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Rapid, iterative assembly of octyl α-1,6-oligomannosides and their 6-deoxy equivalents†

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Mycobacterium tuberculosis is the cause of the deadly human disease tuberculosis. In studies over the last 40 years it has been revealed that this organism possesses a complex cell wall including glycophospholipids such as the phosphatidylinositiol mannosides (PIMs), lipomannan (LM) and lipoarabinomannan (LAM). These glycolipids all contain a common α-1,6-linked mannoside core, and the higher PIMs and LAM possess α-1,2-linked mannosyl residues. It has been shown that simple α-1,6-linked oligomannosides can act as substrates for α-1,6-mannosyltransferases in mycobacteria. Here we report a simple iterative synthesis of a series of hydrophobic octyl α-1,6-linked oligomannosides from mono- through to tetrasaccharides. We have utilized a single thioglycoside donor and alcohol acceptor. Further, we have developed conditions for the conversion of each of these compounds to the 6-deoxy congeners. Deoxygenation of the 6-position of the terminal mannosyl residue should prevent these compounds acting as substrates for the abundant α-1,6-mannosyltransferases in mycobacteria and should permit detection of the elusive α-1,2-mannosyltransferase activity responsible for elaboration of LM to mature LAM and the biosynthesis of the higher PIMs.

Introduction

An estimated one third of the global population (almost 2 billion people) carries *Mycobacterium tuberculosis*, the causative agent of tuberculosis (TB). Each year approximately 9 million of those infected will develop active disease, resulting in up to 2 million deaths. TB is the leading killer of women of child bearing age and is the major cause of death of HIV positive individuals.[1] The advent of the HIV/AIDS pandemic is the principal cause of the dramatic resurgence of TB, particularly in sub-Saharan Africa. In tandem recent outbreaks of drug resistant TB in many industrialized nations have resulted in a resurgence of interest in the disease, and basic research and drug development have again become priorities.

An ideal TB drug target is the biosynthesis of the mycobacterial cell wall, which is unusually thick and lipid rich.[2] Drugs such as isoniazid, ethambutol and ethionamide already target aspects of cell wall biosynthesis.[3,4] The cell wall is critical for the integrity of the bacterium, allowing it to survive and propagate within the human host. Mycobacteria possess a unique set of cell wall glycolipids, the phosphatidylinositol mannosides (PIMs), lipomannan (LM), and lipoarabinomannan (LAM) (Fig. 1).[5] Biochemical studies have revealed that PIMs, LM and LAM are biosynthetically related[6,7] and recent genetic studies have validated this set of molecules as a promising target for therapeutic intervention in the treatment of mycobacterial diseases including tuberculosis.[8,9] Studies on an early step of PIM, LM, and LAM biosynthesis, that catalyzed by the α-mannosyltransferase PimA, have provided clear, unambiguous evidence for the essentiality of these molecules. In particular a study of a conditional mutant of *pimA* in *Mycobacterium smegmatis* have shown this to be an essential gene in this organism and provides strong evidence that PIM, LM and LAM biosynthesis are essential for the survival of mycobacteria.[9]

† Dedicated to Associate Professor Bob Stick on the occasion of his 60th birthday.

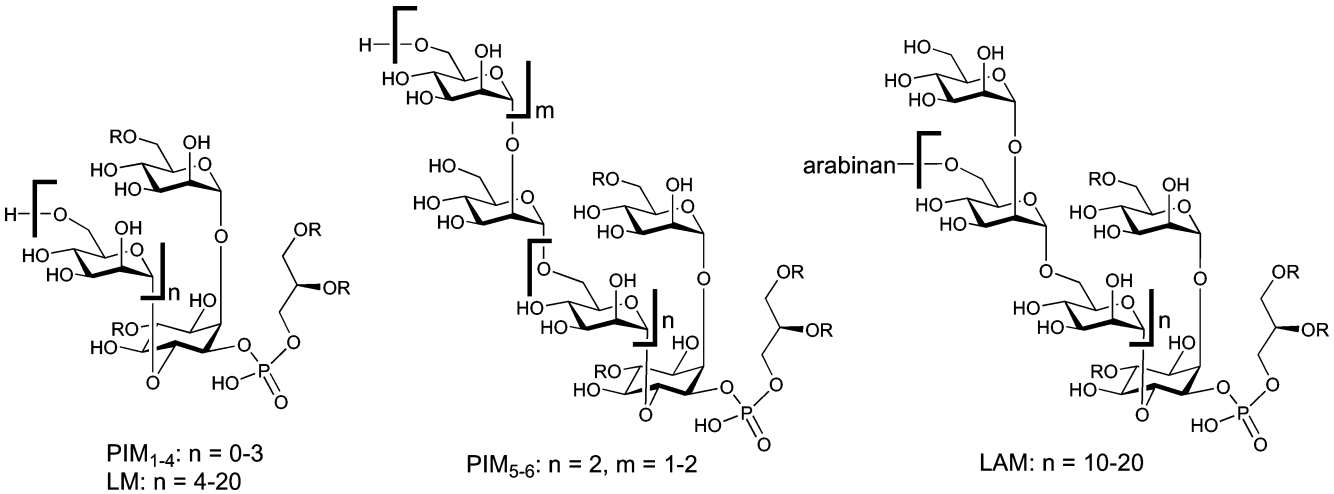

Fig. 1 Typical structures of phosphatidylinositol mannosides (PIMs), lipomannan (LM) and lipoarabinomannan (LAM). Common accepted ranges for the number of mannose residues are given. "R" stands for various fatty acyl groups such as palmitic, stearic and tuberculostearic acids.

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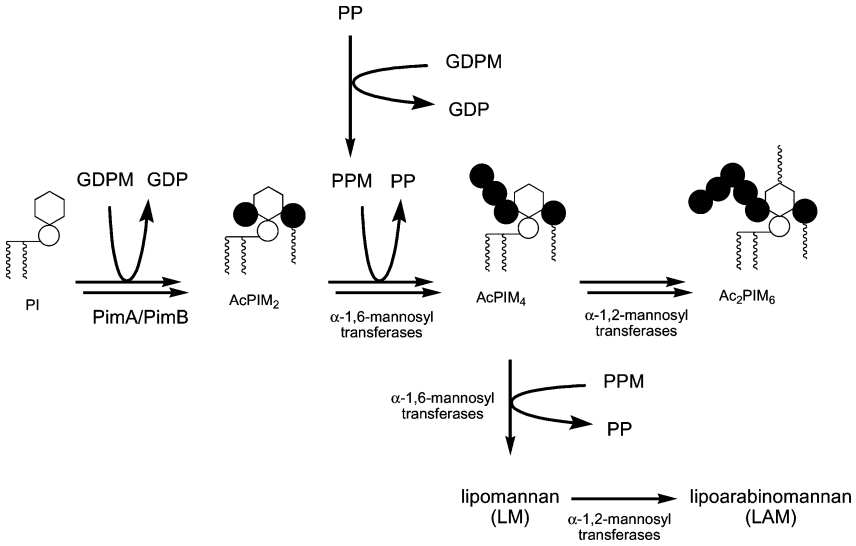


Fig. 2 Abbreviated biosynthesis of PIMs, LM and LAM highlighting the action of α-1,6- and α-1,2-mannosyltransferases. The hexagon indicates inositol, an open circle indicates phosphate and α-mannosyl residues are shown with a closed circle.

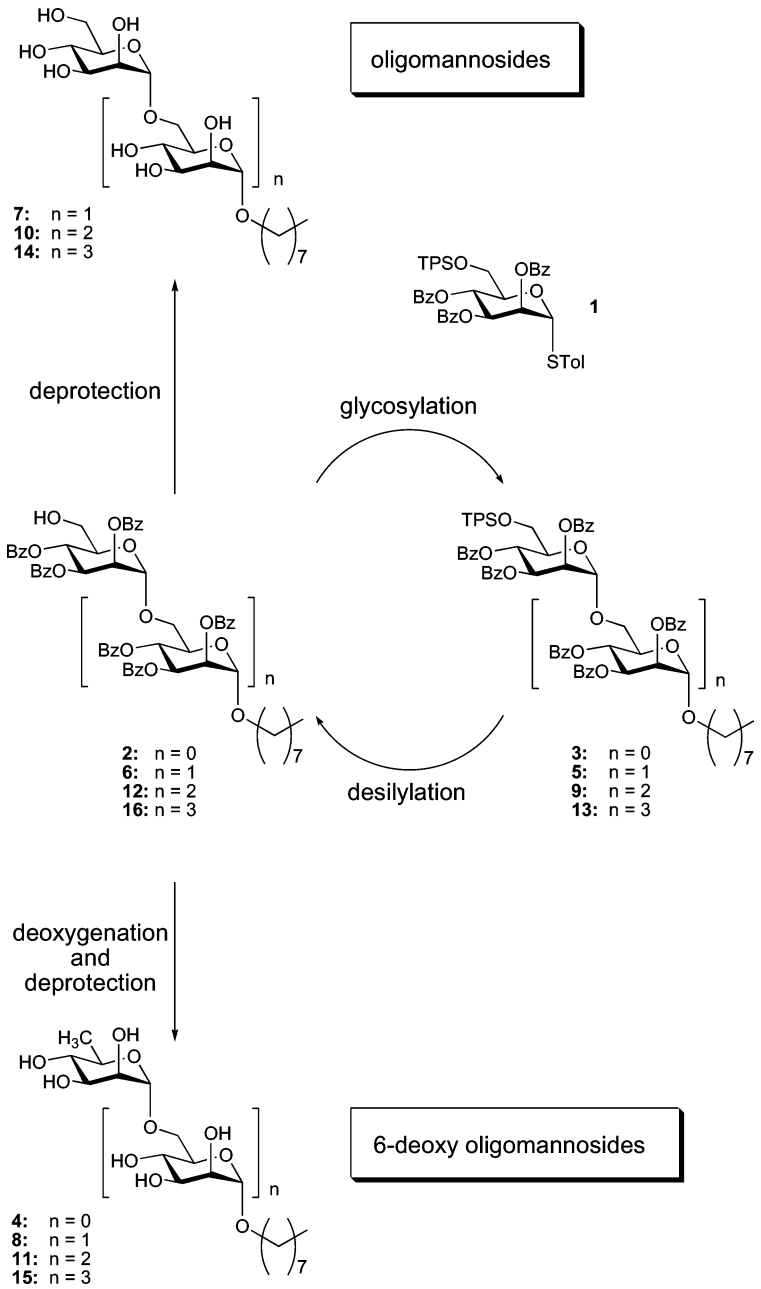
PIM, LM and LAM share a common phosphatidylinositol core. This core is elaborated with α-mannosyl residues, with the first being added to the 6-position (to afford PIM_1) and a chain of α-1,6-linked mannosyl residues being built up on the 2-position, leading sequentially to the higher PIMs, LM, and then LAM (Fig. 2).[6] Mature LAM possesses single α-1,2-linked mannosyl residues off the main α-1,6-linked mannan chain. Efforts to study PIM and LAM biosynthesis have been restricted by the limited availability of substrates for these enzymes. While total syntheses of some PIMs have been reported,[10–13] these challenging routes are not readily accessible for the wider community, and systematic modifications of these molecules is by no means simple. Simplified structures that can act as substrates for enzymes in PIM, LM and LAM biosynthesis offer an alternative method for their study.

In pioneering studies Yokoyama and Ballou showed that mannose, methyl α-mannopyranoside and α-1,6-linked mannose oligomers could act as substrates for α-1,6-mannosyltransferases from *M. smegmatis*.[14] More recently, Brown and co-workers have reported the synthesis of a series of alkyl and alkenyl di- and trimannosides for the study of mycobacterial glycolipid biosynthesis.[15] These compounds were demonstrated to act as substrates for polyprenolmannose-dependent α-1,6-mannosyltranferases within a mycobacterial cell free system. Brown *et al.* showed that each of the dimannosides was extended by *M. smegmatis* extracts to the respective tri- and tetramannosides, whilst the trimannoside underwent extension to both the tetra- and pentamannoside; subsequent characterization of these products showed them all to be α-1,6-linked. Together these studies have shown that much simpler analogues of the PIMs can function as substrates for mycobacterial mannosyltransferases. However, the syntheses of these substrates were rather inefficient, with the mannose oligomers in the work of Yokoyama and Ballou being obtained through laborious degradation of yeast mannan and in the case of Brown *et al.* each compound was synthesized individually through synthetic routes that utilized different donors to prepare the di- and trisaccharides. Zhu and Kong have reported a simple iterative approach to di- through to dodecamannosides using largely unprotected glycosides as acceptors.[16] While quite efficient this route, along with those of Brown and co-workers, does not allow simple modification of the carbohydrate rings, which could be of great value to learn more about the active site architecture of these mannosyltransferases. Additionally, modified substrates may also show inhibitory effects towards these mannosyltransferases and may act as substrates of other mannosyltransferases. Besra and co-workers have recently reported studies of modified α-1,6-dimannosides and have identified moderate inhibitors obtained through modifications of the 2′,6′-positions.[17] Notably, while the di- and trimannosides of Brown and co-workers were excellent substrates for α-1,6-mannosyltransferases, none of these compounds could act as substrates for the much rarer α-1,2-mannosyltransferase(s) involved in the biosynthesis of PIM_5 and PIM_6 and in installing α-1,2-linked mannosyl groups on mature LAM.

Here we report an efficient iterative synthesis of a series of α-1,6-linked hydrophobic mono-, di-, tri-, and tetramannosides. The choice of a hydrophobic octyl glycoside capping group was made as such derivatives allow simple solvent partitioning of products from radiolabelled GDP-mannose in enzymic assays.[18] We have utilized a single glycosyl acceptor **1** and donor **2**, each prepared from mannose pentaacetate. Further, we have developed conditions for the conversion of each of these compounds to the corresponding 6-deoxy congeners. Deoxygenation of the 6-position of the terminal mannosyl residue should prevent these compounds acting as substrates for the abundant α-1,6-mannosyltransferases in mycobacteria and should permit detection of the elusive α-1,2-mannosyltransferase activity responsible for elaboration of LM to mature LAM and the biosynthesis of PIM_5 and PIM_6.

Results and discussion

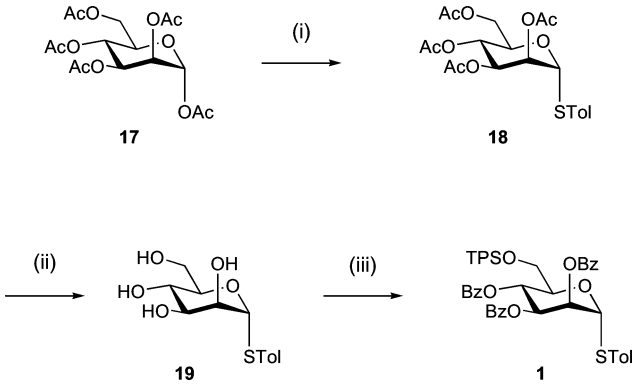
Previous approaches to the synthesis of α-1,6-oligomannosides have largely relied on glycosyl halides or trichloroacetimidates.[15,16,19] While these agents are effective glycosyl donors the lability of the anomeric leaving group does not permit facile modification of the carbohydrate ring prior to glycosylation as is sought here for the preparation of the 6-deoxy congeners. Thioglycosides present themselves as a possible alternative glycosyl donor, with the robustness of the anomeric thio substituent allowing protecting group manipulations prior to glycosylation. Thioglycosides as donors have recently been reported for the synthesis of several modified α-1,6-linked dimannosides.[17,20,21] Here, owing to the repeating nature of the target oligomers, an iterative approach was thought appropriate, using a single glycosyl donor **1** and an alcohol **2** (Scheme 1). The alcohol **2**, derived in turn from the TPS ether **3**, can immediately give rise to the 6-deoxy monomannoside **4** through sequential deoxygenation and deprotection. Alternatively, following condensation of donor **1** and alcohol **2** to give the disaccharide **5**, the silyl ether can be removed, affording the



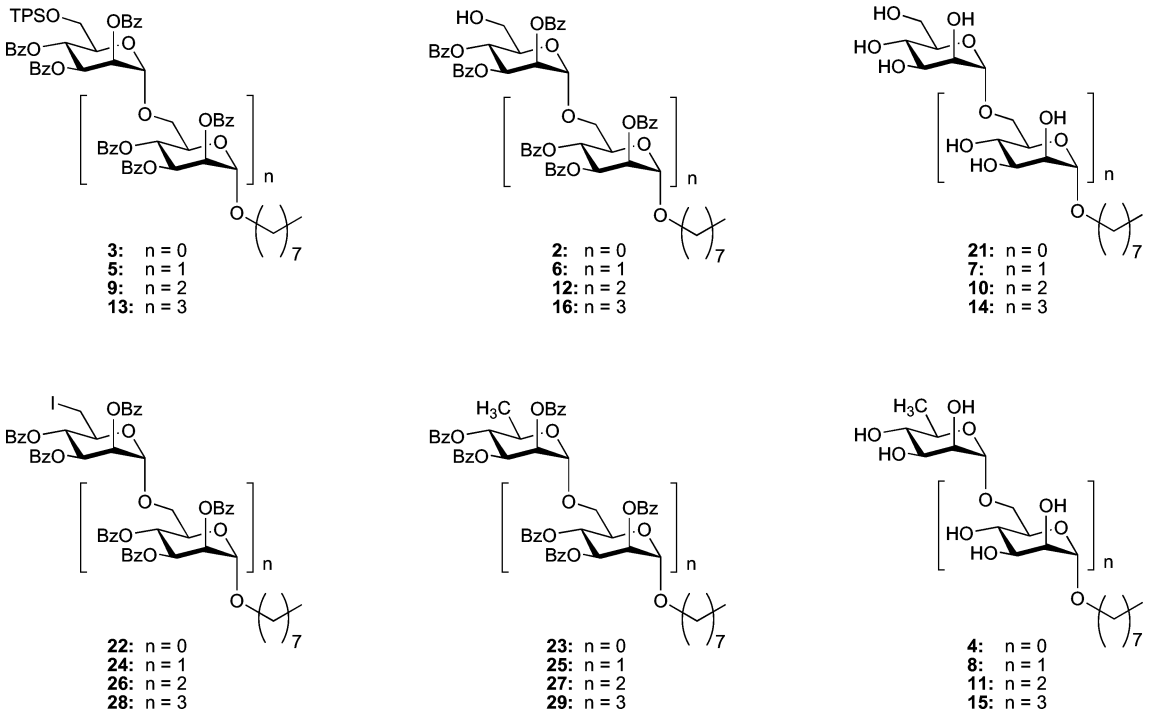
Scheme 1 Iterative synthesis of octyl oligomannosides and 6-deoxy congeners using a single glycosyl donor **1** and acceptor **2**.

disaccharide alcohol **6**. This alcohol can then provide access to the dimannoside **7**, or the 6-deoxy dimannoside **8** through an intermediate deoxygenation step. Iteration of these steps gives access to the higher homologues: glycosylation of the alcohol **6** with donor **1** will furnish the trimannoside **9**, which again can be converted to either of the trimannosides **10** or **11** or in turn become a glycosyl acceptor **12** for extension to a tetramannoside **13**. The tetramannoside **13** can be treated in an identical manner to give the tetramannosides **14** and **15**, *via* the intermediate alcohol **16**.

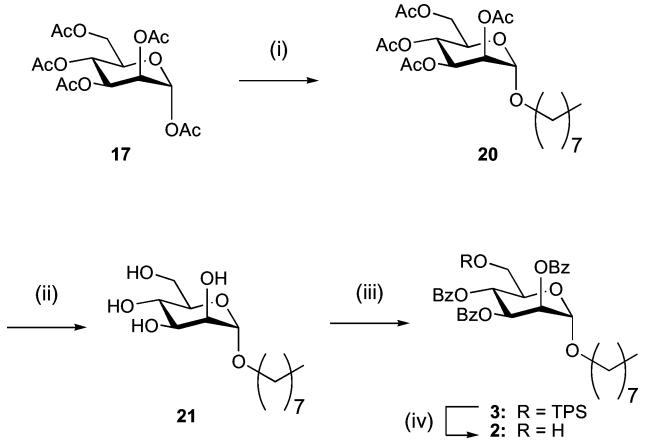
The donor **1** was prepared from mannose pentaacetate **17** in a simple four-step sequence (Scheme 2). Tin(IV) chloride-catalyzed condensation of pentaacetate **17** and thiocresol afforded the thioglycoside **18**, which was deacetylated with catalytic sodium in methanol to afford the tetraol **19**. Thiocresol was chosen as it is a crystalline thiol and significantly less malodorous than thiophenol. Additionally, the 4-methyl group is an excellent spectroscopic reporter of the presence of this substituent in ^{1}H NMR spectra, particularly when other aromatic protecting groups obscure the remaining aromatic protons. The tetraol **19** was selectively protected at the primary position with a bulky TPS ether by treatment with TPSCl according to the procedure



Scheme 2 *Reagents and conditions*: (i) thiocresol, cat. $SnCl_4$, CH_2Cl_2; (ii) cat. NaOMe, MeOH, 27% from mannose; (iii) a) TPSCl, imidazole, DMF, b) BzCl, pyridine, 49%.



of Corey and Venkateswarlu.[22] The TPS ether was chosen over the more readily cleaved TBS alternative as it has been reported that TBS ethers are unstable to halonium ion sources (*e.g.* NIS), conditions that were planned for the eventual glycosylation.[23] Finally, treatment of the intermediate triol with benzoyl chloride and pyridine afforded the target donor **1**. Surprisingly, residual benzoic acid at this step proved challenging to remove, perhaps due to the presence of silanol by-products, with the sugar *after* chromatography requiring a wash with potassium carbonate solution in order to give pure donor **1**.



Scheme 3 *Reagents and conditions*: (i) octanol, cat. $SnCl_4$, CH_2Cl_2; (ii) cat. NaOMe, MeOH, 33% from mannose; (iii) a) TPSCl, imidazole, DMF, b) BzCl, pyridine, 55%; (iv) HCl, MeOH, Et_2O, 58%.

Acquisition of the glycosyl acceptor **2** was the next objective (Scheme 3). Mannose pentaacetate **17** was treated with 1-octanol and stannic chloride to afford the intermediate tetraacetate **20**. The tetraacetate **20** was deacetylated using catalytic sodium methoxide in methanol to afford the octyl mannoside **21**.[24] As for the glycosyl donor, the octyl mannoside **21** was selectively protected at the primary alcohol using TPSCl, with the remaining hydroxyls protected as benzoate esters through treatment with BzCl, pyridine and DMAP, affording the silyl ether **3** in good yield (55%). Again, residual benzoic acid could not be completely removed during work-up or by chromatography but was readily separated afterwards. The silyl ether of **3** was selectively removed using HCl, MeOH and diethyl ether (prepared *in situ* from AcCl) to afford the alcohol **2** in a good yield (58%).

While a 6-deoxy monomannoside **4** was unlikely to act as a particularly efficacious substrate for mycobacterial α-1,2-mannosyltransferases, its synthesis provided a simple model for deoxygenation that could be applied to the higher homologues. The 6-deoxy monomannoside **4** was synthesized from the alcohol **2** over three steps. Initially, the primary alcohol **2** was treated with Ph_3P, imidazole and iodine, to afford the iodide **22** in a good yield (86%). The successful introduction of iodine was revealed in the ^{13}C NMR spectrum, which reported a characteristic chemical shift (δ 5.1 ppm) for C6 attached to I. The iodide **22** underwent reduction upon treatment with Bu_3SnH and catalytic AIBN in toluene, to give the protected 6-deoxy mannoside **23** in a good yield (76%). Here, partitioning between petroleum spirit and acetonitrile was used to separate the bulk of tributyltin species; however, the surprisingly good solubility of the 6-deoxy mannoside **23** in the non-polar phase required repeated back extraction with acetonitrile to ensure good mass recovery. The protected 6-deoxy mannoside **23** underwent global deprotection using catalytic NaOMe in MeOH to give the fully deprotected 6-deoxy mannoside **4**. Purification of 6-deoxy mannoside **4** by flash chromatography was not complete, so **4** was further purified on a C_{18} reverse phase silica column using a water–methanol gradient. This worked in removing trace impurities that had been otherwise inseparable.

Efforts then moved to the coupling of the glycosyl donor **1** and the glycosyl acceptor **2**. The monosaccharides **1** and **2** were treated with *N*-iodosuccinimide and catalytic triflic acid to afford the fully protected disaccharide **5**. The stereoselective formation of the α-anomer in this case can be explained by invoking neighbouring group participation by the benzoyl group at the 2-position of the glycosyl donor **1**.‡ Despite our best efforts the disaccharide **5** could not be purified by flash chromatography, so the crude product was selectively deprotected using HCl, MeOH and Et_2O, yielding alcohol **6**,

‡ Evidence for the exclusive formation of the α-anomer in this and subsequent glycosylations was obtained through examination of the $^1J_{C,H}$ coupling constants for the anomeric carbons of the tetramannoside **16**. Each coupling constant was > 170 Hz, thereby showing that all *O*-glycosidic linkages formed in this manuscript were α.[28]

which was readily purified (71% over two steps). The primary alcohol **6** underwent global deprotection using catalytic NaOMe in MeOH to afford the dimannoside **7**. Again, C_{18} silica gel chromatography was necessary to effect adequate purification of **7**.

The corresponding 6-deoxy dimannoside **8** was synthesized in an identical fashion as for the 6-deoxy monomannoside **4**, by way of conversion of the primary alcohol to the iodide and then its reduction. Thus, the primary alcohol **6** was treated with Ph_3P, imidazole and iodine in toluene to afford the iodide **24** in high yield (94%). The iodide **24** was reduced using Bu_3SnH–cat. AIBN in toluene, affording the 6-deoxy dimannoside **25** (79%). Here, and for the higher homologues, no difficulties were encountered in the acetonitrile–petroleum spirit partitioning step used to remove tributyltin species. Debenzoylation of the protected dimannoside **25** using NaOMe in MeOH yielded the 6-deoxy dimannoside **8** (77%).

The next targets were the trimannosides **10** and **11**. Illustrating the iterative nature of this synthetic route, the primary alcohol **6** was coupled with the glycosyl donor **1** under identical conditions as for the disaccharides, using NIS and TfOH, affording the silyl trimannoside **9** (90%). The silyl trimannoside **9** was selectively deprotected as for **3** and **5**, providing the primary alcohol **12**. As for the corresponding dimannoside, the partially protected trimannoside **12** was treated with catalytic NaOMe in methanol, affording the trimannoside **10** (70%). The 6-deoxy trimannoside **11** was synthesized in the same manner as for the mono- and dimannosides **4** and **8**. The trisaccharide alcohol **12** was treated with Ph_3P, imidazole and iodine in toluene affording the iodide **26** (87%). Treatment of **26** with Bu_3SnH–cat. AIBN in toluene afforded the protected 6-deoxy trimannoside **27** (88%). Deacylation of the protected trimannoside **27** using NaOMe and methanol yielded the 6-deoxy trimannoside **11**.

The robust capabilities of this synthetic approach were demonstrated through the synthesis of the 6-hydroxy and 6-deoxy tetramannosides **14** and **15**. The primary alcohol **12** was coupled with the glycosyl donor **2**, again using NIS–TfOH, to give the fully protected trimannoside **13** isolated in good yield (91%). The silyl ether was removed from **13** using HCl, MeOH and diethyl ether to yield the primary alcohol **16** (78%). The alcohol **16** was globally deprotected in the usual fashion to yield the tetramannoside **14** in a low but acceptable yield (30%). Again, a three step procedure was used to give rise to the 6-deoxy tetramannoside **15**. The alcohol **16** was treated with Ph_3P, imidazole and iodine in toluene to afford the primary iodide **28** (92%). The iodide **28** was reduced using Bu_3SnH–cat. AIBN in toluene, to yield the 6-deoxy protected tetramannoside **29** (93%). Finally, deacetylation using NaOMe and methanol afforded the last of the targets, the 6-deoxy tetramannoside **15** (44%).

Several features of this efficient route merit comment. The method used for selective deprotection of the TPS group, HCl in MeOH–Et_2O, is extremely robust and gave consistent results throughout this sequence.[25] It appears to be independent of the chain length of the oligomers and in no cases were appreciable amounts of methanolysis of any glycosidic linkage observed. Glycosylation of the carbohydrate alcohols was also efficient and, while this route was enacted only to the point of tetrasaccharides as the octyl moiety loses efficiency in solvent partitioning for longer oligomers, higher homologues should be accessible without appreciable reductions in yield. It is noteworthy that the inclusion of an octyl glycoside, originally made with consideration of the ability of this group to assist in solvent partitioning during biochemical assays, provides a useful hydrophobic handle for C_{18} reverse phase silica chromatography of the deprotected compounds.

Preliminary studies have revealed that the di-, tri- and tetrasaccharides **7, 10** and **14** all appear to act as substrates for mannosyltransferases in a cell free *M. smegmatis* system using radiolabelled GDP-mannose as substrate. The mannosyltransferase activity is amphomycin sensitive demonstrating that the transferase activity being detected is polyprenolmannose-dependent. Thus, the disaccharide **7** can be used as a reagent to detect polyprenol-mannose dependent mannosyltransferase(s). Density centrifugation of a cell free extract of *M. smegmatis* resulted in separation of polyprenolmannose synthase and polyprenolmannose-dependent mannosyltransferases, suggesting functional compartmentalization of enzymes involved in mycobacterial glycolipid biosynthesis.[26] Additionally, the 6-deoxy di- and trisaccharides **8** and **11** also appear to act as weak mannosyltransferase substrates. Ongoing studies aim to elucidate the structures of the new products.

Conclusion

We have defined a rapid, stepwise route to a series of α-1,6-linked hydrophobic oligomannosides. The donor **1** and acceptor **2** are prepared from mannose pentaacetate **17** in 3 and 4 steps, respectively. Couplings are performed using highly efficient NIS–TfOH thioglycosylations. The choice of benzoate esters as protecting groups will allow future modification of the synthetic route to install sensitive aglycons for bioconjugations. Deoxygenation of the primary alcohols of the products is achieved through iodination and reductive deoxygenation to give the corresponding 6-deoxy analogues and in future introduction of alternative substituents at this position will be possible. The inclusion of a hydrophobic aglycon allowed for simple purification of the deprotected compounds on reverse phase silica and will assist in solvent partitioning of radiolabelled products in biochemical assays, or the capture of radiolabelled products on hydrophobic membranes. We shall report on the use of these oligomannosides as tools for the study of mycobacterial glycolipid biosynthesis in due course.

Experimental

Thin layer chromatography (TLC) was performed with Merck Silica Gel 60 F_{254}, using mixtures of petroleum spirits–ethyl acetate unless otherwise stated. Detection was effected by either charring in a mixture of 5% sulfuric acid–MeOH and/or by visualization in UV light. NMR spectra were obtained on a Unity 400 machine (Melbourne, Australia). *J* values are given in Hz. Superscript $^{A, B, C, D}$ refer to carbohydrate rings labelled from the reducing end for di-, tri- and tetrasaccharides. Flash chromatography was performed according to the method of Still *et al.* with Merck Silica Gel 60, using adjusted mixtures of ethyl acetate–petroleum spirits unless otherwise stated.[27] Fully deprotected compounds were purified by reverse phase chromatography using C_{18} silica cartridges (900 mg, C_{18}, Alltech Associates). $(CH_2Cl)_2$ was dried over P_2O_5. Toluene was dried over sodium metal. Solvents were evaporated under reduced pressure using a rotary evaporator. Optical rotations were obtained using a JASCO DIP-1000 polarimeter. $[\alpha]_D$ values are given in 10^{-1} cm^2 g^{-1}. The melting point was obtained using an Electrothermal melting point apparatus and is uncorrected. Elemental analyses were performed by C.M.A.S. (Belmont, Victoria). High resolution mass spectra were performed by Sally Duck at the Chemistry Department, Monash University.

1,2,3,4,6-Penta-*O*-acetyl-α-D-mannose 17

Sulfuric acid (2 drops) was added at 0 °C to a stirred mixture of acetic anhydride (27 mL) and D-mannose (4.98 g, 27.8 mmol). The mixture was stirred for 10 min at 0 °C and then allowed to warm to room temperature and stirred for a further 30 min. The mixture was then diluted with ice–water (100 mL), and the organic phase extracted with EtOAc (100 mL). The extract was washed with water (3 × 100 mL) and then sat. aq. $NaHCO_3$. The extract was dried ($MgSO_4$) and the solvent evaporated under reduced pressure to afford the pentaacetate **17** (9.64 g) as a pale yellow oil, δ_H(399.7 MHz; $CDCl_3$; Me_4Si) 1.99, 2.04, 2.08, 2.15, 2.16 (15 H, s, Me), 4.02–4.06 (1 H, m, H5), 4.08 (1H, dd, $J_{5,6}$

2.4, $J_{6,6}$ 12.4, H6), 4.26 (1 H, dd, $J_{5,6}$ 5.2, $J_{6,6}$ 12.4, H6), 5.23–5.34 (3 H, m, H2,3,4), 6.06 (1 H, d, $J_{1,2}$ 2.0, H1); δ_C(100.1 MHz; d_4-MeOH; MeOH) 20.59, 20.66, 20.72, 20.81 (5 C, CH_3), 61.99, 65.40, 68.23, 68.65, 70.51 (5 C, C2,3,4,5,6), 90.51 (1 C, C1), 168.03, 169.48, 169.69, 169.95, 170.61 (5C, C=O).

4-Methylphenyl 1-thio-α-D-mannopyranoside 19

$SnCl_4$ (0.75 mL) was added to a stirred mixture of thiocresol (2.85 g, 22.9 mmol) and the crude pentaacetate **17** (8.54 g, 21.9 mmol) dissolved in CH_2Cl_2 (35 mL). The mixture was stirred for 24 h, then was quenched with HCl (1 M, 100 mL), and stirred for 10 min. The mixture was washed with HCl (1 M, 2 × 100 mL), followed by aq. $NaHCO_3$ (100 mL). The organic extract was dried ($MgSO_4$) and the solvent evaporated under reduced pressure. Flash chromatography (35:65 EtOAc–pet. spirits) afforded the tetraacetate **18** (6.64 g, 14.6 mmol) as a yellow oil. This oil was dissolved in MeOH (30 mL) and treated with a small piece of sodium metal. The solution was stirred for 1 h until TLC (17 : 2 : 1 EtOAc–MeOH–H_2O) indicated the reaction was complete. Dowex-50 resin (H^+ form) was added to neutralize the solution (litmus paper) and, following filtration, the solvent was evaporated from the filtrate to give a pale brown residue. This residue was recrystallized to give the tetraol **19** (2.19 g, 27% from mannose) as white cubic crystals, mp 138.5–140 °C (from MeOH–EtOAc–petroleum spirits); $[\alpha]_D^{19}$ +279 (*c* 0.7 in MeOH); δ_H(399.7 MHz; d_4-MeOH, MeOH) 2.29 (3H, s, CH_3), 3.68–4.09 (4 H, m, H3,4,6,6), 4.04 (1 H, dd, $J_{1,2}$ 1.6, $J_{2,3}$ 2.8, H2), 4.85 (1 H, br s, H5), 5.35 (1 H, d, H1), 7.09–7.39 (4 H, m Ar); δ_C(100.1 MHz; d_4-MeOH, MeOH) 21.09 (1 C, CH_3), 62.53, 68.63, 73.08, 73.57, 75.44 (5 C, C2,3,4,5,6), 90.68 (1 C, C1), 130.71, 132.00, 133.44, 138.84 (4 C, Ar); *m/z* (ESI) 309.0767 ([M + Na]$^+$ $C_{13}H_{18}O_5S$ requires 309.0773).

4-Methylphenyl 2,3,4-tri-*O*-benzoyl-6-*O*-(*tert*-butyldiphenylsilyl)-1-thio-α-D-mannoside 1

tert-Butylchlorodiphenylsilane (1.19 mL, 4.51 mmol) was added to a mixture of the tetraol **19** (0.994 g, 3.47 mmol) and imidazole (0.63 g, 8.69 mmol) in DMF (2.0 mL). The mixture was stirred at 35 °C for 3 h then was quenched with water (5 mL) and stirred for 10 min. The mixture was diluted with EtOAc (30 mL) and washed sequentially with water (3 × 30 mL), HCl (1 M, 40 mL), and sat. aq. $NaHCO_3$ (40 mL). The organic extract was dried ($MgSO_4$) and the solvent evaporated under reduced pressure. To the syrupy residue benzoyl chloride (1.81 mL, 15.6 mmol), pyridine (2.52 mL, 31.2 mmol) and catalytic DMAP (20 mg) were added. The mixture was stirred for 18 h and then quenched with water (2 mL) and stirred for a further 10 min. The mixture was diluted with EtOAc (30 mL) and washed with water (3 × 30 mL) and aq. K_2CO_3 solution (0.5 M). The organic phase was dried ($MgSO_4$) and the solvent evaporated under reduced pressure. Flash chromatography (8 : 92 EtOAc–pet. spirits) yielded a residue, which was washed with aq. K_2CO_3 solution (0.5 M) until TLC indicated no benzoic acid was present. The solvent was evaporated to afford the silyl ether **1** (1.36 g, 49%) as a yellow oil, $[\alpha]_D^{19}$ −39 (*c* 0.6 in $CHCl_3$) (Found: C, 71.75; H, 5.70. $C_{50}H_{48}O_8SSi$ requires C, 71.74; H, 5.78%); δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.04 (9 H, s, *t*-butyl), 2.33 (3 H, s, ArCH_3), 3.85 (1 H dd, $J_{5,6}$ 1.6, $J_{6,6}$ 11.6, H6), 3.94 (1 H, dd, $J_{5,6}$ 4.0, H6), 4.69 (1 H, br d, H5), 5.73 (1 H, d, $J_{1,2}$ 0.8, H1), 5.80 (1 H, dd, $J_{2,3}$ 3.2, $J_{3,4}$ 10.4, H3), 5.97 (1 H, dd, H2), 6.26 (1 H, dd, $J_{4,5}$ 10.0, H4), 7.08–8.17 (29 H, Ar, Ph); δ_C(100.5 MHz; $CDCl_3$; Me_4Si) 9.15 (1 C, $(CH_3)_3C$), 21.12 (1 C, ArCH_3), 26.54 (3 C, $(CH_3)_3C$), 60.36, 62.31, 66.59, 70.96, 72.55 (5 C, C2,3,4,5,6), 86.43 (1 C, C1), 127.53–138.00 (24 C, Ar, Ph), 165.21, 165.45, 165.54 (3 C, C=O); *m/z* (ESI) 859.2733 ([M + Na]$^+$ $C_{50}H_{48}O_8SSi$ requires 859.2737).

Octyl α-D-mannopyranoside 21

$SnCl_4$ (2.92 mL, 24.9 mmol) was added to a mixture of pentaacetate **17** (9.77 g, 25.1 mmol), CH_2Cl_2 (120 mL) and 1-octanol (4.9 mL, 30.8 mmol) containing 4 Å molecular sieves stirring at 0 °C. After 30 min the reaction was allowed to warm to room temperature and left to stir for 19 h. The mixture was filtered, washed with HCl (3 × 100 mL), aq. $NaHCO_3$ (100 mL) and brine solution (30 mL). The organic extract was dried ($MgSO_4$), and the solvent evaporated under reduced pressure. The residue was dissolved in MeOH (30 mL) and treated with a small piece of sodium metal. The solution was stirred for 1 h at which stage TLC (17 : 2 : 1 EtOAc–MeOH–H_2O) indicated conversion to a more polar compound. Dowex-50 resin (H^+ form) was added to neutralize the reaction and, following filtration, the solvent was evaporated from the filtrate to give a pale yellow oil. This oil was purified by flash chromatography (17 : 2 : 1 EtOAc–MeOH–H_2O), to give the tetraol **21** (2.43 g, 33% from mannose) as a yellow oil, $[\alpha]_D^{24}$ +57 (*c* 0.82 in MeOH); δ_H(399.7 MHz; d_4-MeOH, MeOH) 0.89–1.61 (15H, m, $OCH_2(CH_2)_6CH_3$), 3.41 (1 H, m, OCH_2CH_2), 3.50–3.84 (6 H, m, H2,3,5,6,6,OCH_2CH_2), 3.62 (1 H, dd, $J_{3,4}$ 9.6, $J_{4,5}$ 9.2, H4), 4.74 (1 H, dd, $J_{1,2}$ 2.0, H1); δ_C(100.5 MHz; d_4-MeOH) 14.59, 23.85, 27.49, 30.53, 30.67, 30.74, 33.14 (7 C, $OCH_2(CH_2)_6CH_3$), 63.00, 68.70, 72.38, 72.79, 74.64 (6 C, C2,3,4,5,6,OCH_2CH_2), 101.64 (1 C, C1).

Octyl 2,3,4-tri-*O*-benzoyl-6-*O*-(*tert*-butyldiphenylsilyl)-α-D-mannoside 3

tert-Butylchlorodiphenylsilane (2.60 mL, 9.98 mmol) was added to a mixture of the tetraol **21** (2.43 g, 8.32 mmol), and imidazole (1.50 g, 20.8 mmol) in DMF (5 mL). The mixture was stirred at 35 °C for 3 h, then was quenched with water (2 mL) and stirred for 10 min. EtOAc (30 mL) was added and the mixture washed with water (3 × 30 mL), 1 M HCl (40 mL), and aq. $NaHCO_3$ (40 mL). The organic extract was dried ($MgSO_4$) and the solvent evaporated under reduced pressure. To the residue BzCl (4.35 mL, 37.4 mmol), pyridine (6.05 mL, 74.9 mmol) and catalytic DMAP (40 mg) were added with stirring at room temperature. The mixture was stirred for 18 h and then was quenched with water (2 mL) and stirred for a further 10 min. The organic phase was extracted with EtOAc (30 mL) and washed with water (3 × 30 mL) and K_2CO_3 solution (0.5 M). The organic phase was dried ($MgSO_4$) and the solvent evaporated under reduced pressure. Flash chromatography (8 : 92 EtOAc–pet. spirits) yielded a residue, which was washed with aq. K_2CO_3 solution (0.5 M) until TLC indicated no benzoic acid was present. The solvent was evaporated to afford the silyl ether **3** (3.80 g, 55%) as a yellow oil, $[\alpha]_D^{20}$ −60 (*c* 0.8 in $CHCl_3$); δ_H(399.7 MHz; $CDCl_3$; Me_4Si) 0.87–1.72 (15 H, m, $OCH_2(CH_2)_6CH_3$), 1.04 (9 H, s, *t*-butyl), 3.53 (1 H, ddd, *J* 6.4, 9.2, 13.2, OCH_2CH_2), 3.81 (1 H, ddd, *J* 6.8, 9.2, 14.0, OCH_2CH_2), 3.84 (1 H, dd, $J_{5,6}$ 1.6, $J_{6,6}$ 11.2, H6), 3.91 (1 H, dd, $J_{5,6}$ 4.4, $J_{6,6}$ 11.2, H6), 4.15 (1 H, br d, H5), 5.09 (1 H, d, $J_{1,2}$ 1.7, H1), 5.69 (1 H, dd, $J_{2,3}$ 3.2, H2), 5.85 (1 H, dd, $J_{3,4}$ 10.4, H3), 6.10 (1 H, dd, $J_{4,5}$ 10.0, H4), 7.14–8.17 (25 H, Ph); δ_C(100.5 MHz; $CDCl_3$; Me_4Si) 14.09, 19.17, 22.65, 26.14, 26.52, 26.60, 29.24, 29.40, 31.81 (9 C, $OCH_2(CH_2)_6CH_3$, $(CH_3)_3C$), 62.69, 66.78, 68.32, 70.72, 70.88, 71.37 (6 C, C2,3,4,5,6,OCH_2CH_2), 97.45 (1 C, C1), 127.51–135.65 (25 C, Ph), 165.28, 165.59, 165.62 (3 C, C=O); *m/z* (ESI) 865.3745 ($C_{51}H_{58}O_9Si$ [M + Na]$^+$ requires 865.3748).

Octyl 2,3,4-tri-*O*-benzoyl-α-D-mannopyranoside 2

Acetyl chloride (6.13 mL) was added dropwise to MeOH (150 mL) with stirring and the solution cooled to 20 °C. The silyl ether **3** (3.81 g, 4.61 mmol) was dissolved in diethyl ether (150 mL) and this was then added to the methanol solution. The mixture was stirred for 4 days. The solvent was evaporated and

the residue co-evaporated with toluene under reduced pressure. The crude product was purified using flash chromatography (15 : 85 then 20 : 80 then 25 : 75 EtOAc–pet. spirits) yielding the alcohol **2** (1.62 g, 58%) as a pale yellow oil, $[\alpha]_D^{20}$ −115 (*c* 0.8 in $CHCl_3$) (Found: C, 69.53; H, 6.70. $C_{35}H_{40}O_9$: C, 69.52; H, 6.67%); δ_H(399.7 MHz; $CDCl_3$; Me_4Si) 0.85–1.80 (15 H, m, $OCH_2(CH_2)_6CH_3$), 2.69 (1 H, t, $J_{OH,6}$ 6.8, OH), 3.55 (1 H, ddd, *J* 6.8, 9.6, 13.2, OCH_2CH_2), 3.77–3.86 (3 H, m, H6,6, OCH_2CH_2), 4.07 (1 H, br d, H5), 5.10 (1 H, d, $J_{1,2}$ 1.2, H1), 5.68 (1 H, dd, $J_{2,3}$ 3.2, H2), 5.84 (1 H, dd, $J_{3,4}$ 10.0, $J_{4,5}$ 10.0, H4), 6.00 (1 H, dd, H3), 7.23–8.12 (15 H, m, Ph); δ_C(100.5 MHz; $CDCl_3$; Me_4Si) 14.06, 22.61, 26.07, 29.18, 29.33, 31.78 (7 C, $OCH_2(CH_2)_6CH_3$), 61.34, 67.33, 68.61, 69.69, 70.72, 70.81 (6 C, C2,3,4,5,6,OCH_2CH_2), 97.63 (1 C, C1), 128.22–133.58 (18 C, Ph), 165.43, 165.51, 166.46 (3 C, C=O); *m*/*z* (ESI) 627.2559 ($C_{35}H_{40}O_9$ $[M + Na]^+$ requires 627.2570).

General procedure for glycosylation reactions using donor 1 and alcohols 6 and 12

TfOH was added to a mixture of the donor **1**, the alcohol acceptor, NIS and 4 Å molecular sieves in dry dichloroethane at 0 °C under N_2. The solution was stirred for 5 min during which time the mixture went dark purple and TLC showed consumption of starting materials. The reaction was quenched with aq. $NaHCO_3$ and 0.5 M sodium thiosulfate. The solution was filtered and the organic phase extracted with dichloromethane and dried ($MgSO_4$). The solvent was evaporated under reduced pressure, and the residue purified by flash chromatography to afford the protected oligomannosides.

Octyl (2,3,4-tri-*O*-benzoyl-6-*O*-(*tert*-butyldiphenylsilyl)-α-D-mannopyranosyl)-(1→6)-(2,3,4-tri-*O*-benzoyl-α-D-mannopyranosyl)-(1→6)-(2,3,4-tri-*O*-benzoyl-α-D-mannopyranoside) 9. TfOH (8 μL) was added to a mixture of the donor **1** (294 mg, 369 μmol), the alcohol **6** (330 mg, 306 μmol), NIS (94 mg, 418 μmol) with 4 Å molecular sieves in dry dichloroethane (10 mL), with the solution treated as for the general procedure above. The product was purified by flash chromatography (25 : 75 then 30 : 70 then 35 : 65 EtOAc–pet. spirits) affording the protected trimannoside **9** (486 mg, 90%) as a clear oil, $[\alpha]_D^{19}$ −71 (*c* 0.8 in $CHCl_3$) (Found: C, 70.29; H, 5.81. $C_{105}H_{102}O_{25}Si$ requires C, 70.38; H, 5.74%); δ_H(399.7 MHz; $CDCl_3$; Me_4Si) 0.79–1.74 (15 H, m, $OCH_2(CH_2)_6CH_3$), 1.01 (9 H, s, *t*-butyl), 4.05, 4.25, 4.54 (3 H, 3 br d, $H5^A$,5^B,5^C), 3.32–4.33 (8 H, m, $H(6,6)^A$,$(6,6)^B$,$(6,6)^C$,OCH_2CH_2), 4.84, 5.15, 5.21 (3 H, 3 br s, $H1^A$,1^B,1^C), 5.54, 5.80, 5.93 (3 H, 3 m, $H2^A$,2^B,2^C), 5.86 (1 H, dd, $J_{2,3}$ 3.0, $J_{3,4}$ 10.5), 5.98 (1 H, dd, $J_{2,3}$ 3.6, $J_{3,4}$ 9.9), 6.07 (1 H, dd, $J_{2,3}$ 3.0, $J_{3,4}$ 10.2, $H3^A$,3^B,3^C), 5.98 (1 H, dd, $J_{3,4}$ 9.9, $J_{4,5}$ 9.9), 6.14 (1 H, dd, $J_{3,4}$ 9.9, $J_{4,5}$ 9.9), 6.30 (1 H, dd, $J_{3,4}$ 10.2, $J_{4,5}$ 10.2, $H4^A$,4^B,4^C), 7.06–8.24 (55 H, Ph); δ_C(100.5 MHz; $CDCl_3$; Me_4Si) 14.06, 19.06, 22.60, 26.09, 26.52, 29.17, 29.40, 31.77 (9 C, $OCH_2(CH_2)_6CH_3$, $(CH_3)_3C$), 60.33, 62.06, 65.55, 66.19, 66.63, 66.82, 68.58, 69.33, 69.42, 70.35, 70.41, 70.59, 70.65, 71.16 (16 C, $C(2,3,4,5,6)^A$,$(2,3,4,5,6)^B$,$(2,3,4,5,6)^C$,OCH_2CH_2), 97.20, 97.76, 97.84 (3 C, $C1^A$,1^B,1^C), 127.43–135.61 (66 C, Ph), 165.11, 165.13, 165.21, 165.26, 165.43, 165.48, 165.57, 165.76 (9 C, C=O); *m*/*z* (ESI) 1813.6374 ($C_{105}H_{102}O_{25}$ $[M + Na]^+$ requires 1813.6377).

Octyl (2,3,4-tri-*O*-benzoyl-6-*O*-(*tert*-butyldiphenylsilyl)-α-D-mannopyranosyl)-(1→6)-(2,3,4-tri-*O*-benzoyl-α-D-mannopyranosyl)-(1→6)-(2,3,4-tri-*O*-benzoyl-α-D-mannopyranosyl)-(1→6)-(2,3,4-tri-*O*-benzoyl-α-D-mannopyranoside) 13. TfOH (10 μL) was added to a mixture of the donor **1** (229 mg, 0.29 mmol), the alcohol **12** (373 mg, 0.24 mmol), NIS (76 mg, 0.34 mmol) and 4 Å molecular sieves in dry dichloroethane (20 mL). The solution was treated as for the general procedure above. Flash chromatography (35 : 65 then 40 : 60 EtOAc–pet. spirits) afforded the protected tetramannoside **13** (499 mg, 91%) as a yellow oil, $[\alpha]_D^{14}$ −62 (*c* 1.3 in $CHCl_3$) (Found: C, 69.95; H, 5.61. $C_{132}H_{124}O_{33}Si$ requires C, 69.95; H, 5.51%); δ_H(399.7 MHz; $CDCl_3$; Me_4Si) 0.83–1.71 (15 H, m, $OCH_2(CH_2)_6CH_3$), 0.99 (9 H, s, *t*-butyl), 3.76, 4.19, 4.33, 4.53 (4 H, 4 br d, $H5^A$,5^B,5^C,5^D), 3.39–4.20 (10 H, m, $H(6,6)^A$,$(6,6)^B$,$(6,6)^C$,$(6,6)^D$,OCH_2CH_2), 4.86 (1 H, d, $J_{1,2}$ 1.6), 4.95 (1 H, d, $J_{1,2}$ 1.6), 5.15 (1 H, d, $J_{1,2}$ 1.6), 5.24 (1 H, d, $J_{1,2}$ 1.2, $H1^A$,1^B,1^C,1^D), 5.65 (1 H, dd, $J_{1,2}$ 1.6, $J_{2,3}$ 3.2), 5.76 (1 H, dd, $J_{1,2}$ 2.0, $J_{2,3}$ 3.2), 5.79 (1 H, dd, $J_{1,2}$ 1.6, $J_{2,3}$ 3.6), 5.94 (1 H, dd, $J_{1,2}$ 1.2, $J_{2,3}$ 2.4, $H2^A$,2^B,2^C,2^D), 5.89 (1 H, dd, $J_{2,3}$ 3.2, $J_{3,4}$ 10.4), 5.92 (1 H dd, $J_{2,3}$ 4.0, $J_{3,4}$ 12.0), 5.97 (1 H, dd, $J_{2,3}$ 3.2, $J_{3,4}$ 10.0), 6.07 (1 H, dd, $J_{2,3}$ 3.6, $J_{3,4}$ 10.4, $H3^A$,3^B,3^C,3^D), 6.11 (1 H, dd, $J_{3,4}$ 9.6, $J_{4,5}$ 10.0), 6.11 (1 H, dd, $J_{3,4}$ 10.8, $J_{4,5}$ 10.0), 6.21 (1 H, dd, $J_{3,4}$ 10.0, $J_{4,5}$ 10.0), 6.25 (1 H, dd, $J_{3,4}$ 10.0, $J_{4,5}$ 10.4, $H4^A$,4^B,4^C,4^D), 7.05–8.21 (70 H, m, Ph); δ_C(100.5 MHz; $CDCl_3$; Me_4Si) 14.32, 19.30, 22.86, 26.36, 29.45, 29.68, 32.04 (7 C, $OCH_2(CH_2)_6CH_3$), 26.73 (4 C, *t*-butyl), 61.97, 65.75, 66.01, 66.20, 66.57, 66.92, 68.84, 69.53, 69.60, 70.38, 70.56, 70.88, 71.08, 71.30 (21 C, $C(2,3,4,5,6)^A$,$(2,3,4,5,6)^B$,$(2,3,4,5,6)^C$,$(2,3,4,5,6)^D$,OCH_2CH_2), 97.79, 97.97, 98.10, 98.20 (4 C, $C1^A$,1^B,1^C,1^D), 127.64–135.86 (84 C, Ph), 154.41, 165.46, 165.60, 165.69, 165.92, 166.00 (12 C, C=O).

General procedure for removal of the *tert*-butyldiphenylsilyl group from 5, 9 and 13

Acetyl chloride (1.3 mL $mmol^{-1}$) was added dropwise to MeOH (33 mL $mmol^{-1}$) with stirring and the solution cooled to 20 °C. The silyl ether was dissolved in diethyl ether (33 mL $mmol^{-1}$) and this solution was added to the methanol solution and the mixture was stirred for 4 days. The solvent was evaporated and the residue co-evaporated with toluene. The residue was purified by flash chromatography.

Octyl (2,3,4-tri-*O*-benzoyl-α-D-mannopyranosyl)-(1→6)-(2,3,4-tri-*O*-benzoyl-α-D-mannopyranoside) 6. TfOH (5 μl) was added to a mixture of the donor **1** (2.65 g, 3.86 mmol), the acceptor **2** (2.80 g, 4.63 mmol), NIS (1.22 g, 5.41 mmol) and 4 Å molecular sieves in dry dichloroethane at 0 °C under N_2. The solution was stirred for 5 min, during which time the mixture went deep purple, and TLC showed consumption of the starting material. The reaction was quenched with aq. $NaHCO_3$ and 0.5 M sodium thiosulfate. The mixture was filtered and the organic phase extracted with dichloromethane and dried ($MgSO_4$). The solvent was evaporated under reduced pressure to give a residue that could not be resolved by flash chromatography so the crude disaccharide was desilylated as for the general procedure above. This yielded the alcohol **6** (2.95 g, 71%) as a colourless oil, $[\alpha]_D^{20}$ −99 (*c* 0.8 in $CHCl_3$) (Found: C, 69.06; H, 5.84. $C_{62}H_{62}O_{17}$ requires C, 69.00; H, 5.79%); δ_H(399.7 MHz; $CDCl_3$; Me_4Si) 0.81–1.82 (15 H, m, $OCH_2(CH_2)_6CH_3$), 2.61 (1 H, t, $J_{OH,6}$ 7.2 O*H*), 3.51–3.66 (3 H, m, $H6^A$,6^A,OCH_2CH_2), 3.79 (1 H, dd, $J_{5,6}$ 2.0, $J_{6,6}$ 11.2, $H6^B$), 3.92 (1 H, ddd, *J* 6.8, 9.6, 13.6, OCH_2CH_2), 4.02–4.10 (2 H, m, $H5^A$,6^B), 4.39 (1 H, dd, $H5^B$), 5.12 (1 H, d, $J_{1,2}$ 1.2), 5.17 (1 H, $J_{1,2}$ 1.6, $H1^A$,1^B), 5.75–5.77 (2 H, m, $H2^A$,2^B), 5.83 (1 H, dd, $J_{3,4}$ 10.0, $J_{4,5}$ 10.0), 6.05 (1 H, dd, $J_{3,4}$ 10.4, $J_{4,5}$ 10.0, $H4^A$,4^B), 5.94 (1 H, dd, $J_{2,3}$ 3.60, $J_{3,4}$ 10.0), 6.07 (1 H, dd, $J_{2,3}$ 3.2, $J_{3,4}$ 10.0, $H3^A$,3^B), 7.25–8.20 (30 H, m, Ph); δ_C(100.5 MHz; $CDCl_3$; Me_4Si) 14.06, 22.63, 26.16, 29.24, 29.43, 29.64, 31.80 (7 C, $OCH_2(CH_2)_6CH_3$), 60.95, 66.64, 67.07, 68.71, 69.32, 70.30, 70.34, 70.66, 70.92 (11 C, $C(2,3,4,5,6)^A$,$(2,3,4,5,6)^B$,OCH_2CH_2), 97.63, 97.74 (2 C, $C1^A$,1^B), 128.23–133.61 (36 H, Ph), 165.08, 165.28, 165.48, 165.64, 166.55 (6 C, C=O).

Octyl (2,3,4-tri-*O*-benzoyl-α-D-mannopyranosyl)-(1→6)-(2,3,4-tri-*O*-benzoyl-α-D-mannopyranosyl)-(1→6)-(2,3,4-tri-*O*-benzoyl-α-D-mannopyranoside) 12. The protected trimannoside **9** (293 mg, 0.163 mmol) was treated as for the general procedure above. Flash chromatography (30 : 70 then 35 : 65 then 40 : 60 EtOAc–pet. spirits) afforded the trimannoside alcohol **12** (251 mg, 70%) as an oil, $[\alpha]_D^{18}$ −75 (*c* 0.8 in $CHCl_3$)

(Found, C, 68.95; H, 5.49. $C_{89}H_{84}O_{25}$ requires C, 68.80; H, 68.95%); δ_H(399.7 MHz; $CDCl_3$; Me_4Si) 0.83–1.77 (15 H, m, $OCH_2(CH_2)_6CH_3$), 2.26 (1 H, br s, OH), 3.43–3.66 (4 H, m, OCH_2CH_2,H(6,6)^C), 3.82–3.95 (4 H, m, H5^A,6^A,(6,6)^B), 4.24 (1 H, dd, $J_{5,6}$ 4.4, $J_{6,6}$ 10.8, H6^A), 4.28 (1 H, dd, $J_{5,6}$ 4.8), 4.52 (1 H, dd, $J_{4,5}$ 10.0, $J_{5,6}$ 2.8, H5^B,5^C), 4.88 (1 H, d, $J_{1,2}$ 2.0), 5.16 (1 H, d, $J_{1,2}$ 1.6), 5.20 (1 H, d, $J_{1,2}$ 1.6. H1^A,1^B,1^C), 5.57 (1 H, br d), 5.80 (1 H, br s), 5.91 (1 H br s, H2^A,2^B,2^C), 5.77 (1 H, dd, $J_{3,4}$ 10.0, $J_{4,5}$ 10.0), 6.24 (1 H, dd, $J_{3,4}$ 10.0, $J_{4,5}$ 10.0, H4^A,4^B), 5.98 (1 H, dd, $J_{2,3}$ 2.4, $J_{3,4}$ 10.4, H3^A), 6.02–6.07 (3 H, m, H3^B,3^C,4^C), 7.22–8.23 (45 H, m, Ph); δ_C(100.5 MHz; $CDCl_3$; Me_4Si) 14.06, 22.62, 26.16, 29.23, 29.44, 29.65, 31.80 (7 C, $OCH_2(CH_2)CH_3$), 60.90, 65.91, 66.37, 66.72, 66.77, 67.01, 68.67, 69.30, 69.33, 69.49, 70.28, 70.54, 70.67, 70.86 (16 C, C(2,3,4,5,6)^A, (2,3,4,5,6)^B, (2,3,4,5,6)^C, OCH_2CH_2), 97.53, 97.77, 97.88 (3 C, C1^A,1^B,1^C), 128.25–133.61 (54 C, Ph), 165.13, 165.15, 165.17, 165.41, 165.46, 165.48, 165.56, 165.74, 166.55 (9 C, C=O); *m/z* (ESI) 1575.5171 ($C_{89}H_{84}O_{25}$ [M + Na]$^+$ requires 1575.51990.

Octyl (2,3,4-tri-*O*-benzoyl-α-D-mannopyranosyl)-(1→6)-(2,3,4-tri-*O*-benzoyl-α-D-mannopyranosyl)-(1→6)-(2,3,4-tri-*O*-benzoyl-α-D-mannopyranosyl)-(1→6)-(2,3,4-tri-*O*-benzoyl-α-D-mannopyranoside) 16. The protected tetramannoside **13** (389 mg, 17 μmol) was treated as for the general procedure above. Flash chromatography (40 : 60 then 45 : 65 then 50 : 50 EtOAc–pet. spirits) afforded the tetramannoside alcohol **16** (270 mg, 78%) as an oil, $[\alpha]_D^{15}$ −67 (*c* 0.9 in $CHCl_3$) (Found: C, 68.79; H, 5.33. $C_{116}H_{106}O_{33}$ requires C, 68.70; H, 5.27%); δ_H(399.7 MHz; $CDCl_3$; Me_4Si) 0.82–1.82 (15 H, m, $OCH_2(CH_2)_6CH_3$), 2.62 (1 H, br s, OH), 3.37–3.98 (10 H, m, H(6,6)^A,(6,6)^B,(6,6)^C,(6,6)^D,OCH_2CH_2), 4.23 (1 H br dd), 4.28–4.36 (2 H, m), 4.54 (1 H, dd,$J_{4,5}$ 10.4,$J_{5,6}$ 2.8, H5^A,5^B,5^C,5^D), 4.88, 4.99, 5.17, 5.25 (4 H, 4 br d, H1^A,1^B,1^C,1^D), 5.65 (1 H, br dd, H2^A), 5.71–5.76 (2 H, m, H2^B,3^A), 5.68 (1 H, dd,$J_{1,2}$ 1.6,$J_{2,3}$ 3.2, H2^C), 5.91–5.94 (2 H, m, H2^D,3^B), 5.97 (1 H, dd,$J_{2,3}$ 3.2,$J_{3,4}$ 10.0), 6.04 (1 H, dd,$J_{2,3}$ 3.2, $J_{3,4}$ 10.0 H3^C,3^D), 6.07–6.11 (2 H, m), 6.14 (1 H, dd,$J_{3,4}$ 10.0,$J_{4,5}$ 10.0), 6.24 (1 H, dd,$J_{3,4}$ 10.0,$J_{4,5}$ 10.0, H4^A,4^B,4^C,4^D), 7.22–8.21 (60 H, Ph); δ_C(100.5 MHz; $CDCl_3$; Me_4Si) 14.29, 16.82, 22.83, 26.35, 29.42, 29.67, 32.01 (7 C, $OCH_2(CH_2)_6CH_3$), 60.97, 66.11, 66.54, 66.93, 67.23, 68.85, 69.47, 69.59, 69.79, 70.38, 70.50, 70.55, 70.81, 70.87, 71.04 (21 C, C(2,3,4,5,6)^A, (2,3,4,5,6)^B, (2,3,4,5,6)^C, (2,3,4,5,6)^D, OCH_2CH_2), 97.84, 97.97, 98.16, 98.21 (4 C, C1^A,1^B,1^C,1^D), 128.47–133.88 (72 C, Ph), 165.29, 165.39, 165.47, 165.54, 165.66, 165.70, 165.79, 165.97, 166.9 (12 C, C=O).

General procedure for the iodination of the primary alcohols 2, 6, 12 and 16

A mixture of the primary alcohol, imidazole and Ph_3P in toluene was distilled for 10 minutes to azeotropically remove excess water. The temperature was then reduced to 90 °C and iodine was added and the mixture stirred under nitrogen overnight. MeOH (1 mL) was added and the mixture stirred for 30 min. The organic solution was washed with water (3 × 20 mL), 0.25 M sodium thiosulfate (20 mL) and dried over $MgSO_4$ and the solvent removed under reduced pressure. The product was purified by flash chromatography to give the iodide.

Octyl 2,3,4-tri-*O*-benzoyl-6-deoxy-6-iodo-α-D-mannopyranoside 22. A mixture of the alcohol **2** (193 mg, 399 μmol), imidazole (72 mg, 998 μmol) and Ph_3P (157 mg, 599 μmol) in toluene (10 mL) was treated with iodine (152 mg, 0.599 μmol) as for the general procedure above. Flash chromatography (10 : 90 then 15 : 85 then 20 : 80 EtOAc–pet. spirits) gave the iodide **22** (196 mg, 86%) as a yellow gum, $[\alpha]_D^{15}$ −65 (*c* 0.7 in $CHCl_3$) (Found: C, 58.68; H, 5.47. $C_{35}H_{39}IO_8$ requires C, 58.83; H, 5.50%); δ_H(399.7 MHz; $CDCl_3$; Me_4Si) 0.89–1.74 (15 H, m, $OCH_2(CH_2)_6CH_3$), 3.37 (1 H, dd, $J_{5,6}$ 5.4, $J_{6,6}$ 10.8, H6), 3.47 (1 H, dd, $J_{5,6}$ 5.4, $J_{6,6}$ 10.8, H6), 3.58 (1 H, ddd, OCH_2CH_2), 3.95 (1 H, ddd, OCH_2CH_2), 4.07 (1 H, dd, H5), 5.10 (1 H, d, $J_{1,2}$ 1.6, H1), 5.68 (1 H, dd, $J_{2,3}$ 3.2, H2), 5.76 (1 H, dd, $J_{3,4}$ 9.6, $J_{4,5}$ 10.0, H4), 5.90 (1 H, dd, H3); δ_C(100.5 MHz; $CDCl_3$; Me_4Si) 5.10 (1 C, C6), 14.32, 22.86, 26.33, 29.43, 29.51, 29.58, 32.02 (7 C, $OCH_2(CH_2)_6CH_3$), 68.94, 69.81, 70.25, 70.80, 70.98 (5 C, C2,3,4,5,OCH_2CH_2), 97.74 (1 C, C1), 128.45–133.76 (18 C, Ph), 165.56, 165.66, 165.75 (3 C, C=O).

Octyl (2,3,4-tri-*O*-benzoyl-6-deoxy-6-iodo-α-D-mannopyranosyl)-(1→6)-(2,3,4-tri-*O*-benzoyl-α-D-mannopyranoside) 24. A mixture of the alcohol **6** (304 mg, 316 μmol), imidazole (62 mg, 859 μmol) and Ph_3P (135 mg, 514 μmol) in toluene (5 mL) was treated with iodine (130 mg, 512 μmol) as for the general procedure above. Flash chromatography (15 : 85 then 20 : 80 then 25 : 75 EtOAc–pet. spirits) afforded the iodide **24** (0.352 g, 94%) as a yellow oil, $[\alpha]_D^{20}$ −80 (*c* 0.8 in $CHCl_3$) (Found: C, 62.64; H, 5.09. $C_{62}H_{61}IO_{16}$ requires C, 62.63; H, 5.17%); δ_H(399.7 MHz; $CDCl_3$; Me_4Si) 0.85–1.70 (15 H, m, $OCH_2(CH_2)_6CH_3$), 3.24 (2 H, m, H(6,6)^B), 3.63 (1 H, ddd, *J* 6.4, 13.2), 3.93 (1 H, ddd, *J* 6.8, 9.2, OCH_2CH_2), 3.81 (1 H, br d,), 4.08 (1 H, dd, $J_{5,6}$ 6.0, $J_{6,6}$ 10.0, H(6,6)^A), 4.24 (1 H, dd, $J_{4,5}$ 10.8 $J_{5,6}$ 5.6), 4.41 (1 H, dd, $J_{4,5}$ 10.0, $J_{5,6}$ 5.2, H5^A,5^B), 5.13, 5.17 (2 H, 2 br s, H1^A,1^B), 5.74 (1 H, dd, $J_{3,4}$ 10.0, $J_{4,5}$ 10.0), 6.07 (1 H, dd, $J_{3,4}$ 10.0, $J_{4,5}$ 10.0, H4^A,4^B), 5.75–5.77 (2 H, m, H2^A,2^B), 5.94–5.99 (2 H, m, H3^A,3^B), 7.25–8.19 (30 H, m, Ph); δ_C(100.5 MHz; $CDCl_3$; Me_4Si) 4.55 (1 C, C6^B), 14.08, 22.66, 26.19, 29.28, 29.45, 31.83 (7 C, $OCH_2(CH_2)_6CH_3$), 66.55, 67.05, 68.74, 69.11, 69.94, 70.27, 70.57, 70.63 (10 C, C(2,3,4,5,6)^A,(2,3,4,5)^B, OCH_2CH_2), 97.42, 97.61 (2 C, C1^A,1^B), 128.25–133.54 (36 C, Ph), 165.01, 165.24, 165.53, 165.74, 165.65 (6 C, C=O); *m/z* (ESI) 1211.2912 ($C_{62}H_{61}IO_{16}$ [M + Na]$^+$ requires 1211.2902).

Octyl (2,3,4-tri-*O*-benzoyl-6-deoxy-6-iodo-α-D-mannopyranosyl)-(1→6)-(2,3,4-tri-*O*-benzoyl-α-D-mannopyranosyl)-(1→6)-(2,3,4-tri-*O*-benzoyl-α-D-mannopyranoside) 26. A mixture of the alcohol **12** (159 mg, 100 μmol), imidazole (18.4 mg, 255 μmol) and Ph_3P (39.3 mg, 150 μmol) in toluene (5 mL) was treated with iodine (38.1 mg, 150 μmol) as for the general procedure above. Flash chromatography (15 : 85 then 20 : 80 then 25 : 75 EtOAc–pet. spirits) furnished the iodide **26** (144 mg, 87%) as a yellow oil, $[\alpha]_D^{23}$ −63 (*c* 0.54 in $CHCl_3$) (Found C, 64.29; H, 5.02. $C_{89}H_{83}IO_{24}$ requires C, 64.26; H, 5.03%); δ_H(399.7 MHz; $CDCl_3$; Me_4Si) 0.81–1.79 (15 H, m, $OCH_2(CH_2)_6CH_3$), 3.20 (1 H, m, OCH_2CH_2), 3.48 (1 H, br dd, H6^A), 3.64 (1 H, m, OCH_2CH_2), 3.90 (1 H, br dd, H6^A), 3.90–4.08 (4 H, H(6,6)^B,(6,6)^C), 4.26 (1 H, dd, $J_{4,5}$ 11.2, $J_{5,6}$ 4.8), 4.32 (1 H m), 4.52 (1 H, dd, $J_{4,5}$ 10.0, $J_{5,6}$ 2.4, H5^A,5^B,5^C), 4.90 (1 H, d, $J_{1,2}$ 1.2), 5.16 (1 H, d, $J_{1,2}$ 1.6), 5.22 (1 H, d, $J_{1,2}$ 1.2, H1^A,1^B,1^C), 5.57 (1 H, dd, $J_{1,2}$ 1.6, $J_{2,3}$ 3.2), 5.80 (1 H, dd, $J_{1,2}$ 1.6, $J_{2,3}$ 3.2, H2^A,2^B), 5.92–5.95 (2 H, m, H3^A,2^C), 5.99 (1 H, dd, $J_{2,3}$ 3.6, $J_{3,4}$ 10.4, H3^B), 6.08–6.09 (2 H, m, H4^A,3^C), 5.69 (1 H, dd, $J_{3,4}$ 9.6, $J_{4,5}$ 10.0), 6.27 (1 H, dd, $J_{3,4}$ 10.4, $J_{4,5}$ 10.0, H4^B,4^C), 7.22–8.24 (45 H, Ph); δ_C(100.5 MHz; $CDCl_3$; Me_4Si) 4.55 (1 C, C6^C), 14.03, 22.60, 26.13, 29.19, 29.41, 29.44, 31.77 (7 C, $OCH_2(CH_2)_6CH_3$), 52.01, 65.84, 66.35, 66.69, 68.64, 69.08, 69.32, 69.42, 69.84, 70.17, 70.21, 70.48, 70.54, 70.62 (15 C, C(2,3,4,5,6)^A,(2,3,4,5,6)^B,(2,3,4,5)^C,OCH_2CH_2), 97.14, 97.77, 97.88 (3 C, C1^A,1^B,1^C), 128.22–133.50 (54 C, Ph), 165.02, 165.08, 165.15, 165.36, 165.43, 165.50, 165.52, 165.55, 165.73 (9 C, C=O).

Octyl (2,3,4-tri-*O*-benzoyl-6-deoxy-6-iodo-α-D-mannopyranosyl)-(1→6)-(2,3,4-tri-*O*-benzoyl-α-D-mannopyranosy)-(1→6)-(2,3,4-tri-*O*-benzoyl-α-D-mannopyranosyl)-(1→6)-(2,3,4-tri-*O*-benzoyl-α-D-mannopyranoside) 28. A mixture of the alcohol **16** (279 mg, 138 μmol), imidazole (25.0 mg, 344 μmol) and Ph_3P (54.0 mg, 207 μmol) in toluene (10 mL) was treated with iodine (53 mg, 207 μmol) as for the general procedure above. Flash chromatography (40 : 60 then 45 : 55 then 50 : 50 EtOAc–pet. spirits) afforded the iodide **28** (273 mg, 92%) as a clear gum, $[\alpha]_D^{15}$ −55 (*c* 1.35 in $CHCl_3$) (Found: C, 66.09; H, 5.03. $C_{116}H_{105}IO_{32}$

requires C, 66.17; H, 4.95%); δ_H(399.7 MHz; $CDCl_3$; Me_4Si) 0.83–1.78 (15 H, m, $OCH_2(CH_2)_6CH_3$), 3.11–3.70 (2 H, m, $H6^A$, OCH_2CH_2), 3.48 (2 H, m, $H6^A$,6^B), 3.62 (1 H, m, OCH_2CH_2), 3.87–4.03 (5 H, m, $H6^B$,(6,6)^C,(6,6)^D), 4.23–4.35 (3 H, m, $H5^A$,5^B,5^C), 4.53 (1 H, br dd, $H5^D$), 4.88, 5.00, 5.16, 5.25 (4 H, s, $H1^A$,1^B,1^C,1^D), 5.66–5.71 (1 H, m, $H2^A$), 5.69 (1 H, dd, $J_{3,4}$ 9.6, $J_{4,5}$ 10.0, $H4^A$), 5.74 (1 H, dd, $J_{1,2}$ 1.2, $J_{2,3}$ 3.2), 5.80 (1 H, dd, $J_{1,2}$ 1.6, $J_{2,3}$ 3.2), 5.94 (1 H, dd, $J_{1,2}$ 1.2, $J_{2,3}$ 3.2, $H2^B$,2^C,2^D), 5.95–5.99 (3 H, m), 6.08 (1 H, dd, $J_{2,3}$ 3.2, $J_{3,4}$ 10.0, $H3^A$,3^B,3^C,3^D), 6.13 (1 H, dd, $J_{3,4}$ 9.6, $J_{4,5}$ 10.0), 6.17 (1 H, dd, $J_{3,4}$ 10.0, $J_{4,5}$ 10.0), 6.25 (1 H, dd, $J_{3,4}$ 10.0, $J_{4,5}$ 10.4, $H4^B$,4^C,4^D), 7.23–8.24 (60 H, m, Ph); δ_C(100.5 MHz; $CDCl_3$; Me_4Si) 4.79 (1 C, C6-I), 13.66, 14.32, 22.85, 26.38, 29.45, 29.68, 29.89, 32.03 (7 C, $OCH_2(CH_2)_6CH_3$), 66.08, 66.47, 66.88, 68.85, 69.34, 69.59, 69.81, 70.09, 70.32, 70.45, 70.57, 70.64, 70.80 (20 C, C(2,3,4,5,6)^A,(2,3,4,5,6)^B,(2,3,4,5,6)^C,(2,3,4,5)^D,OCH_2CH_2), 97.89, 97.97, 98.17 (4 C, $C1^A$,1^B,1^C,1^D), 128.47–133.78 (72 C, Ph), 165.19, 165.64, 165.41, 165.48, 165.56, 165.69, 165.85, 165.99 (12 C, C=O).

General procedure for tributyltin hydride reduction of iodides 22, 24, 26 and 28

A solution of the iodide and Bu_3SnH in toluene with catalytic AIBN (2–5 mg) was stirred under reflux overnight. The solvent was removed under reduced pressure and the residue was partitioned between MeCN and pet. spirits. The MeCN layer was separated and washed with pet. spirits (5 × 20 mL). The solvent was removed under reduced pressure and the product was purified by flash chromatography to afford the protected 6-deoxy compounds.

Octyl 2,3,4-tri-*O*-benzoyl-6-deoxy-α-D-mannopyranoside 23. The monomannoside iodide **22** (299 mg, 0.42 mmol) and Bu_3SnH (182 mg, 0.63 mmol) and catalytic AIBN in toluene (15 mL) was treated as for the general procedure above. Following partitioning between MeCN and pet. spirit, the pet. spirit phase was extracted with additional MeCN (8 × 10 mL). The solvent was evaporated from the MeCN phase under reduced pressure. Flash chromatography (10 : 90 then 15 : 85 then 20 : 80 EtOAc–pet. spirits) afforded the protected deoxy monomannoside **23** (186 mg, 76%) as a clear oil, $[\alpha]_D^{15}$ −115 (*c* 0.8 in $CHCl_3$) (Found C, 71.46; H, 6.91. $C_{35}H_{40}O_8$ requires C, 71.41; H, 6.85%); δ_H(399.7 MHz; $CDCl_3$; Me_4Si) 0.85–1.73 (15 H, m, $OCH_2(CH_2)_6CH_3$), 1.37 (3 H, d, $J_{5,6}$ 6.0, H6), 3.53 (1 H, m, *J* 6.8, 9.59, 13.2, OCH_2CH_2), 3.69 (1 H, m, *J* 6.8, 9.6, 14.0, OCH_2CH_2), 4.19 (1 H, ddd, $J_{4,5}$ 12.8, $J_{5,6}$ 6.4, H5), 5.00 (H 1, d, H1), 5.66 (1 H, dd, $J_{1,2}$ 1.6, $J_{2,3}$ 3.2, H2), 5.67 (1 H, dd, $J_{3,4}$ 10.0, $J_{4,5}$ 9.6, H4), 5.85 (1 H, dd, $J_{2,3}$ 3.6, $J_{3,4}$ 10.0, H3), 7.24–8.12 (15 H, m, Ph); δ_C(100.5 M, $CDCl_3$) 14.35, 17.91, 22.90, 26.35, 29.48, 29.61, 29.44, 32.07 (8 C, $OCH_2(CH_2)CH_3$, C6), 66.75, 68.68, 70.28, 71.20, 72.13 (5 C, C2,3,4,5,OCH_2CH_2), 97.71 (1 C, C1), 128.46–133.64 (18 C, Ph), 165.72, 165.85, 166.01 (3 C, C=O).

Octyl (2,3,4-tri-*O*-benzoyl-6-deoxy-α-D-mannopyranosyl)-(1→6)-(2,3,4-tri-*O*-benzoyl-α-D-mannopyranoside) 25. The iodide **24** (250 mg, 211 μmol) and Bu_3SnH (85 μL, 316 μmol) and catalytic AIBN in toluene was treated as for the general procedure above. Flash chromatography (20 : 80 then 25 : 75 then 30 : 70 EtOAc–pet. spirits) afforded the protected deoxy dimannoside **25** (0.176 g, 79%) as yellow oil, $[\alpha]_D^{20}$ −93 (*c* 0.7 in $CHCl_3$) (Found: C, 70.31; H, 6.04. $C_{62}H_{62}O_{16}$ requires C, 70.04; H, 5.88%); δ_H(399.7 MHz; $CDCl_3$; Me_4Si) 0.84–1.79 (15 H, m, $OCH_2(CH_2)_6CH_3$), 1.18 (3 H, d, $J_{5,6}$ 6.4, $H6^B$), 3.63 (1 H, ddd, OCH_2CH_2), 3.75 (1 H. br d), 4.07 (1 H, dd, $J_{5,6}$ 5.6, $J_{6,6}$ 10.8, H(6,6)^A), 3.93 (1 H, ddd, OCH_2CH_2), 4.15 (1 H, dd, $J_{4,5}$ 9.6, $J_{5,6}$ 6.0), 4.39 (1 H, m, $H5^A$,5^B), 5.06, 5.12 (2 H, 2 br s, $H1^A$,1^B), 5.64 (1 H, dd, $J_{3,4}$ 10.0, $J_{4,5}$ 10.0), 6.03 (1 H, dd, $J_{3,4}$ 9.6, $J_{4,5}$ 10.4, $H4^A$,4^B), 5.74 (2 H, m, $H2^A$,2^B), 5.89 (1 H, dd, $J_{2,3}$ 3.2, $J_{3,4}$ 10.0), 5.94 (1 H, dd, $J_{2,3}$ 3.2, $J_{3,4}$ 10.0, $H3^A$,3^B), 7.26–8.19 (30 H, Ph); δ_C(100.5 MHz; $CDCl_3$; Me_4Si) 14.08, 17.43, 22.67, 26.21, 29.30, 29.47, 29.68, 31.85 (8 C, $OCH_2(CH_2)_6CH_3$,$C6^B$), 66.56, 66.73, 67.15, 68.71, 69.40, 69.90, 70.37, 70.66, 70.75, 71.67 (10 C, C(2,3,4,5,6)^A,(2,3,4,5)^B,OCH_2CH_2), 97.52, 97.66 (2 H, $C1^A$,1^B), 128.22–133.39 (36 C, Ph), 165.13, 165.39, 165.51, 165.54, 165.71, 165.80 (6 C, C=O); *m/z* (ESI) 1085.3939 ($C_{62}H_{62}O_{16}$ $[M + Na]^+$ requires 1085.3936).

Octyl (2,3,4-tri-*O*-benzoyl-6-deoxy-α-D-mannopyranosyl)-(1→6)-(2,3,4-tri-*O*-benzoyl-α-D-mannopyranosyl)-(1→6)-(2,3,4-tri-*O*-benzoyl-α-D-mannopyranoside) 27. A solution of the iodo trimannoside **26** (133 mg, 80 μmol) and Bu_3SnH (32 μL, 118 μmol) and catalytic AIBN in toluene was treated as for the general procedure above. Flash chromatography (20 : 80 then 25 : 75 then 30 : 70 EtOAc–pet. spirits) afforded the protected deoxy dimannoside **27** (108 mg, 88%) as yellow oil, $[\alpha]_D^{18}$ −76 (*c* 0.8 in $CHCl_3$) (Found: C, 69.37; H, 5.64. $C_{89}H_{84}O_{24}$ requires C, 69.52; H, 5.57%); δ_H(399.7 MHz; $CDCl_3$; Me_4Si) 0.83–1.78 (15 H, m, $OCH_2(CH_2)_6CH_3$), 1.13 (3 H, d, $J_{5,6}$ 6.4, $H6^C$), 3.40 (1 H, br dd, $J_{5,6}$ 1.6, $J_{6,6}$ 10.8, $H6^A$), 3.62 (1 H, m, OCH_2CH_2), 3.84–4.09 (4 H, m, $H6^A$,(6,6)^B,OCH_2CH_2), 4.26 (1 H, dd, $J_{4,5}$ 11.2, $J_{5,6}$ 6.4), 4.27–4.31 (1 H, m), 4.52 (1 H, dd, $J_{4,5}$ 10.0, $J_{5,6}$ 2.4, $H5^A$,5^B,5^C), 4.77 (1H, br s), 5.16 (1 H, d, $J_{1,2}$ 1.6), 5.21 (1 H, d, $J_{1,2}$ 1.2, $H1^A$,1^B,1^C), 5.55 (1 H, dd, $J_{1,2}$ 2.0, $J_{2,3}$ 3.2), 5.79 (1 H, dd, $J_{1,2}$ 2.0, $J_{2,3}$ 3.2), 5.92 (1 H, br d, $H2^A$,2^B,2^C), 5.85 (1 H, dd, $J_{2,3}$ 3.2, $J_{3,4}$ 10.0), 5.98 (1 H, dd, $J_{2,3}$ 3.2, $J_{3,4}$ 10.0, $H3^A$,3^B), 6.05–6.06 (2 H, m, $H4^A$,3^C), 5.59 (1 H, dd, $J_{3,4}$ 10.0, $J_{4,5}$ 10.0), 6.25 (1 H, dd, $J_{3,4}$ 10.4, $J_{4,5}$ 10.0, $H4^B$,4^C), 7.22–8.23 (45 H, Ph); δ_C(100.5 MHz; $CDCl_3$; Me_4Si) 14.05, 17.37, 22.62, 26.15, 29.21, 29.43, 29.65, 31.79 (8 C, $OCH_2(CH_2)_6CH_3$,$C6^C$), 60.35, 65.68, 66.30, 66.63, 66.75, 68.65, 69.34, 69.85, 70.32, 70.50, 70.58, 70.69, 71.57 (15 C, C(2,3,4,5,6)^A, (2,3,4,5,6)^B, (2,3,4,5)^C,OCH_2CH_2), 97.24, 97.76, 97.85 (1 C, $C1^A$,1^B,1^C), 128.23–133.34 (54 C, Ph) 165.13, 165.17, 165.20, 165.42, 165.46, 165.56, 165.75 (9 C, C=O).

Octyl (2,3,4-tri-*O*-benzoyl-6-deoxy-α-D-mannopyranosyl)-(1→6)-(2,3,4-tri-*O*-benzoyl-α-D-mannopyranosyl)-(1→6)-(2,3,4-tri-*O*-benzoyl-α-D-mannopyranosyl)-(1→6)-(2,3,4-tri-*O*-benzoyl-α-D-mannopyranoside) 29. A solution of the iodo tetramannoside **28** (187 mg, 87 μmol) and Bu_3SnH (38.0 mg, 13 μmol) and catalytic AIBN in toluene (10 mL) was treated as for the general procedure above. Flash chromatography (30 : 70 then 35 : 65 then 40 : 60 EtOAc–pet. spirits) to afford the protected deoxy tetramannoside **29** (162 mg, 93%) as a clear gum, $[\alpha]_D^{17}$ −48 (*c* 0.49 in $CHCl_3$) (Found: 69.30; H, 5.40. $C_{116}H_{106}O_{32}$ requires C, 69.24; H, 5.31%); δ_H(399.7 MHz; $CDCl_3$; Me_4Si) 0.83–1.76 (15 H, m, $OCH_2(CH_2)_6CH_3$), 1.03 (3 H, d, $J_{5,6}$ 6.4, $C6^D$), 3.41–3.47 (2 H, m, H(6,6)^A), 3.60 (1 H, m, OCH_2CH_2), 3.79 (1 H, dd, $J_{5,5}$ 3.6, $J_{6,6}$ 11.2, $H6^B$), 3.86–3.07 (m, 4 H, $H6^B$,(6,6)^C,OCH_2CH_2), 4.23 (1 H, br dd), 4.27–4.32 (2 H, m), 4.52–4.55 (dd, $J_{4,5}$ 10.0, $J_{5,6}$ 2.4, $H5^A$,5^B,5^C,5^D), 4.87 (1 H, br d), 4.88 (1 H, d, $J_{1,2}$ 0.8), 5.16 (1 H, d, $J_{1,2}$ 1.6), 5.24 (1 H, br d, $H1^A$,1^B,1^C,1^D), 5.59 (1 H, dd, $J_{3,4}$ 10.0, $J_{4,5}$ 9.6, $H4^A$), 5.65 (1 H, dd, $J_{1,2}$ 1.6, $J_{2,3}$ 2.8), 5.72 (1 H, dd, $J_{1,2}$ 1.6, $J_{2,3}$ 3.2), 5.79 (dd, $J_{1,2}$ 2.0, $J_{2,3}$ 3.2, $H2^A$,2^B,2^C), 5.88 (1 H, dd, $J_{2,3}$ 3.2, $J_{3,4}$ 10.0, $H3^A$), 5.92–5.99 (3 H, m, $H2^D$,3^B,3^C), 6.09–6.12 (2 H, m, $H3^D$,4^B), 6.15 (1 H, dd, $J_{3,4}$ 10.0, $J_{4,5}$ 10.4), 6.26 (1 H, dd, $J_{3,4}$ 10.4, $J_{4,5}$ 10.0. $H4^C$,4^D), 7.22–8.22 (60 H, m, Ph); δ_C(100.5 MHz; $CDCl_3$; Me_4Si) 14.32, 17.44, 22.86, 26.38, 29.46, 29.69, 29.91, 32.05 (8 C, $OCH_2(CH_2)_6CH_3$, $C6^D$), 66.55, 66.82, 66.91, 68.85, 69.29, 69.63, 70.18, 70.38, 70.54, 70.65, 70.83, 71.69 (20 C, C(2,3,4,5,6)^A, (2,3,4,5,6)^B, (2,3,4,5,6)^C, (2,3,4,5)^D, OCH_2CH_2), 97.81, 97.97, 98.16 (4 C, $C1^A$,1^B,1^C,1^D), 128.48–133.56 (72 C, Ph), 165.29, 165.41, 165.45, 165.50, 165.59, 165.71, 165.82, 166.00, 166.06 (9 C, C=O).

General method for global deprotection of 6, 12, 16, 23, 25, 27 and 29

The protected oligomannoside was dissolved in MeOH and treated with a small piece of sodium metal. The solution

was stirred for 1–4 h until TLC (7 : 2 : 1 EtOAc–MeOH–H_2O) indicated the reaction was complete. Dowex-50 resin (H^+ form) was added to neutralize the reaction. Following filtration, the filtrate was treated with Amberlite IRA 400 (OH^- form), the solvent evaporated and the residue purified by flash chromatography. Following this a small portion was purified by C_{18} reverse phase chromatography (100% H_2O to 100% MeOH).

Octyl (α-D-mannopyranosyl)-(1→6)-(α-D-mannopyranoside) 7. The dimannoside alcohol **6** (0.153 g, 153 μmol) was treated as for the general procedure above. Flash chromatography (9 : 1 MeOH–EtOAc then 17 : 2 : 1 then 7 : 2 : 1 EtOAc–MeOH–H_2O) afforded the dimannoside **7** (41.7 mg, 60%) as a pale yellow oil, $[a]_D^{18}$ +50 (*c* 1.2 in MeOH) (lit.,[17,24] +27.3, +55.6 (H_2O)); δ_H(399.7 MHz; d_4-MeOH; MeOH) 0.90–1.60 (15 H, m, $OCH_2(CH_2)_6CH_3$), 3.31–3.44 (2 H, m, OCH_2CH_2), 3.64–3.93 (12 H, m, H(2,3,4,5,6,6)^A, (2,3,4,5,6,6)^B), 4.72, 4.83 (2 H, 2 br s, H1^A,1^B); δ_C(100.5 MHz, d_4-MeOH) 14.59, 23.88, 27.58, 30.56, 30.68, 30.77, 33.16 (7 C, $OCH_2(CH_2)_6CH_3$), 67.53, 68.73, 72.26, 72.34, 72.79, 72.99, 73.23, 74.46 (11 C, C(2,3,4,5,6)^A,(2,3,4,5,6)^B,OCH_2CH_2), 101.51, 101.75 (2 C, C1^A,1^B); *m/z* (ESI) 477.4 ($C_{20}H_{38}IO_{11}$ $[M + Na]^+$ requires 477.2).

Octyl (α-D-mannopyranosyl)-(1→6)-(α-D-mannopyranosyl)-(1→6)-(α-D-mannopyranoside) 10. The trimannoside alcohol **12** (0.153 g, 98.4 μmol) was treated as for the general procedure above. Flash chromatography (9 : 1 EtOAc–MeOH then 17 : 2 : 1 then 7 : 2 : 1 EtOAc–MeOH–H_2O) afforded the trimannoside **10** (42.6 mg, 70%) as clear glass, $[a]_D^{20}$ +78 (*c* 1.1 in MeOH) (Found: C, 50.79; H, 7.79. $C_{26}H_{48}O_{16}$ requires C, 50.64; H, 7.85%); δ_H(399.7 MHz; d_4-MeOH, MeOH) 0.89–1.59 (15 H, m, $OCH_2(CH_2)_6CH_3$), 3.41 (1 H, m, OCH_2CH_2), 3.60–3.87 (19 H, m, H(2,3,4,5,6,6)^A,(2,3,4,5,6,6)^B,(2,3,4,5,6,6)^C,OCH_2CH_2), 4.73, 4.78 (2 H, 2 br s, H1^A,1^B), solvent peak obscured H1^C; δ_C(100.5 MHz, d_4-MeOH) 14.59, 23.88, 27.59, 30.56, 30.68, 30.77, 33.16 (7 C, m, $OCH_2(CH_2)_6CH_3$), 62.99, 67.27, 67.49, 68.78, 72.14, 72.44, 72.63, 73.00, 73.15, 74.55 (16 C, m, C(2,3,4,5,6)^A, (2,3,4,5,6)^B, (2,3,4,5,6)^C, OCH_2CH_2), 100.98, 101.22, 101.58 (3 C, C1^A,1^B,1^C); *m/z* (ESI) 615.4 [$C_{89}H_{84}O_{25}$ $(M - H)^+$ requires 615.3].

Octyl (α-D-mannopyranosyl)-(1→6)-(α-D-mannopyranosyl)-(1→6)-(α-D-mannopyranosyl)-(1→6)-(α-D-mannopyranoside) 14. The tetramannoside alcohol **16** (223 mg, 0.11 mmol) was treated as for the general procedure above. Flash chromatography (7 : 2 : 1 then 5 : 2 : 1 EtOAc–MeOH–H_2O) afforded the tetramannoside **14** (25.3 mg, 30%) as a clear glass, $[a]_D^{11}$ +91 (*c* 0.54 in MeOH); δ_H(399.7 MHz; d_4-MeOH, MeOH) 0.84–1.54 (15 H, m, $OCH_2(CH_2)_6CH_3$), 3.25–3.84 (26 H, H(2,3,4,5,6,6)^A,(2,3,4,5,6,6)^B,(2,3,4,5,6,6)^C,(2,3,4,5,6,6)^D,OCH_2CH_2), 4.68, 4.74, 4.77, 4.80 (4 H, 4 br s, H1^A,1^B,1^C,1^D); δ_C(100.5 MHz, d_4-MeOH) 14.62, 23.89, 27.59, 30.57, 30.69, 30.77, 33.16 (7 C, $OCH_2(CH_2)_6CH_3$), 63.00, 67.08, 67.29, 67.47, 68.75, 72.06, 72.18, 72.36, 72.45, 72.63, 72.83, 72.97, 73.05, 73.10, 75.52 (21 C, C(2,3,4,5,6)^A, (2,3,4,5,6)^B, (2,3,4,5,6)^C, (2,3,4,5,6)^D, OCH_2CH_2), 100.74, 101.07, 101.57 (4 C, C1^A,1^B,1^C,1^D).

Octyl 6-deoxy-α-D-mannopyranoside 4. The protected deoxy monomannoside **23** (161 mg, 0.27 mmol) was treated as for the general procedure above. Flash chromatography (17 : 2 : 1 EtOAc–MeOH–H_2O) afforded the deoxy monomannoside **4** (33 mg, 44%) as a clear gum, $[a]_D^{15}$ +52 (*c* 0.5 in MeOH) (Found: C, 60.71; H, 10.14. $C_{19}H_{28}O_5$ requires C, 60.84; H, 10.21%); δ_H(399.7 MHz; d_4-MeOH, MeOH) 0.86–1.60 (15 H, m, $OCH_2(CH_2)_3CH_3$), 1.25 (3 H, d, $J_{5,6}$ 6.0, H6), 3.26–3.78 (6 H, m, H2,3,4,5,OCH_2CH_2), 4.64 (1 H, d, $J_{1,2}$ 6.0, H1); δ_C(100.5 MHz, d_4-MeOH) 47.41, 47.59, 47.88, 48.06, 48.22, 48.22, 48.23, 48.35 (8 C, $OCH_2(CH_2)_3CH_3$, C6), 50.13, 50.19. 50.32, 50.41 (5 C, C2,3,4,5,OCH_2CH_2), 51.79 (1 C, C1).

Octyl (6-deoxy-α-D-mannopyranosyl)-(1→6)-(α-D-mannopyranoside) 8. The protected deoxy dimannoside **25** (170 mg, 160 μmol) was treated as for the general procedure above. Flash chromatography (9 : 1 MeOH–EtOAc then 17 : 2 : 1 then 7 : 2 : 1 EtOAc–MeOH–H_2O) yielded the deoxy dimannoside **8** (53.9 mg, 77%) as a yellow gum, $[a]_D^{15}$ +62 (*c* 1.1 in MeOH); δ_H(399.7 MHz; d_4-MeOH, MeOH) δ 0.89–1.59 (15 H, m, $OCH_2(CH_2)_6CH_3$), 1.25 (3 H, d, $J_{5,6}$ 6.4, H6^B), 3.31 (2 H, m, OCH_2CH_2), 3.35–3.86 (10 H, H(2,3,4,5,6,6)^A,(2,3,4,5)^B), 4.71 (1 H, d, $J_{1,2}$ 1.2), 4.74 (1 H, d, $J_{1,2}$ 1.2, H1^A,1^B); δ_C(100.5 MHz, d_4-MeOH) 14.59, 18.16, 22.87, 27.57, 30.55, 30.66, 30.76, 33.14 (8 C, $OCH_2(CH_2)_6CH_3$,C6^B), 67.52, 68.70, 69.74, 72.32, 72.57, 73.01, 73.22, 74.18 (10 C, C(2,3,4,5,6)^A,(2,3,4,5,6)^B,OCH_2CH_2), 101.53, 101.73 (2 C, C1^A,1^B); *m/z* (ESI) 461.2360 ($C_{20}H_{38}O_{10}$ $[M + Na]^+$ requires 461.2363).

Octyl (6-deoxy-α-D-mannopyranosyl)-(1→6)-(α-D-mannopyranosyl)-(1→6)-(α-D-mannopyranoside) 11. The protected deoxy trimannoside **27** (108 mg, 70 μmol) was treated as for the general procedure above. Flash chromatography (9 : 1 then 17 : 2 : 1 then 7 : 2 : 1 EtOAc–MeOH–H_2O) afforded the deoxy trimannoside **11** (27.8 mg, 66%) as an opaque yellow gum, $[a]_D^{20}$ +66 (*c* 0.7 in MeOH) (Found: C, 52.03; H, 7.96. $C_{26}H_{48}O_{15}$ requires C, 51.99; H, 8.05%); δ_H(399.7 MHz; d_4-MeOH, MeOH) 0.91–1.62 (15 H, $OCH_2(CH_2)_6CH_3$), 1.28 (3 H, d, $J_{5,6}$ 6.4, H6^C); 3.13–3.89 (17 H, m, H(2,3,4,5,6,6)^A, (2,3,4,5,6,6)^B, (2,3,4,5,6,6)^C, OCH_2CH_2), 4.75, 4.80 (2 H, br s, H1^A,1^B), solvent peak obscured H1^C; δ_C(100.5 MHz, d_4-MeOH, MeOH) 14.59, 18.18, 23.85, 27.56, 30.52, 30.65, 30.74, 33.13 (8 C, $OCH_2(CH_2)_6CH_3$,C6^C), 67.18, 67.44, 68.73, 68.78, 69.79, 72.13, 72.23, 72.41, 72.98, 73.04, 73.10, 74.24 (15 C, C(2,3,4,5,6)^A, (2,3,4,5,6)^B, (2,3,4,5,)^C, OCH_2CH_2) 100.96, 101.20, 101.55 (3 C, C1^A,1^B,1^C).

Octyl (6-deoxy-α-D-mannopyranosyl)-(1→6)-(α-D-mannopyranosyl)-(1→6)-(α-D-mannopyranosyl)-(1→6)-(α-D-mannopyranoside) 15. The protected deoxy tetramannoside **29** (144 mg, 0.072 mmol) was treated as for the general procedure above. Flash chromatography (17 : 2 : 1 then 7 : 2 : 1 then 5 : 2 : 1 EtOAc–MeOH–H_2O) afforded the deoxy tetramannoside **15** (23.9 mg, 44%) as a glass, $[a]_D^{12}$ +80° (*c* 0.8 in MeOH) (Found: C, 52.11; H 7.99. $C_{33}H_{60}O_{19}$ requires C, 51.10; H, 7.95%); δ_H(399.7 MHz; d_4-MeOH, MeOH) 0.76–1.48 (15 H, m, $OCH_2(CH_2)_6CH_3$), 1.13 (3 H, d, $J_{5,6}$ 6.0, H6^D), 3.13–3.76 (24 H, m, H(2,3,4,5,6,6)^A, (2,3,4,5,6,6)^B, (2,3,4,5,6,6)^C, (2,3,4,5)^D, OCH_2CH_2), 4.60 (1H, d, $J_{1,2}$ 1.2), 4.64 (1 H, d, $J_{1,2}$ 1.6), 4.67 (1 H, d, $J_{1,2}$ 2.0), 4.69 (1 H, d, $J_{1,2}$ 1.6, 4H, H1^A,1^B,1^C,1^D); δ_C(100.5 MHz, d_4-MeOH) 14.62, 18.21, 23.89, 27.60, 30.58, 30.69, 30.78, 33.17 (8C, $OCH_2(CH_2)_6CH_3$, C6^D), 67.09, 67.24, 67.45, 68.70, 69.78, 72.10, 72.21, 72.27, 72.38, 72.67, 72.88, 72.96, 73.05, 73.13, 74.26 (20 C, C(2,3,4,5,6)^A, (2,3,4,5,6)^B, (2,3,4,5,6)^C, (2,3,4,5)^D, OCH_2CH_2), 100.76, 101.09, 101.58 (4 C, C1^A,1^B,1^C,1^D).

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