A New Approach to Phosphonate Analogues of Phosphatidyl Derivatives

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A new method for the preparation of the phosphonate analogues of phosphatidyl derivatives using a Horner–Mark [2,3]-sigmatropic rearrangement is described. Phosphonate analogues were prepared in which the *sn*-3 oxygen of the diacylglyceryl moiety is substituted by -HC=CH- or -CH_2CH_2- fragments.

Introduction

Phospholipid analogues are major constituents of cell membranes and play an important role in biochemical processes.[1] Many phospholipids possess biological activity,[2] for example the hormone platelet activating factor (PAF) and lysophosphatidic acid (LPA).[3] The anticancer properties of phospholipid analogues **I** (Figure 1) have been well established in a variety of cell systems.[4,5] Moreover, structurally modified phospholipids have been widely used for drug delivery in liposomes,[6] and in physical and biochemical studies of membrane structure and function.[7]

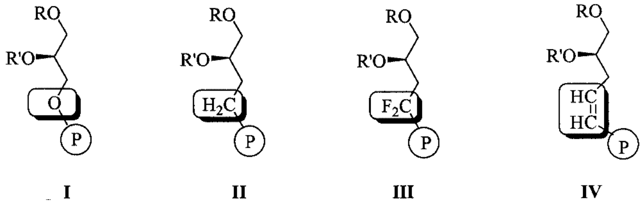

Figure 1. P = Phosphorus-containing moiety; R′ = Me, AlkC(O); R = Alk, AlkC(O)

Recent literature has indicated an interest in the preparation of various phosphonolipids.[8−10] These are analogues of natural phospholipids where the *sn*-3 oxygen of the diacylglyceryl moiety has been replaced with a -CH_2- or a -CF_2- moiety. The presence of a phosphonate group, instead of a phosphate moiety as present in natural phospholipids, renders compounds **II** and **III** (Figure 1) less prone to in vivo chemical or enzymatic hydrolysis, thus increasing their therapeutic lifetime and efficacy.[11] For example, it was shown recently that unnatural phosphonolipids[10a][10b] have potent cytotoxic activity toward various tumor cells, and are potential anticancer drugs in clinical trials.

Several approaches to the preparation of isosteric and nonisosteric phosphonate analogues of phospholipids have been reported. The best known of these are the Arbuzov[8] and Michaelis−Becker[9] reactions, and the interaction of phosphonate anions with epoxides[10a,10b] or primary triflates.[10c,10d] In connection with our work[12] on the application of phosphorylated allenes for the construction of unsaturated organophosphorus compounds, and for a better understanding of the role of the -CH_2- fragment in the phosphonolipids **II** (Figure 1), we report here an efficient and stereoselective methodology for the preparation of a new type of phosphonate analogues **IV** (Figure 1) using a Horner−Mark [2,3]-sigmatropic rearrangement as the key step.

The goal of our current research is the synthesis of new analogues of phosphatidyl derivatives, which will be useful for further biological studies. The target compounds were prepared in which the *sn*-3 oxygen of the diacylglyceryl moiety is substituted by -HC=CH- or -CH_2CH_2- fragments, rendering the compounds resistant to chemical or enzymatic hydrolysis.

Results and Discussion

In a preliminary publication, we reported the synthesis of new phosphonolipids.[12e] Now we provide details of our methods for the construction of unsaturated analogues of phosphatidyl derivatives.

The 5-(phosphoryl)-1,2-diacylpent-4-enes **8a** and **8b** were synthesized by a simple and efficient three-step procedure: synthesis of the acetylenic alcohol **2**; synthesis of the phosphorylated diol **5**; and synthesis of the target phosphonates **8a,b** (Scheme 1). The starting material, 2,3-*O*-isopropylidene-D-glyceraldehyde, was prepared from 1,2:5,6-diisopropylidene-D-mannitol. The D-mannitol can be ketalized by a

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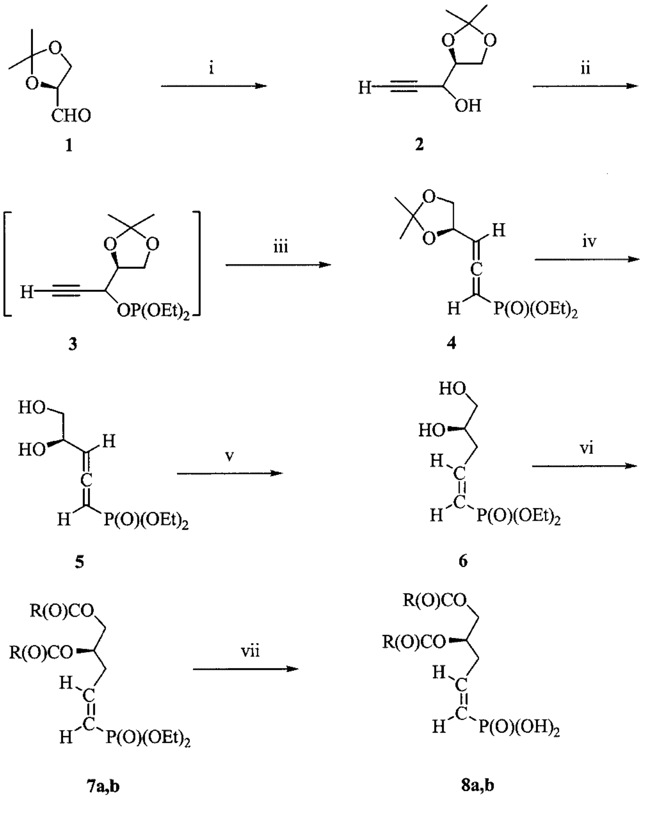
variety of methods[13] to provide 1,2:5,6-diisopropylidene-D-mannitol. We selected the procedure reported by Chittenden, which uses a catalytic amount of $SnCl_2$ and 2,2-dimethoxypropane to ketalize D-mannitol in 50−55% yield.[14] The 1,2:5,6-diisopropylidene-D-mannitol was oxidatively cleaved with silica gel-supported sodium metaperiodate reagent[15] to afford the acetonide-protected D-glyceraldehyde **1**. When 2,3-*O*-isopropylidene-D-glyceraldehyde (**1**) was reacted with a standard Grignard reaction,[16] the target (1,2-*O*-isopropylidene)-4-pentyn-3-ol (**2**) was obtained in high yield after purification by column chromatography. Compound **2** was obtained as a mixture of two diastereomers. These could not be separated by flash chromatography or TLC, but the diastereomeric ratio could be measured by ^{13}C NMR spectroscopy. At 50 MHz small splittings of the signals could be identified as two diastereomers in a 1.2:1 ratio. The structure of the final acetylenic alcohol **2** was confirmed by ^{1}H and ^{13}C NMR spectroscopy and elemental analysis.



R = $C_{15}H_{31}$ (a); $C_{17}H_{35}$ (b).

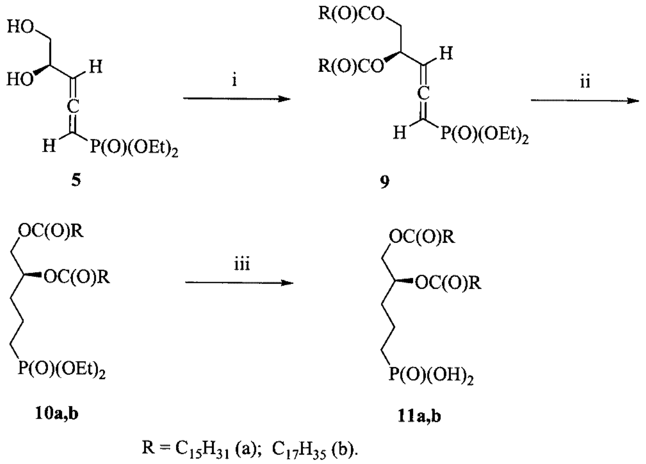
Scheme 1. (i) HC≡CMgBr, THF; (ii) $ClP(OEt)_2$, NEt_3, Et_2O, −40 °C; (iii) room temp., 24 h; (iv) MeOH, HCl, room temp., 2 h; (v) H_2, MeOH, Pd/$BaSO_4$; (vi) RCOOH, DCC DMAP; (vii) $CHCl_3$, Me_3SiBr

The phosphorylated allene **4** was synthesized directly from the acetylenic alcohol **2** in 66% yield by a Horner−Mark [2,3]-sigmatropic rearrangement[17] of the unstable phosphite **3**, which was generated in situ by reaction with diethyl chlorophosphite in the presence of triethylamine in diethyl ether at −40 °C and then kept at 20 °C for 24 h. Compound **4** is stable enough to be handled at ambient temperature. The reaction was monitored by TLC on SiO_2 and by ^{31}P NMR spectroscopy. The isopropylidene protecting group was then easily removed in 1 N HCl solution in methanol at room temperature, to give 5-(diethoxyphosphoryl)penta-3,4-diene-1,2-diol (**5**) in quantitative yield. Analytically pure phosphorylated allene **5** was isolated as a colorless or pale yellow oil by column chromatography on silica gel. The phosphonate **5** was obtained as a mixture of two diastereomers resulting from the chirality of the allenic group. The chemical shift of the phosphorus atom is characteristic of compounds with a four-coordinate phosphorus atom linked to an sp^2-hybridized carbon atom. The extremely low-field position of the central allenic carbon atom resonance (δ = 211.94 ppm) allows the immediate identification of the allenic moiety by ^{13}C NMR spectroscopy.[18]

For preparation of the phosphonate analogues in which the *sn*-3 oxygen of the diacylglyceryl moiety was substituted by HC=CH, we used compound **5** as the starting material. This compound was selectively and stereospecifically hydrogenated in methanol over 5% Pd/$BaSO_4$ at atmospheric pressure, with hydrogen attacking only the C(3)=C(4) double bond of the allene moiety, to give 5-(diethoxyphosphoryl)-pent-4-ene-1,2-diol (**6**), which has a *Z* double bond configuration (Scheme 1). Confirmation of the isomeric structure of this product was based on the ^{1}H NMR spectrum, which shows a doublet of doublets at δ = 5.76 ppm ($J_{Ha,P}$ = 19.1 Hz) and a doublet, doublet of doublets at δ = 6.64 ppm ($J_{Hb,P}$ = 52.9 Hz) for the hydrogen atoms -CH(b)=CH(a)P(O)(OEt), the coupling constant $J_{Hb\text{-}P}$ = 52.9 Hz being typical of an *E* configuration of the phosphorus and vicinal proton (CHb=).[19] After purification by column chromatography on silica gel the purified diol **6** could be acylated with any fatty acid. Thus, carbodiimide-mediated esterification with palmitic or stearic acid gave (2*R*)-5-(diethoxyphosphoryl)-2-(palmitoyloxy)pent-4-enyl palmitate (**7a**) or (2*R*)-5-(diethoxyphosphoryl)-2-(stearoyloxy)pent-4-enyl stearate (**7b**) in satisfactory yield.

Bromotrimethylsilane (TMSBr) has frequently been used as an efficient reagent for dealkylation of phosphonate dialkyl esters to generate the corresponding phosphonic acids.[19] Thus, hydrolysis of the diethyl esters **7a**,**b** with TMSBr proceeded smoothly to afford the phosphonic acids **8a,b** in about 40% yield. The acids were obtained as a white solid after purification by crystallization. The structures were confirmed by ^{1}H, ^{13}C and ^{31}P NMR spectroscopy.

Acylation of both hydroxyl groups of **5** with palmitoyl or stearoyl chloride was accomplished under standard coupling conditions with 4-(dimethylamino)pyridine to give (2*R*)-5-(diethoxyphosphoryl)-2-(palmitoyloxy)penta-3,4-dienyl palmitate (**9a**) or (2*R*)-5-(diethoxyphosphoryl)-2-(stearoyloxy)penta-3,4-dienyl stearate (**9b**) in satisfactory yield (Scheme 2). The palmitate **9a** and stearate **9b** were obtained as white solids after purification by column chromatography. They were obtained as mixtures of two diastereomers (^{31}P NMR spectroscopic data, for **9a,b** δ_P = 14.47 and 14.64 ppm, in an approximate 1:1.2 ratio). The purity of the products **9a** and **9b** was confirmed by IR and NMR spectroscopy, and elemental analysis. For example, compound **9a** exhibits a strong absorption in the range 1752−1755 cm^{-1} and another at 1965 cm^{-1} that are characteristic of the carbonyl and C=C=C groups, respectively. The salient features in the ^{1}H NMR spectrum of **9a** are the multiplets in the regions δ = 5.50−5.53 ppm (*CH*OH), and δ = 5.56−5.57 ppm (HC=).



Scheme 2. (i) RCOCl, NEt_3, DMAP; (ii) H_2, MeOH, Pd/C; (iii) Me_3SiBr, $CHCl_3$

In the next step a solution of compound **9a** or **9b** in ethanol was hydrogenated over 5% Pd/C at atmospheric pressure. The reaction was monitored by TLC on SiO_2 and ^{1}H and ^{31}P NMR spectroscopy. The hydrogenation of the C=C=C fragment converted the diastereomeric mixture into the (*R*)-enantiomer of phosphonates **10a** or **10b** (^{31}P NMR: δ_P = 32.54 ppm). Hydrolysis of the diethyl esters **10a**,**b** with TMSBr proceeded smoothly to afford phosphonic acids **11a**,**b**, which were obtained as white solids after purification by crystallization.

Conclusion

In summary, we have described a convenient and efficient synthesis of 5-phosphoryl-1,2-diacylpent-4-enes and 5-phosphoryl-1,2-diacylpentanes. This general and efficient methodology could be applied to the synthesis of phosphonate analogues of phosphatidyl choline, phosphatidyl ethanolamine and other phosphatidyl derivatives. Further studies on this potentially important synthetic methodology are currently in progress. Applications of phosphorylated allenes to the synthesis of interesting phosphonic acid derivatives will be reported in due course.

Experimental Section

^{1}H NMR spectra were recorded on a Bruker CXP-200 or a Bruker DPX-200 spectrometer at 200 MHz. Chemical shifts for ^{1}H NMR are reported in ppm relative to tetramethylsilane as internal standard. ^{13}C NMR: Bruker DPX-200 (50.3 MHz). Signal multiplicities were determined with DEPT techniques. Chemical shifts refer to tetramethylsilane or to residual solvent signals. ^{31}P NMR: Bruker DPX-200 (81.01 MHz). Chemical shifts refer to external 85% H_3PO_4 in H_2O. Infrared spectra were recorded on a Bruker IFS-113 spectrometer. Samples were typically prepared as films or in CCl_4 solution. Band frequencies ($\tilde{\nu}$) are reported in cm^{-1}. Optical rotations were determined at 20 °C using a Perkin−Elmer automatic polarimeter, model 241. Elemental analyses were determined with a Carlo Erba Instruments EA 1108 element analyzer. Column chromatography on silica gel was performed with Fluka Silica gel 100 (0.035−0.070 mm). All reactions were monitored by TLC on Fluka Silica Gel 60 F-254/TLC-cards (20 × 20 × 0.2 cm) with detection by spraying with $KMnO_4$ solution. All reagents were of commercial quality or were purified before use. Organic solvents were purified and dried by standard procedures. 2,3-*O*-isopropylidene-D-glyceraldehyde (**1**) was prepared according to the published procedures.[15−17]

(2*R*)-1,2-*O*-Isopropylidene-4-pentyn-3-ol (2): Purified, anhydrous THF (100 mL) was placed in a 250 mL-flask, acetylene was introduced through the gas-inlet tube at the rate of 2−3 L/h, and the stirrer was started. After 30 min, a solution of ethylmagnesium bromide [prepared in situ from 0.48 g (0.02 g-atom) of Mg turnings, and 2.4 g (0.022 mol) of ethyl bromide in 25 mL of THF] was added over 2 h. The temperature of the reaction increased by between 5 and 10 °C. The mixture was then stirred at 30−35 °C for 1 h. The mixture was cooled in an ice bath and 2,3-*O*-isopropylidene-D-glyceraldehyde (3.12 g, 0.024 mol) in THF (15 mL) was added over 15 min. The mixture was then stirred and heated to 40−45 °C for a further 2 h. After cooling to room temperature, the reaction mixture was quenched by addition of saturated aqueous NH_4Cl solution (30 mL). The two layers were separated and the aqueous phase was extracted with Et_2O (3 × 15 mL). The combined organic fractions were washed with dried (K_2CO_3), and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, $CHCl_3$/MeOH, 10:1) to give the acetylenic alcohol **2** (2.2 g, 71%) as a colorless oil. TLC: R_f = 0.47 ($CHCl_3$/MeOH, 10:0.3). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.38 (s, 3 H, CH_3), 1.49 (s, 3 H, CH_3), 2.51 (br. d, J = 2.2 Hz, 1 H, OH), 2.67 (d, J = 5.0 Hz, 2 H, HC≡), 2.77 (d, $J_{H,H}$ = 4.9 Hz, 1 H, HC≡), 3.80−4.14 (m, 2 H, OCH_2), 4.24 (m, 1 H, HCO), 4.34 (ddd, $J_{H,H}$ = 2.2, $J_{H,H}$ = 4.6, $J_{H,H}$ = 5.0 Hz, 1 H, HOC*H*-C≡), 4.46 (ddd, $J_{H,H}$ = 2.2, $J_{H,H}$ = 4.7, $J_{H,H}$ = 5.0 Hz, 1 H, HOC*H*-C≡) ppm (a mixture of diastereomers). ^{13}C NMR (50.3 MHz. $CDCl_3$, DEPT): δ = 24.98 (CH_3), 25.06 (CH_3), 26.24 (CH_3), 26.61 (CH_3), 62.36 (CH), 63.74 (CH), 65.23 (CH_2), 65.91 (CH_2), 74.29 (CH), 74.32 (CH), 77.64 (C≡), 78.47 (C≡), 81.01 (C≡), 81.09 (C≡), 110.11 [*C*(CH_3)$_2$], 110.41 [*C*(CH_3)$_2$] ppm (a mixture of diastereomers). $C_8H_{12}O_3$ (156.18): calcd. C 61.52, H 7.74; found C 61.40, H 7.59.

(2*R*)-5-(Diethoxyphosphoryl)-1,2-*O*-isopropylidenepenta-3,4-diene (4): NEt_3 (1.62 g, 0.016 mol) was added to solution of acetylenic alcohol **2** (2.3 g, 0.0148 mol) in Et_2O (50 mL) under N_2 and the mixture was cooled to −40 °C. A solution of diethyl chlorophosphite (2.18 g, 0.014 mol) in Et_2O (10 mL) was then added dropwise and the mixture was stirred at −40 °C for 1 h and at room temp. for 24 h. The solid was removed by filtration and the solvent was evaporated under reduced pressure. The crude product was chromatographed ($CHCl_3$/MeOH, 10:0.5) to give **4** (2.55 g, 66%) as a colorless oil. TLC: R_f = 0.42, 0.44 ($CHCl_3$/MeOH, 10:0.3) (a mixture of diastereomers). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.31 (t, $J_{H,H}$ = 7.1 Hz, 3 H, *CH_3*CH_2O), 1.32 (t, $J_{H,H}$ = 7.1 Hz, 3 H, *CH_3*CH_2O), 1.38 (s, 3 H, CH_3), 1.45 (s, 3 H, CH_3), 3.78 (dd, $J_{H,H}$ =

8.3, $J_{H,H}$ = 6.4 Hz, 1 H, C*H*H-O), 4.10 (m, $J_{H,H}$ = 7.2, $J_{H,P}$ = 6.8 Hz, 4 H, 2CH$_3$*CH$_2$*O), 4.11 (dd, $J_{H,H}$ = 8.2, $J_{H,H}$ = 6.3 Hz, 1 H, CH*H*-O), 4.67 (m, 1 H, =CH-C*H*O), 5.48 (m, 1 H, =CH), 5.56 (m, 1 H, HC=) ppm. ^{13}C NMR (50.3 MHz. CDCl$_3$, DEPT): δ = 16.21 (*CH$_3$*CH$_2$O), 16.34 (*CH$_3$*CH$_2$O), 25.52 (CH$_3$), 25.54 (CH$_3$), 25.57 (CH$_3$), 26.48 (CH$_3$), 62.40 (d, $J_{C,P}$ = 5.6 Hz, CH$_3$*CH$_2$*O), 62.53 (d, $J_{C,P}$ = 5.8 Hz, CH$_3$*CH$_2$*O), 69.15 (d, $J_{C,P}$ = 6.0 Hz, OCH$_2$), 69.23 (d, $J_{C,P}$ = 6.2 Hz, OCH$_2$), 72.39 (d, $J_{C,P}$ = 6.5 Hz, OCH), 72.84 (d, $J_{C,P}$ = 6.5 Hz, OCH), 82.32 (d, $J_{C,P}$ = 196.6 Hz, =CHP), 82.61 (d, $J_{C,P}$ = 196.5 Hz, =CHP), 92.21 (d, $J_{C,P}$ = 16.0 Hz, =CH), 92.29 (d, $J_{C,P}$ = 15.9 Hz, =CH), 109.73 (C), 109.76 (C), 210.55 (=C=), 211.28 (=C=) ppm (a mixture of diastereomers). ^{31}P NMR (81.01 MHz. CDCl$_3$): δ = +14.27, +14.35 ppm (a mixture of diastereomers). C$_{12}$H$_{21}$O$_5$P (276.27): calcd. C 52.17, H 7.66, P 11.21; found C 52.04, H 7.58, P 11.19.

(2*R*)-5-(Diethoxyphosphoryl)penta-3,4-diene-1,2-diol (5): The crude phosphorylated allene **4** (1.4 g) was dissolved in CH$_3$OH (20 mL) and 1−2 drops of 35% aqueous HCl were added. The solution was stirred at room temp. 2 h and the solvent evaporated in vacuo. The crude product was chromatographed (CH$_2$Cl$_2$/MeOH, 10:1.3) to give **5** (2.1 g, 94%) as a colorless oil. TLC: R_f = 0.53, 0.56 (CHCl$_3$/MeOH, 10:1.3) (a mixture of diastereomers). IR (CCl$_4$): $\tilde{\nu}$ = 3387 cm^{-1} (br. OH); 1959 (C=C=C). ^{1}H NMR (200 MHz, CDCl$_3$): δ = 1.31 (t, $J_{H,H}$ = 7.2 Hz, 3 H, *CH$_3$*CH$_2$O), 1.32 (t, $J_{H,H}$ = 7.2 Hz, 3 H, *CH$_3$*CH$_2$O), 3.67 (m, 2 H, C*H$_2$*OH), 3.81 (br. s., 2 H, 2OH), 4.08 (m, $J_{H,H}$ = 7.2, $J_{H,P}$ = 7.0 Hz, 4 H, 2 CH$_3$*CH$_2$*O), 4.40 (m, 1 H, C*H*-OH), 5.44 (m, 1 H, =CH), 5.60 (ddd, $J_{H,H}$ = 6.5, $J_{H,H}$ = 6.6, $J_{H,P}$ = 13.1 Hz, 1 H, HC=) ppm (a mixture of diastereomers). ^{13}C NMR (50.3 MHz, CDCl$_3$, DEPT): δ = 16.14 (*CH$_3$*CH$_2$O), 16.26 (*CH$_3$*CH$_2$O), 62.68 (d, $J_{C,P}$ = 5.4 Hz, CH$_3$*CH$_2$*O), 62.88 (d, $J_{C,P}$ = 5.8 Hz, CH$_3$*CH$_2$*O), 65.79 (d, $J_{C,P}$ = 4.0 Hz, CH$_2$OH), 65.95 (d, $J_{C,P}$ = 4.1 Hz, CH$_2$OH), 69.14 (d, $J_{C,P}$ = 6.3 Hz, CHOH), 69.22 (d, $J_{C,P}$ = 6.4 Hz, CHOH), 81.57 (d, $J_{C,P}$ = 193.7 Hz, =CHP), 81.62 (d, $J_{C,P}$ = 193.6 Hz, =CHP), 94.07 (d, $J_{C,P}$ = 16.0, CH=), 94.42 (d, $J_{C,P}$ = 15.8 Hz, CH=), 211.13 (=C=), 211.94 (=C=) ppm (a mixture of diastereomers). ^{31}P NMR (81.01 MHz. CDCl$_3$): δ = +14.08 ppm. C$_9$H$_{17}$O$_5$P (236.20): calcd. C 45.77, H 7.25, P 13.11; found C 45.75, H 7.19, P 13.09.

(2*R*)-5-(Diethoxyphosphoryl)pent-4-ene-1,2-diol (6): A solution of compound **5** (2.36 g, 10.0 mmol) in methanol (15 mL) was hydrogenated over 5% Pd-BaSO$_4$ (0.2 g) at atmospheric pressure. The mixture was stirred vigorously at room temperature for 1 h, after which time the catalyst was removed by filtration and the filtrate concentrated under reduced pressure. The crude product **6** was purified by column chromatography (silica gel; CHCl$_3$/MeOH, 10:1) to give **6** (1.79 g, 75%) as a colorless oil. $[\alpha]_D^{20}$ = +8.14 (*c* = 1.5, C$_6$H$_6$). TLC: R_f = 0.31 (CHCl$_3$/MeOH, 10:0.3). IR (CCl$_4$): $\tilde{\nu}$ = 3400 cm^{-1} (br. OH). ^{1}H NMR (200 MHz, CDCl$_3$): δ = 1.32 (t, $J_{H,H}$ = 7.2 Hz, 3 H, *CH$_3$*CH$_2$O), 1.33 (t, $J_{H,H}$ = 7.2 Hz, 3 H, *CH$_3$*CH$_2$O), 2.78 (m, 2 H, =CH*CH$_2$*), 3.57 (br. d, 1 H, OH), 3.59 (m, 2 H, *CH$_2$*OH), 3.76 (m, *CH*OH), 3.92 (br. t, 1 H, OH), 4.08 (m, $J_{H,H}$ = 7.1, $J_{H,P}$ = 6.7 Hz, 4 H, 2CH$_3$*CH$_2$*O), 5.76 (dd, $J_{H,H}$ = 12.9, $J_{H,P}$ = 19.1 Hz, 1 H, HC=*CH*P), 6.64 (dddd, $J_{H,H}$ = 8.1, $J_{H,H}$ = 8.8, $J_{H,H}$ = 12.9, $J_{H\text{-}P}$ = 52.9 Hz, 1 H, *HC*=CHP) ppm. ^{13}C NMR (50.3 MHz, CDCl$_3$): δ = 16.10 (*CH$_3$*CH$_2$O), 16.15 (*CH$_3$*CH$_2$O), 34.45 (d, $J_{C,P}$ = 8.3 Hz, =CH-*CH$_2$*), 61.65 (d, $J_{C,P}$ = 5.6 Hz, CH$_3$*CH$_2$*O), 61.73 (d, $J_{C,P}$ = 5.6 Hz, CH$_3$*CH$_2$*O), 64.99 (CH$_2$O), 70.59 (d, $J_{C,P}$ = 2.4 Hz, CHOH), 118.37 (d, $J_{C,P}$ = 188.9 Hz, =CHP), 150.14 (d, $J_{C,P}$ = 4.5 Hz, =CH) ppm. ^{31}P NMR (81.01 MHz. CDCl$_3$): δ = +28.80 ppm. C$_9$H$_{19}$O$_5$P (238.22): calcd. C 45.38, H 8.04, P 13.00; found C 45.30, H 8.12, P12.92.

(2*R*)-5-(Diethoxyphosphoryl)-2-(palmitoyloxy)pent-4-enyl Palmitate (7a): Phosphonate **6** (0.28 g, 1.18 mmol), palmic acid (0.59 g, 2.32 mmol) and dimethylaminopyridine (DMAP, 30 mg, 0.24 mmol) were dissolved in 20 mL of chloroform, and then a solution of DCC (0.52 g, 2.52 mmol) in 10 mL of chloroform was added at room temperature. The reaction mixture was stirred overnight, and the white solid was removed by filtration through Celite. The solvent was evaporated under reduced pressure and the crude product was purified by column chromatography (silica gel; CHCl$_3$/MeOH, 10:0.2) to give **7a** (0.53 g, 63%) as a white solid, (m.p. 46−48 °C). $[\alpha]_D^{20}$ = +1.47 (*c* = 1.5, C$_6$H$_6$). TLC: R_f = 0.52 (CHCl$_3$/MeOH, 1: 0.2). IR (CCl$_4$): $\tilde{\nu}$ = 1758, 1760 cm^{-1} (C=O). ^{1}H NMR (200 MHz, CDCl$_3$): δ = 0.86 (m, 6 H, 2CH$_3$), 1.08−1.41 (m, 54 H, 24CH$_2$ + 2*CH$_3$*CH$_2$O), 1.52 (m, 4 H, 2CH$_2$), 2.25 (m, 4 H, 2CH$_2$), 2.88 (br. m 2 H, *CH$_2$*-CH=), 4.08 (m, $J_{H,H}$ = 7.2, $J_{H,P}$ = 6.8 Hz, 4 H, 2CH$_3$*CH$_2$*O), 4.13 (dd, $J_{H,H}$ = 12.0, $J_{H,H}$ = 3.5 Hz, 2 H, CH-*CH$_2$*O), 5.17 (ddt, $J_{H,H}$ = 3.3, $J_{H,H}$ = 3.5, $J_{H,H}$ = 3.5 Hz, 1 H, HCO), 5.67 (dd, $J_{H,H}$ = 13.1, $J_{H,P}$ = 18.3 Hz, 1 H, CH=*CH*P), 6.40 (ddt, $J_{H,H}$ = 7.38, $J_{H,P}$ = 51.9, $J_{H,H}$ = 13.1 Hz, 1 H, *CH*=CHP) ppm. ^{13}C NMR (50.3 MHz, CDCl$_3$): δ = 13.99 (CH$_3$), 14.11 (CH$_3$), 16.20 (*CH$_3$*CH$_2$O), 16.31 (*CH$_3$*CH$_2$O), 22.57 (CH$_2$), 22.65 (CH$_2$), 24.72 (CH$_2$), 24.83 (CH$_2$), 29.01−29.57 (22 CH$_2$), 31.70 (CH$_2$), 31.83 (CH$_2$), 34.08 (d, $J_{C,P}$ = 12.8 Hz, CH$_2$), 61.42 (d, $J_{C,P}$ = 5.6 Hz, CH$_3$*CH$_2$*O), 61.45 (d, $J_{C,P}$ = 5.6 Hz, CH$_3$*CH$_2$*O), 64.38 (OCH$_2$), 70.04 (d, $J_{C,P}$ = 2.0 Hz, OCH), 119.70 (d, $J_{C,P}$ = 183.1 Hz, =CHP), 147.06 (d, $J_{C,P}$ = 3.6 Hz, *HC*=CHP), 173.05 (C=O), 173.24 (C=O) ppm. ^{31}P NMR (81.01 MHz. CDCl$_3$): δ = +17.17 ppm. C$_{41}$H$_{79}$O$_7$P (715.05): calcd. C 68.87, H 11.14, P 4.33; found C 69.01, H 11.08, P 4.19.

(2*R*)-5-(Diethoxyphosphoryl)-2-(stearoyloxy)pent-4-enyl Stearate (7b): Prepared from **6** (0.24 g, 1.0 mmol) in an analogous manner to that described above for **7a**, but with stearic acid. Purification by silica gel column chromatography (CHCl$_3$/MeOH, 10:0.2) gave **7b** (0.54 g, 70%) as a white solid, (m.p. 44−47 °C), $[\alpha]_D^{20}$ = +1.44 (*c* = 1.5, C$_6$H$_6$). TLC: R_f = 0.54 (CHCl$_3$/MeOH, 10:0.2). IR (CCl$_4$): $\tilde{\nu}$ = 1754, 1758 cm^{-1} (C=O). ^{1}H NMR (200 MHz, CDCl$_3$): δ = 0.87 (m, 6 H, 2CH$_3$), 1.08−1.41 (m, 62 H, 28CH$_2$ + 2*CH$_3$*CH$_2$O), 1.53 (m, 4 H, 2CH$_2$), 2.26 (m, 4 H, 2CH$_2$), 2.89 (br. m, 2 H, *CH$_2$*-CH=), 4.10 (m, $J_{H,H}$ = 7.2, $J_{H,P}$ = 6.9 Hz, 4 H, 2CH$_3$*CH$_2$*O), 4.17 (dd, $J_{H,H}$ = 12.2, $J_{H,H}$ = 3.6 Hz, 2 H, CH-*CH$_2$*O), 5.19 (ddt, $J_{H,H}$ = 3.3, $J_{H,H}$ = 3.5, $J_{H,H}$ = 3.5 Hz, 1 H, HCO), 5.72 (dd, $J_{H,H}$ = 13.0, $J_{H,P}$ = 18.3 Hz, 1 H, CH=*CH*P), 6.50 (ddt, $J_{H,H}$ = 7.4, $J_{H,P}$ = 51.7, $J_{H,H}$ = 13.1 Hz, 1 H, *CH*=CHP) ppm. ^{13}C NMR (50.3 MHz, CDCl$_3$): δ = 13.86 (CH$_3$), 14.05 (CH$_3$), 16.10 (*CH$_3$*CH$_2$O), 16.18 (*CH$_3$*CH$_2$O), 22.42 (CH$_2$), 22.58 (CH$_2$), 24.76 (CH$_2$), 24.88 (CH$_2$), 29.06−29.63 (26 CH$_2$), 31.68 (CH$_2$), 31.8 (CH$_2$), 34.08 (d, $J_{C,P}$ = 12.8 CH$_2$), 61.48 (d, $J_{C,P}$ = 5.6 Hz, CH$_3$*CH$_2$*O), 61.51 (d, $J_{C,P}$ = 5.8 Hz, CH$_3$*CH$_2$*O), 64.43 (OCH$_2$), 70.07 (d, $J_{C,P}$ = 2.2 Hz, OCH), 119.74 (d, $J_{C,P}$ = 183.0 Hz, =CHP), 147.11 (d, $J_{C,P}$ = 3.7 Hz, *HC*=CHP), 173.12 (C=O), 173.32 (C=O) ppm. ^{31}P NMR (81.01 MHz. CDCl$_3$): δ = +17.18 ppm. C$_{45}$H$_{87}$O$_7$P (771.16): calcd. C 70.09, H 11.37, P 4.02; found C 70.11, H 11.25, P 4.13.

(2*R*)-2-(Palmitoyloxy)-5-(phosphoryl)pent-4-enyl Palmitate (8a): A solution of phosphonate **7a** (1.43 g, 2.0 mmol) in 10 mL of alcohol-free chloroform was added to a three-necked round-bottomed flask equipped with a magnetic stir bar and nitrogen inlet. To this solution was added dropwise a solution of bromotrimethylsilane (1.84 g, 12.0 mmol) in 10 mL of alcohol-free chloroform. After 24 h the solvents were removed on a rotary evaporator, and the residue was recrystallized from hexane/chloroform (15:1) to give 0.47 g (36%) of **8a** as a white solid, (m.p. 57−63 °C). $[\alpha]_D^{20}$ = +1.63 (*c* =

1.5, C_6H_6). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.88 (m, 6 H, $2CH_3$), 1.24 (m, 48 H, $24CH_2$), 1.54 (m, 4 H, $2CH_2$), 2.26 (br. m, 4 H, $2CH_2$), 2.89 (br. m 2 H, $\mathit{CH_2}$CH=), 4.15 (br. dd, $J_{H,H}$ = 12.2, $J_{H,H}$ = 4.0 Hz, 2 H, CH-$\mathit{CH_2}$O), 5.20 (m, 1 H, HCO), 5.67 (br. m, 1 H, CH=*CH*P), 6.38 (br. m, $J_{H,P}$ = 52 Hz, 1 H, *CH*=CHP) ppm.^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 13.98 (CH_3), 14.04 (CH_3), 22.68 (CH_2), 22.71 (CH_2), 24.72 (CH_2), 24.90 (CH_2), 28.42−31.42 (22 CH_2), 31.88 (CH_2), 31.96 (CH_2), 35.23 (d, $J_{C,P}$ = 12.2 Hz, CH_2), 64.45 (OCH_2), 70.32 (d, $J_{C,P}$ = 2.0 Hz, OCH), 120.82 (d, $J_{C,P}$ = 182.1 Hz, =CHP), 147.45 (d, $J_{C,P}$ = 3.6 Hz, *HC*=CHP), 174.01 (C=O), 175.24 (C=O) ppm. ^{31}P NMR (81.01 MHz. $CDCl_3$): δ = +20.36 ppm. $C_{37}H_{71}O_7P$ (658.94): calcd. C 67.44, H 10.86, P 4.70; found C 67.36, H 10.80, P 4.61.

(2*R*)-5-(Phosphoryl)-2-(stearoyloxy)pent-4-enyl Stearate (8b): Prepared from **7b** (1.54 g, 2.0 mmol) in an analogous manner to that described above for **8a**. Yield of **8b** (0.57 g, 40%) as a white solid, (m.p. 54−58 °C), $[\alpha]_D^{20}$ = +1.81 (*c* = 1.5, C_6H_6). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.88 (m, 6 H, $2CH_3$), 1.19−1.31 (br. m, 56 H, $28CH_2$), 1.60 (br. m, 4 H, $2CH_2$), 2.24 (br. m, 4 H, $2CH_2$), 2.92 (br. m 2 H, $\mathit{CH_2}$CH=), 4.12 (br. d, $J_{H,H}$ = 12.2 Hz,, 2 H CH-$\mathit{CH_2}$O), 5.12 (m, 1 H, HCO), 5.79 (br. m, 1 H, CH=*CH*P), 6.40 (dm, $J_{H,P}$ = 52 Hz, 1 H, *CH*=CHP) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 12.69 (CH_3), 12.82 (CH_3), 22.70 (CH_2), 22.86 (CH_2), 24.92 (CH_2), 25.00 (CH_2), 28.00−31.20 (26 CH_2), 31.70 (CH_2), 31.82 (CH_2), 35.00 (d, $J_{C,P}$ = 12.2 Hz, CH_2), 64.50 (OCH_2), 70.22 (d, $J_{C,P}$ = 2.0 Hz, OCH), 120.87 (d, $J_{C,P}$ = 180.0 Hz, =CHP), 148.44 (d, $J_{C,P}$ = 3.4 Hz, *HC*=CHP), 175.01 (C=O), 175.20 (C=O) ppm. ^{31}P NMR (81.01 MHz. $CDCl_3$): δ = +20.67 ppm. $C_{41}H_{79}O_7P$ (715.05): calcd. C 68.87, H 11.14, P 4.33; found C 68.96, H 11.04, P 4.22.

(2*R*)-5-(Diethoxyphosphoryl)-2-(palmitoyloxy)penta-3,4-dienyl Palmitate (9a): Palmitoyl chloride (0.66 g, 2.4 mmol) was added dropwise under argon to a stirred solution of **5** (0.236 g, 1.0 mmol), NEt_3 (0.202 g, 2.0 mmol) and 4-dimethylaminopyridine (0.037 g, 0.3 mmol) in DMF (5 mL) cooled to 5 °C. The reaction was stirred at 5 °C for 1 h and for 24 h at 50 °C, quenched by the addition of water, and extracted with chloroform (3 × 10 mL). The combined organic extracts were dried and concentrated. The concentrate was purified by column chromatography (CH_2Cl_2/MeOH, 20:1) to give **9a** (0.58 g, 82%) as a white solid, (m.p. 48−50 °C). TLC: R_f = 0.67 (CH_2Cl_2/MeOH, 24:1). IR (CCl_4): $\tilde{\nu}$ = 1752, 1755 cm^{-1} (C=O), 1965 (C=C=C). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.86 (m, 6 H, $2CH_3$), 1.06−1.41 (m, 54 H, $24CH_2$ + 2 $\mathit{CH_3}CH_2O$), 1.62 (m, 4 H, $2CH_2$), 2.24−2.36 (m, 4 H, $2CH_2$), 4.16 (m, $J_{H,H}$ = 7.2, $J_{H,P}$ = 6.8 Hz, 4 H, 2 $CH_3\mathit{CH_2}O$), 4.23 (m, 2 H, OCH_2), 5.53 (m, 1 H, *CH*OH), 5.57 (m, 2 H, 2HC=) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$, DEPT): δ = 13.97 (CH_3), 13.98 (CH_3), 16.11 ($\mathit{CH_3}CH_2O$), 16.23 ($\mathit{CH_3}CH_2O$), 22.55 (CH_2), 22.56 (CH_2), 24.69 (CH_2), 24.71 (CH_2), 24.72 (CH_2), 24.74 (CH_2), 28.97−29.56 ($16CH_2$), 31.77 (CH_2), 31.79 (CH_2), 33.90 (CH_2), 33.91 (CH_2), 34.05 (CH_2), 34.15 (CH_2), 62.42 (d, $J_{C,P}$ = 5.2 Hz, $CH_3\mathit{CH_2}O$), 62.52 (d, $J_{C,P}$ = 5.8 Hz, $CH_3\mathit{CH_2}O$), 64.00 (d, $J_{C,P}$ = 3.73 Hz, OCH_2), 64.13 (d, $J_{C,P}$ = 4.02 Hz, OCH_2), 67.37 (d, $J_{C,P}$ = 6.3 Hz, OCH), 67.69 (d, $J_{C,P}$ = 6.4 Hz, OCH), 83.26 (d, $J_{C,P}$ = 196.4 Hz, PCH=), 83.46 (d, $J_{C,P}$ = 195.8 Hz, PCH=), 89.28 (d, $J_{C,P}$ = 16.1 Hz, C-*CH*=), 89.38 (d, $J_{C,P}$ = 16.0 Hz, C-*CH*=), 172.48 (O=C), 172.60 (O=C), 173.12 (O=C), 210.62 (=C=), 210.85 (=C=) ppm (a mixture of diastereomers). ^{31}P NMR (81.01 MHz. $CDCl_3$): δ = +14.47, +14.64 ppm (a mixture of diastereomers). $C_{41}H_{77}O_7P$ (713.03): calcd. C 69.06, H 10.88, P 4.34; found C 69.21, H 10.88, P 4.19.

(2*R*)-5-(Diethoxyphosphoryl)-2-(stearoyloxy)penta-3,4-dienyl Stearate (9b): This compound was prepared as described for **9a**. Yield **9b** (0.68 g, 89%), (m.p. 39−42 °C). TLC: R_f = 0.72 (CH_2Cl_2/MeOH, 24:1). IR (CCl_4): $\tilde{\nu}$ = 1752, 1754 cm^{-1} (C=O), 1968 (C=C=C). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.86 (m, 6 H, $2CH_3$), 1.08−1.40 (m, 62 H, $28CH_2$ + $2CH_3$), 1.61 (m, 4 H, $2CH_2$), 2.23−2.38 (m, 4 H, $2CH_2$), 4.16 (m, $J_{H,H}$ = 7.2, $J_{H,P}$ = 6.8 Hz, 4 H, $2CH_3\mathit{CH_2}O$), 4.25 (m, 2 H, OCH_2), 5.53 (m, 1 H, *CH*OH), 5.59 (m, 2 H, 2HC=) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$, DEPT): δ = 14.00 (CH_3), 14.09 (CH_3), 16.11 ($\mathit{CH_3}CH_2O$), 16.17 ($\mathit{CH_3}CH_2O$), 22.58 (CH_2), 22.59 (CH_2), 24.73 (CH_2), 24.75 (CH_2), 22.76 (CH_2), 24.78 (CH_2), 29.08−29.60 ($20CH_2$), 31.82 (CH_2), 31.83 (CH_2) 33.94 (CH_2), 33.95 (CH_2), 34.00 (CH_2), 34.09 (CH_2), 62.44 (d, $J_{C,P}$ = 5.5 Hz, $CH_3\mathit{CH_2}O$), 62.54 (d, $J_{C,P}$ = 5.7 Hz, $CH_3\mathit{CH_2}O$), 64.03 (d, $J_{C,P}$ = 3.84 Hz, OCH_2), 64.18 (d, $J_{C,P}$ = 2.8 Hz, OCH_2), 67.41 (d, $J_{C,P}$ = 6.2 Hz, OCH), 67.73 (d, $J_{C,P}$ = 6.3 Hz, OCH), 83.33 (d, $J_{C,P}$ = 196.4 Hz, PCH=), 83.53 (d, $J_{C,P}$ = 195.9 Hz, PCH=), 89.31 (d, $J_{C,P}$ = 16.0 Hz, C-*CH*=), 89.42 (d, $J_{C,P}$ = 16.0 Hz, C-*CH*=), 172.54 (O=C), 173.13 (O=C), 210.64 (=C=), 210.87 (=C=) ppm (a mixture of diastereomers). ^{31}P NMR (81.01 MHz. $CDCl_3$): δ = +14.47, +14.64 ppm (a mixture of diastereomers). $C_{45}H_{85}O_7P$ (769.14): calcd. C 70.27, H 11.14, P 4.03; found C 70.36, H 11.05, P 3.95.

(2*R*)-5-(Diethoxyphosphoryl)-2-(palmitoyloxy)pentanyl Palmitate (10a): A solution of compound **9a** (0.356 g, 0.5 mmol) in methanol (10 mL) was hydrogenated over 5% Pd/C (0.03 g) at atmospheric pressure. The mixture was vigorously stirred at room temperature for 1 h, whereupon the catalyst was removed by filtration and the filtrate concentrated under reduced pressure. The crude product was purified by column chromatography (silica gel; CH_2Cl_2/MeOH, 24:1) to give **10a** (0.28 g, 78%) as a white solid, (m.p. 29−31 °C). $[\alpha]_D^{20}$ = +1.43 (*c* = 1.5, C_6H_6). TLC: R_f = 0.51 (CH_2Cl_2/MeOH, 24:1). IR (CCl_4): $\tilde{\nu}$ = 1751, 1753 cm^{-1} (C=O). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.87 (m, 6 H, $2CH_3$), 1.06−1.40 (m, 54 H, $24CH_2$ + $2\mathit{CH_3}CH_2O$), 1.61 (m, 10 H, $5CH_2$), 2.12−2.30 (m, 4 H, $2CH_2$), 4.08 (m, $J_{H,H}$ = 7.2, $J_{H\text{-}P}$ = 6.8 Hz, 4 H, $2CH_3\mathit{CH_2}O$), 4.12 (m, 2 H, OCH_2), 5.07 (m, 1 H, *CH*OH) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$, DEPT): δ = 13.93 (CH_3), 13.94 (CH_3), 16.23 ($\mathit{CH_3}CH_2O$), 16.35 ($\mathit{CH_3}CH_2O$), 18.21 (d, $J_{C,P}$ = 4.8 Hz, CH_2), 22.52 (CH_2), 22.53 (CH_2), 24.71 (CH_2), 24.72 (CH_2), 24.84 (CH_2), 24.85 (CH_2), 25.16 (d, $J_{C,P}$ = 141.7 Hz, P-CH_2), 28.97−29.53 (16 CH_2), 31.32 (d, $J_{C,P}$ = 16.2 Hz, CH_2), 31.76 (CH_2), 31.77 (CH_2), 33.95 (CH_2), 34.21 (CH_2), 61.38 (d, $J_{C,P}$ = 6.5 Hz, $2CH_3\mathit{CH_2}O$), 64.54 (OCH_2), 70.29 (OCH), 173.13 (C=O), 173.28 (C=O) ppm. ^{31}P NMR (81.01 MHz. $CDCl_3$): δ = +32.54 ppm. $C_{41}H_{81}O_7P$ (717.06): calcd. C 68.68, H 11.39, P 4.32; found C 68.60, H 11.27, P 4.30.

(2*R*)-5-(Diethoxyphosphoryl)-2-(stearoyloxy)pentanyl Stearate (10b): This compound was prepared as described for **10a**. Yield 0.29 g, (75%), (m.p. 37−39 °C). $[\alpha]_D^{20}$ = +1.38 (*c* = 1.5, C_6H_6). TLC: R_f = 0.54 (CH_2Cl_2/MeOH, 24:1). IR (CCl_4): $\tilde{\nu}$ = 1750, 1753 cm^{-1} (C=O). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.88 (m, 6 H, $2CH_3$), 1.08−1.41 (m, 62 H, $28CH_2$ + $2\mathit{CH_3}CH_2O$), 1.63 (m, 10 H, $5CH_2$), 2.29 (m, 4 H, $2CH_2$), 4.08 (m, $J_{H,H}$ = 7.2, $J_{H,P}$ = 6.8 Hz, 4 H, $2CH_3\mathit{CH_2}O$), 4.12 (m, 2 H, OCH_2), 5.08 (m, 1 H, *CH*OH) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$, DEPT): δ = 14.13 (CH_3), 14.14 (CH_3), 16.40 ($\mathit{CH_3}CH_2O$), 16.51 ($\mathit{CH_3}CH_2O$), 18.43 (d, $J_{C,P}$ = 5.0 Hz, CH_2), 22.71 (CH_2), 22.72 (CH_2), 24.91 (CH_2), 24.93 (CH_2), 25.03 (CH_2), 25.25 (CH_2), 25.41 (d, $J_{C,P}$ = 141.3 Hz, P-CH_2), 29.18−29.73 (23 CH_2), 31.55 (d, $J_{C,P}$ = 16.1 Hz, CH_2), 31.96 (CH_2), 32.10 (CH_2), 34.16 (CH_2), 34.42 (CH_2), 61.56 (d, $J_{C,P}$ = 6.5 Hz, $2CH_3\mathit{CH_2}O$), 64.76 (OCH_2), 70.52 (OCH), 173.32 (C=O), 173.48 (C=O) ppm. ^{31}P NMR (81.01 MHz. $CDCl_3$): δ = +32.54 ppm. $C_{45}H_{89}O_7P$ (773.17): calcd. C 69.91, H 11.60, P 4.01; found C 70.07, H 11.55, P 3.89.

(2*R*)-2-(Palmitoyloxy)-5-(phosphoryl)pentanyl Palmitate (11a): A solution of the phosphonate **10a** (0.717 g, 1.0 mmol) in 10 mL of alcohol-free chloroform was added to a three-necked, round-bottomed flask equipped with a magnetic stir bar and nitrogen inlet. To this solution was added dropwise a solution of bromotrimethylsilane (0.918 g, 6.0 mmol) in 5 mL of alcohol-free chloroform. After 24 h the solvents were removed on a rotary evaporator, and the residue was recrystallized from hexane/chloroform (15:1) to give 0.284 g (43%) of pure **11a** as a white solid, (m.p. 67−70 °C). $[\alpha]_D^{20} = +1.41$ ($c = 1.5$, C_6H_6). ^1H NMR (200 MHz, $CDCl_3$): $\delta = 0.89$ (m, 6 H, $2CH_3$), 1.25 (m, 48 H, $24CH_2$), 1.61 (br. m, 10 H, $5CH_2$), 2.31 (br. m, 4 H, $2CH_2O$), 4.18 (m, 2 H, OCH_2), 5.12 (m, 1 H, *CH*OH) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$, DEPT): $\delta = 14.16$ (CH_3), 14.15 (CH_3), 18.00 (CH_3), 18.19 (CH_2), 22.43 (CH_3), 22.68 (CH_2), 24.70 (CH_3), 24.76 (CH_2), 24.88 (CH_2), 25.25 (d, $J_{C,P} = 144.0$ Hz, P-CH_2), 28.71−29.23 (18 CH_2), 31.32 (CH_2), 31.76 (CH_2), 33.90 (CH_3), 33.95 (CH_2), 34.21 (CH_2), 64.64 (OCH_2), 71.18 (OCH), 177.13 (C=O), 178.28 (C=O) ppm. ^{31}P NMR (81.01 MHz. $CDCl_3$): $\delta = +36.04$ ppm. $C_{37}H_{73}O_7P$ (660.96): calcd. C 67.24, H 11.13, P 4.69; found C 67.09, H 11.05, P 3.50.

(2*R*)-5-(Phosphoryl)-2-(stearoyloxy)pentanyl Stearate (11b): Prepared from **10b** (0.772 g, 1.0 mmol) in an analogous manner to that described above for **11a**. Yield 0.34 g (47%), (m.p. 64−68 °C). $[\alpha]_D^{20} = +1.42$ ($c = 1.5$ C_6H_6). ^1H NMR (200 MHz, $CDCl_3$): $\delta = 0.89$ (m, 6 H, $2CH_3$), 1.24 (m, 56 H, $28CH_2$), 1.62 (br. m, 10 H, $5CH_2$), 2.33 (br. m, 4 H, $2CH_2O$), 4.17 (m, 2 H, OCH_2), 5.11 (m, 1 H, *CH*O) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$, DEPT): $\delta = 14.10$ (CH_3), 14.11 (CH_3), 18.13 (CH_2), 18.14 (CH_2), 22.65 (CH_2), 22.66 (CH_2), 24.70 (CH_2), 24.76 (CH_2), 24.81 ($2CH_2$), 24.87 ($2CH_2$), 25.24 (d, $J_{C,P} = 146.0$ Hz, P-CH_2), 28.80−30.23 (22 CH_2), 31.31 (CH_2), 31.77 (CH_2), 33.88 (CH_2), 34.19 (CH_2), 64.44 (OCH_2), 71.12 (OCH), 177.43 (C=O), 178.40 (C=O) ppm. ^{31}P NMR (81.01 MHz. $CDCl_3$): $\delta = +36.08$ ppm. $C_{41}H_{81}O_7P$ (717.07): calcd. C 68.68, H 11.39, P 4.32; found C 68.56, H 11.25, P 4.20.

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