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Versatile Synthesis of 1-*O*-(ω-Aminolauryl)-I(4,5)P_2

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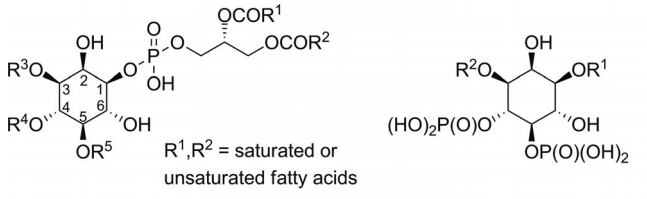
The synthesis of a model 1-*O*-(ω-aminoacyl)-IP_2 derivative, lauryl 4,5-bisphosphate **31**, was realized following a versatile and high-yielding scheme. The flexible synthetic strategy used for this purpose allows the preparation of a range of other useful IP, IP_2 and IP_3 derivatives. In view of the central role played by IPs and PIPs in cellular life, the preparation of functionalized *myo*-inositol derivatives of this type may facilitate the isolation and fluorescent localization of related proteins.

Introduction

myo-Inositol phosphates (IPs) play a key role in biological systems. They function as secondary messengers in important cell-signalling pathways.[1] In particular, phosphatidylinositol (PI, **1**, Figure 1) and its ring-phosphorylated derivatives (PIPs, **2**) comprise a very important class of membrane phospholipids.[2] Naturally occurring PIPs can be categorized according to their inositol ring phosphorylation pattern and the fatty acids present on the glycerol moiety.



1: R^3,R^4,R^5 = H
2: R^3,R^4,R^5 = H or P(O)$(OH)_2$
3: R^3 = H, R^4,R^5 = P(O)$(OH)_2$
4: R^1 = stearoyl, R^2 = P(O)$(OH)_2$
5: R^1 = APB, R^2 = P(O)$(OH)_2$
rac-**6**: R^1 = palmitoyl, R^2 = H

Figure 1. General structures of PI (**1**), PIPs (**2** and **3**) and structures of known 1-*O*-acyl-IPs (**4**–**6**) [APB = 4-(4-aminophenyl)butyryl].

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PIPs are known to undergo phosphorylation at multiple sites to generate diverse phosphoinositides, which, in turn, regulate a series of signal-transduction pathways.[1] They can undergo sequential and reversible phosphorylations at the 3-, 4-, and 5-positions, catalysed by specific kinases. Consequently, they act as important mediators of several biochemical processes that are known to play central roles in fundamental cellular functions, such as intracellular vesicle trafficking, apoptosis, cell proliferation, and metabolism.[3]

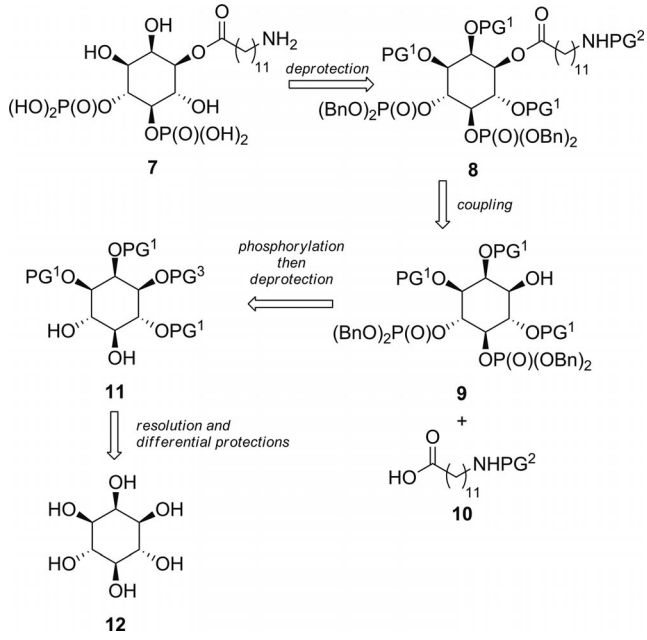
More specifically, PI(4,5)P_2 (**3**, Figure 1) has been implicated in a variety of important cellular functions. It is hydrolyzed by a phosphatidylinositol-specific phospholipase C (PLC) to generate two important secondary messenger molecules, I(1,4,5)P_3 and diacylglycerol.[4] This initiates an important pathway for cell proliferation in which I(1,4,5)P_3 interacts with membrane-bound receptors to release Ca^{2+}, which is a key event in cellular signal transduction.[5] This process mediates cellular responses to hormones, neurotransmitters, and other cellular signalling molecules, including odorants and those responsible for bitter taste.[6] In addition, PI(4,5)P_2 sequesters profilin to the inner surface of the phospholipid bilayer, which facilitates the polymerization of actin.[7] It can also be converted by agonist-stimulated, receptor-mediated activation of phosphoinositide 3-kinase (PI 3-K) to PI(3,4,5)P_3, the key element in a newly discovered intracellular signaling system.[8]

Because of their unique biological profile, several research groups have designed and synthesized a number of PIP analogues.[2,9] These modified PIPs could be helpful probes for examining the stereospecificity and inhibition of several inositol monophosphatase enzymes, and for exploring their potential use as drugs. They mainly belong to the families of inositol-deoxygenated analogues,[10,11] phosphorothioates,[12–14] and phosphonates,[13,15] but other types of PIP analogue have also been synthesized.[16,17]

In order to clarify the diverse biological role of PIPs, it is necessary to identify the related receptor proteins. In practice though, this is prohibited due to the lack of sufficient amounts of PIPs that can be obtained from natural sources. This issue was very nicely addressed by the design and synthesis of ω-amino-PIP analogues for the preparation of photoaffinity-labeled probes,[18,19] biotinylated probes, and others,[17,19,20] as well as affinity probes immobilized on beads,[21] which could help in the investigation and isolation of particular receptor proteins.

A less investigated category of PIP analogues includes those derivatives that completely lack the phosphoglycerol tail, having replaced it by an acyl group, i.e., 1-*O*-acyl-IPs (Figure 1). These compounds have the advantage of being more easily prepared, since they contain only the headgroup of a PIP. Interestingly, 1-*O*-stearoyl-I(3,4,5)P_3 **4** was found to completely inhibit PI 3-kinase,[22] whereas affigel-immobilized I(3,4,5)P_3-APB **5** has shown better binding selectivity to proteins than the corresponding PIP.[11,23] Racemic 1-*O*-palmitoyl-I(4,5)P_2 **6** has also been synthesized as a potential phospholipase C inhibitor.[24]

In a continuation of our previous research work[25] into the synthesis and biological evaluation of polyphosphorylated inositol and carbohydrate derivatives, we wish to report here a versatile and high-yielding synthesis of new 1-*O*-(ω-aminoacyl)-IP_2 **7** (Scheme 1). This model compound could potentially be used for the selective isolation of proteins (as an immobilized probe)[11,23] and/or as a fluorescent probe (after the attachment of a fluorescent label).[26]



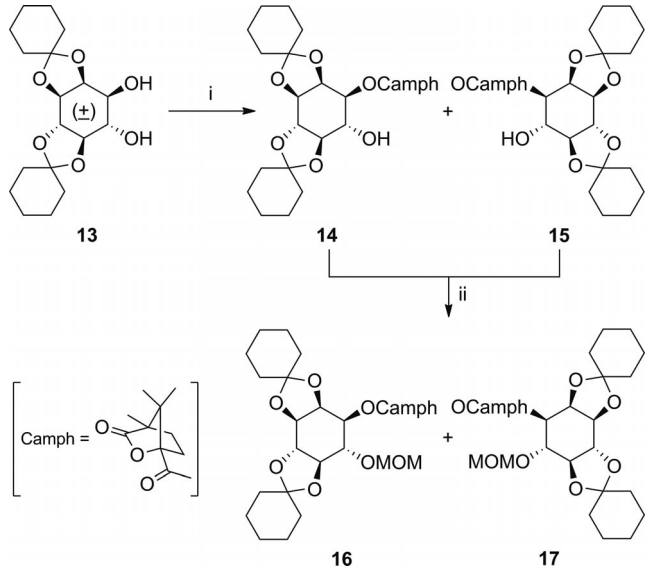
Scheme 1. Retrosynthetic analysis (PG = protecting group).

Results and Discussion

For the synthesis of **7**, we envisaged the retrosynthesis shown in Scheme 1. According to this plan, the target compound could be derived from fully protected ester **8** by deprotection. Obviously, it would be highly desirable to realize this task in a single step, so the protecting groups (PGs) present other than Bn should be chosen carefully. In turn, ester **8** leads back to advanced *myo*-inositol derivative **9** and protected 12-aminolauric acid **10**. The former compound is expected to be derived from diol **11** by sequential phosphorylation and selective deprotection of the 1-position. Finally, **11** could be obtained from parent *myo*-inositol (**12**) by a series of regioselective protecting group manipulations and a key resolution step.

Since this synthetic plan should be widely applicable, and not only relevant to our model compound **7**, the following structural variations were taken into consideration: (a) the number and position of the phosphate groups, i.e., the possibility to construct all seven phosphorylated IPs (variables on the 3-, 4- and 5-positions); (b) the length and saturation of the ω-amino fatty acid; and finally (c) the absolute stereochemistry, i.e., the ability to prepare the corresponding enantiomeric IPs [3-*O*-(ω-aminoacyl)-derivatives].

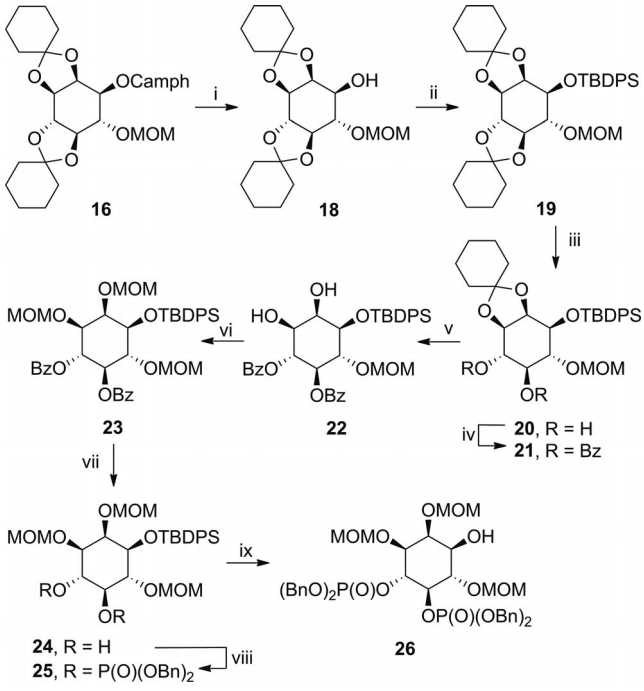
The key resolution step was realized early in our synthesis (Scheme 2). Thus, racemic 2,3:4,5-di-*O*-cyclohexylidene *myo*-inositol (**13**), readily available on a multi-gram scale from *myo*-inositol,[27] was selected as the starting material of choice. Regioselective camphanylation of **13** with 1-(*S*)-(–)-camphanyl chloride by a known procedure[28] yielded a 1:1 mixture of diastereoisomers **14** and **15**. In order to avoid time-consuming chromatographic techniques, we examined the possibility of separating the two diasteroisomers after the next step. After some experimentation, and to our delight, introduction of a methoxymethyl group on the free hydroxy (C-6) furnished a 1:1 mixture of the corresponding fully masked derivatives **16** and **17**, which were easily separated by simple fractional crystallization. The absolute configuration of each diastereoisomer (**16** and **17**) was verified



Scheme 2. (i) Ref.[28] (ii) MOMCl, DIPEA, DMF, room temp., 72 h (89%; 1:1 mixture of **16** and **17**) (MOM = methoxymethyl; DIPEA = diisopropylethylamine).

by their independent preparation from small quantities of pre-purified known camphanyl esters **14** and **15**. This decided the nature of the required protecting group PG[1] (Scheme 1), and thus, significantly, determined the final global deprotection conditions for the realization of our synthetic plan. Moreover, the ability to easily obtain both enantiomers in pure form clearly addresses the issue of the future synthesis of 3-*O*-(ω-aminoacyl)-IPs using the same methodology.

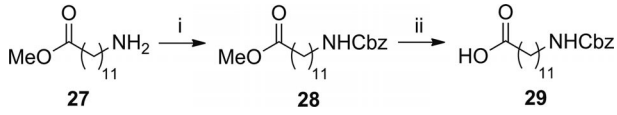
Having solved the issues of optical resolution and PG[1] introduction in the early stages, we proceeded with the stepwise construction of the desired phosphorylated inositol head-group (i.e., **9**). Saponification of camphanyl ester **16** smoothly furnished free alcohol **18** (Scheme 3). At this point, for the introduction of PG[3], the orthogonal TBDPS (*tert*-butyldimethylsilyl) group was chosen. Silylation occurred in excellent yield, although it required a prolonged reaction time. Selective removal of the more labile 4,5-cyclohexylidene group in **19** was achieved almost quantitatively by mild acidic methanolysis, and the resulting *trans*-diol (i.e., **20**) was benzoylated under standard conditions to give ester **21**. The next step required removal of the more stable 2,3-cyclohexylidene ketal. A carefully monitored hydrolysis protocol with aqueous trifluoroacetic acid (TFA) in dichloromethane at low temperature was used to obtain *cis*-diol **22** without cleavage of the other acid-sensitive groups



Scheme 3. (i) LiOH, THF, H_2O, room temp., 1 h (98%); (ii) TBDPSCl, imidazole, pyridine, 65 °C, 5 d (97%); (iii) AcCl, CH_2Cl_2, MeOH, 0 °C, 90 min (99%); (iv) BzCl, pyridine, CH_2Cl_2, 0 °C to room temp., 24 h (96%); (v) 90% aq. TFA, CH_2Cl_2, –20 °C, 2 h (94%); (vi) MOMCl, DIPEA, DMF, 75 °C, 4 d (100%); (vii) 20% w/v MeONa in MeOH, room temp., 1 h (92%); (viii) 1. $(BnO)_2PN(iPr)_2$, 1*H*-tetrazole, MeCN, room temp., 24 h; 2. *m*CPBA, CH_2Cl_2, –40 to 0 °C, 3 h (88%); (ix) TBAF, THF, room temp., 1 h (93%) (*m*CPBA = *meta*-chloroperbenzoic acid).

present. Protecting the resulting free hydroxy groups with the same PG[1] led to known tris-MOM ether **23**,[29] which was further debenzoylated to give 4,5-diol **24**.[29] This compound was then very cleanly phosphorylated to give **25**, in contrast to what has previously been reported,[29] using a modified procedure. Finally, desilylation of **25** on exposure to TBAF (tetrabutylammonium fluoride) gave alcohol **26**. It is worth mentioning that the above described reaction sequence allows, after appropriate modifications (e.g., the use of tin acetal chemistry), the preparation of all seven possible IPs phosphorylated at the 3-, 4- and 5-positions.

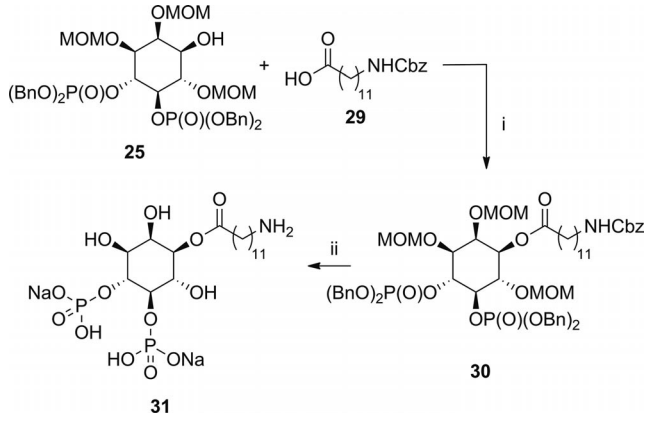
With inositol head precursor **9** prepared, we then proceeded to synthesize the required protected amino acid **10**, and for this purpose, a Cbz (benzyloxycarbonyl) group (PG[2]) was selected. Direct Cbz protection of 12-aminolauric acid to **29** is known,[30] but in our hands, it was practically impossible to obtain the product in a form pure enough to use in the next step. Therefore, we adopted a two-step sequence with the corresponding methyl ester (i.e., **27**)[31] as starting material, which involved Cbz-protection to give **28** and subsequent saponification (Scheme 4). It is obvious that any other ω-amino acid would also be suitable for our synthetic scheme, but the final deprotection step should be compatible with the nature of fatty chain (i.e., whether or not it is saturated).



Scheme 4. (i) CbzCl, Et_3N, DMAP, CH_2Cl_2, 0 °C to room temp., 12 h (89%); (ii) LiOH, THF, H_2O, room temp., 10 h (95%) [DMAP = 4-(dimethylamino)pyridine].

At this point, our synthetic plan involved the coupling reaction of the inositol head and the fatty acid tail partners. To this end, our initial effort to promote the esterification of **29** with **25** under simple conditions [DCC (*N*,*N*′-dicyclohexylcarbodiimide) and DMAP in dry CH_2Cl_2] gave, slowly, but very cleanly, fully protected target compound **30** (Scheme 5).

In contrast, the final deprotection step proved to be quite challenging. Thus, we first tried to simultaneously remove Bn and Cbz groups from **30** by $Pd(OH)_2$ catalyzed hydrogenolysis in *t*BuOH/H_2O under forcing conditions (25 bar of H_2) (Scheme 5). We hoped that the acidity of the liberated phosphates would be enough to cleave the MOM ethers, either in situ or after the addition of EtSH. However, although the Bn groups were efficiently removed in the first 2 h, the Cbz group required more than 24 h to be completely cleaved, and in the meantime, we observed slow decomposition in the ^1H and ^{31}P NMR spectra. Changing the solvent system to EtOH/H_2O or THF/H_2O did not improve this result. We believe that self-catalyzed hydrolysis of phosphates and/or acid-catalyzed hydrolysis of the lauric ester moiety occurred. Since it was impossible to perform hydrogenolysis in the presence of a base,[32] our second approach



Scheme 5. (i) DCC, DMAP, CH_2Cl_2, room temp., 3 d (96%); (ii) 1. TMSBr, CH_2Cl_2, –78 °C to room temp., 2 h; 2. MeOH, room temp., 1 h; 3. $NaHCO_3$, H_2O, 1 h (81%).

involved the removal of Bn and MOM groups using TMSBr (TMS = trimethylsilyl) before the catalytic hydrogenolytic removal of Cbz. Bruzik conditions[29] (neat TMSBr, 30 min; then MeOH, 1 h; then EtSH, 1 h) cleanly furnished the desired fully inositol-head-deprotected derivative, but removal of the remaining Cbz upon hydrogenolysis again proved to be troublesome.[33] Nevertheless, valuable information was obtained from the ^{1}H NMR spectra of the material before hydrogenolysis: the desired compound was accompanied (less than 7%) by the corresponding free amine, i.e., our final target compound. This led us to perform the same protocol with TMSBr but with an increased reaction time (1 h). But at this point, decomposition was again observed in the ^{1}H NMR spectra while the Cbz peaks were still partially present.[34] Finally, using the Prestwich protocol,[12] **30** was exposed to a mixture of TMSBr/CH_2Cl_2 for 2 h and then simply stirred in methanol to uneventfully furnish the target 1-*O*-(ω-aminolauryl)-I(4,5)P_2 (i.e., **7**). According to this result, and in compliance with our original synthetic strategy, unsaturated ω-amino fatty acids could be also used as the acyl partners.

Conclusions

We have presented an efficient synthetic scheme for the preparation of a model 1-*O*-(ω-aminoacyl)-IP, the lauryl derivative **31** (12 steps from known camphanyl ester **14** and 44% overall yield). The same synthetic strategy is expected to be easily applicable to the preparation of other 1- and 3-*O*-(ω-aminoacyl)-IPs, including all possible phosphorylated IPs, with variable phosphorylation a the 3-, 4- and 5- (or 1-, 5- and 6-, respectively) positions, and also including derivatives bearing fatty chains of different lengths and saturation patterns. In view of the central role played by IPs and PIPs in cellular life, the preparation of compounds like these may facilitate the isolation and fluorescent localization of related proteins.

Experimental Section

General Methods: All commercially available reagent-grade chemicals were used without further purification. All solvents were purified by standard procedures before use. Dry solvents were obtained by literature methods and stored over molecular sieves. Whenever possible, reactions were monitored using commercially available precoated TLC plates (layer thickness 0.25 mm) of Kieselgel 60 F254. Compounds were visualized by use of a UV lamp and/or using a suitable stain [*p*-anisaldehyde ethanolic solution, phosphomolybdic acid (PMA), Seebach's stain (PMA + cerium sulfate) and warming]. Column chromatography was performed in the usual way using Merck 60 (40–60 mm) silica gel. Optical rotations were determined at room temperature with an A. Krüss P3000 Automatic Digital Polarimeter. NMR spectra were recorded with a 300 MHz spectrometer (^{1}H: 300 MHz, ^{13}C: 75 MHz, ^{31}P: 100 MHz) in the deuterated solvent indicated. Chemical shifts are given in parts per million and *J* values in Hertz using solvent or TMS as an internal reference. Mass spectra were obtained using the electrospray technique, positive mode (ESI-MS).

1-[1-(*S*)-Camphanyl]-2,3:4,5-di-*O*-cyclohexylidene-6-*O*-methoxymethyl-*myo*-inositol (16) and 3-[1-(*S*)-Camphanyl]-1,2:5,6-di-*O*-cyclohexylidene-4-*O*-methoxymethyl-*myo*-inositol (17): A 1:1 mixture of camphanyl esters **14** and **15** (880 mg, 1.7 mmol)[28] was dissolved in dry DMF (12 mL) under an Ar atmosphere. DIPEA (15 mL, 85 mmol) was added followed by the dropwise addition of MOMCl (5.2 mL, 68 mmol). The mixture was left under vigorous stirring at room temperature for 72 h. Then it was quenched with saturated aqueous NH_4Cl (20 mL) and extracted with EtOAc(2× 75 mL). The combined organic extracts were washed with brine (2× 40 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The residue was purified by flash column chromatography (10→20% EtOAc in hexanes) to give a 1:1 mixture of MOM ethers **16** and **17** (855 mg, 89%). Pure diastereoisomer **16** was obtained upon crystallization from a mixture of acetone/light petroleum spirit (boiling range 35–60 °C); the other diastereomer (**17**) remained in the filtrate. **16**: R_f = 0.22 (25% EtOAc in hexanes). $[a]_D$ = –20.9 (*c* = 2, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.19 (t, *J* = 5.4 Hz, 1 H, 1-H), 4.86, 4.75 (ABq, *J* = 6.6 Hz, 2 H, OCH_2O), 4.61 (t, *J* = 5.3 Hz, 1 H, 2-H), 4.31 (dd, *J* = 8.3, 5.4 Hz, 1 H, 3-H), 4.10 (dd, *J* = 9.3, 5.4 Hz, 1 H, 6-H), 3.83 (dd, *J* = 10.4, 8.3 Hz, 1 H, 4-H), 3.44 (dd, *J* = 10.4, 9.3 Hz, 1 H, 5-H), 3.42 (s, 3 H, OCH_3), 2.50–2.40 (m, 1 H, C*H*H), 2.09–1.89 (m, 2 H, 2 C*H*H), 1.75–1.35 (m, 21 H, 21 C*H*H), 1.12 (s, 6 H, 2 CH_3), 0.99 (s, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.8, 166.6, 113.0, 111.4, 95.7, 90.7, 78.1, 76.9, 75.9, 75.2 74.7, 73.2, 55.7, 54.7, 54.4, 37.3, 36.4, 36.3, 34.6, 30.6, 29.0, 24.9 (2 C), 23.8, 23.7, 23.6, 23.4, 16.6, 16.5, 9.6 ppm. HRMS (ESI): calcd. for $C_{30}H_{44}NaO_{10}$ $[M + Na]^+$ 587.2827; found 587.2831.

17: R_f = 0.22 (25% EtOAc in hexanes). $[a]_D$ = +12.6 (*c* = 1, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.15 (t, *J* = 5.4 Hz, 1 H, 3-H), 4.86, 4.79 (ABq, *J* = 6.4 Hz, 2 H, OCH_2O), 4.61 (t, *J* = 5.4 Hz, 1 H, 2-H), 4.32 (dd, *J* = 8.2, 5.4 Hz, 1 H, 1-H), 4.10 (dd, *J* = 9.0, 5.5 Hz, 1 H, 4-H), 3.84 (dd, *J* = 10.3, 8.2 Hz, 1 H, 6-H), 3.46 (dd, *J* = 10.3, 9.0 Hz, 1 H, 5-H), 3.43 (s, 3 H, OCH_3), 2.52–2.42 (m, 1 H, C*H*H), 2.07–1.87 (m, 2 H, 2 C*H*H), 1.73–1.36 (m, 21 H, 21 C*H*H), 1.12 (s, 3 H, CH_3), 1.06 (s, 3 H, CH_3), 1.03 (s, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.8, 166.7, 113.1, 111.4, 95.6, 90.9, 78.0, 77.2, 75.9, 75.0, 74.9, 73.1, 55.7, 54.8, 54.3, 37.1, 36.5, 36.4, 34.3, 30.6, 28.8, 24.9 (2 C), 23.8, 23.7, 23.6, 23.5, 16.79, 16.75, 9.7 ppm. HRMS (ESI): calcd. for $C_{30}H_{44}NaO_{10}$ $[M + Na]^+$ 587.2827; found 587.2831.

2,3:4,5-Di-*O*-cyclohexylidene-6-*O*-methoxymethyl-*myo*-inositol (18): Lithium hydroxide monohydrate (420 mg, 10 mmol) was added to a solution of campanyl ester **16** (565 mg, 1 mmol) in a 1:1 mixture of THF/H_2O (40 mL). The reaction mixture was stirred at room temperature for 1 h. Then, it was extracted with EtOAc (2× 50 mL). The combined organic extracts were washed with brine (40 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The residue was purified by flash column chromatography (10→35% EtOAc in hexanes) to give alcohol **18** (378 mg, 98%) as a white foam. R_f: = 0.37 (35% EtOAc in hexanes). $[\alpha]_D$ = –11.2 (*c* = 3.4, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 4.86, 4.79 (ABq, *J* = 6.6 Hz, 2 H, OCH_2O), 4.45 (dd, *J* = 7.2, 3.9 Hz, 1 H, 2-H), 4.32 (t, *J* = 7.3 Hz, 1 H, 3-H), 4.06 (dd, *J* = 10.6, 8.0 Hz, 1 H, 4-H), 4.02 (dd, *J* = 8.5, 3.7 Hz, 1 H, 6-H), 3.95 (t, *J* = 3.8 Hz, 1 H, 1-H), 3.45 (dd, *J* = 10.6, 8.4 Hz, 1 H, 5-H), 3.44 (s, 3 H, OCH_3), 2.90 (br. s, 1 H, OH), 1.75–1.55 (m, 16 H, 16 C*H*H), 1.47–1.32 (m, 4 H, 4 C*H*H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 112.8, 111.0, 95.8, 77.9, 77.5, 77.2, 76.7, 75.5, 72.6, 55.6, 36.7, 36.42, 36.37, 33.9, 24.91, 24.88, 23.7, 23.6, 23.5, 23.3 ppm. HRMS (ESI): calcd. for $C_{20}H_{32}NaO_7$ $[M + Na]^+$ 407.2040; found 407.2044.

1-*O*-*tert*-Butyldiphenylsilyl-2,3:4,5-di-*O*-cyclohexylidene-6-*O*-methoxymethyl-*myo*-inositol (19): Alcohol **18** (430 mg, 1.1 mmol) and imidazole (140 mg, 2.1 mmol) were dissolved in dry pyridine (5 mL) under an Ar atmosphere. TBDPSCl (400 µL, 1.5 mmol) was added dropwise, and the mixture was left to stir at 65 °C for 5 d. Then, brine (30 mL) was added, and the mixture was stirred for 15 min and then extracted with EtOAc (3× 50 mL). The combined organic extracts were washed with brine (30 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The residue was purified by flash column chromatography (10→30% EtOAc in hexanes) to give silyl ether **19** (660 mg, 97%) as a thick pale yellow oil. R_f = 0.57 (25% EtOAc in hexanes). $[\alpha]_D$ = +12.2 (*c* = 2, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.80–7.73 (m, 4 H, ArH), 7.42–7.32 (m, 6 H, ArH), 4.54–4.51 (ABq, *J* = 6.4 Hz, 2 H, OCH_2O), 4.14–4.01 (m, 3 H, 2-H, 3-H, 4-H), 3.94 (dd, *J* = 8.3, 6.0 Hz, 1 H, 6-H), 3.93 (br. s, 1 H, 2-H), 3.31 (s, 3 H, OCH_3), 3.26 (t, *J* = 8.9 Hz, 1 H, 5-H), 1.73–1.25 (m, 20 H, 20 C*H*H), 1.12 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 136.1, 136.0, 133.7, 133.6, 129.8, 129.7, 127.7, 127.4, 112.3, 110.8, 96.2, 77.9, 77.8, 77.3, 76.0, 75.7, 74.6, 55.6, 37.3, 36.6, 36.3, 34.1, 27.1, 25.1, 25.0, 23.8, 23.7, 23.68, 23.6, 16.3 ppm. HRMS (ESI): calcd. for $C_{36}H_{50}NaO_7Si$ $[M + Na]^+$ 645.3218; found 645.3208.

1-*O*-*tert*-Butyldiphenylsilyl-2,3-*O*-cyclohexylidene-6-*O*-methoxymethyl-*myo*-inositol (20): Acetal **19** (455 mg, 0.75 mmol) was dissolved in a 5:1 mixture of CH_2Cl_2/MeOH (48 mL), and the mixture was cooled to 0 °C. AcCl (80 µL, 1.15 mmol) was added dropwise, and the mixture was left to stir at 0 °C for 90 min. Then saturated aqueous sodium hydrogen carbonate (6 mL) was added, and the mixture was vigorously stirred at 0 °C for 15 min and then extracted with CH_2Cl_2 (5× 30 mL). The combined organic extracts were washed with brine (20 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The residue was purified by flash column chromatography (10→50% EtOAc in hexanes) to give diol **20** (402 mg, 99%) as a sticky white foam. R_f = 0.19 (50% EtOAc in hexanes). $[\alpha]_D$ = +26.4 (*c* = 3.8, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.79–7.72 (m, 4 H, ArH), 7.41–7.32 (m, 6 H, ArH), 4.62, 4.09 (ABq, *J* = 6.6 Hz, 2 H, OCH_2O), 3.94 (dd, *J* = 8.7, 4.1 Hz, 1 H, 3-H), 3.88 (t, *J* = 4.3 Hz, 1 H, 2-H), 3.72–3.65 (m, 3 H, 1-H, 4-H, 6-H), 3.38 (s, 3 H, OCH_3), 3.12 (t, *J* = 9.2 Hz, 1 H, 5-H), 3.00 (br. s, 2 H, 2 OH), 1.80–1.65 (m, 4 H, 4 C*H*H), 1.55–1.30 (m, 6 H, 6 C*H*H), 1.09 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 135.90, 135.86, 133.9, 133.4, 129.7 (2 C), 127.5, 127.4, 110.3, 98.5, 83.4, 77.7, 75.5 (2 C), 72.5, 71.5, 55.7, 38.1, 34.7, 26.9, 25.0, 23.9, 23.7, 19.3 ppm. HRMS (ESI): calcd. for $C_{30}H_{42}NaO_7Si$ $[M + Na]^+$ 565.2592; found 565.2600.

4,5-Di-*O*-benzoyl-1-*O*-*tert*-butyldiphenylsilyl-2,3-*O*-cyclohexylidene-6-*O*-methoxymethyl-*myo*-inositol (21): Diol **20** (460 mg, 0.85 mmol) was dissolved in dry CH_2Cl_2 (1 mL) and dry pyridine (5 mL) under an Ar atmosphere, and the mixture was cooled to 0 °C. BzCl (250 µL, 2.1 mmol) was added dropwise, and the mixture was left to stir at room temperature for 24 h. Then EtOAc (70 mL) was added and the mixture was washed with saturated aqueous sodium hydrogen carbonate (2× 30 mL) and brine (30 mL), and then dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by flash column chromatography (10% EtOAc in hexanes) to give dibenzoate **21** (610 mg, 96%) as a white foam. R_f = 0.54 (20% EtOAc in hexanes). $[\alpha]_D$ = +16.4 (*c* = 4.5, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.93 (d, *J* = 7.3 Hz, 2 H, ArH), 7.89 (d, *J* = 7.3 Hz, 2 H, ArH), 7.84 (d, *J* = 6.8 Hz, 2 H, ArH), 7.74 (d, *J* = 6.8 Hz, 2 H, ArH), 7.48–7.23 (m, 12 H, ArH), 6.00 (br. t, *J* = 8.7 Hz, 1 H, 4-H), 5.21 (dd, *J* = 9.6, 6.1 Hz, 1 H, 5-H), 4.73, 4.59 (ABq, *J* = 6.4 Hz, 2 H, OCH_2O), 4.33 (dd, *J* = 7.1, 3.8 Hz, 1 H, 2-H), 4.19 (t, *J* = 7.1 Hz, 1 H, 3-H), 4.12 (dd, *J* = 7.1, 6.4 Hz, 1 H, 1-H), 3.98 (t, *J* = 6.5 Hz, 1 H, 6-H), 3.05 (s, 3 H, OCH_3), 1.99–1.70 (m, 4 H, 4 C*H*H), 1.51–1.30 (m, 6 H, 6 C*H*H), 1.16 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.8, 165.4, 136.2, 135.9, 133.5, 133.4, 132.9, 132.7, 130.0, 129.9, 129.8, 129.7, 129.6, 128.3, 128.14, 128.07, 127.7, 127.5, 111.0, 97.5, 77.7, 75.1, 74.7, 74.2 (2 C), 71.3, 55.8, 37.1, 34.3, 27.1, 25.1, 24.0, 23.8, 19.3 ppm. HRMS (ESI): calcd. for $C_{44}H_{50}NaO_9Si$ $[M + Na]^+$ 773.3116; found 773.3129.

4,5-Di-*O*-benzoyl-1-*O*-*tert*-butyldiphenylsilyl-6-*O*-methoxymethyl-*myo*-inositol (22): Acetal **21** (525 mg, 0.7 mmol) was dissolved in CH_2Cl_2 (8 mL) and the solution was cooled to –40 °C. Aqueous TFA (90%; 4 mL) was added dropwise and the mixture was left to stir at –20 °C for 2 h. Then saturated aqueous sodium hydrogen carbonate (20 mL) was added. The resulting slurry was stirred at room temperature for 15 min and then extracted with CH_2Cl_2 (2× 30 mL). The combined organic extracts were washed with brine (20 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The residue was purified by flash column chromatography (10→50% EtOAc in hexanes) to give diol **22** (440 mg, 94%) as a white foam. R_f = 0.20 (25% EtOAc in hexanes). $[\alpha]_D$ = +15.7 (*c* = 2.8, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.97 (br. d, *J* = 7.1 Hz, 2 H, ArH), 7.85 (br. d, *J* = 7.1 Hz, 2 H, ArH), 7.76 (br. d, *J* = 6.3 Hz, 4 H, ArH), 7.40–7.23 (m, 12 H, ArH), 5.67 (t, *J* = 9.9 Hz, 1 H, 4-H), 5.40 (t, *J* = 9.8 Hz, 1 H, 5-H), 4.88 (d, *J* = 6.8 Hz, 1 H, OC*H*HO), 4.51 (d, *J* = 6.8 Hz, 1 H, OC*H*HO), 4.31 (t, *J* = 9.5 Hz, 1 H, 6-H), 3.97 (dd, *J* = 9.2, 2.5 Hz, 1 H, 3-H), 3.72 (br. s, 1 H, 2-H), 3.49 (br. d, *J* = 9.6 Hz, 1 H, 1-H), 3.13 (br. s, 1 H, OH), 2.97 (br. s, 1 H, OH), 2.97 (s, 3 H, OCH_3), 1.12 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.9, 165.9, 135.8, 135.6, 133.5, 133.0, 132.8, 132.6, 130.1, 130.0, 129.9, 129.7, 129.6, 129.3, 128.1 (2 C), 127.9, 127.8, 98.8, 78.7, 74.3, 74.2, 72.4, 72.0, 70.6, 55.8, 27.0, 19.3 ppm. HRMS (ESI): calcd. for $C_{38}H_{43}O_9Si$ $[M + H]^+$ 671.2671; found 671.2666.

4,5-Di-*O*-benzoyl-1-*O*-*tert*-butyldiphenylsilyl-2,3,6-tri-*O*-methoxymethyl-*myo*-inositol (23): Diol **22** (335 mg, 0.5 mmol) was dissolved in dry DMF (10 mL) and DIPEA (3.6 mL) under an Ar atmosphere. MOMCl (1.4 mL, 18 mmol) was added dropwise at room temperature, and the mixture was stirred at 75 °C for 4 d. Then the

reaction mixture was cooled to room temperature and saturated aqueous sodium hydrogen carbonate (20 mL) was added. The resulting slurry was stirred at room temperature for 15 min and then extracted with CH_2Cl_2 (3 × 50 mL). The combined organic extracts were washed with brine (30 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The residue was purified by flash column chromatography (10→20% EtOAc in hexanes) to give MOM ether **23** (378 mg, 100%) as a pale yellow foam. R_f = 0.46 (25% EtOAc in hexanes). $[\alpha]_D$ = +33.1 (c = 2.9, $CHCl_3$). ^1H NMR spectrum was identical with that reported in the literature.[29] ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.8, 165.4, 135.9, 135.8, 133.8, 132.8, 132.7, 130.04, 130.97, 129.9, 129.7, 129.6, 129.5, 128.09 (2 C), 128.06, 127.9, 127.7, 98.5, 97.4, 94.4, 78.3, 75.1, 74.2, 73.3, 72.8, 72.3, 55.8, 55.6, 55.3, 27.1, 19.2 ppm. HRMS (ESI): calcd. for $C_{42}H_{50}NaO_{11}Si$ [M + Na]$^+$ 781.3015; found 781.3019.

1-*O*-*tert*-Butyldiphenylsilyl-2,3,6-tri-*O*-methoxymethyl-*myo*-inositol (24): Following a slightly modified procedure,[29] dibenzoate **23** gave diol **24** in 92% yield. R_f = 0.13 (50% EtOAc in hexanes). $[\alpha]_D$ = +80.6 (c = 2, $CHCl_3$). ^1H and ^{13}C NMR spectra were identical with those reported in the literature.[29] HRMS (ESI): calcd. for $C_{28}H_{43}O_9Si$ [M + H]$^+$ 551.2671; found 551.2661.

Tetrabenzyl 4,5-(1-*O*-*tert*-Butyldiphenylsilyl-2,3,6-tri-*O*-methoxymethyl-*myo*-inositol) Bisphosphate (25): Diol **24** was phosphorylated following a modification of a known procedure.[29] Thus, starting diol **24** (260 mg, 0.47 mmol) was dried under high vacuum for 24 h. Then a solution of 1*H*-tetrazole in acetonitrile (0.45 M; 10 mL, 4.5 mmol) was added under a N_2 atmosphere at room temperature. Dropwise addition (30 min) of dibenzyl *N*,*N*-diisopropylphosphoramidite (0.5 mL, 1.5 mmol) to the resulting suspension followed. The resulting slurry was vigorously stirred at room temperature for 24 h. CH_2Cl_2 (5 mL) was added and the mixture was cooled to –40 °C. A solution of *m*-chloroperbenzoic acid (70%; 740 mg, 3 mmol) in CH_2Cl_2 (5 mL) was added dropwise, and the mixture was left to stir at 0 °C for 3 h. Then the mixture was diluted with CH_2Cl_2 (50 mL) and successively washed with aqueous sodium sulfite (10%; 2× 30 mL), saturated aqueous sodium hydrogen carbonate (2× 25 mL), H_2O (25 mL), and brine (25 mL). The organic phase was dried (Na_2SO_4), and the solvents were removed under reduced pressure (30 °C). The resulting residue was purified by flash column chromatography (10→50% EtOAc in hexanes) to give bisphosphate **25** (445 mg, 88%) as a colorless thick oil. R_f = 0.45 (50% EtOAc in hexanes). $[\alpha]_D$ = +7.0 (c = 2.6, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.78 (br. d, J = 6.5 Hz, 2 H, ArH), 7.71 (d, J = 6.0 Hz, 2 H, ArH), 7.43–7.24 (m, 26 H, ArH), 5.14–4.93 (m, 9 H, 4 OCH_2Ph, OCHHO), 4.79 (q, $^3J_{HH}$ = $^3J_{HP}$ = 9.9 Hz, 1 H, 4-H), 4.76 (d, J = 6.1 Hz, 1 H, OCHHO), 4.59, 4.52 (ABq, J = 6.4 Hz, 2 H, OCH_2O), 4.32 (q, $^3J_{HH}$ = $^3J_{HP}$ = 9.4 Hz, 1 H, 5-H), 4.28, 4.05 (ABq, J = 7.1 Hz, 2 H, OCH_2O), 4.19 (t, J = 9.6 Hz, 1 H, 6-H), 3.87 (br. d, J = 9.7 Hz, 1 H, 1-H), 3.38 (s, 3 H, OCH_3), 3.29 (br. s, 1 H, 2-H), 3.26 (s, 3 H, OCH_3), 3.20 (br. d, J = 9.8 Hz, 1 H, 3-H), 2.97 (s, 3 H, OCH_3), 1.11 (s, 9 H, tBu) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 136.21 (d, $^3J_{CP}$ = 7.5 Hz, 3 C), 136.17 (d, $^3J_{CP}$ = 8.0 Hz), 136.0, 135.8, 133.9, 132.6, 130.0, 129.8, 128.30, 128.25, 128.2, 128.10, 128.05, 128.03, 128.00, 127.91, 127.88, 127.8, 127.72, 127.67, 98.7, 97.3, 95.9, 78.5 (t, J_{CP} = 5.2 Hz), 77.8 (q, J_{CP} = 2.9 Hz), 75.8 (br. s), 75.5, 74.2, 73.7, 69.5 (d, $^2J_{CP}$ = 5.7 Hz), 69.3 (d, $^2J_{CP}$ = 5.7 Hz), 69.2 (d, $^2J_{CP}$ = 5.2 Hz), 69.0 (d, $^2J_{CP}$ = 5.2 Hz), 56.9, 55.6, 55.4, 27.2, 19.1 ppm. ^{31}P NMR (100 MHz, $CDCl_3$, ^{31}P–^1H decoupled): δ = –1.23, –1.51 ppm. HRMS (ESI): calcd. for $C_{56}H_{68}NaO_{15}P_2Si$ [M + Na]$^+$ 1093.3695; found 1093.3679.

Tetrabenzyl 4,5-(2,3,6-Tri-*O*-methoxymethyl-*myo*-inositol) Bisphosphate (26): Silyl ether **25** (320 mg, 0.3 mmol) was dissolved in dry THF (4 mL) under an Ar atmosphere. TBAF solution in THF (1 M; 180 μL, 0.36 mmol) was added dropwise, and the mixture was stirred at room temperature for 1 h. Then it was quenched by the addition of saturated aqueous ammonium chloride (2 mL). EtOAc (10 mL) was added, and the resulting slurry was vigorously stirred for 15 min, and then extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were washed with brine (10 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The residue was purified by flash column chromatography (10→35% EtOAc in hexanes) to give alcohol **26** (231 mg, 93%) as a pale yellow amorphous solid. R_f = 0.20 (35% EtOAc in hexanes). $[\alpha]_D$ = –41.8 (c = 2.0, $CHCl_3$). ^1H and ^{31}P NMR spectra were identical with those reported in the literature.[29] ^{13}C NMR (75 MHz, $CDCl_3$): δ = 135.91 (d, $^3J_{CP}$ = 8.0 Hz, 2 C), 135.87 (d, $^3J_{CP}$ = 8.0 Hz), 135.8 (d, $^3J_{CP}$ = 7.5 Hz), 128.4, 128.3, 128.2, 128.14, 128.10, 128.06, 127.9, 127.8 127.73, 127.69, 98.9, 97.5, 96.7, 83.2, 79.2 (t, J_{CP} = 5.5 Hz), 77.8 (t, J_{CP} = 5.8 Hz), 75.4, 74.9, 70.3, 69.4 (d, $^2J_{CP}$ = 6.3 Hz), 69.3 (d, $^2J_{CP}$ = 6.9 Hz), 69.0 (d, $^2J_{CP}$ = 5.2 Hz, 2 C), 55.8, 55.6, 55.5 ppm. HRMS (ESI): calcd. for $C_{40}H_{50}NaO_{15}P_2$ [M + Na]$^+$ 855.2517; found 855.2525.

Methyl 12-(Benzyloxycarbonylamino)dodecanoate (28): Amine **27** (500 mg, 2.2 mmol)[31] was dissolved in dry CH_2Cl_2 (17 mL) under an Ar atmosphere. DMAP (53 mg, 0.43 mmol) and dry Et_3N (1.5 mL, 11 mmol) were added, and the resulting solution was cooled to 0 °C. Then, CbzCl (0.37 mL, 2.6 mmol) was added dropwise, and the mixture was left to stir at room temperature for 12 h. H_2O (10 mL) was added, and the resulting mixture was vigorously stirred for 15 min. The organic phase was washed with brine (2× 10 mL), and the combined aqueous washes were re-extracted with CH_2Cl_2 (15 mL). Finally, the combined organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by flash column chromatography (10→50% EtOAc in hexanes) to give protected amine **28** (705 mg, 89%) as a thick colorless oil. R_f = 0.60 (50% EtOAc in hexanes). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.35–7.29 (m, 5 H, ArH), 5.09 (s, 2 H, CH_2Ph), 4.78 (br. s, 1 H, NH), 3.65 (s, 3 H, OCH_3), 3.17 (q, J = 6.6 Hz, 2 H, NHCH_2), 2.29 (t, J = 7.5 Hz, 2 H, COCH_2), 1.64–1.56 (m, 2 H, $COCH_2CH_2$), 1.50–1.46 (m, 2 H, $NHCH_2CH_2$), 1.27 (br. s, 14 H, 7 $CH_2CH_2CH_2$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.2, 156.4, 136.7, 128.4, 128.0, 66.5, 51.3, 41.1, 34.0, 29.9, 29.40, 29.39, 29.3, 29.2, 29.14, 29.07, 26.7, 24.9 ppm. HRMS (ESI): calcd. for $C_{21}H_{33}NNaO_4$ [M + Na]$^+$ 386.2302; found 386.2310.

12-(Benzyloxycarbonylamino)dodecanoic Acid (29): Ester **28** (580 mg, 1.6 mmol) was dissolved in a 3:1 mixture of THF/H_2O (12 mL). LiOH monohydrate (202 mg, 4.8 mmol) was added, and the resulting slurry was left to stir vigorously at room temperature for 10 h. Then the mixture was acidified to pH 2 using HCl (1 M). CH_2Cl_2 (25 mL) was added, and the organic phase was washed with brine (2× 10 mL). The combined aqueous washes were re-extracted with CH_2Cl_2 (10 mL). Finally, the combined organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by flash column chromatography (20→60% EtOAc in hexanes) to give acid **29** (530 mg, 95%) as a white waxy solid. R_f = 0.16 (25% EtOAc in hexanes). ^1H NMR spectrum was identical with that reported in the literature.[30] ^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.1, 156.8, 137.0, 128.5, 128.0, 66.7, 41.4, 33.9, 30.0, 29.4, 29.32, 29.26, 29.2, 29.1, 29.0, 26.7, 14.7 ppm. HRMS (ESI): calcd. for $C_{20}H_{31}NNaO_4$ [M + Na]$^+$ 372.2145; found 372.2148.

Tetrabenzyl 4,5-{1-*O*-[12-*N*-(Benzyloxycarbonyl)aminododecanoyl]-2,3,6-tri-*O*-methoxymethyl-*myo*-inositol} Bisphosphate (30): Alcohol **25** (50 mg, 0.06 mmol) and carboxylic acid **29** (63 mg,

0.18 mmol) were dissolved in dry CH_2Cl_2 (5 mL) under an Ar atmosphere. A catalytic amount of DMAP (1 mg) was added, followed by DCC (37 mg, 0.18 mmol). The mixture was stirred at room temperature for 3 d. Then it was concentrated under reduced pressure, and the residue was triturated with a mixture of CH_2Cl_2/Et_2O (9:1). The crystallized urea was removed by filtration and the filtrate was concentrated to give a residue, which was further purified by flash column chromatography (40→70% EtOAc in hexanes) to give ester **30** (67 mg, 96%) as a colorless thick oil. R_f = 0.27 (65% EtOAc in hexanes). $[\alpha]_D$ = –27.5 (c = 0.36, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.36–7.25 (m, 25 H, ArH), 5.15–4.94 (m, 10 H, 5 OCH_2Ph), 4.90 (q, $^3J_{HH}$ = $^3J_{CP}$ = 9.4 Hz, 1 H, 4-H), 4.81 (dd, J = 10.3, 2.3 Hz, 1 H, 1-H), 4.77, 4.64 (ABq, J = 6.7 Hz, 2 H, OCH_2O), 4.68 (br. s, 1 H, NH), 4.62, 4.57 (ABq, J = 6.9 Hz, 2 H, OCH_2O), 4.57, 4.47 (ABq, J = 6.9 Hz, 2 H, OCH_2O), 4.42 (q, $^3J_{HH}$ = $^3J_{CP}$ = 9.3 Hz, 1 H, 5-H), 4.13 (br. s, 1 H, 2-H), 4.05 (t, J = 9.7 Hz, 1 H, 6-H), 3.61 (dd, J = 10.1, 1.8 Hz, 1 H, 3-H), 3.38 (s, 3 H, OCH_3), 3.26 (s, 3 H, OCH_3), 3.22 (s, 3 H, OCH_3), 3.17 (q, J = 6.6 Hz, 2 H, NHCH_2), 2.35 (t, J = 6.4 Hz, 2 H, $COCH_2$), 1.68–1.58 (m, 2 H, $COCH_2CH_2$), 1.51–1.46 (m, 2 H, $NHCH_2CH_2$), 1.26 (br. s, 14 H, 7 $CH_2CH_2CH_2$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.8, 156.4, 136.8, 136.3–136.0 (m, 4 C), 128.52, 128.50, 128.44, 128.41, 128.38, 128.33, 128.29, 128.2, 128.1, 128.0, 127.9, 99.0, 97.5, 97.2, 79.3 (t, J_{CP} = 5.5 Hz), 77.5–77.2 (m, 2 C), 75.3, 74.3, 71.5, 69.8 (d, $^3J_{CP}$ = 5.9 Hz), 69.6 (d, $^3J_{CP}$ = 5.9 Hz), 69.5 (d, $^3J_{CP}$ = 5.1 Hz), 69.3 (d, $^3J_{CP}$ = 5.1 Hz), 66.6, 56.2, 55.9, 55.7, 41.2, 34.2, 30.0, 29.7, 29.5, 29.4, 29.3, 29.2 (2 C), 26.7, 24.5 ppm. ^{31}P NMR (100 MHz, $CDCl_3$, ^{31}P–^{1}H decoupled): δ = –1.34, –1.46 ppm. HRMS (ESI): calcd. for $C_{60}H_{79}NNaO_{18}P_2$ [M + Na]$^+$ 1186.4665; found 1186.4658.

Disodium 4,5-[1-*O*-(12-Amindodecanoyl)-*myo*-inosityl] Bisphosphate (31): TMSBr (ca. 0.4 mL) was distilled into a flask cooled to –78 °C containing a solution of ester **30** (23 mg, 0.02 mmol) in dry CH_2Cl_2 (0.6 mL) under an Ar atmosphere. The mixture was left to stir in the dark for 2 h. Then it was concentrated under reduced pressure at room temperature, and the residue was placed under high vacuum for 6 h. MeOH (1 mL) was added, and the mixture was stirred for 1 h at room temperature. Evaporation under reduced pressure at room temperature and washing with $CHCl_3$ (3× 1 mL) yielded a waxy solid. Aqueous sodium hydrogen carbonate (0.1 M; 0.4 mL, 0.04 mmol) was added along with *t*BuOH (1 mL), and the mixture was concentrated under reduced pressure at room temperature. Additional quantities of *t*BuOH (2× 1 mL) were used to azeotropically remove traces of water by evaporation under reduced pressure at room temperature. The residue was further dried under high vacuum for 12 h to give sodium phosphate **31** (9.4 mg, 81%) as an amorphous white solid. $[\alpha]_D$ = +2.1 (c = 0.15, H_2O). ^{1}H NMR (acid form, 300 MHz, CD_3OD): δ = 4.75 (obscured, 1 H, 1-H), 4.50 (q, $^3J_{HH}$ = $^3J_{CP}$ = 8.2 Hz, 1 H, 4-H), 4.18 (br. q, $^3J_{HH}$ = $^3J_{CP}$ = 9.2 Hz, 1 H, 5-H), 4.06 (br. s, 1 H, 2-H), 4.03 (t, J = 9.6 Hz, 1 H, 6-H), 3.67 (br. d, J = 8.5 Hz, 1 H, 3-H), 2.91 (br. q, J = 6.4 Hz, 2 H, NHCH_2), 2.40 (t, J = 7.5 Hz, 2 H, $COCH_2$), 1.64 (br. s, 4 H, $COCH_2CH_2$, $NHCH_2CH_2$), 1.33, 1.29 (2 br. s, 14 H, 7 $CH_2CH_2CH_2$) ppm. ^{13}C NMR (acid form, 75 MHz, CD_3OD): δ = 173.5, 79.9 (t, J_{CP} = 5.1 Hz), 79.1 (br. s), 78.7, 77.4, 75.6, 72.1, 40.8, 35.1, 31.1, 30.12, 30.14, 30.0, 29.9, 29.8, 29.7, 26.6, 24.7 ppm. ^{31}P NMR (acid form, 100 MHz, CD_3OD, ^{31}P–^{1}H decoupled): δ = 3.39, 2.89 ppm. HRMS (ESI): calcd. for $C_{18}H_{35}NNaO_{13}P_2$ [M – Na]$^-$ 558.1487; found 558.1491.

Supporting Information (see footnote on the first page of this article): Copies of the ^{1}H NMR and ^{13}C NMR spectra for all compounds.

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[34] As expected, removal of the Cbz group not only resulted in disappearance of the corresponding peaks in the ^1H NMR spectra, but also caused significant shielding of certain methylene protons (on C-12 of the lauric moiety).

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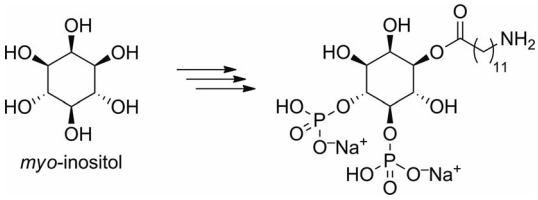

1-*O*-(ω-Aminolauryl)-I(4,5)P_2 was prepared from *myo*-inositol using a versatile and high-yielding scheme. The same synthetic strategy is expected to be easily applicable to the preparation of other 1- and 3-*O*-(ω-aminoacyl)-IPs, with potential use in the isolation and localization of proteins.

Keywords: Bioorganic chemistry / Natural products / Inositols / Phosphates / Fatty acids / Lipids

