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Total Synthesis of Phosphatidylinositol Mannosides of *Mycobacterium tuberculosis*

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Abstract: The total synthesis of phosphatidylinositol mannosides (PIMs), a key class of antigenic glycolipids found on the cell wall of *Mycobacterium tuberculosis*, is described. The synthetic strategy relied on a [4 + 3] glycosylation of tetramannoside **1** and pseudotrisaccharide **2**, which allowed for convergent access to the glycan backbone of the phosphatidylinositol dimannoside (PIM_2) and hexamannoside (PIM_6). A short practical synthesis of tuberculostearic acid was achieved based on a copper-catalyzed cross-coupling reaction. Union of the glycan and lipid parts resulted in the first total synthesis of native PIM_2 and PIM_6.

Introduction

Tuberculosis (TB) is among the most devastating infectious diseases in the world. Once considered to be a third world disease, TB has been recently declared a "global health emergency" by the World Health Organization. Estimated to infect eight million people annually, the disease has now spread to one-third of the world's population, culminating in two million deaths per year.[1] TB is caused by *Mycobacterium tuberculosis*, one of the most effective bacterial human pathogens. The cell wall of *M. tuberculosis* is covered by a thick glycocalyx that is critical for the integrity of bacteria and allows them to infect, survive, and propagate within the human host.[2,3] The major components of the mycobacterial envelope are the mycolyl arabinogalactan−peptidoglycan complex (mAGP) and the lipoarabinomannan (LAM) associated lipoglycans. LAMs have been shown to exert profound physiological effects and emerge as the most potent nonpeptidic molecules to modulate the host immune response.[4,5]

LAMs contain a phosphatidyl *myo*-inositol (PI) anchor that is extended by mannosyltransferases, to phosphatidylinositol mono-, di-, tri-, and tetramannosides (PIM_1→PIM_2→PIM_3→PIM_4) (Figure 1). PIM_4 is postulated to be a key biosynthetic intermediate. Modification of PIM_4 with α1-2-linked mannose leads to more polar penta- and hexamannosides (PIM_5 and PIM_6). Alternatively, PIM_4 can be further extended with α1-6-linked mannose to form the linear mannan core. This backbone can be modified with additional α1-2-linked mannose to lead to mature branched lipomannan (LM), which undergoes subsequent arabinosylation to form LAMs.[6,7] Although the gross structural features of LM and LAMs have been elucidated, the degree of branching on the mannan and arabinan backbone and the attachment site(s) for the arabinan chains on the mannan core still remain unknown. In contrast to the structural uncertainties associated with LM and LAM, the glycan sequences and compositions of PIMs have been well established.[8,9] Recent studies clearly defined the lipid composition of this class of glycolipids.[10,11] PIMs not only are important biosynthetic precursors to LM and LAM but also are present in the

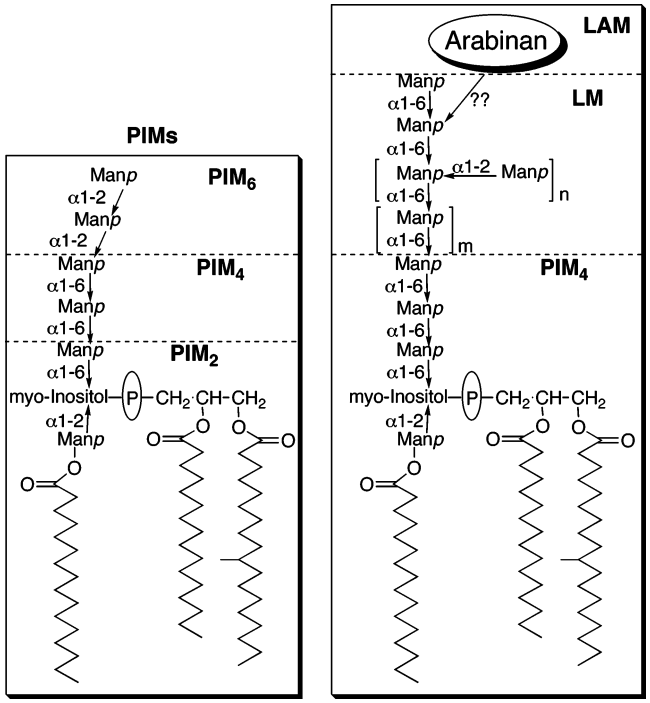

Figure 1. Structural features of PIMs, LM, and LAM (typical lipid composition shown).

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10.1021/ja0565368 CCC: $33.50

mycobacterial cell wall, predominantly in the form of PIM_2 and PIM_6, and elicit a variety of immune responses. PIMs act as agonists of Toll-like receptor 2 (TLR2), a pattern recognition receptor involved in innate immunity. PIMs activate primary macrophages to secrete tumor necrosis factor-α via TLR2.[10,11] It has been demonstrated that PIMs interact with human CD1 molecules and recruit human natural killer T cells via CD1d.[12,13]

The structural uniqueness of PIMs has attracted the attention of synthetic chemists since the early 1990s. PIM_2-related glycolipids were initially prepared in 1992,[14−16] followed by further syntheses.[17,18] More recently, the synthesis of PIM_1 and PIM_2 analogues were reported by Schmidt and Fraser-Reid.[19−21] All previous syntheses focused on the efficient preparation of the carbohydrate motif using different glycosylation strategies whereby different phospholipids were introduced that did not mirror the natural scenario. It should be noted that the lipid composition of antigenic glycolipids usually plays a vital role in inducing an immune response.[22] Syntheses of higher PIMs have not been reported to date.

We became interested in the chemistry and biology of PIMs in view of their biological relevance to the immunopathogenesis of tuberculosis. As part of our program in pursuit of novel glycolipid-based immunomodulators and carbohydrate-based vaccines against TB, we set out to synthesize these lipoglycans. Herein, we report the first total syntheses of native PIM_2 and PIM_6.

Results and Discussion

Synthetic Strategies. PIM_2 is the biosynthetic precursor to PIM_6 so that both glycan backbones have the 2,6-di-*O*-mannosyl-D-*myo*-inositol pseudotrisaccharide in common (Figure 2). The carbohydrate core is anchored in the cell membrane via a phosphatidyl−diacylglycerol moiety. Further lipidation can occur on C-3 of the inositol unit and C-6 of the mannose linked to C-2 of inositol and is responsible for the microheterogeneous character of PIMs. However, recent studies have shown that the dominant forms of PIM_2 and PIM_6 are triacylated species containing (*R*)-10-methyloctadecanoic acid and palmitic acid on glycerol and palmitic acid on the mannose residue.[10,11] Based on these observations, we set out to synthesize these dominant structures (Figure 2). Considering the structural similarities of PIM_2 and PIM_6, we envisioned a convergent strategy whereby a [4 + 3] glycosylation between fragments **1** and **2** would form PIM_6, while **2** itself can be readily converted to PIM_2. The two sites on the glycan backbone to be lipidated are masked with orthogonal allyl and triisopropyl silyl (TIPS) groups. Incorporation of the lipids at a late stage in the synthesis will facilitate future access to PIM analogues containing different lipid chains.

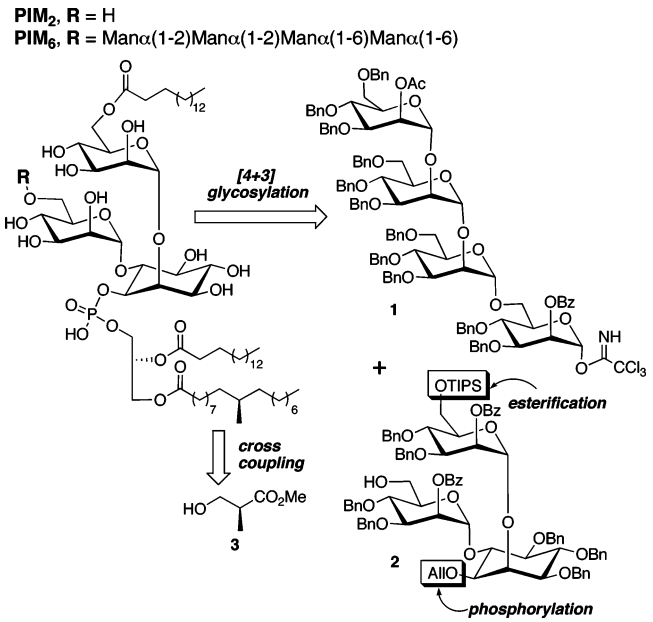

Figure 2. Structure and retrosynthesis of PIM_2 and PIM_6.

A Short Synthesis of Tuberculostearic Acid. (*R*)-10-Methyloctadecanoic acid was originally isolated from tubercle bacilli and thus named tuberculostearic acid (TBSA).[23,24] TBSA is the basic cell wall constituent of mycobacteria and has been explored as a diagnostic marker for the detection of TB.[25,26] Three total syntheses of TBSA were reported in the late 1940s, aiming at the structural confirmation of this chiral fatty acid.[27−29] However, the synthetic sequences are all lengthy and tedious in nature. We imagined an alternative strategy to gain access to this unique fatty acid, using the readily available methyl (*S*)-3-hydroxy-2-methylpropionate (Roche ester) **3** as chiral building block (Figure 2), followed by iterative Cu-catalyzed cross-coupling reactions between alkyl Grignard reagents and alkyl tosylates.[30] The total synthesis of PIM_2 and PIM_6 commenced with the implementation of this new route to TBSA (Scheme 1).

Enantiopure Roche ester was first converted to tosylate **4**,[31] then coupled with heptylmagnesium bromide, mediated by catalytic dilithium copper tetrachloride (Li_2CuCl_4). Cleavage of the THP moiety gave alcohol **5**, which was transformed to tosylate **6** and subjected to a further Cu-catalyzed cross-coupling with the Grignard reagent derived from THP-protected 8-bromooctanol **7**.[32] Removal of the THP moiety then afforded (*R*)-10-methyloctadodecanol **8**. After screening several oxidation protocols, a TEMPO-catalyzed oxidation was found to be optimal,[33] furnishing the analytically pure TBSA **9** in high yield

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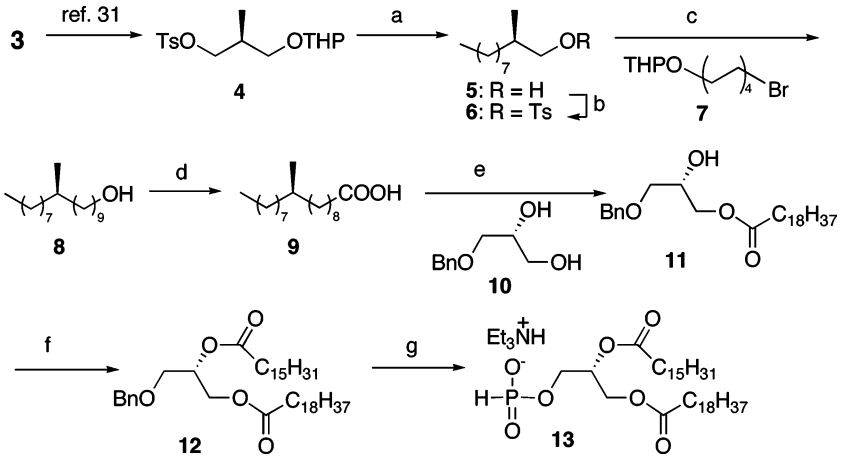
Scheme 1. Synthesis of TBSA **9** and Phospholipid **13**[a]



[a] Reagents and conditions: (a) $C_7H_{15}MgBr$, Li_2CuCl_4 (cat.), THF, then *p*TsOH, MeOH, 80%, two steps; (b) TsCl, Py, quant.; (c) **7** with Mg, THF, Li_2CuCl_4 (cat.), then *p*TsOH, MeOH/Hexane, 76%; (d) TEMPO (cat.), NaOCl (cat.), $NaClO_2$, CH_3CN, 93%; (e) **9**, DMAP (cat.), DCC, CH_2Cl_2, 75%; (f) $C_{15}H_{31}COOH$, DMAP (cat.), DCC, CH_2Cl_2, 88%; (g) (i) H_2, Pd/C, EtOH/AcOH, 93%, (ii) PCl_3, Im, Et_3N, 67%.

without the need for chromatographic purification. With several grams of TBSA in hand, its incorporation into the phospholipids commmenced. Regioselective acylation of the *sn*-1-hydroxyl group of 3-*O*-benzyl-*sn*-glycerol **10** with stoichiometric amounts of TBSA, DCC, and DMAP gave ester **11** in 75% yield. The *sn*-2-hydroxyl was further capped with palmitic acid to afford diester **12**. While removal of the benzyl substituent is required to proceed to the following phosphorylation, we found that 2→3-acyl migration of the plamitoyl group occurred even during the reaction, albeit to a small extent.[34] Consequently, to synthesize H-phophonate **13**, the reaction mixture had to be purified by rapid chromatography and used immediately after purification. In this fashion, enantiopure **13** was obtained in good overall yield.

Preparation of the Mannose Building Blocks and Assembly of the Tetramannoside Fragment. To maximize synthetic convergency, three key mannose building blocks, derived from two mannose ortho esters, were used to assemble the mannose portions in PIM_2 and PIM_6. Hydrolysis of the ortho esters, **14a** and **15a**, using *p*-TsOH gave the corresponding hemiacetals that were readily converted to mannosyl trichloroacetimidates **14b** and **15c** in good yield. Treatment of **15a** with excess allyl alcohol and $BF_3{\cdot}Et_2O$ activation, followed by removal of the TIPS substituent with in situ generated HCl in methanol, gave mannoside **15b**. Construction of tetramannoside **1** commenced with the coupling of mannosides **14b** and **15b** to furnish known disaccharide **16** (Scheme 2).[35] Disaccharide **16** was elongated via intermediate **17** to tetrasaccharide **18** using iterative TMSOTf-catalyzed glycosylation with **14b** and mildly acidic conditions to cleave the temporary acetate protecting groups in the presence of the benzoyl ester. Removal of the anomeric allyl group with $PdCl_2$, and treatment with Cl_3CCN and DBU, afforded tetramannoside **1** in 52% yield over two steps.

Assembly of Inositol-Containing Fragment 2 and Total Synthesis of PIM_2. The construction of the key inositol-containing fragment **2** commenced with the synthetic elaboration of enantiopure *myo*-inositol derivative **19** that is readily available from methyl α-D-glucose.[36] While the literature method relied on a deacylation and subsequent regioselective allylation via a stannylene acetal to introduce the allyl group on the C-1 of inositol (**19**→**20**), we found this method to give variable yields with low conversion rates, especially during large-scale operation. Consequently, we developed a two-stage protection−deprotection sequence, where the C-2 and C-6 hydroxyl groups of inositol **19** were temporarily masked as ethoxyethyl (EE) ethers (Scheme 3). Base-catalyzed deacylation, followed by allylation and removal of the EE groups under acidic conditions, gave **20** in 82% over four steps. This method provided reproducible yields on a 20-mmol scale and had been applied during our previous syntheses of glycosylphosphatidylinositols, a different class of glycolipids.[35,37−40]

Regioselective alkylation of inositol **20**, using 2-naphthylmethyl bromide (NAPBr), gave **21** in 81% yield. Our overall synthetic design required the C-6 hydroxyl of mannose to be attached to the C-6 of inositol to be masked with a temporary orthogonal protecting group. This protective group has to be selectively removed in the presence of allyl, benzyl, benzoyl, and silyl ethers at the late stage of the synthesis (**25**→**2**, Scheme 3) to allow for the union with tetramannoside **1** and thus access PIM_6. A levulinoyl (Lev) ester was chosen to meet these criteria. Initially we attempted the glycosylation of **21** with mannosyl trichloroacetimidate **15d** (derived from **15b**, synthesis not shown) equipped with the levolinoyl group to directly access pseudodisaccharide **23**. To our surprise, **23** was isolated as a diastereomeric mixture at the anomeric carbon ($\alpha{:}\beta = 9{:}1$) even though a participating benzoyl ester is present at C-2 of mannoside **15d**. This observation can be explained by the reduced reactivity of glycosylating agent **15d** due to the incorporation of the levulinoyl group. Thus, a reactivity

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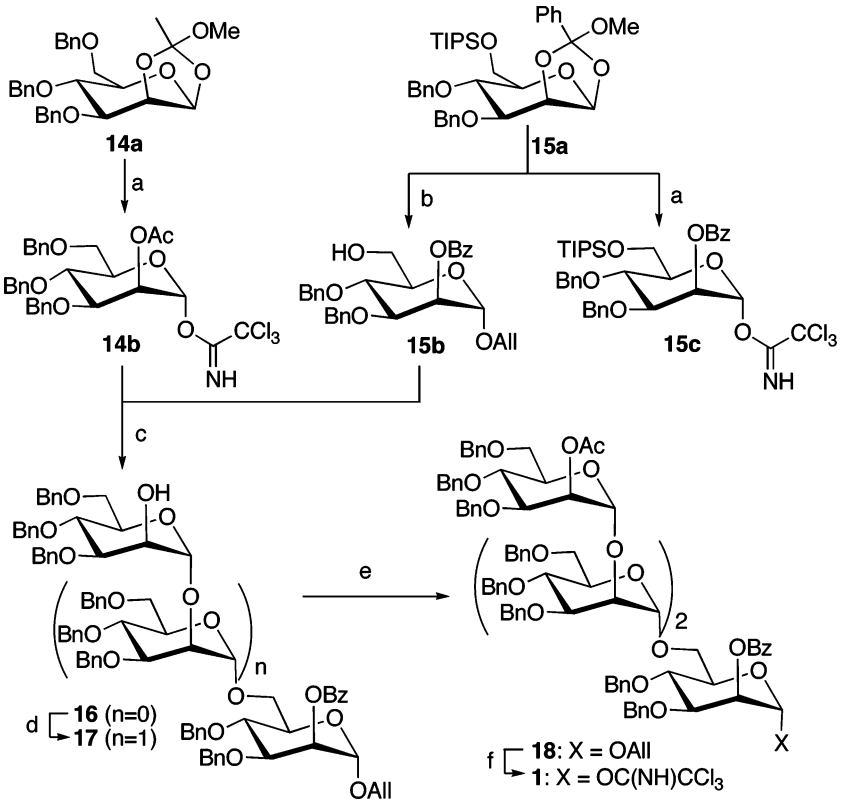
Scheme 2. Preparation of Mannose Building Blocks and Assembly of Tetramannoside **1**[a]



[a] Reagents and conditions: (a) (i) DME/H_2O, *p*TsOH, (ii) Cl_3CCN, DBU, 84% (**14b**), 80% (**15c**), 2 steps; (b) (i) AllOH, $BF_3{\cdot}Et_2O$, 4 Å MS, (ii) AcCl in MeOH/CH_2Cl_2, 86% two steps; (c) (i) TMSOTf (cat.), CH_2Cl_2, (ii) AcCl in MeOH/CH_2Cl_2, 80%, two steps; (d) (i) **14b**, TMSOTf (cat.), CH_2Cl_2, (ii) AcCl in MeOH/CH_2Cl_2, 74%, two steps; (e) (i) **14b**, TMSOTf (cat.), CH_2Cl_2, 83%; (f) (i) $PdCl_2$, NaOAc, AcOH/H_2O, (ii) Cl_3CCN, DBU, CH_2Cl_2, 52%, two steps.

mismatch between the "armed" glycosyl acceptor **21** and the "disarmed" glycosyl donor **15d** occurred, resulting in poor selectivity. Further evidence supporting this explanation was sought by switching to the more reactive glycosylating agent **15c**. Union of **15c** and **21** proceeded with complete α-selectivity to give the corresponding pseudodisaccharide. Immediate removal of the TIPS group under acidic conditions gave **22** in 84% yield. The hydroxyl group of **22** was then masked as the Lev ester to form **23**, and the NAP group was removed by treatment with DDQ in CH_2Cl_2/MeOH to ready **24** for the following mannosylation. Coupling of **24** and **15c** proceeded again with complete stereoselectivity to furnish **25** in 80% yield. However, this seemingly obvious selectivity is caused by more than the participating effect of C-2 benzoate in mannosyl trichloroacetimidate **15c**. In a recent study by Fraser-Reid,[41] a substrate similar to **24** (**24′**, R^2 = TBDPS, instead of Lev) gave poor yield and no stereoselectivity upon glycosylation with an analogue of **15c** (**15c′**, TBS group in C-6 instead of TIPS). A reactivity mismatch between the relatively unreactive glycosyl donor **15c′** and the more reactive glycosyl acceptor **24′** explains this observation. The disarming effect of the Lev group on **24** contributed to the perfect selectivity in our system, as the reactivity of **24** was lower than **24′** and consequently matched that of glycosylating agent **15c**. These observations (**21** + **15d** → **23**, **24** + **15c** → **25**) highlight the importance of reactivity matching between glycosyl donors and acceptors to control the stereochemistry of glycosylations.[42]

With key intermediate **25** in hand, removal of the Lev group furnished pseudo-trisaccharide **2** for the synthesis of PIM_6. Alternatively, to access PIM_2, the ester groups in **25** were replaced with benzyl ethers to give **26**. Silyl ether cleavage provided **27** in excellent yield, and subsequent esterification with palmitic acid also proceeded smoothly. Removal of the allyl group from **28** under the agency of $PdCl_2$ led to **29** in 51% yield, while a ketone byproduct resulting from a Wacker-type oxidation accumulated in 30% yield. Consequently, an alternative protocol using a cationic iridium catalyst to facilitate the removal of the allyl group was explored.[43] Though the isomerization of allyl to the corresponding enol proceeded smoothly, clean scission of the enol could never be achieved. Therefore, albeit obtained in moderate yield, **29** was further phosphorylated with H-phosphonate **13** to afford the fully protected PIM_2 (**30**) in 85% yield.

The end game required the removal of all of the benzyl ethers present in **30** via hydrogenolysis. Unexpectedly, the conventional method using $Pd(OH)_2$ on carbon in $CHCl_3$/MeOH/H_2O resulted in partial cleavage of the lipids from the carbohydrate backbone. Consequently, several catalysts and solvent conditions were screened, with Pd/C in EtOAc/THF/PrOH/H_2O proving optimal and giving PIM_2 in a respectable 82% yield.[44]

Total Synthesis of PIM_6. The synthetic ventures outlined above rendered fragments **1** and **2** available to us. The union of **1** and **2** was promoted by TMSOTf in the presence of 4 Å

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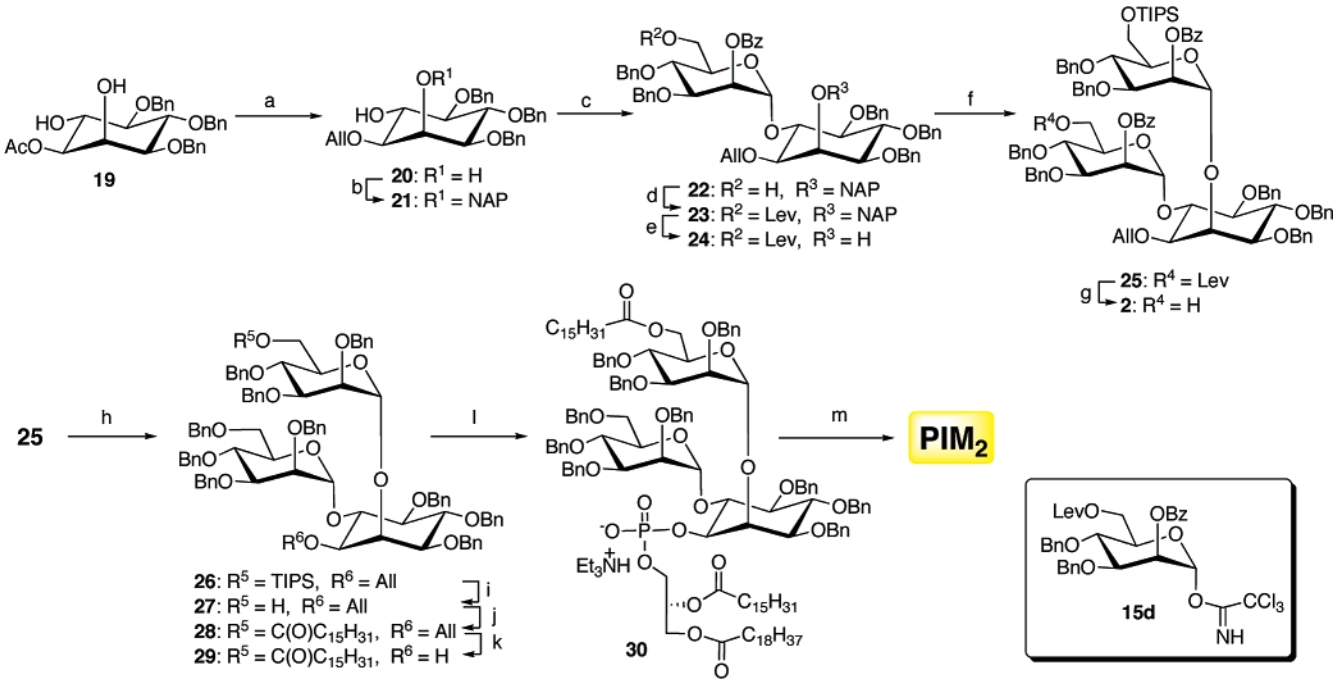
Scheme 3. Assembly of Inositol Dimannnoside **2** and Total Synthesis of PIM_2[a]



[a] Reagents and conditions: (a) (i) CH_2=CHOEt, PPTS, then NaOMe, MeOH, (ii) AllBr, NaH, then 2N HCl, 84%, two steps; (b) NAPBr, NaH, TBAI, DMF, 81%; (c) **15c**, TMSOTf (cat.), CH_2Cl_2, then AcCl in MeOH/CH_2Cl_2, 85%; (d) LevOH, DCC, DMAP, CH_2Cl_2, 93%; (e) DDQ, CH_2Cl_2/MeOH, 81%; (f) **15c**, TMSOTf (cat.), CH_2Cl_2, 80%; (g) $H_2NNH_2 \cdot H_2O$, Py/AcOH, 89%; (h) NaOMe, MeOH, then BnBr, NaH, DMF, 80%; (i) AcCl in MeOH/CH_2Cl_2, 97%; (j) $C_{15}H_{31}COOH$, DCC, DMAP, 86%; (k) $PdCl_2$, NaOAc, AcOH/H_2O, 51%; (l) **13**, PivCl, Py, then I_2, Py/H_2O, 85%; (m) H_2, Pd/C, EtOAc/THF/PrOH/H_2O, 82%.

MS to give pseudo-heptasaccharide **31** in 91% yield with complete stereocontrol. The acetyl and benzoyl esters were then cleaved to yield tetraol **32** that was subsequently converted to benzyl ether protected **33**. Mildly acidic conditions allowed for the efficient cleavage of the silyl group, while further esterification of **34** led to the palmitoyl derivative **35**. Cleavage of the C-1 allyl group in inositol using $PdCl_2$ proved more problematic. The target compound **36** was isolated in a mere 40% yield with an equal amount of the oxidized ketone byproduct also obtained. This low yield prompted us to further explore different deallylation protocols in addition to using the cationic iridium complex that had been shown to be ineffective in the synthesis of PIM_2. In particular, the recently reported cationic $CpRu^{II}$ complex with quinaldic acid in MeOH seemed attractive.[45] Employing this system, the single allyl substituent in **35** was removed cleanly to afford **36** in 72% yield, although stiochiometric amount of ruthenium catalyst was required. Phosphorylation of **36** with H-phosphonate **13** then gave fully protected PIM_6 **37** in 81% yield. Global debenzylation of **37** using the modified Pd/C in EtOAc/THF/PrOH/H_2O protocol furnished the native PIM_6 in 76% yield (Scheme 4).

Conclusion

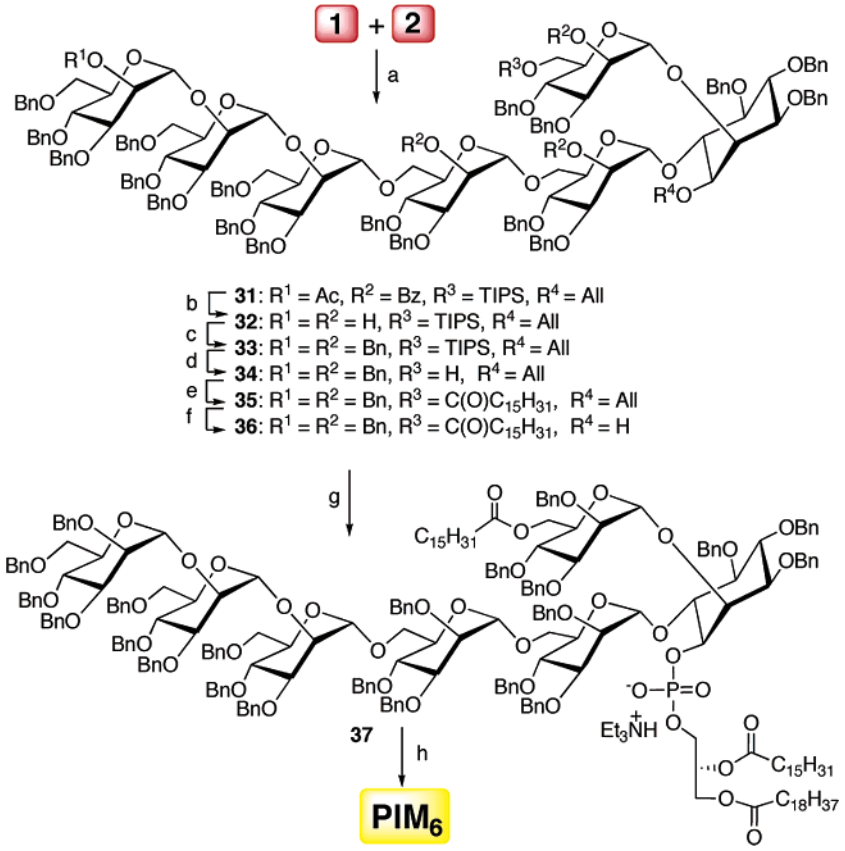
We achieved the first total syntheses of the native PIM_2 and PIM_6 present in the cell wall of *M. tuberculosis*. A series of efficient synthetic transformations elaborated three building blocks **14a**, **15a**, **20** into the pseudo-trisaccharide **25** and -heptasaccharide **31**. The overall efficiency of the assembly process benefited from a set of properly selected protecting groups. Blocking groups were selected by virtue of orthogonality, participating effect, and, importantly, reactivity tuning effects on the glycosylating agents. Thus, complete stereoselectivity for each glycosylation throughout the entire synthetic process was ensured. Tuberculostearic acid was synthesized in rapid fashion from Roche ester. Late stage incorporation of the lipids into the glycan backbone maximized synthetic convergence and ensured easy access to PIM motifs with different lipids. These PIMs and their analogues will be important tools to establish a structure−activity relationship of these lipoglycans and their effect on the immunopathogenesis of tuberculosis. Such biological effects are currently being explored in our laboratory.

Experimental Section

(*R*)-10-Methyloctadecan-1-ol (8): To a solution of tosylate **6** (1.68 g, 5.12 mmol) in dry THF (15 mL) at −78 °C was added dropwise via cannula a solution of Grignard reagent derived from **7** in THF (freshly prepared from THP-protected 8-bromooctanol **7**[32] (6.0 g, 20.5 mmol) and magnesium turnings (0.52 g, 21.5 mmol) in THF (22 mL)), followed by a solution of dilithium copper tetrachloride (5.1 mL, 0.51 mmol, 0.1 M in THF). The resulting mixture was gradually warmed to 0 °C over 90 min and stirred at 0 °C for an additional 12 h. The reaction mixture was then carefully poured into an ice-cooled saturated aqueous NH_4Cl solution (60 mL) and extracted with EtOAc (30 mL × 3). The combined organic layers were washed with water (50 mL) and brine (50 mL), dried over Na_2SO_4, and then concentrated in vacuo. The residue was purified by flash silica gel column chromatography to give a mixture of THP-protected 10-methyloctadecanol and THP-protected octanol. This mixture was then dissolved in methanol (10 mL) and hexane (6 mL), and *p*TsOH·H_2O (9.8 mg) was added. The resulting solution was heated at 40 °C for 4 h and then neutralized with saturated aqueous $NaHCO_3$ solution (20 mL). The aqueous phase was extracted with EtOAc (25 mL × 3), and the combined organic layers were washed with water (40 mL) and brine (40 mL). Concentration in vacuo led to

(45) Tanaka, S.; Saburi, H.; Ishibashi, Y.; Kitamura, M. *Org. Lett.* **2004**, *6*, 1873−1875.

Scheme 4. Total Synthesis of PIM_6[a]



[a] Reagents and conditions: (a) TMSOTf (cat.), 4 Å MS, CH_2Cl_2, 91%; (b) NaOMe, MeOH, 97%; (c) BnBr, NaH, DMF, 90%; (d) AcCl in MeOH/CH_2Cl_2, 94%; (e) $C_{15}H_{31}COOH$, DCC, DMAP, 92%; (f) $[CpRu(CH_3CN)_3]PF_6$, quinaldic acid, CH_2Cl_2, MeOH, 72%; (g) **13**, PivCl, Py, then I_2, Py/H_2O, 81%; (h) H_2, Pd/C, EtOAc/THF/PrOH/H_2O, 76%.

the crude residue that was purified by a short silica gel column and dried under high vacuum ($P < 0.5$ Torr) at room temperature overnight to give **8** (1.11 g, 76% over 2 steps) as a colorless oil. R_f 0.31 (Hexanes/EtOAc = 4:1); $[\alpha]_D^{rt} = -0.02$ ($c = 8.0$, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.83 (d, $J = 6.6$ Hz, 3H), 0.88 (t, $J = 6.6$ Hz, 3H), 1.01−1.12 (m, 1H), 1.19−1.40 (m, 29H), 1.53−1.60 (m, 2H), 3.64 (t, $J = 6.6$ Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.1, 19.7, 22.7, 25.7, 27.1, 27.1, 29.4, 29.5, 29.6, 29.7, 29.7, 30.0, 30.1, 32.0, 32.8, 32.8, 37.1, 37.1, 63.1; IR (film) 3327, 2934, 2853, 1456, 1376, 1057 cm^{-1}. Anal. Calcd for $C_{19}H_{40}O$: C, 80.21; H, 14.17. Found: C, 80.13; H, 14.25

(*R*)-10-Methyloctadecanoic Acid (9): To a solution of (*R*)-10-methyloctadecan-1-ol **8** (0.91 g, 3.21 mmol) in CH_3CN (18 mL) were added TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy free radical) (74.3 mg, 0.48 mmol), aqueous sodium dihydrogenphosphate (NaH_2PO_4) (13.5 mL, 0.67 M), and 80% sodium chlorite ($NaClO_2$) (0.72 g in 3.5 mL of water, 6.34 mmol) in sequential order. A solution of dilute sodium hypochlorite (NaOCl) was prepared by diluting household bleach (2 mL, 13−14% chlorine content) with water (18 mL). 3.8 mL of this solution were added to the reaction mixture dropwise, and the solution was heated to 35 °C with stirring for 7 h. After the reaction mixture cooled to room temperature, 20 mL of water were added and the pH was adjusted to 8.0 by the addition of ca. 6 mL of 2.0 N NaOH. The reaction mixture was then poured into an ice-cold sodium sulfite solution (2.0 g in 30 mL of water). After the solution stirred for 10 min at room temperature, 20 mL of methyl *tert*-butyl ether (MTBE) were added and the solution stirred for an additional 10 min. The organic layer was then separated and discarded. Further MTBE (30 mL) was added to the aqueous phase. The solution was then acidified with 2.0 N HCl to ca. pH 3. The organic layer was separated, and the aqueous layer was extracted with MTBE (30 mL × 2). The combined organic phases were then washed with water (30 mL × 2) and brine (30 mL) and concentrated to give the pure tuberculostearic acid **9** as a white semisolid (0.89 g, 93%). R_f 0.48 (Hexanes/EtOAc = 3:1); $[\alpha]_D^{rt} = -0.02$ ($c = 10.5$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83 (d, $J = 6.7$ Hz, 3H), 0.88 (t, $J = 6.9$ Hz, 3H), 1.04−1.15 (m, 2H), 1.17−1.40 (m, 25H), 1.60−1.70 (m, 2H), 2.35 (t, $J = 7.5$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 19.7, 22.7, 24.7, 27.0, 27.1, 29.1, 29.3, 29.4, 29.5, 29.7, 30.0, 31.1, 32.0, 32.8, 34.1, 37.0, 37.1, 179.8; IR (film) 3000 (br), 2923, 2851, 1707, 1456, 754 cm^{-1}. Anal. Calcd for $C_{19}H_{38}O$: C, 76.19; H, 13.12. Found: C, 76.22; H, 12.99.

3-*O*-Benzyl-1-*O*-((*R*)-10-methyloctadecanoyl)-*sn*-glycerol (11): To a solution of tuberculostearic acid **9** (0.81 g, 2.74 mmol) and 3-*O*-benzyl-*sn*-glycerol **10** (0.60 g, 3.30 mmol) in CH_2Cl_2 (25 mL) at 0 °C were added (dimethylamino)pyridine (DMAP) (33.0 mg, 0.27 mol) and dicyclohexylcarbodiimide (DCC) (5.5 mL, 5.5 mmol, 1 M in CH_2Cl_2). The mixture was stirred at 0 °C for 1 h before being warmed to room temperature and stirred for an additional 12 h. The mixture was then filtered through Celite, the solvent was removed in vacuo, and the residue was purified by flash silica gel column chromatography to give **11** (0.94 g, 75%) as a colorless oil. R_f 0.35 (Hexanes/EtOAc = 4:1); $[\alpha]_D^{rt} = +1.49$ ($c = 3.5$, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.83 (d, $J = 6.6$ Hz, 3H), 0.88 (t, $J = 6.9$ Hz, 3H), 1.04−1.15 (m, 2H), 1.18−1.45 (m, 25H), 1.57−1.68 (m, 2H), 2.32 (t, $J = 7.5$ Hz, 2H), 2.51 (d, $J = 4.8$ Hz, 1H), 3.49 (dd, $J = 9.6$, 6.6 Hz, 1H), 3.56 (dd, $J = 9.6$, 6.6 Hz, 1H), 4.01−4.06 (m, 1H), 4.14 (dd, $J = 10.5$, 6.1 Hz, 1H), 4.19 (dd, $J = 10.5$, 6.1 Hz, 1H), 4.56 (s, 2H), 7.28−7.37 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.1, 19.7, 22.7, 24.7, 27.1, 27.1, 29.1, 29.3, 29.4, 29.5, 29.7, 29.9, 30.0, 31.9, 32.8, 34.2, 37.1, 65.4, 68.9, 70.9, 73.5, 127.7, 127.9, 128.5, 137.7, 174.0; IR (film) 3456, 2918, 2851, 1733, 1456, 1107 cm^{-1}. Anal. Calcd for $C_{29}H_{50}O_4$: C, 75.28; H, 10.89. Found: C, 75.17; H, 10.78.

3-*O*-Benzyl-1-*O*-((*R*)-10-methyloctadecanoyl)-2-*O*-palmitoyl-*sn*-glycerol (12): To a solution of glycerol **11** (0.81 g, 1.76 mmol) and palmitic acid (0.90 g, 3.51 mmol) in CH_2Cl_2 (15 mL) were added DMAP (86.0 mg, 0.35 mmol) and DCC (3.5 mL, 3.5 mmol, 1 M in CH_2Cl_2) at room temperature. The mixture was stirred for 20 h and then filtered through Celite, the solvent was removed under reduced pressure, and the residue oil was purified by flash silica gel column chromatography to give **12** (1.08 g, 88%) as a colorless oil. R_f 0.45 (Hexanes/EtOAc = 10:1); $[\alpha]_D^{rt} = +5.45$ ($c = 3.9$, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.83 (d, $J = 6.6$ Hz, 3H), 0.88 (t, $J = 6.9$ Hz, 6H), 1.04−1.12 (m, 2H), 1.18−1.40 (m, 45H), 1.57−1.64 (m, 4H), 2.27 (t, $J = 7.4$ Hz, 2H), 2.31 (t, $J = 7.2$ Hz, 2H), 3.59 (m, 2H), 4.18 (dd, $J = 12.0$, 6.4 Hz, 1H), 4.34 (dd, $J = 12.0$, 3.8 Hz, 1H), 4.54 (dd, $J = 11.6$, 9,8 Hz, 2H), 5.22−5.26 (m, 1H), 7.27−7.46 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.1, 19.7, 22.7, 24.9, 27.1, 27.1, 29.1−30.0, 31.9, 32.8, 34.1, 34.4, 37.1, 62.7, 68.3, 70.0, 73.3, 127.6, 127.8, 128.4, 137.8, 173.1, 173.4; IR (film) 2923, 2851, 1738, 1456, 1369, 1159, 1107 cm^{-1}. Anal. Calcd for $C_{45}H_{80}O_5$: C, 77.09; H, 11.50. Found: C, 77.30; H, 11.48.

Triethylammonium 1-*O*-[(*R*)-10-methyloctadecanoyl]-2-*O*-palmitoyl-*sn*-glycero-3-*H*-phosphonate (13): To a solution of glycerol **12** (0.82 g, 1.17 mmol) in ethanol (20 mL) were added acetic acid (1.5 mL) and palladium on charcoal (Pd/C) (45 mg, 10% Pd content). The mixture was stirred at room temperature under an atmosphere of hydrogen for 4 h before being filtered through a pad of Celite and the solvents being removed in vacuo at 25 °C. The residue was purified immediately by flash silica gel column chromatography to give 1-*O*-[(*R*)-10-methyloctadecanoyl]-2-*O*-palmitoyl-*sn*-glycerol (0.66 g, 93%) as a colorless oil. R_f 0.35 (Hexanes/EtOAc = 4:1); $[\alpha]_D^{rt} = -2.8$ ($c = 1.1$, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.83 (d, $J = 6.9$ Hz, 3H), 0.88 (t, $J = 6.9$ Hz, 6H), 1.04−1.09 (m, 2H), 1.19−1.38 (m, 45H), 1.57−1.66 (m, 4H), 2.04 (t, $J = 6.9$ Hz, 1H), 2.32 (t, $J = 7.5$ Hz, 2H), 2.34 (t, $J = 7.5$ Hz, 2H), 3.70−3.77 (m, 2H), 4.23 (dd, $J = 12.0$, 3.3 Hz, 1H), 4.32 (dd, $J = 10.0$, 2.7 Hz, 1H), 5.08 (tt, $J = 5.0$, 5.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.1, 19.7, 22.7, 24.9, 25.0, 27.1, 27.1, 29.1−30.0, 32.0, 32.8, 34.1, 34.3, 37.1, 37.1, 61.6, 62.0, 72.1, 173.4, 173.8; IR (film) 3477, 2923, 2851, 1738, 1458, 1164 cm^{-1}. Anal. Calcd for $C_{38}H_{74}O_5$: C, 74.70; H, 12.21. Found: C, 74.84; H, 12.35.

Imidazole (1.67 g, 24.5 mmol), coevaporated with toluene (10 mL × 3) and dried in vacuo for 1 h, was dissolved in toluene (20 mL), and the solution was cooled to 0 °C. PCl_3 (0.47 mL, 5.4 mmol) in toluene (5 mL) and then Et_3N (1.95 mL, 14.0 mmol) were added, and the reaction mixture stirred for 30 min before being cooled to −10 °C. A solution of 1-*O*-[(*R*)-10-methyloctadecanoyl]-2-*O*-palmitoyl-*sn*-glycerol (0.65 g, 1.06 mmol) in a mixture of toluene (15 mL) and CH_2Cl_2 (5 mL) was then added dropwise to the reaction mixture via a syringe pump over a period of 60 min. After the addition the mixture was allowed to stir for a further 60 min at −10 °C before being quenched by the addition of water/pyridine (1:4, 30 mL). The aqueous layer was extensively extracted with $CHCl_3$, and the combined organic layers were washed with triethylammonium borate (TEAB) buffer and dried over Na_2SO_4. Evaporation in vacuo gave the crude residue that was purified by flash column chromatography with Et_3N-deactivated silica gel to afford H-phosphonate **13** as a white gummy solid (0.54 g, 65%) after lyophilization with dioxane. R_f 0.31 (CH_2Cl_2/MeOH = 4:1); $[\alpha]_D^{rt} = +3.70$ ($c = 1.9$, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.77 (d, $J = 6.6$ Hz, 3H), 0.82 (t, $J = 6.9$ Hz, 6H), 0.93−1.62 (m, 55H), 1.34 (t, $J = 6.9$ Hz, 9H), 2.20−2.30 (m, 4H), 3.00−3.12 (m, 6H), 3.94−4.00 (m, 2H), 4.11 (dd, $J = 12.0$, 6.3 Hz, 1H), 4.31 (dd, $J = 12.0$, 3.0 Hz, 1H), 5.10−5.20 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 8.78, 14.2, 19.8, 22.7, 25.0, 27.2, 29.1−30.1, 32.0, 32.8, 34.1, 34.3, 37.1, 45.9, 62.3, 70.1, 172.8, 173.1. ^{31}P NMR (121 MHz, $CDCl_3$) δ 4.86; IR (film) 3425 (br), 2923, 2851, 2605, 2492, 1738, 1461, 1169 cm^{-1}. HRMS-MALDI (*m*/*z*): $[M]^-$ Calcd for $C_{38}H_{74}O_7P^-$, 673.5178; Found, 673.5190.

Allyl (3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→2)-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-2-*O*-benzoyl-3,4-di-*O*-benzyl-α-D-mannopyranoside (17): Imidate **14b** (1.16 g, 1.82 mmol) and disaccharide **16**[35] (1.42 g, 1.82 mmol) were combined and coevaporated (×3) with toluene before being placed under nitrogen and dissolved in 20 mL of CH_2Cl_2. The solution was then cooled to 0 °C, TMSOTf (28 μL, 0.15 mmol) was added dropwise, and the solution stirred for 40 min before being quenched by the addition of NEt_3 (40 μL) and the solvent being removed under reduced pressure to give the crude trisaccharide. The residue was purified by gradient flash chromatography (toluene/EtOAc, 50:1 to 20:1) to give a mixture of the trisaccharide (R_f 0.33, Hexanes/EtOAc = 3:1) with trichloroacetamide as a colorless oil. The oil was then dissolved in CH_2Cl_2 (10.5 mL) and MeOH (50 mL) before AcCl (520 μL) was added slowly dropwise. The reaction was stirred at room temperature for 48 h, additional AcCl (100 μL) was added, and the reaction stirred for an additional 24 h. The solution was then quenched by the addition of NEt_3 (800 μL), the solvent was removed under reduced pressure, and the residue was purified by gradient flash chromatography (Hexanes/EtOAc, 5:1 to 3:1) to give pure **17** (1.56 g, 74% over two steps) as a white foam; (R_f 0.11 Hexanes/EtOAc = 3:1). $[\alpha]_D^{rt} = +30.5$ ($c = 0.31$, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.19 (m, 2H), 7.52−7.23 (m, 43 H), 5.95 (m, 1H), 5.73 (dd, $J = 3.0$, 1.9 Hz, 1H), 5.36 (m, 1H), 5.28−5.24 (m, 2H), 5.17 (d, $J = 1.6$ Hz, 1H), 5.01 (d, $J = 1.6$ Hz, 1H), 4.98−4.88 (m, 4H), 4.77−4.50 (m, 12H), 4.26−4.18 (m, 4H), 4.06−3.67 (m, 15H), 2.64 (bs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.7, 138.5, 138.4, 138.3, 138.2, 138.0, 137.9, 133.3, 133.2, 129.9, 129.8, 128.5, 128.4, 128.2, 128.1, 127.8, 127.6, 127.5, 127.4, 127.3, 127.2, 118.0, 101.1, 99.0, 96.7, 79.9, 79.4, 78.5, 75.0, 74.6, 74.3, 74.2, 73.2, 73.1, 72.1, 71.9, 71.5, 70.8, 69.0, 68.9, 68.5, 68.0, 66.2; IR ($CHCl_3$) 3423, 3066, 3009, 2917, 2859, 1716, 1359, 1268, 1112, 1095, 1049, 986 cm^{-1}. HRMS-MALDI (*m*/*z*): $[M + Na]^+$ Calcd for $C_{84}H_{88}O_{17}$, 1391.5919; Found, 1391.5889.

Allyl (2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→2)-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→2)-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-2-*O*-benzoyl-3,4-di-*O*-benzyl-α-D-mannopyranoside (18): Imidate **14b** (543 mg, 0.85 mmol) and trisaccharide **17** (993 mg, 0.71 mmol) were combined and coevaporated (×3) with toluene before being placed under nitrogen and dissolved in 12 mL of CH_2Cl_2. The solution was then cooled to 0 °C, TMSOTf (12.9 μL, 71.0 μmol) was added dropwise, and the solution stirred for 40 min before being quenched by the addition of NEt_3 (20 μL). The solvent was then removed under reduced pressure, and the residue was purified by gradient flash chromatography (toluene/EtOAc, 50:1 to 20:1) to give pure **18** (1.08 g, 83%) as a colorless oil; (R_f 0.50, toluene/EtOAc =10:1). $[\alpha]_D^{rt} = +25.8$ ($c = 1.88$, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10 (m, 2H), 7.41−7.08 (m, 53 H), 5.87 (m, 1H), 5.65 (dd, $J = 3.0$, 1.8 Hz, 1H), 5.60 (dd, $J = 3.0$, 1.8 Hz, 1H), 5.28 (m, 1H), 5.26 (d, $J = 1.2$ Hz, 1H), 5.18 (m, 1H), 5.13 (d, $J = 1.2$ Hz, 1H), 5.07 (d, $J = 1.3$ Hz, 1H), 4.92−4.81 (m, 7H), 4.69−4.32 (m, 16 H), 4.16−3.36 (m, 24H), 2.17 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.1, 165.7, 138.5, 138.4, 138.3, 138.1, 138.0, 137.9, 133.2, 129.9, 129.8, 128.4, 128.2, 128.1, 127.9, 127.8, 127.6, 127.5, 127.4, 118.1, 100.5, 99.4, 98.9, 96.7, 79.3, 79.2, 78.6, 78.2, 75.0, 74.9, 74.6, 74.2, 74.1, 73.3, 73.1, 72.2, 72.1, 72.0, 71.8, 71.7, 71.5, 70.8, 69.2, 69.0, 68.6, 68.5, 68.0, 66.3, 21.2; IR ($CHCl_3$) 3066, 3008, 2923, 2867, 1733, 1720, 1496, 1453, 1364, 1090, 1055, 1028, 981, 911 cm^{-1}. HRMS-MALDI (*m*/*z*): $[M + Na]^+$ Calcd for $C_{113}H_{118}O_{23}$, 1865.7962; Found, 1865.7922.

(2-*O*-Acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→2)-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→2)-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-2-*O*-benzoyl-3,4-di-*O*-benzyl-α-D-mannopyranosyl trichloroacetimidate (1). To a solution of tetrasaccharide **18** (226 mg, 0.12 mmol) in 12 mL of AcOH and 1.2 mL of H_2O were added NaOAc (59 mg, 0.72 mmol) and $PdCl_2$ (33 mg, 0.18 mmol), and the solution stirred at room temperature for 14 h. The solution was then filtered through a small silica gel plug, and the solvent was

removed under reduced pressure. The brown residue was extracted with EtOAc (50 mL × 2), washed with saturated aqueous $NaHCO_3$ (50 mL × 3) and brine (50 mL), and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by gradient flash chromatography (Hexanes/EtOAc, 3:1 to 2:1) to give the hemiacetal that was then dissolved in CH_2Cl_2 (1.5 mL); the solution was then cooled to 0 °C. Trichloroacetonitrile (66 μL, 0.66 mmol) then DBU (1.9 μL, 13.0 μmol) were added, and the solution stirred for 30 min before being filtered though a small silica gel plug. The solvent was removed under reduced pressure, and the resultant yellow oil was purified by gradient flash chromatography (Hexanes/EtOAc, 5:1 to 3:1) to give pure **1** (131 mg, 52% over two steps) as a colorless oil; (R_f 0.38, Hexanes/EtOAc = 3:1); $[\alpha]_D^{rt} = +24.3$ ($c = 0.94$, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.09 (s, 3H), 3.49 (dd, $J = 11.0$, 1.5 Hz, 1H), 3.54 (dd, $J = 11.0$, 1.5 Hz, 1H), 3.61−3.69 (m, 4H), 3.72−3.98 (m, 13H), 4.03 (dd, $J = 3.0$, 2.5 Hz, 1H), 4.08 (dd, $J = 3.0$, 2.5 Hz, 1H), 4.26 (d, $J = 12.0$ Hz, 1H), 4.35−4.44 (m, 6H), 4.47−4.67 (m, 11H), 4.76−4.82 (m, 4H), 4.96 (d, $J = 1.5$ Hz, 1H), 5.04 (d, $J = 1.5$ Hz, 1H), 5.17 (d, $J = 2.0$ Hz, 1H), 5.51 (dd, $J = 3.5$, 2.0 Hz, 1H), 5.70 (dd, $J = 3.0$, 2.0 Hz, 1H), 6.29 (d, $J = 1.5$ Hz, 1H), 7.01−7.39 (m, 58H), 8.04 (dd, $J = 7.5$, 2.0 Hz, 2H), 8.04 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.4, 66.3, 68.0, 68.9, 69.0, 69.3, 69.6, 72.0, 72.1, 72.2, 72.2, 72.3, 72.4, 72.6, 73.4, 73.5, 73.6, 73.9, 73.9, 74.4, 94.9, 75.0, 75.2, 75.3, 75.3, 75.4, 75.5, 78.1, 78.5, 79.7, 91.0, 95.4, 99.1, 99.7, 100.9, 127.5−128.8 (CH−Aryl), 129.8, 130.1, 131.7, 137.3−138.9 (C_q−Aryl), 159.8, 165.7, 170.3; IR ($CHCl_3$) 3064.4, 3008, 2926, 2868, 1731, 1675, 1454, 1363, 1093, 1052, 975, 909 cm^{-1}. HRMS-MALDI (*m*/*z*): $[M + Na]^+$ Calcd for $C_{112}H_{114}O_{23}NCl_3$, 1968.6745; Found, 1968.6705.

1-*O*-Allyl-3,4,5-tri-*O*-benzyl-2-*O*-naphthylmethyl-D-*myo*-inositol (21): Inositol **20** (1.34 g, 2.7 mmol) and TBAI (1.0 g, 2.7 mmol) were dissolved in DMF (60 mL). The solution was then cooled to 0 °C, and NaH (60% in mineral oil, 0.48 g, 10.3 mmol) was added in one portion. After stirring for 30 min at 0 °C, the reaction mixture was cooled to −20 °C, 2-naphthylmethyl bromide in DMF (5 mL) was added dropwise, and the reaction stirred overnight (ca. 10 h) allowing it to warm to room temperature. The reaction was then quenched with water and extracted with Et_2O (50 mL × 4), and the combined organic layers were further washed with water and brine and dried over Na_2SO_4. The solvents were removed under reduced pressure to give the crude residue that was purified by flash silica gel chromatography to give **21** (1.44 g, 81%) as a white solid. R_f 0.31 (Hexanes/EtOAc = 4:1, eluted twice); $[\alpha]_D^{rt} = -10.8$ ($c = 1.2$, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.48 (d, $J = 1.9$ Hz, 1H), 3.12 (dd, $J = 9.8$, 3.2 Hz, 1H), 3.40 (t, $J = 9.2$ Hz, 1H), 3.41 (dd, $J = 9.8$, 3.2 Hz, 1H), 3.98 (ddt, $J = 12.7$, 5.7, 1.4 Hz, 1H), 4.05 (ddt, $J = 12.7$, 5.7, 1.4 Hz, 1H), 4.08 (q, $J = 2.3$ Hz, 1H), 4.10 (t, $J = 9.5$ Hz, 1H), 4.19 (dt, $J = 9.8$, 1.9 Hz, 1H), 4.63 (d, $J = 11.7$ Hz, 1H), 4.70 (d, $J = 11.7$ Hz, 1H), 4.85 (d, $J = 10.7$ Hz, 1H), 4.86 (d, $J = 11.2$ Hz, 1H), 4.90 (d, $J = 11.2$ Hz, 1H), 4.92 (d, $J = 10.2$ Hz, 1H), 4.95 (d, $J = 10.2$ Hz, 1H), 4.98 (d, $J = 12.2$ Hz, 1H), 5.01 (d, $J = 12.2$ Hz, 1H), 5.17 (ddt, $J = 10.4$, 2.9, 1.3 Hz, 1H), 5.24 (ddt, $J = 17.0$, 2.9, 1.3 Hz, 1H), 5.88 (m, 1H), 7.25−7.43 (m, 15H), 7.44−7.49 (m, 2H), 7.53−7.55 (m, 1H), 7.58−7.83 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 71.2, 72.8, 73.0, 73.3, 74.0, 75.4, 75.9, 79.9, 81.2, 81.5, 83.5, 117.4, 125.7, 125.9, 126.2, 126.4, 127.5, 127.6, 127.65, 127.67, 127.85, 127.89, 128.1, 128.2, 128.3, 128.4, 133.0, 133.2, 134.5, 136.3, 138.4, 138.8, 138.9; IR (film) 3477, 3056, 3015, 2882, 1497, 1451, 1359, 1118, 1062 cm^{-1}. HRMS-MALDI (*m*/*z*): $[M + Na]^+$ Calcd for $C_{41}H_{42}O_6$, 653.2874; Found, 653.2882.

(2-*O*-Benzoyl-3,4-di-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-1-*O*-allyl-3,4,5-tri-*O*-benzyl-2-*O*-naphthylmethyl-D-*myo*-inositol (22): Inositol **21** (0.83 g, 1.32 mmol) and imidate **15c** (1.11 g, 1.45 mmol) were combined and coevaporated (×3) with toluene before being placed under nitrogen and dissolved in CH_2Cl_2 (20 mL). The solution was then cooled to 0 °C, TMSOTf (24.0 μL, 0.13 mmol) was added dropwise, and the solution stirred for 30 min before being quenched by the addition of NEt_3 (35 μL). The solvent was then removed under reduced pressure, and the residue dried under high vaccum before being dissolved in a mixture of MeOH (10 mL) and CH_2Cl_2 (10 mL). The solution was then cooled to 0 °C, AcCl (400 μL) was added dropwise, and the solution stirred at 0 °C for 1 h before warming to room temperature and stirred for an additional 6 h. Neutralization by the addition of Et_3N (500 mL), followed by the removal of the solvents under reduced pressure, gave the crude material that was purified by flash silica gel column chromatography to afford **22** (1.20 g, 85% over two steps) as a white foam. R_f 0.41 (Hexanes/EtOAc = 3:1); $[\alpha]_D^{rt} = -4.0$ ($c = 1.3$, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.60 (brs, 1H), 3.25−3.49 (m, 5H), 3.90−4.09 (m, 6H), 4.16 (t, $J = 9.5$ Hz, 1H), 4.24 (t, $J = 9.5$ Hz, 1H), 4.56−4.69 (m, 5H), 4.80−5.03 (m, 7H), 5.14 (dd, $J = 10.5$, 1.5 Hz, 1H), 5.23 (dd, $J = 15.5$, 1.5 Hz, 1H), 5.57 (d, $J = 1.8$ Hz, 1H), 5.69 (dd, $J = 2.7$, 1.5 Hz, 1H), 5.86−6.00 (m, 1H), 7.09 (m, 31H), 7.73−7.82 (m, 4H), 8.06−8.09 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 61.4, 69.2, 71.4, 71.6, 72.9, 73.0, 74.0, 74.0, 75.1, 75.8, 75.9, 76.1, 78.0, 80.9, 81.3, 81.6, 82.0, 98.3, 117.8, 125.7−128.4 (CH−Aryl), 129.8, 129.9, 132.9, 133.1, 134.2, 136.1, 138.0, 138.7, 165.5; IR (film): 3477, 3026, 2872, 1718, 1595, 1497, 1451, 1359, 1261, 1113, 1067, 907 cm^{-1}. HRMS-MALDI (*m*/*z*): $[M + Na]^+$ Calcd for $C_{66}H_{68}O_{12}$, 1099.4603; Found, 1099.459.

(2-*O*-Benzoyl-3,4-di-*O*-benzyl-6-*O*-levuniloyl-α-D-mannopyranosyl)-(1→6)-1-*O*-allyl-3,4,5-tri-*O*-benzyl-2-*O*-naphthylmethyl-D-*myo*-inositol (23): To a solution of disaccharide **22** (1.20 g, 1.12 mmol) and levunilic acid (170 μL, 1.67 mmol) in CH_2Cl_2 (24 mL) at room temperature were added diisopropylcarbodiimide (DIPC) (260 μL, 1.67 mmol) and DMAP (272 mg, 2.24 mmol). The reaction mixture was stirred at room temperature for 2 h and then filtered through a pad of Celite. The solvents were removed under reduced pressure, and the residue oil was purified by flash silica gel column chromatography to give **23** (1.22 g, 93%) as a white foam. R_f 0.32 (Hexanes/EtOAc = 2:1); $[\alpha]_D^{rt} = -3.60$ ($c = 1.8$, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.03 (s, 3H), 2.46 (t, $J = 7.0$ Hz, 2H), 2.51−2.56 (m, 2H), 3.21 (dd, $J = 10.0$, 2.0 Hz, 1H), 3.32 (q, $J = 9.5$ Hz, 1H), 3.33 (dd, $J = 10.0$, 2.0 Hz, 1H), 3.82 (t, $J = 9.5$ Hz, 1H), 3.89−4.10 (m, 7H), 4.21 (t, $J = 9.5$ Hz, 1H), 4.42 (d, $J = 11.0$ Hz, 1H), 4.53−4.61 (m, 4H), 4.75−4.79 (m, 3H), 4.88−4.95 (m, 4H), 5.07 (dd, $J = 10.5$, 1.5 Hz, 1H), 5.15 (dd, $J = 15.5$, 1.5 Hz, 1H), 5.55 (d, $J = 1.5$ Hz), 5.62 (dd, $J = 3.0$, 2.0 Hz, 1H), 5.81−5.89 (m, 1H), 7.04−7.07 (m, 2H), 7.10−7.30 (m, 13H), 7.37−7.43 (m, 4H), 7.48−7.55 (m, 2H), 7.68−7.75 (m, 4H), 8.04−8.05 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.8, 30.0, 37.9, 63.0, 68.9, 69.3, 72.8, 72.8, 73.8, 74.9, 75.6, 75.7, 75.8, 78.1, 80.9, 81.4, 81.5, 82.0, 98.0, 117.7, 125.7−128.4 (CH−Aryl), 129.9, 130.1, 133.0, 133.2, 134.3, 136.2−138.6 (C_q−Aryl), 165.5, 172.3. HRMS-MALDI (*m*/*z*): $[M + Na]^+$ Calcd for $C_{73}H_{74}O_{14}$, 1197.4971; Found, 1197.500.

(2-*O*-Benzoyl-3,4-di-*O*-benzyl-6-*O*-levuniloyl-α-D-mannopyranosyl)-(1→6)-1-*O*-allyl-3,4,5-tri-*O*-benzyl-D-*myo*-inositol (24): To a solution of disaccharide **23** (1.12 g, 0.95 mmol) at 0 °C was added dichlorodicyanobenzoquinone (DDQ) (650 mg, 2.86 mmol) in two portions over 20 min. The reaction mixture was stirred for a further 15 min at 0 °C before being warmed to room temperature and stirred for 1 h. Dilution with CH_2Cl_2, washing of the organic phase with aqueous sodium ascorbate solution, saturated aqueous $NaHCO_3$ solution, and water, followed by drying over Na_2SO_4 and removal of the solvents under reduced pressure, gave the crude residue. Purification by silica gel column chromatography gave **24** (801 mg, 81%) as a white foam. R_f 0.57 (Hexanes/EtOAc = 1:1); $[\alpha]_D^{rt} = -16.1$ ($c = 1.3$, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.07 (s, 3H), 2.35 (brs, 1H), 2.45−2.55 (m, 2H), 2.58−2.70 (m, 2H), 3.25 (dd, $J = 9.5$, 2.5 Hz, 1H), 3.28 (t, $J = 9.5$ Hz, 1H), 3.37 (dd, $J = 9.5$, 2.5 Hz, 1H), 3.82 (t, $J = 9.5$ Hz, 2H), 3.88−4.15 (m, 10H), 4.44 (d, $J = 11.0$ Hz, 1H), 4.55 (d, $J = 11.5$ Hz, 1H), 4.58 (d, $J = 10.5$ Hz, 1H), 4.87 (s, 2H), 4.75−4.80 (m, 3H), 4.85 (d, $J = 11.0$ Hz, 1H), 4.89 (d, $J = 10.5$ Hz, 1H), 5.11 (dd, $J = 10.5$, 1.5 Hz, 1H), 5.20 (dd, $J = 15.5$, 1.5 Hz, 1H), 5.47 (d, $J =$

2.0 Hz, 1H), 5.59 (dd, J = 3.0, 1.5 Hz, 1H), 5.86−5.94 (m, 1H), 7.04−7.54 (m, 28H), 8.03−8.04 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.1, 30.0, 38.2, 63.2, 66.9, 69.2, 69.9, 71.5, 71.6, 72.9, 74.0, 75.2, 75.4, 76.0, 76.1, 78.3, 80.8, 80.7, 81.2, 81.7, 98.1, 118.6, 127.5−130.1 (CH−Aryl), 130.3, 133.4, 134.4, 131.1−138.7 (C_q−Aryl), 165.8, 172.5, 206.6; IR (film) 3497, 3015, 2882, 1718, 1353, 1268, 1102, 1061 cm^{-1}. HRMS-MALDI (m/z): [M + Na]$^+$ Calcd for $C_{62}H_{66}O_{14}$, 1057.4345; Found, 1057.433.

(2-*O*-Benzoyl-3,4-di-*O*-benzyl-6-*O*-levuniloyl-α-D-mannopyranosyl)-(1→6)-3,4,5-tri-*O*-benzyl-2-*O*-(2-*O*-benzoyl-3,4-di-*O*-benzyl-6-*O*-triisopropylsilyl-α-D-mannopyranosyl)-1-*O*-allyl-D-*myo*-inositol (25): Disaccharide **24** (760 mg, 0.73 mmol) and imidate **15c** (670 mg, 0.88 mmol) were combined and coevaporated (× 3) with toluene before being placed under nitrogen and dissolved in CH_2Cl_2 (15 mL). The solution was then cooled to 0 °C, TMSOTf (13.5 μL, 74.0 μmol) was added dropwise, and the solution stirred for 30 min before being quenched by the addition of NEt_3 (20 μL). The solvent was then removed under reduced pressure, and the residue was purified by flash column chromatography to give pure **25** (956 mg, 80%) as a white foam. R_f 0.46 (Hexanes/EtOAc = 2:1); $[\alpha]_D^{rt}$ = +2.10 (c = 1.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.00−1.02 (m, 21H), 2.04 (s, 3H), 2.43−2.70 (m, 4H), 3.23−3.31 (m, 3H), 3.65 (d, J = 11.5 Hz, 1H), 3.77 (d, J = 11.5 Hz, 1H), 3.83−4.12 (m, 11H), 4.28 (d, J = 1.5 Hz, 1H), 4.42−4.88 (m, 14H), 5.01 (dd, J = 10.5, 1.5 Hz, 1H), 5.13 (d, J < 1.0 Hz, 1H), 5.15 (dd, J = 17.0, 1.5 Hz, 1H), 5.50 (d, J < 1.0 Hz, 1H), 5.62−5.63 (m, 2H), 5.79−5.90 (m, 1H), 7.08−7.54 (m, 41H), 7.98−8.05 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.1, 18.2, 18.3, 28.1, 30.0, 38.2, 62.4, 63.1, 69.0, 69.5, 70.0, 71.5, 71.6, 71.9, 72.7, 72.8, 73.9, 74.1, 75.3, 75.4, 76.0, 76.2, 76.6, 78.1, 78.5, 79.3, 81.3, 81.6, 81.6, 98.5, 99.3, 118.3, 127.3−128.8 (CH−Aryl), 130.2, 130.4, 130.5, 133.0, 133.4, 134.1, 138.1−139.3 (C_q−Aryl), 165.5, 165.7, 172.5, 206.9; HRMS-MALDI (m/z): [M + Na]$^+$ Calcd for $C_{98}H_{112}O_{20}Si$, 1659.7408; Found, 1659.708.

(2-*O*-Benzoyl-3,4-di-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-1-*O*-allyl-2-*O*-(2-*O*-benzoyl-3,4-di-*O*-benzyl-6-*O*-triisopropylsilyl-α-D-mannopyranosyl)-3,4,5-tri-*O*-benzyl-D-*myo*-inositol (2): To a solution of trisaccharide **25** (480 mg, 0.29 mmol) in a mixture of CH_2Cl_2 (6 mL), pyridine (0.72 mL), and AcOH (0.48 mL) at 0 °C was added hydrazine monohydrate (57 μL, 1.16 mmol). The reaction mixture was stirred at room temperature for 90 min before being quenched by the addition of acetone (1 mL). The solvents were then removed under reduced pressure, and the residue was purified by silica gel column chromatography to give **2** (401 mg, 89%) as a white foam. R_f 0.41 (Hexanes/EtOAc = 2:1); $[\alpha]_D^{rt}$ = +2.37 (c = 2.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.02−1.11(m, 21H), 1.91 (dd, J = 10.0, 3.0 Hz, 1H), 3.31−3.37 (m, 3H), 3.45−3.55 (m, 2H), 3.63 (dd, J = 11.0, 1.5 Hz, 1H), 3.82 (dd, J = 11.5, 2.5 Hz, 1H), 3.90−4.18 (m, 10H), 4.35 (t, J = 2.5 Hz, 1H), 4.60−4.66 (m, 6H), 4.72 (m, 1H), 4.80−4.96 (m, 7H), 5.06 (dd, J = 10.5, 1.5 Hz, 1H), 5.21 (dd, J = 17.0, 1.5 Hz, 1H), 5.24 (d, J = 1.5 Hz, 1H), 5.57 (d, J = 2.0 Hz, 1H), 5.68 (dd, J = 3.0, 2.0 Hz, 1H), 5.71(dd, J = 3.0, 2.0 Hz, 1H), 5.86−5.94 (ddt, J = 17.0, 10.5, 6.0 Hz, 1H), 7.12−7.40 (m, 37H), 7.44−7.47 (m, 3H), 7.52−7.59 (m, 2H), 8.04−8.07 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.0, 18.0, 18.0, 61.3, 62.2, 69.0, 69.2, 70.7, 71.2, 71.4, 71.6, 71.8, 72.0, 72.5, 73.9, 74.1, 75.2, 75.8, 75.9, 76.1, 77.8, 78.0, 79.0, 81.2, 81.4, 81.5, 98.3, 98.6, 118.1, 127.1−130.0 (CH−Aryl), 130.1, 132.9, 133.1, 133.9, 137.9−139.0 (C_q−Aryl), 165.4, 165.6. HRMS-MALDI (m/z): [M + Na]$^+$ Calcd for $C_{93}H_{106}O_{18}Si$, 1561.7041; Found, 1561.7013.

(2,3,4,6-Tetra-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-1-*O*-allyl-3,4,5-tri-*O*-benzyl-2-*O*-(2,3,4-tri-*O*-benzyl-6-*O*-triisopropylsilyl-α-D-mannopyranosyl)-D-*myo*-inositol (26): To a solution of trisaccharide **25** (360 mg, 0.22 mmol) in a mixture of CH_2Cl_2 (2 mL) and MeOH (4 mL) at room temperature was added NaOMe (0.22 mL, 0.11 mmol, 0.5 M in MeOH). The reaction mixture was stirred for 10 h at room temperature before the solvents were removed under reduced pressure. The residue was passed through a pad of silica gel (EtOAc with 2% MeOH as eluent), and the filtrate evaporated to give the crude triol. To a solution of crude triol in DMF (6 mL) at 0 °C was added BnBr (118 mL, 0.99 mmol) and NaH (15.8 mg, 1.1 mmol, 60% in mineral oil). The reaction mixture was stirred overnight while warming to room temperature. MeOH was added cautiously to quench the reaction before water (10 mL) was added. The aqueous layer was then extracted with Et_2O (20 mL × 4), and the combined organic layers were washed with additional water and brine and then dried over Na_2SO_4. Evaporation of the solvents under reduced pressure gave the crude residue that was purified by silica gel column chromatography to give **26** (282 mg, 80% over two steps) as a white foam. R_f 0.45 (Hexanes/EtOAc = 4:1); $[\alpha]_D^{rt}$ = +28.5 (c = 2.8, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.99−1.01 (m, 21H), 3.13 (dd, J = 5.0, 1.5 Hz, 1H), 3.20−3.27 (m, 3H), 3.37 (dd, J = 11.5, 2.5 Hz, 1H), 3.59 (d, J = 11.0 Hz, 1H), 3.71−4.01 (m, 12H), 4.08−4.20 (m, 3H), 4.33 (t, J = 1.5 Hz, 1H), 4.45 (d, J = 11.0 Hz, 1H), 4.53−4.73 (m, 14H), 4.82−4.89 (m, 4H), 5.05 (dd, J = 10.5, 1.5 Hz, 1H), 5.17 (dd, J = 17.0, 1.5 Hz, 1H), 5.20 (d, J < 1.0 Hz, 1H), 5.49 (d, J < 1.0 Hz, 1H), 5.65−5.72 (m, 1H), 7.04−7.37 (m, 50H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.3, 18.2, 18.3, 62.8, 68.9, 69.4, 71.1, 72.1, 72.2, 72.4, 72.5, 72.7, 73.2, 73.5, 74.5, 74.5, 75.1, 75.3, 75.7, 75.8, 75.9, 76.1, 76.4, 79.3, 79.4, 80.4, 81.7, 81.8, 82.2, 98.2, 98.9, 118.1, 127.4−128.6 (CH−Aryl), 134.2, 138.2−139.5 (C_q−Aryl). HRMS-MALDI (m/z): [M + Na]$^+$ Calcd for $C_{100}H_{116}O_{16}Si$, 1623.7925; Found, 1623.790.

(2,3,4,6-Tetra-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-1-*O*-allyl-3,4,5-tri-*O*-benzyl-2-*O*-(2,3,4-tri-*O*-benzyl-α-D-mannopyranosyl)-D-*myo*-inositol (27): To a solution of trisaccharide **26** (280 mg, 0.175 mmol) in a mixture of CH_2Cl_2 (2 mL) and MeOH (6 mL) at 0 °C was added AcCl (120 μL) dropwise. The reaction mixture was warmed to room temperature after 30 min and stirred for a further 6 h before being quenched by Et_3N (160 μL). The solvents were removed in vacuo, and the crude residue was purified by silica gel column chromatography to give **27** (245 mg, 97%) as a white foam. R_f 0.35 (Hexanes/EtOAc = 2:1); $[\alpha]_D^{rt}$ = +29.3 (c = 1.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.76 (brs, 1H), 3.16 (dd, J = 10.0, 2.0 Hz, 1H), 3.22−3.30 (m, 3H), 3.38 (dd, J = 9.0, 3.0 Hz, 1H), 3.51−3.60 (m, 2H), 3.79−3.91 (m, 6H), 3.96−4.04 (m, 5H), 4.16−4.24 (m, 3H), 4.47 (d, J = 11.0 Hz, 1H), 4.55−4.78 (m, 15H), 4.84−4.94 (m, 4H), 5.12 (dd, J = 10.5, 1.5 Hz, 1H), 5.15 (d, J < 1.0 Hz, 1H), 5.22 (dd, J = 17.0, 1.5 Hz, 1H), 5.50 (d, J = 2.0 Hz, 1H), 5.69−5.77 (m, 1H), 7.04−7.38 (m, 50H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 62.1, 68.6, 71.0, 71.4, 71.8, 71.9, 72.2, 72.2, 72.3, 72.4, 72.8, 73.2, 74.5, 74.8, 74.9, 75.0, 75.1, 75.6, 75.7, 75.9, 76.0, 78.7, 78.9, 80.2, 81.4, 81.5, 81.7, 98.7, 99.1, 117.8, 127.2−128.5 (CH−Aryl), 133.9, 137.8−139.1 (C_q−Aryl). HRMS-MALDI (m/z): [M + Na]$^+$ Calcd for $C_{91}H_{96}O_{16}$, 1467.6591; Found, 1467.6563.

(2,3,4,6-Tetra-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-1-*O*-allyl-3,4,5-tri-*O*-benzyl-2-*O*-(2,3,4-tri-*O*-benzyl-6-*O*-palmitoyl-α-D-mannopyranosyl)-D-*myo*-inositol (28): To a solution of trisaccharide **27** (225 mg, 0.156 mmol) in CH_2Cl_2 (3 mL) at room temperature were added palmitic acid (158 mg, 0.623 mmol), DMAP (76.0 mg, 0.623 mmol), and DCC (0.62 mL, 0.62 mmol, 1M in CH_2Cl_2). The reaction mixture was stirred for 10 h before the solvents were removed in vacuo. The residue was purified by silica gel column chromatography to give **28** (225 mg, 86%) as a colorless syrup. R_f 0.54 (Hexanes/EtOAc = 3:1); $[\alpha]_D^{rt}$ = +30.9 (c = 1.2, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.83 (t, J = 7.0 Hz, 3H), 1.15−1.26 (m, 24H), 1.46−1.54 (m, 2H), 2.18 (t, J = 7.5 Hz, 2H), 3.10 (dd, J = 9.5, 2.0 Hz, 1H), 3.16−3.24 (m, 3H), 3.33 (dd, J = 11.0, 3.0 Hz, 1H), 3.71−3.86 (m, 6H), 3.91−3.97 (m, 5H), 4.08−4.15 (m, 4H), 4.23 (t, J = 1.5 Hz, 1H), 4.40−4.72 (m, 16H), 4.78−4.88 (m, 4H), 5.04 (dd, J = 10.5, 1.5 Hz, 1H), 5.15 (dd, J = 17.0, 1.5 Hz, 1H), 5.15 (d, J < 1.0 Hz, 1H), 5.46 (d, J = 1.5 Hz, 1H), 5.62−5.70 (m, 1H), 6.99−7.33 (m, 50H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.3, 22.9, 25.0, 29.4−29.9, 32.1, 34.4, 63.2, 68.8, 70.4, 71.3, 71.6, 71.7, 72.1, 72.5, 72.5, 72.6, 72.7, 73.4, 74.3, 74.7, 75.0, 75.1, 75.3, 75.8, 75.9, 76.0, 76.2, 78.7, 79.0, 80.4, 81.6, 81.7, 81.9,

98.8, 98.9, 118.0, 127.4−128.7 (CH−Aryl), 134.1, 137.9−139.3 (C_q−Aryl), 173.9; HRMS-MALDI (*m*/*z*): $[M + Na]^+$ Calcd for $C_{107}H_{126}O_{17}$, 1705.8887; Found, 1705.886.

(2,3,4,6-Tetra-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-3,4,5-tri-*O*-benzyl-2-*O*-(2,3,4-tri-*O*-benzyl-6-*O*-palmitoyl-α-D-mannopyranosyl)-D-*myo*-inositol (29): Trisaccharide **28** (80 mg, 47.5 μmol), NaOAc (39 mg, 0.48 mmol), and $PdCl_2$ (41 mg, 0.24 mmol) were dissolved in a mixture of AcOH/H_2O (19:1) (3 mL) with the aid of sonication. The reaction mixture was stirred vigorously at room temperature for 6 h and then quenched carefully by the addition of saturated aqueous $NaHCO_3$ solution and solid Na_2CO_3. The aqueous layer was then extracted with CH_2Cl_2 (4 × 10 mL), and the combined organic layers were dried over Na_2SO_4 before the solvents were removed in vacuo. The residue was purified by flash silica gel column chromatography to give **29** (40 mg, 51%) as a faint yellow syrup. R_f 0.29 (Hexanes/EtOAc = 3:1); $[\alpha]_D^{rt} = +42.1$ (*c* = 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.83 (t, *J* = 7.0 Hz, 3H), 1.16−1.27 (m, 24H), 1.45−1.55 (m, 2H), 2.20 (t, *J* = 7.5 Hz, 2H), 3.18−3.23 (m, 2H), 3.37−3.40 (m, 2H), 3.53−3.58 (m, 2H), 3.69−4.15 (m, 15H), 4.30−4.78 (m, 20H), 4.85 (t, *J* = 11.0 Hz, 2H), 5.15 (d, *J* < 1.0 Hz, 1H), 5.36 (d, *J* < 1.0 Hz, 1H), 7.09−7.35 (m, 50H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.3, 22.9, 25.1, 29.4−29.9, 32.1, 34.4, 63.3, 69.7, 70.3, 71.3, 71.9, 72.0, 72.3, 72.3, 72.8, 74.4, 74.5, 74.7, 75.3, 75.4, 75.5, 75.8, 75.9, 78.4, 79.1, 79.5, 80.4, 80.4, 81.4, 95.8, 99.1, 127.6−128.8 (CH−Aryl), 137.8−138.8 (C_q−Aryl), 173.9. HRMS-MALDI (*m*/*z*): $[M + Na]^+$ Calcd for $C_{104}H_{122}O_{17}$, 1665.8574; Found, 1665.854.

Triethylammonium (2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-3,4,5-tri-*O*-benzyl-2-*O*-(2,3,4-tri-*O*-benzyl-6-*O*-palmitoyl-α-D-mannopyranosyl)-1-*O*-(1-*O*-((*R*)-10-methyloctadecanoyl)-2-*O*-palmitoyl-*sn*-glycerylphosphonato)-D-*myo*-inositol (30): Trisaccharide **29** (32 mg, 19.4 μmol) and *H*-phosphonate **13** (112 mg, 0.144 mmol) were coevaporated with anhydrous pyridine (3 mL × 3) and dried under a high vacuum overnight. Aided by sonication, the mixture was dissolved in anhydrous pyridine (2 mL) at room temperature. Pivaloyl chloride (35.4 μL, 0.289 mmol) was then added, and the resulting mixture stirred at room temperature for 10 h. Iodine (36.6 mg, 0.144 mmol) in a mixture of pyridine/water (19:1, 0.2 mL) was added to oxidize P(III) to P(V), and the reaction stirred for 6 h at room temperature. The solution was then diluted with $CHCl_3$ and washed with aqueous $Na_2S_2O_3$ solution, and the aqueous layer was re-extracted with $CHCl_3$. The combined organic layers were washed with TEAB buffer and dried over Na_2SO_4. Evaporation under reduced pressure gave the crude residue, which was purified by flash column chromatography with Et_3N-deactivated silica gel to give **30** (40 mg, 85%) as a pale yellow syrup. R_f 0.42 ($CHCl_3$/MeOH = 20:1); $[\alpha]_D^{rt} = +14.2$ (*c* = 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.77 (d, *J* = 6.5 Hz, 3H), 0.82 (t, *J* = 7.0 Hz, 9H), 1.00−1.30 (m, 84H), 1.41−1.51 (m, 6H), 2.09−2.17 (m, 6H), 2.86−3.04 (m, 6H), 3.26−3.40 (m, 4H), 3.59 (t, *J* = 1.5 Hz, 1H), 3.73 (t, *J* = 9.5 Hz, 1H), 3.82−4.24 (m, 16H), 4.37−4.85 (m, 19H), 5.15 (brm, 1H), 5.47 (d, *J* < 1.0 Hz, 1H), 5.61 (d, *J* < 1.0 Hz, 1H), 6.96−7.35 (m, 50H), 11.9 (brs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 8.8, 14.3, 19.9, 22.9, 25.0, 27.3, 29.3−30.4, 32.1, 34.2, 34.4, 37.3, 46.1, 62.5, 63.1, 64.6, 69.0, 70.4, 70.8, 71.4, 71.8, 72.0, 72.1, 72.4, 73.3, 74.0, 74.2, 74.9, 75.1, 75.2, 75.8, 76.4, 78.8, 79.0, 79.8, 81.5, 98.3, 98.6, 127.3−128.6 (CH−Aryl), 138.2−139.4 (C_q−Aryl), 173.2, 173.5, 173.7; ^{31}P NMR (121 MHz, $CDCl_3$) δ −0.70; HRMS-MALDI (*m*/*z*): $[M]^-$ Calcd for $C_{142}H_{194}O_{24}P^-$, 2314.3707; Found, 2314.365.

Sodium α-D-Mannopyranosyl-(1→6)-2-*O*-(6-*O*-palmitoyl-α-D-mannopyranosyl)-1-*O*-(1-*O*-((*R*)-10-methyloctadecanoyl)-2-*O*-palmitoyl-*sn*-glycerylphosphonato)-D-*myo*-inositol (PIM_2): A solution of the triethylammonium salt **30** (10 mg, 4.1 μmol) in 1:1 $CHCl_3$−MeOH (2 mL) was stirred in the presence of Dowex 50W X 4 (Na^+) resin for 3 h, filtered, then concentrated under reduced pressure. The residue was dissolved in a mixture of EtOAc/THF/1-PrOH/H_2O (1 mL, 2:1:1:1) with Pd/C (25 mg, 10% Pd content) and stirred under an atmosphere of hydrogen for 20 h. The reaction mixture was filtered through a short Celite plug with 1-PrOH/H_2O (1:1) as eluent, concentrated, and lyophilized to give **PIM_2** in Na^+ form (4.8 mg, 82%) as a white solid. R_f 0.50 ($CHCl_3$/MeOH/H_2O = 60:35:8); ^{1}H NMR (500 MHz, $CDCl_3$/CD_3OD/D_2O = 60:35:8) δ 0.75 (d, *J* = 6.5 Hz, 3H), 0.79 (t, *J* = 7.0 Hz, 9H), 1.11−1.29 (m, 75H), 1.47−1.55 (m, 6H), 2.23 (t, *J* = 7.5 Hz, 2H), 2.28 (t, *J* = 7.5 Hz, 4H), 3.21 (t, *J* = 9.5 Hz, 1H), 3.39 (dd, *J* = 10.0, 2.5 Hz, 1H), 3.52−4.50 (m, 20H), 5.03 (d, *J* < 1.0 Hz, 1H), 5.10 (d, *J* < 1.0 Hz, 1H), 5.18 (m, 1H); ^{31}P NMR (121 MHz, $CDCl_3$/CD_3OD/D_2O = 60:35:8) δ −0.50. HRMS-ESI (*m*/*z*): $[M]^-$ Calcd for $C_{72}H_{134}O_{24}P^-$, 1413.9003; Found, 1413.9001.

(2-*O*-Acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→2)-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→2)-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-(2-*O*-benzoyl-3,4-di-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-(2-*O*-benzoyl-3,4-di-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-1-*O*-allyl-2-*O*-(2-*O*-benzoyl-3,4-di-*O*-benzyl-6-*O*-triisopropylsilyl-α-D-mannopyranosyl)-3,4,5-tri-*O*-benzyl-D-*myo*-inositol (31): Pseudotrisaccharide **2** (207 mg, 0.135 mmol) and tetramannosyl imidate **1** (301 mg, 0.155 mmol) were combined and coevaporated (×3) with toluene before being placed under nitrogen and dissolved in CH_2Cl_2 (15 mL) with freshly activated 4 Å MS (300 mg). The solution was stirred for 30 min at room temperature and cooled to 0 °C, and then TMSOTf (2.4 μL, 13.5 μmol) in CH_2Cl_2 (100 μL) was added dropwise. The solution was stirred for 40 min before being quenched by the addition of Et_3N (10 μL), the solvent was removed under reduced pressure, and the residue was purified by flash column chromatography to give pure **31** (395 mg, 91%) as a white foam. R_f 0.58 (Hexanes/EtOAc = 2:1); $[\alpha]_D^{rt} = +23.5$ (*c* = 1.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.99−1.04 (m, 21H), 2.08 (s, 3H), 3.16−3.19 (m, 4H), 3.26−3.48 (m, 9H), 3.55−3.66 (m, 4H), 3.76−4.17 (m, 26H), 4.22−4.34 (m, 8H), 4.39−4.65 (m, 14H), 4.68−4.88 (m, 12H), 4.80 (d, *J* < 1.0 Hz, 1H), 4.91 (d, *J* = 1.5 Hz, 1H), 5.00 (d, *J* = 10.5 Hz, 1H), 5.02 (dd, *J* = 10.5, 1.5 Hz, 1H), 5.08 (d, *J* = 1.5 Hz, 1H), 5.18 (dd, *J* = 17.0, 1.5 Hz, 1H), 5.20 (d, *J* = 1.5 Hz, 1H), 5.24 (d, *J* = 1.5 Hz, 1H), 5.52 (d, *J* = 2.0 Hz, 1H), 5.53 (dd, *J* = 3.0, 2.0 Hz, 1H), 5.64 (dd, *J* = 3.0, 2.0 Hz, 1H), 5.72 (dd, *J* = 3.0, 2.0 Hz, 1H), 5.75 (dd, *J* = 3.0, 2.0 Hz, 1H), 5.82−5.91 (m, 1H), 6.86−7.48 (m, 99H), 7.97−8.12 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.3, 18.2, 18.2, 21.4, 62.5, 68.6, 68.7, 68.9, 68.9, 69.0, 69.2, 69.4, 70.7, 70.8, 70.9, 71.3, 71.5, 71.7, 71.8, 71.9, 72.1, 72.3, 72.4, 72.4, 72.7, 72.8, 73.5, 73.6, 73.7, 74.1, 74.2, 74.3, 74.4, 74.7, 74.8, 74.8, 75.0, 75.2, 75.3, 75.4, 75.4, 76.0, 76.1, 78.0, 78.6, 78.6, 79.1, 79.3, 79.4, 79.8, 81.3, 81.6, 81.8, 98.6, 98.9, 99.1, 99.4, 99.6, 100.6, 118.4, 127.0−128.8, 130.1, 130.1, 130.2, 130.4, 130.4, 130.5, 133.0, 133.3, 133.4, 134.1, 137.8−139.3 (C_q−Aryl), 165.5, 165.5, 165.9, 170.3. HRMS-MALDI (*m*/*z*): $[M + Na]^+$ Calcd for $C_{203}H_{218}O_{40}Si$, 3346.469; Found, 3346.461.

(2,3,4,6-Tetra-*O*-benzyl-α-D-mannopyranosyl)-(1→2)-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→2)-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-(2,3,4-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-(2,3,4-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-2-*O*-(2,3,4-tri-*O*-benzyl-6-*O*-palmitoyl-α-D-mannopyranosyl)-3,4,5-tri-*O*-benzyl-D-*myo*-inositol (36): [$CpRu(CH_3CN)_3$]PF_6 (5.6 mg, 13.0 μmol), quinaldic acid (2.2 mg, 13.0 μmol), and methanol (0.5 mL) were placed in a 10-mL Schlenk tube under an argon stream. The mixture was degassed thoroughly by freeze−pump−thaw (3 cycles) and stirred at room temperature for 30 min. Heptasaccharide **35** (27 mg, 7.9 μmol) was dissolved in CH_2Cl_2 (0.5 mL) and transferred to the Schlenk tube via syringe. The solution was resubjected to freeze−pump−thaw cycles (×3) and then heated to 40 °C for 10 h. The solvents were then removed under reduced pressure, and the residue was purified by silica gel column chromatography to give **36** (19 mg, 72%) as a colorless syrup. R_f 0.48 (Hexanes/EtOAc = 2:1); $[\alpha]_D^{rt} = +48.1$ (*c* = 0.7, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.83 (t, *J* = 7.0 Hz, 3H), 1.14−1.26 (m, 24H), 1.43−1.50 (m, 2H), 2.10 (t, *J* = 7.5 Hz, 2H), 3.14 (t, *J* = 9.5 Hz, 2H), 3.23 (dd, *J* = 9.5, 2.5 Hz, 1H), 3.28−3.39 (m, 3H), 3.45−4.11 (m, 38H), 4.18−4.62 (m, 39H), 4.66 (d, *J* = 10.5 Hz, 1H), 4.73−

4.85 (m, 8H), 4.75 (d, J = 2.0 Hz, 1H), 4.91 (d, J = 1.5 Hz, 1H), 5.11 (d, J = 1.5 Hz, 1H), 5.13 (d, J = 1.5 Hz, 1H), 5.15 (d, J = 1.5 Hz, 1H), 5.39 (d, J = 1.5 Hz, 1H), 6.96−7.29 (m, 110H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.3, 22.9, 25.0, 29.4−29.9, 32.1, 34.3, 63.3, 66.4, 67.0, 69.1, 69.2, 69.5, 70.3, 71.4, 71.5, 71.8, 72.1, 72.2, 72.2, 72.3, 72.6, 72.8, 72.8, 73.0, 73.4, 73.5, 73.6, 74.2, 74.2, 74.6, 74.6, 74.7, 74.8, 75.0, 75.0, 75.1, 75.2, 75.2, 75.4, 75.5, 75.7, 78.6, 79.0, 79.1, 80.1, 80.1, 80.6, 80.8, 81.5, 96.2, 98.8, 98.8, 99.5, 99.5, 100.8, 127.3−128.7 (CH−Aryl), 138.6−139.1 (C_q−Aryl), 173.8. HRMS-MALDI (m/z): $[M + Na]^+$ Calcd for $C_{212}H_{234}O_{37}$, 3396.6388; Found, 3396.637.

Triethylammonium (2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-(1→2)-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→2)-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-(2,3,4-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-(2,3,4-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-2-*O*-(2,3,4-tri-*O*-benzyl-6-*O*-palmitoyl-α-D-mannopyranosyl)-3,4,5-tri-*O*-benzyl-1-*O*-(1-*O*-((*R*)-10-methyloctadecanoyl)-2-*O*-palmitoyl-*sn*-glycerylphosphonato)-D-*myo*-inositol (37): Heptasaccharide **36** (15 mg, 4.45 μmol) and *H*-phosphonate **13** (34.5 mg, 44.5 μmol) were coevaporated with anhydrous pyridine (2 mL × 3) and dried under high vacuum overnight. The mixture was dissolved in anhydrous pyridine (1 mL) at room temperature, aided by sonication. Pivaloyl chloride (11.0 μL, 88.9 μmol) was added, and the resulting mixture was stirred at room temperature for 12 h. Iodine (11.3 mg, 44.5 μmol) in a mixture of pyridine/water (19:1, 0.1 mL) was added to oxidize P(III) to P(V), and the reaction stirred for 6 h at room temperature. The solution was then diluted with $CHCl_3$ and washed with aqueous $Na_2S_2O_3$ solution. The aqueous layer was extracted with $CHCl_3$, and the combined organic layers were washed with TEAB buffer and dried over Na_2SO_4. Evaporation under reduced pressure gave the crude residue, which was purified by flash column chromatography with Et_3N-deactivated silica gel to give **37** (15 mg, 81%) as a pale yellow syrup. R_f 0.36 ($CHCl_3$/MeOH = 20:1); $[\alpha]_D^{rt}$ = +26.7 (c = 0.8, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3/CD_3OD$ = 1:1) δ 0.84 (d, J = 6.5 Hz, 3H, CH_3CH−TBacid), 0.86−0.91 (m, 9H), 1.04−1.39 (m, 84H), 1.48−1.56 (m, 6H), 2.15−2.22 (m, 6H), 3.08 (q, J = 7.3 Hz, 6H), 3.11 (t, J = 10.0 Hz, 2H), 3.29−3.68 (m, 12H), 3.78−4.15 (m, 25H), 4.18−4.83 (m, 50H), 4.81 (d, J < 1.0 Hz, 1H), 4.86−4.93 (m, 5H), 4.92 (d, J < 1.0 Hz, 1H), 5.02 (d, J = 11.0 Hz, 1H), 5.21 (d, J = 1.5 Hz, 1H), 5.22 (d, J = 1.5 Hz, 1H), 5.23−5.26 (m, 1H), 5.54 (d, J < 1.0 Hz, 1H), 5.67 (d, J < 1.0 Hz, 1H), 7.00−7.54 (m, 110H); ^{13}C NMR (150 MHz, $CDCl_3/CD_3OD$ = 1:1) δ 8.96, 14.3, 20.0, 23.2, 25.4, 25.4, 25.5, 27.6, 27.6, 29.6−30.5, 32.4, 33.3, 34.5, 34.6, 34.7, 37.6, 37.6, 47.1, 63.1, 63.7, 64.3, 66.7, 66.8, 69.4, 69.7, 70.5, 71.0, 71.2, 71.5, 71.7, 71.8, 72.0, 72.4, 72.6, 72.6, 72.7, 72.8, 72.9, 73.0, 73.0, 73.0, 73.7, 73.9, 73.9, 74.4, 74.6, 74.8, 74.9, 75.1, 75.2, 75.3, 75.3, 75.4, 75.5, 75.9, 76.1, 76.5, 76.7, 78.6, 79.1, 79.5, 79.7, 79.9, 80.4, 80.9, 81.7, 82.0, 98.9, 98.9, 99.4, 99.7, 100.0, 101.1, 127.4−129.1 (CH−Aryl), 138.4−140.0 (C_q−Aryl), 173.8, 174.2, 174.3; ^{31}P NMR (121 MHz, $CDCl_3/CD_3OD$ = 1:1) δ −0.60; HRMS-MALDI (m/z): $[M]^-$ Calcd for $C_{250}H_{306}O_{44}P^-$, 4045.1507; Found, 4045.136.

Sodium α-D-mannopyranosyl-(1→2)-α-D-mannopyranosyl-(1→2)-α-D-mannopyranosyl-(1→6)-α-D-mannopyranosyl-(1→6)-α-D-mannopyranosyl-(1→6)-2-*O*-(6-*O*-palmitoyl-α-D-mannopyranosyl)-1-*O*-(1-*O*-((*R*)-10-methyloctadecanoyl)-2-*O*-palmitoyl-*sn*-glycerylphosphonato)-D-*myo*-inositol (PIM$_6$): A solution of the triethylammonium salt **37** (15 mg, 3.6 μmol) in 1:1 $CHCl_3$−MeOH (2 mL) was stirred in the presence of Dowex 50W X 4 (Na^+) resin for 3 h, filtered, and then concentrated under reduced pressure. The residue was then dissolved in a mixture of EtOAc/THF/1-PrOH/H_2O (2 mL, 2:1:1:1) with Pd/C (100 mg, 10% Pd content) and stirred under an atmosphere of hydrogen for 20 h. The reaction mixture was filtered through a short Celite plug with 1-PrOH/H_2O (1:1) as eluent, concentrated, and lyophilized to give **PIM$_6$** in Na^+ form (5.7 mg, 76%) as a white solid. R_f 0.23 ($CHCl_3$/MeOH/H_2O = 60:35:8); ^{1}H NMR (600 MHz, d_6-DMSO) δ 0.80 (d, J = 6.5 Hz, 3H), 0.84 (t, J = 7.0 Hz, 9H), 1.04−1.30 (m, 75H), 1.45−1.52 (m, 6H), 2.23−2.30 (m, 6H), 3.00−4.20 (m, 53 H), 4.40 (br, 1H), 4.58 (br, 1H), 4.63 (br, 1H), 4.68 (br, 1H), 4.75 (br, 1H), 4.81 (br, 1H), 4.90 (br, 1H); ^{31}P NMR (243 MHz, d_6-DMSO) δ 1.85. HRMS-ESI (m/z): $[M]^-$ Calcd for $C_{96}H_{174}O_{44}P^-$, 2062.1121; Found, 2062.1148.

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Supporting Information Available: Experimental procedures for compounds **5**, **6**, **14b**, **15b**, **15c**, **20**, **32**−**35**, spectral copies (^{1}H, ^{13}C, ^{31}P, HSQC, MS) of all new compounds, and full citations for refs 12, 13, 22. This material is available free of charge via the Internet at http://pubs.acs.org.

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