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Synthesis and Structure of Phosphatidylinositol Dimannoside

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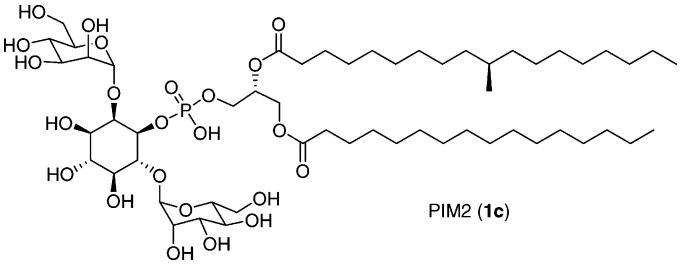

PIM2 (**1c**)

(*R*)-Tuberculostearic acid (**2**) was synthesized in seven steps from (*S*)-citronellol (**5**). The carbon chain of **2** was assembled by copper-catalyzed cross coupling of (*S*)-citronellol tosylate (**6**) and hexylmagnesium bromide; subsequent ozonolysis and reaction with 6-benzyloxyhexylmagnesium bromide furnished alcohol **10**. Functional group manipulation afforded (*R*)-**2** in 49% overall yield from **5**. DCC coupling of (*R*)-**2** with 3-*O*-benzyl-1-*O*-palmitoyl-*sn*-glycerol (**16**), followed by hydrogenolytic removal of the benzyl group and treatment with benzyl bis(diisopropyl)phosphoramidite, afforded phosphoramidite **20**. Tetrazole-mediated coupling of **20** with PIM1 head group **21** gave **22**, and subsequent debenzylation afforded phosphatidylinositol mono-mannoside, PIM1 (**23**). Similarly, coupling of **20** and **24** and removal of the benzyl protecting groups gave PIM2 (**1c**). Both **23** and **1c** have a clearly defined acylation pattern, which was confirmed by mass spectrometry, with *sn*-1 palmitoyl and *sn*-2 tuberculostearoyl groups on the glycerol moiety. Both **23** and **1c** were shown to modulate the release of the pro-inflammatory cytokine, IL-12, in a dendritic cell assay.

Introduction

Phosphatidylinositol mannosides (PIMs), present in the cell walls of mycobacteria, are attracting a great deal of attention as they elicit a range of immune responses and constitute the biosynthetic precursors of lipomannan and lipoarabinomannan. PIMs act as agonists of Toll-like receptor 2 (TLR2), which is involved with innate immunity.[1,2] They are also known to recruit natural killer T-cells[1,3] and cause T-cell expansion via binding to the lipid presentation molecule, CD1b.[1,4,5] As part of an ongoing program investigating the potential of PIMs for modulating immune responses we recently reported the syntheses of diacylated phosphatidylinositol mannosides, PIM1, PIM2, and PIM4.[6,7] Mixtures of PIMs isolated from *Mycobacterium bovis* and synthetic PIM1 and PIM2 **1a**, which contain the stearoyl acyl residue, were shown to suppress the recruitment of eosinophils in a mouse model of allergic asthma.[6,8] Synthetic PIM2 **1b** and PIM4, containing palmitoyl residues, were shown

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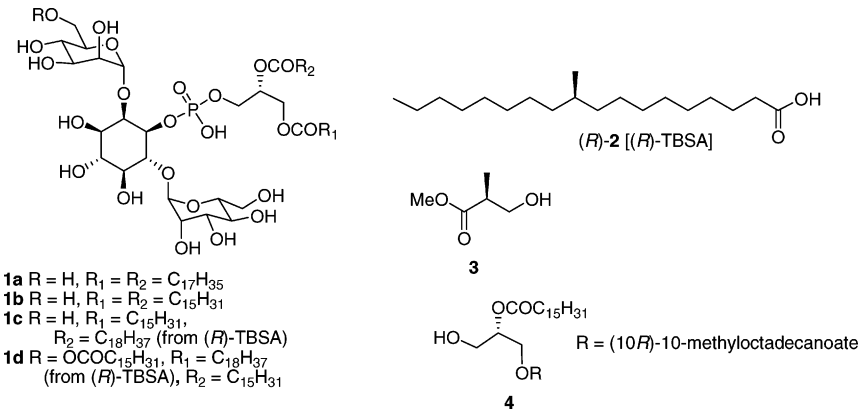

1a R = H, $R_1 = R_2 = C_{17}H_{35}$
1b R = H, $R_1 = R_2 = C_{15}H_{31}$
1c R = H, $R_1 = C_{15}H_{31}$, $R_2 = C_{18}H_{37}$ (from (*R*)-TBSA)
1d R = $OCOC_{15}H_{31}$, $R_1 = C_{18}H_{37}$ (from (*R*)-TBSA), $R_2 = C_{15}H_{31}$

to be effective in inducing IFN-γ production when given as an adjuvant with a model antigen in an in vivo system.[7] Structure−activity relationships of PIMs are complicated by the fact that these molecules exist in nature in multiacylated forms, and obtaining single entities from cell wall material is challenging. Although structures of the pseudo-oligosaccharide moieties of PIMs have been well established,[9−11] those of the diacyl-glyceryl component are still unclear. Gilleron et al.[1] carried out a comprehensive study of this unit of PIMs from *Mycobacterium bovis* Bacilluss Calmette Guérin using negative-ion ESI-MS/MS mass spectrometry to elucidate the acylation pattern. The specific location of these acyl groups was deduced on the basis of work by Hsu and Turk,[12] who showed that loss of a fatty acid at the *sn*-2 position occurs more readily than that at the *sn*-1 position of deprotonated molecular ions of phosphatidylinositols. Gilleron et al.[1] concluded from their mass spectral data that PIM2 existed as a 62:38 mixture of two compounds with differing acylation patterns. The major form **1c** contained a palmitate residue at the *sn*-1 position of the glycerol unit and an (*R*)-tuberculostearate (TBSA) residue at the *sn*-2 position. The minor form **1b** possessed palmitate residues at both of these sites. The glyceryl moieties of tri- and tetra-acylated PIM2 species were shown to have palmitate at the *sn*-1 and tuberculostearate at the *sn*-2 positions only. In a later paper, Gilleron et al.[2] depicted a structure of the hexa-mannoside, AcPIM6. In this case they showed the tuberculostearate residue at the *sn*-1 and palmitate at the *sn*-2 positions of the glycerol unit.

Liu et al.[13] recently reported the total synthesis of "native" AcPIM2 and AcPIM6 based upon the later structural assignment of Gilleron et al.[2] They synthesized (*R*)-tuberculostearic acid (TBSA, **2**) from the Roche ester **3** and prepared differentially acylated diacylglycerol **4**. Glycerol **4** was coupled to protected PIM head groups to furnish AcPIM2 **1d** and AcPIM6. In this paper, we report an alternative synthesis of (*R*)-TBSA (**2**) from (*S*)-citronellol (**5**), the regioisomer of **4** and PIM2 **1c**, where the acylation pattern is consistent with the 2001 findings of Gilleron et al.[1] We aim to gain insight into the structures of these natural products.

Discussion

Several syntheses of racemic and two of enantiopure (*R*)-tuberculostearic acid (**2**) have been reported to date.[13−17] The elegant synthesis of (*R*)-**2**, by Liu et al.,[13] relied on building up the carbon chain from a derivative of Roche ester **3** by copper-catalyzed cross-coupling reactions. Our approach is somewhat similar and builds upon the work of Djerassi and co-workers,[18] who reported the synthesis of 10-methylhexadecanoic acid from citronellol. In our synthesis (Scheme 1) commercially available (*S*)-citronellol (**5**) was tosylated to give **6**,[19] which was then coupled with hexylmagnesium bromide catalyzed by dilithium copper tetrachloride to give hydrocarbon **7** (Scheme 1). Due to difficulties in separating **7** from dodecane produced from the Grignard homocoupling reaction the mixture was used as is for subsequent reaction. Ozonolysis of the alkene furnished aldehyde **8** in 88% from tosylate **6**. Attempts to extend the carbon chain of **8** using Wittig chemistry proved low yielding, and cross coupling with Grignard reagent **9** after reduction and subsequent tosylation of **8** failed. Thus, aldehyde **8** was directly reacted with Grignard reagent **9** to give the secondary alcohol **10** as a mixture of epimers in 78% yield. Tosylation of **10** gave **11**, and subsequent elimination on alumina furnished a mixture of alkenes **12**. Simultaneous removal of the alkene and benzyl group was achieved by treatment with hydrogen to give the known alcohol **13**[13] in 58% yield from **10**. Oxidation of **13** with acidified potassium permanganate under phase-transfer conditions afforded (*R*)-tuberculostearic acid (**2**) in 98% yield.

With tuberculostearic acid in hand our attention turned to synthesis of the diacylated glycerol derivative. We felt that the most efficient method to prepare a protected diacyl glycerol derivative was via nucleophilic opening of benzyl glycidol by a carboxylate salt.[20] This was achieved from (*R*)-benzyl glycidol (**14**), which is readily available by hydrokinetic resolution of (*rac*)-**14**[21,22] using Jacobsen's methodology.[23] The resolution of **14**, using catalyst (*S*,*S*)-**15** (Schaus et al.[23] reported that the

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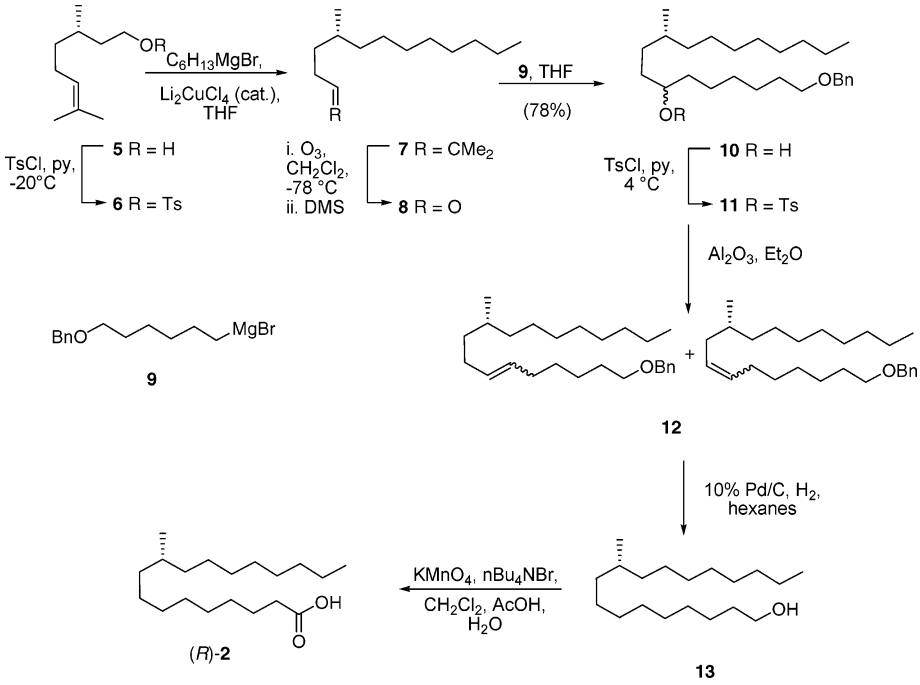
SCHEME 1. Synthesis of (*R*)-Tuberculostearic acid (2)

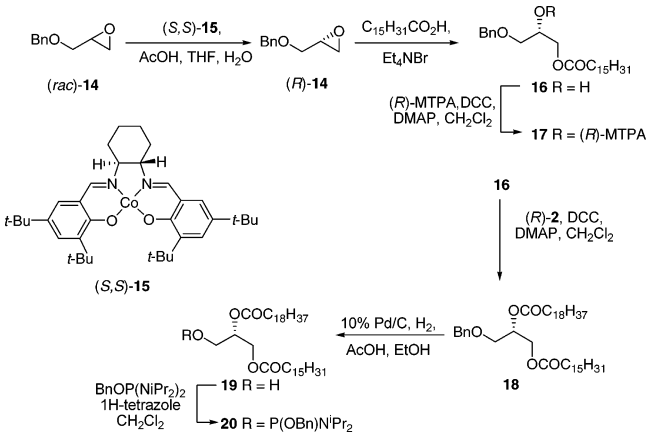


hydrokinetic resolution of **14** with (*R*,*R*)-**15** gave (*R*)-benzyl glycidol), afforded (*R*)-**14**, which had an optical rotation consistent with that reported by Mikkilineni et al.[24] and also that of a commercial sample (Aldrich). Reaction of (*R*)-**14** with palmitic acid and tetraethylammonium bromide in a melt[25] yielded, after careful column chromatography, mono-acylglycerol **16** in 64% yield. The ee of **16** was estimated as greater than 95% from the ^{1}H and ^{19}F NMR spectra of the corresponding (*R*)-MTP-ester **17**. Carbodimide coupling of **16** and TBSA (*R*)-**2** gave the corresponding differentially acylated diacyl glycerol **18** in 97% yield. Removal of the benzyl protecting group was achieved without significant acyl migration under the hydrogenolytic conditions as reported for debenzylation of the corresponding regioisomer by Liu et al.[13] to afford **19** in 93% yield.

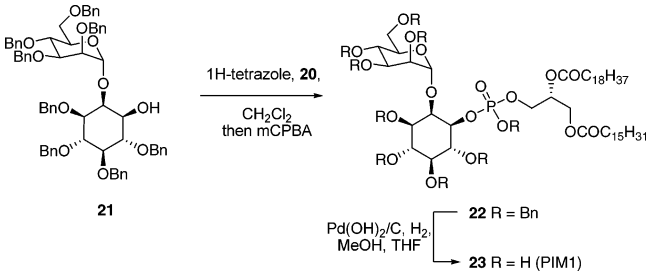
The next step in the synthesis was the tetrazole-mediated coupling of phosphoramidite **20** with PIM1 head group **21**[6] (Scheme 3). After an in situ oxidation, the reaction furnished protected PIM1 **22** as a mixture of isomers about the phosphorus atom in a 51% yield. Hydrogenolysis of the benzyl groups of **22** gave PIM1 (**23**) in 86% yield as a white amorphous solid after lyopholization. Of note in the ^{1}H NMR spectrum recorded in a mixture of $CDCl_3$, CD_3OD and D_2O was a multiplet at δ 5.29−5.34 due to *sn*-2 proton and a broad one-proton singlet at δ 5.14 attributed to the anomeric proton, H-1′.

PIM2 (**1c**) was synthesized in a similar manner (Scheme 4). Tetrazole-mediated coupling of phosphoramidite **20** with PIM2 head group **24**[7] gave, after an in situ oxidation, protected PIM2

SCHEME 2. Synthesis of Phosphoramidite 20



SCHEME 3. Synthesis of PIM1 (23)



25 as a mixture of isomers about the phosphorus atom in a 48% yield. Hydrogenolytic removal of the benzyl groups of **22** gave PIM2 (**1c**) in 86% yield as a white amorphous solid after lyopholization. The ^{1}H NMR spectrum recorded in a mixture of $CDCl_3$, CD_3OD, and D_2O showed a multiplet at δ 5.22−5.33 due to *sn*-2 proton and two broad one-proton singlets at δ 5.10 and 5.13 attributed to the two anomeric protons, H-1′ and H-1″.

The negative-ion ESI MS/MS CID spectrum of **1c** showed two fragments at *m*/*z* 877.4 and 920.4. The former was the more

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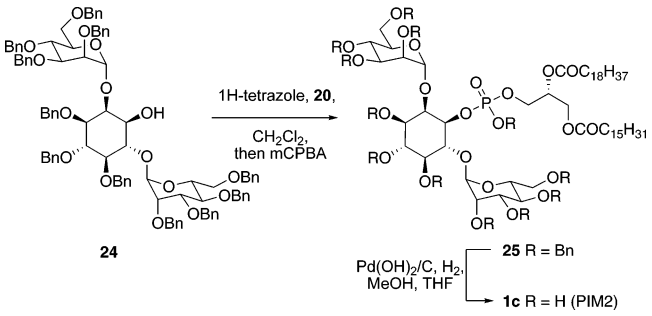
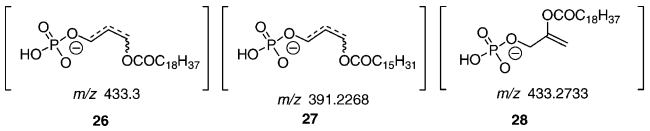
SCHEME 4. Synthesis of PIM2 (1c)



significant peak that arose by elimination of the tuberculostearate (C_{19}) residue from the *sn*-2 position of the glyceryl moiety of the molecular ion. The latter less significant peak was due to loss of the *sn*-1 palmitate (C_{16}) residue. This result is consistent with the acylation pattern of **1c** and the findings of Hsu and Turk,[12] who have shown that the acid on the *sn*-2 position of a glyceryl phosphate is more readily lost. Very recently, Gilleron et al. revisited their structural characterization of natural PIMs.[26] In this work they have used negative-ion ES-IRMPD and MALDI-TOF/TOF CID mass spectrometry on tetra-acylated PIM2 (Ac_2PIM2) from *Mycobacterium bovis* Bacilluss Calmette Guérin to establish the acylation pattern. In this study they proposed that the C_{19} fatty acid is located on the *sn*-1 and the C_{16} acid at is on the *sn*-2 position of the glycerol contrary to their earlier assignment. The basis for this new assignment was the presence of a peak at *m*/*z* 433.3 that was assigned to fragment **26** consistent with loss of the C16 fatty acid from the *sn*-2 position. In the current study, prominent in the ESI MS/MS CID spectrum of **1c** is a peak at *m*/*z* 391.2268 attributed to ion **27**, clearly establishing the presence of the C_{16} fatty acid at the *sn*-1 position. A much smaller peak at *m*/*z* 433.2733 was attributed to **28**. A similar pattern of peaks due to ions **27** and **28** were apparent in a negative-ion MALDI-TOF/TOF CID spectrum of PIM1 (**23**).



Given the potential of PIMs to modulate immune responsiveness,[1,2] we elected to test the obtained products to ascertain if they could modulate the release of pro-inflammatory cytokines. To that aim, dendritic cells (DCs) from mice were exposed to 50 μg of synthesized compounds and the release of the key Th1 cytokine interleukin-12 (IL-12)[27] was assessed (Figure 1). It was found that PIM2 (**1b**),[7] possessing palmitoyl residues at the *sn*-1 and *sn*-2 positions, was significantly more active than PIM1 (**23**) and PIM2 (**1c**) at enhancing IL-12, suggesting that the modified products, although immunologically active, are less potent than **1b** at stimulating DCs. This result confirms that subtle changes in the composition of the acyl residues in the PIM structure affect the bioactivity of these compounds, at least in this in vitro system. The crystal structure of the lipid antigen presenting molecule, CD1d, with a PIM2 (**1b**) ligand has

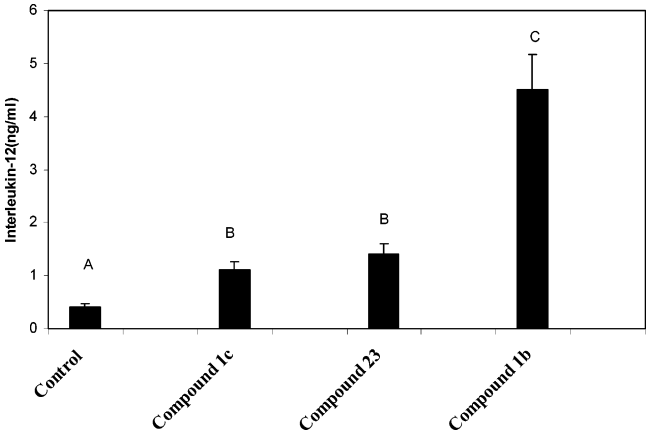


FIGURE 1. Bone marrow cells from BALB/c mice were cultured in the presence of 100 U of granulocyte-macrophage stimulating factor (GM-CSF) and interleukin-4 (IL-4) for 10 days. Cells (95% DCs) were stimulated with 50 μg of indicated products or diluent (control). Levels of interleukin-12 (IL-12) released by DCs were measured by a commercial ELISA kit. Columns identified by different letters are significantly different from each other (ANOVA test). Each data point represents results from four mice cell cultures. Bars indicate standard errors of the means.

recently been published.[28] The *sn*-2 palmitate inserts into the hydrophobic F′ pocket, making an optimal fit, whereas the *sn*-1 palmitate only partially fills the larger hydrophobic A′ pocket. In the current work, if binding of CD1d to PIM is important, it would follow that for tight binding the larger tuberculostearic acid would need to insert into the larger A′ pocket, and this would only occur if it was attached to the *sn*-1 position of the glycerol moiety.

In summary, we developed simple syntheses of (*R*)-tuberculostearic acid (**2**) from commercially available (*S*)-citronellol and differentially acylated glycerol **19** incorporating **2** from (*R*)-benzyl glycidol. The latter was then utilized in the total syntheses of the PIM1 (**23**) and PIM2 (**1c**), both of which possess a defined acylation pattern. Our MS/MS studies on **1c** and **23** unambiguously confirm the findings of Turk[12] and Gilleron[26] that loss of the *sn*-2 fatty acid residue is more facile than that of the *sn*-1 fatty acid. The fatty acid composition and distribution on the glycerol moiety of natural PIM molecules can now be validated using this method. Although PIM1 (**23**) and PIM2 (**1c**), both of which possess an 'unnatural' acylation pattern of the glycerol moiety, were immunologically active in a dendritic cell assay which measured the release of the Th1 cytokine IL-12; they were significantly less active than PIM2 (**1b**). We plan to synthesize a library of PIM variants, including those with tuberculostearoyl and palmitoyl residues at the *sn*-1 and *sn*-2 positions of the glyceryl unit, to establish a structure−activity relationship. Careful study of these newly synthesized variants may provide some clues in the mechanisms of immunomodulation of PIMs.

Experimental Section

(*R*)-2,6-Dimethyl-tetradec-2-ene (7). LiCl (0.525 g, 12.4 mmol) and $CuCl_2$ (0.915 g, 6.81 mmol) were stirred in THF (100 mL) under a N_2 atmosphere for 5 min; then tosylate **6**[19] (9.72 g, 31.3 mmol) was added. The solution was cooled to 0 °C, and freshly

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prepared hexylmagnesium bromide, from 1-bromohexane (17.8 g, 108 mmol) and magnesium (3.59 g, 148 mmol) in THF (150 mL), was added dropwise to the mixture, which was stirred at 0 °C for a further 1 h. The solution was then stirred 24 h at room temperature. Saturated NH_4Cl solution (200 mL) was added, and the mixture was filtered though Celite, diluted with ether (400 mL), washed with water (150 mL), brine (150 mL), and dried ($MgSO_4$). Removal of the solvent and purification of the residue by silica gel column chromatography (hexanes as eluent) gave an inseparable mixture of the title compound **7** and dodecane as a colorless oil (9.76 g). ^{1}H NMR (500 MHz, $CDCl_3$) δ inter alia 0.87−0.91 (m, 6H), 1.08−1.20 (m, 2H), 1.30−1.46 (m, 17H), 1.62 (s, 3H), 1.70 (s, 3H), 1.89−2.08 (m, 2H), 5.10−5.14 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.2, 17.7, 19.7, 22.8, 25.7, 25.8, 27.2, 29.5, 29.8, 30.2, 32.1, 32.6, 37.1, 37.3, 125.2, 131.0. Anal. Calcd for $C_{16}H_{32}$: C, 85.63; H, 14.37. Found: C, 85.66; H, 14.16.

(*R*)-4-Methyl-dodecanal (8). Ozone was bubbled though a solution of **7** and dodecane (9.76 g, 31.3 mmol) from the previous reaction in CH_2Cl_2 (400 mL) at −78 °C until the solution turned blue. Oxygen was bubbled through the solution to remove excess ozone; then dimethyl sulfide (4.6 mL, 63 mmol) was added. The stirred solution was warmed to room temperature over 2 h, then diluted with dichloromethane (200 mL), and washed with water (300 mL) and brine (300 mL). The solution was dried ($MgSO_4$), and the solvent was removed. Purification of the residue by silica gel column chromatography (light petroleum to light petroleum/CH_2Cl_2 = 3:1) gave the title compound **8** (5.85 g, 88% from **6**) as a colorless oil. $[\alpha]_D^{18}$ +1.1 (c = 0.44, CH_2Cl_2); υ_{max} (film), 2925, 2855, 2713, 1728 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.86−0.90 (m, 6H), 1.08−1.16 (m, 2H), 1.21−1.34 (m, 12H), 1.39−1.48 (m, 2H), 1.62−1.65 (m, 1H), 2.36−2.48 (m, 2H), 9.77 (t, J = 2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.2, 19.4, 22.7, 27.0, 29.0, 29.4, 29.7, 30.0, 32.0, 32.5, 36.7, 41.8, 203.1. Anal. Calcd for $C_{13}H_{26}O$: C, 78.72; H, 13.21. Found: C, 78.57; H, 13.12.

(7*R,10*R*)-1-Benzyloxy-10-methyloctadecan-7-ol (10).** A solution of aldehyde **8** (2.38 g, 11.2 mmol) in THF (20 mL) was added to 6-benzyloxylhexylmagnesium bromide (**9**), prepared from 6-benzyloxy-1-bromohexane (7.0 g, 26 mmol) and magnesium turnings in THF (60 mL), dropwise at room temperature. The reaction was stirred at room temperature for 16 h; then saturated NH_4Cl solution (100 mL) was added. The mixture was diluted with CH_2Cl_2 (100 mL), washed with 1 M HCl (50 mL), and dried ($MgSO_4$). Removal of the solvent and purification of the residue by silica gel column chromatography (light petroleum/Et_2O = 4:1) gave the title compound **10** (3.291 g, 75%, mixture of diastereoisomers) as a colorless oil. υ_{max} (film), 3364, 2926, 2854, 1454 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.86 (dd, J = 3.3, 6.6 Hz, 3H), 0.89 (d, J = 7.0 Hz, 3H), 1.06−1.14 (m, 2H), 1.19−1.52 (m, 26H), 1.58−1.66 (m, 2H), 3.47 (t, J = 6.6 Hz, 2H), 3.52−3.58 (m, 1H), 4.50 (s, 2H) 7.25−7.35 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.2, 19.7, 19.8, 22.8, 25.6, 25.7, 26.3, 27.1, 27.2, 29.4, 29.6, 29.7, 29.8, 30.1, 32.0, 32.9, 32.9, 33.0, 35.0, 35.1, 37.0, 37.2, 37.4, 37.5, 70.5, 72.4, 72.5, 72.9, 127.5, 127.7, 128.4, 138.8. Anal. Calcd for $C_{26}H_{46}O_2$: C, 79.94; H, 11.87. Found: C, 79.67; H, 11.89.

(7*R,10*R*)-1-Benzyloxy-10-methyl-7-tosyloxyoctadecane (11).** Tosyl chloride (2.3 g, 13 mmol) was added to a solution of **10** (3.29 g, 8.43 mmol) in a 1:1 mixture of pyridine and CH_2Cl_2 (20 mL) at 0 °C. The mixture was maintained at 0 °C for 3 days. The reaction mixture was concentrated in vacuo, diluted with CH_2Cl_2 (100 mL), washed with 1 M HCl (50 mL), and dried ($MgSO_4$). Removal of the solvent and purification of the residue by silica gel column chromatography (light petroleum/CH_2Cl_2 = 1:1, then light petroleum/EtOAc = 4:1) gave the title compound **11** (4.30 g, 93%) as a colorless oil; υ_{max} (film), 2926, 1454, 1599, 1454 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.76 (d, J = 6.6 Hz, 3H), 0.89 (d, J = 7.0 Hz, 3H), 0.95−1.24 (m, 2H), 1.10−1.35 (m, 27H), 1.50−1.61 (m, 2H), 2.42 (s, 3H), 3.44 (t, J = 6.6 Hz, 2H), 4.50 (s, 2H), 4.50−4.56 (m, 1H), 7.26−7.35 (m, 7H), 7.76−7.80 (m 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.2, 19.4, 19.5, 21.7, 22.8, 24.7, 24.8, 29.2, 29.4, 29.70, 29.74, 29.8, 30.0, 30.1, 31.68, 31.72, 31.8, 31.9, 32.0, 32.58, 32.61, 34.1, 34.2, 36.8, 36.9, 70.4, 73.0, 85.0, 127.6, 127.7, 127.8, 128.4, 129.6, 129.7, 134.9, 138.7, 144.4. Anal. Calcd for $C_{33}H_{52}O_4S$: C, 72.75; H, 9.62; S, 5.89. Found: C, 72.49; H, 9.55; S, 5.55.

(*R*)-1-Benzyloxy-10-methyloctadec-6- and -7-ene (12). Diethyl ether (50 mL) was added to freshly activated neutral alumina (28 g), and the mixture was cooled to room temperature. Tosylate **11** (2.10 g, 3.83 mmol) in ether (25 mL) was added, and the resultant slurry was stirred for 17 h under nitrogen. The mixture was filtered, and the alumina was washed with diethyl ether (100 mL). Concentration of the combined filtrates and purification of the residue by silica gel chromatography (light petroleum/Et_2O = 9:1) gave the title compounds **12** (1.08 g, 75%) as a colorless oil; υ_{max} (film), 2923, 2854, 1455, 1112 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.82−0.90 (m, 6H), 1.05−1.19 (m, 2H), 1.20−1.44 (m, 20H), 1.58−1.66 (m, 2H), 1.94−2.07 (m, 2H), 3.47 (dt, J = 1.0, 7.0 Hz, 2H), 5.31−5.39 (m, 2H), 7.26−7.36 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.2, 19.57, 19.64, 19.66, 19.69, 22.8, 24.9, 25.8, 26.0, 26.1, 26.16, 26.18, 27.09, 27.12, 27.17, 27.23, 27.3, 27.4, 29.0, 29.3, 29.4, 29.5, 29.6, 29.7, 29.75, 29.82, 30.0, 30.1, 30.2, 32.0, 32.3, 32.48, 32.6, 32.7, 33.3, 33.51, 34.6, 36.7, 36.8, 37.0, 37.1, 40.2, 70.4, 70.5, 70.6, 72.92, 72.94, 127.5, 127.7, 128.4, 128.6, 129.0, 129.5, 130.0, 130.3, 130.6, 130.8, 131.5, 138.76, 138.78. Anal. Calcd for $C_{26}H_{43}O$: C, 84.03; H, 11.66. Found: C, 84.05; H, 11.89.

(*R*)-(−)-10-Methyl-octadecan-1-ol (13). A mixture of 10% palladium on carbon (0.305 g), **12** (2.46 g, 6.37 mmol), and hexanes (100 mL) was stirred under an atmosphere of hydrogen for 72 h. The reaction mixture was filtered though Celite, and the solvent was removed. Purification of the residue by silica gel chromatography (light petroleum/Et_2O = 9:1) gave the title compound **13** (1.84 g, 96%) as a colorless oil. $[\alpha]_D^{29}$ −0.03 (c = 2.75, CH_2Cl_2) {Lit.[13] $[\alpha]_D$ −0.02 (c = 8.0, $CHCl_3$)}; υ_{max} (film), 3336, 2922, 1459, 1370, 1057 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.83 (d, J = 6.6 Hz, 3H), 0.88 (t, J = 6.6 Hz, 3H), 1.02−1.14 (m, 1H), 1.18−1.44 (m, 29H), 1.50−1.65 (2H, m), 3.64 (t, J = 6.6 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.2, 19.8, 22.8, 24.7, 27.1, 27.2, 29.1, 29.3, 29.4, 29.5, 26.8, 30.0, 30.1, 32.0, 32.8, 34.1, 37.1, 37.2, 63.3. Anal. Calcd for $C_{19}H_{40}O$: C, 80.21; H, 14.17. Found: C, 80.56; H, 14.06.

(*R*)-10-Methyloctadecanoic acid [(*R*)-(2)]. Alcohol **13** (0.255 g, 0.898 mmol), tetrabutylammonium bromide (0.157 g, 0.487 mmol), and potassium permanganate (0.443 g, 2.80 mmol) were refluxed in a mixture of CH_2Cl_2 (50 mL), acetic acid (2 mL), and water (30 mL) for 4 h. The solution was cooled, and 1 M HCl (50 mL) was added. Sodium sulfite (0.5 g) was added, and the aqueous phase was extracted with CH_2Cl_2 (50 mL). The organic extracts were dried ($MgSO_4$), and the solvent was removed. Purification of the residue by silica gel column chromatography (light petroleum/Et_2O = 4:1) gave the title compound (*R*)-**2** (0.263 g, 98%) as a colorless oil. $[\alpha]_D^{30}$ −0.03 (c = 4.75, $CHCl_3$) {Lit.[13] $[\alpha]_D$ −0.02 (c = 10.5, $CHCl_3$)}; υ_{max} (film), 3016, 2923, 1705, 1459, 1057 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.83 (d, J = 6.7 Hz, 3H), 0.88 (t, J = 6.9 Hz, 3H), 1.05−1.10 (m, 1H), 1.18−1.39 (m, 29H), 1.60−1.66 (2H, m), 2.35 (t, J = 7.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.2, 19.8, 22.8, 24.8, 27.1, 27.2, 29.1, 29.3, 29.4, 29.5, 26.8, 30.0, 30.1, 32.0, 32.8, 34.1, 37.1, 37.2, 180.2. Anal. Calcd for $C_{19}H_{38}O_2$: C, 76.45, H, 12.83. Found: C, 76.09; H, 12.93.

(*R*)-Benzyl Glycidyl Ether (−)-(14). A mixture of (*S*,*S*)-**15** (76.0 mg, 126 μmol), (±)-benzyl glycidyl ether (**14**) (4.15 g, 25.3 mmol), AcOH (28 μL, 0.49 mmol), and THF (0.25 mL) was cooled to 0 °C; then H_2O (240 μL, 13.3 mmol) was added with stirring. The mixture was warmed to rt, and after 16 h, (*R*)-benzyl glycidyl ether (−)-(**14**) (2.05 g, 49%) was isolated by vacuum distillation (bpt, 120 °C 0.7 mm/Hg) followed by further purification by silica gel column chromatography (light petroleum/Et_2O = 9:1); $[\alpha]_D^{20}$ −5.7 (c = 5, $C_6H_5CH_3$); Aldrich: (−)-Benzyl (*R*)-glycidyl ether, cat. No. 363529 $[\alpha]_D^{20}$ −5.4 (c = 5, $C_6H_5CH_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.60−2.64 (m, 1H); 2.80 (1H, t, J = 4.6 Hz); 3.07−3.12

(m, 1H); 3.44 (dd, J = 6.2, 5.3 Hz, 1H); 3.77 (dd, J = 8.4, 3.0 Hz, 1H); 4.59 (dt, J = 15.8, 11.7 Hz, 2H), 7.26−7.40 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 44.3, 50.9, 70.8, 73.3, 127.8, 128.4, 137.9.

3-*O*-Benzyl-1-*O*-palmitoyl-*sn*-glycerol[29] (16). A melt of (*R*)-benzyl glycidol (*R*)-**14** (1.06 g, 6.46 mmol), palmitic acid (1.68, 6.53 mmol), and tetraethylammonium bromide (30 mg, 0.14 mmol) at 100 °C was stirred for 3 h. The reaction mixture was purified by silica gel chromatography (toluene to toluene/EtOAc = 95:5) to give the title compound **16** (1.75 g, 64%) as a white wax. $[\alpha]_D^{15}$ +0.6 (c = 3.00, CH_2Cl_2); υ_{max} (film), 3494, 2917, 2852, 1715 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, J = 6.9 Hz, 3H), 1.20−1.34 (m, 24H), 1.57−1.67 (m, 2H), 2.32 (t, J = 7.5 Hz, 2H), 2.51 (bs, 1H), 3.49 (dd, J = 6.2, 9.6 Hz, 1H), 3.56 (dd, J = 4.4, 9.6 Hz, 1H), 4.00−4.06 (m, 1H), 4.14 (dd, J = 6.1, 11.5 Hz, 1H), 4.19 (dd, J = 4.4, 11.5 Hz, 1H), 4.56 (s, 2H), 7.27−7.38 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.1, 22.7, 24.9, 29.1, 29.3, 29.4, 29.5, 29.6, 29.65, 29.69, 31.9, 34.1, 65.3, 68.9, 70.9, 73.5, 127.7, 127.8, 128.4, 137.7, 173.9.

3-*O*-Benzyl-2-*O*-((*R*)-α,α,α-methoxytrifluoromethylphenylacetyl)-1-*O*-palmitoyl-*sn*-glycerol (17). A mixture of **16** (20 mg, 48 μmol), DCC (20 mg, 97 μmol), (*R*)-MTPA (26 mg, 111 μmol), and DMAP (7.0 mg, 57 μmol) was dissolved in CH_2Cl_2 (5 mL) at room temperature and stirred overnight. The reaction mixture was filtered through Celite and concentrated. The residue was purified by silica chromatography (light petroleum/Et_2O = 9:1) to give MTPA-ester **17** (27 mg, 89%) as a white wax. $[\alpha]_D^{26}$ 31.0 (c = 1.40, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, J = 7.0 Hz, 3H), 1.20−1.40 (m, 24H), 1.50−1.60 (m, 2H), 2.21 (dt, J = 2.4, 5.2 Hz, 2H), 3.54 (d, J = 1.0 Hz, 3H), 3.69 (d, J = 5.5 Hz, 2H), 4.14 (dd, J = 6.8, 12.3 Hz, 1H), 4.37 (dd, J = 3.53, 12.0 Hz, 1H), 4.55 (dd, J = 11.8, 17.9 Hz, 2H), 5.50−5.54 (m, 1H), 7.28−7.40 (m, 8H), 7.56 (d, J = 7.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.2, 22.8, 24.8, 29.2, 29.3, 29.4, 29.5, 29.67, 29.71, 29.8, 32.0, 34.0, 55.5, 62.3, 68.3, 72.7, 73.4, 127.5, 127.7, 127.9, 128.4, 128.5, 129.6, 132.2, 137.4, 166.1, 173.3; ^{19}F NMR (470 MHz, $CDCl_3$) δ −72.5. HRMS-ESI: $[M + Na]^+$ calcd for $C_{36}H_{51}F_3O_6Na$, 659.3535; found, 659.3530.

3-*O*-Benzyl-2-*O*-((*R*)-10-methyloctadecanoyl)-1-*O*-palmitoyl-*sn*-glycerol (18). A mixture of **16** (344 mg, 817 μmol), DCC (343 mg, 1.66 mmol), (*R*)-**2** (268 mg, 898 μmol), and DMAP (5.9 mg, 48 μmol) was dissolved in CH_2Cl_2 (15 mL) at rt and stirred overnight. The reaction mixture was filtered through Celite and concentrated. The residue was purified by silica gel column chromatography (light petroleum/Et_2O = 19:1) to give the title compound **18** (556 mg, 97%) as a white wax. $[\alpha]_D^{20}$ 5.2 (c = 3.00, $CHCl_3$); ^{1}H NMR: (500 MHz, $CDCl_3$) δ 0.83 (d, J = 6.4 Hz, 3H), 0.88 (t, J = 6.9 Hz, 6H), 1.02−1.12 (m, 1H), 1.19−1.40 (m, 48H), 1.55−1.65 (m, 4H), 2.28 (t, J = 7.6 Hz, 3H), 2.32 (t, J = 7.6 Hz, 3H), 3.56−3.62 (m, 2H), 4.19 (dd, J = 6.4, 12.1 Hz, 1H), 4.34 (dd, J = 3.7, 12.0 Hz, 1H), 4.52 (d, J = 12.1 Hz, 1H), 4.56 (d, J = 12.1 Hz, 1H), 5.22−5.27 (m, 1H), 7.26−7.36 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.2, 19.8, 22.8, 24.9, 25.0, 27.1, 27.2, 29.18, 29.20, 29.36, 29.39, 29.43, 29.44, 29.56, 29.61, 29.70, 29.73, 29.74, 29.8, 30.0, 30.1, 32.0, 32.8, 34.2, 34.4, 37.2, 62.7, 68.3, 70.1, 73.4, 127.7, 127.8, 128.5, 137.8, 173.2, 173.5. HRMS-ESI: $[M + Na]^+$ calcd for $C_{45}H_{80}O_5Na$, 723.5903; found: 723.5931. Anal. Calcd for $C_{45}H_{80}O_5$: C, 77.09; H, 11.50. Found: C, 76.72; H, 11.29.

2-*O*-((*R*)-10-methyloctadecanoyl)-1-*O*-palmitoyl-*sn*-glycerol (19). A mixture of glycerol **18** (200 mg, 285 μmol) and 10% Pd/C (30 mg, 28 μmol) in ethanol (15 mL) and AcOH (0.15 mL) was stirred at room temperature for 1.5 h under an atmosphere of H_2. The mixture was filtered through Celite, and the solvent was removed. Purification of the residue by silica gel column chromatography (CH_2Cl_2/light petroleum 1:1 to CH_2Cl_2 to CH_2Cl_2/EtOAc = 19:1) gave the title compound **19** (163 mg, 93%) as a colorless oil. $[\alpha]_D^{20}$ −2.6 (c = 0.40, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.83 (d, J = 6.5 Hz, 3H), 0.88 (t, J = 7.0 Hz, 6H), 1.10−1.13 (m, 1H), 1.17−1.40 (m, 48H), 1.57−1.66 (m, 4H), 2.30−2.36 (m, 6H), 3.69−3.76 (m, 2H), 4.23 (dd, J = 6.0, 12.1 Hz, 1H), 4.32 (dd, J = 5.5, 11.8 Hz, 1H), 5.06−5.11 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.2, 19.8, 22.8, 24.9, 25.0, 27.1, 29.2, 29.3, 29.36, 29.43, 29.5, 29.6, 29.67, 29.72, 29.8, 30.0, 30.1, 32.0, 32.8, 34.2, 34.4, 37.2, 61.6, 62.1, 72.2, 173.5, 173.9; HRMS-ESI: $[M + Na]^+$ calcd for $C_{38}H_{74}O_5Na$, 633.5434; found, 633.5462. Anal. Calcd for $C_{38}H_{74}O_5$: C, 74.70; H, 12.21. Found: C, 74.87; H, 11.99.

Benzyl (2-*O*-(*R*)-10-Methyloctadecanoyl-1-*O*-hexadecanoyl-*sn*-glycero)-diisopropylphosphoramidite (20). 1*H*-Tetrazole (15.0 mg, 0.214 mmol) was added to a stirred solution of alcohol **19** (100 mg, 0.164 mmol) and benzyl bis(diisopropyl)phosphoramidite (124 mg, 0.367 mmol) in dry CH_2Cl_2 (7 mL) cooled to 0 °C under an argon atmosphere. After stirring at rt for 1.5 h, the solvent was removed in vacuo and the residue purified by silica gel column chromatography (Et_3N/EtOAc/light petroleum = 3:10:90), affording the title compound **20** (128 mg, 0.151 mmol, 92%) as an oil. $[\alpha]_D^{20}$ 5.4 (c = 1.7, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.81−0.91 (m, 9H), 1.02−1.38 (m, 63H), 1.52−1.62 (m, 4H), 2.21−2.31 (m, 4H), 3.58−3.80 (m, 4H), 4.12−4.19 (m, 1H), 4.30−4.38 (m, 1H), 4.61−4.77 (m, 2H), 5.17−5.24 (m, 1H), 7.19−7.37 (m, 5H); ^{13}C NMR (75 MHz) δ 14.2, 19.8, 22.7, 24.6, 24.7, 24.8, 25.0, 27.1, 29.2, 29.4, 29.5, 29.6, 29.7, 30.1, 32.0, 32.8, 34.2, 34.4, 37.2, 43.1, 43.3, 61.5, 61.7, 61.9, 62.6, 65.3, 65.6, 70.9, 127.0, 127.3, 128.3, 139.4, 173.4, 173.4; ^{31}P NMR (121.5 MHz, $CDCl_3$) δ 150.0, 150.2; HRMS-ESI: $[M + H]^+$ calcd for $C_{51}H_{95}O_6NP$, 848.6897; found, 848.6885.

3,4,5,6-Tetra-*O*-benzyl-2-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl-1-*O*-(2-*O*-(*R*)-10-methyloctadecanoyl-1-*O*-hexadecanoyl-*sn*-glycero-3-benzylphosphoryl)-D-*myo*-inositol (22). 1*H*-Tetrazole (16 mg, 0.23 mmol) was added to a stirred solution of 3,4,5,6-tri-*O*-benzyl-2-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-D-*myo*-inositol (21) (94 mg, 0.088 mmol) and phosphoramidite 20 (149 mg, 0.176 mmol) in dry CH_2Cl_2 (6 mL) cooled to 0 °C under an argon atmosphere. After stirring at rt for 1.5 h, the reaction mixture was cooled to −40 °C and a solution of *m*-CPBA (50%, 61 mg, 0.18 mmol) in CH_2Cl_2 (4 mL) was added dropwise to the reaction mixture. After warming to rt over 2 h the reaction was quenched with addition of 10% aqueous Na_2SO_3 solution (50 mL) and the combined mixture extracted with Et_2O (100 mL). The ethereal extract was washed with saturated $NaHCO_3$ solution (3 × 50 mL) and dried ($MgSO_4$). After filtration the solvent was removed in vacuo and the residue purified by silica gel column chromatography (EtOAc/light petroleum = 1:9 to 1:4), followed by a second column (CH_2Cl_2 to EtOAc/CH_2Cl_2 = 1:25), giving the title compound 21 (83 mg, 51%) as an oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.83 (d, J = 6.3 Hz, 3H), 0.89 (t, J = 6.9 Hz, 6H), 1.03−1.11 (m, 2H), 1.15−1.35 (m, 49H), 1.45−1.59 (m, 4H), 2.17−2.25 (m, 4H), 3.21−3.55 (m, 4H) 3.66−4.34 (m, 12H), 4.44−5.07 (m, 18H), 5.07−5.13 (m, 1H), 5.34−5.38 (m, 1H), 7.14−7.44 (m, 45H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.8, 14.2, 19.8, 22.8, 24.8, 24.85, 24.89, 27.2, 29.1, 29.17, 29.21, 29.38, 29.40, 29.42, 29.43, 29.58, 29.64, 29.7, 29.8, 30.09, 30.12, 31.3, 32.0, 32.9, 34.0, 34.07, 34.11, 37.2, 38.2, 59.6, 61.58, 61.60, 65.6, 65.78, 65.82, 66.0, 67.5, 68.7, 68.8, 69.4, 69.5, 69.70, 69.74, 69.8, 71.8, 71.9, 72.1, 72.15, 72.19, 72.24, 73.4, 73.7, 74.0, 74.4, 74.5, 74.6, 74.7, 75.1, 75.4, 75.5, 75.7, 75.8, 76.2, 77.3, 78.5, 78.7, 79.0, 79.1, 79.3, 79.34, 79.6, 79.7, 80.7, 80.8, 82.98, 83.01, 98.9, 127.3, 127.40, 127.42, 127.48, 127.51, 127.6, 127.66, 127.70, 127.77, 127.83, 127.9, 128.0, 128.06, 128.07, 128.07, 128.11, 128.15, 128.23, 128.26, 128.31, 128.33, 128.38, 128.42, 128.44, 128.49, 128.53, 128.57, 128.63, 128.68, 128.72, 128.8, 130.96, 130.97, 131.2, 135.5, 135.6, 138.0, 138.1, 138.31, 138.34, 138.39, 138.43, 138.43, 138.45, 138.53, 138.54, 138.87, 138.88, 172.8, 173.09, 173.13; ^{31}P NMR (202 MHz, $CDCl_3$) δ −0.64 (0.7P) and −0.34 (0.3P). HRMS-ESI: $[M + Na]^+$ calcd for $C_{113}H_{149}NaO_{18}P$, 1849.0413; found, 1849.0452. Anal. Calcd for $C_{133}H_{149}O_{18}P$: C, 74.31; H, 8.22. Found: C, 74.23; H, 8.32.

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2-(*O*-α-D-Mannopyranosyl)-1-*O*-(2-*O*-(*R*)-10-methyloctadecanoyl-1-*O*-hexadecanoyl-*sn*-glycero-3-phosphoryl)-D-*myo*-inositol (23). $Pd(OH)_2$/C (20% , 19 mg) was added to a stirred solution of **22** (51 mg, 0.028 mmol) in a 3:2 mixture of MeOH and THF (5 mL). The mixture was stirred under a hydrogen atmosphere for 4 h at rt and filtered through Celite, washed with further 3:2 MeOH and THF (30 mL), and concentrated in vacuo. The residue was purified on silica gel ($CHCl_3$/MeOH/H_2O = 90:10:0 to 70:40:6) to afford the title compound **23** (26 mg, 91%). ^{1}H NMR (500 MHz, $CDCl_3$:MeOD:D_2O 70:40:6) δ 0.85 (d, J = 6.6 Hz, 3H), 0.89 (t, J = 6.9 Hz, 6H), 1.05−1.12 (m, 2H), 1.17−1.40 (m, 49H), 1.65−1.55 (m, 4H), 2.31 (t, J = 7.6, Hz, 2H), 2.34 (t, J = 7.5, Hz, 2H), 3.27 (t, J = 9.1 Hz, 1H), 3.47−3.52 (m, 1H), 3.57−3.67 (m, 2H), 3.62−3.84 (m, 4H), 3.84−3.68 (m, 1H), 3.93−4.10 (m, 5H), 4.27−4.35 (m, 1H), 4.31 (bs, 1H), 4.44 (dd, J = 12.0, 2.5 Hz, 2H), 5.14 (s, 1H), 5.29−5.23 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$: MeOD: D_2O 70: 40: 6) δ 16.7, 22.4, 25.4, 27.7, 27.8, 29.87, 29.92, 32.0, 32.1, 32.2, 32.4, 32.5, 32.6, 32.8, 32.9, 34.7, 35.6, 36.9, 37.1, 39.91, 39.93, 57.3, 58.3, 62.9, 63.0, 64.0, 65.9, 66.5, 69.8, 71.4, 73.1, 73.3, 73.35, 73.42, 73.45, 75.3, 75.7, 76.9, 77.4, 78.2, 78.9, 79.3, 81.5, 90.9, 104.3, 176.9, 177.2; ^{31}P NMR (121 MHz, $CDCl_3$: MeOD: D_2O 70: 40: 6) δ −0.06. HRMS-ESI: $[M - H]^-$ calcd for $C_{50}H_{94}O_{18}P$, 1013.6183; found, 1013.6172.

3,4,5-Tri-*O*-benzyl-2,6-di-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl-1-*O*-(2-*O*-(*R*)-10-methyloctadecanoyl-1-*O*-hexadecanoyl-*sn*-glycero-3-benzylphosphoryl)-D-*myo*-inositol (25). 1*H*-Tetrazole (18 mg, 0.26 mmol) was added to a stirred solution of 3,4,5-tri-*O*-benzyl-2,6-di-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-D-*myo*-inositol (24) and phosphoramidite 20 (215 mg, 0.253 mmol) in dry CH_2Cl_2 (6 mL) cooled to 0 °C under an argon atmosphere. After stirring at rt for 1.5 h the reaction mixture was cooled to −40 °C and a solution of *m*-CPBA (50%, 88 mg, 0.25 mmol) in CH_2Cl_2 (4 mL) was transferred by cannula into the reaction mixture. After warming to rt over 2 h the reaction was quenched with addition of 10% aqueous Na_2SO_3 solution (50 mL) and the combined mixture extracted with Et_2O (100 mL). The ethereal extract was washed with saturated $NaHCO_3$ solution (3 × 50 mL) and dried ($MgSO_4$). After filtration the solvent was removed in vacuo and the residue purified by silica gel column chromatography (EtOAc/light petroleum = 1:9 to 1:4) followed by a second column (CH_2Cl_2 to EtOAc/CH_2Cl_2 = 1:25) to give the title compound 21 (69 mg, 0.031 mmol, 48%) as an oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.81−0.91 (m, 9H), 1.01−1.13 (m, 2H), 1.14−1.34 (m, 49H), 1.42−1.58 (m, 4H), 2.09−2.24 (m, 4H), 3.21−3.52 (m, 6H), 3.75−4.26 (m, 17H), 4.40−5.15 (m, 24H), 5.27−5.36 (m, 1H), 5.49 (brs, 1H), 6.98−7.39 (m, 60H), ^{13}C NMR (75 MHz) δ 14.2, 19.8, 22.8, 24.9, 27.2, 29.2, 29.4, 29.8, 30.1, 32.0, 32.9, 33.9, 34.1, 37.2, 61.4−81.1 (CH and CH_2), 98.5, 99.6, 127.2−128.9 (CH-Aryl),137.8−139.2 (C_q-Aryl), 172.6, 173.0; ^{31}P NMR (121.5 MHz, $CDCl_3$) δ 1.16, 0.94. HRMS-ESI: $[M + Na]^+$ calcd for $C_{140}H_{177}O_{23}NaP$, 2280.2316; found, 2280.2317.

2,6-(Di-*O*-α-D-mannopyranosyl)-1-*O*-(2-*O*-(*R*)-10-methyloctadecanoyl-1-*O*-hexadecanoyl-*sn*-glycero-3-phosphoryl)-D-*myo*-inositol (1c). $Pd(OH)_2$/C (20%, 37 mg) was added to a stirred solution of 25 (32 mg, 0.014 mmol) in a 3:2 mixture of MeOH and THF (5 mL). The mixture was stirred under a hydrogen atmosphere for 3 h at rt when the hydrogen was replaced with argon, and the mixture was filtered through Celite, washed with 3:2 MeOH and THF (30 mL), and concentrated in vacuo. The residue was purified on silica gel ($CHCl_3$/MeOH/H_2O = 70:40:1 to 70:40:6) to afford the title compound 5 (14 mg, 86%). ^{1}H NMR (300 MHz, $CDCl_3$/CD_3OD/D_2O, 70:40:6) δ 0.82−0.90 (m, 9H), 1.05−1.13 (m, 2H), 1.55−1.66 (m, 4H), 1.21−1.34 (m, 49H), 2.27−2.40 (m, 4H), 3.25−3.31(m, 1H), 3.43−3.50 (m, 1H), 3.57−3.86 (m, 10H), 3.91−4.09 (m, 7H), 4.30 (br s, 1H), 4.40−4.43 (m, 1H), 5.10 (br s, 1H), 5.13 (br s, 1H), 5.22−5.32 (m, 1H); ^{31}P NMR (121.5 MHz, $CDCl_3$/CD_3OD/D_2O, 70:40:6) δ −3.7. HRMS-ESI: $[M - H]^-$ calcd for $C_{56}H_{104}O_{23}P$, 1175.6706; found, 1175.6725. Anal. Calcd for $C_{56}H_{105}O_{23}P.1.5SiO_2$: C, 53.07; H, 8.35. Found: C, 53.11; H, 8.27.

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Supporting Information Available: General experimental remarks, experimental details for the synthesis of **6**, NMR spectra for all compounds reported in the Experimental Section, and mass spectra for **1c** and **23**. This material is available free of charge via the Internet at http://pubs.acs.org.

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