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Synthesis of phosphatidylinositol mannosides (PIMs)

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Abstract

Two strategies towards the synthesis of phosphatidylinositol mannosides (PIMs) were elaborated which permit selective access to the *O*-1-, *O*-2-, and the *O*-6 position of the *myo*-inositol residue. Starting materials are 1,2:5,6- and 1,2:4,5-di-*O*-cyclohexylidene-DL-*myo*-inositol, respectively. In the latter case, the required assignment to the D- or L-series is based on the transformation of one enantiomer into known (−)-liriodentritol. The efficiency and potential versatility of the two approaches is exemplified in the synthesis of PIMs (D)-**1a** and its pseudoenantiomer (L)-**1b**, both having myristoyl residues as part of the phosphatidyl moiety.

Keywords: Phosphatidylinositol; Phosphatidylinositol mannoside; Synthesis; Glycosidation; Structural assignment

1. Introduction

Important constituents of the mycobacterial cell wall are arabinogalactan-peptidoglycan (AGP) and lipoarabinomannan (LAM) complexes. The LAM structure is composed of a phosphatidylinositol dimannoside (PIM_2) which carries a mannan (→lipomannan, LM) or an arabinomannan moiety (→LAM) (Scheme 1).[1] Precursors for the biosynthesis of LAMs are phosphatidylinositols (PIs) which are α-mannopyranosylated at *O*-2 (→PIM) or at *O*-2- and *O*-6 (→PIM_2).[2] Chain extension of the α-(1→6)-linked mannopyranosyl residue with additional α-(1→6)- and α-(1→2)-linked mannopyranosyl residues will lead to LMs and by further adding arabinofuranosyl residues finally LAMs are obtained.

In mycobacterial infections, the lipoglycans localize to caveolae/lipid rafts of host membranes which serve as signal transduction platforms, thus eliciting a profound biological response. Such responses involve induced expression and secretion of TNF-α and IL-6 and inhibition of T-cell proliferative responses.[1,3] LAMs have also been shown to inhibit expression of IL-2, IL-5, and GM-CSF genes in human T-cells and the IFN-γ-mediated activation of macrophages.

Because the PIM substructure of LAMs is able to inhibit LAM insertion into caveolae, the PIM substructures may contain the necessary structural characteristics to target to caveolae. Therefore, such compounds have to be investigated if they are mimics of the naturally occurring PIMs, thus inducing biological responses normally attributed to the natural compound if they act as biologically inert carriers delivering specific pharmaceutically active compounds to caveolae. Hence, we initiated a program to the synthesis of PIMs and structural variants, thus requiring regioselective access to the *O*-1, *O*-2, and *O*-6 position of (D)- or (L)-*myo*-inositol.[4,5]

In this paper, the synthesis of phosphatidyl-(D)-inositol mannoside with $R^6 = H$ (Scheme 1, (D)-**1a**) and of its pseudoenantiomer (L)-**1b** with (L)-inositol configuration (which is actually a diastereomer of (D)-**1a**) is reported. Structural analogs of (D)-**1a** were previously synthesized by routes which did not consider eventual attachments to the O-6 position of the inositol moiety.[6] Also, the successful synthesis of PIM_2 was already reported starting from racemic inositol derivatives.[7] The resolution of unsymmetrically substituted *myo*-inositol derivatives with the help of an α-linked mannosyl residue at the *O*-2 position turned out to be laborious. Therefore, in our synthesis, designed chiral

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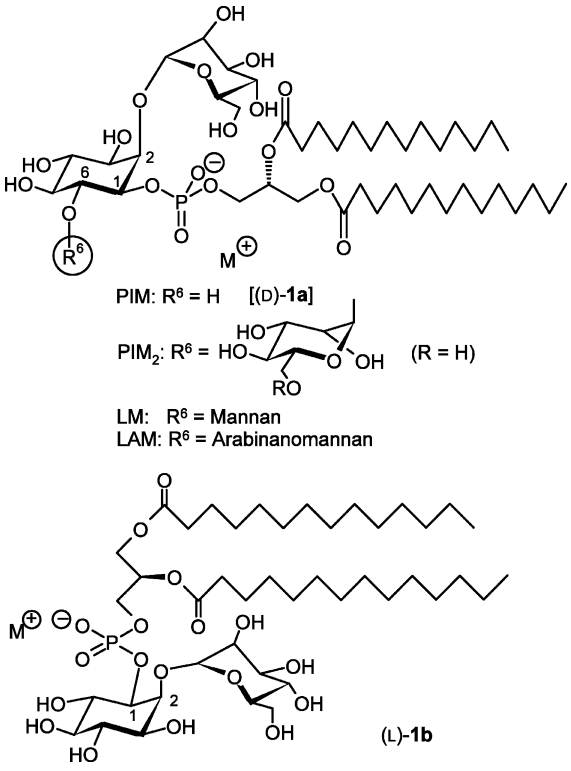
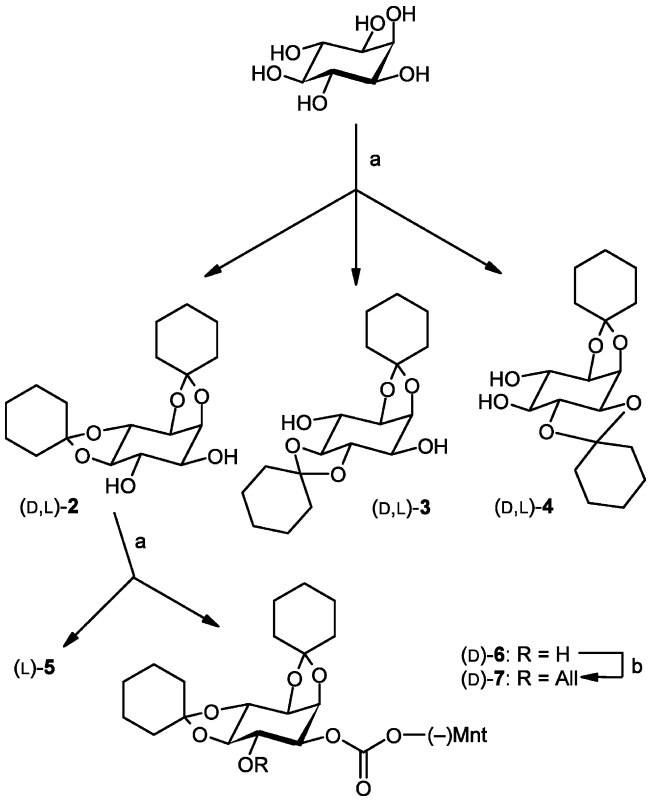


Scheme 1. Structure of PIMs, LM and LAM and of target molecules (D)-**1a** and (L)-**1b**.



Scheme 2. Reagents and conditions: (a) Ref. 8; (b) All-Br, Ag_2O, DMF, 0 °C; KI (86%); see also Ref. 9.

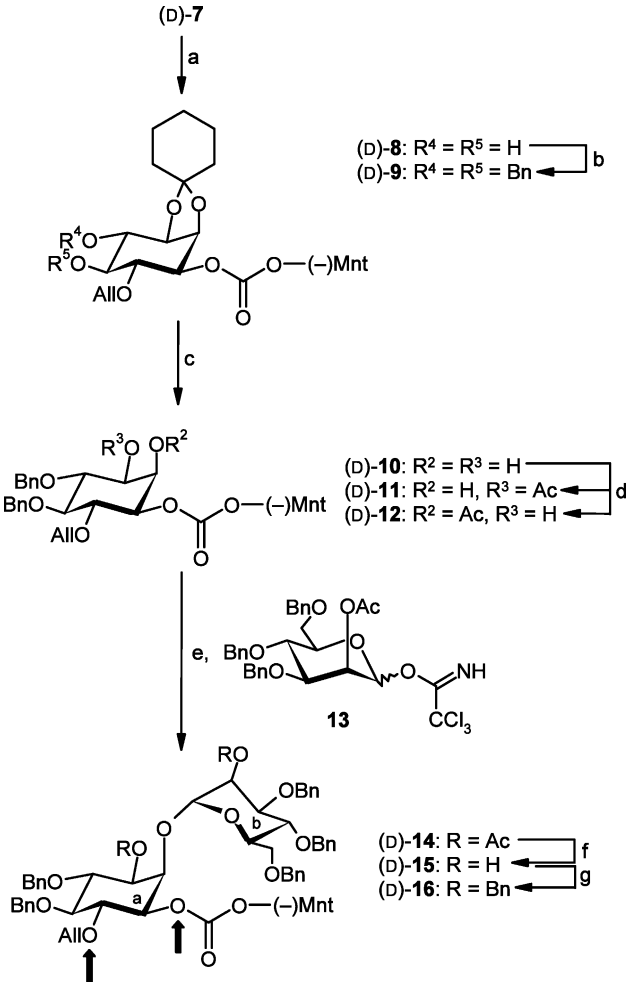
auxiliaries for efficient resolution were employed. The designed synthesis takes also into account future regioselective attachment of residues at the O-6 position of the inositol moiety, thus permitting the synthesis of PIM_2, LMs, and LAMs and structural variants thereof.[5]

2. Results and discussion

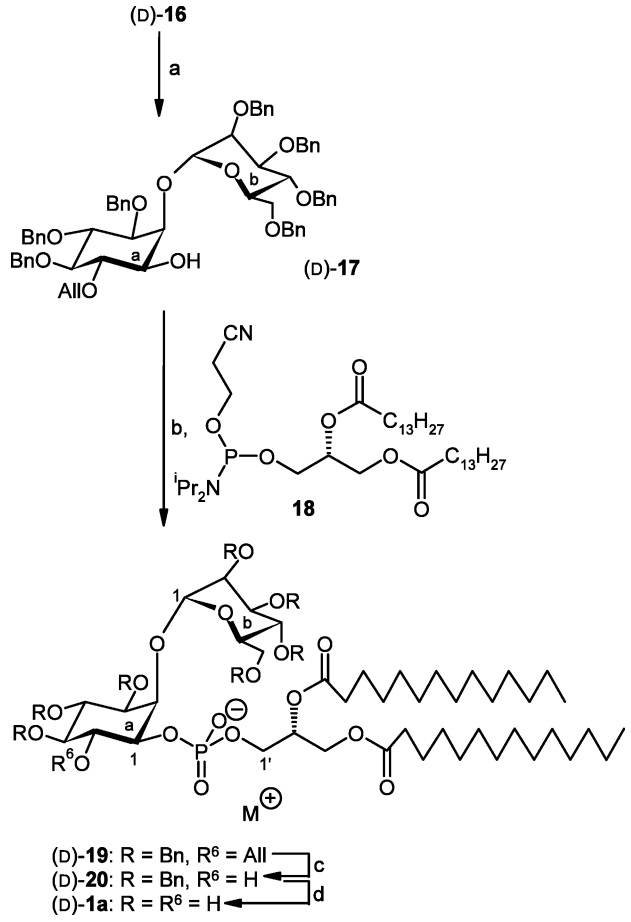
Following a literature procedure,[8] *myo*-inositol (Scheme 2) can be readily transformed into di-*O*-cyclohexylidene derivatives **2**–**4** which are separated by crystallisation (**3**) and by chromatography (**2** and **4**).

Compound **2** has been frequently employed for the synthesis of phosphatidylinositol derived compounds, particularly glycosylphosphatidylinositol (GPI) anchors[8,9] which require access to the *O*-1 and *O*-6 position of *myo*-inositol. Therefore, resolution of (DL)-**2** with the help of (−)-menthyloxycarbonyl derivatives (L)-**5** and (D)-**6** is well studied.[8b,9] In order to take into account the desired selective access to the *O*-6 position for later PIM related syntheses, O-6 allylation with allyl bromide in the presence of silver oxide in DMF at 0 °C was carried out, thus avoiding menthyloxycarbonyl migration, which was observed under more drastic conditions. Excess silver ions were removed by treatment with potassium iodide; workup led to desired (D)-**7**.[9]

Selective 4,5-*O*-cyclohexylidene group removal on (D)-**7** under acid catalysis with pyridinium *p*-toluenesulfonate (PPTSA)–*p*-toluenesulfonic acid (PTSA) furnished 4,5-O unprotected (D)-**8** (Scheme 3), which on treatment with benzyl bromide in the presence of silver oxide afforded cleanly 4,5-di-*O*-benzyl protected derivative (D)-**9**. Following 2,3-*O*-decyclohexylidenation with camphorsulfonic acid (CSA) as catalyst in methanol afforded 2,3-*O* unprotected (D)-**10**, which on treatment with acetyl chloride in the presence of dimethyltin dichloride[10] in THF and potassium carbonate as base afforded a 7:3-mixture of desired monoacetylated (D)-**11** and (D)-**12**. After chromatographic separation, reaction of (D)-**11** as acceptor with known **13**[8a,9,11] as mannosyl donor and tin(II) trifluoromethanesulfonate as catalyst furnished, by applying the inverse procedure,[12] α-linked inositol mannoside (D)-**14** in 95% yield. *O*-Deacetylation of (D)-**14** with dimethylamine in ethanol gave (D)-**15** in 79% yield. Following *O*-benzylation with benzyl bromide and sodium hydride as base in DMF at room temperature furnished the hepta-*O*-benzyl derivative (D)-**16** which is now accessible to selective modifications at *O*-1 and/or *O*-6 position. Full structural assignment could be based on NMR data. The α configuration of



Scheme 3. Reagents and conditions: (a) 13:1 PPTSA–PTSA, CH_2Cl_2, MeOH, 45 °C (68%); (b) BnBr, Ag_2O, CH_2Cl_2, rt (71%); (c) CSA, MeOH, 45 °C (89%); (d) AcCl, Me_2SnCl_2, THF, rt, K_2CO_3 (65%, 7:3); (e) $Sn(OTf)_2$, Et_2O, rt (95%); (f) $HNMe_2$ in EtOH (79%); (g) BnBr, NaH, DMF, rt (85%).

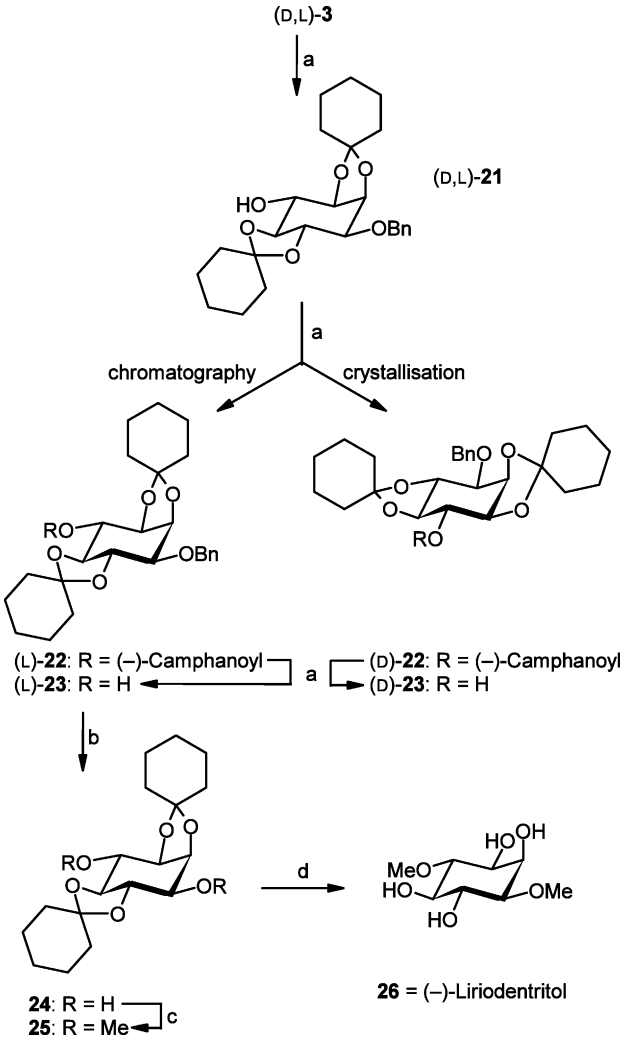


Scheme 4. Reagents and conditions: (a) K_2CO_3, MeOH, 60 °C (86%); (b) tetrazole, CH_2Cl_2; *t*-BuO_2H; Me_2NH, EtOH (78%); (c) $Pd(PPh_3)_4$, Tol-SO_2Na, HOAc, CH_2Cl_2, rt (58%); (d) Pd/C, H_2, 7.5:7.5:1 CH_2Cl_2–MeOH–H_2O (73%).

the mannosyl residue was ascertained by the $J_{C1b,H1b}$ coupling of 171.3 Hz.[13]

For the transformation of pseudodisaccharide (D)-**16** into the phosphatidyl residue carrying target molecule, the menthyloxycarbonyl group at *O*-1 was removed by treatment with potassium carbonate in methanol at 60 °C, thus affording *O*-1 unprotected (D)-**17** (Scheme 4). Reaction of (D)-**17** with the known diacylglycerol carrying phosphitamide **18**[14] in the presence of tetrazole as catalyst and then oxidation with *tert*-butylhydroperoxide and base catalyzed removal of the cyanoethyl group furnished the *O*-protected target molecule (D)-**19** which was structurally assigned by the NMR and MS data. *O*-Deallylation with palladium(0) as catalyst and sodium *p*-toluene sulfinate as nucleophile[15] in acetic acid–dichloromethane at room temperature afforded (D)-**20** in 58% yield. Hydrogenolytic *O*-debenzylation with palladium on carbon as catalyst led to the desired unprotected target molecule (D)-**1a**. Full structural assignment of this compound was based on NMR (HMQC, DQF-COSY, SED-^{31}P, ROESY) and MS data.

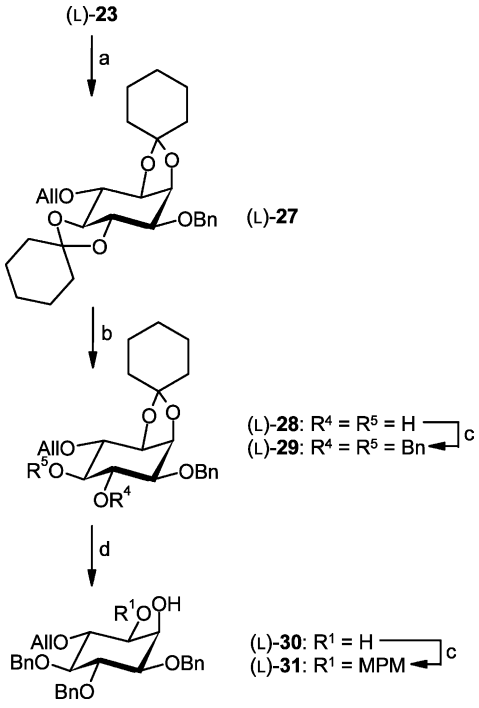
Although the synthesis of (D)-**1a** from (DL)-**2** is rather straightforward, the ready availability of (DL)-**3** by crystallisation from the reaction mixture led us to design an alternative procedure for the synthesis of pseudoenantiomer (L)-**1b**; this procedure should be also applicable to the (D)-series of PIMs and LAMs. In the new procedure, the possible migration of the menthyloxycarbonyl or any other acyl group, thus requiring mild silver oxide-supported introduction of allyl and benzyl groups, should be avoided. The first steps followed a procedure by Vacca and coworkers[16]: (DL)-**3** was selectively benzylated at the more reactive *O*-3 position [→(DL)-**21**] (Scheme 5) and then the (−)-camphanoyl residue was attached to the *O*-6 resulting in (D)- and (L)-**22**, which could be simply separated by crystallisation and flash chromatography on silica gel; thus (D)- and (L)-**22** were readily obtained in >99% enantiomeric excess. Base catalyzed removal of the camphanoyl residues furnished (L)- and (D)-**23**. Because the previous



Scheme 5. Reagents and conditions: (a) Ref. 16; (b) $Pd(OH)_2$/C, H_2, THF (98%); (c) MeI, NaH, DMF, rt (92%); (d) CSA, CH_2Cl_2, MeOH, rt, 24 h (78%).

configurational assignment of these compounds was not clear,[16] the configuration of (L)-**23** was ascertained by transformation into known (−)-liriodentritol (**26**).[17] Hydrogenolytic *O*-debenzylation of (L)-**23** with Pearlman's catalyst in THF, thus avoiding partial *O*-decyclohexylidenation, gave 3,*O*-6 unprotected **24** in high yield. *O*-Methylation with methyl iodide and sodium hydride as base in DMF afforded di-*O*-methyl derivative **25**, which on CSA-catalyzed *O*-decyclohexylidenation furnished **26** in 78% yield.

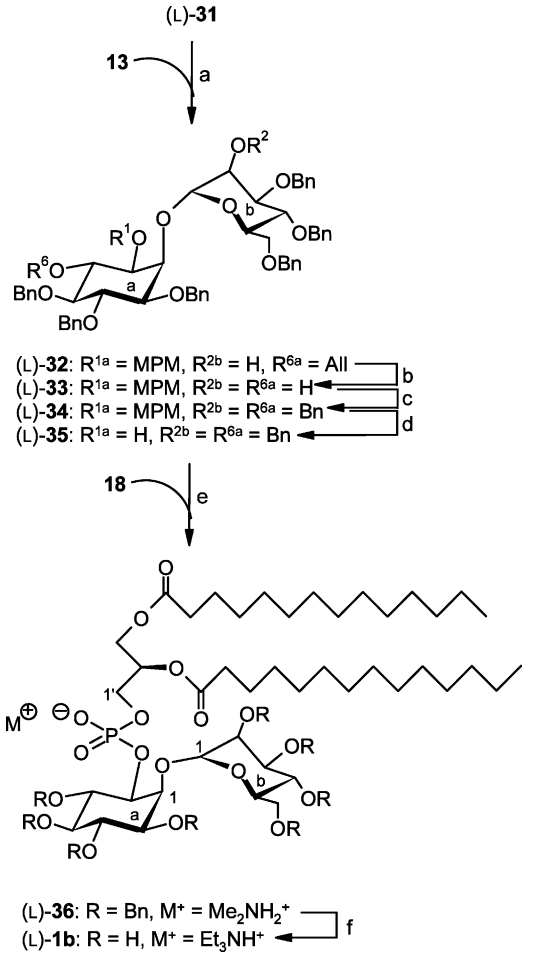
This compound was in all aspects identical with natural (−)-liriodentritol, thus leading to unequivocal structural assignment of (L)- and (D)-**23**. Hence, the synthesis of (L)-**1b** could be based on (L)-**23**. Allylation of (L)-**23** with allyl bromide in the presence of sodium hydride as base in DMF afforded fully protected *myo*-inositol derivative (L)-**27** in high yield (Scheme 6). Selective removal of the 4,5-*O*-cyclohexylidene group with PPTSA/PTSA in the presence of methanol [→(L)-



Scheme 6. Reagents and conditions: (a) All-Br, NaH, DMF, 1 h, rt (qu); (b) 13:1 PPTSA–PTSA, CH_2Cl_2, MeOH, 40 °C (78%); (c) BnBr, NaH, DMF, rt (84%); (d) CSA, 10:1 MeOH, CH_2Cl_2 10:1, 24 h, rt (95%); (e) Bu_2SnO, Tol, 3 h, refl., MPMCl, TBAI, 1.5 h, 110 °C (79%).

28] and then *O*-benzylation under standard conditions afforded the tri-*O*-benzyl derivative (L)-**29**. CSA-catalyzed cleavage of the 1,2-*O*-cyclohexylidene group in the presence of methanol led to the 1,2-*O*-unprotected derivative (L)-**30**, again in high yield. Regioselective *O*-1 protection by treatment with dibutyltin oxide in refluxing toluene and then with 4-methoxyphenylmethyl (MPM) chloride in the presence of tetrabutylammonium iodide (TBAI) furnished *O*-2 unprotected (L)-**31** which—compared with (D)-**11**—offers also the desired regioselective access to the *O*-1, *O*-2, and *O*-6 position; however, (L)-**31** is much more reluctant to further transformation than (D)-**11**.

Mannosylation of (L)-**31** with **13**[8a,9,11] as mannosyl donor in the presence of TMSOTf as catalyst in Et_2O as solvent at room temperature furnished the desired α-linked pseudodisaccharide which on treatment with methylamine in ethanol led to *O*-deacetylation, thus furnishing (L)-**32** in 71% yield (Scheme 7). The α configuration of the mannosyl residue was ascertained by the $J_{C1b\text{-}H1b}$ coupling of 173.3 Hz.[13] Then *O*-6 deallylation of (L)-**32** under standard conditions was carried out because selective access to *O*-6 was not required for the synthesis of (L)-**1b**. Thus, *O*-2b, *O*-6a unprotected (L)-**33** was obtained, which was subjected to dibenzylation again under standard conditions to furnish octa-*O*-benzyl (L)-**34** in 86% yield. Mild oxidative



Scheme 7. Reagents and conditions: (a) TMSOTf, Et_2O, rt; H_2NMe, EtOH (71%); (b) $(Ph_3P)_3RhCl$, DBU, EtOH, 90 °C; HCl, Me_2CO (87%); (c) BnBr, NaH, DMF, rt (86%); (d) CAN, MeCN, Tol, H_2O, 0 °C→rt, 75 min (94%); (e) tetrazole, CH_2Cl_2; *t*-BuO_2H; Me_2NH, EtOH (76%); (f) Pd/C, H_2, CH_2Cl_2, MeOH, H_2O, rt (74%).

cleavage of the MPM group with ceric(IV)ammonium nitrate (CAN) furnished *O*-1 unprotected (L)-**35** in high yield; transformation of (L)-**34** into (L)-**35** with DDQ as oxidizing agent was accompanied by decomposition of the starting material.[5] Diacylglycerol containing phosphitamide **18**[14] could be successfully linked to (L)-**35** in the presence of tetrazole as catalyst; ensuing oxidation with *tert*-butylhydroperoxide and then base-catalyzed removal of the cyanoethyl group led to *O*-benzyl-protected target molecule (L)-**36** in 76% yield. Hydrogenolytic removal of the eight *O*-benzyl groups could be successfully carried out with palladium on carbon as catalyst in a 7.5:7.5:1-mixture of dichloromethane–methanol–water providing pure (L)-**1b** in 74% yield. The structure of (L)-**1b** is fully supported by the NMR and MS data.

In conclusion, efficient syntheses of phosphatidylinositol mannosides (PIMs) could be developed. The decisive intermediates, particularly those obtained from 1,2:4,5-di-*O*-cyclohexylidene-*myo*-inositol, permit any structural variation at *O*-1, *O*-2, and/or *O*-6 position, thus giving access to a wide variety of PIMs, LMs, and LAMs.

3. Experimental

3.1. General methods

Solvents were purified by distillation and dried by normal procedures, except for distilled CH_2Cl_2 which was passed through a column of commercially available neutral alumina (ICN Alumina N, activity grade super I) as an alternative drying procedure. ^{13}C Assignments were based on heteronuclear multiple-quantum correlation (HMQC). Boiling range of the petroleum ether: 35–70 °C. Thin layer chromatography (TLC) was performed on E. Merck Silica Gel 60 F_{254} plates (0.2 mm). The plates were visualized by immersion in mostain [200 mL 10% H_2SO_4, 10 g $(NH_4)_6Mo_7O_{24}\cdot 4H_2O$, 200 mg $Ce(SO_4)_2$] or ninhydrin soln 1% in EtOH) or 10% H_2SO_4 or $KMnO_4$ soln (1% in water, 1% $NaHCO_3$) followed by heating (165 °C). Preparative flash chromatography was carried out on Baker Silica Gel 60 (30–60 mm) at a pressure of 0.02–0.04 MPa. FABMS was recorded on a modified Finnigan MAT 312/AMD 5000. ^1H, ^{13}C NMR and ^{31}P spectra were recorded on a Bruker AC 250 Cryospec and a Bruker DRX 600 instrument. Proton chemical shifts are reported in ppm relative to Me_4Si as internal standard. Assignments of protons and carbons were carried out with the aid of 600 MHz spectra: COSY, HMQC, ROESY, TOCSY. Measurements of optical rotations were performed on a Perkin–Elmer polarimeter 241 MC (1 dm cell). Melting points: Gallenkamp metal block; not corrected. MALDIMS were obtained on a Kratos Analytical Kompac Maldi 2 instrument with 2,5-dihydroxybenzoic acid as matrix (positive mode) or 6-aza-2-thiothymin (ATT) (negative mode).

3.2. 6-*O*-Allyl-2,3-*O*-cyclohexylidene-1-*O*-(1*R*)-menthyloxycarbonyl-D-*myo*-inositol [(D)-8]

Bis-ketal (D)-**7**[9] (48.75 g, 0.1 mol) was dissolved in a mixture of dry 1:1 CH_2Cl_2–MeOH (600 mL) and heated up to 45 °C. To this soln was added 10 mL of a mixture of 13:1 PPTSA–PTSA (0.86 m in dry DCM). The reaction was followed by TLC. Stirring was maintained for 1 h and 10 min before the reaction was quenched with NEt_3. The residue obtained upon evaporation was purified by flash chromatography (3:1→1:1 petroleum ether–EtOAc) to yield (D)-**8** (28.3 g, 68%) as a colourless foam; TLC (1:1 petroleum ether–EtOAc); R_f 0.47; $[\alpha]_D$ −49° (*c* 1, $CHCl_3$); mp 129.2 °C; ^1H NMR (250 MHz,

$CDCl_3$): δ 0.75–1.16 (3 d, m, 12 H, 3 Me, H_{Mnt}), 1.38–1.79 (m, 14 H, 10 $H_{cyclohexylidene}$, H_{Mnt}), 1.9–2.12 (m, 4 H, H_{Mnt}, 2 OH), 3.41 (dd, 1 H, $J_{5,4}$ 10.3, $J_{5,6}$ 8.6 Hz, H-5), 3.71 (dd, 1 H, $J_{6,5} = J_{6,1}$ 8.5 Hz, H-6), 3.79 (dd, 1 H, $J_{4,3}$ 7.4, $J_{4,5}$ 10.3 Hz, H-4), 4.08 (dd, 1 H, $J_{3,2}$ 5.5, $J_{3,4}$ 7.3 Hz, H-3), 4.18–4.38 (m, 2 H, OCH_2CH=CH_2), 4.5 (dd, 1 H, $J_{2,1}$ 4.1, $J_{2,3}$ 5.4 Hz, H-2), 4.56–4.63 (m, 1 H, H_{Mnt}), 4.92 (dd, 1 H, $J_{1,2}$ 4.1, $J_{1,6}$ 8.4 Hz, H-1), 5.19–5.36 (m, 2 H, CH=CH_2), 5.85–6.01 (m, 1 H, CH=CH_2). Anal. Calcd for $C_{26}H_{42}O_8$ (482.61): C, 64.71; H, 8.77. Found: C, 64.69; H, 8.60.

3.3. 6-*O*-Allyl-4,5-di-*O*-benzyl-2,3-*O*-cyclohexylidene-1-*O*-(1*R*)-menthyloxycarbonyl-D-*myo*-inositol [(D)-9]

To a mixture of (D)-**8** (30.89 g, 64 mmol), silver (I) oxide (118 g, 8 equiv) and dry DCM (350 mL) was treated BnBr (45.6 mL, 6 equiv, exothermic). After stirring for 3 h at room temperature (rt), the mixture was filtered over celite and concentrated under diminished pressure. The obtained residue was purified on silica gel (20:1 petroleum ether–EtOAc) to give 29.8 g (71%) of (D)-**9** as colourless oil; TLC (6:1 petroleum ether–EtOAc): R_f 0.7; $[\alpha]_D$ −31.9° (*c* 1, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.72–1.13 (3 d, m, 12 H, 3 Me, H_{Mnt}), 1.3–1.75 (m, 14 H, 10 $H_{cyclohexylidene}$, H_{Mnt}), 1.9–2.12 (m, 2 H, H_{Mnt}), 3.45 (dd, 1 H, $J_{5,6}$ 9.5, $J_{5,4}$ 8.3 Hz, H-5), 3.79 (dd, 1 H, $J_{6,5}$ 9.5 Hz, H-6), 3.81 (dd, 1 H, H-4), 4.19–4.23 (m, 3 H, CH_2CH=CH_2, H-3), 4.44 (dd, 1 H, $J_{2,1}$ 3.8, $J_{2,3}$ 5.7 Hz, H-2), 4.48–4.6 (m, 1 H, H_{Mnt}), 4.78 (m, 2 H, CH_2Ph), 4.8 (2 d, 2 H, CH_2Ph), 4.95 (dd, 1 H, $J_{1,2}$ 3.8, $J_{1,6}$ 8.3 Hz, H-1), 5.1–5.3 (m, 2 H, CH=CH_2), 5.82–5.9 (m, 1 H, CH=CH_2), 7.2–7.4 (m, 10 H, Ph). Anal. Calcd for $C_{40}H_{54}O_8$ (662.86): C, 72.45; H, 8.21. Found: C, 72.55; H, 8.21; MALDIMS: *m*/*z* 685.3 $[M+Na]^+$, 701.3 $[M+K]^+$.

3.4. 6-*O*-Allyl-4,5-di-*O*-benzyl-2,3-1-*O*-(1*R*)-menthyloxycarbonyl-D-*myo*-inositol [(D)-10]

For the cleavage of the ketal protecting group, compound (D)-**9** (16.74 g, 25 mmol) was dissolved in 10:1 MeOH–CH_2Cl_2 (220 mL). To this soln was added camphor-10-sulfonic acid (0.75 g, 3.23 mmol) and the reaction mixture was stirred for 8.5 h at 45 °C. Next, the mixture was neutralized with Et_3N, diluted with toluene and concentrated under diminished pressure. The residue was purified on silica gel (6:1 petroleum ether–EtOAc) to give 13.1 g (89%) of product (D)-**10** as a colourless foam; TLC (2:1 petroleum ether–EtOAc): R_f 0.55; ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.72–1.13 (3 d, m, 12 H, 3 Me, H_{Mnt}), 1.32–1.72 (m, 4 H, H_{Mnt}), 1.88–2.3 (m, 4 H, H_{Mnt}, 2 OH), 3.49 (dd, 1 H, H-5), 3.55 (dd, 1 H, $J_{3,2}$ 2.7, $J_{3,4}$ 9.6 Hz, H-3), 3.76 (dd, 1 H, H-6), 3.89 (dd, 1 H, H-4), 4.15–4.35 (m, 3 H, CH_2CH=CH_2, $J_{2,3} = J_{2,1}$ = 2.6 Hz, H-2), 4.48–4.6 (m, 1 H, H_{Mnt}), 4.66–4.97 (4 d, 4 H, CH_2Ph), 4.7 (dd, 1 H, $J_{1,2}$ 2.7, $J_{1,6}$ 10.1 Hz, H-1), 5.08–5.28 (m, 2 H, CH=CH_2), 5.8–5.98 (m, 1 H, CH=CH_2), 7.21–7.39 (m, 10 H, Ph). MALDIMS $[M+Na]^+$: Calcd 605.7, Found 605.4; $[M+K]^+$ Calcd 621.8, Found 621.4. Anal. Calcd for $C_{34}H_{46}O_8$ (582.7): C, 70.08; H, 7.96. Found: C, 69.67; H, 7.99.

3.5. 3-*O*-Acetyl-6-*O*-allyl-4,5-di-*O*-benzyl-1-*O*-(1*R*)-menthyloxycarbonyl-D-*myo*-inositol [(D)-11]

The diol (D)-**10** (10.58 g, 18 mmol), dissolved in dry THF (100 mL), was treated with anhyd K_2CO_3 (5.62 g, 2.24 equiv) and dimethyltin dichloride (4.39 g, 1.1 equiv) and stirred for 0.5 h under AP. To this reaction mixture was added acetyl chloride (1.56 mL, 1.2 equiv) and stirred overnight. Then K_2CO_3 was filtered off and the reaction mixture was concentrated under diminished pressure. Silica gel column chromatography (15:1 toluene–EtOAc) afforded (D)-**11** (7.3 g, 65%) as a white solid; TLC (6:1 toluene–EtOAc): R_f 0.56; $[\alpha]_D$ −23.5° (*c* 1, $CHCl_3$); mp 144.5 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.7–1.08 (3 d, m, 12 H, 3 Me, H_{Mnt}), 1.33–1.63 (m, 4 H, H_{Mnt}), 1.8–1.9, 1.98–2.05 (m, 2 H, H_{Mnt}), 1.94 (s, 3 H, OAc), 3.48 (dd, 1 H, $J_{5,6} = J_{5,4}$ 9.5 Hz, H-5), 3.82 (dd, 1 H, $J_{6,1} = J_{6,5}$ 9.82 Hz, H-6), 3.93 (dd, 1 H, $J_{4,5} = J_{4,3}$ 9.82 Hz, H-4), 4.1–4.16, 4.23–4.27 (m, 2 H, CH_2CH=CH_2), 4.19 (dd, 1 H, $J_{2,3} = J_{2,1}$ 2.6 Hz, H-2), 4.45–4.52 (m, 1 H, H_{Mnt}), 4.57–4.82 (4 d, dd, 5 H, CH_2Ph, $J_{1,2}$ 2.6, $J_{1,6}$ 10.2 Hz, H-1), 4.85 (dd, 1 H, $J_{3,4}$ 10.2, $J_{3,2}$ 2.8 Hz, H-3), 5.03–5.21 (m, 2 H, CH=CH_2), 5.8–5.9 (m, 1 H, CH=CH_2), 7.14–7.3 (m, 10 H, Ph). Anal. Calcd for $C_{36}H_{48}O_9$ (624.77): C, 69.21; H, 7.74. Found: C, 69.16; H, 7.74.

3.6. 3-*O*-Acetyl-6-*O*-allyl-4,5-di-*O*-benzyl-*O*-1-(1*R*)-menthyloxycarbonyl-2-*O*-(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-D-*myo*-inositol [(D)-14]

To a soln of acceptor (D)-**11** (8.02 g, 18 mmol), in anhyd ether (50 mL), was added under Ar $Sn(OTf)_2$ (268 mg, 0.05 equiv). Then donor **13**[8a,9,11] (16.35 g, 0.026 mol, dissolved in 50 mL anhyd ether) was added drop-wise over 5 min to the reaction mixture. Stirring was maintained for 1 h, then the reaction was quenched with triethylamine and the mixture concentrated. The residue was purified by flash chromatography (24:1 toluene–EtOAc) to give (D)-**14** (13.4 g, 95%) as a colourless foam; TLC (12:1 toluene–acetone, 1% Et_3N): R_f 0.57. $[\alpha]_D$ +5.9° (*c* 1, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.7–1.11 (3 d, m, 12 H, 3 Me, H_{Mnt}), 1.3–1.7 (m, 4 H, H_{Mnt}), 1.78 (s, 3 H, OAc), 1.81–2.16 (m, 2 H, H_{Mnt}), 2.1 (s, 3 H, OAc), 3.5–3.6 (m, 2 H), 3.66–3.95 (m, 6 H), 4.17–4.37 (m, 3 H, OCH_2CH=CH_2), 4.4–4.68 (m, 6 H), 4.7–4.9 (m, 7 H), 5.0–5.05 (d, 1 H, H-2b), 5.12–5.31 (m, 2 H, CH=CH_2), 5.45 (d, 1 H, H-1b), 5.8–5.99 (m, 1 H, CH=CH_2), 7.1–7.4 (m, 25

H, Ph). MALDI-MS: 1122.2 $[M+Na]^+$. Anal. Calcd for $C_{65}H_{78}O_{15}$ (1099.32): C, 71.02; H, 7.15. Found: C, 71.07; H, 7.20.

3.7. 6-*O*-Allyl-4,5-di-*O*-benzyl-1-*O*-(1*R*)-menthyloxycarbonyl-2-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-D-*myo*-inositol [(D)-15]

Compound (D)-**14** (13.4 g, 12 mmol) was dissolved in 100 mL of methylamine soln (33% in anhyd EtOH) and stirred for 24 h at rt. The reaction mixture was concentrated, diluted with toluene and evaporated. Silica gel column chromatography of the residue (10:1 toluene–EtOAc) afforded (D)-**15** (9.8 g, 79%) as a colourless foam; TLC (3:1 petroleum ether–EtOAc): R_f 0.48; $[\alpha]_D$ −3.7° (*c* 1, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): δ 0.72–1.12 (3 d, m, 12 H, 3 Me, H_{Mnt}), 1.33–1.72 (m, 4 H, H_{Mnt}), 1.8–2.2 (m, 4 H, H_{Mnt}, 2 OH), 3.4–3.8 (m, 8 H), 4.01–4.12 (m, 2 H), 4.12–4.32 (m, 3 H, $OCH_2CH{=}CH_2$, H-2), 4.4–4.89 (m, 12 H), 4.96 (d, 1 H, H-1b), 5.09–5.3 (m, 2 H, $CH{=}CH_2$), 5.81–5.99 (m, 1 H, $CH{=}CH_2$), 7.11–7.4 (m, 25 H, Ph). MALDIMS: 1037.4 $[M+Na]^+$, 1053.3 $[M+K]^+$. Anal. Calcd for $C_{61}H_{74}O_{13}$ (1015.25·0.5 H_2O): C, 71.53; H, 7.38. Found: C, 71.63; H, 7.33.

3.8. 6-*O*-Allyl-3,4,5-tri-*O*-benzyl-1-*O*-(1*R*)-menthyloxycarbonyl-2-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-D-*myo*-inositol [(D)-16]

To a soln of (D)-**15** (9.8 g, 9.65 mmol), in anhyd DMF (100 mL), was added BnBr (5.73 mL, 5 equiv). After cooling to 0 °C, NaH was added portion-wise (579 mg, 2.5 equiv). The reaction mixture was allowed to reach rt and after 2.5 h stirring the mixture was quenched with 1:3 CH_3COOH–EtOAc and the mixture concentrated under diminished pressure. The residue was purified on silica gel (10:1 petroleum ether–EtOAc) to give 9.75 g (85%) of (D)-**16** as a colourless oil. TLC (3:1 petroleum ether–EtOAc): R_f 0.73. $[\alpha]_D$ −1.8° (*c* 1, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$): δ 0.61–1.08 (3 d, m, 12 H, 3 Me, H_{Mnt}), 1.25–1.64 (m, 4 H, H_{Mnt}), 1.8–1.9, 2.02–2.08 (m, 2 H, H_{Mnt}), 3.16–3.19, 3.36–3.42 (m, H, H-6b), 3.28–3.37 (m, 2 H, H-5a, H-3a), 3.52 (dd, 1 H, H-6a), 3.63 (dd, 1 H, H-4a), 3.64–3.73 (m, 2 H, H-2b, H-3b), 3.9–4.05 (m, 2 H, H-4b, H-5b), 4.08–4.2 (m, 2 H, $CH_2CH{=}CH_2$), 4.2–4.26, 4.33–4.4, 4.45–4.54, 4.66–4.85 (m, 15 H, CH_2Ph, H_{Mnt}), 4.32 (dd, 1 H, H-2a), 4.6 (dd, 1 H, H-1a), 4.97–5.04, 5.1–5.2 (m, 2 H, $CH{=}CH_2$), 5.27 (d, 1 H, H-1b), 5.79–5.9 (m, 1 H, $CH{=}CH_2$), 6.98–7.48 (m, 35 H, Ph); ^{13}C NMR (150.9 MHz, $CDCl_3$): δ 68.3 (C-6b), 70.1–75.6 (CH_2Ph), 71.7 (C-4b), 72.9 (C-2b), 73.5 (C-2a), 74.4 (C-5b), 74.5 ($OCH_2CH{=}CH_2$), 77.1 (C-1a), 78.5 (C-3a), 78.7 (C-3b), 79.0 (C-6a), 79.1 (C-Mnt), 80.9 (C-4a), 83.1 (C-5a), 98.2 (C-1b), 117.0 ($CH{=}CH_2$), 134.8 ($CH{=}CH_2$). Anal. Calcd for $C_{75}H_{86}O_{13}$ (1195.5): C, 75.35; H, 7.25. Found: C, 75.08; H, 7.49. MALDIMS: 1217.4 $[M+Na]^+$.

3.9. 6-*O*Allyl-3,4,5-tri-*O*-benzyl-2-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-D-*myo*-inositol [(D)-17]

To a soln of (D)-**16** (3.1 g, 2.6 mmol), in 10:1 anhyd MeOH–Et_2O (110 mL), was added K_2CO_3 (3 g, 21.7 mmol) and the mixture was stirred for 6 h at 60 °C. After evaporation, the residue was purified by silica gel column chromatography (6:1 toluene–EtOAc) to afford (D)-**17** (2 g, 86%) as a colourless oil. TLC (3:1 petroleum ether–EtOAc): R_f 0.17; $[\alpha]_D$ +35.1° (*c* 1, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$) δ 3.28–3.42 (m, 5 H), 3.52–3.6 (m, 1 H), 3.68–3.9 (m, 3 H), 3.98–4.15 (m, H), 4.31–4.98 (m, 16 H), 5.1–5.29 (m, 2 H, $CH{=}CH_2$), 5.46 (d, 1 H, H-1b), 5.79–5.96 (m, 1 H, $CH{=}CH_2$), 7.11–7.4 (m, 35 H, Ph). MALDIMS: 1035.2 $[M+Na]^+$, 1051.2 $[M+K]^+$. Anal. Calcd for $C_{64}H_{68}O_{11}$ (1013.24): C, 75.87; H, 6.77. Found: C, 75.96; H, 7.02.

3.10. 6-*O*-Allyl-3,4,5-tri-*O*-benzyl-2-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-D-*myo*-inosit-1-yl-[(2*R*)-2,3-bis-(myristoyloxy)propyl]-phosphate [(D)-19]

Tetrazole (360 mg, 2.6 equiv) and cyanethoxy-*N*,*N*-diisopropylphosphoramidite (**18**)[14] (2.82 g, 2 equiv) were dried for 1 h under high diminished pressure. Compound (D)-**17** (2 g, 1.97 mmol, dissolved in 100 mL anhyd CH_2Cl_2) was added to the mixture of tetrazole and **18**. Stirring was maintained at rt under Ar atmosphere for 2 h. The two diastereomers (3:1 petroleum ether–EtOAc, R_f 0.50 and 0.56) were then treated with *tert*-butylhydroperoxide (4.7 m in isooctane, 7.85 mL). After 1 h, the reaction mixture was concentrated to 10 mL, treated with dimethylamine soln (36 mL, 33% in anhyd EtOH) and stirred for 1 h. Then the reaction mixture was again concentrated to 10 mL, diluted with CH_2Cl_2, a satd $NaHCO_3$-soln was added, and the two layers were separated. The organic layer was washed with brine, dried (Na_2SO_4) and concentrated. The residue was purified by flash chromatography (9:1 → 1:10 toluene–acetone) to afford (D)-**19** (2.6 g, 78%) as a slightly yellow oil; TLC (10:1 $CHCl_3$–MeOH): R_f 0.34; ^{31}P NMR (242.9 MHz, 1:1 CD_3OD–$CDCl_3$): δ −3.97 (s, 1P); ^1H NMR (600 MHz, 1:1 $CDCl_3$–CD_3OD): δ 0.8–0.95 (t, 6 H, Me), 1.04–1.4 (m, 40 H, CH_2-chain), 1.4–1.7 (m, 4 H, $COCH_2$–CH_2–R), 2.18–2.3 (m, 4 H, $COCH_2$–CH_2–R), 3.1 (m, H-6b), 3.29–3.43 (m, 3 H, H-6b, H-5a, H-3a), 3.59 (dd, 1 H, H-6a), 3.72 (dd, 1 H, H-4a), 3.79 (dd, 1 H, H-2b), 3.82 (dd, 1 H, H-3b), 4.0–4.18 (m, 7 H, H-4b, H-5b, H-1a, H-1′, H-3′), 4.25–4.4 (m, 2 H, $OCH_2CH{=}CH_2$), 4.2–4.25, 4.4–4.9 (m, 14 H, CH_2Ph), 4.58 (dd, 1 H, H-2a), 5.13–5.32 (m, 3 H, $CH{=}CH_2$, H-2′), 5.61 (d, 1 H, H-1b), 5.9–6.1 (m, H, $CH{=}CH_2$), 7.1–7.52 (m, 35 H, Ph); ^{13}C NMR (1:1 150.9

MHz, $CDCl_3$–CD_3OD): δ 62.8 (C-3′), 64.2 (C-1′), 68.4 (C-6b), 70.6 (C-2′), 71.2–76.8 (CH_2Ph), 71.7 (C-5b), 73.7 (C-2b), 73.8 (C-2a), 74.5 (C-4b), 74.8 ($OCH_2CH=CH_2$), 77.0 (C-1a), 78.5 (C-3b), 79.0 (C-3a), 80.3 (C-6a), 81.1 (C-4a), 83.2 (C-5a), 98.0 (C-1b). $C_{95}H_{127}O_{18}P$ (1587.09). MALDIMS: 1587.6 $[M-H]^-$.

3.11. 3,4,5-Tri-*O*-benzyl-2-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-D-*myo*-inosit-1-yl-[(2*R*)-2,3-bis[(myristoyloxy)-propyl]phosphate [(D)-20]

To a soln of (D)-**19** (310 mg, 0.2 mmol), in CH_2Cl_2 (2 mL), was added under Ar atmosphere $Pd(PPh_3)_4$ (22 mg, 0.1 equiv), *p*-toluenesulfinic acid sodium salt (40.6 mg, 1.2 equiv) and AcOH (26.1 μL, 2.4 equiv). The reaction mixture was followed by TLC (4:1 $CHCl_3$–MeOH, R_f 0.73→0.69). After 2 h stirring at rt, the reaction was completed. The mixture was concentrated under diminished pressure and purified by silica gel column chromatography (48:1 $CHCl_3$→$CHCl_3$–MeOH) to yield (D)-**20** (180 mg, 58%) as a colourless oil; TLC (4:1 $CHCl_3$–MeOH); R_f 0.69; ^{1}H NMR (250 MHz, 1:1 $CDCl_3$–CD_3OD): δ 0.82–0.95 (t, 6 H, Me), 1.17–1.4 (m, 40 H, CH_2), 1.45–1.65 (m, 4 H, $COCH_2$–CH_2–R), 2.2–2.3 (m, 4 H, $COCH_2$–CH_2–R), 3.15–3.25 (m, 1 H), 3.3–3.5 (m, 3 H), 3.73–4.3 (m, 11 H), 4.39–4.98 (m, 16 H), 5.22–5.35 (m, 1 H, H-2′), 5.53 (d, 1 H, H-1b), 7.1–7.5 (m, 35 H, Ph).

3.12. Triethylammonium [2-*O*-(α-D-mannopyranosyl)-D-*myo*-inosit-1-yl]-[(2*R*)-2,3-bis(myristoyloxy)propyl]-phosphate [(D)-1a]

A stirred mixture of (D)-**20** (170 mg, 0.1 mmol, 7.5:7.5:1 CH_2Cl_2–MeOH–water 3 mL) and Pd/C (0.2 equiv) was degassed under diminished pressure and saturated with H_2 (H_2-filled balloon) three times. The suspension was stirred at rt overnight, filtered over celite, washed with 7.5:7.5:1 CH_2Cl_2–MeOH–water (2 mL) and treated with some Et_2N. The solvents were removed under diminished pressure by lyophilization to afford (D)-**1a** (82 mg, 73%) as a white powder; TLC (65:35:8 $CHCl_3$–MeOH–0.2% $CaCl_2$): R_f 0.26; ^{31}P NMR (242.9 MHz, Me_2SO-d_6): δ −1.31 (s, 1 P); ^{1}H NMR (600 MHz, Me_2SO-d_6): δ 0.75–0.91 (t, 6 H, Me), 1.05–1.37 (m, 49 H, CH_2-chain, Me_{Et3N}), 1.39–1.57 (m, 4 H, $COCH_2CH_2R$), 2.17–2.35 (m, 4 H, $COCH_2CH_2R$), 2.93 (dd, 1 H, H-5a), 3.08 (m, 6 H, $HN(CH_2–CH_3)_3$), 3.18 (dd, 1 H, H-3a), 3.32 (dd, 1 H, H-4a), 3.47 (m, 2 H, H-6a, H-6b), 3.48 (dd, H, H-4b), 3.51 (dd, 1 H, H-3b), 3.54 (m, 1 H, H-6b), 3.64 (dd, 1 H, H-2b), 3.72 (dd, 1 H, H-1a), 3.77 (m, 1 H, H-1,3), 3.84 (ddd, 1 H, H-5b), 3.89 (m, 1 H, H-1,3), 4.00 (dd, 1 H, H-2a), 4.1 (m, 1 H, H-1,3), 4.31 (m, 1 H, H-1,3), 5.02 (d, 1 H, H-1b), 5.09 (m, 1 H, H-2′). ^{13}C NMR (150.9 MHz, Me_2SO-d_6): δ 9.3 (3C, Me_{Et3N}), 14.8 (2C, Me), 22.9, 29.8, 32.5 (20 C, $(CH_2)_n$) 25.1 (2 C, $COCH_2CH_2R$), 34.0 (2 C, $COCH_2CH_2R$), 45.9 (3 C, CH_2CH_{3NEt3}), 61.6 (C-6b), 63.1 (C-1,3), 63.6 (C-1,3), 68.2 (C-6a), 71.0 (C-2′), 71.1 (C-2b), 71.2 (C-3a), 71.4 (C-3b), 73.0 (C-4b), 73.3 (C-5b), 76.1 (C-5a), 72.2 (C-1a), 77.9 (C-2a), 100.7 (C-1b); MALDIMS: Calcd $(M-H)^-$: *m*/*z* 915.7, Found *m*/*z* 914.9.

3.13. 3-*O*-Benzyl-1,2:4,5-di-*O*-cyclohexylidene-6-*O*-camphanoyl-L-*myo*-inositol [(L)-22]

Compound (D)-**22** was synthesized following a procedure of Vacca and coworkers.[16a] Separation procedure: The mother liquors were evaporated and flash chromatography (8:1 petroleum ether–EtOAc) yielded 11 g of crude (L)-**22** which was dissolved in CH_2Cl_2, treated with 100 g silica gel and evaporated to dryness. Column chromatography (∅ 7 cm, l = 40 cm) yielded pure (L)-**22** (8.6 g) as a colourless solid. TLC (3:1 petroleum ether–EtOAc): R_f 0.44.

3.14. 3-*O*-Benzyl-1,2:4,5-di-*O*-cyclohexylidene-6-*O*-camphanoyl-D-*myo*-inositol [(D)-22]

TLC (3:1 petroleum ether–EtOAc): R_f 0.37.

3.15. 1,2:4,5-Di-*O*-cyclohexylidene-L-*myo*-inositol [(L)-24]

A mixture of (L)-**23** (950 mg, 2.21 mmol), anhyd THF (25 mL) and Pearlman's catalyst (10 mol%) was degassed under diminished pressure and saturated with H_2 three times. The suspension was stirred at rt for 2 h, then neutralized with Et_3N, filtered over celite, washed with THF and concentrated. Compound (L)-**24** (736 mg, 98%) was obtained as a white solid; TLC (1:1 petroleum ether–EtOAc): R_f 0.32; mp 190 °C; $[\alpha]_D$ +17.3° (*c* 0.75, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.25–1.86 (m, 20 H, $H_{cyclohexylidene}$), 3.39–2.7 (2 s, 2 H, OH), 3.32 (dd, 1 H, *J* 10.7, *J* 9.3 Hz, H-5), 3.72–3.93 (m, 2 H), 3.95–4.12 (m, 2 H), 4.49 (dd, 1 H, $J_{2,3}=J_{2,1}$ 4.8 Hz, H-2). Anal. Calcd for $C_{18}H_{28}O_6\cdot 0.25\ H_2O$ (344.9): C, 62.68; H, 8.33. Found: C, 62.76; H, 8.35.

3.16. 2,3:5,6-Di-*O*-cyclohexylidene-1,4-di-*O*-methyl-D-*myo*-inositol (25)

To a soln of compound **24** (440 mg, 1.29 mmol), in dry DMF (5 mL), were added ICH_3 (200 μL, 3.2 mmol) and NaH (116 mg, 4.8 mmol). After 3 h stirring at rt, the reaction mixture was diluted with satd aq NH_4Cl-soln and CH_2Cl_2. The organic layer was washed with water (×2), dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (2:1 petroleum ether–EtOAc) to afford **25** (438 mg, 92%) as a white solid. TLC (1:1 petroleum ether–EtOAc): R_f 0.76; mp 118 °C; $[\alpha]_D$ +8° (*c* 1, $CHCl_3$); ^{1}H NMR (600 MHz,

$CDCl_3$): δ 1.25–1.5, 1.51–1.82 (m, 20 H, $H_{cyclohexylidene}$), 3.31 (dd, 1 H, $J5,6 = J_{5,4}$ 9.8 Hz, H-5), 3.47 (dd, 1 H, $J_{4,5}$ 10.6, $J_{4,3}$ 6.4 Hz, H-4), 3.58 (s, 3 H, OMe), 3.60 (s, 3 H, OMe), 3.62 (dd, 1 H, $J_{1,2}$ 4.2, $J_{1,6}$ 10.1 Hz, H-1), 3.96 (dd, 1 H, $J_{6,1} = J_{6,5}$ 9.8 Hz, H-6), 4.06 (dd, 1 H, $J_{3,4} = J_{3,2}$ 5.6 Hz, H-3), 4.52 (dd, 1 H, $J_{2,3} = J_{2,1}$ 4.6 Hz, H-2). Anal. Calcd for $C_{20}H_{32}O_6$ (368.5): C, 65.19; H, 8.75. Found: C, 65.16; H, 8.75.

3.17. 1,4-Di-*O*-methyl-D-*myo*-inositol/(−)-Liriodentritol (26)

To a soln of **25** (160 mg, 0.41 mmol) in 1:1 MeOH–CH_2Cl_2 (2 mL), was added camphor-10-sulfonic acid (15 mg, 0.065 mmol) at rt and the soln was stirred for 24 h. The white precipitate, which was formed, was filtered, washed with CH_2Cl_2 and dried under high diminished pressure. Compound **26** was obtained in 78% yield (67 mg); TLC (5:1 $CHCl_3$–MeOH): R_f 0.07; mp 226 °C. $[\alpha]_D$ −25° (*c* 1.5, water); $[\alpha]_D$ −25° (*c* 2, water); ^{1}H NMR (600 MHz, Me_2SO-d_6): δ 2.78 (dd, 1 H, $J_{1,2}$ 2.5, $J_{1,6}$ 9.6 Hz, H-1), 3.0 (ddd, 1 H, $J_{5,6} = J_{5,4}$ 9.1, $J_{5\text{-OH}}$ 4.7 Hz, H-5), 3.08 (dd, 1 H, $J_{4,5} = J_{4,3}$ 9.4 Hz, H-4), 3.18 (ddd, 1 H, $J_{3,4}$ 9.4, $J_{3,2}$ 2.7, $J_{3\text{-OH}}$ 6.4 Hz, H-3), 3.28 (s 3 H, Ome at O-1), 3.43 (s, 3 H, OMe at O-4), 3.43 (ddd, 1 H, $J_{6,1}$ 9.6, $J_{6,5}$ 9.1, $J_{O\text{-}6H}$ 4.9 Hz, H-6), 3.88 (ddd, 1 H, $J_{2,3}$ 2.72, $J_{2,1}$ 2.5, $J_{O\text{-}6H}$ 4.0 Hz, H-2), 4.54 (d, 1 H, *J* 6.7 Hz, OH-3), 4.56 (d, 1 H, *J* 4.0 Hz, OH-2), 4.58 (d, 1 H, *J* 4.9 Hz, OH-6), 4.65 (d, 1 H, *J* 4.7 Hz, OH-5); ^{13}C NMR (150.9 MHz, Me_2SO-d_6): δ 56.59 ($OMe_{C\text{-}1}$), 56.68 ($OMe_{C\text{-}4}$), 68.53 (C-2), 71.08 (C-3), 71.93 (C-6), 74.67 (C-5), 81.39 (C-1), 83.10 (C-4). Anal. Calcd for $C_8H_{16}O_6$ (208.2): C, 46.14; H, 7.75. Found: C, 46.00; H, 7.71.

3.18. 6-*O*-Allyl-3-*O*-benzyl-1,2:4,5-di-*O*-cyclohexylidene-L-*myo*-inositol [(L)-27]

A soln of (L)-**23** (23 g, 54 mmol), in dry DMF (580 mL), was treated with allyl bromide (5.9 mL, 75.43 mmol), then NaH (2.3 g, 0.90 mmol) was added. The reaction mixture was stirred at rt for 45 min, quenched with MeOH and concentrated under diminished pressure. The residue was diluted with EtOAc, washed with water and brine. The organic layer was dried with $MgSO_4$ and concentrated under diminished pressure. The resulting syrup was applied to a short column of silica gel which was eluted with 9:1→3:1 petroleum ether–EtOAc to give (L)-**27** (25.1 g, quant.) as a white solid; TLC (3:1 petroleum ether–EtOAc): R_f 0.67; mp 90.2 °C; $[\alpha]_D$ + 41.7° (*c* 1, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.3–1.85 (m, 20 H, $H_{cyclohexylidene}$), 3.27 (dd, 1 H, $J_{5,6} = J_{5,4}$ 10 Hz, H-5), 3.63 (dd, 1 H, $J_{6,1}$ 6.5, $J_{6,5}$ 10.6 Hz, H-6), 3.73 (dd, 1 H, $J_{3,4}$ 10.3, $J_{3,2}$ 4.1 Hz, H-3), 4.00 (dd, 1 H, $J_{1,2}$ 5.0, $J_{1,6}$ 6.8 Hz, H-1), 4.03 (dd, 1 H, $J_{4,5} = J_{4,3}$ 9.7 Hz, H-4), 4.25–4.31 (m, 2 H, CH_2CH=CH_2), 4.33 (dd, 1 H, $J_{2,3} = J_{2,1}$ 4.4 Hz, H-2), 4.80–4.91 (m, 2 H, CH_2–Ph), 5.14–5.21, 5.3–5.35 (m, 2 H, $CH_2CH{=}CH_2$), 5.90–5.99 (m, 1 H, $CH_2CH{=}CH_2$), 7.24–7.44 (m, 5 H, ArH). Anal. Calcd for $C_{28}H_{38}O_6$ (470.6): C, 71.46; H, 8.14. Found: C, 71.43; H, 8.14.

3.19. 6-*O*-Allyl-3-*O*-benzyl-1,2-*O*-cyclohexylidene-L-*myo*-inositol [(L)-28]

Bis-ketal (L)-**27** (12 g, 25.5 mmol) was dissolved in 1:1 dry CH_2Cl_2–MeOH (200 mL) and heated up to 40 °C. To this soln was added 0.3 mL of a mixture of 13:1 PPTSA–PTSA (0.86 m) in dry DCM. The reaction was followed by TLC (1:1 petroleum ether–EtOAc, R_f 0.2). Stirring was maintained for 1 h 10 before the reaction was quenched with Et_3N. The residue obtained upon evaporation was purified by flash chromatography (1:1 petroleum ether–EtOAc, dissolved in a minimum of EtOAc–MeOH) to yield (L)-**28** (7.8 g, 78%) as a white solid; mp 138 °C; $[\alpha]_D$ −18.1° (*c* 1, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.3–1.8 (m, 10 H, $H_{cyclohexylidene}$), 2.73 (s, 2 H, OH), 3.33 (dd, 1 H, $J_{5,6} = J_{5,4}$ 9.7 Hz, H-5), 3.46 (dd, 1 H, $J_{4,5}$ 9.7, $J_{4,3}$ 7.0 Hz, H-4), 3.52 (dd, 1 H, $J_{1,2}$ 4.1, $J_{1,6}$ 9.7 Hz, H-1), 3.94 (dd, 1 H, $J_{6,1} = J_{6,5}$ 9.4 Hz, H-6), 4.01 (dd, 1 H, $J_{3,4}$ 7.0, $J_{3,2}$ 5.0 Hz, H-3), 4.18–4.21, 4.39–4.42 (m, 2 H, CH_2CH=CH_2), 4.31 (dd, 1 H, $J_{2,3} = J_{2,1}$ 4.7 Hz, H-2), 4.73–4.79 (m, 2 H, CH_2–Ph), 5.17–5.20, 5.27–5.30 (m, 2 H, $CH_2CH{=}CH_2$), 5.91–5.98 (m, 1 H, $CH_2CH{=}CH_2$), 7.25–7.44 (m, 5 H, ArH). Anal. Calcd for $C_{22}H_{30}O_6$ (390.5): C, 67.67; H, 7.74. Found: C, 67.48; H, 7.61.

3.20. 6-*O*-Allyl-3,4,5-tri-*O*-benzyl-1,2-*O*-cyclohexylidene-L-*myo*-inositol [(L)-29]

To a soln of (L)-**28** (14.43 g, 37 mmol), in dry DMF (430 mL), was added BnBr (11 mL, 92.6 mmol). NaH (2.7 g, 113 mmol) was slowly added to the soln and after stirring for 4 h at rt, the reaction mixture was treated with MeOH. After usual workup (EtOAc–water) the organic layer was dried ($MgSO_4$) and concentrated under diminished pressure. Flash chromatography (10:1 petroleum ether–EtOAc) gave (L)-**29** (84%) as a colourless syrup; TLC (8:1 petroleum ether–EtOAc): R_f 0.35; $[\alpha]_D$ +43.1° (*c* 1, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.3–1.88 (m, 10 H, $H_{cyclohexylidene}$), 3.35 (dd, 1 H, *J* 8.6, *J* 9.8 Hz, $H_{inositol}$), 3.63–3.75 (m, 2 H, $H_{inositol}$), 3.91 (dd, 1 H, *J* 8.6 Hz, $H_{inositol}$), 4.0 (dd, 1 H, *J* 5.5, *J* 7.1 Hz, $H_{inositol}$), 4.2–4.31, 4.32–4.43 (m, 2 H, H-2, CH_2CH=CH_2), 4.70–4.89 (m, 6 H, CH_2–Ph), 5.12–5.36 (m, 2 H, $CH_2CH{=}CH_2$), 5.89–6.08 (m, 1 H, $CH_2CH{=}CH_2$), 7.20–7.47 (m, 15 H, ArH). Anal. Calcd for $C_{36}H_{42}O_6$ (570.7): C, 75.76; H, 7.42. Found: C, 75.78; H, 7.40.

3.21. 6-*O*-Allyl-3,4,5-tri-*O*-benzyl-L-*myo*-inositol [(L)-30]

For cleavage of the ketal, compound (L)-**29** (20.8 g, 25 mmol) was dissolved in 10:1 MeOH–CH_2Cl_2 (330 mL). To this soln was added camphor-10-sulfonic acid (1.1 g, 4.73 mmol) and the reaction mixture was stirred for 24 h at rt. Next the mixture was neutralized with Et_3N, diluted with toluene and concentrated under diminished pressure. The obtained residue was purified on silica gel (1:1 petroleum ether–EtOAc) to give 17 g (95% yield) of product (L)-**30** as a white solid; TLC (2:1 petroleum ether–EtOAc): R_f 0.25; mp 123 °C; $[\alpha]_D$ +31° (*c* 1, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.5 (s, 2 H, OH), 3.41 (dd, 1 H, $J_{5,6} = J_{5,4}$ 9.4 Hz, H-5), 3.44–3.47 (m, 2 H, H-1, H-3), 3.70 (dd, 1 H, $J_{6,1} = J_{6,5}$ 9.4 Hz, H-6), 3.92 (dd, 1 H, $J_{4,5} = J_{4,3}$ 9.4 Hz, H-4), 4.21 (dd, 1 H, $J_{2,3} = J_{2,1}$ 3.0 Hz, H-2), 4.22–4.28, 4.39–4.44 (m, 2 H, CH_2CH=CH$_2$), 4.68–4.70, 4.76–4.89 (m, 6 H, CH_2–Ph), 5.16–5.18; 5.25–5.29 (m, 2 H, CH$_2$CH=CH_2), 5.92–5.98 (m, 1 H, CH$_2$CH=CH$_2$), 7.25–7.34 (m, 15 H, ArH). Anal. Calcd for $C_{30}H_{34}O_6$ (490.6): C, 73.45; H, 6.99. Found: C, 73.50; H, 6.87.

3.22. 6-*O*-Allyl-3,4,5-tri-*O*-benzyl-1-*O*-(4-methoxybenzyl)-L-*myo*-inositol [(L)-31]

Compound (L)-**30** (15.1 g, 30.77 mmol), in anhyd toluene (500 mL), was treated with dibutyltin oxide (8.43 g, 1.1 equiv) and the reaction mixture was refluxed in a Dean and Stark apparatus for 3 h. To the reaction mixture was added TBAI (17 g, 46 mmol) and 4-methoxybenzyl chloride (9.1 mL, 67 mmol). Stirring was maintained at 110 °C for 1.5 h, then evaporated and diluted with EtOAc, washed with water, brine, dried ($MgSO_4$) and concentrated. Silica gel column chromatography of the residue (6:1 → 5:1 petroleum ether–EtOAc) yielded (L)-**31** (14.85 g, 79%) as a slightly brown solid; TLC (2:1 petroleum ether–EtOAc): R_f 0.43; mp 106 °C; $[\alpha]_D$ +9.1° (*c* 1, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.41 (s, 1 H, OH), 3.29 (dd, 1 H, *J* 9.6, *J* 2.7 Hz, $H_{inositol}$), 3.36 (dd, 1 H, *J* 9.7, *J* 2.8 Hz, $H_{inositol}$), 3.38 (dd, 1 H, *J* 9.5 Hz, $H_{inositol}$), 3.81 (s, 3 H, OMe), 3.81 (dd, 1 H, *J* 9.5 Hz, $H_{inositol}$), 3.94 (dd, 1 H, *J* 9.6 Hz, $H_{inositol}$), 4.16 (dd, 1 H, *J* 2.7 Hz, $H_{inositol}$), 4.28, 4.95 (m, 2 H, CH_2CH=CH$_2$), 4.59–4.74, 4.78–4.93 (m, 8 H, CH_2–Ph), 5.12–5.34 (m, 2 H, CH$_2$CH=CH_2), 5.90–6.08 (m, 1 H, CH$_2$CH=CH$_2$), 6.83–6.92 (m, 2 H, H_{PMB}), 7.22–7.40 (m, 17 H, ArH). Anal. Calcd for $C_{38}H_{42}O_7$ (610.8): C, 73.64; H, 6.99. Found: C, 73.70; H, 6.74.

3.23. 6-*O*-Allyl-3,4,5-tri-*O*-benzyl-1-*O*-(4-methoxybenzyl)-2-*O*-(2,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1 → 2)-L-*myo*-inositol [(L)-32]

A mixture of imidate **13**[8a,9,11] (20 g, 31.4 mmol), and acceptor (L)-**31** (11.6 g, 19 mmol) was dissolved in anhyd ether (220 mL, ultrasound). Trimethylsilyl triflate (0.52 mL) was added and the mixture was stirred for 10 s, then quenched with triethylamine, diluted with toluene and concentrated. The residue was purified by flash chromatography (5:1 → 4:1 petroleum ether–EtOAc) to give the crude product. TLC: (2:1 petroleum ether–EtOAc, 1% Et_3N), R_f 0.72. Without further purification, the crude product was dissolved in 200 mL 33% methylamine soln in anhyd EtOH and stirred for 6 h at rt. The reaction mixture was concentrated, diluted with toluene and evaporated. Silica gel column chromatography of the residue (3:1 → 2:1 petroleum ether–EtOAc) afforded (L)-**32** (14 g, 71% over 2 steps). TLC (3:1 petroleum ether–EtOAc): R_f 0.40. $[\alpha]_D$ +41° (*c* 1, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.38 (s, 1 H, OH), 3.20 (dd, 1 H, $J_{1,2}$ 2.0, $J_{1,6}$ 9.9 Hz, H-1a), 3.28–3.40 (m, 3 H, H-5a, H-3a, H-6b), 3.50 (dd, 1 H, J_{gem} 10.7, J_{vic} 3.2 Hz, H-6b), 3.69 (dd, 1 H, $J_{6,1} = J_{6,5}$ 9.5 Hz, H-6a), 3.76 (s, 3 H, OMe), 3.78–3.86 (m, 2 H, H-4a, H-3b), 3.92 (dd, 1 H, $J_{4,5} = J_{4,3}$ 9.7 Hz, H-4b), 4.06 (m, 1 H, H-2b), 4.12–4.17 (m, 1 H, H-5b), 4.25–4.31 (m, 1 H, CH$_2$=CH–CH$_2$), 4.32 (m, 1 H, H-2a), 4.34–4.40, 4.5–4.56, 4.57–4.73, 4.74–4.88 (m, 15 H, CH_2–Ph, CH$_2$=CH–CH_2), 5.13 (dd, 1 H, J_{gem} 10.3 Hz, CH_2=CH–CH$_2$), 5.25 (dd, 1 H, CH_2=CH–CH$_2$), 5.38 (d, 1 H, $J < 1$ Hz, H-1b), 5.89–6.0 (m, 1 H, CH$_2$=CH–CH$_2$), 6.72–6.81 (m, 2 H, H_{PMB}), 7.06–7.38 (m, 32 H, ArH); ^{13}C NMR (150.9 MHz, $CDCl_3$): δ 55.20 (OMe), 68.55 (C-6b), 68.65 (C-2b), 70.90 (C-5b), 72.10–76.19 (9C, CH$_2$–CH=CH$_2$, CH$_2$Ph, C-4b), 78.44 (C-1a), 79.61 (C-3b), 80.75 (C-3a), 81.04 (C-6a), 81.42 (C-4a), 83.44 (C-5a), 99.97 (C-1b), 113.65 (C_{PMB}), 116.57 (CH$_2$–CH=CH$_2$), 127.46–138.70 (40 C, Ph, CH$_2$–CH=CH$_2$), 159.00 (C_{OMe}). Anal. Calcd for $C_{65}H_{70}O_{12}$ (1043.3): C, 74.80; H, 6.76. Found: C, 74.92; H, 6.51.

3.24. 3,4,5-Tri-*O*-benzyl-1-*O*-(4-methoxybenzyl)-2-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-(1 → 2)-L-*myo*-inositol [(L)-33]

Compound (L)-**32** (3 g, 2.88 mmol) was dissolved in EtOH (45 mL) by heating, then DBU (43 μL, 0.29 mmol) and $(Ph_3P)_3RhCl$ (750 mg, 0.81 mmol) were added. The mixture was stirred for 1.5 h under reflux and then concentrated under diminished pressure (propenyl intermediate: R_f 0.54, 2:1 petroleum ether–EtOAc). The residue was dissolved in 1:9 1 m HCl–acetone (50 mL), and the soln was heated under reflux for 15 min. Acidity was neutralized by adding triethylamine, then the mixture was diluted with EtOAc,

washed with water, dried ($MgSO_4$) and concentrated. Flash chromatography (4:1 → 5:2 petroleum ether–EtOAc) of the residue gave (L)-**33** (2.5 g, 87%); TLC (2:1 petroleum ether–EtOAc): R_f 0.38. $[\alpha]_D$ +8.5° (*c* 0.25, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$): δ 2.39 (s, 2 H, OH), 3.06 (dd, 1 H, $J_{1,2}$ 2.4, $J_{1,6}$ 10.0 Hz, H-1a), 3.32 (dd, 1 H, $J_{5,6} = J_{5,4}$ 9.1 Hz, H-5a), 3.34 (dd, 1 H, $J_{3,4}$ 10.0, $J_{3,2}$ 2.4 Hz, H-3a), 3.42 (dd, 1 H, $J_{gem} = 10.4$, $J_{vic} = 2.1$ Hz, H-6b), 3.56 (dd, 1 H, J_{gem} 10.6, J_{vic} 3.8 Hz, H-6b), 3.77 (s, 3 H, OMe), 3.8 (dd, 1 H, $J_{4,5} = J_{4,3}$ 9.4 Hz, H-4a), 3.84 (dd, 1 H, $J_{3,4}$ 9.4, $J_{3,2}$ 3.2 Hz, H-3b), 3.9 (dd, 1 H, $J_{4,5} = J_{4,3}$ 9.7 Hz, H-4b), 3.94 (dd, 1 H, $J_{6,1} = J_{6,5}$ 9.7 Hz, H-6a), 4.05 (dd, 1 H, $J_{2,3} < 1$ Hz, H-2b), 4.15 (ddd, 1 H, J_{vic} 1.8, 3.5, $J_{5,4}$ 10.0 Hz, H-5b), 4.35 (dd, 1 H, $J_{2,3} = J_{2,1}$ 2.4 Hz, H-2a), 4.36–4.47, 4.56–4.61, 4.63–4.73, 4.77–4.88 (m, 14 H, CH_2–Ph), 5.37 (d, 1 H, $J < 1$ Hz, H-1b), 6.78–6.80 (m, 2 H, H_{PMB}), 7.08–7.39 (m, 32 H, ArH); ^{13}C NMR (150.9 MHz, $CDCl_3$): δ 55.24 (OMe), 68.65 (C-2b), 68.79 (C-6b), 71.02 (C-5b), 71.35–75.79 (10 C, CH_2Ph, C-2a, C-6a, C-4b), 77.63 (C-1a), 79.68 (C-3b), 80.81 (C-3a), 81.28 (C-4a), 83.31 (C-5a), 100.0 (C-1b), 113.86 (C_{PMB}), 127.52–138.62 (39 C, Ph), 159.18 (C_{OMe}). Anal. Calcd for $C_{62}H_{66}O_{12}\cdot 0.25\ H_2O$ (1007.7): C, 73.90; H, 6.65. Found: C, 73.81; H, 6.67.

3.25. 3,4,5,6-Tetra-*O*-benzyl-1-*O*-(4-methoxybenzyl)-2-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-(1 → 2)-L-*myo*-inositol [(L)-34]

To a soln of (L)-**33** (2.5 g, 2.49 mmol), in dry DMF (50 mL), was added BnBr (0.75 mL, 6.31 mmol) and NaOH (150 mg, 6.25 mmol). The reaction mixture was stirred at rt for 3 h, quenched with MeOH and concentrated. The residue was partitioned between EtOAc and water. The organic layer was washed with brine, dried ($MgSO_4$) and evaporated under diminished pressure. Silica gel column chromatography (4:1 petroleum ether–EtOAc) afforded (L)-**34** (2.5 g, 86%) as a colourless syrup; TLC (4:1 petroleum ether–EtOAc): R_f 0.27; $[\alpha]_D$ +20° (*c* 1, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): δ 3.23–3.49 (m, 4 H), 3.59 (dd, 1 H, J_{gem} 10.6, J_{vic} 3.5 Hz, H-6b), 3.66–3.88 (m, 4 H), 3.76 (s, 3 H, OMe), 4.0–4.2 (m, 2 H), 4.32–4.96 (m, 19 H, CH_2–Ph, H-2a), 5.42 (d, 1 H, *J* 1.4 Hz, H-1b), 6.70–6.80 (m, 2 H, H_{PMB}), 7.09–7.42 (m, 42 H, ArH). Anal. Calcd for $C_{76}H_{78}O_{12}$ (1183.5): C, 77.10; H, 6.64. Found: C, 77.06; H, 6.73.

3.26. 3,4,5,6-Tetra-*O*-benzyl-2-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-(1 → 2)-L-*myo*-inositol [(L)-35]

A soln of (L)-**34** (2.6 g, 2.20 mmol), in 60:3:4 MeCN–toluene–water (3 mL), was cooled to 0 °C and treated with $Ce(NH_4)_2(NO_3)_6$ (6 g, 10.94 mmol). After 0.5 h at 0 °C, the reaction was allowed to reach rt. The mixture was stirred for 1.5 h, diluted with EtOAc, washed with satd aq $NaHCO_3$-soln, dried ($MgSO_4$) and concentrated. Flash chromatography (4:1 → 3:1 petroleum ether–EtOAc) of the residue gave (L)-**35** (2.2 g, 94%) as a colourless syrup; TLC (5:2 petroleum ether–EtOAc): R_f 0.26. $[\alpha]_D$ +10.8° (*c* 1, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): δ 2.45 (s, 1 H, OH), 3.37–3.49 (m, 3 H), 3.53–3.81 (m, 6 H), 3.90 (dd, 1 H, *J* 8.7 Hz), 4.01–4.11 (m, 1 H), 4.21 (dd, 1 H, $J_{2,1} = J_{2,3}$ 2.3 Hz, H-2a), 4.42–4.93 (m, 16 H, CH_2–Ph), 5.22 (d, 1 H, *J* 1.20 Hz, H-1b), 7.13–7.41 (m, 40 H, ArH). MALDIMS$^+$ (matrix DHB, THF):, *m/z* 1086.3 $[M+Na]^+$. Found: *m/z* 1086.8. Anal. Calcd for $C_{68}H_{70}O_{11}\cdot H_2O$ (1081.3): C, 75.53; H, 6.71. Found: C, 75.48; H, 6.50.

3.27. Dimethylammonium [3,4,5,6-tetra-*O*-benzyl-2-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-L-*myo*-inosit-1-yl]-[(2*R*)-2,3-bis(myristoyloxy)propyl]-phosphate [(L)-36]

Tetrazole (172 mg, 2.46 mmol) was dried for 1 h under high diminished pressure. Compound (L)-**35** (1 g, 0.94 mmol) was dissolved in anhyd CH_2Cl_2 (50 mL), added to the tetrazole and stirred at rt under Ar. To this reaction mixture was added dropwise benzyl *N*,*N*-diisopropylphosphoramidite (**18**)[14] (1.35 g, 1.89 mmol) and the soln was stirred for 2 h, then treated with *tert*-butylhydroperoxide in isooctane (4.7 M, 3.76 mL). After 15 min, the reaction mixture was concentrated to 10 mL, treated with dimethylamine soln (20 mL, 33% in anhyd EtOH) and stirred for 1 h. Then the reaction mixture was again concentrated to 10 mL, diluted with CH_2Cl_2, saturated $NaHCO_3$-soln was added and the two layers were separated. The organic layer was washed with brine, dried ($MgSO_4$) and concentrated. The residue was purified by flash chromatography (9:1 → 1:10 toluene–acetone) to afford (L)-**36** (1.17 g, 76%) as a colourless syrup; ^{31}P NMR (242.9 MHz, 1:1 CD_3OD–$CDCl_3$): δ −2.927 (s, 1P); ^1H NMR (600 MHz, 1:1 CD_3OD–$CDCl_3$): δ 0.89 (t, 6 H, Me), 1.1–1.40 (s, 40 H, $(CH_2)_n$), 1.45–1.60 (m, 4 H, $COCH_2CH_2R$), 2.15–2.30 (m, 4 H, $COCH_2CH_2R$), 3.40–3.54 (m, 2 H, H-3a, H-5a), 3.67 (dd, 1 H, $J_{4,5} = J_{4,3}$ 9.4 Hz, H-4a), 3.71–3.78 (m, 2 H, H-2b, H-6a), 3.79–3.84 (m, 1 H, H-3b), 3.87–3.99 (m, 4 H, H-1, H-3, H-6b), 4.0–4.07, (m, 2 H, H-1a, H-1), 4.09–4.18 (m, 2 H, H-4b, H-5b), 4.19–4.25 (m, 1 H, H-3), 4.38–4.93 (m, 17 H, CH_2–Ph, H-2a), 5.14–5.20 (m, 1 H, H-2), 5.31 (d, 1 H, $J < 1$ Hz, H-1b), 7.10–7.42 (m, 40 H, ArH). MALDIMS$^-$ (matrix ATT, water): $[M-H]^-$, *m/z* 1636.2. Found: *m/z* 1635.8. FABMS$^+$ (matrix NBOH + NaI, $CHCl_3$): $[(M^-Na^+)+Na]^+$, *m/z* 1684. Found: *m/z* 1684.

3.28. Triethylammonium-[2-*O*-(α-D-mannopyranosyl)-l-*myo*-inosit-1-yl]-[(2*R*)-2,3-bis(myristoyloxy)propyl]-phosphate [(L)-1b]

A vigorously stirred mixture of (L)-**36** (394 mg, 0.24 mmol), 7.5:7.5:1 CH_2Cl_2–MeOH–water (5 mL) and Pearlman's catalyst (0.2 equiv) was degassed under diminished pressure and saturated with H_2 (H_2-filled balloon) three times. The suspension was stirred at rt overnight, filtered over celite and washed with 7.5:7.5:1 CH_2Cl_2–MeOH–water (2 mL). The filtrate was diluted with water, treated with Et_3N and further removal of the solvents by lyophilization afforded (L)-**1b** (162 mg, 74%) as a white solid; ^{31}P NMR (242.9 MHz, Me_2SO-d_6): δ 0.963 (s, 1P); ^{1}H NMR (600 MHz, Me_2SO-d_6): δ 0.76–0.91 (t, 6 H, Me), 1.0–1.40 (m, 49 H, $(CH_2)_n$, Me_{Et_3N}), 1.41–1.57 (m, 4 H, $COCH_2CH_2R$), 2.15–2.32 (m, 4 H, $COCH_2CH_2R$), 2.85–2.95 (dd, 1 H, H-5a), 2.96–3.15 (m, 6 H, $HN(CH_2–CH_3)_3$), 3.22 (dd, 1 H, H-4b), 3.23 (m, 1 H, H-6b), 3.24 (m, 1 H, H-3a), 3.34, (dd, 1 H, H-4a), 3.45 (dd, 1 H, H-3b), 3.46 (dd, 1 H, H-6a), 3.61 (dd, 1 H, H-1), 3.64 (dd, 1 H, H-2b), 3.72 (m, 1 H, H-6b), 3.76 (m, 1 H, H-1), 3.9 (m, 1 H, H-1), 4.00 (dd, 1 H, H-2a), 4.06 (m, 1 H, H-3), 4.08 (ddd, 1 H, H-5b), 4.28 (m, 1 H, H-3), 4.95 (d, 1 H, H-1b), 5.09 (m, 1 H, H-2); ^{13}C NMR (150.9 MHz, Me_2SO-d_6): δ 8.5 (3 C, Me_{Et_3N}), 13.87 (2 C, Me), 22.04/28.42–29.03/31.26 $(CH_2)_n$) 24.36/24.47 (2 C, $COCH_2CH_2R$), 33.34/33.57 (2 C, $COCH_2CH_2R$), 45.1 (3 C, $CH_2CH_{3Et_3N}$), 62.04 (C-3′), 62.55 (C-1′), 62.6 (C-6b), 68.53 (C-4b), 70.05 (C-2b), 70.24 (C-2′), 70.51 (C-6a), 71.65 (C-3a), 71.95 (C-3b), 72.16 (C-4a), 72.28 (C-5b), 73.85 (C-1a), 75.21 (C-5a), 76.97 (C-2a), 100.2 (C-1b), 172.25/172.51 (2C, *C*OR). FABMS$^-$ (matrix 1:1:1 Me_2SO–glycerol–NBOH): $[M-H]^-$, *m/z* 915.7. Found: *m/z* 915, $[M-C_{14}H_{27}O]^-$, *m/z* 705.3. Found: 705.

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References

1. (a) Draper, P. In *The Biology of Mycobacteria*; Ratledge, C.; Standford, J., Eds. *The Anatomy of Mycobacteria*; Vol. 2; Academic Press: London, 1982; pp 9–52;
(b) Brennan, P. J.; Nikaido, H. *Annu. Rev. Biochem.* **1995**, *64*, 887–888;
(c) Chatterjee, D.; Khoo, K.-H. *Cell. Mol. Life Sci.* **2001**, *58*, 2018–2042;
(d) Chatterjee, D.; Khoo, K.-H. *Glycobiology* **1998**, *8* (2), 113–120.
2. (a) Brennan, P. J.; Ballou, C. E. *J. Biol. Chem.* **1967**, *242*, 3046–3056;
(b) Besra, G. S.; Morehouse, C. B.; Rittner, C. M.; Waechter, C. J.; Brennan, P. J. *Am. Soc. Biochem. Mol. Biol.* **1997**, *272*, 18460–18466.
3. Theler, J. -M.; Brennan, P. J.; Nasir-ud-Din; Ilangumaran, S.; Arni, S.; Poincelet, M.; Hoessli, D. C. *J. Immunol.* **1995**, *155*, 1334–1342.
4. Stadelmaier, A. *Diplomarbeit*, Universität Konstanz, **1999**.
5. Stadelmaier, A. *Dissertation*, Universität Konstanz, **2003**.
6. (a) Stepanov, A. E.; Shvets, V. I.; Evstigneeva, R. P. *Zh. Obshch. Kim.* **1977**, *47*, 1653–1656;
(b) Zamyatina, A. Y.; Shvets, V. I. *Chem. Phys. Lipids* **1995**, *76*, 225–240;
(c) Elie, C. J. J.; Dreef, C. E.; Verduyn, R.; Van der Marel, G. A.; Van Boom, J. H. *Tetrahedron* **1989**, *45*, 3477–3486.
7. (a) Elie, C. J. J.; Verduyn, R.; Dreef, C. E.; Van der Marel, G. A.; Van Boom, J. H. *J. Carbohydr. Chem.* **1992**, *11*, 715–739;
(b) Watanabe, Y.; Yamamoto, T.; Ozaki, S. *J. Org. Chem.* **1996**, *61*, 14–15;
(c) Watanabe, Y.; Yamamoto, T.; Okazaki, T. *Tetrahedron* **1997**, *53*, 903–918.
8. (a) Massy, D. J. R.; Wyss, P. *Helv. Chim. Acta* **1990**, *73*, 1037–1057;
(b) Mayer, T. G.; Schmidt, R. R. *Liebigs Ann. Recueil* **1997**, 859–863;
(c) Pekari, K.; Schmidt, R. R. In *Lipases and Lipids: Structure, Function and Biotechnological Applications*; Kokotos, G.; Constantinou-Kokotou, V., Eds. Recent results in glycosyl phosphatidyl inositol (GPI) anchor synthesis; Crete University Press: Heraklion, 2000; pp 233–252.
9. Pekari, K.; Tailler, D.; Weingart, R.; Schmidt, R. R. *J. Org. Chem.* **2001**, *66*, 7432–7442.
10. Maki, T.; Iwasaki, F.; Matsumura, Y. *Tetrahedron Lett.* **1998**, *39*, 5601–5604.
11. (a) Mayer, T. G.; Kratzer, B.; Schmidt, R. R. *Angew. Chem.* **1994**, *106*, 2289–2293; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 2177–2181.;
(b) Kartha, K. P. R.; Jennings, H. J. *J. Carbohydr. Chem.* **1990**, 777–781;
(c) Borén, H. B.; Ekborg, G.; Ekland, K. *Acta Chem. Scand.* **1973**, *27*, 2639–2644;
(d) Kaur, K. J.; Hindsgaul, O. *Carbohydr. Res.* **1992**, *226*, 219–231;
(e) Ponpipom, M. M. *Carbohydr. Res.* **1977**, *59*, 311–317;
(f) Yamazaki, F.; Kitajima, T.; Nukada, T.; Ito, Y.; Ogawa, T. *Carbohydr. Res.* **1990**, *201*, 31–50.
12. Schmidt, R. R.; Toepfer, A. *Tetrahedron Lett.* **1991**, *32*, 3353–3356.
13. (a) Bock, K.; Pederson, C. *J. Chem. Soc. Perkin Trans. II* **1974**, 293–297;
(b) Yonezawa, T.; Morishma, I. *J. Mol. Spectrosc.* **1968**, *27*, 210–217;

(c) Albrand, J. P.; Cogne, A.; Gagnaire, D.; Robert, J. B. *Tetrahedron* **1971**, *27*, 2453–2461.

14. (a) Mayer, T. G.; Weingart, R.; Münstermann, F.; Kawada, T.; Teymuras, T.; Schmidt, R. R. *Eur. J. Org. Chem.* **1999**, *10*, 2563–2572;
(b) Beaucage, S. L.; Caruthers, M. H. *Tetrahedron Lett.* **1981**, *22*, 1859–1862;
(c) Beaucage, S. L.; Iyer, R. P. *Tetrahedron* **1993**, *49*, 10441–10488;
(d) Bannwarth, W.; Trzeciak, A. *HeIv. Chim. Acta* **1987**, *70*, 175–186.
15. Honda, M.; Morita, H.; Nagakura, I. *J. Org. Chem.* **1997**, *62*, 8932–8936.
16. (a) Vacca, J. P.; deSolms, S. J.; Huff, J. R.; Billington, D. C.; Baker, R.; Kulagowski, J. J.; Mawer, I. M. *Tetrahedron* **1989**, *45*, 5679–5702;
(b) Billington, D. C.; Baker, R.; Kulagowski, J. J.; Mawer, I. M. *J. Chem. Soc., Chem. Commun.* **1987**, 314–316.
17. (a) Aguiló, A.; Martín-Lomas, M.; Penadés, S. *Tetrahedron Lett.* **1992**, *33*, 401–404;
(b) Anderson, L. *The Carbohydrates, Chemistry and Biochemistry*, 2nd ed.; Pigman, W., Horton, D., Eds.; Academic Press, New York, 1972, Vol. 1A, pp. 519–579.;
(c) Plouvier, V. *Bull. Soc. Chim. Biol.* **1963**, *45*, 1079–1118;
(d) Angyal, S. J.; Bender, V. *J. Chem. Soc.* **1961**, 4718–4720;
(e) Post, G. G.; Anderson, L. *J. Am. Chem. Soc.* **1962**, *84*, 471–478;
(f) Post, G. G.; Anderson, L. *J. Am. Chem. Soc.* **1962**, *84*, 478–480.