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Synthesis and Mass Spectral Characterization of Mycobacterial Phosphatidylinositol and Its Dimannosides

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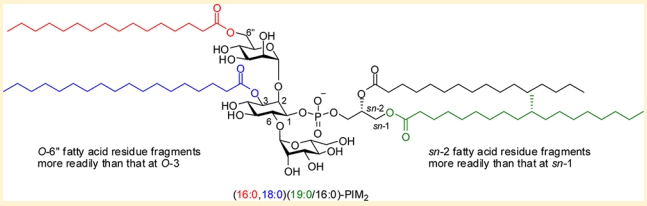
Supporting Information

ABSTRACT: A family of naturally occurring mycobacterial phosphatidylinositol (PI) and its dimannosides (PIM_2, $AcPIM_2$, and Ac_2PIM_2) that all possess the predominant natural 19:0/16:0 phosphatidyl acylation pattern were prepared to study their mass spectral fragmentations. Among these, the first synthesis of a fully lipidated PIM (i.e., (16:0,18:0)(19:0/16:0)-PIM_2) was achieved from (±)-1,2:4,5-diisopropylidene-D-*myo*-inositol in 16 steps in 3% overall yield. A key feature of the strategy was extending the utility of the *p*-(3,4-dimethoxyphenyl)benzyl protecting group for its use at the *O*-3 position of inositol to allow installation of the stearoyl residue at a late stage in the synthesis. Mass spectral studies were performed on the synthetic PIMs and compared to those reported for natural PIMs identified from a lipid extract of *M. bovis* BCG. These analyses confirm that fragmentation patterns can be used to identify the structures of specific PIMs from the cell wall lipid extract.



INTRODUCTION

The waxy cell wall of mycobacteria continues to be of interest to a number of research groups as it is essential for pathogen viability inside an infected host.[1,2] This makes it a target for drug design[3] and also provides a rich source of material that has a wide range of immune-modulatory activities. Because of this, we have developed a program aimed at the structural determination, synthesis, and testing of various cell wall components from mycobacteria in an endeavor to contribute to the growing body of evidence that will allow immunological insight into the mechanism of action for mycobacterial products. In particular, we have focused on the phosphatidylinositol mannoside (PIM) subclass of molecules because of their diverse biological activity.[4] Both synthetic and natural preparations of these molecules have been investigated in various immunological models. For example, synthetic PIM glycans display strong adjuvant activity when conjugated to the carrier protein BSA,[5] and natural PIM extracts can induce a cell-mediated immune response in a vaccination protocol utilizing the model antigen OVA.[6] In the latter example, the activity of the PIM compounds was attributed to their ability to form liposomes and deliver the vaccine to antigen presenting cells. PIMs have also been shown to bind various cell surface receptors including DC-SIGN,[7] CD1d,[8] TLR2/4,[9,10] and $\alpha_5\beta_1$ integrin.[11] Along with their adjuvant properties, PIM compounds have also been shown to block LPS signaling,[12] reduce allergic airway disease in murine models of asthma,[13] induce T-cell adhesion to fibronectin,[11] and modulate T-cell proliferation.[14−16] Although synthetic examples from most PIM subclasses have been prepared to date, there are few examples of synthetic PIM compounds that are present in the mycobacterial cell wall (i.e., most synthetic preparations of PIMs do not contain natural acylation patterns). Standard organic extraction protocols of mycobacteria afford PI, PIM_2, $AcPIM_2$, and Ac_2PIM_2 as major cell wall components. These fractions are heterogeneous mixtures with each compound type consisting of a number of molecules with different fatty acid substituents. Isolation of discrete PIMs is implausible because of the similarity of these molecules and this complicates structural elucidation.

Hsu et al. have undertaken a comprehensive mass spectral study of a fractionated cell wall extract from *Mycobacterium bovis* Bacillus Calmette Guérin to determine the acylation pattern of the major PI and PIM molecules.[17] They found that the most abundant PIMs contain a palmitoyl (16:0) and a (*R*)-tuberculostearoyl (19:0) fatty acid attached to the glycerol moiety of the phosphatidyl group. The fragmentation patterns of deprotonated molecular ions of these compounds shown by negative-ion electrospray ionization tandem mass spectrometry (MS^2) indicated that the 16:0 acyl group fragmented more readily than the 19:0 fatty acid. From this observation, they proposed that the more abundant PIMs had a 19:0 and a 16:0 fatty acid at the *sn*-1 and *sn*-2 glyceryl sites respectively, exemplified by (19:0/16:0)-PIM_2 (**1**). These observations were also reported by Gilleron et al.[18] in their mass spectral study of a PIM extract from *M. bovis*. The hypothesis that the *sn*-2 acyl group fragments more readily than that at the *sn*-1 position was

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confirmed by Dyer et al.[19] from a mass spectral study of a non-natural synthetic PIM_2. NMR studies of higher acylated PIMs[20,21] have identified two additional acylation sites. These are the primary position of the mannose residue attached at *O*-2 of inositol for AcPIMs together with the *O*-3 position of inositol for Ac_2PIMs (Figure 1).

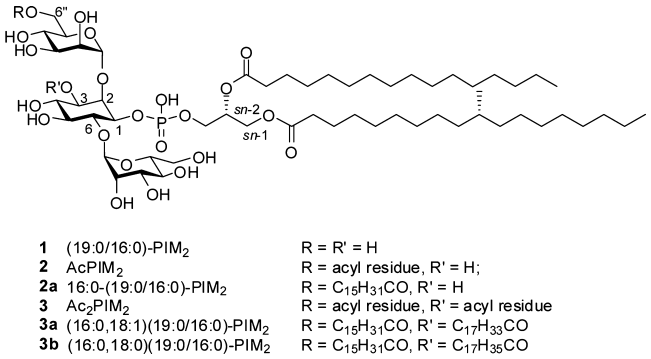


Figure 1. Acylation sites of PIM_2 species.

By analysis of mass spectra (MS, MS^2, MS^3) of a *M. bovis* extract, Hsu et al.[22] proposed that the most abundant $AcPIM_2$ species (**2**) possessed the expected 19:0/16:0 phosphatidyl acylation pattern and a palmitoyl residue at *O*-6″, i.e., 16:0-(19:0/16:0)-PIM_2 (**2a**). They also showed that the major species from the fully lipidated PIM subgroup (Ac_2PIM_2) possessed the same phosphatidyl moiety as (19:0/16:0)-PIM_2 (**1**). By analogy to (16:0-(19:0/16:0)-PIM_2 (**2a**), it was suggested that the acyl group attached to *O*-6″ of the major Ac_2PIM_2 subclass was most commonly palmitoyl (16:0). The acyl residue at *O*-3 of inositol was predominately oleoyl (18:1), stearoyl (18:0), or (*R*)-tuberculostearoyl (19:0). The assignments were made on the assumption that the acyl group attached to *O*-6″ fragments more easily than that at *O*-3. However, the structural analyses of these fully acylated PIMs are not definitive as only limited data pertaining to atom connectivity can be obtained using mass spectrometry alone. Thus, the assignments of the acylation pattern at these positions on the mannose and inositol residues are only speculative until proven by comparison of the spectroscopic data to that of the discrete entity obtained through isolation or, more commonly, via careful and methodical synthesis.

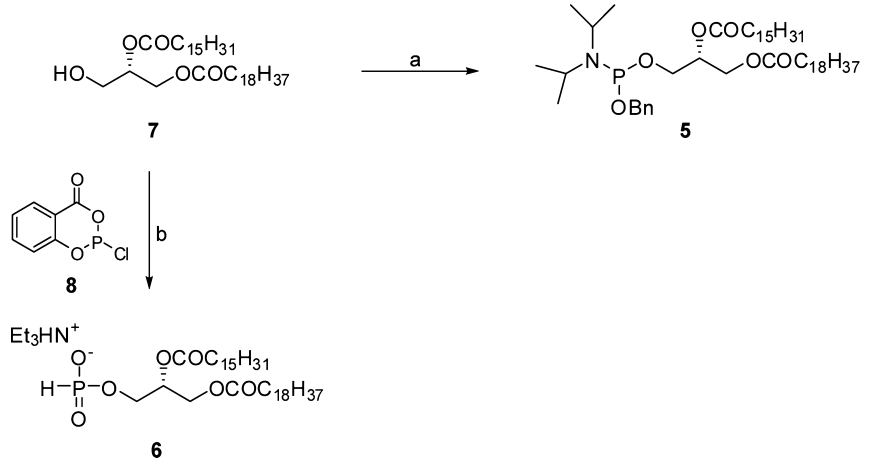
Although a number of studies have produced synthetic PIMs,[5,19,23−33] only two have reported compounds that contain the most abundant natural acylation pattern. Specifically, both the Seeberger[34] and Lear[35] groups have synthesized (16:0-(19:0/16:0)-PIM_2 (**2a**), and Seeberger et al.[34] have also synthesized 16:0-(19:0/16:0)-PIM_6. Unfortunately, no detailed mass spectral analyses were performed, and therefore, no comparison with data obtained from natural extracts could be made. To definitively ascertain the acylation patterns of fully lipidated PIMs, we report here the synthesis of a structurally defined set of these molecules containing the natural 19:0/16:0 acylated phosphatidyl moiety. These encompass the major components of the PIM_2 family proposed to be present in mycobacterial cell walls. A detailed mass spectral study of these compounds has substantiated the fragmentation interpretation of Hsu et al.[17,22] Furthermore, inclusion of a fourth acyl group provides the first synthetic example of an Ac_2PIM_2 to be reported and significantly extends the available library of synthetic PIMs that will be tested in biological assays.

Our targets were (19:0/16:0)-PI (**4**) (Scheme 2), (19:0/16:0)-PIM_2 (**1**), 16:0-(19:0/16:0)-PIM_2 (**2a**), and an Ac_2PIM_2 (**3**) (Figure 1). The synthesis of the first three targets was by modification of syntheses already developed for other PIM compounds.[9,13,15,19,24,25,36,37] However, for Ac_2PIM_2, a different synthetic strategy was required that would allow sequential glycosylation at *O*-6 and *O*-2 of *myo*-inositol, acylation at *O*-3, and phosphatidylation at *O*-1. In their study, Hsu et al.[22] focused on the fragmentation pattern of an Ac_2PIM_2 which they tentatively assigned the structure as (16:0,18:1)(19:0/16:0)-PIM_2 (**3a**). We chose to target another analogous abundant natural Ac_2PIM_2 with a structure believed to be (16:0,18:0)-(19:0/16:0)-PIM_2 (**3b**). This compound (**3b**) would be synthetically more readily accessible and would still allow comparison of the mass spectral data to those from natural samples.

RESULTS AND DISCUSSION

The current study required a phosphatidylation reagent with tuberculostearoyl (19:0) and palmitoyl (16:0) fatty esters at the *sn*-1 and *sn*-2 positions of the glycerol, respectively. It was

Scheme 1. Synthesis of Phosphoramidite 5 and *H*-Phosphonate 6[a]



[a]Reagents and conditions: (a) $BnOP(NiPr_2)_2$, 1*H*-tetrazole, CH_2Cl_2, 80%; (b) **8**, THF, Py, TEAB buffer, quant.

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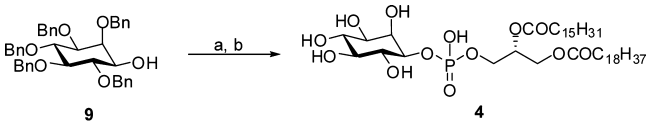
decided to utilize both phosphoramidite **5** and *H*-phosphonate **6** as both of these compounds have been used successfully in previous syntheses of PIM compounds (Scheme 1). The required diacylglycerol **7** was synthesized from (*R*)-benzyl glycidyl ether using the procedure reported by Horst et al.[38] Treatment of diacylglycerol **7** with benzyloxybis-(diisopropylamino)phosphine and 1*H*-tetrazole afforded phosphoramidite **5** in 80% yield. *H*-Phosphonate **6** was prepared in quantitative yield by reaction of **7** with chlorophosphite **8**. The data were consistent with those reported by Seeberger et al.[34]

The first target (19:0/16:0)-PI (**4**) was prepared by phosphatidylation of known intermediate **9**[28] with *H*-phosphonate **6**[34] and then global debenzylation to furnish the previously unreported compound **4** in 86% yield, which was shown to be 96% pure by HPLC analysis (Scheme 2).

Scheme 2. Synthesis of (19:0/16:0)-PI (4)[a]

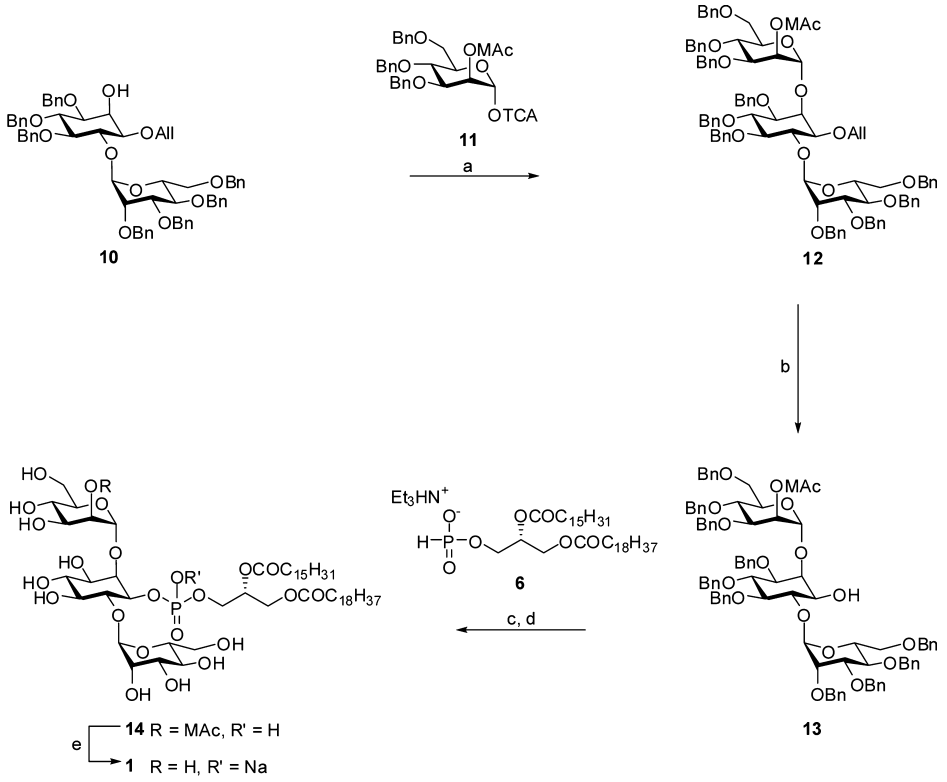


[a]Reagents and conditions: (a) (i) **6**, PivCl, Py, (ii) I_2, Py/H_2O, (iii) Amberlite IRC86 (H^+) resin; (b) $Pd(OH)_2/C$, H_2, MeOH, THF, 86%.

Increasing in complexity, the syntheses of (19:0/16:0)-PIM_2 (**1**) and 16:0-(19:0/16:0)-PIM_2 (**2a**) were accomplished. We chose pseudodisaccharide **10**[9,28] as the starting material for the synthesis of **1** and **2a** as this compound can be easily prepared in multiple gram amounts (Scheme 3). Pseudodisaccharide **10** was mannosylated with trichloroacetimidate donor **11**,[13] which incorporates a methoxyacetate (MAc) group at *O*-2. This directing group imparts high α-selectivity giving compound **12** in 85% yield with no β-anomer detected and has the added advantage that it can be readily removed in the presence of other ester groups.[12,13] Oxymercuration was used to cleave the enol ether adduct of the Ir(I)-promoted allyl ether isomerization to avoid loss of the acid labile MAc group, and the resulting alcohol **13** was coupled with *H*-phosphonate **6** followed by in situ oxidation with iodine. Hydrogenolysis gave partially protected PIM_2 **14**, and finally, the methoxyacetate group was removed with dilute NaOMe in CH_2Cl_2/MeOH to afford (19:0/16:0)-PIM_2 (**1**) in 78% yield, which was shown to be 95% pure by HPLC.

The synthesis of AcPIM$_2$ 16:0-(19:0/16:0)-PIM$_2$ (**2a**) began with the mannosylation of **10** with orthogonally protected mannosyl phosphate donor **15**[39] (Scheme 4). Promotion of the reaction with excess TBSOTf resulted in glycosylation, albeit with partial exchange of the *O*-6″ silyl protecting group to give **16** as a 2:1 mixture of triisopropyl- and *tert*-butyldimethyl silyl ethers in 67% yield. Standard modification procedures, namely debenzoylation under Zemplén conditions, followed by benzylation and subsequent removal of the allyl and silyl ether protecting groups afforded **17** in 77% yield over three steps. Selective acylation of diol **17** with palmitoyl chloride gave the AcPIM$_2$ headgroup **18** in 85% yield. The 1*H*-tetrazole-mediated coupling of phosphoramidite **5** with **18** followed by in situ oxidation furnished protected AcPIM$_2$ **19** in 88% yield. Hydrogenolysis of the benzyl groups of **19** gave 16:0-(19:0/

Scheme 3. Synthesis of PIM_2 (1)[a]



[a]Reagents and conditions: (a) **11**, TMSOTf, toluene, 0 °C, 85%; (b) (i) $(COD)(MePh_2P)_2Ir^+PF_6^-$, H_2, THF, (ii) HgO, $HgCl_2$, $(CH_3)_2CO/H_2O$, 85%; (c) (i) **6**, PivCl, Py, (ii) I_2, Py/H_2O, (iii) Amberlite IRC86 (H^+) resin; (d) $Pd(OH)_2/C$, H_2, MeOH, THF, 81%, two steps; (e) (i) 2.5 mM NaOMe, CH_2Cl_2/MeOH, (ii) Amberlite IRC86 (Na^+) resin, 78%.

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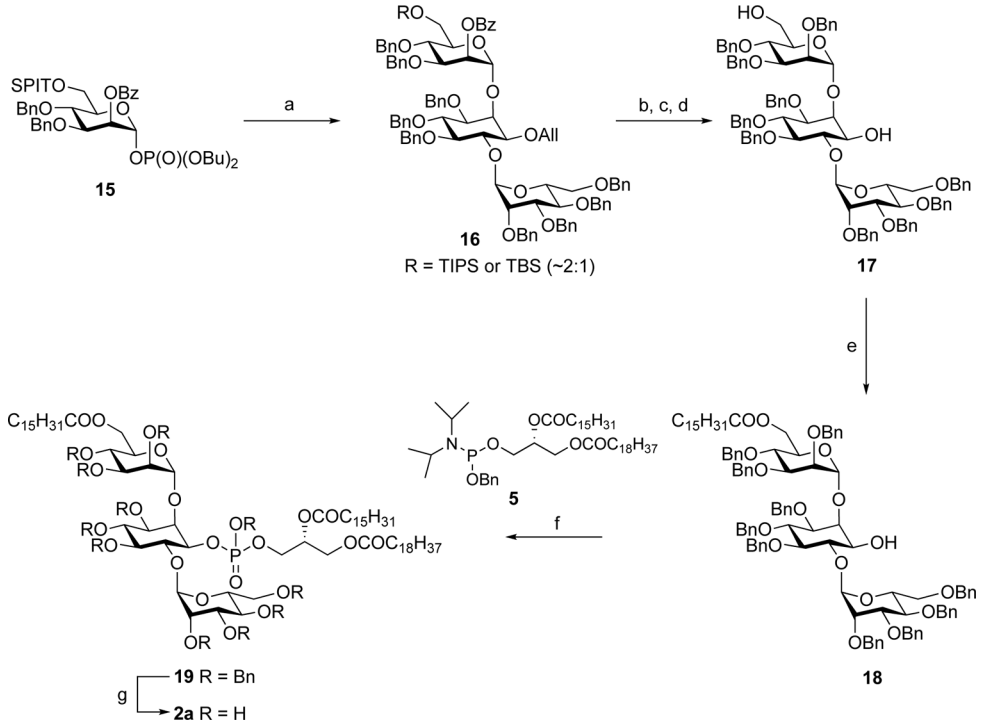
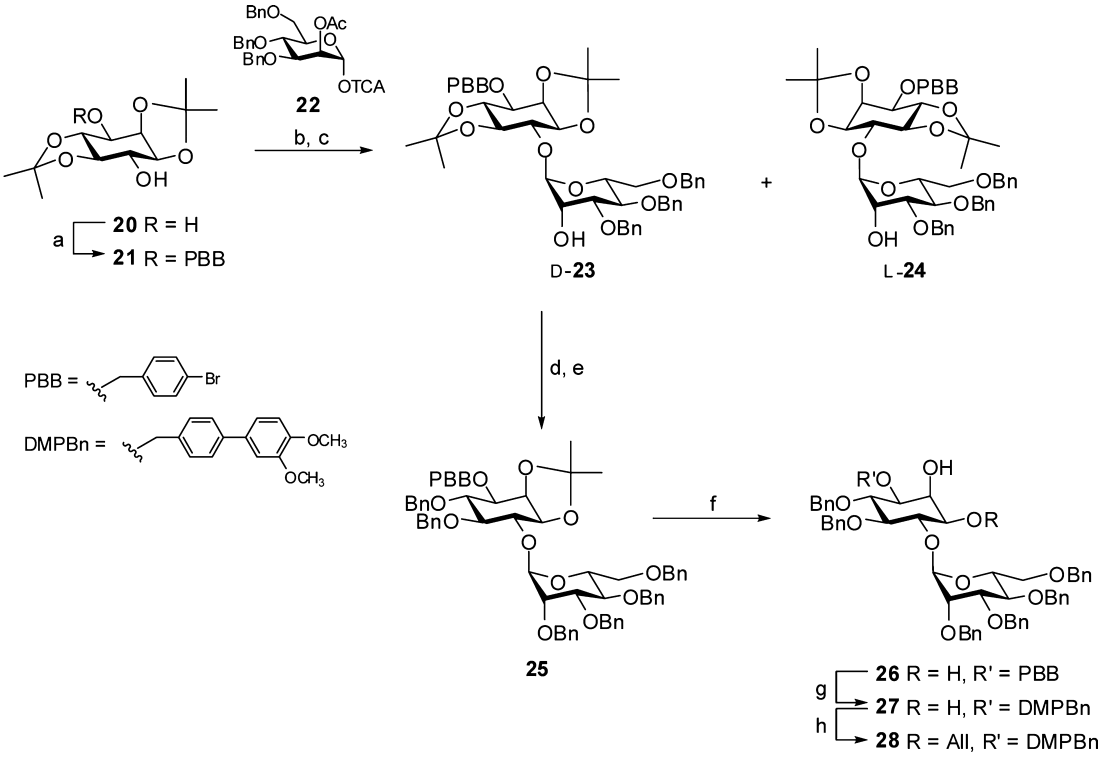
Scheme 4. Synthesis of AcPIM$_2$ (2a)[a]



[a]Reagents and conditions: (a) **10**, TBSOTf, toluene, 0 °C, 67%; (b) NaOMe, CH_2Cl_2/MeOH; (c) BnBr, NaH, DMF; (d) (i) $(COD)(MePh_2P)_2Ir^+PF_6^-$, H_2, THF, (ii) AcCl, MeOH/CH_2Cl_2, 77%, three steps; (e) $C_{15}H_{31}COCl$, Py/CH_2Cl_2, 85%, (f) (i) **5**, 1*H*-tetrazole, MeCN, (ii) *m*-CPBA, CH_2Cl_2, 88%; (g) $Pd(OH)_2$/C, H_2, MeOH/THF, 90%.

Scheme 5. Resolution of *myo*-Inositol 20[a]



[a]Reagents and conditions: (a) 4-bromobenzyl bromide, NaH, THF, 65%; (b) **22**, TMSOTf, 4 Å M.S., CH_2Cl_2, −30 °C; (c) NaOMe, MeOH, D-**23**, 42%, two steps, L-**24**, 41%, two steps; (d) TFA, H_2O, CH_2Cl_2, 0 °C, 2.5 h; (e) BnBr, NaH, DMF, 79%, two steps; (f) TFA, MeOH, CH_2Cl_2, 12 h, 79%; (g) K_3PO_4, Bu_4NBr, $Pd(OAc)_2$, 3,4-dimethoxyphenylboronic acid, EtOH, 90%; (h) (i) Bu_2SnO, toluene, (ii) CsF, AllBr, DMF, 73%.

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16:0)-PIM_2 (**2a**) in 90% yield, which was shown to have a purity of 98% by HPLC.

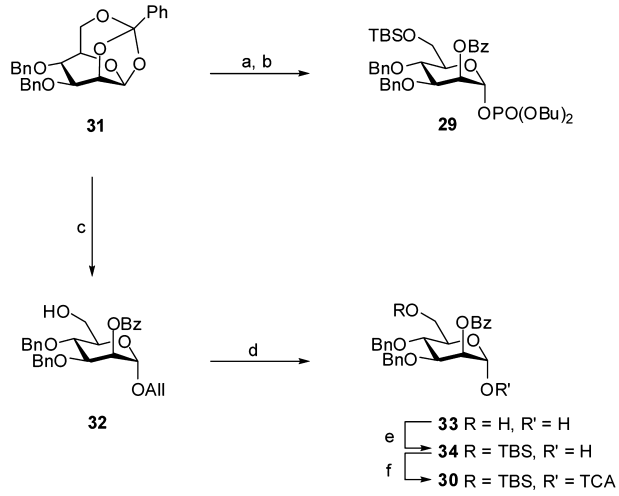
With the first three targets in hand, our attention turned to the synthesis of (16:0,18:0)(19:0/16:0)-PIM_2 (**3b**) (Scheme 5). Bis-isopropylidene-*myo*-inositol **20**[40−42] was chosen as a convenient starting material as it is readily available and displays appropriate reactivity (i.e., *O*-3 is more reactive than *O*-6). We planned to use a relay deprotection method at *O*-3 whereby this position was protected as a *p*-bromobenzyl (PBB) ether.[43,44] This group was chosen due to the variety of reactions which can mediate its selective removal, for example, aromatic substitution followed by treatment with either a Lewis acid, protic acid, or oxidant.[43,44]

Inositol **21** was prepared by selective alkylation of **20** with *p*-bromobenzyl bromide in 65% yield. The mannosylation of **21** with TCA donor **22**[45,46] and subsequent deacetylation permitted chromatographic separation of the diastereomeric mannosides D-**23** and L-**24** in 42% and 41% yields, respectively. The D-*myo*-inositol configuration of **23** was confirmed by synthesis from D-**20**, prepared by resolution of (±)-**20** via the corresponding bis-(*S*)-*O*-acetylmandeloyl esters.[47,48] Selective acidic hydrolysis of the *trans*-fused isopropylidene group and subsequent benzylation of the resulting triol gave **25**, which was then treated with methanolic TFA to afford diol **26**. The incompatibility of the PBB and allyl ether protecting groups in the Pd-catalyzed amination reaction led to transforming the PBB ether into a *p*-(3,4-dimethoxyphenyl)benzyl (DMPBn) ether via a Suzuki−Miyaura coupling with 3,4-dimethoxyphenylboronic acid in excellent yield. Stannylene acetal promoted alkylation of **27** was used to selectively install the allyl ether at *O*-1 to afford **28** in 73% yield.

To avoid the problems of silyl exchange as encountered in the synthesis of **2a** (**10** → **16**, Scheme 4), mannosylation of **28** with phosphate donor **29**, bearing a TBS ether at *O*-6, was attempted. Although the reaction afforded a significant amount of the target pseudotrisaccharide, a product resulting from additional glycosylation at *O*-6″ was also observed, presumably by cleavage of the TBS ether and subsequent glycosylation. To overcome this, a more reactive donor requiring only catalytic amounts of a promoter was used. The known TCA mannosyl donor **30**[49] was prepared in four steps from tricyclic orthoester **31**[39] via an alternative method (Scheme 6). The Lewis acid promoted reaction of **31** and allyl alcohol afforded **32** which was deallylated under standard conditions affording diol **33** in 87% yield. Selective silylation of the primary hydroxyl group was achieved using TBSOTf to afford **34**, which was then converted to imidate **30**.

Mannosylation at *O*-2 of **28** with TCA donor **30** gave pseudotrisaccharide **35** in high yield (Scheme 7). Routine protecting group manipulations, namely debenzoylation to give **36** and benzylation, afforded **37**. Mild acidic conditions cleaved the silyl ether to give **38**, and subsequent acylation with palmitic acid afforded **39** in 79% yield from **35**. Attempted removal of the DMPBn ether of **39** with DDQ, as described for mono- and disaccharide substrates,[43] resulted in a complex mixture of products due to the uncontrolled loss of benzyl protecting groups. Seeberger et al. had noted that this protecting group could not be selectively removed from a protected hexasaccharide in the synthesis of a GPI anchor.[50] This problematic deprotection was circumvented by hydrolysis of the DMPBn group using TFA and cation scavenger **40**[51] to cleanly afford **41** in 74% yield. Acylation of alcohol **41** with

Scheme 6. Synthesis of Mannosyl Donors 29 and 30[a]



[a]Reagents and conditions: (a) $HOP(O)(OBu)_2$, CH_2Cl_2; (b) TBSCl, DMAP, Py, CH_2Cl_2, 73%, two steps; (c) AllOH, $BF_3{\cdot}Et_2O$, CH_2Cl_2, 99%; (d) (i) $(COD)(MePh_2P)_2Ir^+PF_6^-$, H_2, THF, (ii) AcCl, MeOH/CH_2Cl_2, 85%; (e) TBSOTf, *sym*-collidine, CH_2Cl_2, 79%; (f) Cl_3CCN, DBU, CH_2Cl_2, 83%.

stearic acid and deallylation of **42** gave the Ac_2PIM_2 headgroup **43**.

Phosphorylation of pseudotrisaccharide **43** with phosphoramidite **5** was unsuccessful; however, treatment with *H*-phosphonate **6** and in situ oxidation furnished protected Ac_2PIM_2 **44** as the triethylammonium salt in 87% yield. Cation exchange and global deprotection under hydrogenolytic conditions afforded Ac_2PIM_2 **3b** as the sodium salt in high purity (96% by HPLC). A well-resolved ^1H NMR spectrum of **3b** was obtained in the mixed solvent system $CDCl_3/CD_3OD/D_2O$ (70:40:6) at 30 °C.

With all four synthetic targets in hand, we set about comparing their corresponding fragmentation patterns by negative ion ESI-MS^n both to each other and to those reported from natural sources. All MS^2 and pseudo-MS^3 spectra are provided in the Supporting Information.

At the core of the PIM family is (19:0/16:0)-PI (**4**), which shows a deprotonated molecular ion $[M - H]^-$ at *m*/*z* 851.6. ESI-MS^2 fragmentation of this parent ion gave two major peaks at *m*/*z* 595.3, attributed to the loss of the *sn*-2 palmitoyl (16:0) residue, and at *m*/*z* 433.3, resulting from the loss of the inositol and the *sn*-2 fatty acid. Related, less intense peaks from the analogous losses of the *sn*-1 tuberculostearoyl (19:0) and inositol moieties were observed at *m*/*z* 553.3 and 391.2, which reaffirms that the *sn*-2 fatty acid fragments more readily than that at the *sn*-1 position (Figure 2). Overall, the fragmentation pattern revealed in the MS^2 spectrum of our synthetic target matched that of the natural product reported by Hsu et al.[17] (Figure S1, Supporting Information).

(19:0/16:0)-PIM_2 (**1**), with a parent ion $[M - H]^-$ at *m*/*z* 1175.7 was fragmented, giving rise to two daughter ions at *m*/*z* 919.4 and 877.4 corresponding to the loss of the *sn*-2 and *sn*-1 acyl residues respectively from the phosphatidyl moiety (Figure S2B, Supporting Information). The dominant ion of the pair at *m*/*z* 919.4 was consistent with the data reported by Hsu et al.[17] for the preferential loss of the *sn*-2 palmitoyl ester. This MS^2 spectrum of **1** also displays signals of *m*/*z* 433.3 and 391.2 also seen in the MS^2 spectrum of **4** above. These data confirm that

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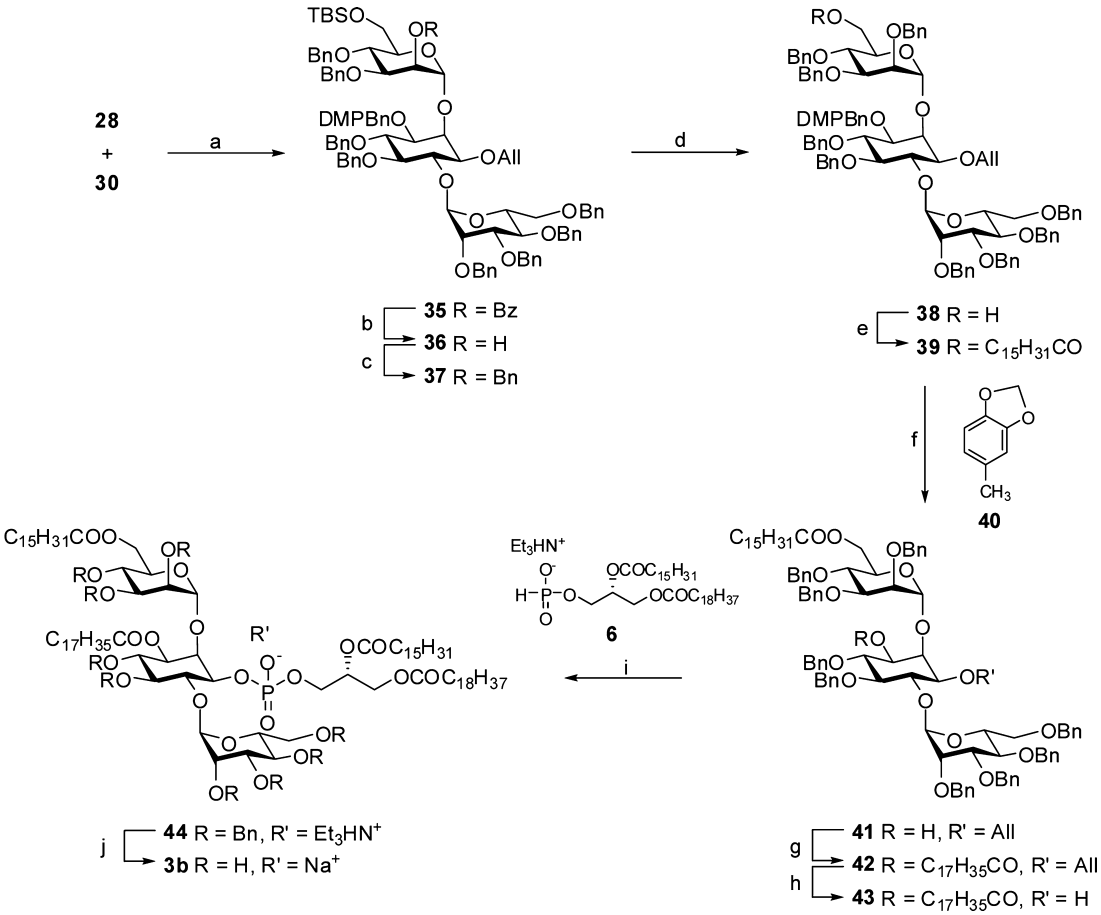
Scheme 7. Synthesis of Ac_2PIM_2 (3b)[a]



[a]Reagents and conditions: (a) TMSOTf, 4 Å M.S., toluene, 0 °C, 99%; (b) NaOMe, CH_2Cl_2/MeOH, 93%; (c) BnBr, NaH, DMF, 99%; (d) AcCl, CH_2Cl_2/MeOH, 92%; (e) $C_{15}H_{31}COOH$, DMAP, DCC, CH_2Cl_2, 93%; (f) **40**, 30% TFA, CH_2Cl_2, 74%; (g) $C_{17}H_{35}COOH$, DMAP, DCC, CH_2Cl_2, 84%; (h) (i) $(COD)(MePh_2P)_2Ir^+PF_6^-$, H_2, THF, (ii) HgO, $HgCl_2$, $(CH_3)_2CO/H_2O$, 61%; (i) (i) **6**, PivCl, Py, (ii) I_2, Py/H_2O, 87%; (j) (i) Dowex 50WX4-400 (Na+) resin, $CHCl_3$/MeOH, (ii) $Pd(OH)_2/C$, H_2, MeOH, THF, 99%.

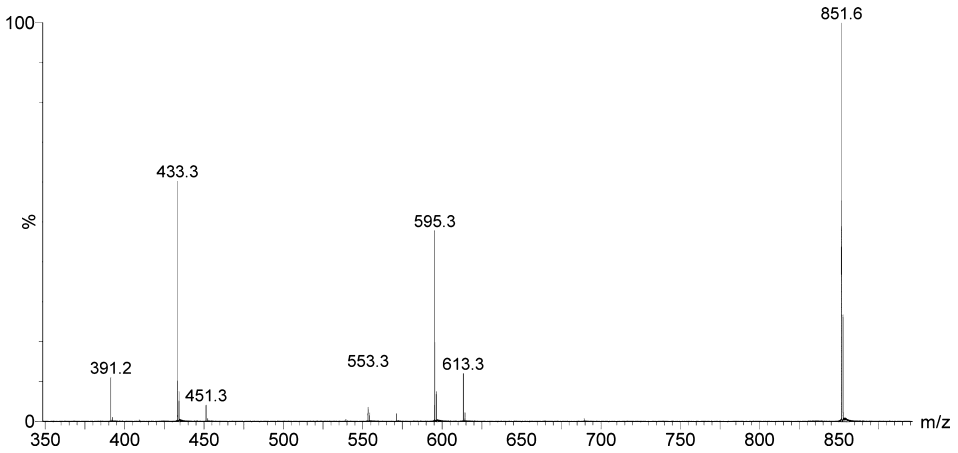


Figure 2. Negative-ion ESI-TOF MS^2 spectrum of the ion at m/z 851.6 of 19:0/16:0-PI (**4**).

the natural acylation pattern of the phosphatidyl group of the more abundant PIMs is as synthesized here (i.e., contains a 19:0 and 16:0 fatty acid at the *sn*-1 and *sn*-2 positions respectively).

The fragmentation of the $[M - H]^-$ ion at m/z 1413.9 of 16:0-(19:0/16:0)-PIM_2 (**2a**) showed a similar *sn*-2 fragmentation bias as observed for **4** and **1** (Figure S3, Supporting Information). This MS^2 spectrum also showed a product ion at m/z 803.3 which is attributed to the loss of the diacyl glycerol unit. Pseudo-MS^3 data obtained for m/z 803 of **2a** compares well to the equivalent m/z 803 MS^3 (1413→803) spectrum of the natural extract obtained by Hsu et al.[22] with prominent ions at m/z 385.0 and 547.1 attributable to the loss of the *O*-2

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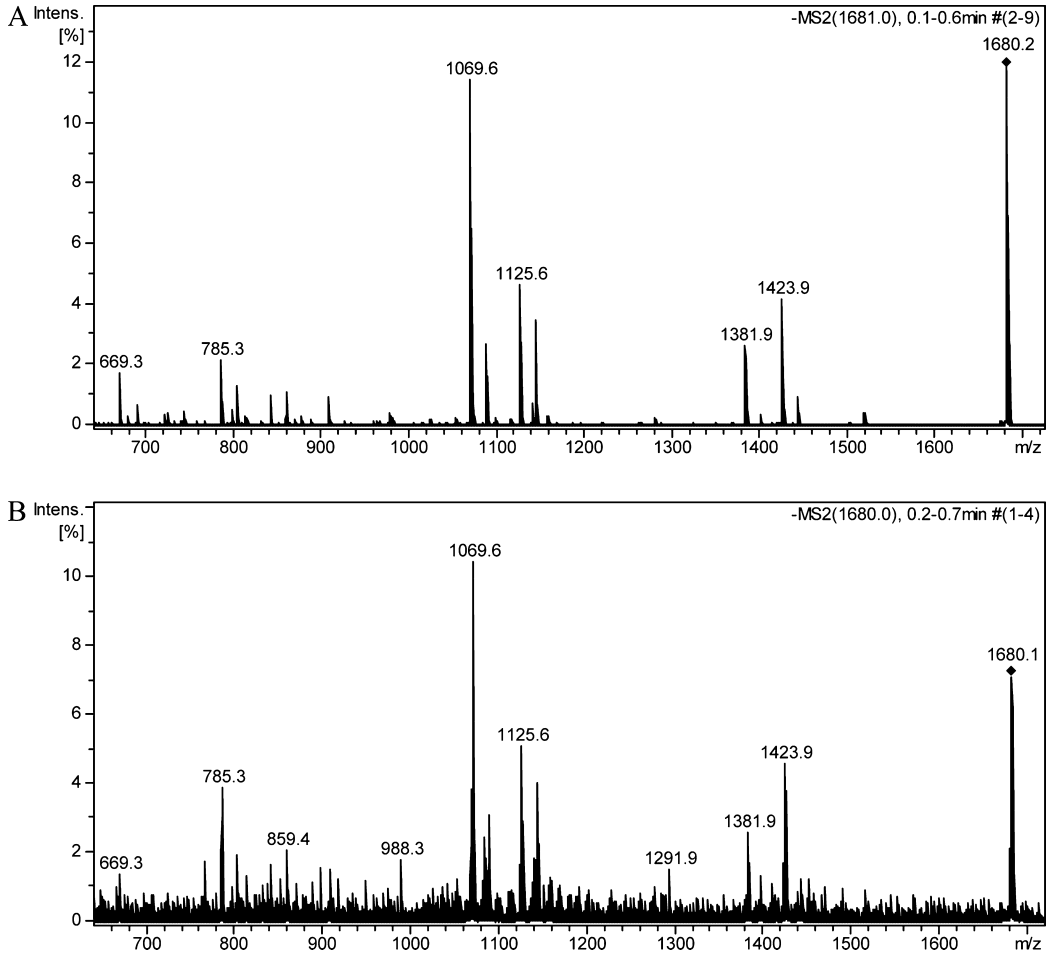

Figure 3. Negative-ion ESI-TOF MS^2 spectrum of synthetic Ac_2PIM_2 **3b** (A) and negative ion ESI-TOF MS^2 spectrum of the ion at m/z 1680.1 (B) from a lipid extract of *M. bovis* AN5.

palmitoylated mannosyl pyranose residue and the palmitic acid residue respectively (Figure S4, Supporting Information).

The MS^2 and pseudo-MS^3 spectra of Ac_2PIM_2, (16:0,18:0)-(19:0/16:0)-PIM_2 (**3b**) ($[M\text{-}H]^-$, m/z 1680.2), were compared to those reported by Hsu et al.[22] for the ion at m/z 1678.1 from the natural extract, the structure of which was proposed to be (16:0,18:1)(19:0/16:0)-PIM_2 (**3a**) (Figure S5, Supporting Information). The fragmentation pattern of the 16:0 and 19:0 fatty acids on the phosphatidyl moiety in the MS^2 spectrum of the $[M - H]^-$ molecular ion was consistent with those observed for PI **4**, PIM_2 **1**, and $AcPIM_2$ **2a**. The MS^2 spectrum displayed an ion at m/z 1069.6 arising from the loss of the diacylglycerol moiety, which was critical for the analysis of the fragmentation behavior of the *O*-6″ and *O*-3 fatty acids. The pseudo-MS^3 spectrum of the ion at m/z 1069.6 showed a more intense signal at m/z 813.4 arising from loss of the *O*-6″ palmitoyl fatty acid compared to the signal at m/z 785.3 attributed to the loss of the *O*-3 stearoyl fatty acid. Hsu et al. observed the same pattern of intensities for the loss of the palmitoyl and oleoyl fatty acids in the MS^3 spectrum for the analogous fragment ion at m/z 1067.7 (1678→1067) for **3a** from the natural extract (Figure S6, Supporting Information).

Further analysis of the pseudo-MS^3 spectrum of the ion at m/z 1069.6 of **3b** shows the fragment ion at m/z 907.5 attributed to the loss of the *O*-6 mannose moiety. Additional fragmentation of this ion results in the signals at m/z 651.3 and 669.3, due to the loss of the O-6″ 16:0 acyl residue as an acid and ketene, respectively, which are much more intense than those at m/z 623.3 and 641.3 from the analogous loss of the *O*-3 18:0 residue. Given that the structure of **3b** is defined by synthesis and the palmitoyl fatty acid is at *O*-6″ of mannose, this confirms the proposal of Hsu et al. that the fatty acid on the mannose moiety fragments more readily than that on the inositol. Furthermore, this also confirms the acylation pattern for natural Ac_2PIM_2 **3a**.

To enable direct comparison of the mass spectral data of **3b** with Ac_2PIM_2 from a mycobacterial source, we investigated a lipid extract of *M. bovis AN5*. The MS^2 spectrum of the m/z 1680.2 ion from the MS of **3b** was compared to that of the corresponding ion from the bacterial extract (Figure 3). The fragmentation pattern and relative intensities of the molecular ions matched, thereby confirming the specific acylation pattern of Ac_2PIM_2 from the natural extract.

■ CONCLUSIONS

In conclusion, we have reported the first syntheses of PI, PIM_2, and Ac_2PIM_2 along with $AcPIM_2$, all possessing the naturally predominant 19:0/16:0 acylation pattern on the phosphatidyl moiety. The synthesis of Ac_2PIM_2 **3b** was enabled by extending the utility of the DMPBn protecting group methodology pioneered by Seeberger. Complete characterization was achieved by a combination of NMR and MS with purity established by HPLC. Comprehensive mass spectral analyses show that the glyceryl *sn*-2 acyl group fragments more readily

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than that at the *sn*-1 position of the phosphatidyl group. For Ac_2PIM_2 **3b** pseudo-MS^3 analyses show that the *O*-6″ acyl group on the *O*-2 mannosyl residue fragments more readily than that at the *O*-3 position of inositol. This study confirms that mass spectrometry provides a powerful tool for definitively elucidating the acylation patterns of PIMs from natural mycobacterial extracts.

EXPERIMENTAL SECTION

^{1}H NMR spectra were obtained at 400 or 500 MHz and referenced to tetramethylsilane (TMS) (0.0 ppm) or the residual solvent peak (^{1}H $CHCl_3$ δ 7.26 ppm). ^{13}C NMR spectra were recorded at 75 or 125 MHz and referenced either to TMS (0.0 ppm) or internal solvent ($CDCl_3$ δ 77.0 ppm). ^{31}P NMR spectra were recorded at 202 MHz with H_3PO_4 (δ 0.0 ppm) as the external reference. Electrospray ionization (ESI) mass spectra were recorded on Q-TOF mass spectrometers. Anhydrous solvents were sourced commercially and used without further treatment unless stated. Powdered molecular sieves were flame-dried under vacuum immediately prior to use. Flash column chromatography was carried out using Davisil LC60 Å 40−63 μm silica gel unless otherwise stated. All flash chromatography solvents were AR-grade. Petroleum ether used was bp 60−80 °C range. All compounds were isolated after silica gel column chromatography and fractions collected were one spot by TLC. Thin-layer chromatography (TLC) plates were visualized under an UV lamp and/or with a spray consisting of 5% w/v dodecamolybdophosphoric acid in ethanol with subsequent heating. HPLC purity of target compounds: **4** (95.6%), **1** (95.1%), **2a** (99.0%), and **3b** (96.2%).

The HPLC analyses of **4** and **1** used system 1; HPLC: column: Phenomenex Synergi 4 μm Fusion-RP (80 Å, 3.0 × 250 mm). Detection: charged aerosol detector (filter = none). Flow rate: 0.5 mL/min. Column temperature: 40 °C. Solvents: A, H_2O; B, water containing 50 mM NH_4OAc adjusted to pH 5.0; C, methanol. Gradient program: 0−10 min 10−0% A, 10% B, 80−90%C, 10−28 min hold (0% A, 10% B, 90% C), 28−30 min return to starting conditions then equilibrate for 10 min prior to next injection. Chromatograms were corrected for detector nonlinearity. The HPLC analysis of **2a** used system 2; Phenomenex Synergi 4 μm Fusion-RP (80 Å, 4.6 × 250 mm). Detection: as for system 1. Flow rate: 0.8 mL/min. Column temperature: 40 °C. Solvents: A 1:1 water/MeOH + 50 mM NH_4OAc adjusted to pH 5.0 prior to dilution; B, MeOH; C, 2-propanol. Gradient program; 0−20 min 10% A, 60−50% B, 30−40% C; 20−21 min hold (10% A, 50% B, 40% C); 21−23 min return to starting conditions then equilibrate for 17 min prior to next injection. The HPLC analysis of compound **3b** used system 3; HPLC: column Phenomenex Jupiter C4 5 μm (300 Å, 4.6 × 250 mm); detection: as for system 1. Flow rate: 0.8 mL/min. Column temperature: 40 °C. Solvents: A, 75:15:10 $CHCl_3$/MeOH/H_2O containing 20 mM NH_4OAc and 1%AcOH; solvent B, 1:1 $CHCl_3$/MeOH containing 20 mM NH_4OAc and 1% AcOH. Gradient program: 0−15 min 100−30% A, 0−70% B, 15−20 min hold (30% A, 70% B), 20−25 min return to starting conditions and equilibrate for 10 min prior to next injection. Chromatograms for systems 2 and 3 were not corrected for detector nonlinearity.

Benzyl (1-*O*-((*R*)-10-Methyloctadecanoyl)-2-*O*-hexadecanoyl-*sn*-glycero)diisopropylphosphoramidite (5). 1*H*-Tetrazole was added to a solution of benzyloxybis(diisopropylamino)phosphine (0.620 g, 1.83 mmol) and diacylglycerol **7** (0.560 g, 0.917 mmol) in dry CH_2Cl_2 (10 mL) and 4 Å sieves under argon at rt. After 2 h, the reaction mixture was diluted with CH_2Cl_2, washed with saturated $NaHCO_3$, dried ($MgSO_4$), and filtered and the solvent removed in vacuo. The residue was purified by column chromatography on silica gel (Et_3N/EtOAc/petroleum ether = 3:15:80) to afford the *title compound* **5** (0.620 g, 80%) as a colorless oil: $[\alpha]_D^{22}$ +6.34 (*c* = 1.34, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$)) δ 0.84 (d, *J* = 6.5 Hz, 3H), 0.88 (t, *J* = 7.0 Hz, 6H), 1.05−1.38 (m, 63H), 1.57−1.64 (m, 4H), 2.27−2.31 (m, 4H), 3.59−3.82 (m, 4H), 4.15−4.20 (m, 1H), 4.32−4.37 (m, 1H), 4.63−4.76 (m, 2H), 5.17−5.21 (m, 1H), 7.31−7.35 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 19.8, 22.8, 24.6, 24.7, 24,8, 25.0, 27.2, 29.2, 29.4, 29.5, 29.57, 29.61, 29.8, 30.07, 30.12, 32.0, 32.9, 34.2, 34.4, 37.2, 43.1, 43.3, 61.6, 61.7, 61.9, 62.6, 65.4, 65.6, 70.1, 127.0, 127.4, 128.3, 173.1, 173.4; ^{31}P NMR (202 MHz, $CDCl_3$) δ 148.7, 148.9; HRMS-ESI $[M + H]^+$ calcd for $C_{51}H_{95}NO_6P$ 848.6897, found 848.6912.

Triethylammonium 1-*O*-((*R*)-10-Methyloctadecanoyl)-2-*O*-hexadecanoyl-*sn*-glycero-3-*H*-phosphonate (6).[34] Diacylglycerol **7** (0.21 g, 0.35 mmol) was dried by coevaporation with pyridine (3 × 5 mL) and then dissolved in dry THF/pyridine (10:1, 5.5 mL). This solution was added dropwise over a period of 30 min to a stirred solution of salicyl chlorophosphite **8** (0.088 g, 0.44 mmol) in dry THF (5 mL) under argon at rt. The reaction mixture was stirred for 3 h, after which time TLC analysis ($CHCl_3$/CH_3OH/H_2O = 100:15:1) showed complete conversion of the starting material into a product of lower R_f. The reaction mixture was quenched with 1 M aqueous triethylammonium bicarbonate (TEAB) buffer (20 mL), stirred for 15 min, and then extracted into $CHCl_3$ (3 × 30 mL). The combined organic layers were washed with TEAB buffer (3 × 20 mL) and dried ($MgSO_4$). After filtration, the solvent was removed in vacuo to give the title compound **6** (0.322 g, quant) as a colorless oil which was used without further purification: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.83 (d, *J* = 6.6 Hz, 3H), 0.88 (t, *J* = 6.9 Hz, 6H), 1.21−1.32 (m, 51H), 1.34 (t, *J* = 7.3 Hz, 9H), 1.56−1.63 (m, 4H), 2.27−2.32 (m, 4H), 3.10 (q, *J* = 7.3, Hz, 6H), 4.03 (dd, *J* = 5.3, 8.0 Hz, 2H), 4.18 (dd, *J* = 6.4, 11.9 Hz, 1H), 4.38 (dd, *J* = 3.7, 11.9 Hz, 1H), 5.21−5.25 (m, 1H), 6.88 (d, $^1J_{PH}$ = 628 Hz, 1H), 12.87 (brs, 1H); ^{31}P NMR (202 MHz, $CDCl_3$) δ 4.34 (d, $^1J_{PH}$ = 628 Hz); HRMS-ESI $[M + H]^+$ calcd for $C_{44}H_{91}NO_7P$ 776.6533, found 776.6543; HRMS-ESI $[M - Et_3HN]^-$ calcd for $C_{38}H_{74}O_7P$ 673.5172, found 673.5181.

1-*O*-(1-*O*-((*R*)-10-Methyloctadecanoyl)-2-*O*-hexadecanoyl-*sn*-glycero-3-phosphoryl)-D-*myo*-inositol (4). Alcohol **9** (0.030 g, 0.047 mmol) and *H*-phosphonate **6**[34] (0.055 g, 0.071 mmol) were coevaporated from dry pyridine (3 × 5 mL) then placed under high vacuum for 30 min. The reagents were dissolved in dry distilled pyridine (5 mL), pivaloyl chloride (0.033 mL, 0.238 mmol) was added, and the reaction mixture was stirred for 2 h at rt. Iodine (0.036 g, 0.143 mmol) in pyridine/H_2O (9:1, 5 mL) was added, and the mixture was stirred for 1 h before being diluted with $CHCl_3$ (20 mL) and washed with 10% aq $Na_2S_2O_3$ (20 mL). The aqueous phase was re-extracted with $CHCl_3$ (2 × 20 mL) then EtOAc (20 mL), the combined organic layers were dried ($MgSO_4$) and filtered, and the solvent was removed in vacuo. The residue was dissolved in CH_2Cl_2/MeOH (1:1, 10 mL), treated with Amberlite IRC86 resin (H^+ form), and filtered, solvent was removed, and the residue was semipurified by column chromatography on silica gel ($CHCl_3$/MeOH = 1:0 to 9:1). $Pd(OH)_2$/C (20%, 34 mg, 0.048 mmol) was added to the residue in THF/MeOH (2:3, 10 mL), and the reaction mixture was stirred under an atmosphere of H_2. After 4 h, the reaction was filtered through Celite and the solvent removed in vacuo. The residue was purified by column chromatography on silica gel ($CHCl_3$/MeOH/H_2O = 70:40:0 to 70:40:6) to afford the *title compound* **4** (0.035 g, 86%, 95.6% pure by HPLC) as a white solid: ^{1}H NMR (500 MHz, $CDCl_3$/CD_3OD/D_2O = 70:40:6) δ 0.85 (d, *J* = 6.5 Hz, 3H), 0.88 (t, *J* = 7.0 Hz, 6H), 1.06−1.40 (m, 51H), 1.57−1.64 (m, 4H), 2.30−2.36 (m, 4H), 3.26 (t, *J* = 9.5 Hz, 1H), 3.45 (dd, *J* = 3.0, 9.5 Hz, 1H), 3.64 (dd, *J* = 9.5, 9.5 Hz, 1H), 3.76 (t, *J* = 9.5 Hz, 1H), 3.87−3.93 (m, 1H), 4.00−4.09 (m, 2H), 4.18−4.21 (m, 2H), 4.43 (dd, *J* = 2.8, 12.2 Hz, 1H), 5.24−28 (m 1H); ^{13}C NMR (125 MHz, $CDCl_3$/CD_3OD/D_2O = 70:40:6) δ 13.8, 19.5, 22.5, 24.78, 24.84, 27.0, 29.0, 29.1, 29.2, 29.5, 29.6, 29.9, 31.8, 32.7, 34.0, 34.2, 37.0, 62.9, 63.7, 70.5, 70.6, 71.1, 71.6, 71.6, 72.4, 74.4, 76.5, 174.0, 174.3; ^{31}P NMR (202 MHz, $CDCl_3$/CD_3OD/D_2O = 70:40:6) δ 0.4; HRMS-ESI $[M - H]^-$ calcd for $C_{44}H_{84}O_{13}P$ 851.5650, found 851.5649.

1-*O*-Allyl-2-*O*-(2-*O*-methoxyacetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-3,4,5-tri-*O*-benzyl-D-*myo*-inositol (12). TMSOTf (5 μL, 0.028 mmol) was added to a mixture of alcohol **10**[9,28] (0.230 g, 0.227 mmol) and trichloroacetimidate **11**[13] (0.270 g, 0.405 mmol) in dry toluene at 0 °C. After 45 min, the reaction was quenched with Et_3N and filtered through Celite and the solvent removed in vacuo. The

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residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:9 to 2:3) to afford the *title compound* **12** (0.30 g, 85%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.18 (dd, J = 2.0, 9.5 Hz, 1H), 3.26−3.40 (m, 5H), 3.42 (s, 3H), 3.53 (dd, J = 3.0, 10.5 Hz, 1H), 3.80−4.21 (m, 14H), 4.21−4.30 (m, 2H), 4.43 (d, J = 10.5 Hz, 1H), 4.47 (d, J = 11.0 Hz, 1H), 4.57−4.94 (m, 18H), 5.11 (d, J = 10.5 Hz, 1H), 5.16 (s, 1H), 5.23 (d, J = 17.5 Hz, 1H), 5.76 (dddd, J = 5.0, 5.0, 10.5, 17.5 Hz, 1H), 7.11−7.43 (m, 50H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 59.3, 68.4, 68.5, 69.0, 70.8, 71.4, 71.8, 72.0, 72.1, 72.5, 73.2, 73.4, 74.0, 74.7, 74.9, 75.0, 75.3, 75.7, 75.9, 76.7, 77.3, 77.4, 78.7, 80.0, 80.9, 81.3, 81.5, 98.8 ($^1J_{C-H}$ = 171 Hz), 99.0 ($^1J_{C-H}$ = 172 Hz), 117.4, 127.17, 127.20, 127.24, 127.35, 127.37, 127.51, 127.53, 127.54, 127.56, 127.58, 127.7, 127.8, 127.89, 127.90, 127.95, 127.99, 128.1, 128.16, 128.17, 128.23, 128.24, 128.34, 128.37, 128.44, 128.52, 133.9, 137.9, 138.0, 138.1, 138.4, 138.58, 138.61, 138.7, 138.9, 139.1, 169.3; HRMS-ESI [M + Na]$^+$ calcd for $C_{94}H_{100}NaO_{18}$ 1539.6802, found 1539.6793.

2-*O*-(2-*O*-Methoxyacetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-3,4,5-tri-*O*-benzyl-D-*myo*-inositol (13). (1,5-Cyclooctadiene)bis(methyldiphenylphosphine)iridium(I) hexafluorophosphate (0.030 g, 0.040 mmol) was added to a stirred solution of **12** (0.300 g, 0.200 mmol) in dry THF at rt under an atmosphere of argon. The argon atmosphere was replaced with H_2 for ca. 1 min, followed by a gentle stream of argon being passed over the reaction. After 2 h, the solvent was removed in vacuo and the residue dissolved in acetone/H_2O (9:1, 40 mL). To the solution were added mercury(II) chloride (0.117 g, 0.403 mmol) and mercury(II) oxide (0.111 g, 0.508 mmol), and the reaction was stirred under reflux for 90 min. Once cooled to rt, the suspension was filtered through Celite and the solvent removed in vacuo. The residue was dissolved in CH_2Cl_2 (50 mL), washed with 10% aq KI (50 mL), dried ($MgSO_4$), and filtered and the solvent evaporated. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:4 to 1:1) to afford the *title compound* **13** (0.25 g, 85%) as a white foam: ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.30−3.43 (m, 4H), 3.48 (s, 3H), 3.48−3.51 (m, 1H), 3.56−3.64 (m, 3H), 3.79 (brs, 1H), 3.83−4.03 (m, 6H), 4.11−4.23 (m, 5H), 4.35 (d, J = 12.0 Hz, 1H), 4.39 (d, J = 12.0 Hz, 1H), 4.47−4.50 (m, 3H), 4.55−4.92 (m, 15H), 5.32 (d, J = 1.5 Hz, 1H), 5.38 (brs, 1H), 5.60 (brs, 1H), 7.17−7.40 (m, 50H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 59.4, 68.6, 69.2, 69.4, 69.7, 71.4, 71.6, 72.0, 72.20, 72.22, 72.23, 72.6, 73.4, 73.5, 74.2, 74.6, 75.0, 75.1, 75.2, 75.4, 75.7, 76.1, 77.4, 77.7, 78.6, 79.5, 80.1, 80.6, 81.3, 96.1, 99.3, 127.46, 127.56, 127.59, 127.60, 127.65, 127.67, 127.69, 127.72, 127.79, 127.84, 128.04, 128.07, 128.09, 128.34, 128.35, 128.37, 128.45, 128.49, 128.53, 128.54, 138.0, 138.1, 138.25, 138.34, 138.5, 138.6, 138.69, 138.73, 169.7; HRMS-ESI [M + Na]$^+$ calcd for $C_{91}H_{96}NaO_{18}$ 1499.6489, found 1499.6437.

6-*O*-α-D-Mannopyranosyl-2-*O*-(2-*O*-methoxyacetyl-α-D-mannopyranosyl)-1-*O*-(1-*O*-((*R*)-10-methyloctadecanoyl)-2-*O*-hexadecanoyl-*sn*-glycero-3-phosphoryl)-D-*myo*-inositol (14). Alcohol **13** (0.047 g, 0.032 mmol) and *H*-phosphonate **6**[34] (0.065 g, 0.082 mmol) were coevaporated from dry pyridine (3 × 5 mL) and then placed under high vacuum for 30 min. The reagents were dissolved in dry pyridine (5 mL) before the addition of pivaloyl chloride (0.035 mL, 0.254 mmol) and stirred for 2 h at rt. Iodine (0.040 g, 0.159 mmol) in pyridine/H_2O (9:1, 5 mL) was added and the reaction mixture stirred for 1 h before being diluted with $CHCl_3$ (20 mL) and washed with 10% aq $Na_2S_2O_3$ (20 mL). The aqueous phase was re-extracted with $CHCl_3$ (2 × 20 mL) and then EtOAc (20 mL), the combined organic layers were dried ($MgSO_4$) and filtered, and the solvent was removed in vacuo. The residue was dissolved in CH_2Cl_2/MeOH (1:1, 10 mL), treated with Amberlite IRC86 resin (H^+ form) and filtered, and solvent removed in vacuo, and the residue was semipurified by column chromatography on silica gel ($CHCl_3$/MeOH = 1:0 to 9:1). $Pd(OH)_2$/C (20%, 34 mg, 0.048 mmol) was added to the residue dissolved in THF/MeOH (2:3, 10 mL), and the reaction mixture was stirred under an atmosphere of H_2. After 4 h, the reaction was filtered through Celite and the solvent removed in vacuo. The residue was purified by column chromatography on silica gel ($CHCl_3$/MeOH/H_2O = 70:40:0 to 70:40:6) to afford the *title compound* **14** (0.032 g, 81%) as a white solid: ^{1}H NMR (500 MHz, $CDCl_3$/CD_3OD/D_2O = 70:40:6) δ 0.81 (d, J = 6.5 Hz, 3H), 0.86 (t, J = 6.5 Hz, 6H), 1.05−1.33 (m, 51H), 1.55−1.58 (m, 4H), 2.28 (t, J = 7.5 Hz, 2H), 2.33 (t, J = 7.5 Hz, 2H), 3.29−2.35 (m, 1H), 3.41 (s, 3H), 3.46 (brd, J = 11 Hz, 1H), 3.55−3.69 (m, 4H), 3.73−3.84 (m, 5H), 3.94−4.23 (m, 11H), 5.10 (s, 1H), 5.15 (s, 1H), 5.20−5.23 (m, 1H), 5.25 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$/CD_3OD/D_2O = 70:40:6) δ 14.4, 20.1, 23.2, 25.4, 25.5, 27.57, 27.61, 29.65, 29.72, 29.3, 29.85, 29.89, 29.94, 30.07, 30.12, 30.15, 30.16, 30.20, 30.23, 30.51, 30.54, 32.4, 33.3, 34.6, 34.7, 37.60, 37.63, 59.5, 61.6, 62.2, 63.5, 64.1, 67.4, 68.0, 69.5, 69.8, 70.7, 71.0, 71.1, 73.27, 73.34, 73.5, 73.8, 73.9, 77.1, 78.9, 79.1, 98.6, 102.1, 171.3, 174.6, 174.9; ^{31}P NMR (202 MHz, $CDCl_3$/CD_3OD/D_2O = 70:40:6) δ 3.21; HRMS-ESI [M − H]$^-$ calcd for $C_{59}H_{108}O_{25}P$ 1247.6923, found 1247.6884.

Sodium 2,6-Di-*O*-α-D-mannopyranosyl-1-*O*-(1-*O*-((*R*)-10-methyloctadecanoyl)-2-*O*-hexadecanoyl-*sn*-glycero-3-phosphoryl)-D-*myo*-inositol (1). A freshly prepared solution of sodium methoxide in MeOH (0.5 M, 0.02 mL) was added dropwise to a stirred solution of **14** (0.015 g, 0.012 mmol) in CH_2Cl_2/MeOH (1:7, 4 mL). After 10 min, the reaction mixture was quenched by the addition of IRC-86 resin (H^+ form) and filtered. The resulting solution was treated with IRC-86 resin (Na^+ form) and filtered and the solvent removed in vacuo. The residue was purified by column chromatography on silica gel ($CHCl_3$/MeOH/H_2O = 70:40:6) to afford the *title compound* **1** (11 mg, 78%, 95.1% pure by HPLC) as a white solid: ^{1}H NMR (500 MHz, $CDCl_3$:CD_3OD:D_2O = 70:40:6) δ 0.75 (d, J = 6.5 Hz, 3H), 0.79 (t, J = 6.5 Hz, 6H), 1.05−1.35 (m, 51H), 1.53−1.58 (m, 4H), 2.23 (t, J = 7.5 Hz, 2H), 2.28 (t, J = 7.5 Hz, 2H), 3.19 (t, J = 9.5 Hz, 1H), 3.33−3.39 (m, 1H), 3.49−3.73 (m, 10H), 3.85−3.96 (m, 7H), 4.09−4.13 (m, 1H), 4.20 (brs, 1H), 4.33 (brs, 1H), 5.00 (s, 1H), 5.02 (s, 1H), 5.17−5.19 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$/CD_3OD/D_2O = 70:40:6) δ 14.5, 20.2, 23.2, 25.5, 25.6, 27.66, 27.70, 29.7, 29.8, 29.9, 29.98, 30.04, 30.2, 30.25, 30.32, 30.60, 30.63, 32.5, 33.4, 34.7, 34.8, 37.69, 37.72, 61.9, 62.1, 63.5, 64.3, 67.7, 70.8, 71.0, 71.1, 71.2, 71.3, 73.4, 73.6, 74.0, 79.1, 79.2, 102.2, 174.8, 175.1; ^{31}P NMR (202 MHz, $CDCl_3$/CD_3OD/D_2O = 70:40:6) δ 3.09; HRMS-ESI [M − H]$^-$ calcd for $C_{56}H_{104}O_{23}P$ 1175.6711, found 1175.6676.

1-*O*-Allyl-2-*O*-(2-*O*-benzoyl-3,4-di-*O*-benzyl-6-*O*-triisopropylsilyl-α-D-mannopyranosyl)-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-3,4,5-tri-*O*-benzyl-D-*myo*-inositol (16). TBSOTf (95 μL, 0.413 mmol) was added to a mixture of alcohol **10**[9,28] (0.384 g, 0.379 mmol) and dibutylphosphate **15**[5] (0.280 g, 0.344 mmol) in dry toluene at 0 °C. After 45 min, the reaction was quenched with Et_3N, filtered through Celite and the solvent removed *in vacuo*. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether =1:9 to 1:4) to afford a mixture of the triisopropyl and *tert*-butyldimethyl silylated pseudotrisaccharides (approximately 2:1 by ^{1}H NMR) **16** (0.49 g) as a colorless oil. From the mixture a sample containing mostly the triisopropylsilyl protected material was obtained for NMR and HRMS analysis: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.05−1.08 (m, 18H), 3.22 (dd, J = 2.0, 10.0 Hz, 1H), 3.32−3.38 (m, 3H), 3.48 (dd, J = 3.0, 11.5 Hz, 1H), 3.67 (d, J = 10.5 Hz, 1H), 3.87−4.07 (m, 8H), 4.11−4.17 (m, 3H), 4.20−4.30 (m, 3H), 4.37 (s, 1H), 4.55 (d, J = 11.0 Hz, 1H), 4.65−4.78 (m, 10H), 4.82−4.85 (m, 2H), 4.89−4.98 (m, 6H), 5.08 (d, J = 13.0 Hz, 1H), 5.24 (d, J = 17.0 Hz, 1H), 5.26 (s, 1H), 5.60 (s, 1H), 5.76 (s, 1H), 5.74−5.81 (m, 1H), 7.16−7.49 (m, 47H), 7.59 (t, J = 6.5, 6.5 Hz, 1H), 8.15 (d, J = 8.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.2, 18.2, 25.8, 26.2, 62.4, 68.8, 69.4, 70.9, 71.1, 71.8, 72.2, 72.4, 72.6, 72.8, 73.4, 74.1, 74.9, 75.0, 75.3, 75.4, 75.9, 76.0, 77.9, 79.2, 80.2, 81.2, 81.7, 81.9, 99.0, 99.1, 117.7, 127.2−128.5, 130.2, 130.5, 133.0, 134.1, 138.2, 138.3, 138.4, 138.6, 138.9, 139.0, 139.1, 139.2, 139.3, 165.4; HRMS-ESI [M + Na]$^+$ calcd for $C_{100}H_{114}NaO_{17}Si$ 1637.7723, found 1637.7739.

6-*O*-(2,3,4,6-Tetra-*O*-benzyl-α-D-mannopyranosyl)-2-*O*-(2,3,4-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4,5-tri-*O*-benzyl-D-*myo*-inositol (17). Sodium methoxide in MeOH (6 mL, 30% solution) was added dropwise to a stirred solution of **16** (0.550 g) in CH_2Cl_2/MeOH (1:2, 6 mL). After 18 h, the reaction mixture was

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diluted with saturated NH_4Cl (30 mL), the aqueous phase extracted with $CHCl_3$ (2 × 30 mL), dried ($MgSO_4$), and filtered, and the solvent removed in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:9 to 3:7) to afford the corresponding mixture of TIPS and TBS ether protected alcohols (0.455 g) as a colorless oil. NaH (60% dispersion in oil, 38 mg, 0.942 mmol) was added to a stirred solution of the residue (0.475 g) and benzyl bromide (131 μL, 1.10 mmol) in dry DMF (10 mL) at 0 °C and the resulting suspension allowed to slowly warm to rt over 18 h. The reaction mixture was partioned between Et_2O and H_2O (1:1, 50 mL) and the aqueous phase extracted into Et_2O (2 × 25 mL). The combined organic layers were washed with saturated NaCl (100 mL), dried ($MgSO_4$), and filtered and the solvent removed in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:9 to 3:7) to afford the corresponding mixture of TIPS and TBS ether protected intermediate (0.470 g) as a colorless oil. (1,5-Cyclooctadiene)bis(methyldiphenylphosphine)iridium(I) hexafluorophosphate (58 mg, 0.069 mmol) was added to a stirred solution of the residue (0.550 g) in dry THF at rt under an argon atmosphere. The argon was replaced with H_2 for ca. 2 min followed by a gentle stream of argon being passed over the reaction. After 2 h, the solvent was removed in vacuo, and the residue was dissolved in MeOH/CH_2Cl_2 (1:4, 20 mL). Acetyl chloride (250 μL) was added, and the reaction was stirred for 18 h. Solid $NaHCO_3$ was added to quench the reaction, and then the resulting mixture partitioned between $CHCl_3$ and H_2O (1:1, 50 mL). The aqueous layer was extracted with $CHCl_3$ (2 × 30 mL), the combined organic fractions were dried ($MgSO_4$) and filtered, and the solvent was removed in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:9 to 1:1) to afford the *title compound* **17** (0.45 g, 93%) as a white solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.69 (brs, 1H), 3.24−3.29 (m, 2H), 3.40 (brs, 1H), 3.44−3.48 (m, 1H), 3.55−3.61 (m, 4H), 3.76−3.99 (m, 9H), 4.07−4.13 (m, 2H), 4.36−4.41 (m, 2H), 4.46−4.67 (m, 12H), 4.69−4.76 (m, 3H), 4.81−4.89 (m, 3H), 5.26 (s, 1H), 5.28 (s, 1H), 7.15−7.37 (m, 50H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 62.3, 69.6, 71.4, 72.0, 72.1, 72.3, 72.6, 73.4, 74.6, 74.86, 74.91, 75.1, 75.2, 75.3, 75.6, 76.6, 78.5, 79.4, 80.0, 80.3, 81.2, 95.7 ($^1J_{C,H}$ = 168.5 Hz), 99.8 ($^1J_{C,H}$ = 173.2 Hz), 127.47, 127.53, 127.6, 127.7, 127.8, 127.9, 128.0, 128.1, 128.2, 128.27, 128.31, 128.35, 128.39, 128.43, 128.45; HRMS-ESI $[M + Na]^+$ calcd for $C_{88}H_{92}NaO_{16}$ 1427.6283, found 1427.6290.

6-*O*-(2,3,4,6-Tetra-*O*-benzyl-α-D-mannopyranosyl)-2-*O*-(2,3,4-tri-*O*-benzyl-6-*O*-hexadecanoyl-α-D-mannopyranosyl)-3,4,5-tri-*O*-benzyl-D-*myo*-inositol (18).[34] Palmitoyl chloride (13 μL, 0.043 mmol) was added to a stirred solution of diol **17** (0.050 g, 0.036 mmol) in dry pyridine/CH_2Cl_2 (4:1, 2.5 mL) and 4 Å sieves. The reaction was stirred at 30 °C for 2 h, diluted with CH_2Cl_2 (30 mL), washed with 0.5 M HCl (20 mL), dried ($MgSO_4$), and filtered and the solvent removed in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:4 to 1:3) to afford the title compound **18** (0.050 g, 85%) as a colorless oil. ^{1}H and ^{13}C NMR (500 MHz, $CDCl_3$) data were consistent to those in the literature.[34]

1-*O*-(1-*O*-((*R*)-10-Methyloctadecanoyl)-2-*O*-hexadecanoyl-*sn*-glycero-3-benzylphosphoryl)-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-2-*O*-(2,3,4-tri-*O*-benzyl-6-*O*-hexadecanoyl-α-D-mannopyranosyl)-3,4,5-tri-*O*-benzyl-D-*myo*-inositol (19). Alcohol **18** (0.07 g, 0.043 mmol) and phosphoramidite **5** (0.150 g, 0.177 mmol) were coevaporated from dry acetonitrile (2 × 30 mL) and then placed under high vacuum for 30 min. The reagents were dissolved in dry acetonitrile (15 mL) before the addition of 1*H*-tetrazole (13 mg, 0.192 mmol) at 0 °C and stirred for 2 h at rt. Dry CH_2Cl_2 (10 mL) was added, the solution was cooled to −30 °C, and a dried ($MgSO_4$) solution of *m*-CPBA (~50%, 0.066 g, 0.192 mmol) in CH_2Cl_2 (3 mL) was added to the reaction. After being warmed to rt over 1 h, the reaction was diluted with Et_2O/H_2O (1:1, 60 mL) and washed with saturated $NaHCO_3$ (30 mL) and then 10% aq Na_2SO_3 (30 mL). The combined aqueous phases were re-extracted with Et_2O (2 × 30 mL), the combined organic layers were dried ($MgSO_4$) and filtered, and the solvent was removed in vacuo. The crude residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:4 to 2:3) followed by further purification on silica gel (EtOAc/$CHCl_3$ = 0:1 to 3:97) to afford the *title compound* **19** (0.090 g, 88%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.83 (d, J = 6.5 Hz, 6H), 0.88 (t, J = 7 Hz, 18H), 1.03−1.39 (m, 150H), 1.45−1.59 (m, 12H), 2.12−2.22 (m, 12H), 3.24−3.33 (m, 5H), 3.36−3.40 (m, 3H), 3.76−3.81 (m, 2H), 3.88−4.20 (m, 35H), 4.43−4.45 (m, 10H), 4.57−4.67 (m, 15H), 4.72−4.84 (m, 8H), 4.88−4.91 (m, 6H), 4.94−5.07 (m, 5H), 5.11−5.15 (m, 1H), 5.27 (d, J = 1.5 Hz, 1H), 5.32 (d, J = 1.5 Hz, 1H), 5.48 (d, J = 1.5 Hz, 1H), 5.49 (d, J = 1.5 Hz, 1H), 7.01−7.37 (m, 110H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.1, 19.7, 22.7, 24.8, 27.1, 29.16, 29.23, 29.3, 29.4, 29.5, 29.6, 29.7, 30.1, 31.9, 32.8, 33.88, 33.93, 34.0, 34.2, 37.1, 61.4, 61.5, 66.1, 68.7, 69.4, 70.1, 70.2, 70.5, 71.6, 71.7, 71.8, 72.0, 72.3, 72.5, 73.1, 74.0, 74.3, 74.5, 74.7, 74.8, 74.9, 75.1, 75.6, 75.7, 76.2, 78.1, 78.3, 78.8, 80.0, 80.4, 80.9, 81.0, 98.5, 98.6, 99.3, 127.0, 127.2, 127.4, 127.5, 127.7, 127.8, 127.9, 128.0, 128.11, 128.14,128.2, 128.3, 128.4, 128.5, 128.8, 128.87, 128.92, 129.0, 135.1, 137.5, 137.65, 137.74, 138.16, 138.22, 128.3, 138.5, 138.7, 138.9, 139.0, 139.1, 172.5, 172.7, 173.0, 173.5; ^{31}P NMR (202 MHz, $CDCl_3$) δ −0.16, −0.29; HRMS-ESI $[M + Na]^+$ calcd for $C_{149}H_{201}NaO_{24}P$ 2428.4143, found 2428.4148.

6-*O*-α-D-Mannopyranosyl-1-*O*-(1-*O*-((*R*)-10-methyloctadecanoyl)-2-*O*-hexadecanoyl-*sn*-glycero-3-phosphoryl)-2-*O*-(6-*O*-hexadecanoyl-α-D-mannopyranosyl)-D-*myo*-inositol (2a).[34] Pd(OH)$_2$/C (20%, 37 mg, 0.053 mmol) was added to a solution of **19** (0.085 g, 0.035 mmol) in THF/MeOH (2:3, 10 mL). The reaction mixture was stirred under an atmosphere of H_2 for 4 h at rt and then filtered through Celite and the solvent removed in vacuo. The residue was purified by column chromatography on silica gel ($CHCl_3$/MeOH/H_2O = 70:40:1 to 70:40:6) to afford the title compound **2a** (0.045 g, 90%, 98% pure by HPLC) as a white solid: $[\alpha]_D^{22}$ +39.0 (c = 0.12, $CHCl_3$/MeOH/H_2O = 70:40:6); ^{1}H NMR (500 MHz, $CDCl_3$/CD_3OD/D_2O = 70:40:6) δ 0.85 (d, J = 6.5 Hz, 3H), 0.89 (t, J = 7.0 Hz, 9H) 1.07−1.43 (m, 75H), 1.56−1.64 (m, 6H), 2.30−2.39 (m, 6H), 3.29 (t, J = 9.0 Hz, 1H), 3.46 (dd, J = 2.5, 10.5 Hz, 1H), 3.57−3.69 (m, 3H), 3.73−3.83 (m, 5H), 3.96−4.45 (m, 12H), 5.09 (s, 1H), 5.12 (s, 1H), 5.24−5.29 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$/CD_3OD/D_2O = 70:40:6) δ 13.8, 19.5, 22.6, 24.7, 24.8, 24.9, 26.98, 27.03, 29.1, 29.2, 29.3, 29.4, 29.6, 29.9, 31.8, 32.7, 33.9, 34.0, 34.1, 37.0, 61.1, 62.9, 63.4, 63.6, 66.9, 67.1, 70.0, 70.1, 70.3, 70.5, 70.6, 70.7, 72.8, 73.0, 73.3, 76.8, 78.5, 78.7, 101.5, 101.6, 173.9, 174.2, 175.0; ^{31}P NMR (202 MHz, $CDCl_3$/CD_3OD/D_2O = 70:40:6) δ −0.5; HRMS-ESI $[M - H]^-$ calcd for $C_{72}H_{134}O_{24}P$ 1413.9003, found 1413.9014.

(±)-3-*O*-(4-Bromobenzyl)-1,2:4,5-di-*O*-isopropylidene-*myo*-inositol (21). To a solution of diol **20** (2.01 g, 7.71 mmol) in dry THF (100 mL) were added NaH (60% dispersion in oil, 0.383 g, 15.97 mmol) and 4-bromobenzyl bromide (2.15 g, 8.60 mmol), and the mixture was refluxed overnight under an atmosphere of nitrogen. The mixture was quenched with H_2O, extracted into EtOAc (3 × 100 mL), and washed with H_2O (150 mL) and saturated NaCl (150 mL). The organic extract was dried ($MgSO_4$) and filtered and the solvent removed in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:2 to 1:1) to give the *title compound* **21** (2.14 g, 65%, R_f = 0.39, EtOAc/petroleum ether 1:1) and (±)-3,6-di-*O*-(4-bromobenzyl)-1,2:4,5-di-*O*-isopropylidene-*myo*-inositol (0.709 g, 15%, R_f = 0.88, EtOAc/petroleum ether 1:1), both as white solids. Data for **21**: mp 139−142 °C (EtOAc/PE); ν_{max} (ATR-IR) 3474, 2982, 2936, 2884, 1487, 1466, 1403, 1382, 1374, 1344, 1237, 1217, 1161, 1137, 1112, 1083, 1062, 1046 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.35 (s, 3H), 1.45 (s, 3H), 1.48 (s, 3H), 1.55 (s, 3H), 2.40 (d, J = 2.9 Hz, 1H), 3.26 (dd, J = 9.4, 10.6 Hz, 1H), 3.77 (dd, J = 4.3, 10.1 Hz, 1H), 3.89 (dd, J = 6.7, 10.6 Hz, 1H), 3.96 (dd, J = 4.9, 6.6 Hz, 1H), 4.03 (t, J = 9.7 Hz, 1H), 4.34 (t, J = 4.5 Hz, 1H), 4.75 (d, J = 12.6 Hz, 1H), 4.83 (d, J = 12.6 Hz, 1H), 7.28−7.31 (m, 2H), 7.46−7.49 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 26.0, 27.01, 27.03, 28.3, 71.2, 74.5, 74.7, 76.6, 77.3, 78.4, 81.7, 110.4, 112.6, 121.9, 130.0, 131.6, 136.9; HRMS-ESI $[M + Na]^+$ calcd for $C_{19}H_{25}{}^{79}BrNaO_6$ 451.0727, found 451.0705.

Data for (±)-3,6-di-*O*-(4-bromobenzyl)-1,2:4,5-di-*O*-isopropylidene-*myo*-inositol: mp 146−147 °C (EtOAc/PE); ν_{max} (ATR-IR)

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2985, 2931, 2896, 2880, 1487, 1463, 1402, 1368, 1352, 1339, 1240, 1217, 1159, 1132, 1089, 1067, 1053 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.34 (s, 3H), 1.41 (s, 3H), 1.45 (s, 3H), 1.47 (s, 3H), 3.33 (dd, J = 9.4, 10.5 Hz, 1H), 3.63 (dd, J = 6.5, 10.6 Hz, 1H), 3.73 (dd, J = 4.2, 10.1 Hz, 1H), 3.99 (t, J = 9.8 Hz, 1H), 4.06 (dd, J = 5.1, 6.4 Hz, 1H), 4.33 (t, J = 4.6 Hz, 1H), 4.74 (d, J = 13.8 Hz, 3H), 4.82 (d, J = 12.7 Hz, 1H), 7.25−7.30 (m, 4H), 7.43−7.49 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 26.0, 27.08, 27.12, 28.0, 71.15, 71.29, 74.6, 76.7, 77.1, 78.8, 80.2, 81.1, 110.1, 112.3, 121.4, 121.9, 129.56, 129.99, 131.36, 131.58, 137.0, 137.4; HRMS-ESI $[M + Na]^+$ calcd for $C_{26}H_{30}{}^{79}Br_2NaO_6$ 619.0301, found 619.0293.

3-*O*-(4-Bromobenzyl)-6-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-1,2:4,5-di-*O*-isopropylidene-D-*myo*-inositol (23) and 3-*O*-(4-Bromobenzyl)-6-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-1,2:4,5-di-*O*-isopropylidene-L-*myo*-inositol (24). TMSOTf (119 μL, 0.658 mmol) was added to a mixture of alcohol **21** (2.83 g, 6.58 mmol), trichloroacetimidate **22** (5.03 g, 7.90 mmol), and 4 Å molecular sieves in dry CH_2Cl_2 (20 mL) at −30 °C. After being stirred for 30 min, the reaction was quenched with Et_3N, filtered through Celite, and evaporated to dryness. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:9 to 1:2) to give a mixture of diastereoisomers 6-*O*-(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3-*O*-(4-bromobenzyl)-1,2:4,5-di-*O*-isopropylidene-D-*myo*-inositol and 6-*O*-(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3-*O*-(4-bromobenzyl)-1,2:4,5-di-*O*-isopropylidene-L-*myo*-inositol (5.81 g). Sodium methoxide (prepared from reacting Na (0.192 g, 8.36 mmol) with MeOH (10 mL)) was added dropwise to a stirred solution of the diastereoisomers (5.81 g, 6.43 mmol) in MeOH (25 mL) until the pH of the solution remained greater than 11. The reaction mixture was stirred overnight then extracted into EtOAc (3 × 100 mL), and the combined organic extracts were washed with H_2O (100 mL). The solution was dried ($MgSO_4$) and filtered, and the solvent was removed in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:9 to 1:2) to give the *title compounds* **23** (2.39 g, 42%, two steps, R_f = 0.31, EtOAc/petroleum ether 2:3) and **24** (2.32 g, 41%, two steps, R_f = 0.52, EtOAc/petroleum ether 2:3) both as white foams. Data for **23**: $[\alpha]_D^{29}$ +2.9 (c = 1.06, $CHCl_3$); ν_{max} (ATR-IR) 3495, 3063, 3029, 2986, 2932, 1488, 1454, 1373, 1219, 1156, 1116, 1086, 1067, 1045 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.33 (s, 3H), 1.38 (s, 6H), 1.56 (s, 3H), 2.49 (brs, 1H), 3.20 (dd, J = 9.4, 10.7 Hz, 1H), 3.66 (dd, J = 1.9, 10.8 Hz, 1H), 3.70 (dd, J = 4.2, 10.2 Hz, 1H), 3.80 (dd, J = 3.7, 10.8 Hz, 1H), 3.88 (dd, J = 3.3, 9.3 Hz, 1H), 3.92−4.06 (m, 5H), 4.11 (dd, J = 1.4, 3.0 Hz, 1H), 4.28 (t, J = 4.5 Hz, 1H), 4.51 (d, J = 12.2 Hz, 1H), 4.54 (d, J = 10.6 Hz, 1H), 4.67−4.75 (m, 4H), 4.81, 4.82 (2 × overlapping d, J = 12.7, 10.7 Hz, 2H), 5.33 (d, J = 1.4 Hz, 1H), 7.18−7.20 (m, 2H), 7.25−7.37 (m, 15H), 7.46−7.49 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 26.1, 26.98, 27.16, 28.2, 68.6, 70.7, 71.1, 72.0, 73.4, 74.5, 75.4, 76.6, 76.9, 77.4, 79.9, 80.2, 81.6, 98.9, 110.3, 112.2, 121.8, 127.57, 127.76, 127.79, 127.90, 127.91, 128.22, 128.34, 128.43, 128.57, 130.0, 131.6, 137.0, 138.13, 138.42, 138.43; HRMS-ESI $[M + Na]^+$ calcd for $C_{46}H_{53}{}^{79}BrNaO_{11}$ 883.2663, found 883.2637. Anal. Calcd for $C_{46}H_{53}BrO_{11}$: C, 64.11; H, 6.20; Br, 9.27. Found: C, 63.84; H, 6.27; Br, 9.24.

Data for **24**: $[\alpha]_D^{30}$ +79.5 (c = 1.04, $CHCl_3$); ν_{max} (ATR-IR) 3486, 3062, 3029, 2985, 2934, 2896, 1488, 1454, 1403, 1373, 1315, 1219, 1156, 1123, 1069, 1047, 1027 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.29 (s, 3H), 1.41 (s, 3H), 1.43 (s, 3H), 1.47 (s, 3H), 2.49 (brs, 1H), 3.24 (dd, J = 9.5, 10.5 Hz, 1H), 3.65 (dd, J = 1.9, 10.6 Hz, 1H), 3.69 (dd, J = 4.2, 10.1 Hz, 1H), 3.84 (dd, J = 2.9, 10.6 Hz, 1H), 3.88−3.92 (m, 2H), 3.95−4.02 (m, 3H), 4.06 (dt, J = 2.3, 10.1 Hz, 1H), 4.10 (dd, J = 1.7, 3.2 Hz, 1H), 4.29 (t, J = 4.5 Hz, 1H), 4.49 (d, J = 12.1 Hz, 1H), 4.51 (d, J = 10.8 Hz, 1H), 4.66−4.75 (m, 4H), 4.82, 4.83 (2 × overlapping d, J = 12.7, 10.7 Hz, 2H), 5.33 (d, J = 1.5 Hz, 1H), 7.17−7.19 (m, 2H), 7.24−7.39 (m, 15H), 7.46−7.49 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.9, 27.08, 27.09, 28.2, 68.4, 68.6, 70.8, 71.1, 71.9, 73.6, 74.2, 74.5, 75.3, 76.5, 76.8, 77.2, 79.0, 79.6, 80.1, 98.1, 110.0, 112.6, 121.8, 127.64, 127.68, 127.77, 127.88, 128.01, 128.07, 128.4, 128.6, 130.0, 131.6, 137.0, 138.12, 138.25, 138.6; HRMS-ESI $[M + Na]^+$ calcd for $C_{46}H_{53}{}^{79}BrNaO_{11}$ 883.2663, found 883.2646. Anal. Calcd for $C_{46}H_{53}BrO_{11}$: C, 64.11; H, 6.20; Br, 9.27. Found: C, 63.84; H, 6.23; Br, 9.31.

3-*O*-(4-Bromobenzyl)-1,2:4,5-di-*O*-isopropylidene-D-*myo*-inositol (D-21). To a solution of diol D-**20**[47,48] (0.315 g, 1.21 mmol) in dry THF (60 mL) were added NaH (60% dispersion in oil, 0.087 g, 3.63 mmol) and 4-bromobenzyl bromide (0.333 g, 1.33 mmol), and the mixture was refluxed overnight under an atmosphere of nitrogen. The reaction mixture was quenched with H_2O and extracted into EtOAc (3 × 50 mL) and washed with H_2O (20 mL) and brine (20 mL). The organic extract was dried ($MgSO_4$) and filtered and the solvent removed in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:2) to give the *title compound* D-**21** (0.812 g, 67%) as a white solid: $[\alpha]_D^{27}$ −37.0 (c = 0.95, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 1.36 (s, 3H), 1.45 (s, 3H), 1.48 (s, 3H), 1.55 (s, 3H), 2.40 (d, J = 2.8 Hz, 1H), 3.27 (dd, J = 9.4, 10.4 Hz, 1H), 3.77 (dd, J = 4.3, 10.1 Hz, 1H), 3.88 (dd, J = 6.7, 10.6 Hz, 1H), 3.96 (dd, J = 4.9, 6.6 Hz, 1H), 4.03 (t, J = 9.7 Hz, 1H), 4.35 (t, J = 4.5 Hz, 1H), 4.75 (d, J = 12.6 Hz, 1H), 4.84 (d, J = 12.6 Hz, 1H), 7.28−7.31 (m, 2H), 7.46−7.49 (m, 2H); HRMS-ESI $[M + Na]^+$ calcd for $C_{19}H_{25}{}^{79}BrNaO_6$ 451.0727, found 451.0722. ^1H NMR and all other analytical data, excluding the optical rotation, were consistent with (±)-3-*O*-(4-bromobenzyl)-1,2:4,5-di-*O*-isopropylidene-*myo*-inositol **21**.

3-*O*-(4-Bromobenzyl)-6-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-1,2:4,5-di-*O*-isopropylidene-D-*myo*-inositol (D-23). TMSOTf (19 μL, 0.103 mmol) was added to a mixture of alcohol D-**21** (0.440 g, 1.03 mmol), trichloroacetimidate **22**[51] (0.784 g, 1.23 mmol), and 4 Å molecular sieves in dry CH_2Cl_2 (15 mL) at −30 °C. After being stirred for 30 min, the reaction was quenched with Et_3N, filtered through Celite, and evaporated to dryness. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:4 to 1:2) to give pseudodisaccharide 6-*O*-(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3-*O*-(4-bromobenzyl)-1,2:4,5-di-*O*-isopropylidene-D-*myo*-inositol (0.882 g) as a white foam. Sodium methoxide (prepared from reacting Na (0.069 g, 1.27 mmol) with MeOH (5 mL)) was added dropwise to a stirred solution of the pseudodisaccharide (0.882 g, 0.975 mmol) in MeOH (5 mL) until the pH of the solution remained greater than 11. The reaction mixture was then allowed to stir overnight. The reaction mixture was extracted into EtOAc (3 × 50 mL), and the combined organic extracts were washed with H_2O (50 mL). The solution was dried ($MgSO_4$) and filtered, and the solvent was removed in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:2) to give the *title compound* D-**23** (0.819 g, 80%) as a white foam. ^1H NMR and all other analytical data were consistent with those of **23**, prepared from (±)-**21**.

3-*O*-(4-Bromobenzyl)-4,5-di-*O*-benzyl-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-1,2-di-*O*-isopropylidene-D-*myo*-inositol (25). To a solution of **23** (2.11 g, 2.45 mmol) in CH_2Cl_2 (20 mL) were added H_2O (44 μL, 2.45 mmol) and TFA (0.377 mL, 4.89 mmol) at 0 °C. The solution was stirred for 2.5 h, diluted with CH_2Cl_2 (40 mL), and washed with saturated $NaHCO_3$ (20 mL) and saturated NaCl (20 mL). The organic phase was dried ($MgSO_4$) and filtered, and the solvent was evaporated under reduced pressure to give 3-*O*-(4-bromobenzyl)-6-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-1,2-di-*O*-isopropylidene-D-*myo*-inositol (2.01 g) as a white foam which was used without further purification: HRMS-ESI $[M + Na]^+$ calcd for $C_{43}H_{49}BrO_{11}Na$ 843.2350, found 843.2328. To a solution of crude triol (2.01 g, 2.45 mmol) in dry DMF (20 mL) were added NaH (60% dispersion in oil, 0.528 g, 22 mmol) and benzyl bromide (2.61 mL, 22 mmol) at 0 °C, and the reaction mixture was stirred overnight. The reaction was quenched by careful addition of H_2O (5 mL) and then extracted into EtOAc (3 × 100 mL). The combined organic layers were washed with H_2O (100 mL) and saturated NaCl (100 mL), dried ($MgSO_4$), and filtered, and the solvent was removed in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:9 to 1:2) to give the *title compound* **25** (2.12 g, 79%, two steps) as a white foam: $[\alpha]_D^{29}$ +9.3 (c = 1.00, $CHCl_3$); ν_{max} (ATR-IR) 3062, 3029, 2984, 2865, 1496, 1453, 1362, 1242, 1201, 1089, 1070, 1041, 1026 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.35 (s,

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3H), 1.53 (s, 3H), 3.27 (dd, J = 7.8, 9.6 Hz, 1H), 3.51 (dd, J = 1.7, 11.1 Hz, 1H), 3.62−3.65 (m, 2H), 3.80 (dd, J = 1.9, 3.1 Hz, 1H), 3.85 (t, J = 8.0 Hz, 1H), 3.88 (dd, J = 3.2, 9.5 Hz, 1H), 3.95−3.99 (m, 2H), 4.05−4.10 (m, 2H), 4.26 (dd, J = 3.8, 5.8 Hz, 1H), 4.35 (d, J = 12.2 Hz, 1H), 4.51 (d, J = 10.9 Hz, 1H), 4.57 (d, J = 10.9 Hz, 4H), 4.62 (d, J = 12.2 Hz, 1H), 4.67−4.71 (m, 4H), 4.74 (d, J = 12.5 Hz, 1H), 4.78 (d, J = 12.5 Hz, 1H), 4.89 (d, J = 10.9 Hz, 1H), 5.49 (d, J = 1.7 Hz, 1H), 7.02−7.06 (m, 2H), 7.12−7.16 (m, 3H), 7.20−7.32 (m, 25H), 7.36−7.44 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.8, 27.6, 68.9, 71.8, 71.9, 72.3, 72.4, 73.1, 74.49, 74.55, 74.84, 74.90, 75.0, 75.3, 76.8, 77.3, 79.2, 79.6, 80.9, 81.1, 96.3, 110.2, 121.7, 127.3, 127.49, 127.56, 127.71, 127.73, 127.83, 127.87, 127.89, 128.06, 128.17, 128.21, 128.29, 128.30, 128.31, 128.41, 128.44, 129.6, 131.5, 137.3, 137.9, 138.37, 138.45, 138.56, 138.58, 139.0; HRMS-ESI [M + Na]$^+$ calcd for $C_{64}H_{67}{}^{79}BrNaO_{11}$ 1113.3759, found 1113.3707.

3-*O*-(4-Bromobenzyl)-4,5-di-*O*-benzyl-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-D-*myo*-inositol (26). To a solution of **25** (4.054 g, 3.71 mmol) in CH_2Cl_2 (100 mL) were added MeOH (0.230 mL, 5.57 mmol) and TFA (1.43 mL, 18.56 mmol), and the reaction mixture was stirred at rt overnight. The reaction mixture was diluted with CH_2Cl_2 (50 mL) and washed with saturated $NaHCO_3$ (50 mL) and saturated NaCl (50 mL). The organic phase was dried ($MgSO_4$) and filtered, and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:2 to 1:1) to give the *title compound* **26** (2.12 g, 79%) as a white foam: $[\alpha]_D^{31}$ +24.4 (c = 1.03, $CHCl_3$); ν_{max} (ATR-IR) 3434, 3087, 3062, 3029, 2864, 1592, 1496, 1453, 1360, 1208, 1070, 1048, 1027 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.55 (brs, 1H), 2.99 (d, J = 8.6 Hz, 1H), 3.28 (t, J = 9.4 Hz, 1H), 3.38 (dd, J = 2.8, 9.5 Hz, 1H), 3.48−3.55 (m, 3H), 3.84−3.86 (m, 1H), 3.88−3.92 (m, 2H), 3.95 (t, J = 9.2 Hz, 1H), 4.03 (t, J = 9.5 Hz, 1H), 4.02−4.07 (m, 2H), 4.35 (d, J = 12.1 Hz, 1H), 4.46 (d, J = 11.1 Hz, 1H), 4.55−4.63 (m, 6H), 4.70−4.79 (m, 5H), 4.84 (d, J = 11.1 Hz, 1H), 5.51 (d, J = 2.0 Hz, 1H), 7.09−7.14 (m, 3H), 7.14−7.19 (m, 3H), 7.22−7.31 (m, 24H), 7.35−7.38 (m, 2H), 7.41−7.44 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 69.2, 70.3, 71.89, 71.92, 71.95, 72.31, 72.33, 73.2, 74.78, 74.81, 74.9, 75.6, 75.8, 78.0, 79.4, 79.8, 80.7, 81.1, 97.0, 121.9, 127.42, 127.45, 127.47, 127.54, 127.64, 127.69, 127.7, 127.8, 127.85, 127.87, 127.88, 128.0, 128.22, 128.25, 128.26, 128.34, 128.37, 128.43, 129.5, 131.7, 136.8, 138.29, 138.31, 138.36, 138.53, 138.55, 138.8; HRMS-ESI [M + Na]$^+$ calcd for $C_{61}H_{63}{}^{79}BrNaO_{11}$ 1073.3446, found 1073.3400.

4,5-Di-*O*-benzyl-3-*O*-(4-(3,4-dimethoxyphenyl)benzyl)-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-D-*myo*-inositol (27). To an oven-dried Schlenk flask were added diol **26** (0.934 g, 0.89 mmol), 3,4-dimethoxyphenylboronic acid (0.194 g, 1.07 mmol), tetrabutylammonium bromide (0.029 g, 0.09 mmol), potassium phosphate (K_3PO_4) (0.565 g, 2.66 mmol), and EtOH (25 mL). The resulting mixture was subjected to the freeze−pump−thaw cycle three times to exclude air. $Pd(OAc)_2$ (10 mg, 0.045 mmol) was then added under a flow of argon, and the reaction mixture was stirred at rt for 3 h. Once the reaction was complete, the solution was filtered through a plug of Celite and washed with EtOAc (100 mL). The reaction mixture was washed with saturated aq $NaHCO_3$ (100 mL), and the aqueous layer was back-extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with H_2O (50 mL) and saturated NaCl (50 mL), dried ($MgSO_4$), and filtered, and the solvent was removed in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:2 to 2:3) to give the *title compound* **27** (0.881 g, 99%) as a white foam: $[\alpha]_D^{28}$ +20.7 (c = 1.01, $CHCl_3$); ν_{max} (ATR-IR) 3460, 3062, 3029, 2906, 2865, 1604, 1589, 1526, 1502, 1453, 1399, 1360, 1327, 1250, 1217, 1171, 1140, 1072, 1049, 1025 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.64 (s, 1H), 2.96 (d, J = 6.5 Hz, 1H), 3.29 (t, J = 9.4 Hz, 1H), 3.45 (dd, J = 2.7, 9.5 Hz, 1H), 3.49−3.52 (m, 2H), 3.53 (dd, J = 2.8, 9.6 Hz, 1H), 3.85−3.87 (m, 1H), 3.88−3.99 (m, 3H), 3.93 (s, 3H), 3.95 (s, 3H), 4.01−4.06 (m, 2H), 4.09 (t, J = 2.7 Hz, 1H), 4.34 (d, J = 12.1 Hz, 1H), 4.46 (d, J = 11.1 Hz, 1H), 4.54−4.61 (m, 4H), 4.69−4.76 (m, 5H), 4.79 (d, J = 10.8 Hz, 1H), 4.84 (d, J = 11.1 Hz, 1H), 4.87 (d, J = 10.8 Hz, 1H), 5.54 (d, J = 1.9 Hz, 1H), 6.95 (d, J = 8.4 Hz, 1H), 7.08−7.19 (m, 7H), 7.20−7.30 (m, 23H), 7.37 (d, J = 8.1 Hz, 4H), 7.50−7.53 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 56.02, 56.05, 69.1, 70.3, 71.9, 72.3, 72.52, 72.55, 73.2, 74.8, 74.9, 75.6, 75.8, 77.8, 79.5, 79.8, 80.7, 81.2, 97.0, 110.5, 111.6, 119.4, 127.0, 127.38, 127.41, 127.43, 127.5, 127.61, 127.63, 127.69, 127.85, 127.88, 127.9, 128.0, 128.20, 128.23, 128.24, 128.32, 128.34, 128.40, 128.44, 133.8, 136.4, 138.31, 138.33, 138.38, 138.5, 138.7, 138.8, 140.8, 148.8, 149.2; HRMS-ESI [M + Na]$^+$ calcd for $C_{69}H_{72}NaO_{13}$ 1131.4865, found 1131.4854. Anal. Calcd for $C_{69}H_{72}O_{13}\cdot H_2O$: C, 73.51; H, 6.62. Found: C, 73.59; H, 6.74.

1-*O*-Allyl-4,5-di-*O*-benzyl-3-*O*-(4-(3,4-dimethoxyphenyl)-benzyl)-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-D-*myo*-inositol (28). Diol **27** (1.72 g, 1.55 mmol) and dibutyltin oxide (0.463, 1.86 mmol) were dried together under high vacuum for 30 min and then flushed with argon. To this was added anhydrous toluene (30 mL), and the reaction mixture was heated at reflux for 2 h during which time the suspension changed to a clear yellow solution. Once cooled to rt, the solvent was removed in vacuo to give a yellow foam. Cesium fluoride (0.353 g, 2.34 mmol) was added and the mixture dried under high vacuum together for 30 min and then flushed with argon. Anhydrous DMF (20 mL) was added, followed by allyl bromide (0.201 mL, 2.34 mmol), and the reaction mixture was heated at 50 °C overnight. After cooling, the reaction mixture was diluted with CH_2Cl_2 (200 mL) and partitioned with H_2O (100 mL). The aqueous layer was re-extracted with CH_2Cl_2 (2 × 50 mL), the combined organic layers were washed with saturated NaCl (100 mL), dried ($MgSO_4$), and filtered, and the solvent was removed in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:4 to 2:3) to give the *title compound* **28** (1.30 g, 73%, R_f = 0.71, EtOAc/petroleum ether 1:1) and 2-*O*-allyl-4,5-di-*O*-benzyl-3-*O*-(4-(3,4-dimethoxyphenyl)benzyl)-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-D-*myo*-inositol (0.128 g, 7%, R_f = 0.82, EtOAc/petroleum ether 1:1), both as white foams. Data for **28**: $[\alpha]_D^{26}$ +14.2 (c = 1.00, $CHCl_3$); ν_{max} (ATR-IR) 3488, 3062, 3029, 2865, 1604, 1588, 1526, 1501, 1453, 1399, 1360, 1327, 1250, 1216, 1171, 1050, 1025 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.43 (brs, 1H), 3.22 (dd, J = 2.5, 9.6 Hz, 1H), 3.28 (t, J = 9.5 Hz, 1H), 3.36 (dd, J = 1.6, 11.3 Hz, 1H), 3.40−3.45 (m, 2H), 3.84 (dd, J = 2.0, 2.8 Hz, 1H), 3.88−4.07 (m, 5H), 3.93 (s, 3H), 3.96 (s, 3H), 4.10 (t, J = 9.7 Hz, 1H), 4.15 (t, J = 9.6 Hz, 1H), 4.22 (t, J = 2.6 Hz, 1H), 4.27 (d, J = 12.0 Hz, 1H), 4.48 (d, J = 11.0 Hz, 1H), 4.62 (d, J = 12.1 Hz, 1H), 4.64−4.78 (m, 7H), 4.81 (d, J = 10.6 Hz, 1H), 4.85 (d, J = 11.1 Hz, 2H), 4.93 (d, J = 10.6 Hz, 1H), 5.15 (dq, J = 10.4, 1.3 Hz, 1H), 5.25 (dq, J = 17.2, 1.6 Hz, 1H), 5.53 (d, J = 1.8 Hz, 1H), 5.79 (dddd, J = 5.7, 5.7, 10.2, 17.2 Hz, 1H), 6.96 (d, J = 8.3 Hz, 1H), 7.05−7.17 (m, 7H), 7.17−7.32 (m, 21H), 7.34−7.43 (m, 6H), 7.50−7.54 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 56.02, 56.05, 66.5, 68.7, 70.7, 71.9, 72.11, 72.16, 72.4, 73.2, 74.9, 75.22, 75.26, 75.8, 76.0, 79.8, 80.0, 80.5, 81.4, 81.5, 98.4, 110.4, 111.6, 117.9, 119.4, 127.0, 127.2, 127.3, 127.37, 127.44, 127.60, 127.61, 127.8, 127.87, 127.91, 128.0, 128.10, 128.14, 128.17, 128.24, 128.3, 128.4, 128.44, 133.8, 134.3, 136.5, 138.2, 138.6, 138.70, 138.71, 138.8, 139.1, 140.7, 148.8, 149.3; HRMS-ESI [M + Na]$^+$ calcd for $C_{72}H_{76}NaO_{13}$ 1171.5178, found 1171.5082. Anal. Calcd for $C_{72}H_{76}O_{13}.H_2O$: C, 74.08; H, 6.73. Found: C, 74.52; H, 6.65.

Data for 2-*O*-allyl-4,5-di-*O*-benzyl-3-*O*-(4-(3,4-dimethoxyphenyl)-benzyl)-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-D-*myo*-inositol: $[\alpha]_D^{31}$ +23.5 (c = 1.00, $CHCl_3$); ν_{max} (ATR-IR) 3506, 3062, 3029, 2927, 2863, 1604, 1589, 1526, 1502, 1453, 1398, 1360, 1327, 1249, 1216, 1170, 1140, 1090, 1049, 1026 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.44 (d, J = 10.4 Hz, 1H), 3.26 (t, J = 9.3 Hz, 1H), 3.42 (dd, J = 2.3, 9.9 Hz, 1H), 3.44−3.49 (m, 2H), 3.52 (dd, J = 4.0, 10.9 Hz, 1H), 3.86 (t, J = 2.6 Hz, 1H), 3.88 (m, 1H), 3.89−4.06 (m, 5H), 3.93 (s, 3H), 3.96 (s, 3H), 4.16 (ddt, J = 1.3, 6.2, 12.7 Hz, 1H), 4.30 (d, J = 12.0 Hz, 1H), 4.46 (d, J = 11.0 Hz, 1H), 4.52−4.62 (m, 5H), 4.68−4.78 (m, 5H), 4.79 (d, J = 10.7 Hz, 1H), 4.86 (d, J = 11.0 Hz, 1H), 4.90 (d, J = 10.7 Hz, 1H), 5.21 (dq, J = 10.5, 1.3 Hz, 1H), 5.28 (dq, J = 17.2, 1.6 Hz, 1H), 5.61 (d, J = 1.4 Hz, 1H), 5.94 (dddd, J = 5.3, 6.1, 10.4, 16.6 Hz, 1H), 6.95 (d, J = 8.4 Hz, 1H), 7.04−7.17 (m, 8H), 7.20−7.30 (m, 22H), 7.36−7.40 (m, 4H), 7.50−7.53 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 56.03, 56.06, 69.0, 71.75, 71.76, 72.2, 72.9,

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73.1, 73.2, 73.9, 74.6, 74.9, 74.87, 75.81, 75.84, 77.9, 78.2, 79.5, 81.1, 81.3, 81.5, 97.3, 110.5, 111.6, 117.38, 119.42, 126.9, 127.31, 127.34, 127.39, 127.47, 127.52, 127.58, 127.7, 127.84, 127.87, 127.9, 128.0, 128.16, 128.20, 128.22, 128.3, 128.4, 133.8, 135.0, 136.7, 138.3, 138.52, 138.53, 138.6, 138.7, 139.0, 140.6, 148.8, 149.3; HRMS-ESI $[M + Na]^+$ calcd for $C_{72}H_{76}NaO_{13}$ 1171.5178, found 1171.5157.

Dibutyl (2-*O*-Benzoyl-3,4-di-*O*-benzyl-6-*O*-*tert*-butyldimethylsilyl-α-D-mannopyranosyl) Phosphate (29). To a solution of tricyclic orthoester **31**[39] (0.70 g, 1.57 mmol) and 4 Å molecular sieves in dry CH_2Cl_2 (20 mL) was added dibutyl phosphate (3.10 mL, 15.7 mmol) in one portion. The reaction mixture was stirred at rt overnight, cooled to 0 °C, and quenched with Et_3N (3 mL). The solution was warmed to rt and filtered through a plug of Et_3N-deactivated silica gel and further eluted with CH_2Cl_2 (20 mL), and the solvent was removed in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether with 1% Et_3N = 1:4 to 2:3) to give dibutyl (2-*O*-benzoyl-3,4-di-*O*-benzyl-6-*O*-*tert*-butyldimethylsilyl-α-D-mannopyranosyl) phosphate (0.954 g) as a colorless oil. *tert*-Butyldimethylsilyl chloride (TBSCl) (0.572 mL, 3.30 mmol) was added to a stirred solution of dibutyl (2-*O*-benzoyl-3,4-di-*O*-benzyl-6-*O*-*tert*-butyldimethylsilyl-α-D-mannopyranosyl) phosphate (0.868 g, 1.32 mmol), pyridine (6 mL, 74.2 mmol), and DMAP (0.323 g, 2.64 mmol) in anhydrous CH_2Cl_2 (20 mL). The reaction mixture was allowed to stir at rt overnight. The solvent was removed in vacuo, and the residue was purified by column chromatography on silica gel (EtOAc/petroleum ether with 1% Et_3N = 1:9 to 1:2) to give the *title compound* **29** (0.793 g, 78%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.09 (s, 3H), 0.10 (s, 3H), 0.92−0.96 (m, 15H), 1.37−1.46 (m, 4H), 1.63−1.70 (m, 4H), 3.83 (dd, J = 1.7, 11.4 Hz, 1H), 3.89 (dt, J = 2.1, 9.7 Hz, 1H), 4.03−4.12 (m, 6H), 4.18 (t, J = 9.7 Hz, 1H), 4.59 (d, J = 11.4 Hz, 1H), 4.68 (d, J = 10.8 Hz, 1H), 4.79 (d, J = 11.4 Hz, 1H), 4.90 (d, J = 10.8 Hz, 1H), 5.66 (t, J = 2.6 Hz, 1H), 5.74 (dd, J = 2.0, 6.4 Hz, 1H), 7.22−7.35 (m, 10H), 7.43−7.47 (m, 2H), 7.57−7.61 (m, 1H), 8.09−8.12 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ −5.4, −5.1, 13.6, 18.4, 18.7, 26.0, 32.3, 61.6, 67.9, 67.95, 68.0, 68.8, 69.9, 72.0, 73.4, 74.3, 75.4, 96.1, 127.7, 128.0, 128.1, 128.38, 128.43, 128.45, 129.7, 130.1, 133.4, 138.0, 138.6, 165.5; ^{31}P NMR (202 MHz, $CDCl_3$) δ −3.01; HRMS-ESI $[M + Na]^+$ calcd for $C_{41}H_{59}NaO_{10}PSi$ 793.3513, found 793.3505.

2-*O*-Benzoyl-3,4-di-*O*-benzyl-α-D-mannopyranose (33). (1,5-Cyclooctadiene)bis(methyldiphenylphosphine)iridium(I) hexafluorophosphate (0.050 g, 0.059 mmol) was added to a stirred solution of allyl ether **32** (2.40 g, 4.76 mmol) in dry THF (20 mL) at rt under an atmosphere of argon. The argon atmosphere was replaced with H_2 for ca. 1 min, followed by a gentle stream of argon being passed over the reaction. The reaction mixture was stirred for 2.5 h, the solvent was removed in vacuo, and the residue was dissolved in CH_2Cl_2/MeOH (2:1, 30 mL). Acetyl chloride (0.3 mL, 4.22 mmol) was added to the solution, and the reaction was stirred overnight. The reaction mixture was quenched with saturated $NaHCO_3$ (20 mL), and H_2O (50 mL) was added. The mixture was extracted with CH_2Cl_2 (3 × 100 mL), the combined organic extracts were dried ($MgSO_4$) and filtered, and the solvent was removed in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:2 to 1:1) to give the *title compound* **33** (1.88 g, 85%) as a white foam: ν_{max} (ATR-IR) 3389, 3063, 3031, 2929, 1719, 1601, 1584, 1496, 1452, 1345, 1268, 1210, 1178, 1095, 1070, 1042, 1026 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.33 (brs, 1H), 3.61 (d, J = 3.3 Hz, 1H), 3.77 (dd, J = 4.9, 11.3 Hz, 1H), 3.86 (dd, J = 2.1, 11.8 Hz, 1H), 3.91 (t, J = 9.6 Hz, 1H), 3.99 (ddd, J = 2.7, 4.7, 9.8 Hz, 1H), 4.16 (dd, J = 3.2, 9.2 Hz, 1H), 4.58 (d, J = 11.4 Hz, 1H), 4.64 (d, J = 11.0 Hz, 1H), 4.77 (d, J = 11.4 Hz, 1H), 4.92 (d, J = 11.0 Hz, 1H), 5.28 (dd, J = 1.9, 3.5 Hz, 1H), 5.59 (dd, J = 1.9, 3.1 Hz, 1H), 7.24−7.35 (m, 10H), 7.45−7.48 (m, 2H), 7.56−7.60 (m, 1H), 8.05−8.08 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 62.4, 69.6, 71.6, 71.9, 74.3, 75.3, 77.7, 92.6, 127.7, 127.9, 128.0, 128.3, 128.4, 128.5, 128.6, 130.0, 133.4, 138.0, 138.1, 165.8; HRMS-ESI $[M + Na]^+$ calcd for $C_{27}H_{28}NaO_7$ 487.1727, found 487.1712.

2-*O*-Benzoyl-3,4-di-*O*-benzyl-6-*O*-*tert*-butyldimethylsilyl-α-D-mannopyranose (34).[49] *tert*-Butyldimethylsilyl trifluoromethanesulfonate (TBSOTf) (0.317 mL, 1.20 mmol) was added dropwise over ca. 10 min to a solution of diol **33** (0.506 g, 1.09 mmol) and *sym*-collidine (0.435 mL, 3.27 mmol) in dry CH_2Cl_2 (25 mL) under an argon atmosphere at rt. The reaction mixture was stirred for 1 h, diluted with CH_2Cl_2 (50 mL), washed with H_2O (2 × 30 mL), and dried ($MgSO_4$). The solution was filtered, and the solvent removed in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether =1:9 to 1:2) to give the title compound **34** (0.498 g, 79%) as a white solid: mp 139−142 °C (EtOAc/PE); ν_{max} (ATR-IR) 3363, 3036, 2933, 2899, 2859, 1723, 1605, 1584, 1453, 1352, 1290, 1248, 1125, 1105, 1076, 1059 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.088 (s, 3H), 0.094 (s, 3H), 0.94 (s, 9H), 2.59 (d, J = 3.7 Hz, 1H), 3.84 (dd, J = 1.6, 11.2 Hz, 1H), 3.94 (ddd, J = 1.4, 3.6, 9.7 Hz, 1H), 4.00 (dd, J = 3.7, 11.2 Hz, 1H), 4.06 (t, J = 9.6 Hz, 1H), 4.15 (dd, J = 3.2, 9.5 Hz, 1H), 4.59 (d, J = 11.4 Hz, 1H), 4.66 (d, J = 10.8 Hz, 1H), 4.79 (d, J = 11.4 Hz, 1H), 4.91 (d, J = 10.8 Hz, 1H), 5.34 (brs, 1H), 5.64 (dd, J = 1.9, 3.2 Hz, 1H), 7.22−7.34 (m, 10H), 7.43−7.47 (m, 2H), 7.56−7.60 (m, 1H), 8.10−8.12 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ −5.3, −5.1, 18.5, 26.1, 62.4, 69.6, 71.7, 72.7, 74.2, 75.3, 77.8, 92.8, 127.6, 127.7, 128.0, 128.1, 128.3, 128.4, 130.1, 133.2, 138.2, 138.7, 165.9; HRMS-ESI $[M + Na]^+$ calcd for $C_{33}H_{42}NaO_7Si$ 601.2592, found 601.2624.

2-*O*-Benzoyl-3,4-di-*O*-benzyl-6-*O*-*tert*-butyldimethylsilyl-α-D-mannopyranosyl Trichloroacetimidate (30).[49] Mannoside **34** (2.43 g, 4.20 mmol) was dissolved in dry CH_2Cl_2 (100 mL) and cooled to 0 °C under an atmosphere of nitrogen. To the solution were added trichloroacetonitrile (3.79 mL, 37.8 mmol) and DBU (0.063 mL, 0.420 mmol), and the reaction was stirred for 1 h at this temperature. The solvent was removed in vacuo, and the residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:9) to give the title compound **30** (2.51 g, 83%) as a colorless oil: ν_{max} (ATR-IR) 2952, 2927, 2855, 1727, 1674, 1601, 1587, 1496, 1454, 1361, 1260, 1165, 1148, 1095, 1069, 1047 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.10 (s, 3H), 0.11 (s, 3H), 0.95 (s, 9H), 3.86−3.92 (m, 2H), 4.03 (dd, J = 2.9, 11.3 Hz, 1H), 4.14 (dd, J = 3.3, 9.7 Hz, 1H), 4.23 (t, J = 9.6 Hz, 1H), 4.62 (d, J = 11.4 Hz, 1H), 4.69 (d, J = 10.6 Hz, 1H), 4.81 (d, J = 11.4 Hz, 1H), 4.92 (d, J = 10.6 Hz, 1H), 5.73 (dd, J = 2.1, 3.2 Hz, 1H), 6.39 (d, J = 2.0 Hz, 1H), 7.23−7.36 (m, 10H), 7.45−7.49 (m, 2H), 7.58−7.62 (m, 1H), 8.12−8.15 (m, 2H), 8.66 (brs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ −5.3, −5.1, 18.4, 26.0, 61.7, 67.9, 72.0, 73.5, 75.4, 75.6, 77.5, 95.9, 127.8, 128.2, 128.3, 128.4, 128.5, 129.7, 130.2, 133.4, 137.7, 138.5, 160.1, 165.6; HRMS-ESI $[M + Na]^+$ calcd for $C_{35}H_{42}{}^{35}Cl_3NNaO_7Si$ 744.1688, found: 744.1684.

1-*O*-Allyl-2-*O*-(2-*O*-benzoyl-3,4-di-*O*-benzyl-6-*O*-*tert*-butyldimethylsilyl-α-D-mannopyranosyl)-4,5-di-*O*-benzyl-3-*O*-(4-(3,4-dimethoxyphenyl)benzyl)-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-D-*myo*-inositol (35). Alcohol **28** (0.417 g, 0.363 mmol) and trichloroacetimidate **30** (0.324 g, 0.448 mmol) were coevaporated from dry toluene (2 × 20 mL) and dried under high vacuum for 30 min and then flushed with nitrogen. Anhydrous toluene (30 mL) was added followed by 4 Å molecular sieves, and the solution was cooled to 0 °C. TMSOTf (4 μL, 0.018 mmol) was added, and the reaction mixture was stirred for 1 h at 0 °C. The reaction was quenched with Et_3N (0.2 mL), filtered through Celite, and washed with DCM (50 mL) and the solvent evaporated to dryness. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:4 to 1:2) to give the *title compound* **35** (0.360 g, 99%) as a white foam: $[\alpha]_D^{27}$ +26.0 (c = 1.80, $CHCl_3$); ν_{max} (ATR-IR) 3062, 3030, 2927, 2856, 1724, 1603, 1587, 1526, 1501, 1453, 1397, 1360, 1266, 1251, 1216, 1170, 1094, 1026 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ −0.02 (s, 3H), 0.02 (s, 3H), 0.90 (s, 9H), 3.18 (dd, J = 2.0, 9.7 Hz, 1H), 3.29, 3.29 (overlapping dd, t, J = 1.5, 11.2, 9.3 Hz, 2H), 3.34 (dd, J = 2.5, 9.9 Hz, 1H), 3.40 (dd, J = 3.1, 11.3 Hz, 1H), 3.51 (d, J = 11.3 Hz, 1H), 3.74 (d, J = 10.3 Hz, 1H), 3.83−3.85 (m, 1H), 3.86−3.97 (m, 4H), 3.92 (s, 3H), 3.94 (s, 3H), 4.02 (dd, J = 5.3, 12.8 Hz, 1H), 4.07−4.12 (m, 4H), 4.16 (t, J = 9.8 Hz, 1H), 4.20 (d, J = 12.0 Hz, 1H), 4.34 (t, J = 2.2 Hz, 1H), 4.48 (d, J = 10.9 Hz, 1H), 4.59−4.70 (m, 8H), 4.75−4.81 (m, 3H), 4.85, 4.85 (2 × overlapping d, J = 10.7, 11.5 Hz, 2H), 4.90 (d, J = 10.8 Hz, 2H), 4.92 (d, J = 10.6 Hz, 1H), 5.03 (dq, J = 10.5, 1.4 Hz, 1H), 5.20 (d, J = 1.8 Hz, 1H), 5.21 (dq, J = 17.2,

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1.6 Hz, 1H), 5.55 (d, J = 1.7 Hz, 1H), 5.69−5.77 (m, 2H), 6.94 (d, J = 8.4 Hz, 1H), 7.05−7.06 (m, 1H), 7.09 (dd, J = 2.0, 8.2 Hz, 1H), 7.11−7.14 (m, 4H), 7.15−7.31 (m, 30H), 7.31−7.36 (m, 7H), 7.39−7.45 (m, 5H), 7.54−7.57 (m, 1H), 8.08−8.11 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ −5.4, −5.1, 18.4, 26.1, 56.0, 56.1, 61.9, 68.6, 69.0, 70.8, 71.5, 71.6, 72.06, 72.08, 72.10, 72.2, 72.5, 73.3, 73.9, 74.8, 74.96, 75.02, 75.3, 75.8, 75.9, 77.0, 77.6, 79.1, 80.1, 81.0, 81.5, 81.7, 99.0 ($^1J_{C-H}$ = 173 Hz), 99.2 ($^1J_{C-H}$ = 174 Hz), 110.4, 111.5, 117.5, 119.4, 126.8, 127.2, 127.3, 127.40, 127.41, 127.47, 127.59, 127.61, 127.66, 127.67, 127.86, 127.88, 127.95, 127.97, 128.09, 128.11, 128.12, 128.21, 128.22, 128.28, 128.31, 128.39, 128.41, 128.5, 130.1, 130.3, 132.9, 133.86, 133.95, 136.7, 138.1, 138.2, 138.5, 138.7, 138.85, 138.93, 139.1, 139.2, 140.3, 148.7, 149.2, 165.2; HRMS-ESI $[M + Na]^+$ calcd for $C_{105}H_{116}NaO_{19}Si$ 1731.7772, found 1731.7702. Anal. Calcd for $C_{105}H_{116}O_{19}Si.H_2O$: C, 72.98; H, 6.88. Found: C, 72.76; H, 7.15.

1-*O*-Allyl-4,5-di-*O*-benzyl-2-*O*-(3,4-di-*O*-benzyl-6-*O*-*tert*-butyldimethylsilyl-α-D-mannopyranosyl)-3-*O*-(4-(3,4-dimethoxyphenyl)benzyl)-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-D-*myo*-inositol (36). Sodium methoxide (prepared from reacting Na (0.27 g, 11.74 mmol) with MeOH (5 mL)) was added dropwise to a stirred solution of **35** (1.62 g, 0.948 mmol) in CH_2Cl_2/MeOH (1:9, 50 mL) until the pH of the solution remained greater than 11. The reaction mixture was then allowed to stir overnight, partitioned with H_2O (50 mL), extracted with CH_2Cl_2 (3 × 50 mL), dried ($MgSO_4$), and filtered and the solvent removed in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:4 to 1:2) to give the *title compound* **36** (1.42 g, 93%) as a white foam: $[\alpha]_D^{27}$ +47.8 (c = 1.57, $CHCl_3$); ν_{max} (ATR-IR) 3488, 3061, 3030, 2926, 2854, 1604, 1588, 1526, 1501, 1453, 1398, 1360, 1250, 1216, 1170, 1091, 1026 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ −0.01 (s, 3H), 0.01 (s, 3H), 0.86 (s, 9H), 2.35 (brs, 1H), 3.21 (dd, J = 1.8, 9.7 Hz, 1H), 3.29, 3.31 (overlapping t, dd, J = 9.4, 1.5, 11.2 Hz, 2H), 3.34 (dd, J = 2.5, 9.9 Hz, 1H), 3.42 (dd, J = 3.1, 11.1 Hz, 1H), 3.58 (dd, J = 1.4, 11.4 Hz, 1H), 3.69 (dd, J = 3.7, 11.4 Hz, 1H), 3.83 (dd, J = 1.9, 3.0 Hz, 1H), 3.87−3.95 (m, 5H), 3.94 (s, 3H), 3.95 (s, 3H), 3.96−4.00 (m, 1H), 4.05−4.11 (m, 3H), 4.12−4.18 (m, 2H), 4.22 (d, J = 12.0 Hz, 1H), 4.40 (t, J = 2.1 Hz, 1H), 4.47 (d, J = 11.0 Hz, 1H), 4.59 (d, J = 12.0 Hz, 1H), 4.62−4.72 (m, 7H), 4.75, 4.76 (2 × overlapping d, J = 12.5, 11.3 Hz, 2H), 4.80, 4.81 (2 × overlapping d, J = 10.7, 12.1 Hz, 2H), 4.87, 4.87 (2 × overlapping d, J = 10.9, 11.0 Hz, 2H), 4.91 (d, J = 10.5 Hz, 1H), 4.95 (d, J = 10.7 Hz, 1H), 5.17 (dq, J = 10.4, 1.4 Hz, 1H), 5.23 (d, J = 1.7 Hz, 1H), 5.26 (dq, J = 17.2, 1.6 Hz, 1H), 5.53 (d, J = 1.6 Hz, 1H), 5.79 (dddd, J = 5.5, 5.5, 10.8, 17.1 Hz, 1H), 6.96 (d, J = 8.4 Hz, 1H), 7.07 (d, J = 2.1 Hz, 1H), 7.08−7.14 (m, 5H), 7.15−7.46 (m, 40H); ^{13}C NMR (125 MHz, $CDCl_3$) δ −5.3, −5.1, 18.4, 26.0, 56.0, 56.1, 62.3, 68.4, 68.7, 69.9, 70.9, 71.89, 71.96, 72.0, 72.11, 72.14, 72.19, 73.2, 74.0, 74.8, 75.0, 75.3, 75.7, 76.05, 76.1, 79.2, 79.5, 80.1, 81.58, 81.6, 81.7, 98.7, 100.0, 110.4, 111.5, 117.8, 119.4, 126.8, 127.27, 127.36, 127.44, 127.45, 127.57, 127.63, 127.85, 127.89, 127.91, 127.93, 127.97, 128.12, 128.14, 128.21, 128.25, 128.27, 128.31, 128.35, 128.38, 128.6, 133.9, 134.0, 136.6, 138.05, 138.11, 138.58, 138.61, 138.7, 138.9, 139.0, 139.1, 140.3, 148.7, 149.2; HRMS-ESI $[M + Na]^+$ calcd for $C_{98}H_{112}NaO_{18}Si$ 1627.7510, found 1627.7554. Anal. Calcd for $C_{98}H_{112}O_{18}Si.H_2O$: C, 72.48; H, 7.08. Found: C, 72.60; H, 7.30.

1-*O*-Allyl-4,5-di-*O*-benzyl-3-*O*-(4-(3,4-dimethoxyphenyl)-benzyl)-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-2-*O*-(2,3,4-tri-*O*-benzyl-6-*O*-*tert*-butyldimethylsilyl-α-D-mannopyranosyl)-D-*myo*-inositol (37). To a solution of alcohol **36** (1.22 g, 0.76 mmol) in anhydrous DMF (30 mL) were added NaH (60% dispersion in oil, 0.055 g, 2.28 mmol) and benzyl bromide (0.271 mL, 2.28 mmol) at 0 °C, and the reaction mixture was allowed to stir overnight. The reaction was quenched with H_2O (5 mL) and extracted into CH_2Cl_2 (3 × 100 mL). The combined organic layers were washed with H_2O (100 mL) and saturated NaCl (100 mL), dried ($MgSO_4$), and filtered, and the solvent was removed in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:9 to 1:2) to give the *title compound* **37** (0.75 g, 99%) as a colorless oil: $[\alpha]_D^{27}$ +37.7 (c = 1.16, $CHCl_3$); ν_{max} (ATR-IR) 3063, 3030, 2927, 2856, 1604, 1588, 1526, 1500, 1454, 1397, 1360, 1249, 1216, 1170, 1091, 1049, 1026 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ −0.02 (s, 3H), 0.01 (s, 3H), 0.86 (s, 9H), 3.18 (dd, J = 1.9, 9.7 Hz, 1H), 3.26 (t, J = 9.4 Hz, 1H), 3.28 (dd, J = 1.6, 11.2 Hz, 1H), 3.31 (dd, J = 2.6, 10.0 Hz, 1H), 3.39 (dd, J = 3.0, 11.1 Hz, 1H), 3.56 (dd, J = 1.4, 11.3 Hz, 1H), 3.70 (dd, J = 3.5, 11.4 Hz, 1H), 3.81−3.95 (m, 6H), 3.92 (s, 3H), 3.94 (s, 3H), 3.95−3.98 (m, 1H), 4.00−4.09 (m, 4H), 4.18 (t, J = 9.8 Hz, 1H), 4.20 (d, J = 11.9 Hz, 1H), 4.37 (t, J = 2.4 Hz, 1H), 4.47 (d, J = 11.0 Hz, 1H), 4.57−4.73 (m, 12H), 4.76 (d, J = 10.9 Hz, 1H), 4.79 (d, J = 12.2 Hz, 1H), 4.85 (d, J = 11.0 Hz, 1H), 4.91, 4.91, 4.92 (3 × overlapping d, J = 10.5, 10.7, 11.0 Hz, 3H), 5.09 (dq, J = 10.4, 1.2 Hz, 1H), 5.21 (dq, J = 17.1, 1.5 Hz, 1H), 5.23 (d, J = 1.5 Hz, 1H), 5.52 (d, J = 1.8 Hz, 1H), 5.72 (dddd, J = 5.6, 5.6, 10.8, 17.1 Hz, 1H), 6.94 (d, J = 8.3 Hz, 1H), 7.05 (d, J = 2.1 Hz, 1H), 7.07−7.13 (m, 5H), 7.14−7.39 (m, 43H), 7.42 (d, J = 8.1 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ −5.3, −5.1, 18.4, 26.0, 56.0, 56.1, 62.4, 68.6, 69.8, 71.0, 71.8, 71.9, 72.3, 72.4, 72.5, 72.8, 73.3, 74.4, 74.8, 74.9, 75.0, 75.2, 75.6, 75.7, 76.0, 76.1, 79.06, 79.11, 80.2, 81.4, 81.6, 82.0, 98.3, 98.7, 110.4, 111.5, 117.9, 119.4, 126.8, 127.26, 127.29, 127.34, 127.36, 127.41, 127.46, 127.51, 127.54, 127.60, 127.63, 127.82, 127.84, 127.87, 127.94, 127.97, 128.03, 128.07, 128.12, 128.15, 128.20, 128.23, 128.24, 128.25, 128.27, 128.32, 128.4, 128.5, 133.9, 134.0, 136.7, 138.1, 138.5, 138.56, 138.6, 138.62, 138.8, 138.9, 139.2, 139.3, 140.2, 148.7, 149.2; HRMS-ESI $[M + Na]^+$ calcd for $C_{105}H_{118}NaO_{18}Si$ 1717.7980, found 1717.8070.

1-*O*-Allyl-4,5-di-*O*-benzyl-3-*O*-(4-(3,4-dimethoxyphenyl)-benzyl)-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-2-*O*-(2,3,4-tri-*O*-benzyl-α-D-mannopyranosyl)-D-*myo*-inositol (38). Acetyl chloride (0.30 mL, 4.22 mmol) was added to a solution of **37** (0.417 g, 0.246 mmol) in CH_2Cl_2/MeOH (3:7, 20 mL) and the mixture stirred at rt for 1 h. The reaction mixture was diluted with CH_2Cl_2 (40 mL) and washed with H_2O (40 mL). The aqueous layer was re-extracted with CH_2Cl_2 (2 × 20 mL), the combined organic layers were washed with saturated NaCl (40 mL), dried ($MgSO_4$), filtered, and the solvent was removed in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:2 to 1:1) to give the *title compound* **38** (0.226 g, 92%) as a white foam: $[\alpha]_D^{21}$ +39.1 (c = 1.60, $CHCl_3$); ν_{max} (ATR-IR) 3483, 3062, 3029, 2925, 2864, 1604, 1588, 1526, 1498, 1453, 1397, 1361, 1250, 1216, 1171, 1067, 1025 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.84 (brs, 1H), 3.17 (dd, J = 2.0, 9.7 Hz, 1H), 3.25 (t, J = 9.4 Hz, 1H), 3.28 (dd, J = 1.4, 11.0 Hz, 1H), 3.31 (dd, J = 2.5, 10.0 Hz, 1H), 3.38 (dd, J = 3.0, 11.2 Hz, 1H), 3.59−3.63 (m, 2H), 3.80−3.82 (m, 1H), 3.82 (t, J = 9.6 Hz, 1H), 3.85−3.94 (m, 4H), 3.93 (s, 6H), 3.95−4.04 (m, 4H), 4.07 (dt, J = 3.1, 9.6 Hz, 1H), 4.18 (t, J = 9.8 Hz, 1H), 4.19 (d, J = 11.9 Hz, 1H), 4.27 (t, J = 2.2 Hz, 1H), 4.47 (d, J = 11.0 Hz, 1H), 4.57 (d, J = 11.9 Hz, 1H), 4.59−4.80 (m, 13H), 4.85 (d, J = 11.0 Hz, 1H), 4.89−4.95 (m, 3H), 5.12 (dq, J = 10.4, 1.4 Hz, 1H), 5.17 (d, J = 1.5 Hz, 1H), 5.23 (dq, J = 17.2, 1.6 Hz, 1H), 5.51 (d, J = 1.9 Hz, 1H), 5.74 (dddd, J = 5.4, 5.6, 10.4, 17.1 Hz, 1H), 6.94 (d, J = 8.4 Hz, 1H), 7.06 (d, J = 2.0 Hz, 1H), 7.07−7.12 (m, 5H), 7.14−7.39 (m, 43H), 7.43 (d, J = 8.2 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 56.0, 56.1, 62.2, 68.6, 71.1, 71.3, 71.8, 71.9, 72.1, 72.2, 72.3, 72.4, 72.9, 73.3, 74.5, 74.8, 74.9, 75.0, 75.1, 75.6, 75.7, 75.9, 76.1, 78.8, 78.9, 80.2, 81.4, 81.5, 81.7, 98.7, 99.1, 110.4, 111.5, 117.8, 119.4, 126.8, 127.26, 127.29, 127.37, 127.44, 127.47, 127.49, 127.57, 127.61, 127.65, 127.67, 127.69, 127.83, 127.84, 127.88, 127.93, 128.01, 128.06, 128.11, 128.13, 128.15, 128.17, 128.19, 128.2, 128.3, 128.38, 128.4, 128.5, 133.8, 133.9, 136.4, 138.0, 138.28, 138.30, 138.5, 138.6, 138.68, 138.74, 138.8, 139.1, 140.4, 148.7, 149.2; HRMS-ESI $[M + Na]^+$ calcd for $C_{99}H_{104}NaO_{18}$ 1603.7115, found 1603.7135. Anal. Calcd for $C_{99}H_{104}O_{18}.H_2O$: C, 71.89; H, 6.83. Found: C, 71.57; H, 6.55.

1-*O*-Allyl-4,5-di-*O*-benzyl-3-*O*-(4-(3,4-dimethoxyphenyl)-benzyl)-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-2-*O*-(2,3,4-tri-*O*-benzyl-6-*O*-hexadecanoyl-α-D-mannopyranosyl)-D-*myo*-inositol (39). To a solution of alcohol **38** (0.50 g, 0.316 mmol) in anhydrous CH_2Cl_2 (20 mL) were added palmitic acid (0.324 g, 1.26 mmol), DMAP (0.154 g, 1.26 mmol), and DCC (0.261 g, 1.26 mmol). The reaction mixture was stirred at rt overnight and the solvent removed in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:9 to 1:2) to give the

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title compound **39** (0.295 g, 93%) as a colorless oil: $[\alpha]_D^{27}$ +35.0 (*c* = 1.07, $CHCl_3$); ν_{max} (ATR-IR) 3029, 2923, 2853, 1733, 1604, 1587, 1526, 1499, 1454, 1360, 1250, 1216, 1171, 1091, 1054, 1026 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, *J* = 7.0 Hz, 3H), 1.18−1.32 (m, 24H), 1.52−1.58 (m, 2H), 2.24 (t, *J* = 7.6 Hz, 2H), 3.17 (dd, *J* = 1.9, 9.7 Hz, 1H), 3.25 (t, *J* = 9.4 Hz, 1H), 3.27 (dd, *J* = 1.6, 11.3 Hz, 1H), 3.31 (dd, *J* = 2.6, 10.0 Hz, 1H), 3.38 (dd, *J* = 2.9, 11.2 Hz, 1H), 3.77−3.82 (m, 2H), 3.84−3.92 (m, 4H), 3.93 (s, 3H), 3.94 (s, 3H), 3.95−4.04 (m, 4H), 4.07 (dd, *J* = 1.7, 12.0 Hz, 1H), 4.16−4.24 (m, 4H), 4.30 (t, *J* = 2.1 Hz, 1H), 4.46 (d, *J* = 11.0 Hz, 1H), 4.51 (d, *J* = 10.8 Hz, 1H), 4.56, 4.57 (2 × overlapping d, *J* = 11.6, 11.9 Hz, 2H), 4.61−4.75 (m, 10H), 4.78 (d, *J* = 10.8 Hz, 1H), 4.85 (d, *J* = 11.0 Hz, 1H), 4.89−4.94 (m, 3H), 5.09 (dq, *J* = 10.5, 1.3 Hz, 1H), 5.21 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.21 (d, *J* = 1.2 Hz, 1H), 5.52 (d, *J* = 1.8 Hz, 1H), 5.71 (dddd, *J* = 5.5, 5.6, 10.7, 17.0 Hz, 1H), 6.94 (d, *J* = 8.0 Hz, 1H), 7.05−7.12 (m, 6H), 7.14−7.38 (m, 43H), 7.43 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.2, 22.8, 24.9, 29.27, 29.34, 29.4, 29.6, 29.69, 29.72, 29.75, 29.76, 32.0, 34.3, 56.02, 56.06, 63.1, 68.6, 70.2, 71.2, 71.4, 71.5, 72.0, 72.1, 72.3, 72.4, 72.5, 73.3, 74.1, 74.5, 74.8, 75.0, 75.2, 75.6, 75.7, 75.9, 76.1, 78.5, 78.8, 80.2, 81.4, 81.5, 81.8, 98.7, 98.8, 110.6, 111.5, 117.9, 119.4, 127.0, 127.28, 127.3, 127.38, 127.46, 127.49, 127.51, 127.55, 127.59, 127.63, 127.68, 127.75, 127.78, 127.85, 127.98, 128.0, 128.1, 128.13, 128.16, 128.2, 128.25, 128.3, 128.33, 128.34, 128.36, 128.4, 128.6, 133.9, 134.0, 136.3, 138.0, 138.2, 138.3, 138.5, 138.57, 138.58, 138.76, 138.82, 139.1, 140.6, 148.7, 149.2, 173.7; HRMS-ESI $[M + Na]^+$ calcd for $C_{115}H_{134}NaO_{19}$ 1841.9412, found 1841.9352.

1-*O*-Allyl-4,5-di-*O*-benzyl-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-2-*O*-(2,3,4-tri-*O*-benzyl-6-*O*-hexadecanoyl-α-D-mannopyranosyl)-D-*myo*-inositol (41). Inositol compound **39** (0.260 g, 0.143 mmol) and scavenger **40**[51] (0.194 g, 1.43 mmol) were dissolved in CH_2Cl_2 (10.5 mL). To the solution was added TFA (4.5 mL, 30% TFA solution in relation to reaction solvent), and the reaction was stirred at rt for 1 h. The reaction was quenched with aq $NaHCO_3$ (20 mL) and extracted into CH_2Cl_2 (3 × 30 mL). The combined organic layers were washed with H_2O (20 mL), saturated NaCl (20 mL), dried ($MgSO_4$), and filtered, and the solvent was removed in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:4 to 1:2) to give the *title compound* **41** (0.168 g, 74%) as a colorless oil: $[\alpha]_D^{30}$ +17.7 (*c* = 1.19, $CHCl_3$); ν_{max} (ATR-IR) 3479, 3063, 3030, 2922, 2852, 1734, 1604, 1496, 1453, 1360, 1250, 1208, 1091, 1055, 1027 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, *J* = 6.9 Hz, 3H), 1.17−1.33 (m, 24H), 1.52−1.60 (m, 2H), 2.10 (d, *J* = 3.0 Hz, 1H), 2.29 (t, *J* = 6.7 Hz, 2H), 3.23 (dd, *J* = 2.2, 9.7 Hz, 1H), 3.25 (t, *J* = 9.4 Hz, 1H), 3.33 (dd, *J* = 1.5, 11.1 Hz, 1H), 3.36−3.41 (m, 2H), 3.57 (t, *J* = 9.6 Hz, 1H), 3.80 (dd, *J* = 3.0, 9.1 Hz, 1H), 3.82−3.93 (m, 4H), 3.94−4.02 (m, 5H), 4.12 (t, *J* = 2.4 Hz, 1H), 4.17 (t, *J* = 9.7 Hz, 1H), 4.19−4.23 (m, 2H), 4.29 (dd, *J* = 4.8, 12.0 Hz, 1H), 4.46 (d, *J* = 11.0 Hz, 1H), 4.54 (d, *J* = 10.6 Hz, 1H), 4.58 (d, *J* = 11.9 Hz, 2H), 4.64−4.75 (m, 9H), 4.81 (d, *J* = 11.1 Hz, 1H), 4.85, 4.86 (2 × overlapping d, *J* = 11.0, 10.7 Hz, 2H), 4.93 (d, *J* = 10.6 Hz, 1H), 5.03 (d, *J* = 1.7 Hz, 1H), 5.10 (dq, *J* = 10.4, 1.2 Hz, 1H), 5.22 (dq, *J* = 17.2, 1.5 Hz, 1H), 5.54 (d, *J* = 1.6 Hz, 1H), 5.70 (dddd, *J* = 5.5, 5.5, 10.8, 17.0 Hz, 1H), 7.07−7.39 (m, 45H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.2, 22.8, 24.9, 29.1, 29.3, 29.36, 29.43, 29.6, 29.69, 29.73, 29.74, 29.76, 29.77, 32.0, 34.3, 63.4, 68.7, 70.6, 70.92, 70.94, 71.7, 72.0, 72.3, 72.4, 72.7, 73.3, 74.4, 74.7, 74.8, 74.9, 75.27, 75.3, 75.5, 75.6, 75.99, 76.02, 78.9, 80.2, 81.2, 81.7, 81.8, 98.7, 99.6, 117.8, 127.27, 127.31, 127.4, 127.49, 127.51, 127.53, 127.62, 127.66, 127.81, 127.82, 127.84, 127.86, 128.01, 128.09, 128.13, 128.18, 128.20, 128.25, 128.26, 128.34, 128.37, 128.39, 128.5, 128.6, 128.8, 134.0, 138.0, 138.1, 138.2, 138.3, 138.4, 138.6, 138.7, 138.8, 139.1, 173.8; HRMS-ESI $[M + Na]^+$ calcd for $C_{100}H_{120}NaO_{17}$ 1615.8418, found 1615.8481.

1-*O*-Allyl-4,5-di-*O*-benzyl-3-*O*-octadecanoyl-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-2-*O*-(2,3,4-tri-*O*-benzyl-6-*O*-hexadecanoyl-α-D-mannopyranosyl)-D-*myo*-inositol (42). To a solution of alcohol **41** (0.092 g, 0.058 mmol) in anhydrous CH_2Cl_2 (2 mL) were added stearic acid (0.066 g, 0.231 mmol), DMAP (0.028 g, 0.231 mmol), and DCC (0.048 g, 0.231 mmol). The reaction mixture was stirred at rt overnight and the solvent removed in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:9 to 1:6) to give the *title compound* **42** (0.049 g, 84%) as a colorless oil: $[\alpha]_D^{28}$ +26.9 (*c* = 1.15, $CHCl_3$); ν_{max} (ATR-IR) 3063, 3030, 2922, 2852, 1737, 1605, 1496, 1454, 1360, 1207, 1093, 1048, 1027 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, *J* = 7.0 Hz, 6H), 1.13−1.32 (m, 52H), 1.41−1.49 (m, 2H), 1.56−1.63 (m, 2H), 1.99 (dt, *J* = 7.6, 16.4 Hz, 1H), 2.12 (dt, *J* = 7.7, 16.4 Hz, 1H), 2.28 (t, *J* = 7.2 Hz, 2H), 3.30−3.35 (m, 3H), 3.43 (dd, *J* = 3.1, 11.2 Hz, 1H), 3.79 (dd, *J* = 9.3, 10.4 Hz, 1H), 3.83 (dd, *J* = 2.0, 2.9 Hz, 1H), 3.84−3.90 (m, 3H), 3.90−3.96 (m, 3H), 3.97−4.05 (m, 3H), 4.15 (dd, *J* = 1.9, 11.8 Hz, 1H), 4.17−4.23 (m, 3H), 4.36 (dd, *J* = 4.3, 11.8 Hz, 1H), 4.48 (d, *J* = 11.0 Hz, 1H), 4.52−4.76 (m, 13H), 4.79 (dd, *J* = 2.7, 10.5 Hz, 1H), 4.83 (d, *J* = 10.5 Hz, 1H), 4.87 (d, *J* = 11.0 Hz, 1H), 4.96 (d, *J* = 10.7 Hz, 1H), 5.11 (dq, *J* = 10.5, 1.3 Hz, 1H), 5.19 (d, *J* = 1.8 Hz, 1H), 5.22 (dq, *J* = 17.3, 1.6 Hz, 1H), 5.54 (d, *J* = 1.8 Hz, 1H), 5.70 (dddd, *J* = 5.6, 5.6, 10.6, 17.1 Hz, 1H), 7.03−7.39 (m, 45H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.2, 22.8, 24.7, 24.9, 29.2, 29.3, 29.38, 29.41, 29.44, 29.5, 29.6, 29.71, 29.73, 29.74, 29.75, 29.77, 29.78, 29.79, 29.80, 32.0, 34.1, 34.2, 63.1, 68.7, 70.5, 71.1, 71.4, 71.5, 71.6, 72.0, 72.3, 72.5, 72.6, 73.3, 74.1, 74.2, 74.8, 75.0, 75.4, 75.49, 75.52, 76.3, 78.7, 79.6, 80.1, 81.5, 81.6, 98.2, 98.7, 118.2, 127.29, 127.32, 127.4, 127.53, 127.54, 127.57, 127.65, 127.69, 127.81, 127.83, 127.86, 128.14, 128.18, 128.21, 128.23, 128.25, 128.27, 128.36, 128.4, 128.41, 128.5, 128.6, 133.7, 137.8, 138.07, 138.14, 138.18, 138.4, 138.6, 138.7, 138.8, 139.1, 173.1, 173.7; HRMS-ESI $[M + Na]^+$ calcd for $C_{118}H_{154}NaO_{18}$ 1882.1027, found 1882.0917.

4,5-Di-*O*-benzyl-3-*O*-octadecanoyl-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-2-*O*-(2,3,4-tri-*O*-benzyl-6-*O*-hexadecanoyl-α-D-mannopyranosyl)-D-*myo*-inositol (43). (1,5-Cyclooctadiene)bis(methyldiphenylphosphine)iridium(I) hexafluorophosphate (6 mg, 7 μmol) was added to a stirred solution of allyl ether **42** (85 mg, 0.046 mmol) in dry THF (5 mL) at rt under an atmosphere of argon. The argon atmosphere was replaced with H_2 for ca. 1 min, followed by a gentle stream of argon being passed over the reaction. The reaction mixture was stirred for 2 h, the solvent removed in vacuo, and the residue dissolved in acetone/H_2O (9:1, 10 mL). To the solution were added mercury(II) chloride (0.025 g, 0.091 mmol) and mercury(II) oxide (0.024 g, 0.110 mmol), and the resulting solution was then heated at 100 °C for 3 h. Once cooled to rt, the reaction mixture was filtered through Celite and washed with CH_2Cl_2 (50 mL) and the solvent removed in vacuo. The residue was dissolved in CH_2Cl_2 (30 mL), washed with 5% aq KI (10 mL), dried ($MgSO_4$), and filtered and the solvent evaporated. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:9 to 1:4) to give the *title compound* **43** (0.051 g, 61%) as a colorless oil: $[\alpha]_D^{31}$ +32.6 (*c* = 1.54, $CHCl_3$); ν_{max} (ATR-IR) 3470, 3063, 3030, 2922, 2852, 1737, 1605, 1496, 1454, 1360, 1207, 1092, 1048, 1027 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, *J* = 6.6 Hz, 6H), 1.14−1.35 (m, 52H), 1.45−1.52 (m, 2H), 1.55−1.63 (m, 2H), 2.06 (dt, *J* = 7.6, 16.2 Hz, 1H), 2.17 (dt, *J* = 7.6, 16.2 Hz, 1H), 2.30 (t, *J* = 7.6 Hz, 2H), 3.32 (t, *J* = 9.2 Hz, 1H), 3.46 (dd, *J* = 7.1, 10.0 Hz, 1H), 3.58 (d, *J* = 4.9 Hz, 1H), 3.62 (dd, *J* = 1.8, 10.0 Hz, 1H), 3.72−3.87 (m, 7H), 3.89−3.97 (m, 3H), 4.04 (t, *J* = 2.5 Hz, 1H), 4.11−4.14 (m, 1H), 4.16 (dd, *J* = 1.7, 11.7 Hz, 1H), 4.34 (d, *J* = 10.7 Hz, 1H), 4.38 (d, *J* = 11.6 Hz, 1H), 4.40 (dd, *J* = 3.8, 11.6 Hz, 1H), 4.46−4.65 (m, 12H), 4.70 (d, *J* = 11.7 Hz, 1H), 4.72 (d, *J* = 12.9 Hz, 1H), 4.78 (dd, *J* = 2.7, 10.6 Hz, 1H), 4.83 (d, *J* = 11.3 Hz, 1H), 4.94 (d, *J* = 10.7 Hz, 1H), 5.22 (d, *J* = 2.3 Hz, 1H), 5.32 (d, *J* = 1.7 Hz, 1H), 7.16−7.39 (m, 45H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.2, 22.7, 24.8, 25.0, 29.25, 29.32, 29.39, 29.4, 29.5, 29.6, 29.7, 29.78, 29.8, 32.0, 34.21, 34.25, 63.1, 69.6, 70.3, 70.9, 71.48, 71.51, 71.8, 72.1, 72.2, 72.7, 73.5, 73.9, 74.3, 74.6, 75.0, 75.2, 75.3, 75.5, 76.8, 78.6, 79.4, 80.2, 80.4, 95.7, 98.7, 127.57, 127.60, 127.65, 127.72, 127.74, 127.8, 127.86, 127.99, 128.01, 128.07, 128.11, 128.19, 128.28, 128.32, 128.37, 128.40, 128.42, 128.44, 128.46, 128.5, 128.6, 137.62, 138.0, 138.16, 138.17, 138.27, 138.33, 138.42, 138.43, 138.45, 173.0, 173.8; HRMS-ESI $[M + Na]^+$ calcd for $C_{115}H_{150}NaO_{18}$ 1842.0714, found 1842.0754.

Triethylammonium 4,5-Di-*O*-benzyl-3-*O*-octadecanoyl-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-2-*O*-(2,3,4-tri-*O*-

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benzyl-6-*O*-hexadecanoyl-α-D-mannopyranosyl)-1-*O*-(1-*O*-((*R*)-10-methyloctadecanoyl)-2-*O*-hexadecanoyl-*sn*-glycero-3-phosphoryl)-D-*myo*-inositol (44). Alcohol **43** (0.060 g, 0.033 mmol) and *H*-phosphonate **6** (0.128 g, 0.165 mmol) were coevaporated with pyridine (3 × 5 mL) and then dried under high vacuum for 30 min. The residue was dissolved in dry distilled pyridine (4 mL) at rt under argon. Pivaloyl chloride (0.057 mL, 0.461 mmol) was added in one portion, and the reaction mixture was stirred at rt for 3 h. A freshly prepared solution of iodine (0.084 g, 0.330 mmol) in pyridine/H_2O (9:1, 10 mL) was added, and the mixture was stirred for 1 h. The solution was diluted with $CHCl_3$ (20 mL), stirred for 15 min, then washed with 10% aq $Na_2S_2O_3$ solution (30 mL). The aqueous layer was re-extracted with $CHCl_3$ (2 × 20 mL), and the combined organic layers were washed with TEAB buffer (1 M, 3 × 20 mL). The solution was dried ($MgSO_4$) and filtered and the solvent removed in vacuo. The residue was purified by column chromatography on silica gel (CH_2Cl_2/Et_3N/MeOH = 99:1:0 to 98:1:1) to give the *title compound* **44** (0.074 g, 87%) as a colorless oil: $[\alpha]_D^{17}$ +9.5 (*c* = 1.15, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.83 (d, *J* = 6.6 Hz, 3H), 0.88 (t, *J* = 7.0 Hz, 12H), 1.03−1.33 (m, 112H), 1.40−1.59 (m, 8H), 1.97 (dt, *J* = 7.6, 16.3 Hz, 1H), 2.09 (dt, *J* = 7.5, 16.2 Hz, 1H), 2.18 (t, *J* = 7.5 Hz, 4H), 2.25 (t, *J* = 7.6 Hz, 2H), 2.87−2.94 (m, 6H), 3.34−3.46 (m, 3H), 3.77 (t, *J* = 9.9 Hz, 1H), 3.85 (dd, *J* = 3.0, 9.4 Hz, 1H), 3.88−3.92 (m, 1H), 3.94−4.36 (m, 15H), 4.39−4.88 (m, 18H), 4.96 (d, *J* = 10.8 Hz, 1H), 5.14−5.19 (m, 1H), 5.50 (s, 1H), 5.71 (s, 1H), 7.01−7.47 (m, 45H), 12.17 (brs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 8.5, 14.2, 19.8, 22.8, 24.78, 24.89, 24.94, 24.97, 27.2, 29.19, 29.24, 29.35, 29.44, 29.55, 29.64, 29.67, 29.74, 29.79, 30.1, 32.0, 32.9, 34.0, 34.1, 34.21, 34.23, 37.2, 45.5, 52.8, 62.4, 63.0, 64.5, 64.55, 69.0, 70.35, 70.39, 70.6, 71.0, 71.58, 71.66, 71.69, 71.9, 72.0, 72.4, 73.2, 73.4, 74.0, 74.7, 74.8, 75.2, 75.3, 75.48, 75.54, 76.4, 76.5, 78.4, 79.5, 81.5, 98.2, 98.4, 127.1, 127.2, 127.3, 127.51, 127.58, 127.68, 127.7, 127.8, 127.9, 128.1, 128.16, 128.19, 128.26, 128.37, 128.41, 128.6, 137.9, 138.1, 138.31, 138.33, 138.6, 138.75, 138.8, 139.24, 139.25, 172.8, 173.1, 173.4, 173.7; ^{31}P NMR (202 MHz, $CDCl_3$) δ −1.20; HRMS-ESI [M − Et_3HN]$^-$ calcd for $C_{153}H_{222}O_{25}P$ 2490.5838, found 2490.5854.

Sodium 3-*O*-Octadecanoyl-6-*O*-α-D-mannopyranosyl-2-*O*-(6-*O*-hexadecanoyl-α-D-mannopyranosyl)-1-*O*-(1-*O*-((*R*)-10-methyloctadecanoyl)-2-*O*-hexadecanoyl-*sn*-glycero-3-phosphoryl)-D-*myo*-inositol (3b). A solution of triethylammonium salt **44** (0.017 g, 6.55 μmol) in $CHCl_3$/MeOH (1:1, 10 mL) was stirred in the presence of Dowex 50WX4-400 (Na^+) resin for 3 h. The resin was filtered off, and the solvent was removed in vacuo. The residue was purified by column chromatography on silica gel (MeOH/CH_2Cl_2 = 1:99 to 3:97). The residue was dissolved in THF/MeOH (2:3, 5 mL), $Pd(OH)_2$/C (20%, 20 mg) was added, and the reaction mixture was stirred under an atmosphere of H_2 for 2 h at rt. The solution was then filtered through Celite and washed with $CHCl_3$/MeOH/H_2O (70:40:6, 3 × 30 mL) and the solvents removed in vacuo. The residue was purified by column chromatography on silica gel ($CHCl_3$/MeOH/H_2O = 70:40:0 to 70:40:2) to give the *title compound* **3b** (0.011 g, 99%, 96% pure by HPLC) as a white solid: ^{1}H NMR (500 MHz, $CDCl_3$/CD_3OD/D_2O = 70:40:6) δ 0.80 (d, *J* = 6.6 Hz, 3H), 0.84 (t, *J* = 6.9 Hz, 12H), 1.18−1.31 (m, 103H), 1.51−1.62 (m, 8H), 2.24−2.42 (m, 8H), 3.32 (t, *J* = 9.3 Hz, 1H), 3.63 (t, *J* = 9.7 Hz, 2H), 3.69−3.80 (m, 6H), 3.91−4.01 (m, 5H), 4.07−4.27 (m, 5H), 4.32 (dd, *J* = 5.0, 11.9 Hz, 1H), 4.37 (dd, *J* = 2.7, 12.1 Hz, 1H), 4.70 (dd, *J* = 2.3, 10.4 Hz, 1H), 5.05 (s, 1H), 5.07 (s, 1H), 5.17−5.22 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$:CD_3OD:D_2O = 70:40:6) δ 13.4, 19.1, 22.2, 24.35, 24.36, 24.4, 24.5, 26.6, 26.7, 28.72, 28.77, 28.83, 28.86, 28.87, 28.87, 28.88, 28.9, 29.0, 29.04, 29.11, 29.14, 29.17, 29.18, 29.19, 29.23, 29.25, 29.26, 29.28, 29.29, 29.5, 29.6, 31.4, 31.5, 32.3, 33.5, 33.6, 33.65, 33.66, 36.6, 36.7, 60.7, 62.4, 63.11, 63.14, 63.4, 66.5, 66.8, 69.7, 70.0, 70.1, 70.18, 70.24, 70.4, 70.6, 71.3, 72.5, 72.8, 75.8, 76.27, 76.33, 78.3, 101.2, 101.3, 173.2, 173.4, 173.7, 174.2; ^{31}P NMR (202 MHz, $CDCl_3$/CD_3OD/D_2O = 70:40:6) δ −0.57; HRMS-ESI [M + Na]$^+$ calcd for $C_{90}H_{168}Na_2O_{25}P$ 1726.1402, found 1726.1412; HRMS-ESI [M − Na]$^-$ calcd for $C_{90}H_{168}O_{25}P$ 1680.1618, found 1680.1652.

■ ASSOCIATED CONTENT

Supporting Information

Full experimental procedures and characterizations of prepared compounds and copies of ^{1}H and ^{13}C NMR spectra for all novel compounds. Mass spectra and HPLC chromatograms for compounds **4**, **1**, **2a**, and **3b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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