), 17.4, 13.9, 13.5, 13.4, 13.2, 12.9. HRMS (ESI) Calcd for $[C_{44}H_{71}N_3O_{10}]Na^+$: 880.4570. Found: 880.4573.

8-Azidooctyl 5-*O*-(2-*O*-benzyl-α-D-arabinofuranosyl)-2,3-di-*O*-benzyl-α-D-arabinofuranoside (43). Disaccharide **42** (1.8 g, 2. 0 mmol) was benzylated with benzyl bromide (0.4 mL, 2.6 mmol) and NaH (120 mg, 5. 0 mmol) in DMF (10 mL) as described for the preparation of **27**. Following workup, the crude product was dissolved in THF (75 mL) and the solution was cooled to 0°C before *n*-Bu_4NF (4.8 mL of a 1.0 M solution in THF, 4.8 mmol) was added under an argon atmosphere. The reaction mixture was stirred for 2 h and then concentrated; the product was purified by chromatography (hexane/EtOAc, 5:1) to give **43** (880 mg, 62%) as an oil: R_f 0.21 (hexanes/EtOAc, 3:1); $[\alpha]_D$ + 11.3° (*c* 0.9, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$, δ) 7.37–7.25 (m, 15 H), 5.12 (s, 1 H), 4.99 (s, 1 H), 4.59–4.39 (m, 6 H), 4.19–4.16 (m, 1 H), 4.10–3.64 (m, 10 H), 3.35 (ddd, 1 H, *J* = 6.8, 6.8, 1.6 Hz), 3.22 (dd, 2 H, *J* = 6.8, 6.8 Hz), 1.60–1.54 (m, 4 H), 1.35–1.31 (m, 8 H); ^{13}C NMR (100 MHz, $CDCl_3$, δ) 138.0, 137.7, 137.4, 128.9 (2), 128.8, 128.5, 128.4 (2), 128.2 (2), 106.4, 105.5, 87.8, 87.4, 87.2, 84.0, 80.8, 75.6, 72.4, 72.3, 72.0, 67.9, 66.1, 63.0, 51.8, 29.8, 29.6, 29.5, 29.2, 27.0, 26.4. HRMS (ESI) Calcd for $[C_{39}H_{51}N_3O_9]Na^+$: 728.3517. Found: 728.3469.

8-Azidooctyl 5-*O*-[3,5-di-*O*-(2-*O*-benzoyl-3,5-di-*O*-benzyl-α-D-arabinofuranosyl)-2-*O*-benzyl-α-D-arabinofuranosyl]-2,3-di-*O*-benzyl-α-D-arabinofuranoside (44). Disaccharide **43** (800 mg, 1.13 mmol) was glycosylated with thioglycoside **18** (1.6 g, 2.96 mmol), as described for the preparation of **30** using powdered 4 Å molecular sieves (1.0 g), *N*-iodosuccinimide (660 mg, 2.94 mmol) and silver triflate (87 mg, 0.33 mmol) in CH_2Cl_2 (20 mL). The product was purified by chromatography (hexanes/EtOAc, 6:1) to give **44** (1.41 g, 81%) as an oil: R_f 0.31 (hexanes/EtOAc, 4:1); $[\alpha]_D$ + 42.3° (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$, δ) 7.94–7.90 (m, 4 H), 7.35–7.17 (m, 41 H), 5.47 (s, 1 H), 5.36 (s, 1 H), 5.31 (s, 2 H), 5.15 (s, 1 H), 5.00 (s, 1 H), 4.78 (d, 1 H, *J* = 11.3 Hz), 4.71 (d, 1 H, *J* = 11.3 Hz), 4.60–4.30 (m, 17 H), 4.15–3.87 (m, 6 H), 3.70 (dd, 1 H, *J* = 5.9, 2.6 Hz), 3.62–3.52 (m, 7 H), 3.36 (ddd, 1 H,

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J = 6.8, 6.8, 1.6 Hz), 3.26 (dd, 2 H, J = 6.8, 6.8 Hz), 1.58–1.51 (m, 4 H), 1.30–1.20 (m, 8 H); ^{13}C NMR (100 MHz, $CDCl_3$, δ) 165.7 (2), 138.6 (2), 138.3, 138.2, 130.3, 130.2, 128.8 (3), 128.7 (2), 128.4, 128.3 (2), 128.2, 128.1, 128.0 (3), 106.8, 106.7, 106.5, 106.0, 89.1, 88.7, 84.0, 83.6, 82.9, 82.7, 82.6, 82.1, 80.6, 73.8 (2), 72.8, 72.5 (2), 72.4, 72.3, 69.8, 69.5, 68.1, 51.9, 30.0, 29.7, 29.5, 29.3, 27.1, 26.5. HRMS (ESI) Calcd for $[C_{91}H_{99}N_3O_{19}]Na^+$: 1561.6798. Found: 1561.6824.

8-Azidooctyl 5-*O*-[3,5-di-*O*-(3,5-di-*O*-benzyl-α-D-arabinofuranosyl)-2-*O*-benzyl-α-D-arabinofuranosyl]-2,3-di-*O*-benzyl-α-D-arabinofuranoside (45). Tetrasaccharide **44** (1.35 g, 0.88 mmol) was debenzoylated as described for the preparation of **24** using 1.0 M $NaOCH_3$ in CH_3OH (0.5 mL) in CH_2Cl_2 (15 mL) and CH_3OH (10 mL). The product was purified by chromatography (hexanes/EtOAc, 3:1) to give **45** (980 mg, 85%) as an oil: R_f 0.29 (hexanes/EtOAc, 2:1); $[\alpha]_D$ + 17.6° (*c* 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, δ) 7.30–7.21 (m, 35 H), 5.13 (s, 1 H), 5.07 (s, 1 H), 5.04 (s, 1 H), 4.97 (s, 1 H), 4.60–3.80 (m, 29 H), 3.68–3.66 (m, 3 H), 3.55–3.54 (m, 2 H), 3.44–3.36 (m, 2 H), 3.27 (ddd, 1 H, J = 6.8, 6.8, 1.6 Hz), 3.20–3.16 (m, 3 H), 1.58–1.54 (m, 4 H), 1.30–1.26 (m, 8 H); ^{13}C NMR (100 MHz, $CDCl_3$, δ) 138.8, 138.3 (2), 137.9 (2), 128.9 (2), 128.8, 128.7, 128.4 (2), 128.3 (2), 128.2 (3), 128.1, 128.0 (2), 109.6, 107.6, 106.5, 106.4, 85.0, 83.5 (2), 82.8, 80.3, 78.9, 78.8, 74.0, 72.7, 72.5, 72.3, 72.2, 70.2, 70.1, 68.0, 66.1, 51.8, 29.9, 29.6, 29.5, 29.2, 27.0, 26.4. HRMS (ESI) Calcd for $[C_{77}H_{91}N_3O_{17}]Na^+$: 1352.6240. Found: 1352.6174.

8-Azidooctyl 5-*O*-{3,5-di-*O*-[2-*O*-(2,3,5-tri-*O*-benzyl-β-D-arabinofuranosyl)-3,5-di-*O*-benzyl-α-D-arabinofuranosyl]-2-*O*-benzyl-α-D-arabinofuranosyl]-2,3-di-*O*-benzyl-α-D-arabinofuranoside (46). Tetrasaccharide **45** (500 mg, 0.37 mmol) and thioglycoside **19** (593 mg, 1.12 mmol) were dissolved in CH_2Cl_2 (30 mL) and powdered 4 Å molecular sieves (2.0 g) were added. The reaction mixture was cooled to − 78°C and stirred for 20 min before the addition of *N*-iodosuccinimide (25 mg, 1.1 mmol) and silver triflate (28 mg, 0.10 mmol). After being stirred for 2 h at − 78°C, Et_3N was added until the solution changed from red to yellow and then the reaction mixture was diluted with CH_2Cl_2 and filtered through Celite. The filtrate was washed in succession with a saturated aqueous solution of $Na_2S_2O_3$, water, and brine, before being dried (Na_2SO_4) and concentrated. Chromatography of the resulting residue (hexanes/EtOAc, 10:1) gave **46** (65 mg, 81%) as an oil: R_f 0.45 (hexanes/EtOAc, 4:1); $[\alpha]_D$ + 26.2° (*c* 0.9, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, δ) 7.29–7.16 (m, 65 H), 5.11 (s, 2 H), 5.09–5.07 (m, 2 H), 4.95 (d, 1 H, J = 4.8 Hz), 4.93 (s, 1 H), 4.61–4.05 (m, 45 H), 3.99–3.51 (m, 12 H), 3.21 (ddd, 1 H, J = 6.8, 6.8, 1.6 Hz), 3.19 (dd, 2 H, J = 6.8, 6.8 Hz), 1.56–1.54 (m, 4 H), 1.28–1.26 (m, 8 H); ^{13}C NMR (100 MHz, $CDCl_3$, δ) 138.7 (2), 138.2, 138.1, 128.3 (3), 128.7 (2), 128.6, 128.4, 128.2 (2), 128.1 92), 128.0 (2), 127.9, 107.0, 106.6 106.5, 105.7, 100.7, 100.4, 89.0, 86.4, 86.2, 84.6, 84.5 (2), 84.4, 83.6, 83.5 (2), 82.1, 81.6, 80.6, 80.5, 80.4, 80.3, 73.7 (2), 73.5, 73.4, 72.7 (2), 72.6, 72.4 (2), 72.2, 70.4, 70.3, 68.0, 66.4, 65.8, 51.8, 29.9, 29.7, 29.5, 29.2, 27.1, 26.5. HRMS (ESI) Calcd for $[C_{129}H_{143}N_3O_{25}]Na^+$: 2157.9936. Found: 2157.9967.

8-Aminooctyl 5-*O*-{3,5-di-*O*-(2-*O*-[2,3,5-tri-*O*-benzyl-β-D-arabinofuranosyl]-3,5-di-*O*-benzyl-α-D-arabinofuranosyl)-2-*O*-benzyl-α-D-arabinofuranosyl]-2,3-di-*O*-benzyl-α-D-arabinofuranoside (47). To a solution of **46** (300 mg, 0.14 mmol) in THF:water (10 mL, 10:1) was added Ph_3P (73 mg, 0.27 mmol) at 0°C. The reaction

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mixture was stirred for 10 h while warming to rt and then concentrated to an oil, which was purified by chromatography (CH_2Cl_2/CH_3OH, 10:1) to give **47** (235 mg, 78%) as an oil: R_f 0.20 (CH_2Cl_2/CH_3OH, 8:1); $[\alpha]_D$ + 33.1°(*c* 1.1, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$, δ) 7.35–7.10 (m, 65 H), 5.16 (s, 1 H), 5.15 (s, 1 H), 5.11–5.10 (m, 2 H), 4.98 (d, 1 H, *J* = 4.8 Hz), 4.96 (s, 1 H), 4.62–4.30 (m, 34 H), 4.09–3.88 (m, 16 H), 3.67–3.47 (m, 12 H), 3.32 (ddd, *J* = 6.8, 6.8, 1.6 Hz), 3.16 (dd, 2 H, *J* = 6.8, 6.8 Hz), 1.52–1.27 (m, 12 H); ^{13}C NMR (100 MHz, $CDCl_3$, δ) 138.8 (2), 138.6, 138.3, 129.0, 128.9 (3), 128.8, 128.7, 128.5 (2), 128.4, 128.3, 128.2 (2), 128.1 (2), 128.0, 107.2, 106.6 (2), 105.9, 100.9, 100.6, 89.1, 84.6, 84.5, 83.7, 83.6(3), 73.8, 73.6, 73.5, 72.8(2), 72.7 (2), 72.6, 72.5 (2), 72.3, 70.5, 68.1, 66.4, 42.3, 30.9, 29.9, 29.8, 28.1, 27.3, 26.6. HRMS (ESI) Calcd for $[C_{129}H_{146}N_3O_{25}]Na^+$: 2110.0212. Found: 2110.0141.

8-Trifluoroacetamidooctyl 5-*O*-(3,5-di-*O*-(2-*O*-(β-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl}-α-D-arabinofuranoside (48). To a solution of **47** (200 mg, 0.09 mmol) in pyridine (5 mL) was added trifluoroacetic anhydride (0.04 mL, 2.8 mmol). The reaction mixture was stirred for 24 h, then diluted with CH_2Cl_2, washed with water, and concentrated. Purification of the product by chromatography (CH_2Cl_2/CH_3OH, 10:1) gave an oil, which was immediately dissolved in CH_3OH (10 mL) and then 10% Pd/C (30 mg) was added. The solution was stirred overnight under a H_2 atmosphere and then the catalyst was filtered away. The filtrate was concentrated to a residue, which was purified by chromatography on latrobeads (CH_2Cl_2/CH_3OH, 1:1) to give **48** (64 mg, 65%) as an oil: R_f 0.12 (CH_2Cl_2/CH_3OH,5:1)); $[\alpha]_D$ + 7.1° (*c* 0.4, H_2O); ^1H NMR (400 MHz, D_2O, δ) 5.16 (s, 1 H), 5.12 (s, 1 H), 5.07 (d, 1 H, *J* = 4.8 Hz), 5.02–5.01 (m, 2 H), 4.92 (s, 1 H), 4.20–3.49 (m, 32 H), 3.25 (ddd, 1 H, *J* = 6.8, 6.8, 1.6 Hz), 3.21 (dd, 2 H, *J* = 6.8, 6.8 Hz), 1.52–1.49 (m, 4 H), 1.25–1.18 (m, 8 H); ^{13}C NMR (100 MHz, D_2O, δ) 179.0, 107.5, 106.0, 105.8, 101.1, 100.9, 87.4, 87.1, 83.2, 83.1, 82.9, 82.3, 82.1, 81.9, 81.6, 79.5, 76.6, 75.0, 74.5, 74.4, 68.9, 63.3, 63.2, 60.9, 40.1, 28.9, 28.6, 28.5, 28.0, 26.1, 25.4. HRMS (ESI) Calcd for $[C_{40}H_{66}F_3NO_{26}]Na^+$: 1056.3717. Found: 1056.3672.

ACKNOWLEDGMENTS

This work was supported by The National Institutes of Health. CSC's contributions to this work were supported by an American Chemical Society Division of Organic Chemistry Fellowship sponsored by Aventis Pharmaceuticals.

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Received October 25, 2002
Accepted February 5, 2003

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