Supplementary Information

Fatty acid chain length drives lysophosphatidylserine-dependent immunological outputs

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Table of Contents

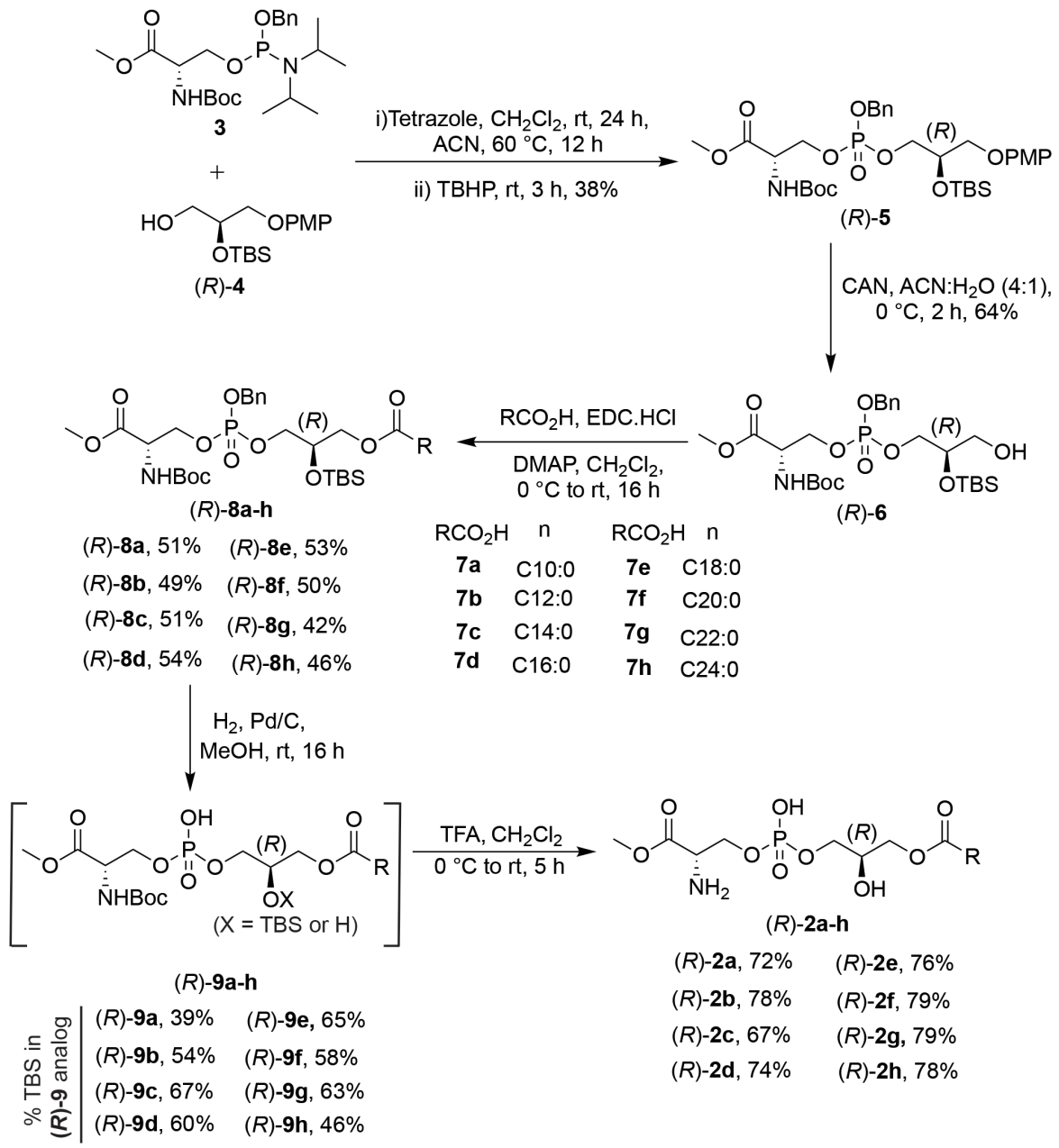


Figure S1. Synthetic strategy for making (*R*)-Me-lyso-PSs. See **Supplementary Information** section “Chemical compound synthesis and characterization” for complete details.

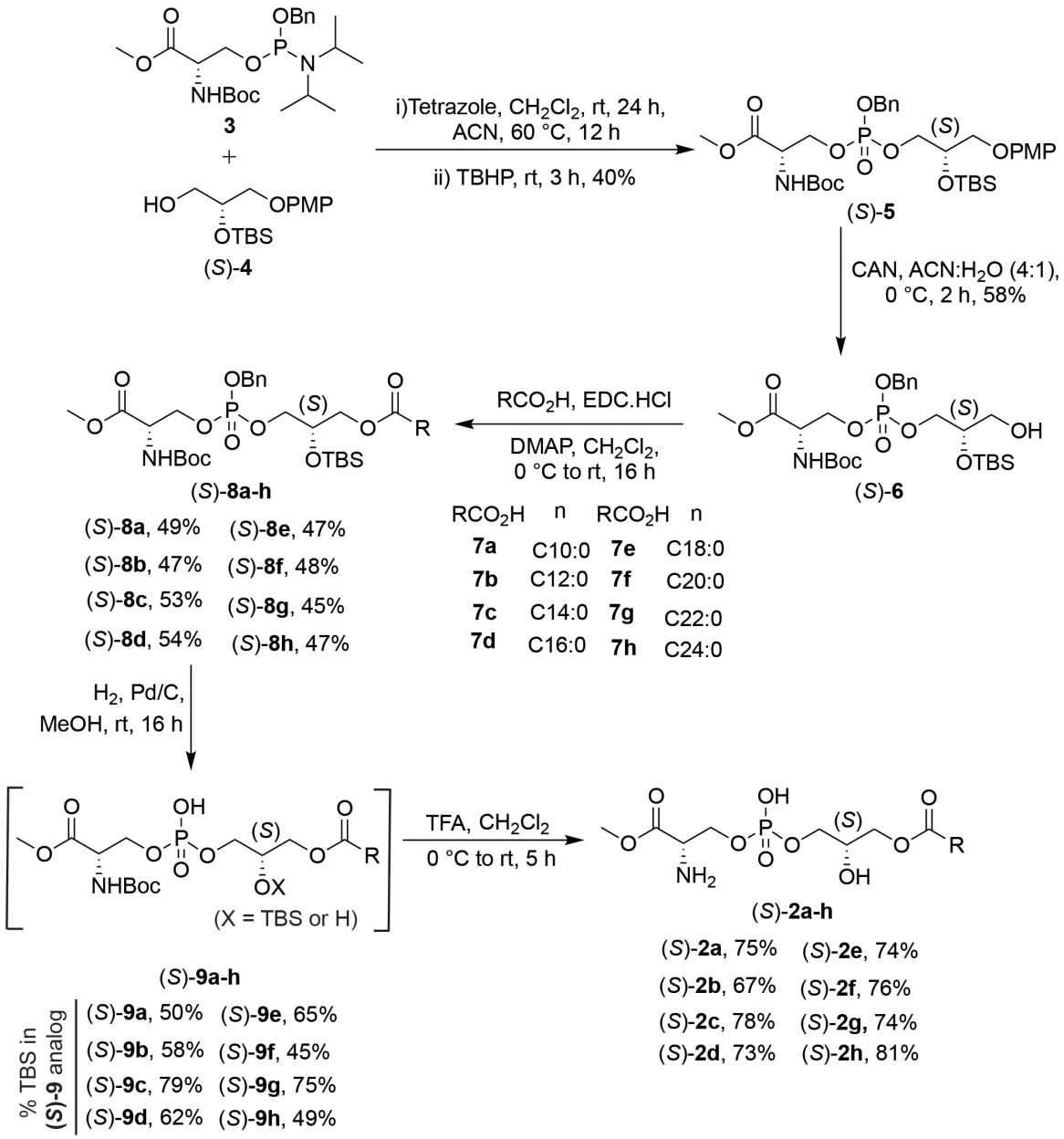


Figure S2. Synthetic strategy for making (*S*)-Me-lyso-PSs. See **Supplementary Information** section “Chemical compound synthesis and characterization” for complete details.

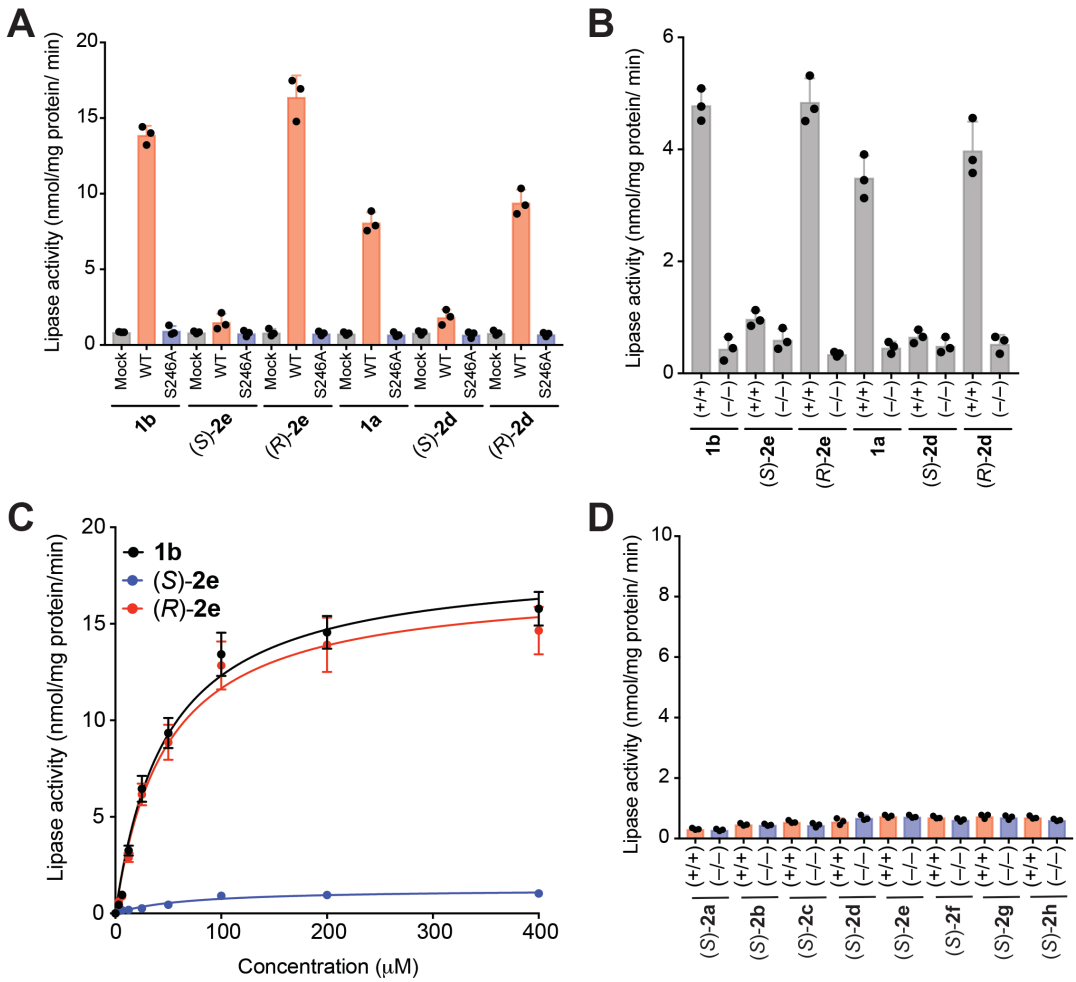


Figure S3. Lyso-PS lipase substrate assays performed with recombinant hABHD12 and endogenous mABHD12. (**A**) HEK293T membrane lysates (10 μg) transfected with wild type (WT) hABHD12 or the catalytically inactive S246A hABHD12 mutant or a mock-transfection control; and (**B**) Brain membrane lysates (20 μg) from wild type (+/+) and ABHD12 knockout (–/–) mice were assayed against 100 μM of commercial lyso-PSs (**1a** and **1b**) or (*R*)-Me-lyso-PS (**2d** and **2e**) or (*S*)-Me-lyso-PS (**2d** and **2e**) using established protocols (Joshi et al., 2018, Singh et al., 2020). The data shows that hABHD12 and mABHD12 have similar lipase activity for commercial lyso-PSs and (*R*)-Me-lyso-PS, while (*S*)-Me-lyso-PS is a poor substrate for this enzyme. (**C**) Enzyme kinetic assays for WT hABHD12 against varying concentrations of **1b**, (*R*)-**2e** and (*S*)-**2e** (0 – 400 μM) showing comparative enzyme kinetic profiles for **1b** and (*R*)-**2e**, but not (*S*)-**2e** (n = 3/data point). The line connecting the data points for a particular group represents a fit to a classical Michaelis-Menten enzyme kinetics equation(Joshi et al., 2018). All enzyme kinetic parameters are reported in **Table 1**. (**D**) Brain membrane lysates from wild type (+/+) and ABHD12 knockout (–/–) mice were assayed against 100 μM of (*S*)-Me-lyso-PS with varying chain lengths ((*S*)-**2a-h**) using established protocols (Joshi et al., 2018, Singh et al., 2020). The data shows that (*S*)-Me-lyso-PSs are not substrates for endogenous mABHD12, suggesting that the lyso-PS lipase activity of endogenous mABHD12 is stereoselective. The plot is at the same scale as the data presented in **Figure 2B** for relative comparison. All data is represented as mean ± standard deviation from three independent experiments for all experimental groups.

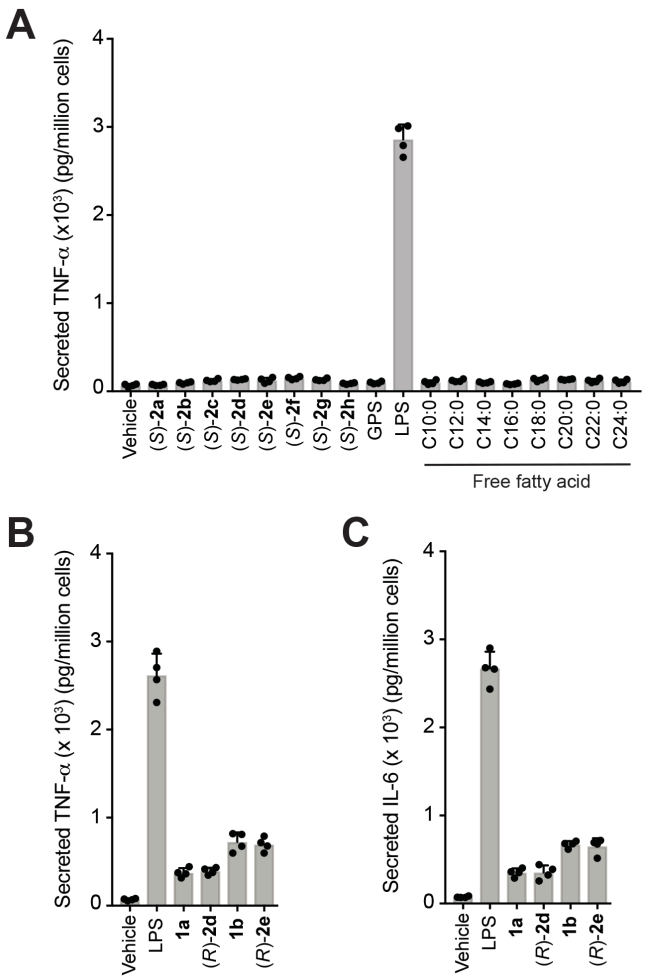


Figure S4. Pro-inflammatory cytokine secretion profiles from wild type (WT) primary peritoneal macrophages (PPM) following different treatments. (**A**) Treatment of WT PPM with either (*S*)-Me-lyso-PSs or free fatty acids (FFAs) (all at 1 μM, 4 h, 37 ^{o}C) fails to elicit secretion of TNF-α compared to LPS (positive) control. (**B**, **C**) The treatment of WT PPM with commercially available lyso-PSs **1a** and **1b** and their synthetic (*R*)-Me-lyso-PS counterparts (*R*)-**2d**, and (*R*)-**2e** respectively (all at 1 μM, 4 h, 37 ^{o}C), produce comparable secretion of (**B**) TNF-α and (**C**) IL-6, suggesting that canonical lyso-PS and (*R*)-Me-lyso-PS of the same chain length function similarly in producing pro-inflammatory cytokines from PPM. All the data presented in (**A**) and (**B**) represents mean ± standard deviation from four independent experiments for all experimental groups.

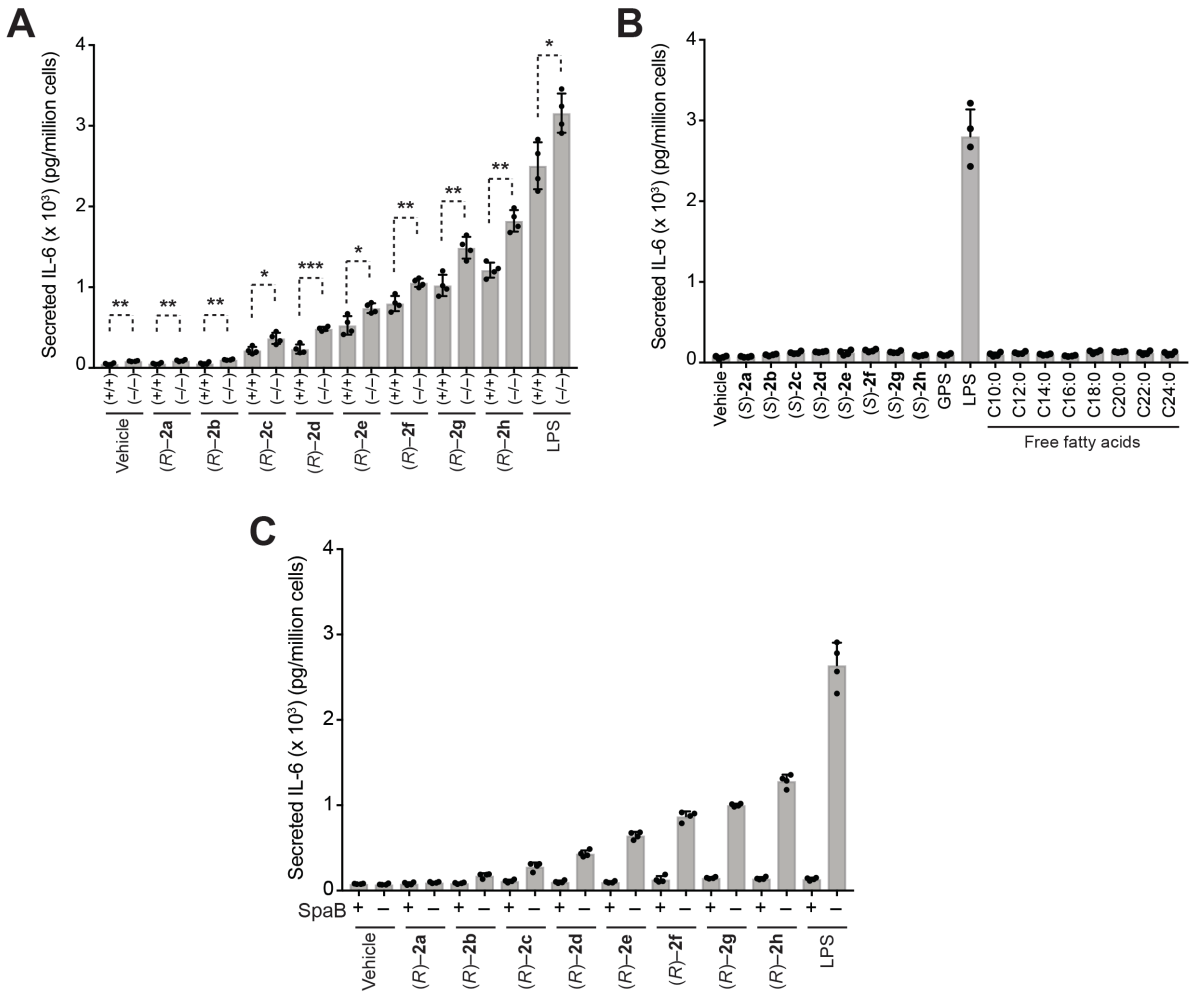


Figure S5. Secretion profiles of the pro-inflammatory cytokine IL-6 from PPM following different treatments. (**A**) The secretion of IL-6 from wild type (+/+) and ABHD12 knockout (–/–) PPM following treatment with different (*R*)-Me-lyso-PSs ((*R*)-**2a-h**) (all at 1 μM, 4 h, 37 °C), shows that VLC (*R*)-Me-lyso-PSs produce the highest secretion of IL-6, and that deletion of ABHD12 (diminished lyso-PS lipase activity (Kamat et al., 2015)), results in heightened IL-6 secretion from ABHD12 knockout PPM compared to WT PPM. These results are similar to those observed for TNF-α reported in **Fig. 2A**. (**B**) Treatment of WT PPM with (*S*)-Me-lyso-PSs or free fatty acids (FFAs) (all at 1 μM, 4 h, 37 °C) fails to elicit secretion of IL-6 compared to LPS (positive) control. (**C**) Pharmacological antagonism of TLR2 by Sparstolonin B (SpaB) (Liang et al., 2011, Liang et al., 2013) results in significantly decreased secretion of IL-6 following treatment with different (*R*)-Me-lyso-PSs ((*R*)-**2a-h**) (all at 1 μM, 4 h, 37 °C), especially the VLC (*R*)-Me-lyso-PSs, suggesting that these signal through TLR2. These results are similar to those observed for TNF-α reported in **Figure 3B**. All the data presented in (**A**), (**B**) and (**C**) represents mean ± standard deviation from four independent experiments for all experimental groups. *p < 0.05, **p < 0.01, and ***p < 0.001 for (–/–) group versus (+/+) group, by Student's t-test.

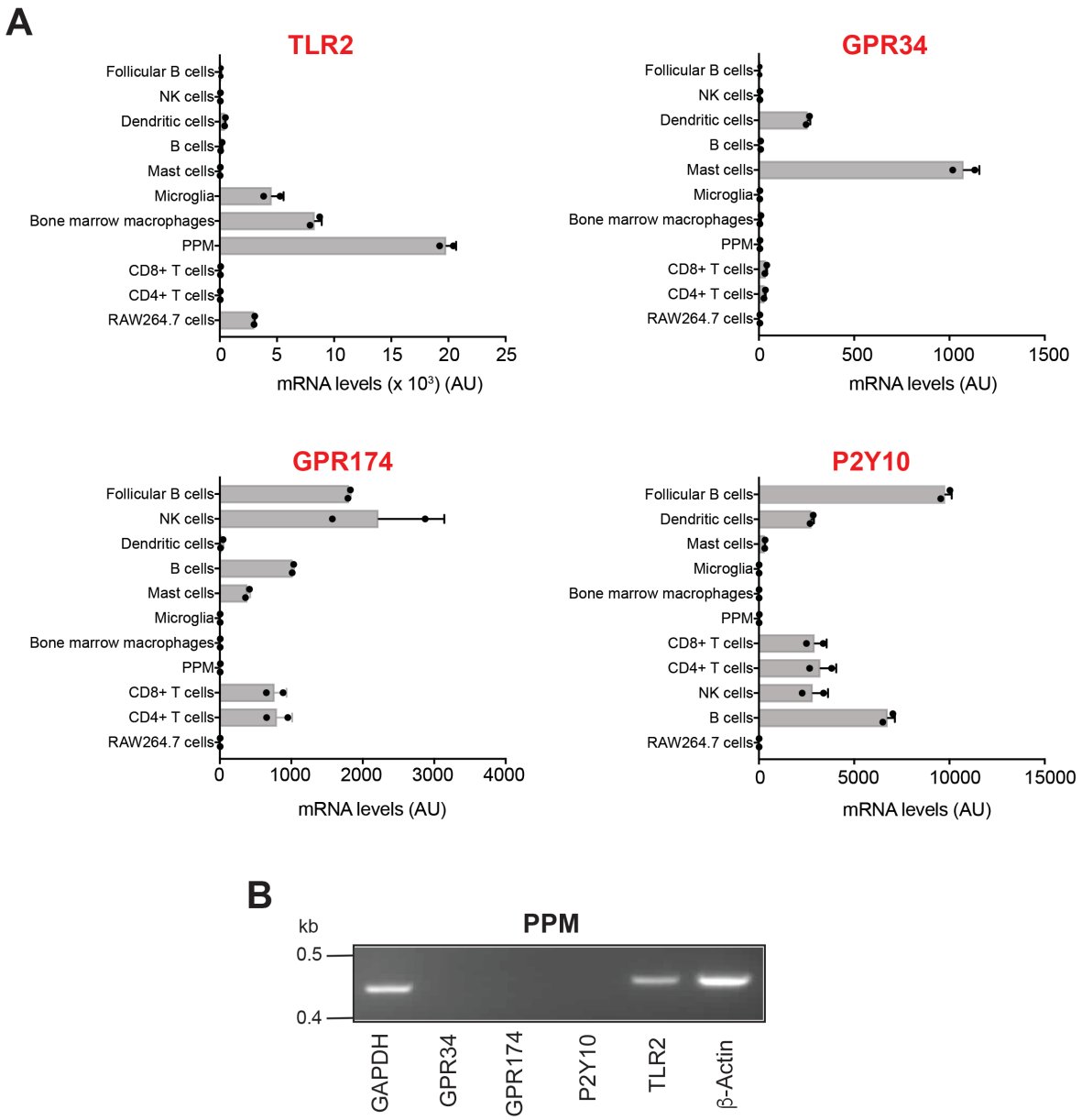


Figure S6. TLR2 is the only putative lyso-PS receptor expressed in macrophages. (**A**) The mRNA expression profiles obtained from the large-scale gene expression database BioGPS (Wu et al., 2016, Wu et al., 2009), in different mouse immune cells, for the different putative lyso-PS receptors (TLR2, GPR34, GPR174 and P2Y10) postulated in literature (van der Kleij et al., 2002, Inoue et al., 2012), showing that TLR2 is the only receptor amongst these to have robust expression in all macrophages (PPM, bone marrow derived macrophages, microglia, and RAW264.7 cells). (**B**) RT-PCR analysis confirms the gene expression profile reported in (**A**), that TLR2, but not GPR34, GPR174 and P2Y10, is present in WT PPM. In this experiment, GAPDH and β-actin were used as controls in this experiment. This RT-PCR experiment was done twice with reproducible results each time.

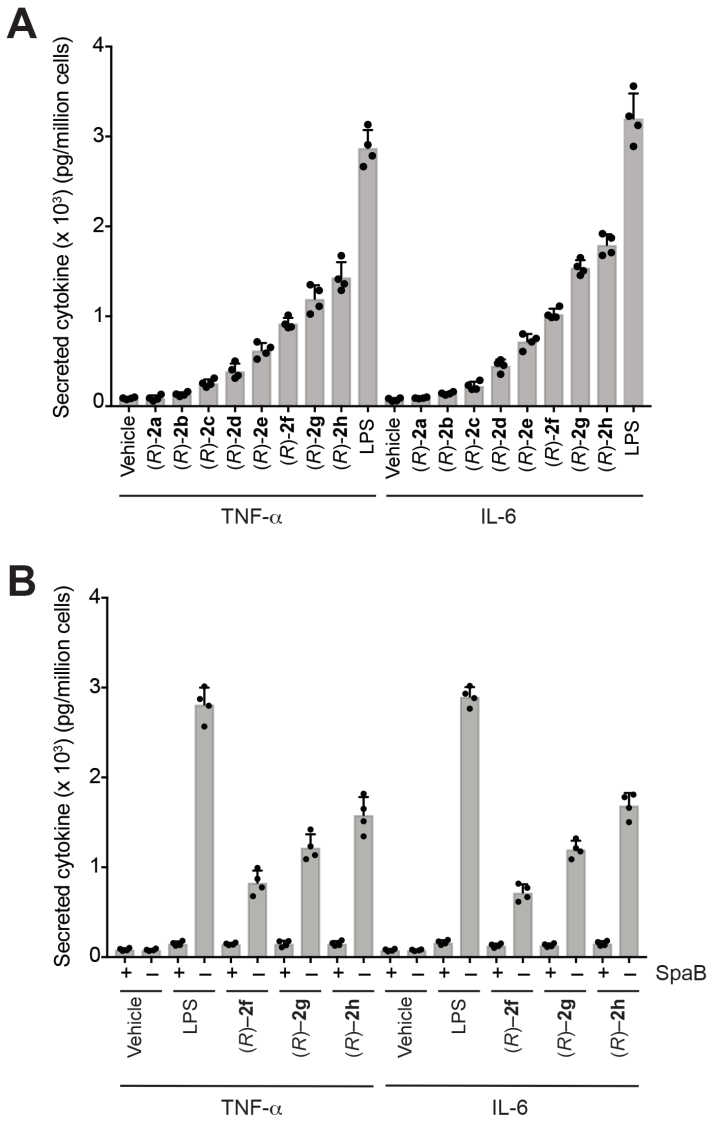


Figure S7. Pro-inflammatory cytokine secretion profile from human THP-1 macrophages. (**A**) The secretion profiles of pro-inflammatory cytokines TNF-α and IL-6 from THP-1 macrophages following treatment with different (*R*)-Me-lyso-PSs ((*R*)-**2a-h**) (all at 1 μM, 4 h, 37 °C). The data shows that VLC (*R*)-Me-lyso-PSs ((*R*)-**2g** and (*R*)-**2h**) produced the highest secretion of TNF-α and IL-6 from THP-1 macrophages, consistent with results seen from mouse PPM presented in **Figure 3A**. (**B**) Pharmacological antagonism of TLR2 by SpaB (10 μM, 4 h, 37 °C) (Liang et al., 2011, Liang et al., 2013) results in significantly decreased secretion of TNF-α and IL-6 from THP-1 macrophages following treatment with different VLC (*R*)-Me-lyso-PSs ((*R*)-**2f-h**) (all at 1 μM, 4 h, 37 °C), suggesting that these signal through TLR2 in THP1 macrophages (Mendoca et al., 2018, Sun et al., 2015, Cho et al., 2011). These results are similar to those observed reported for PPM in **Figures 3B** and **S5**. All the data presented in (**A**) and (**B**) represents mean ± standard deviation from four independent experiments for all experimental groups.

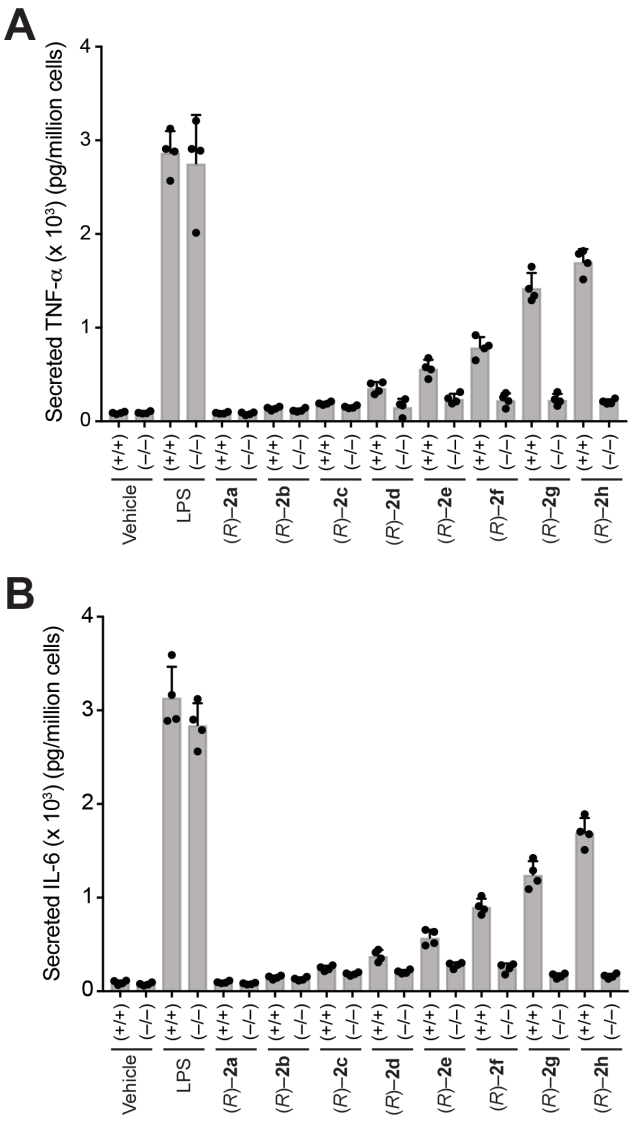


Figure S8. Pro-inflammatory cytokine secretion from PPM obtained from TLR2 knockout mice. The secretion profiles of pro-inflammatory cytokines (**A**) TNF-α and (**B**) IL-6 from PPM obtained from wild type (+/+) or TLR2 knockout (–/–) mice, following treatment with different (*R*)-Me-lyso-PSs ((*R*)-**2a-h**) or LPS (all at 1 μM, 4 h, 37 °C). The data shows that VLC (*R*)-Me-lyso-PSs ((*R*)-**2g** and (*R*)-**2h**) produced the highest secretion of both pro-inflammatory cytokines in (+/+) PPM, but not (–/–) PPM, consistent VLC lyso-PSs signalling through TLR2 in primary macrophages. This data is the full extension of the results presented in **Figure 3C**. All the data presented in (**A**) and (**B**) represents mean ± standard deviation from four independent experiments for all experimental groups.

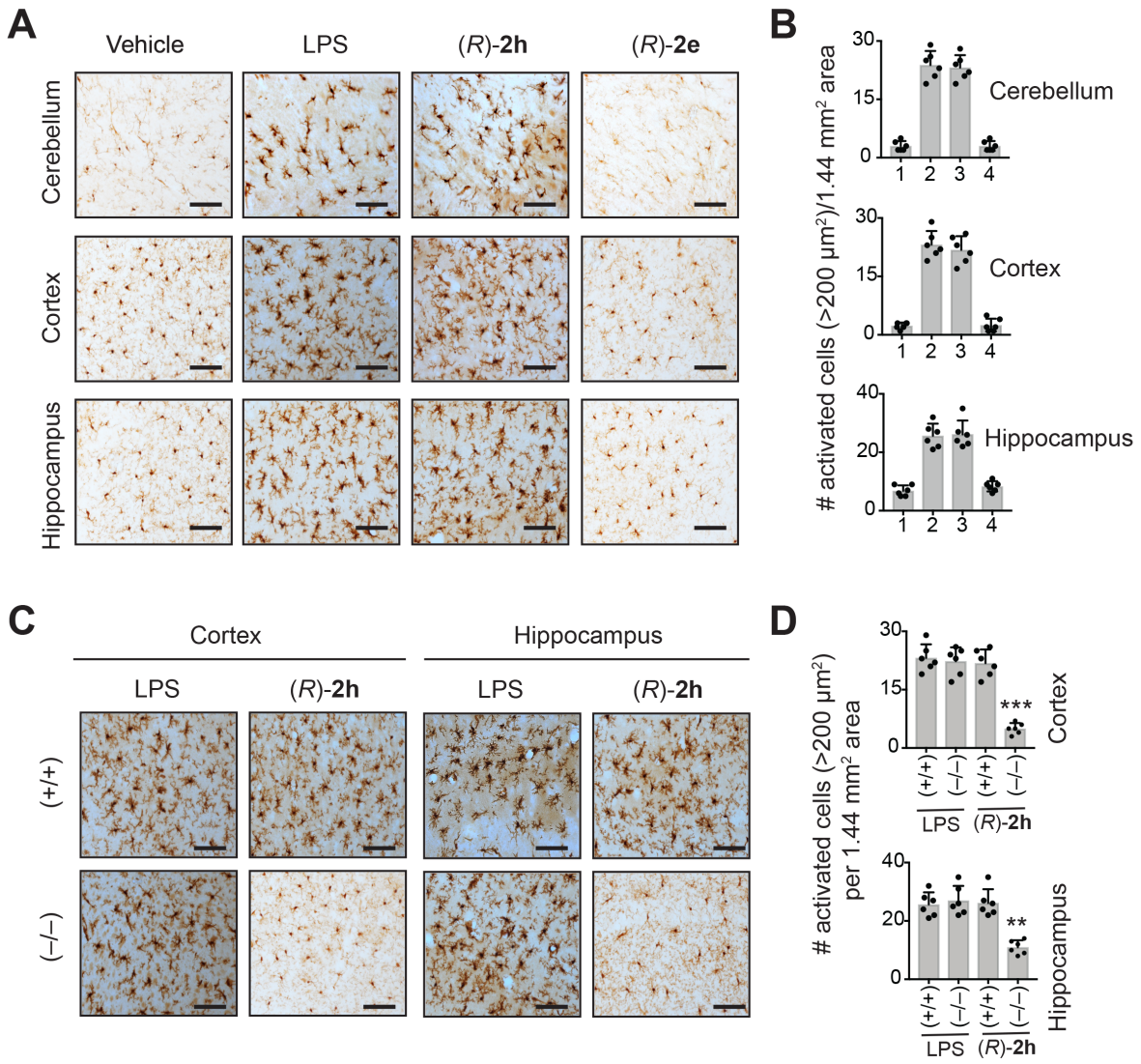


Figure S9. Analysis of activated microgliosis in the mouse brain following injection of a VLC (*R*)-Me-lyso-PS. (**A**) Representative images from Iba-1 immunostaining for microglial activation (black bar = 250 μm) and (**B**) quantification of enlarged cells (>200 μm^2) in the different brain regions (cerebellum, cortex and hippocampus) (per 1.44 mm^2) of wild type mice following intravenous injection of vehicle (PBS), LPS or (*R*)-**2h** or (*R*)-**2e** (all 1 mg/kg body weight, 10 h). The treatment groups are as follows: 1 = vehicle, 2 = LPS, 3 = (*R*)-**2h**, and 4 = (*R*)-**2e** (**C**) Representative images from Iba-1 immunostaining for microglial activation (black bar = 250 μm) and quantification of enlarged cells (>200 μm^2) in the cortex and hippocampus (per 1.44 mm^2) of wild type (+/+) or TLR2 knockout (–/–) mice following intravenous injection of LPS or (*R*)-**2h** (both at 1 mg/kg body weight, 10 h), showing diminished activated microglia in TLR2 knockout mice**.** All data in (**B**) and (**D**) is represented as mean ± standard deviation (n = 5/group). **p < 0.01, and ***p < 0.001 versus (+/+) group by Student's t-test.

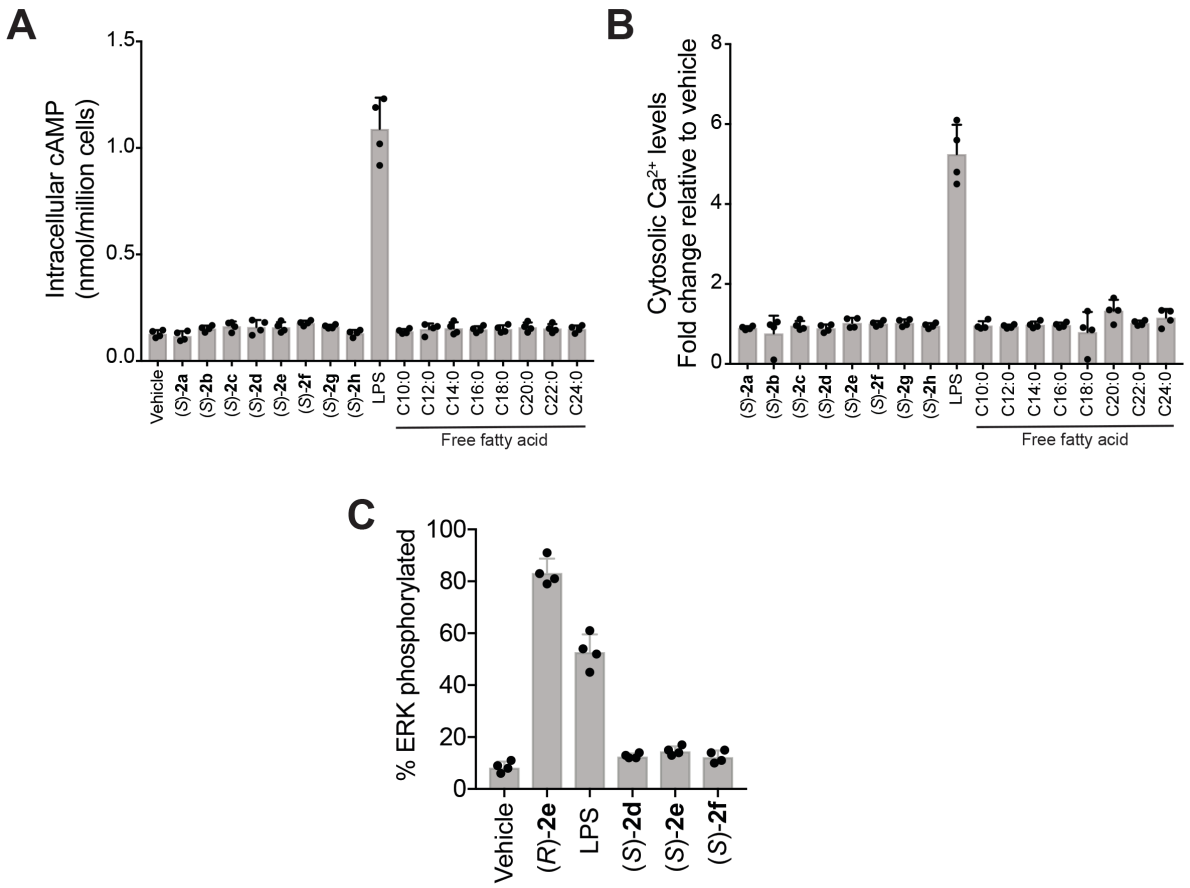


Figure S10. The intracellular cyclic AMP (cAMP), relative cytosolic Ca^{2+} concentrations and ERK phosphorylation in wild type (WT) PPM following different treatments. (**A**, **B**, **C**) Treatment of WT PPM with (*S*)-Me-lyso-PSs or free fatty acids (FFAs) (all at 1 μM, 10 mins, 37 ^{o}C) fails to produce (**A**) increased intracellular cAMP or (**B**) increased cytosolic Ca^{2+} flux or (**C**) increased ERK phosphorylation, compared to LPS (positive) control. All the data presented in (**A**), (**B**) and (**C**) represents mean ± standard deviation from four independent experiments for all experimental groups.

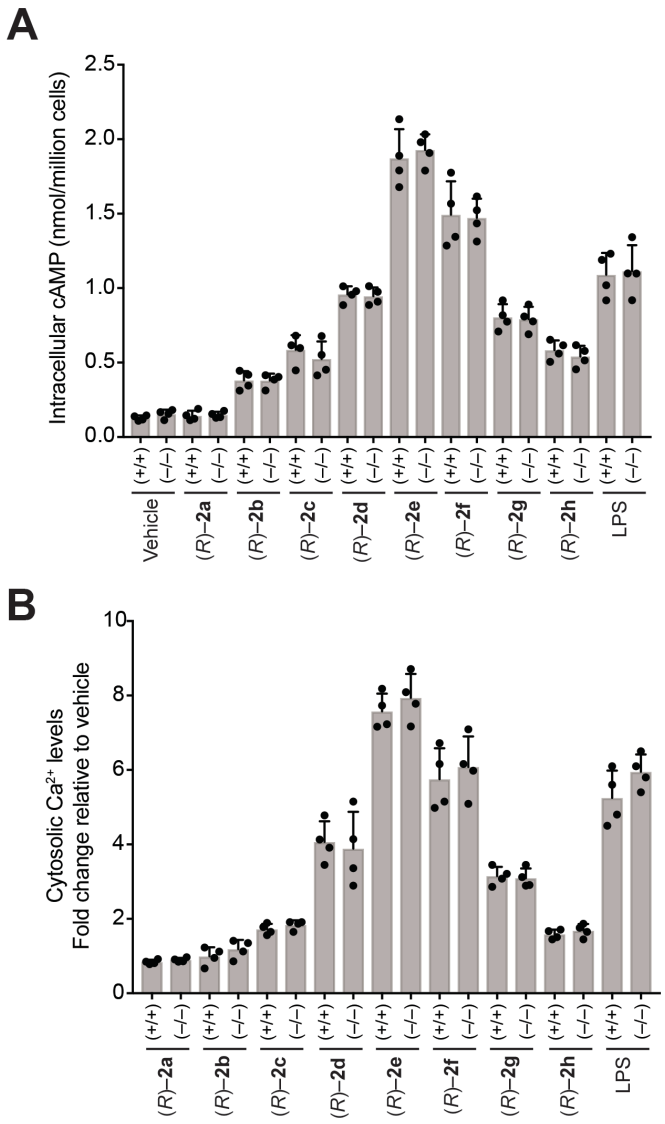


Figure S11. The intracellular cyclic AMP (cAMP) and cytosolic Ca^{2+} concentrations in PPM obtained from wild type (+/+) and TLR2 knockout (–/–) mice following (*R*)-Me-lyso-PS treatments. The concentrations of (**A**) intracellular cAMP and (**B**) cytosolic Ca^{2+} from PPM obtained from (+/+) or (–/–) mice, following treatment with different (*R*)-Me-lyso-PSs ((*R*)-**2a-h**) (all at 1 μM, 10 mins, 37 ^{o}C). The data shows in agreement with results in **Figures 4A** and **4B**, that long chain (*R*)-Me-lyso-PSs ((*R*)-**2e** and (*R*)-**2d**) produced the highest increase for both phenotypes in (+/+) and (–/–) PPM. This data suggests that there exists a TLR2 independent signalling pathway that prefers long chain lyso-PS lipids as ligands in PPM. All the data presented in (**A**) and (**B**) represents mean ± standard deviation from four independent experiments for all experimental groups.

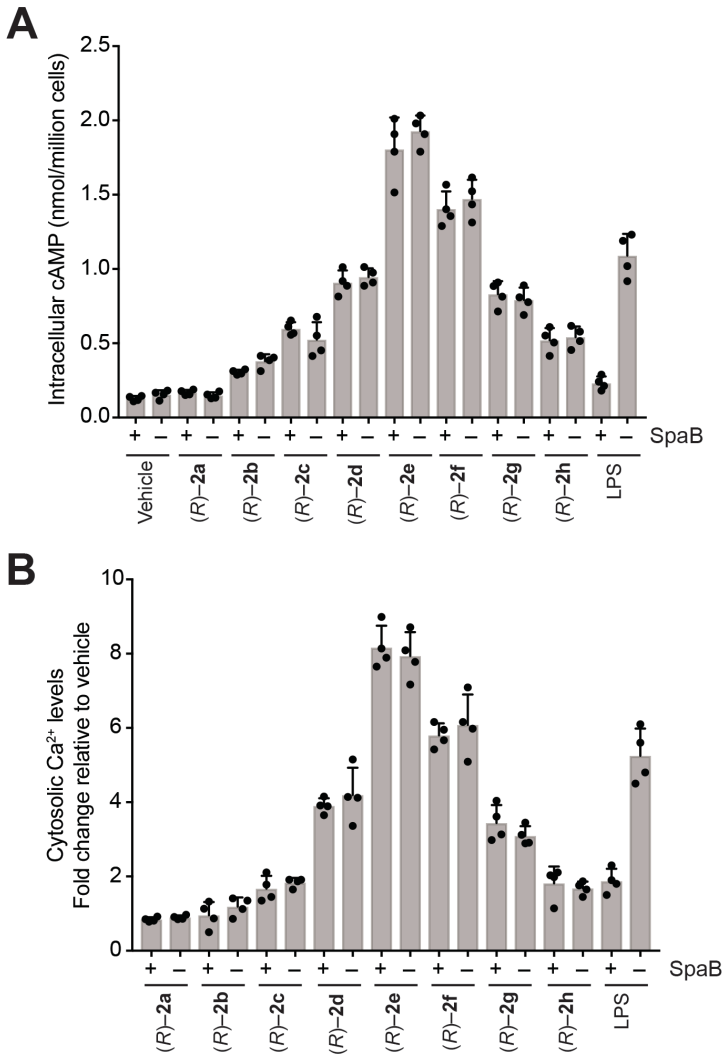


Figure S12. The intracellular cyclic AMP (cAMP) and cytosolic Ca^{2+} levels in SpaB treated PPM following (*R*)-Me-lyso-PS treatments. The concentrations of (**A**) intracellular cAMP and (**B**) cytosolic Ca^{2+} from SpaB treated (10 μM, 4 h, 37 ^{o}C) wild type PPM, following treatment with different (*R*)-Me-lyso-PSs ((*R*)-**9a-h**) (all at 1 μM, 10 mins, 37 ^{o}C). The data shows in agreement with results in **Figures 4A** and **4B**, that long chain (*R*)-Me-lyso-PSs ((*R*)-**2e** and (*R*)-**2d**) produced the highest increase for both phenotypes. This data suggests that the pharmacological antagonism of TLR2 by SpaB has no effect on either phenotype and like the data presented in **Figure S11**, there must exist a TLR2 independent signalling pathway that prefers long chain lyso-PS lipids as ligands in PPM. All the data presented in (**A**) and (**B**) represents mean ± standard deviation from four independent experiments for all experimental groups.

Note: since SpaB is a dual TLR2-TLR4 antagonist, we see a decrease in the LPS (positive control) treated groups for both phenotypes.

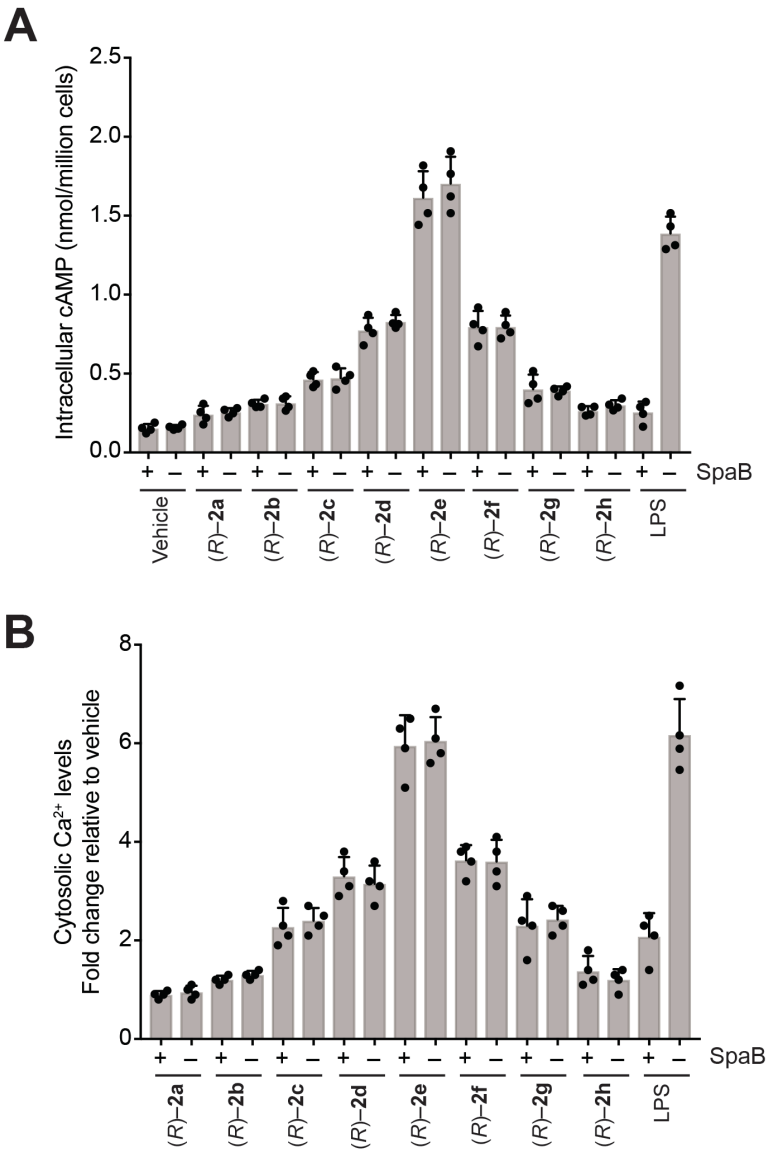


Figure S13. The intracellular cyclic AMP (cAMP) and cytosolic Ca^{2+} levels in SpaB treated human THP-1 macrophages following (*R*)-Me-lyso-PS treatments. The concentrations of (**A**) intracellular cAMP and (**B**) cytosolic Ca^{2+} from Spa B treated (10 μM, 4 h, 37 ^{o}C) THP-1 macrophages, following treatment with different (*R*)-Me-lyso-PSs ((*R*)-**2a-h**) (all at 1 μM, 10 mins, 37 ^{o}C). The data shows in agreement with results in **Figures 4A** and **4B**, that long chain (*R*)-Me-lyso-PSs ((*R*)-**2e** and (*R*)-**2d**) produced the highest increase for both phenotypes. This data seems to suggest that the pharmacological antagonism of TLR2 by SpaB has no effect on either phenotype and that there exists a TLR2 independent signalling pathway in human macrophages as well, that prefers long chain lyso-PS lipids as ligands. All the data presented in (**A**) and (**B**) represents mean ± standard deviation for four independent experiments for all experimental groups.

Note: since SpaB is a dual TLR2-TLR4 antagonist, we see a decrease in the LPS (positive control) treated groups for both phenotypes.

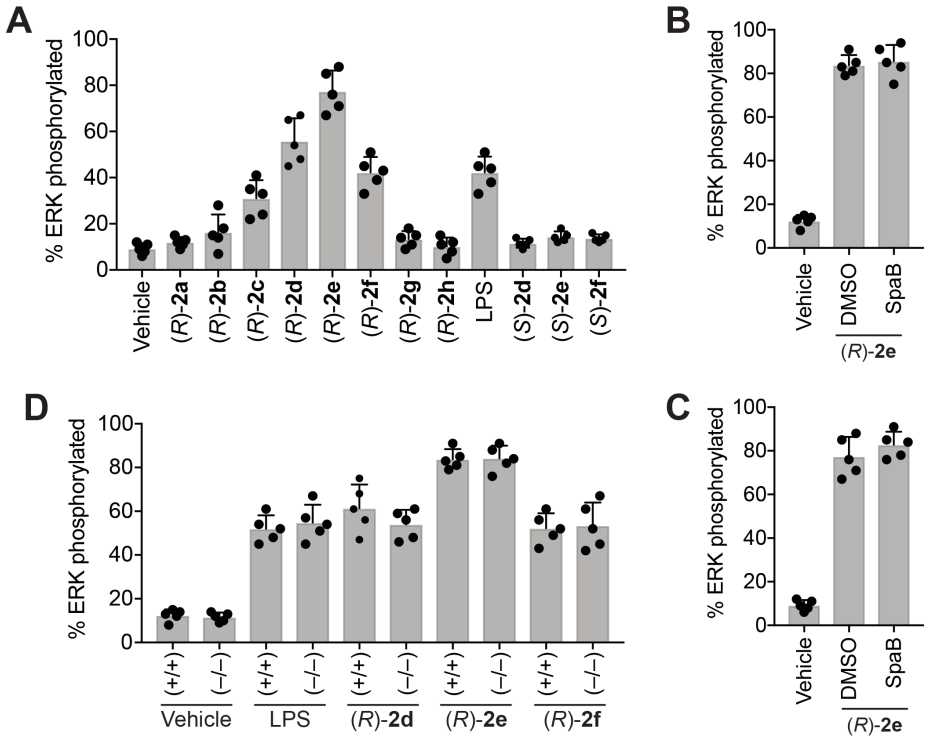


Figure S14. The ERK phosphorylation profile in mammalian macrophages following TLR2 antagonism or genetic deletion. (**A**) The percentage of ERK phosphorylated in THP-1 macrophages following treatment with vehicle (DMSO) or LPS or (*R*)-**2a-h** or (*S*)-**2d-f** (all at 1 μM, 10 mins, 37 °C). Consistent with results from **Figure 4C**, the long chain (*R*)-Me-lyso-PSs, especially (*R*)-**2e**, induces highest ERK phosphorylation in human THP-1 macrophages, while all long chain (*S*)-Me-lyso-PS fail to elicit much ERK phosphorylation. (**B**, **C**) The antagonism of TLR2 by SpaB pre-treatment (10 μM, 4 h, 37 °C) in (**B**) WT PPM or (**C**) THP-1 macrophages, followed by (*R*)-**2e** treatment (1 μM, 10 mins, 37 °C) does not change the ERK phosphorylation profile in these macrophages following (*R*)-**2e** treatment. (**D**) The percentage of ERK phosphorylated in PPM from wild type (+/+) or TLR2 (–/–) knockout mice, following treatment with vehicle (DMSO) or LPS or long chain (*R*)-Me-lyso-PSs (*R*)-**2d-f** (all at 1 μM, 10 mins, 37 °C), showing no significant changes in ERK phosphorylation following long chain (*R*)-Me-lyso-PS treatment between the two genotypes. Taken together, all the data in this figure suggests that ERK phosphorylation by lyso-PS lipids is independent of TLR2 signaling. All the data presented (**A**), (**B**), (**C**) and (**D**) represents mean ± standard deviation from five independent experiments for all experimental groups.

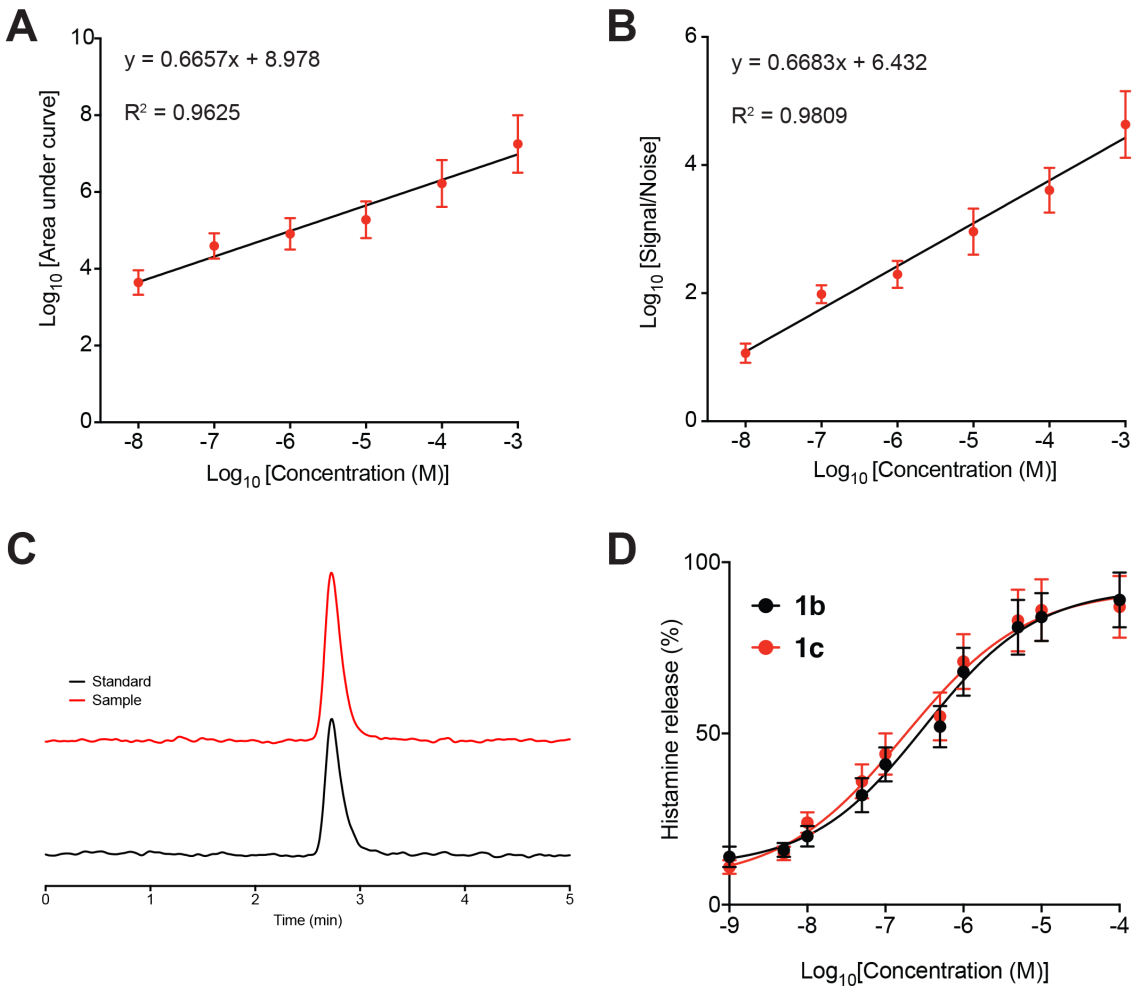


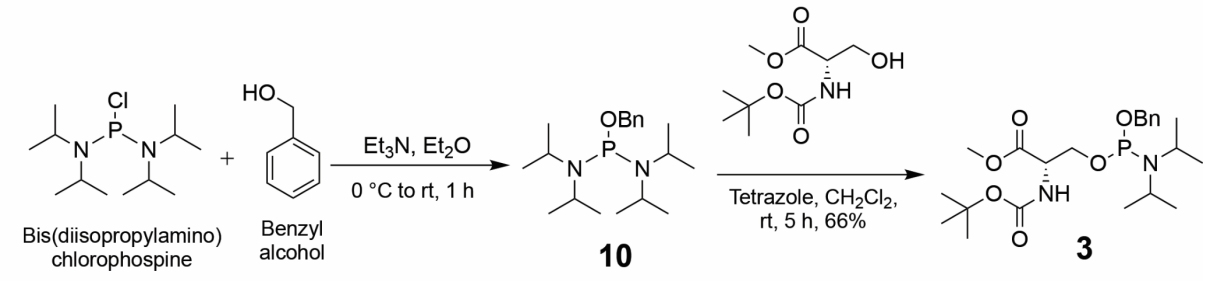
Figure S15. A LC-MS/MS method for measuring histamine release from mast cells (Chimalakonda et al., 2015). Calibration curves using histamine standard showing the linearity of the histamine measurement over 5-orders of magnitude, based on (**A**) measuring the log of area under the curve to the standard concentration; and (**B**) measuring the log of the ratio of signal to noise as a function of the standard concentration. The data in (**A**) and (**B**) represent mean ± standard deviation from four independent experiments. Based on these data, the limit of detection (LOD) and limit of quantification (LOQ) for histamine in this LC-MS assay are 1.2 nM and 7.5 nM respectively. (**C**) A representative LC-MS trace showing the co-elution of histamine standard (100 nM) (black trace) and experimental histamine extract (~ 100 nM) (red trace) in the LC-MS assay (Chimalakonda et al., 2015). (**D**) Comparing the histamine released from mast cells following treatment with authentic lyso-PSs **1b**, and **1c**, showing that increasing unsaturation does not affect the mast cell degranulation process. Each data point represents mean ± standard deviation from six independent experiments.

Chemical synthesis and compound characterization.

General synthetic procedure:

All the chemicals were purchased from Sigma-Aldrich unless otherwise mentioned and used as received. Analytical thin-layer chromatography (TLC) was performed using Silica Gel 60 F254 pre-coated plates (0.25 mm thickness, Merck), and visualized by irradiation with a UV lamp and/or staining with phosphomolybdic acid, ninhydrin or potassium permanganate ($KMnO_4$) solutions. Column chromatography was performed on Rankem silica gel (60–120 mesh) and (100-200 mesh). ^{1}H, ^{13}C, ^{31}P and DEPT-135 spectra were recorded on JEOL 400 MHz or Bruker 400 MHz (or 100 MHz for ^{13}C) NMR spectrometers. The internal standards for the recorded NMR spectra were either residual solvent signals ($CHCl_3$, δ_H = 7.26 ppm, δ_C = 77.2 ppm and CD_3OD, δ_H =3.31, δ_C = 49.0) or an internal standard tetramethylsilane (δ_H = 0.00 ppm, δ_C = 0.00 ppm). Chemical shifts (δ) are reported in p.p.m. and coupling constants (J) in Hz, multiplicities are reported by the following abbreviations: s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sext (sextet), m (multiplet), dd (doublet of doublet); broad multiplate are reported without abbreviation. High-resolution mass spectra (HRMS) were obtained from HRMS-ESI-QuadrupoleTime of Flight (QTOF) LC/MS (Sciex). Preparative High-Performance Liquid Chromatography (Prep-HPLC) was performed using a Combi flash EZ Prep UV using a Kromasil®-C-18 preparative column (250 mm × 21.2 mm, 10 µm). Analytical HPLC was performed on an Agilent Technologies 1260 infinity equipped with a UV detector (λ = 214 and 254 nm) with an Eclipse plus C-18 reversed phase column (250 mm × 4.6 mm, 5 µm).

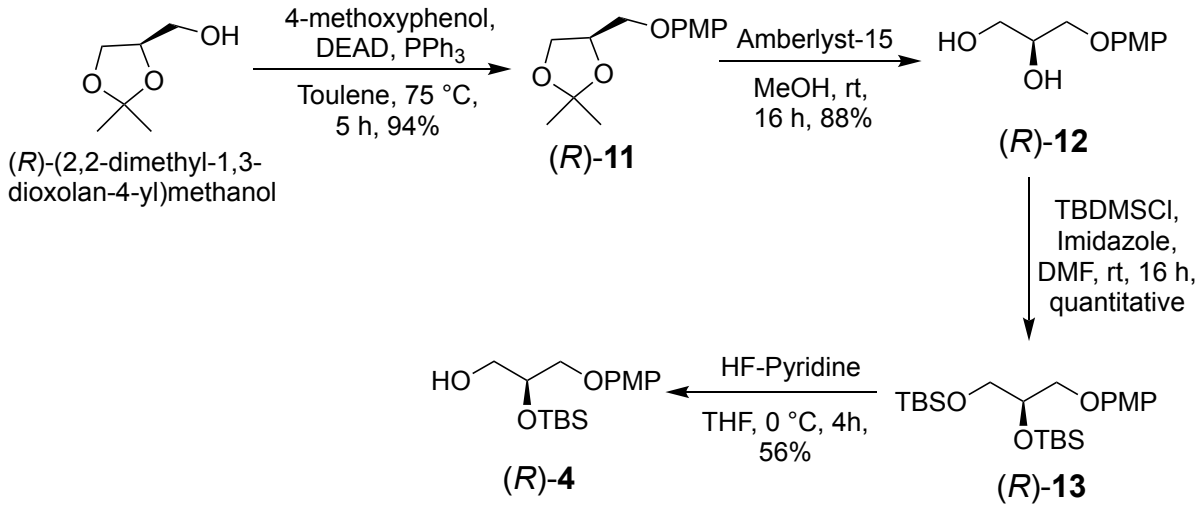
Synthesis of methyl *O*-((benzyloxy)(diisopropylamino)phosphaneyl)-*N*-(*tert*-butoxycarbonyl)-*L*-serinate (Compound **3**): The compound **10** described here was synthesized using a previously reported procedure, and the analytical data collected by us is consistent with literature reported values(Iwashita et al., 2009). The compound **3** described here was synthesized using a previously published methodology and the analytical data for compound **3** collected by us is comparable to a similar reported compound(Iwashita et al., 2009).



1-(benzyloxy)-*N,N,N',N'*-tetraisopropylphosphanediamine (Compound **10**): To a solution of bis(diisopropylamino)chlorophosphine (3.0 g, 11.2 mmol) in dry diethyl ether (Et_2O) (30 mL) in Schlenk flask, a mixture of benzyl alcohol (1.0 mL, 10.0 mmol) and triethylamine (Et_3N) (1.4 mL, 10.0 mmol) in Et_2O (5 mL) was added at 0 °C under nitrogen (N_2) atmosphere. The reaction mixture was stirred for 30 min at 0 °C, then warmed to room temperature during 30 min. The reaction mixture was diluted with cold hexane (15 mL), stirred for 10 min. The hexane solution was then transferred into another Schlenk flask by cannula and concentrated under nitrogen atmosphere to yield compound **10**. The crude product was used as such for the next step without purification: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31-7.22 (m, 5H), 4.58 (d, J = 7.3 Hz, 2H), 3.53-3.46 (m, 4H), 1.13-1.10 (m, 24H); ^{31}P NMR (400 MHz, $CDCl_3$) δ 124.21.

Compound **3**: The crude compound **10** (3.2 g, 94.5 mmol) was dissolved in anhydrous dichloromethane (CH_2Cl_2) (25 mL) in Schlenk flask and a solution of 1*H*-tetrazole (0.8 mL, 85.9 mmol) in 0.45 M acetonitrile (ACN) was added at room temperature. To this solution, *N*-Boc-*L*-Serine-methyl ester (1.8 g, 85.9 mmol) was added under N_2 atmosphere, and in a few minutes, a white solid precipitated. The mixture was stirred for 5 h at room temperature and the residual solvent was evaporated under reduced pressure. The residue was purified by neutral alumina column chromatography using 10% EtOAc in *n*-hexane to yield compound **3** (2.8 g, 61.3 mmol, 66% yield) as a colourless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.25 (m, 5H), 5.55-5.37 (m, 1H), 4.77-4.60 (m, 2H), 4.45-4.43 (m, 1H), 4.13-4.02 (m, 1H), 3.91-3.79 (m, 1H), 3.72 (2s, 3H), 3.67-3.54 (m, 2H), 1.45-1.43 (m, 9H), 1.22-1.13 (m, 12H); ^{31}P NMR (400 MHz, $CDCl_3$) δ 149.68, 149.15; ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 155.5 (2s), 139.3 (2d, $J_{c\text{-}p}$ = 8 Hz), 128.4 (d, $J_{c\text{-}p}$ = 5 Hz), 127.5 (d, $J_{c\text{-}p}$ = 7 Hz), 127.1 (d, $J_{c\text{-}p}$ = 13 Hz), 79.9 (2s), 65.5 (dd, $J_{c\text{-}p}$ = 18, 9 Hz), 64.3 (2d, $J_{c\text{-}p}$ = 16 Hz), 54.9 (t, $J_{c\text{-}p}$ = 8 Hz), 52.5 (2s), 43.2 (d, $J_{c\text{-}p}$ = 12 Hz), 28.4, 24.7, 24.6, 24.5; DEPT-135 NMR (100 MHz, $CDCl_3$) δ 128.4 (d, $J_{c\text{-}p}$ = 4 Hz, CH), 127.4 (d, $J_{c\text{-}p}$ = 8 Hz, CH), 127.1 (d, $J_{c\text{-}p}$ =12 Hz, CH), 65.5 (dd, $J_{c\text{-}p}$ = 18, 8 Hz, CH_2), 64.2 (2d, $J_{c\text{-}p}$ = 16 Hz, CH_2), 54.9 (t, $J_{c\text{-}p}$ = 8 Hz, CH), 52.4 (2s, CH_3), 43.2 (d, $J_{c\text{-}p}$ = 12 Hz, CH), 28.4 (CH_3), 24.7 (CH_3), 24.6 (CH_3), 24.5 (CH_3); HRMS-ESI: [(M + H)$^+$-Boc] calcd for $C_{17}H_{30}N_2O_4P$, 357.1938; found, 357.1939.

Synthesis of (*S*)-2-((*tert*-butyldimethylsilyl)oxy)-3-(4-methoxyphenoxy)propan-1-ol (Compound (*R*)-**4**): The compounds (*R*)-**11**, (*R*)-**12**, (*R*)-**13** and (*R*)-**4** described in this section were synthesized using a previously reported procedure, and the analytical data collected for this compound by us is consistent with literature reported values(Iwashita et al., 2009).



(*R*)-4-((4-methoxyphenoxy)methyl)-2,2-dimethyl-1,3-dioxolane (Compound (*R*)-**11**): The commercially available (*R*)-(-)-2,2-dimethyl-1,3-dioxolane-4-methanol (5.0 g, 37.83 mmol) was dissolved in anhydrous toluene, following which triphenylphosphine (PPh_3) (11.91 g, 45.40 mmol), and *p*-methoxyphenol (14.09 g, 113.49 mmol) were added under a N_2 atmosphere. To this solution, diethyl azodicarboxylate (DEAD) (8.57 g, 49.18 mmol) in toluene (24.6 mL) was added dropwise, and the reaction mixture was stirred at 75 °C for 5 h. The mixture was concentrated under reduced pressure, and the residue was purified by silica gel (60-120 mesh) column chromatography using 10% EtOAc in *n*-hexane as an eluent to yield the desired product (*R*)-**11** (8.5 g, 35.6 mmol, 94% yield) as a colourless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.86-6.80 (m, 4H), 4.45 (quint, J = 6.0 Hz, 1H), 4.14 (tt, J = 7.4, 1.2 Hz, 1H), 4.02 (ddt, J = 9.5, 5.4, 1 Hz, 1H), 3.89-3.85 (m, 2H), 3.75 (m, 3H), 1.46 (s, 3H), 1.39 (s, 3H); HRMS-ESI: $[M + H]^+$ calcd for $C_{13}H_{19}O_4$, 239.1278; found, 239.1280.

(*S*)-3-(4-methoxyphenoxy)propane-1,2-diol (Compound (*R*)-**12**): The compound (*R*)-**11** (8.5 g, 35.6 mmol) was dissolved in anhydrous methanol (MeOH) (37 mL), and Amberlyst-15 (11.2 g, 35.6 mmol) was added at room temperature. The reaction mixture was stirred for 16 h at room temperature. After completion of the reaction, the Amberlyst-15 was filtered off and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel (60-120 mesh) column chromatography using 80% EtOAc in *n*-hexane as an eluent to give the desired product (*R*)-**12** (6.2 g, 31.3 mmol, 88% yield) as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.85-6.80 (m, 4H), 4.07 (sext, J = 4.8 Hz, 1H), 4.00-3.94 (m, 2H), 3.84-3.79 (m, 1H), 3.76 (s, 3H), 3.74-3.69 (m, 1H), 3.08 (m, 1H), 2.62 (m, 1H) ; HRMS-ESI: $[M + H]^+$ calcd for $C_{10}H_{15}O_4$, 199.0965; found, 199.0967.

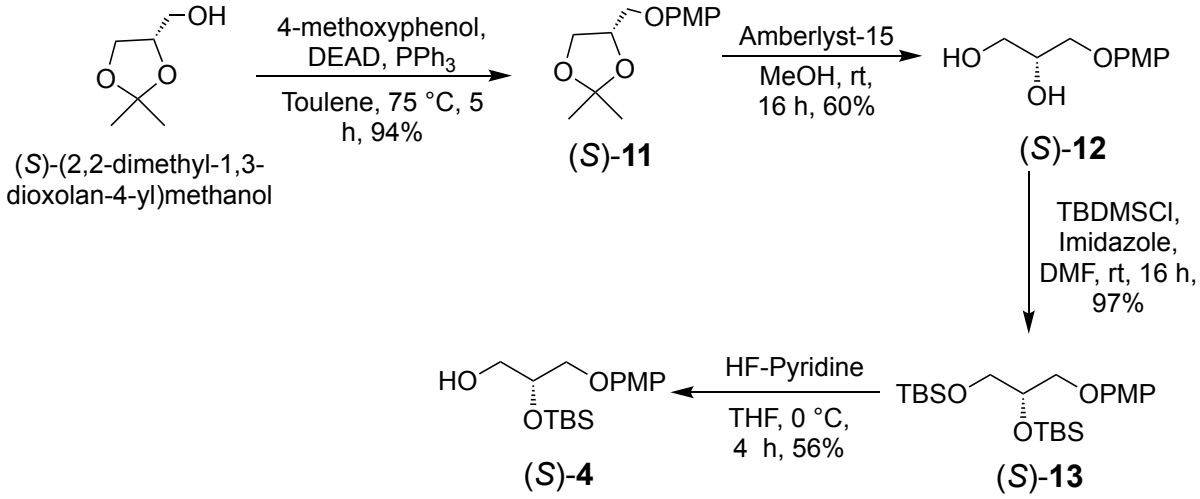
(*R*)-5-((4-methoxyphenoxy)methyl)-2,2,3,3,8,8,9,9-octamethyl-4,7-dioxa-3,8-disiladecane (Compound (*R*)-**13**): The compound (*R*)-**12** (6.2 g, 31.3 mmol) was dissolved in anhydrous dimethylformamide (DMF) (50 mL) following which imidazole (6.4 g, 94 mmol) and *tert*-butyldimethylsilyl chloride (TBDMSCl) (11.8 g, 78.2 mmol) were sequentially added at room temperature. The mixture was stirred for 16 h at room temperature after which it was diluted with water (30 mL) and Et_2O (30 mL), and the aqueous layer was separated and extracted three times with Et_2O (15 mL x 3). The combined organic layer was dried over Na_2SO_4 and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel (60-120 mesh) column chromatography using 5% Et_2O in *n*-hexane as an eluent to obtain the desired product (*R*)-**13** (13.3 g, 31.1 mmol, quantitative) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.87-6.82 (m, 4H), 4.07-4.02 (m, 2H), 3.86-3.81 (m, 1H), 3.78 (s, 3H), 3.66 (d, J = 5.5 Hz, 2H), 0.92 (s, 18H), 0.13 (2s, 6 H), 0.09 (s, 6H); HRMS-ESI: $[M + H]^+$ calcd for $C_{22}H_{43}O_4Si_2$, 427.2694; found 427.2693.

Compound (*R*)-**4**: The compound (*R*)-**13** (13.3 g, 31.1 mmol) was dissolved in dry tetrahydrofuran (THF) (70 mL), following which the HF-pyridine complex (70%w/w) (5.3 mL) and pyridine (25 mL) were sequentially added at room temperature under N_2 atmosphere. The reaction mixture was stirred for 4 h at 0°C and then diluted with water (50 mL). The desired product was extracted three times with EtOAc (50 mL x 3), and washed with brine, dried over Na_2SO_4, filtered and the filtrate was concentrated under reduced pressure. The resultant residue was purified by silica gel (60-120 mesh) column chromatography using 25% EtOAc in *n*-hexane as an eluent to yield the desired product (*R*)-**4** (5.2 g, 16.6 mmol, 56% yield) as a colourless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.83 (s, 4H), 4.11-4.07 (m, 1H), 3.95-3.86 (m, 2H), 3.77 (s, 3H), 3.75-3.65 (m, 2H), 2.00 (broad, 1H), 0.92 (s, 9H), 0.14 (s, 3H), 0.13 (s, 3H); HRMS-ESI: $[M + H]^+$ calcd for $C_{16}H_{29}O_4Si$, 313.1830; found, 313.1837.

Synthesis of (*R*)-2-((*tert*-butyldimethylsilyl)oxy)-3-(4-methoxyphenoxy)propan-1-ol (Compound (*S*)-**4**): The compounds (*S*)-**11**, (*S*)-**12**, (*S*)-**13** and (*S*)-**4** described in this section were synthesized using a previously reported procedure, and the analytical data collected for this compound by us is consistent with literature reported values(Ikubo et al., 2015).

(*S*)-4-((4-methoxyphenoxy)methyl)-2,2-dimethyl-1,3-dioxolane (Compound (*S*)-**11**): The commercially available (*S*)-(-)-2,2-dimethyl-1,3-dioxolane-4-methanol (5.0 g, 37.83 mmol) was dissolved in anhydrous toluene, following which PPh_3 (11.91 g, 45.40 mmol), and *p*-methoxyphenol (14.09 g, 113.49 mmol) were added under N_2 atmosphere. To the solution, DEAD (8.57 g, 49.18 mmol) in toluene (24.6 mL) was added dropwise, and the reaction mixture was stirred at 75 °C for 5 h. After completing the reaction, the mixture was

concentrated under reduced pressure, and the residue was purified by silica gel (60-120 mesh) column chromatography using 10% EtOAc in *n*-hexane as an eluent to provide the desired product (*S*)-**11** (8.5 g, 35.6 mmol, 94% yield) as a colourless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.86-6.80 (m, 4H), 4.45 (quint, J = 5.9 Hz, 1H), 4.15 (dd, J = 8.4, 6.4 Hz, 1H), 4.01 (dd, J = 9.4, 5.5 Hz, 1H), 3.90-3.86 (m, 2H), 3.75 (s, 3H), 1.46 (s, 3H), 1.40 (s, 3H); HRMS-ESI: $[M + H]^+$ calcd for $C_{13}H_{19}O_4$, 239.1278; found, 239.1279.



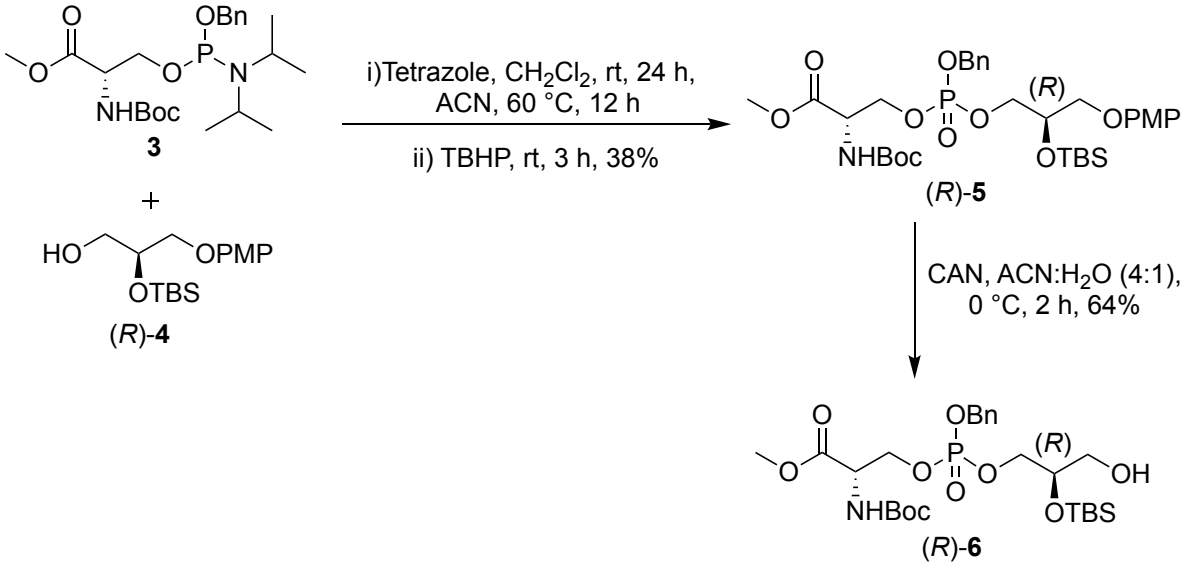
(*R*)-3-(4-methoxyphenoxy)propane-1,2-diol (Compound (*S*)-**12**): The compound (*S*)-**11** (8.4 g, 35.3 mmol) was dissolved in anhydrous MeOH (36 mL), and Amberlyst-15 (11.1 g, 35.3 mmol) was added at room temperature. The reaction mixture was stirred for 16 h at room temperature. After completion of the reaction, Amberlyst-15 was filtered off and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel (60-120 mesh) column chromatography using 80% EtOAc in *n*-hexane as an eluent to give the desired product (*S*)-**12** (4.19 g, 21.2 mmol, 60% yield) as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.87-6.82 (m, 4H), 4.09 (sext, J = 4.9 Hz, 1H), 4.03-3.97 (m, 2H), 3.86-3.81 (m, 1H), 3.77 (s, 3H), 3.76-3.72 (m, 1H), 2.65 (m, 1H), 2.08 (m, 1H); HRMS-ESI: $[M + H]^+$ calcd for $C_{10}H_{15}O_4$, 199.0965; found, 199.0966.

(*S*)-5-((4-methoxyphenoxy)methyl)-2,2,3,3,8,8,9,9-octamethyl-4,7-dioxa-3,8-disiladecane (Compound (*S*)-**13**): The compound (*S*)-**12** (4.1 g, 20.7 mmol) was dissolved in anhydrous DMF (33 mL), following which imidazole (4.23 g, 62.1 mmol) and TBDMSCl (7.8 g, 51.8 mmol) was sequentially added at room temperature. The mixture was stirred for 16 h at room temperature after which it was diluted with water (25 mL) and Et_2O (25 mL), and the aqueous layer was separated and extracted three times with Et_2O (15 mL x 3). The combined organic layer was dried over Na_2SO_4, filtered and the filtrate was concentrated

under reduced pressure. The resultant residue was purified by silica gel (60-120 mesh) column chromatography using 5% Et_2O in *n*-hexane as an eluent to obtain the desired product (*S*)-**13** (8.55 g, 20.1 mmol, 97% yield) as a colourless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.87-6.81 (m, 4H), 4.06-4.02 (m, 2H), 3.84-3.80 (m, 1H), 3.77 (s, 3H), 3.65 (d, J = 5.5 Hz, 2H), 0.91 (s, 18H), 0.12 (2s, 6H), 0.08 (s, 6H); HRMS-ESI: $[M + H]^+$ calcd for $C_{22}H_{43}O_4Si_2$, 427.2694; found 427.2692.

Compound (*S*)-**4**: The compound (*S*)-**13** (8.5 g, 19.9 mmol) was dissolved in dry THF (45 mL), following which the HF-pyridine complex (70%w/w) (3.5 mL) and pyridine (16 mL) were sequentially added at room temperature under N_2 atmosphere. The reaction mixture was stirred for 4 h at 0°C and then diluted with water (30 mL). The desired product was extracted three times with EtOAc (30 mL x 3). The combined organic layer was washed with brine, dried over Na_2SO_4, filtered and the filtrate was concentrated under reduced pressure. The resultant residue was purified by silica gel (60-120 mesh) column chromatography using 25% EtOAc in *n*-hexane as an eluent to provide the desired product (*S*)-**4** (3.32 g, 10.7 mmol, 56% yield) as a colourless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.83 (s, 4H), 4.12-4.07 (m, 1H), 3.95-3.86 (m, 2H), 3.76 (s, 3H), 3.75-3.65 (m, 2H), 1.98 (broad, 1H), 0.91 (s, 9H), 0.14 (s, 3H), 0.12 (s, 3H); HRMS-ESI: $[M + H]^+$ calcd for $C_{16}H_{29}O_4Si$, 313.1830; found, 313.1832.

Synthesis of Methyl *O*-((benzyloxy)((*R*)-2-((*tert*-butyldimethylsilyl)oxy)-3-(4-methoxyphenoxy)propoxy)phosphoryl)-*N*-(*tert*-butoxycarbonyl)-*L*-serinate (Compound (*R*)-**5**): The compound (*R*)-**5** described in this section were synthesized using a previously published methodology with minor modifications, and the analytical data for (*R*)-**5** collected by us is comparable to similar compounds reported in literature(Ikubo et al., 2015).

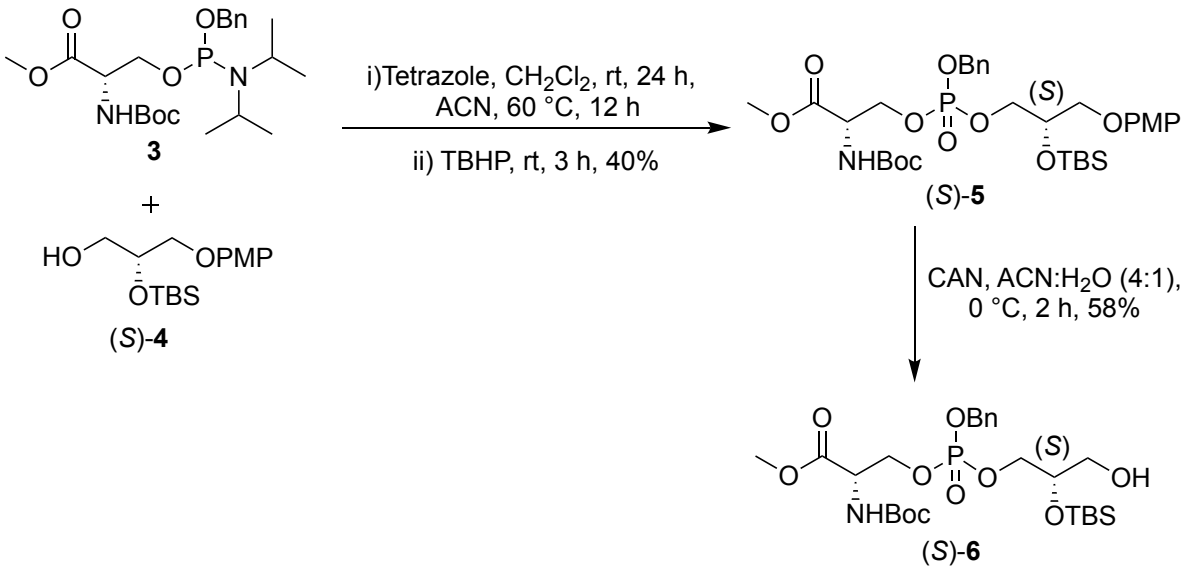


The compound **3** (2.2 g, 4.82 mmol) was dissolved in anhydrous CH_2Cl_2 (2.5 ml), and this solution was co-evaporated with ACN three times (3 x 2.5 mL). The residue was dissolved in anhydrous CH_2Cl_2 (25 mL), to which a solution of 1*H*-tetrazole in ACN (~0.45 M) (1.1 mL, 1.2 mmol) was added at room temperature. To this, compound (*R*)-**4** (3.7 g, 11.8 mmol) in CH_2Cl_2 (5 mL) was added dropwise under N_2 atmosphere, and the resulting mixture was stirred at room temperature for 24 h. To this, anhydrous ACN (30 mL) was added and the resulting mixture was heated to 60 °C for 12 h. The reaction mixture was cooled to room temperature and the intermediate formation was confirmed by TLC, following which a solution of *t*-butyl hydroperoxide (TBHP) in decane (5.0-6.0 M) (1.4 mL, 14.46 mmol) was added dropwise and the reaction mixture was stirred at room temperature for another 3 h. The reaction mixture was diluted with 15 mL water and extracted with CH_2Cl_2 (3 x 25 mL). The combined organic layer was washed with brine solution, dried over Na_2SO_4, filtered and the filtrate was concentrated under reduced pressure. The crude product was purified by flash column chromatography using 85% MeOH in H_2O as an eluent to afford compound (*R*)-**5** (1.25 g, 1.83 mmol, 38% yield) as a colourless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.29 (m, 5H), 6.85-6.77 (m, 4H), 5.58-5.51(m, 1H), 5.09-5.02 (m, 2H), 4.54-4.37 (m, 2H), 4.29-4.22 (m, 1H), 4.18-4.09 (m, 2H), 4.06-3.99 (m, 1H), 3.92-3.80 (m, 2H), 3.74 (s, 3H), 3.73-3.70 (m, 3H), 1.44 (s, 9H), 0.89 (s, 9H), 0.13-0.08 (m, 6H); ^{31}P NMR (400 MHz, $CDCl_3$) δ -0.41; ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 155.4, 154.2, 152.8, 135.7 (d, $J_{c\text{-}p}$ = 7Hz), 128.9, 128.8, 128.1 (d, $J_{c\text{-}p}$ = 4Hz), 115.6 (2s), 114.8, 80.5, 70.0 (d, $J_{c\text{-}p}$ = 7 Hz), 69.8 (t, $J_{c\text{-}p}$ = 6Hz), 69.6 (d, $J_{c\text{-}p}$ = 6 Hz), 69.0 (t, $J_{c\text{-}p}$ = 7 Hz), 67.7 (broad), 55.9, 54.1 (d, $J_{c\text{-}p}$ = 8Hz), 52.9, 28.4, 25.9, 18.3, -4.5, -4.6; DEPT-135 NMR (100 MHz, $CDCl_3$) δ 128.7 (CH), 128.6 (CH), 127.9 (d, $J_{c\text{-}p}$ = 4 Hz, CH), 115.3 (2s, CH), 114.6 (CH), 69.8 (d, $J_{c\text{-}p}$ = 9 Hz, CH), 69.6 (t, $J_{c\text{-}p}$ = 5 Hz, CH_2), 69.4 (d, $J_{c\text{-}p}$ = 5 Hz, CH_2), 68.8 (t, $J_{c\text{-}p}$ = 7 Hz, CH_2), 67.5 (broad, CH_2), 55.7 (CH_3), 53.9 (d, $J_{c\text{-}p}$ = 7 Hz, CH), 52.7 (CH_3), 28.2 (CH_3), 25.7 (CH_3), -4.8 (CH_3), -4.9 (CH_3); HRMS-ESI: [(M + H)$^+$-Boc] calcd. for $C_{27}H_{43}NO_9PSi$, 584.2439; found, 584.2441.

Synthesis of Methyl *O*-((benzyloxy)((*R*)-2-((*tert*-butyldimethylsilyl)oxy)-3-hydroxypropoxy)phosphoryl)-*N*-(*tert*-butoxycarbonyl)-*L*-serinate (Compound (*R*)-**6**): The compound (*R*)-**6** described in this section were synthesized using a previously published methodology, and the analytical data for (*R*)-**6** collected by us is comparable to similar compounds reported in literature(Ikubo et al., 2015). To a solution of (*R*)-**5** (1.2 g, 1.76 mmol) in ACN: H_2O (4:1) (10 mL), ceric ammonium nitrate (CAN) (2.41 g, 4.4 mmol) was added dropwise at 0 °C under N_2 atmosphere. The reaction mixture was stirred for 2 h at 0 °C and then diluted with water (5 mL). The whole mixture was extracted three times with EtOAc (3 x 20 mL), and the combined organic layer was washed with brine solution, dried over Na_2SO_4, filtered and the filtrate was concentrated under reduced pressure. The crude

product was purified by silica gel (100-200 mesh) column chromatography using 60% EtOAc in *n*-hexane as an eluent to afford the desired product (*R*)-**6** (0.648 g, 1.12 mmol, 64% yield) as a brown oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.29 (m, 5H), 5.64-5.45 (m, 1H), 5.06-5.00 (m, 2H), 4.50-4.32 (m, 2H), 4.26-4.16 (m, 1H), 4.03-3.89 (m, 2H), 3.86-3.79 (m, 1H), 3.70 (2s, 3H), 3.59-3.47 (m, 2H), 2.60 (broad, 1H), 1.41 (s, 9H), 0.85 (2s, 9H), 0.05 (2s, 6H); ^{31}P NMR (400 MHz, $CDCl_3$) δ -0.70, -0.85; ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 155.3 (2s), 135.5 (d, $J_{c\text{-}p}$ = 6Hz), 128.8, 128.7, 128.1, 80.4, 71.2 (d, $J_{c\text{-}p}$ = 8Hz), 69.8 (2d, $J_{c\text{-}p}$ = 5Hz), 67.9 (t, $J_{c\text{-}p}$ = 5Hz), 67.7 (2d, $J_{c\text{-}p}$ = 5Hz), 62.9, 54.0 (d, $J_{c\text{-}p}$ = 7Hz), 52.8 (2s), 28.3, 25.8, 18.1, -4.7, -4.8; DEPT-135 NMR (100 MHz, $CDCl_3$) δ 128.8 (CH), 128.7 (CH), 128.0 (CH), 71.1 (d, $J_{c\text{-}p}$ = 7Hz, CH), 69.7 (2d, $J_{c\text{-}p}$ = 6Hz, CH_2), 67.9 (t, $J_{c\text{-}p}$ = 5Hz, CH_2), 67.6 (2d, $J_{c\text{-}p}$ = 6Hz, CH_2), 62.9 (CH_2), 53.9 (d, $J_{c\text{-}p}$ = 8Hz, CH), 52.7 (2s, CH_3), 28.3 (CH_3), 25.7 (CH_3), -4.8 (CH_3), -4.9 (CH_3); HRMS-ESI: [(M + H)$^{+}$-Boc] calcd. for $C_{20}H_{37}NO_8PSi$, 478.2021; found, 478.2023.

Synthesis of Methyl *O*-((benzyloxy)((*S*)-2-((*tert*-butyldimethylsilyl)oxy)-3-(4-methoxyphenoxy)propoxy)phosphoryl)-*N*-(*tert*-butoxycarbonyl)-*L*-serinate (Compound (*S*)-**5**): The compound (*S*)-**5** described in this section were synthesized using a previously published methodology with minor modifications, and the analytical data for (*S*)-**5** collected by us is comparable to similar compounds reported in literature(Ikubo et al., 2015).



The compound **3** (1.0 g, 2.19 mmol) was dissolved in anhydrous CH_2Cl_2 (1.5 ml), and this solution was co-evaporated with ACN three times (3 x 1.5 mL). The residue was dissolved in anhydrous CH_2Cl_2 (12 mL), to which a solution of 1*H*-tetrazole in ACN (~0.45 M) (0.5 mL, 0.55 mmol) was added at room temperature. To this, compound (*S*)-**4** (1.68 g, 5.36 mmol) in CH_2Cl_2 (2.3 mL) was added dropwise under N_2 atmosphere, and the resulting mixture stirred

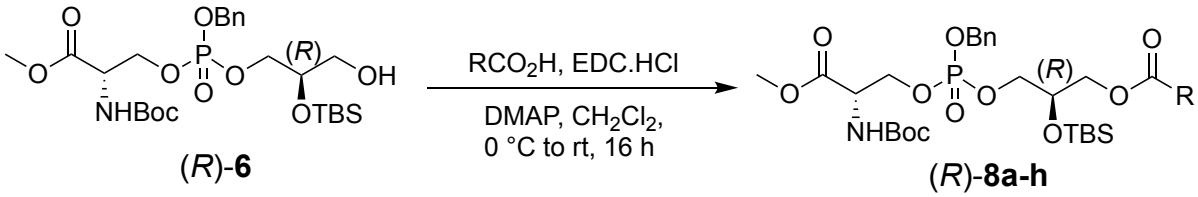
at room temperature for 24 h. To this, anhydrous ACN (14 mL) was added and the resulting reaction mixture was heated to 60 °C. The reaction mixture was stirred for 12 h at this temperature. The reaction mixture was cooled to room temperature and the intermediate formation was confirmed by TLC, following which a solution of TBHP in decane (5.0-6.0 M) (0.64 mL, 6.57 mmol) was added dropwise and the reaction mixture was stirred for another 3 h at room temperature . The reaction mixture was diluted with 7.5 mL water and extracted with CH_2Cl_2 (3 X 15 mL). The combined organic layer was washed with brine solution, dried over Na_2SO_4, filtered and the filtrate was concentrated under reduced pressure. The crude product was purified by flash column chromatography using 95% MeOH in H_2O as an eluent to afford the compound (*S*)-**5** (0.6 g, 1.46 mmol, 40%) as a colourless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.29 (m, 5H), 6.84-6.76 (m, 4H), 5.52-5.42 (m, 1H), 5.09-5.01 (m, 2H), 4.52-4.56 (m, 2H), 4.27-4.20 (m, 1H), 4.17-4.07 (m, 2H), 4.04-3.97 (m, 1H), 3.90-3.78 (m, 2H), 3.75 (s, 3H), 3.72-3.70 (m, 3H), 1.43 (s, 9H), 0.88 (2s, 9H), 0.11-0.07 (m, 6H); ^{31}P NMR (400 MHz, $CDCl_3$) δ -0.40; ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 155.3, 154.1, 152.7, 135.6 (d, $J_{c\text{-}p}$ = 6Hz), 128.8, 128.7, 128.1 (d, $J_{c\text{-}p}$ = 3Hz), 115.4, 114.7, 80.4, 69.9 (d, $J_{c\text{-}p}$ = 8 Hz), 69.7 (t, $J_{c\text{-}p}$ = 6Hz), 69.5 (broad), 68.9 (d, $J_{c\text{-}p}$ = 6Hz), 67.6 (broad), 55.8, 54.0 (d, $J_{c\text{-}p}$ = 7Hz), 52.8, 28.4, 25.8, 18.2, -4.6, -4.7; DEPT-135 NMR (100 MHz, $CDCl_3$) δ 128.8 (CH), 128.7 (CH), 128.1 (d, $J_{c\text{-}p}$ = 2 Hz, CH), 115.4 (CH), 114.7 (CH), 69.9 (d, $J_{c\text{-}p}$ = 8 Hz, CH), 69.7 (t, $J_{c\text{-}p}$ = 5 Hz, CH_2), 69.5 (broad, CH_2), 68.9 (d, $J_{c\text{-}p}$ = 6 Hz, CH_2), 67.6 (broad, CH_2), 55.8 (CH_3), 54.0 (d, $J_{c\text{-}p}$ = 7 Hz, CH), 52.8 (CH_3), 28.4 (CH_3), 25.8 (CH_3), -4.7 (CH_3), -4.8 (CH_3); HRMS-ESI: $[(M + H) – Boc]^+$ calcd for $C_{27}H_{43}NO_9PSi$, 584.2445; found, 584.2443.

Synthesis of Methyl *O*-((benzyloxy)((*S*)-2-((*tert*-butyldimethylsilyl)oxy)-3-hydroxypropoxy)phosphoryl)-*N*-(*tert*-butoxycarbonyl)-*L*-serinate (Compound (*S*)-**6**): The compound (*S*)-**6** described in this section were synthesized using a previously published methodology, and the analytical data for (*S*)-**6** collected by us is comparable to similar compounds reported in literature(Ikubo et al., 2015). To a solution of (*S*)-**5** (0.45 g, 0.658 mmol) in ACN: H_2O (4:1) (3.8 mL), CAN (0.9 g, 1.65 mmol) was added dropwise at 0 °C under N_2 atmosphere. The reaction mixture was stirred for 2 h at 0 °C and then diluted with H_2O (1.9 mL). The whole was extracted three times with EtOAc (3 x 20 mL). The combined organic layer was washed with brine solution, dried over Na_2SO_4, filtered and the filtrate was concentrated under reduced pressure. The crude product was purified by silica gel (100-200 mesh) column chromatography using 60% EtOAc in *n*-hexane as an eluent to afford the desired product (*S*)-**6** (0.220 g, 0.381 mmol, 58% yield) as a brown oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.32 (m, 5H), 5.70-5.46 (m, 1H), 5.12-5.02 (m, 2H), 4.53-4.34 (m, 2H), 4.30-4.19 (m, 1H), 4.07-3.90 (m, 2H), 3.88-3.81 (m, 1H), 3.74 (2s, 3H), 3.63-3.52 (m, 2H), 2.31 (broad, 1H), 1.44 (s, 9H), 0.88 (2s, 9H), 0.07 (2s, 6H); ^{31}P NMR (400 MHz, $CDCl_3$) δ -0.54, -

0.81; ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 155.4, 135.6 (2d, $J_{c\text{-}p}$ = 6 Hz), 128.9 (d, $J_{c\text{-}p}$ = 2 Hz), 128.8 (d, $J_{c\text{-}p}$ = 1Hz), 128.2 (d, $J_{c\text{-}p}$ = 5 Hz), 80.5, 71.1 (2d, $J_{c\text{-}p}$ = 5 Hz), 69.9 (2d, $J_{c\text{-}p}$ = 4 Hz), 67.8 (2d, $J_{c\text{-}p}$ = 6 Hz), 67.5 (2d, $J_{c\text{-}p}$ = 6Hz), 63.0, 54.0 (d, $J_{c\text{-}p}$ = 7 Hz), 52.9 (2s), 28.4, 25.8, 18.2, -4.6, -4.8; DEPT-135 NMR (100 MHz, $CDCl_3$) δ 128.8 (d, $J_{c\text{-}p}$ = 2Hz, CH), 128.7 (broad, CH), 128.1 (d, $J_{c\text{-}p}$ = 5 Hz, CH), 71.0 (2d, $J_{c\text{-}p}$ = 5 Hz, CH), 69.8 (2d, $J_{c\text{-}p}$ = 5 Hz, CH_2), 67.7 (2d, $J_{c\text{-}p}$ = 6Hz, CH_2), 67.4 (2d, $J_{c\text{-}p}$ = 5 Hz, CH_2), 62.9 (CH_2), 53.9 (d, $J_{c\text{-}p}$ = 7 Hz, CH), 52.8 (2s, CH_3), 28.3 (CH_3), 25.7 (CH_3), -4.7 (CH_3), -4.9 (CH_3); HRMS-ESI: : $[(M + H) – Boc]^+$ calcd. for $C_{20}H_{37}NO_8PSi$, 478.2021; found, 478.2023.

General procedure (A1) for the synthesis of compounds (*R*)-8a-h:

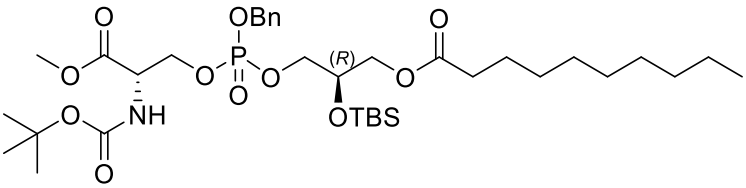
The compounds (*R*)-**8a-h** described in this section were synthesized using a previously reported methodology in literature(Ikubo et al., 2015).



(*R*)-**6** (*R*)-**8a-h**

RCO_2H	n	RCO_2H	n
7a	C10:0	**7e**	C18:0
7b	C12:0	**7f**	C20:0
7c	C14:0	**7g**	C22:0
7d	C16:0	**7h**	C24:0

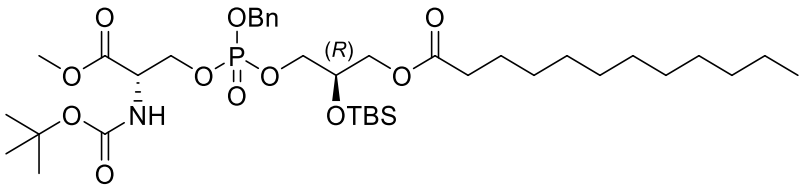
To a solution of the alcohol (*R*)-**6** (1.0 equiv) and fatty acid **7** (0.9 equiv) in anhydrous CH_2Cl_2, 4-dimethylaminopyridine (DMAP 0.25 equiv) and 1-(3-dimethylamino propyl)-3-ethylcarbodiimide hydrochloride (EDC·HCl, 0.9 equiv) were sequentially added at 0 °C. After stirring the mixture 16 h at room temperature, the reaction was quenched with saturated solution of $NaHCO_3$ and extracted three times with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered and the filtrate was concentrated under reduced pressure below 25 °C. The residue was purified by silica gel (100-200 mesh) column chromatography using 25% EtOAc in *n*-hexane as an eluent to afford the corresponding desired product (*R*)-**8.**



(2*R*)-3-(((benzyloxy)((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)phosphoryl)oxy)-2-((*tert*-butyldimethylsilyl)oxy)propyl decanoate

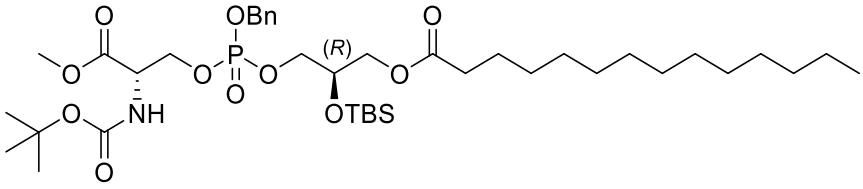
(Compound (*R*)-**8a**): Following the general procedure (**A1**), (*R*)-**6** (80 mg, 0.138 mmol), **7a**

(Decanoic acid, C10:0) (21 mg, 0.124 mmol), EDC·HCl (24 mg, 0.124 mmol), DMAP (4 mg, 0.0346 mmol) and CH_2Cl_2 (5 mL) were used. The crude mixture was purified by silica gel (100-200 mesh) column chromatography using 25% EtOAc in *n*-hexane as an eluent to provide the desired product (*R*)-**8a** (52 mg, 0.0710 mmol, 51%) as a colourless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.31 (m, 5H), 5.43 (m, 1H), 5.06 (dd, J = 8.7, 3.2 Hz, 2H), 4.54-4.34 (m, 2H), 4.29-4.20 (m, 1H), 4.15-4.06 (m, 1H), 4.04-3.86 (m, 4H), 3.74 (2s, 3H), 2.29 (td, J = 7.6, 2.2 Hz, 2H), 1.61 (quint, J = 7.0 Hz, 2H), 1.44 (s, 9H), 1.36-1.21 (m, 12H), 0.92-0.82 (m, 12H), 0.08 (2s, 6H); ^{31}P NMR (400 MHz, $CDCl_3$) δ -1.08; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.5, 169.8, 155.3, 135.8 (d, $J_{c\text{-}p}$ = 6.0 Hz), 128.9, 128.8, 128.1 (d, $J_{c\text{-}p}$ = 2 Hz), 80.5, 69.9 (2d, $J_{c\text{-}p}$ = 5 Hz), 69.3 (d, $J_{c\text{-}p}$ = 8 Hz), 68.6 (t, $J_{c\text{-}p}$ = 6Hz), 67.7 (m), 64.9, 54.2 (m), 52.8, 34.3, 32.0, 29.5, 29.4, 29.3, 28.5, 25.8, 25.0, 22.8, 18.2, 14.2, -4.6, -4.7; DEPT-135 NMR (100 MHz, $CDCl_3$) δ 128.7 (CH), 128.6 (CH), 127.9 (d, $J_{c\text{-}p}$ = 2 Hz, CH), 69.7 (2d, $J_{c\text{-}p}$ = 5 Hz, CH_2), 69.1 (d, $J_{c\text{-}p}$ = 8 Hz, CH), 68.5 (t, $J_{c\text{-}p}$ = 7 Hz, CH_2), 67.5 (m, CH_2), 64.7 (CH_2), 54.1 (m, CH), 52.6 (CH_3), 34.1 (CH_2), 31.8 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 29.1 (CH_2), 28.3 (CH_3), 25.6 (CH_3), 24.8 (CH_2), 22.6 (CH_2), 14.0 (CH_3), -4.8 (CH_3), -4.9 (CH_3); MALDI (ESI-TOF) for $C_{35}H_{62}NO_{11}PSi$ $[M+K]^+$: calcd., 770.34; found, 770.35; $[M+Na]^+$: calcd., 754.37; found, 754.38.

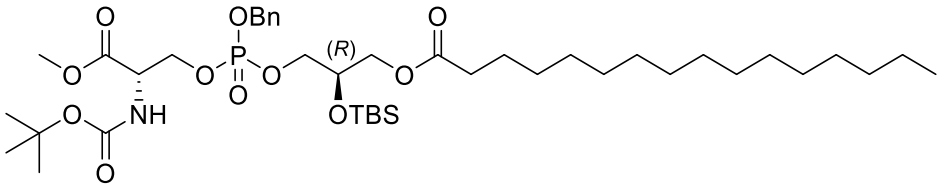


(2*R*)-3-(((benzyloxy)((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)phosphoryl)oxy)-2-((*tert*-butyldimethylsilyl)oxy)propyl dodecanoate (Compound (*R*)-**8b**): Following the general procedure (**A1**), (*R*)-**6** (70 mg, 0.121 mmol), **7b** (Dodecanoic acid, C12:0) (22 mg, 0.108 mmol), EDC·HCl (20 mg, 0.109 mmol), DMAP (3 mg, 0.0302 mmol) and CH_2Cl_2 (5 mL) were used. The crude mixture was purified by silica gel (100-200 mesh) column chromatography using 25% EtOAc in *n*-hexane as an eluent to provide the desired product (*R*)-**8b** (45 mg, 0.0592 mmol, 49%) as a colourless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.31 (m, 5H), 5.47 (dd, J = 14.4, 8.4 Hz, 1H), 5.05 (dd, J = 8.7, 3.2 Hz, 2H), 4.53-4.35 (m, 2H), 4.27-4.18 (m, 1H), 4.13-4.04 (m, 1H), 4.02-3.85 (m, 4H), 3.73 (2s, 3H), 2.29 (td, J = 7.5, 2.2 Hz, 2H), 1.60 (quint, J = 7.0 Hz, 2H), 1.44 (s, 9H), 1.33-1.20 (m, 16H), 0.90-0.82 (m, 12H), 0.07 (2s, 6H); ^{31}P NMR (400 MHz, $CDCl_3$) δ -1.09; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6, 169.8, 155.3, 136.0 (d, $J_{c\text{-}p}$ = 7 Hz), 128.9, 128.8, 128.1 (d, $J_{c\text{-}p}$ = 2 Hz), 80.5, 69.8 (t, $J_{c\text{-}p}$ = 5Hz), 69.1 (d, $J_{c\text{-}p}$ = 8 Hz), 68.5 (t, $J_{c\text{-}p}$ = 6 Hz), 67.7 (m), 64.8, 54.0 (d, $J_{c\text{-}p}$ = 8 Hz), 52.9, 34.2, 32.0, 29.7, 29.6, 29.4, 29.3, 28.4, 25.8, 25.0, 22.8, 18.1, 14.2, -

4.7, -4.8; DEPT-135 NMR (100 MHz, $CDCl_3$) δ 128.8 (CH), 128.7 (CH), 128.1 (d, $J_{c\text{-}p}$ = 2 Hz, CH), 69.7 (t, $J_{c\text{-}p}$ = 5 Hz, CH_2), 69.0 (d, $J_{c\text{-}p}$ = 8 Hz, CH), 68.4 (t, $J_{c\text{-}p}$ = 6 Hz, CH_2), 67.6 (m, CH_2), 64.7 (CH_2), 53.9 (d, $J_{c\text{-}p}$ = 7 Hz, CH), 52.7 (CH_3), 34.1 (CH_2), 31.9 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 28.3 (CH_3), 25.6 (CH_3), 24.9 (CH_2), 22.7 (CH_2), 14.1 (CH_3), -4.8 (CH_3), -4.9 (CH_3); MALDI (ESI-TOF) for $C_{37}H_{66}NO_{11}PSi$ $[M+K]^+$: calcd., 798.38, found., 798.35, $[M+Na]^+$: calcd., 782.40; found, 782.38.

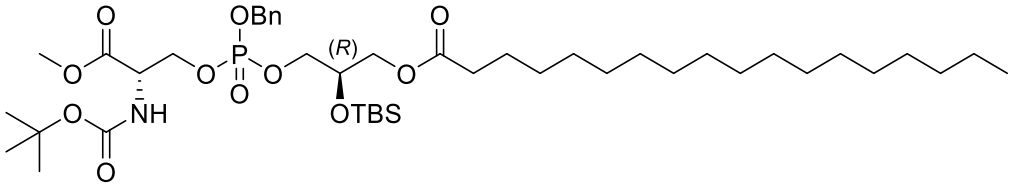


(2*R*)-3-(((benzyloxy)((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)phosphoryl)oxy)-2-((*tert*-butyldimethylsilyl)oxy)propyl tetradecanoate (Compound (*R*)-**8c**): Following the general procedure (**A1**), (*R*)-**6** (80 mg, 0.138 mmol), **7c** (Myristic acid, C14:0) (28 mg, 0.124 mmol), EDC·HCl (24 mg, 0.124 mmol), DMAP (4 mg, 0.0345 mmol) and CH_2Cl_2 (5 mL) were used. The crude mixture was purified by silica gel (100-200 mesh) column chromatography using 25% EtOAc in *n*-hexane as an eluent to provide the desired product (*R*)-**8c** (56 mg, 0.0711 mmol, 51%) as a colourless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.30 (m, 5H), 5.47 (dd, *J* = 14.2, 8.4 Hz, 1H), 5.05 (dd, *J* = 8.7, 3.2 Hz, 2H), 4.53-4.36 (m, 2H), 4.28-419 (m, 1H), 4.13-4.04 (m, 1H), 4.02-3.85 (m, 4H), 3.73 (2s, 3H), 2.29 (td, *J* = 7.5, 2.2 Hz, 2H), 1.60 (quint, *J* = 7.0 Hz, 2H), 1.44 (s, 9H), 1.33-1.20 (m, 20H), 0.90-0.83 (m, 12H), 0.07 (s, 6H); ^{31}P NMR (400 MHz, $CDCl_3$) δ -1.08; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6, 169.8, 155.3, 135.6 (d, $J_{c\text{-}p}$ = 7 Hz), 128.9, 128.8, 128.3 (d, $J_{c\text{-}p}$ = 2 Hz), 80.4, 69.8 (t, $J_{c\text{-}p}$ = 5 Hz), 69.1 (d, $J_{c\text{-}p}$ = 9 Hz), 68.5 (t, $J_{c\text{-}p}$ = 7 Hz), 67.7 (t, $J_{c\text{-}p}$ = 4 Hz), 64.8, 54.0 (d, $J_{c\text{-}p}$ = 7 Hz), 52.9, 34.2, 32.0, 29.8, 29.7, 29.6, 29.5, 29.4, 29.3, 28.4, 25.8, 25.0, 22.8, 18.1, 14.2, -4.7, -4.8; DEPT-135 NMR (100 MHz, $CDCl_3$) δ 128.8 (CH), 128.7 (CH), 128.0 (d, $J_{c\text{-}p}$ = 2 Hz, CH), 69.7 (t, $J_{c\text{-}p}$ = 5 Hz, CH_2), 69.0 (d, $J_{c\text{-}p}$ = 9 Hz, CH), 68.4 (t, $J_{c\text{-}p}$ = 7 Hz, CH_2), 67.6 (m, CH_2), 64.7 (CH_2), 53.9 (d, $J_{c\text{-}p}$ = 7 Hz, CH), 52.7 (CH_3), 34.1 (CH_2), 31.9 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 28.3 (CH_3), 25.6 (CH_3), 24.5 (CH_2), 22.3 (CH_2), 14.1 (CH_3), -4.8 (CH_3), -4.9 (CH_3); MALDI (ESI-TOF) for $C_{39}H_{70}NO_{11}PSi$ $[M+K]^+$: calcd., 826.41; found, 826.44; $[M+Na]^+$: calcd., 810.43; found, 810.44.



(2*R*)-3-(((benzyloxy)((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)phosphoryl)oxy)-2-((*tert*-butyldimethylsilyl)oxy)propyl palmitate

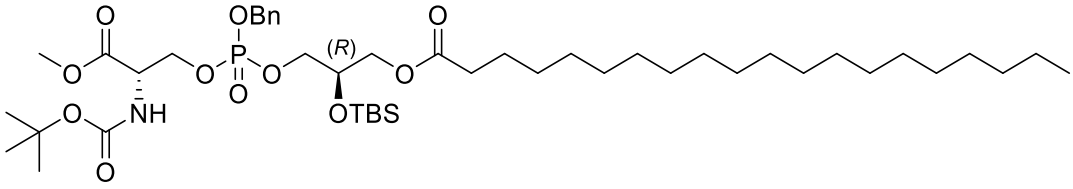
(Compound (*R*)-**8d**): Following the general procedure (**A1**), (*R*)-**6** (80 mg, 0.138 mmol), **7d** (Palmitic acid, C16:0) (32 mg, 0.124 mmol), EDC·HCl (24 mg, 0.124 mmol), DMAP (4 mg, 0.0345 mmol) and CH_2Cl_2 (5 mL) were used. The crude mixture was purified by silica gel (100-200 mesh) column chromatography using 25% EtOAc in *n*-hexane as an eluent to provide the desired product (*R*)-**8d** (61 mg, 0.0747 mmol, 54%) as a colourless oil: ^{1}H NMR (400 MHz, CDCl3) δ 7.41-7.31 (m, 5H), 5.47 (dd, J = 14.5, 8.4 Hz, 1H), 5.05 (dd, J = 8.7, 3.2 Hz, 2H), 4.53-4.36 (m, 2H), 4.27-4.19 (m, 1H), 4.13-4.04 (m, 1H), 4.02-3.84 (m ,4H), 3.73 (2s, 3H), 2.29 (td, J = 7.5, 2.6 Hz, 2H), 1.60 (quint, J = 7.0 Hz, 2H), 1.44 (s, 9H), 1.34-1.20 (m, 24H), 0.89-0.84 (m, 12H), 0.07 (2s, 6H); ^{31}P NMR (400 MHz, $CDCl_3$) δ -1.09; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4, 169.8, 155.3, 135.6 (d, $J_{c\text{-}p}$ = 5 Hz), 128.9, 128.8, 128.1 (d, $J_{c\text{-}p}$ = 3 Hz), 80.4, 69.8 (t, $J_{c\text{-}p}$ = 5 Hz), 69.1 (d, $J_{c\text{-}p}$ = 9 Hz), 68.5 (t, $J_{c\text{-}p}$ = 7 Hz), 67.7 (t, $J_{c\text{-}p}$ = 4 Hz), 64.8, 54.0 (d, $J_{c\text{-}p}$ = 7 Hz), 52.9, 34.2, 32.0, 29.8, 29.7, 29.6, 29.5, 29.4, 29.3, 28.4, 25.8, 25.0, 22.8, 18.2, 14.2, -4.7, -4.8; DEPT-135 NMR (100 MHz, $CDCl_3$) δ 128.8 (CH), 128.7 (CH), 128.1 (d, $J_{c\text{-}p}$ = 2 Hz, CH), 69.7 (t, $J_{c\text{-}p}$ = 5 Hz, CH_2), 69.0 (d, $J_{c\text{-}p}$ = 9 Hz, CH), 68.4 (t, $J_{c\text{-}p}$ = 7 Hz, CH_2), 67.6 (t, $J_{c\text{-}p}$ = 4 Hz, CH_2), 64.7 (CH_2), 53.9 (d, $J_{c\text{-}p}$ = 7 Hz, CH), 52.7 (CH_3), 34.1 (CH_2), 31.9 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 28.3 (CH_3), 25.6 (CH_3), 24.9 (CH_2), 22.7 (CH_2), 14.1 (CH_3), -4.8 (CH_3), -4.9 (CH_3); MALDI (ESI-TOF) for $C_{41}H_{74}NO_{11}PSi$ $[M+K]^+$: calcd., 854.44; found, 854.44; $[M+Na]^+$: calcd., 838.46; found, 838.47.



(2*R*)-3-(((benzyloxy)((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)phosphoryl)oxy)-2-((*tert*-butyldimethylsilyl)oxy)propyl stearate

(Compound (*R*)-**8e**): Following the general procedure (**A1**), (*R*)-**6** (70 mg, 0.121 mmol), **7e** (Stearic acid, C18:0) (31 mg, 0.109 mmol), EDC·HCl (20 mg, 0.109 mmol), DMAP (3 mg, 0.0209 mmol) and CH_2Cl_2 (4 mL) were used. The crude mixture was purified by silica gel (100-200 mesh) column chromatography using 25% EtOAc in *n*-hexane as an eluent to

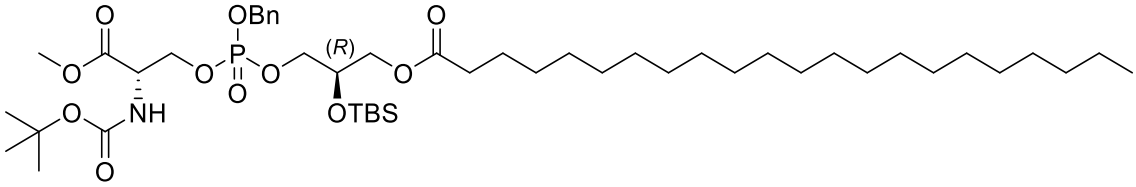
provide the desired product (*R*)-**8e** (54 mg, 0.0640 mmol, 53%) as a colourless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.31 (m, 5H), 5.47 (dd, J = 14.2, 8.5 Hz, 1H), 5.06 (dd, J = 8.7, 3.2 Hz, 2H), 4.53-4.36 (m, 2H), 4.27-4.19 (m, 1H), 4.13-4.04 (m, 1H), 4.03-3.85 (m, 4H), 3.73 (2s, 3H), 2.29 (td, J = 7.5, 2.4 Hz, 2H), 1.60 (quint, J = 7.0 Hz, 2H), 1.44 (s, 9H), 1.33-1.20 (m, 28H), 0.89-0.84 (m, 12H), 0.07 (2s, 6H); ^{31}P NMR (400 MHz, $CDCl_3$) δ -1.08; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6, 169.8, 155.3, 135.6 (d, J = 5 Hz), 128.9, 128.8, 128.1 (d, $J_{c\text{-}p}$ = 2 Hz), 80.5, 69.8 (t, $J_{c\text{-}p}$ = 5 Hz), 69.1 (d, $J_{c\text{-}p}$ = 8 Hz), 68.5 (t, $J_{c\text{-}p}$ = 7 Hz), 67.7 (t, $J_{c\text{-}p}$ = 4 Hz), 64.8, 54.0 (d, $J_{c\text{-}p}$ = 7 Hz), 52.9, 34.3, 32.1, 29.8, 29.7, 29.6, 29.5, 29.4, 29.3, 28.4, 25.8, 25.0, 22.8, 18.2, 14.2, -4.7, -4.8; DEPT-135 NMR (100 MHz, $CDCl_3$) δ 128.8 (CH), 128.7 (CH), 128.1 (d, $J_{c\text{-}p}$ = 2 Hz, CH), 69.7 (t, $J_{c\text{-}p}$ = 5 Hz, CH_2), 69.0 (d, $J_{c\text{-}p}$ = 8 Hz, CH), 68.4 (t, $J_{c\text{-}p}$ = 7 Hz, CH_2), 67.6 (t, $J_{c\text{-}p}$ = 4 Hz, CH_2), 64.7 (CH_2), 53.9 (d, $J_{c\text{-}p}$ = 7 Hz, CH), 52.7 (CH_3), 34.1 (CH_2), 31.9 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 28.3 (CH_3), 25.6 (CH_3), 24.9 (CH_2), 22.7 (CH_2), 14.1 (CH_3), -4.8 (CH_3), -4.9 (CH_3); MALDI (ESI-TOF) for $C_{43}H_{78}NO_{11}PSi$ $[M+K]^+$: calcd., 882.47; found, 882.47; $[M+Na]^+$: calcd., 866.49; found, 866.50.



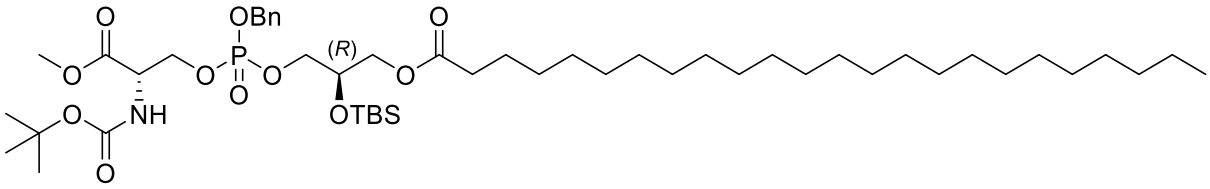
(2*R*)-3-(((benzyloxy)((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)phosphoryl)oxy)-2-((*tert*-butyldimethylsilyl)oxy)propyl icosanoate

(Compound (*R*)-**8f**): Following the general procedure (**A1**), (*R*)-**6** (90 mg, 0.155 mmol), **7f** (Arachidic acid, C20:0) (43 mg, 0.140 mmol), EDC·HCl (27 mg, 0.140 mmol), DMAP (5 mg, 0.0388 mmol) and CH_2Cl_2 (5.5 mL) were used. The crude mixture was purified by silica gel (100-200 mesh) column chromatography using 25% EtOAc in n-hexane as an eluent to provide the desired product (*R*)-**8f** (67 mg, 0.0768 mmol, 50% yield) as a colourless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.30 (m, 5H), 5.47 (dd, J = 14.4, 8.4 Hz, 1H), 5.05 (dd, J = 8.7, 3.2 Hz, 2H), 4.54-4.35 (m, 2H), 4.27-4.19 (m, 1H), 4.13-4.04 (m, 1H), 4.02-3.85 (m, 4H), 3.73 (2s, 3H), 2.29 (td, J = 7.5, 2.4 Hz, 2H), 1.60 (quint, J = 7.0 Hz, 2H), 1.44 (s, 9H), 1.33-1.20 (m, 32H), 0.90-0.84 (m, 12H), 0.07 (2s, 6H); ^{31}P NMR (400 MHz, $CDCl_3$) δ -1.09; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6, 169.8, 155.3, 135.6 (d, $J_{c\text{-}p}$ = 7 Hz), 128.9, 128.8, 128.1 (d, $J_{c\text{-}p}$ = 2Hz), 80.4, 69.8 (t, $J_{c\text{-}p}$ = 5 Hz), 69.1 (d, $J_{c\text{-}p}$ = 9 Hz), 68.5 (t, $J_{c\text{-}p}$ = 7Hz), 67.7 (t, $J_{c\text{-}p}$ = 5 Hz), 64.8, 54.1 (d, $J_{c\text{-}p}$ = 7 Hz), 52.9, 34.3, 32.1, 29.8, 29.7, 29.6, 29.5, 29.4, 29.3, 28.4, 25.8, 25.0, 22.8, 18.2, 14.2, -4.7, -4.8; DEPT-135 NMR (100 MHz, $CDCl_3$) δ 128.8 (CH), 128.7 (CH), 128.1 (d, $J_{c\text{-}p}$ = 2Hz, CH), 69.7 (t, $J_{c\text{-}p}$ = 5 Hz, CH_2), 69.0 (d, $J_{c\text{-}p}$ = 8 Hz, CH), 68.4 (t, $J_{c\text{-}$

$_p$ = 7 Hz, CH_2), 67.6 (t, $J_{c\text{-}p}$ = 4 Hz, CH_2), 64.7 (CH_2), 53.9 (d, $J_{c\text{-}p}$ = 7 Hz, CH), 52.7 (CH_3), 34.1 (CH_2), 31.9 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 28.3 (CH_3), 25.6 (CH_3), 24.9 (CH_2), 22.7 (CH_2), 14.1 (CH_3), -4.8 (CH_3), -4.9 (CH_3); MALDI (ESI-TOF) for $C_{45}H_{82}NO_{11}PSi$ $[M+K]^+$: calcd., 910.50; found, 910.49; $[M+Na]^+$: calcd., 894.52; found, 894.52.



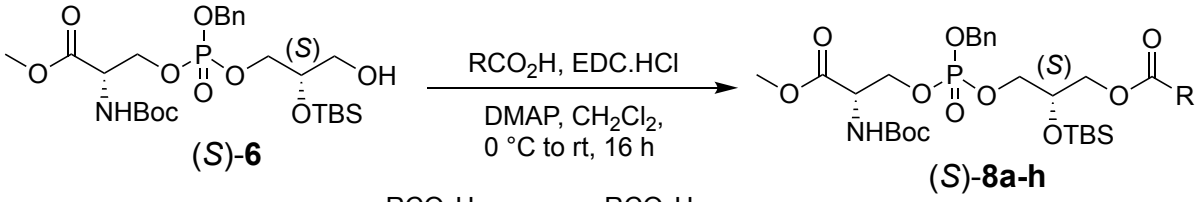
(2*R*)-3-(((benzyloxy)((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)phosphoryl)oxy)-2-((*tert*-butyldimethylsilyl)oxy)propyl docosanoate (Compound (*R*)-**8g**): Following the general procedure (**A1**), (*R*)-**6** (80 mg, 0.139 mmol), **7g** (Behenic acid, C22:0) (38 mg, 0.125 mmol), EDC·HCl (24 mg, 0.125 mmol), DMAP (4 mg, 0.0348 mmol) and CH_2Cl_2 (5 mL) were used. The crude mixture was purified by silica gel (100-200 mesh) column chromatography using 25% EtOAc in *n*-hexane as an eluent to provide the desired product (*R*)-**8g** (53 mg, 0.0589 mmol, 42% yield) as a colourless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42-7.31 (m, 5H), 5.47 (dd, J = 14.0, 8.5 Hz, 1H), 5.06 (dd, J = 8.7, 3.2 Hz, 2H), 4.53-4.36 (m, 2H), 4.28-4.19 (m, 1H), 4.14-4.04 (m, 1H), 4.03-3.85 (m, 4H), 3.73 (2s, 3H), 2.29 (td, J = 7.5, 2.5 Hz, 2H), 1.60 (quint, J = 7.0 Hz, 2H), 1.44 (s, 9H), 1.33-1.21 (m, 36H), 0.91-0.84 (m, 12H), 0.07 (2s, 6H); ^{31}P NMR (400 MHz, $CDCl_3$) δ -1.08; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6, 169.8, 155.4, 135.6 (d, $J_{c\text{-}p}$ = 6 Hz), 128.9, 128.8, 128.1 (d, J = 2 Hz), 80.5, 69.8 (t, $J_{c\text{-}p}$ = 5 Hz), 69.2 (d, $J_{c\text{-}p}$ = 8 Hz), 68.5 (t, $J_{c\text{-}p}$ = 7 Hz), 67.8 (t, $J_{c\text{-}p}$ = 4 Hz), 64.8, 54.0 (d, $J_{c\text{-}p}$ = 7 Hz), 52.9, 34.3, 32.1, 29.8, 29.6, 29.5, 29.4, 29.3, 28.4, 25.8, 25.0, 22.8, 18.2, 14.3, -4.7, -4.8; DEPT-135 NMR (100 MHz, $CDCl_3$) δ 128.8 (CH), 128.7 (CH), 128.1 (d, $J_{c\text{-}p}$ = 2 Hz, CH), 69.7 (t, $J_{c\text{-}p}$ = 5 Hz, CH_2), 69.0 (d, $J_{c\text{-}p}$ = 8 Hz, CH), 68.4 (t, $J_{c\text{-}p}$ = 7 Hz, CH_2), 67.6 (t, $J_{c\text{-}p}$ = 4 Hz, CH_2), 64.7 (CH_2), 53.9 (d, $J_{c\text{-}p}$ = 7 Hz, CH), 52.8 (CH_3), 34.1 (CH_2), 31.9 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 28.3 (CH_3), 25.6 (CH_3), 24.9 (CH_2), 22.7 (CH_2), 14.1 (CH_3), -4.8 (CH_3), -4.9 (CH_3); MALDI (ESI-TOF) for $C_{47}H_{86}NO_{11}PSi$ $[M+K]^+$: calcd., 938.53; found, 938.54; $[M+Na]^+$: calcd., 922.56; found, 922.57.



(2*R*)-3-(((benzyloxy)((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)phosphoryl)oxy)-2-((*tert*-butyldimethylsilyl)oxy)propyl tetracosanoate (Compound (*R*)-**8h**): Following the general procedure (**A1**), (*R*)-**6** (80 mg, 0.139 mmol), **7h** (Lignoceric acid, C24:0) (46 mg, 0.125 mmol), EDC·HCl (24 mg, 0.125 mmol), DMAP (4 mg, 0.0348 mmol) and CH_2Cl_2 (5 mL) were used. The crude mixture was purified by silica gel (100-200 mesh) column chromatography using 25% EtOAc in *n*-hexane as an eluent to provide the desired product (*R*)-**8h** (59 mg, 0.0589 mmol, 46% yield) as a colourless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.30 (m, 5H), 5.47 (dd, J = 14.6, 8.4 Hz, 1H), 5.06 (dd, J = 8.7, 3.2 Hz, 2H), 4.53-4.34 (m, 2H), 4.27-4.19 (m, 1H), 4.14-4.04 (m, 1H), 4.03-3.84 (m, 4H), 3.73 (2s, 3H), 2.29 (td, J = 7.5, 2.4 Hz, 2H), 1.60 (quint, J = 7.0 Hz, 2H), 1.44 (s, 9H), 1.33-1.20 (m, 40H), 0.89-0.84 (m, 12H), 0.07 (2s, 6H); ^{31}P NMR (400 MHz, $CDCl_3$) δ -1.09; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6, 169.8, 155.3, 135.6 (d, $J_{c\text{-}p}$ = 6 Hz), 128.9, 128.8, 128.1 (d, $J_{c\text{-}p}$ = 2 Hz), 80.4, 69.8 (t, $J_{c\text{-}p}$ = 5 Hz), 69.1 (d, $J_{c\text{-}p}$ = 8 Hz), 68.5 (t, $J_{c\text{-}p}$ = 7 Hz), 67.7 (t, $J_{c\text{-}p}$ = 4 Hz), 64.8, 54.1 (d, $J_{c\text{-}p}$ = 7 Hz), 52.9, 34.2, 32.0, 29.8, 29.7, 29.6, 29.5, 29.4, 29.3, 28.4, 25.8, 25.0, 22.8, 18.1, 14.2, -4.7, -4.8; DEPT-135 NMR (100 MHz, $CDCl_3$) δ 128.8 (CH), 128.7 (CH), 128.01 (d, $J_{c\text{-}p}$ = 2 Hz, CH), 69.7 (t, $J_{c\text{-}p}$ = 5 Hz, CH_2), 69.0 (d, $J_{c\text{-}p}$ = 9 Hz, CH), 68.4 (t, $J_{c\text{-}p}$ = 7 Hz, CH_2), 67.6 (t, $J_{c\text{-}p}$ = 4 Hz), 64.7 (CH_2), 53.9 (d, $J_{c\text{-}p}$ = 7 Hz, CH), 52.7 (CH_3), 34.1 (CH_2), 31.9 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 28.3 (CH_3), 25.6 (CH_3), 24.5 (CH_2), 22.7 (CH_2), 14.1 (CH_3), -4.8 (CH_3), -4.9 (CH_3); MALDI (ESI-TOF) for $C_{49}H_{90}NO_{11}PSi$ $[M+K]^+$: calcd., 966.57; found, 966.58; $[M+Na]^+$: calcd., 950.59; found, 950.61.

General procedure (A2) for the synthesis of compounds (*S*)-8a-h:

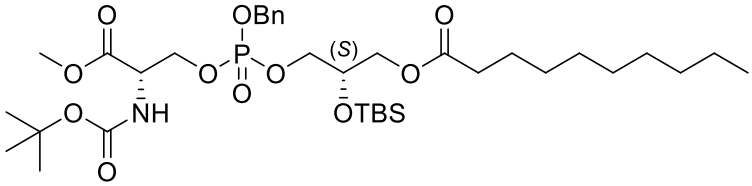
The compounds (*S*)-**8a-h** described in this section were synthesized using a previously reported methodology in literature(Ikubo et al., 2015).



(*S*)-**6** (*S*)-**8a-h**

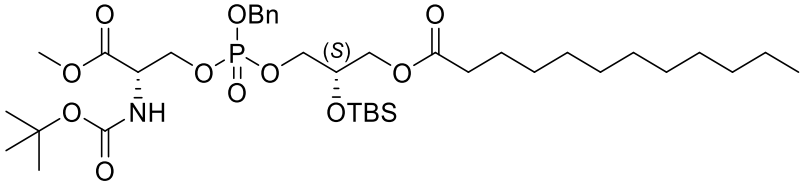
RCO_2H	n	RCO_2H	n
7a	C10:0	**7e**	C18:0
7b	C12:0	**7f**	C20:0
7c	C14:0	**7g**	C22:0
7d	C16:0	**7h**	C24:0

To a solution of the alcohol (*S*)-**6** (1.0 equiv) and fatty acid **7** (0.9 equiv) in anhydrous CH_2Cl_2, DMAP (0.25 equiv) and EDC·HCl (0.9 equiv) were sequentially added at 0 °C. After stirring the mixture 16 h at room temperature, the reaction was quenched with saturated solution of $NaHCO_3$ and extracted three times with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered and the filtrate was concentrated under reduced pressure below 25 °C. The crude mixture was purified by silica gel (100-200 mesh) column chromatography using 25% EtOAc in *n*-hexane as an eluent to afford the corresponding product (*S*)-**8.**

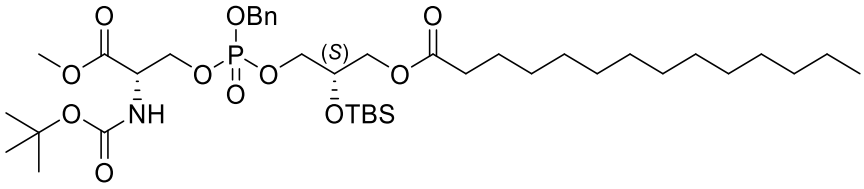


(2*S*)-3-(((benzyloxy)((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)phosphoryl)oxy)-2-((*tert*-butyldimethylsilyl)oxy)propyl decanoate (Compound (*S*)-**8a**): Following the general procedure (**A2**), (*S*)-**6** (80 mg, 0.138 mmol), **7a** (Decanoic acid, C10:0) (21 mg, 0.124 mmol), EDC·HCl (24 mg, 0.124 mmol), DMAP (4 mg, 0.0346 mmol) and CH_2Cl_2 (5 mL) were used. The crude mixture was purified by silica gel (100-200 mesh) column chromatography using 25% EtOAc in *n*-hexane as an eluent to afford the desired product (*S*)-**8a** (50 mg, 0.0683 mmol, 49%) as a colourless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.30 (m, 5H), 5.46 (t, J = 9.7 Hz, 1H), 5.05 (t, J = 8.1 Hz, 2H), 4.54-4.35 (m, 2H), 4.28-4.19 (m, 1H), 4.14-4.05 (m, 1H), 4.03-3.85 (m, 4H), 3.74 (2s, 3H), 2.29 (t, J = 7.5 Hz, 2H), 1.60 (t, J = 7.0 Hz, 2H), 1.44 (s, 9H), 1.32-1.20 (m, 12H), 0.89-0.84 (m, 12H), 0.07 (2s, 6H); ^{31}P NMR (400 MHz, $CDCl_3$) δ -1.05, -1.09; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6, 169.8, 155.3, 135.6 (d, $J_{c\text{-}p}$ = 6.0 Hz), 128.9, 128.8, 128.1 (d, $J_{c\text{-}p}$ = 2Hz),

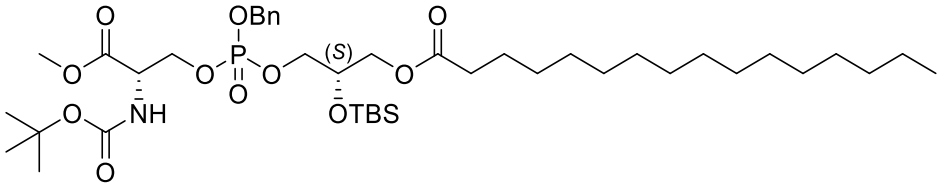
80.4, 69.8 (t, $J_{c\text{-}p}$ = 5 Hz), 69.1 (d, $J_{c\text{-}p}$ = 9 Hz), 68.5 (m), 67.7 (t, $J_{c\text{-}p}$ = 4Hz), 64.8, 54.1 (d, $J_{c\text{-}p}$ = 7 Hz), 52.9, 34.2, 32.0, 29.5, 29.4, 29.3, 28.4, 25.8, 25.0, 22.8, 18.1, 14.2, -4.7, -4.8; DEPT-135 NMR (100 MHz, $CDCl_3$) δ 128.8 (CH), 128.6 (CH), 128.1 (d, $J_{c\text{-}p}$ = 1 Hz, CH), 69.7 (t, $J_{c\text{-}p}$ = 5 Hz, CH_2), 69.0 (d, $J_{c\text{-}p}$ = 8 Hz, CH), 68.4 (m, CH_2), 67.6 (t, $J_{c\text{-}p}$ = 4 Hz, CH_2), 64.7 (CH_2), 53.9 (d, $J_{c\text{-}p}$ = 8 Hz, CH), 52.7 (CH_3), 34.1 (CH_2), 31.9 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 29.1 (CH_2), 28.3 (CH_3), 25.6 (CH_3), 24.9 (CH_2), 22.7 (CH_2), 14.1 (CH_3), -4.8 (CH_3), -4.9 (CH_3); MALDI (ESI-TOF) for $C_{35}H_{62}NO_{11}PSi$ $[M+K]^+$: calcd., 770.34; found, 770.35; $[M+Na]^+$: calcd., 754.37; found, 754.37.



(2*S*)-3-(((benzyloxy)((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)phosphoryl)oxy)-2-((*tert*-butyldimethylsilyl)oxy)propyl dodecanoate (Compound (*S*)-**8b**): Following the general procedure (**A2**), (*S*)-**6** (65 mg, 0.112 mmol), **7b** (Dodecanoic acid, C12:0) (20 mg, 0.101 mmol), EDC·HCl (19 mg, 0.101 mmol), DMAP (2.8 mg, 0.0280 mmol) and CH_2Cl_2 (4.6 mL) were used. The crude mixture was purified by silica gel (100-200 mesh) column chromatography using 25% EtOAc in *n*-hexane as an eluent to afford the desired product (*S*)-**8b** (43 mg, 0.0566 mmol, 47%) as a colourless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.31 (m, 5H), 5.47 (t, *J* = 9.7 Hz, 1H), 5.06 (t, *J* = 8.0 Hz, 2H), 4.54-4.36 (m, 2H), 4.28-4.19 (m, 1H), 4.14-4.05 (m, 1H), 4.02-3.85 (m, 4H), 3.73 (2s, 3H), 2.29 (t, *J* = 7.6 Hz, 2H), 1.60 (quint, *J* = 7.0 Hz, 2H), 1.44 (s, 9H), 1.33-1.20 (m, 16H), 0.90-0.83 (m, 12H), 0.07 (2s, 6H); ^{31}P NMR (400 MHz, $CDCl_3$) δ -1.06, -1.09; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6, 169.8, 155.3, 135.6 (d, $J_{c\text{-}p}$ = 7 Hz), 128.9, 128.8, 128.1 (d, $J_{c\text{-}p}$ = 2 Hz), 80.5, 69.8 (t, $J_{c\text{-}p}$ = 5Hz), 69.2 (d, $J_{c\text{-}p}$ = 9 Hz), 68.5 (m), 67.7 (t, $J_{c\text{-}p}$ = 4Hz), 64.8, 54.1 (d, $J_{c\text{-}p}$ = 6 Hz), 52.9, 34.3, 32.0, 29.7, 29.6, 29.5, 29.4, 29.3, 28.4, 25.8, 25.0, 22.8, 18.2, 14.2, -4.7, -4.8; DEPT-135 NMR (100 MHz, $CDCl_3$) δ 128.8 (CH), 128.7 (CH), 128.0 (d, $J_{c\text{-}p}$ = 2 Hz, CH), 69.7 (t, $J_{c\text{-}p}$ = 5 Hz, CH_2), 69.0 (d, $J_{c\text{-}p}$ = 9 Hz, CH), 68.4 (m, CH_2), 67.6 (t, $J_{c\text{-}p}$ = 4 Hz, CH_2), 64.7 (CH_2), 53.9 (d, $J_{c\text{-}p}$ = 7 Hz, CH), 52.8 (CH_3), 34.1 (CH_2), 31.9 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 28.3 (CH_3), 25.6 (CH_3), 24.9 (CH_2), 22.7 (CH_2), 14.1 (CH_3), -4.8 (CH_3), -4.9 (CH_3); MALDI (ESI-TOF) for $C_{37}H_{66}NO_{11}PSi$ $[M+K]^+$: calcd., 798.38, found., 798.35, $[M+Na]^+$: calcd., 782.40; found, 782.38.

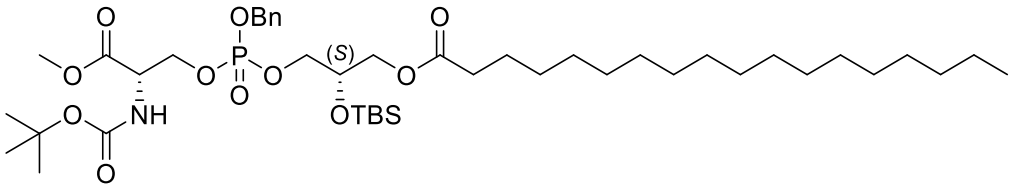


(2*S*)-3-(((benzyloxy)((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)phosphoryl)oxy)-2-((*tert*-butyldimethylsilyl)oxy)propyl tetradecanoate (Compound (*S*)-**8c**): Following the general procedure (**A2**), (*S*)-**6** (75 mg, 0.129 mmol), **7c** (Myristic acid, C14:0) (26 mg, 0.116 mmol), EDC·HCl (23 mg, 0.116 mmol), DMAP (3.8 mg, 0.0323 mmol) and CH_2Cl_2 (4.8 mL) were used. The crude mixture was purified by silica gel (100-200 mesh) column chromatography using 25% EtOAc in *n*-hexane as an eluent to afford the desired product (*S*)-**8c** (54 mg, 0.0686 mmol, 53%) as a colourless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.30 (m, 5H), 5.47 (t, J = 9.7 Hz, 1H), 5.06 (t, J = 8.0 Hz, 2H), 4.54-4.35 (m, 2H), 4.28-419 (m, 1H), 4.14-4.04 (m, 1H), 4.03-3.85 (m, 4H), 3.73 (2s, 3H), 2.29 (t, J = 7.5 Hz, 2H), 1.60 (quint, J = 7.0 Hz, 2H), 1.44 (s, 9H), 1.33-1.19 (m, 20H), 0.91-0.81 (m, 12H), 0.07 (2s, 6H); ^{31}P NMR (400 MHz, $CDCl_3$) δ -1.06, -1.09; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6, 169.8, 155.3, 135.6 (d, $J_{c\text{-}p}$ = 7 Hz), 128.9, 128.8, 128.1(broad), 80.5, 69.8 (t, $J_{c\text{-}p}$ = 5 Hz), 69.1 (d, $J_{c\text{-}p}$ = 8 Hz), 68.5 (t, $J_{c\text{-}p}$ = 7 Hz), 67.7 (t, $J_{c\text{-}p}$ = 4 Hz), 64.8, 54.1 (d, $J_{c\text{-}p}$ = 7 Hz), 52.9, 34.2, 32.0, 29.8, 29.7, 29.6, 29.5, 29.4, 29.3, 28.4, 25.8, 25.0, 22.8, 18.1, 14.2, -4.7, -4.8; DEPT-135 NMR (100 MHz, $CDCl_3$) δ 128.8 (CH), 128.7 (CH), 128.0 (broad, CH), 69.7 (t, $J_{c\text{-}p}$ = 5 Hz, CH_2), 69.0 (d, $J_{c\text{-}p}$ = 8 Hz, CH), 68.4 (m, CH_2), 67.6 (t, $J_{c\text{-}p}$ = 4 Hz, CH_2), 64.7 (CH_2), 53.9 (d, $J_{c\text{-}p}$ = 7 Hz, CH), 52.7 (CH_3), 34.1 (CH_2), 31.9 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 28.3 (CH_3), 25.6 (CH_3), 24.9 (CH_2), 22.7 (CH_2), 14.1 (CH_3), -4.8 (CH_3), -4.9 (CH_3); MALDI (ESI-TOF) for $C_{39}H_{70}NO_{11}PSi$ $[M+K]^+$: calcd., 826.41; found, 826.43; $[M+Na]^+$: calcd., 810.43; found, 810.44.



(2*S*)-3-(((benzyloxy)((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)phosphoryl)oxy)-2-((*tert*-butyldimethylsilyl)oxy)propyl palmitate (Compound (*S*)-**8d**): Following the general procedure (**A2**), (*S*)-**6** (70 mg, 0.121 mmol), **7d** (Palmitic acid, C16:0) (28 mg, 0.109 mmol), EDC·HCl (21 mg, 0.109 mmol), DMAP (3.5 mg, 0.0302 mmol) and CH_2Cl_2 (4.5 mL) were used. The crude mixture was purified by silica gel (100-200 mesh) column chromatography using 25% EtOAc in n-hexane as an eluent to afford the desired product (*S*)-**8d** (53 mg, 0.0649 mmol, 54%) as a colourless oil: ^{1}H NMR

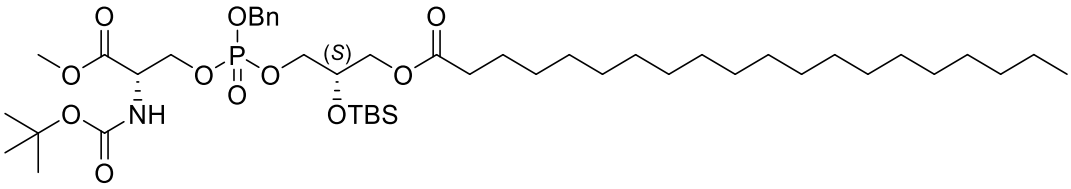
(400 MHz, CDCl3) δ 7.41-7.30 (m, 5H), 5.47 (t, J = 9.7 Hz, 1H), 5.05 (t, J = 8.1 Hz, 2H), 4.54-4.35 (m, 2H), 4.28-4.19 (m, 1H), 4.15-4.05 (m, 1H), 4.03-3.84 (m ,4H), 3.73 (2s, 3H), 2.29 (t, J = 7.5 Hz, 2H), 1.60 (quint, J = 7.0 Hz, 2H), 1.44 (s, 9H), 1.35-1.19 (m, 24H), 0.91-0.82 (m, 12H), 0.07 (2s, 6H); ^{31}P NMR (400 MHz, $CDCl_3$) δ -1.05, -1.09; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6, 169.8, 155.3, 135.6 (d, $J_{c\text{-}p}$ = 5 Hz), 128.9, 128.8, 128.1 (d, $J_{c\text{-}p}$ = 1 Hz), 80.4, 69.8 (t, $J_{c\text{-}p}$ = 5 Hz), 69.1 (d, $J_{c\text{-}p}$ = 9 Hz), 68.5 (m), 67.7 (t, $J_{c\text{-}p}$ = 4 Hz), 64.8, 54.0 (d, $J_{c\text{-}p}$ = 7 Hz), 52.8, 34.2, 32.0, 29.8, 29.7, 29.6, 29.5, 29.4, 29.3, 28.4, 25.8, 25.0, 22.8, 18.1, 14.2, -4.7, -4.8; DEPT-135 NMR (100 MHz, $CDCl_3$) δ 128.8 (CH), 128.7 (CH), 128.0 (d, $J_{c\text{-}p}$ = 2 Hz, CH), 69.7 (t, $J_{c\text{-}p}$ = 5 Hz, CH_2), 69.0 (d, $J_{c\text{-}p}$ = 8 Hz, CH), 68.4 (m, CH_2), 67.6 (t, $J_{c\text{-}p}$ = 4 Hz, CH_2), 64.7 (CH_2), 53.9 (d, $J_{c\text{-}p}$ = 7 Hz, CH), 52.7 (CH_3), 34.1 (CH_2), 31.9 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 28.3 (CH_3), 25.6 (CH_3), 24.9 (CH_2), 22.7 (CH_2), 14.1 (CH_3), -4.8 (CH_3), -4.9 (CH_3); MALDI (ESI-TOF) for $C_{41}H_{74}NO_{11}PSi$ $[M+K]^+$: calcd., 854.44; found, 854.47; $[M+Na]^+$: calcd., 838.46; found, 838.48.



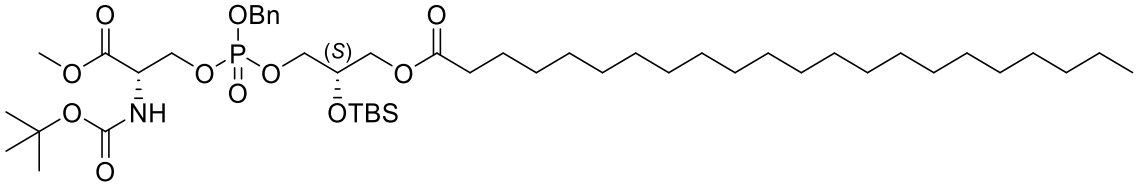
(2*S*)-3-(((benzyloxy)((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)phosphoryl)oxy)-2-((*tert*-butyldimethylsilyl)oxy)propyl stearate

(Compound (*S*)-**8e**): Following the general procedure (**A2**), (*S*)-**6** (80 mg, 0.138 mmol), **7e** (Stearic acid, C18:0) (35 mg, 0.125 mmol), EDC·HCl (23 mg, 0.125 mmol), DMAP (3.5 mg, 0.0239 mmol) and CH_2Cl_2 (4.5 mL) were used. The crude mixture was purified by silica gel (100-200 mesh) column chromatography using 25% EtOAc in *n*-hexane as an eluent to afford the desired product (*S*)-**8e** (55 mg, 0.0652 mmol, 47%) as a colourless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.31 (m, 5H), 5.47 (t, J = 9.7 Hz, 1H), 5.06 (t, J = 8.0 Hz, 2H), 4.54-4.34 (m, 2H), 4.28-4.19 (m, 1H), 4.14-4.04 (m, 1H), 4.03-3.85 (m, 4H), 3.73 (2s, 3H), 2.29 (t, J = 7.5 Hz, 2H), 1.60 (quint, J = 6.9 Hz, 2H), 1.44 (s, 9H), 1.33-1.18 (m, 28H), 0.90-0.83 (m, 12H), 0.07 (2s, 6H); ^{31}P NMR (400 MHz, $CDCl_3$) δ -1.06, -1.09; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6, 169.8, 155.3, 135.6 (d, J = 5 Hz), 128.9, 128.8, 128.1 (d, $J_{c\text{-}p}$ = 2 Hz), 80.4, 69.8 (t, $J_{c\text{-}p}$ = 5 Hz), 69.2 (d, $J_{c\text{-}p}$ = 8 Hz), 68.5 (m), 67.7 (t, $J_{c\text{-}p}$ = 4 Hz), 64.8, 54.1 (d, $J_{c\text{-}p}$ = 7 Hz), 52.9, 34.2, 32.0, 29.8, 29.7, 29.6, 29.5, 29.4, 29.3, 28.4, 25.8, 25.0, 22.8, 18.1, 14.2, -4.7, -4.8; DEPT-135 NMR (100 MHz, $CDCl_3$) δ 128.8 (CH), 128.7 (CH), 128.0 (d, $J_{c\text{-}p}$ = 1 Hz, CH), 69.7 (t, $J_{c\text{-}p}$ = 5 Hz, CH_2), 69.0 (d, $J_{c\text{-}p}$ = 9 Hz, CH), 68.4 (m, CH_2), 67.6 (t, $J_{c\text{-}p}$ = 4 Hz, CH_2), 64.7 (CH_2), 53.9 (d, $J_{c\text{-}p}$ = 7 Hz, CH), 52.7 (CH_3), 34.1 (CH_2), 31.9 (CH_2), 29.7 (CH_2),

29.6 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 28.3 (CH_3), 25.6 (CH_3), 24.9 (CH_2), 22.7 (CH_2), 14.1 (CH_3), -4.8 (CH_3), -4.9 (CH_3); MALDI (ESI-TOF) for $C_{43}H_{78}NO_{11}PSi$ $[M+K]^+$: calcd., 882.47; found, 882.48; $[M+Na]^+$: calcd., 866.49; found, 866.50.

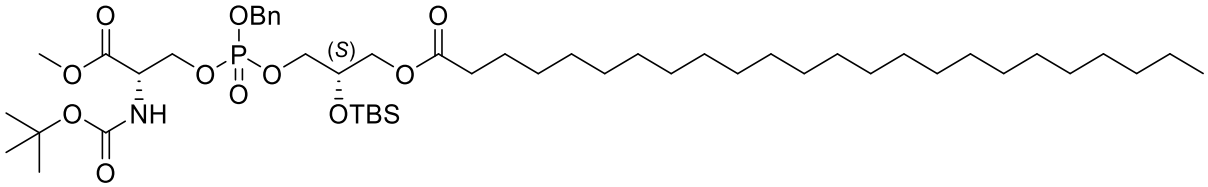


(2*S*)-3-(((benzyloxy)((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)phosphoryl)oxy)-2-((*tert*-butyldimethylsilyl)oxy)propyl icosanoate (Compound (*S*)-**8f**): Following the general procedure (**A2**), (*S*)-**6** (85 mg, 0.147 mmol), **7f** (Arachidic acid, C20:0) (41 mg, 0.132 mmol), EDC·HCl (26 mg, 0.132 mmol), DMAP (4.7 mg, 0.0366 mmol) and CH_2Cl_2 (5 mL) were used. The crude mixture was purified by silica gel (100-200 mesh) column chromatography using 25% EtOAc in n-hexane as an eluent to afford the desired product (*S*)-**8f** (62 mg, 0.0711 mmol, 48%) as a colourless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.30 (m, 5H), 5.47 (t, J = 9.8 Hz, 1H), 5.05 (t, J = 7.9 Hz, 2H), 4.54-4.35 (m, 2H), 4.28-4.19 (m, 1H), 4.13-4.05 (m, 1H), 4.02-3.85 (m, 4H), 3.73 (2s, 3H), 2.29 (t, J = 7.5, Hz, 2H), 1.60 (quint, J = 7.0 Hz, 2H), 1.44 (s, 9H), 1.31-1.21 (m, 32H), 0.90-0.84 (m, 12H), 0.07 (2s, 6H); ^{31}P NMR (400 MHz, $CDCl_3$) δ -1.06, -1.10; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6, 169.8, 155.3, 135.6 (d, $J_{c\text{-}p}$ = 5 Hz), 128.9, 128.8, 128.1 (d, $J_{c\text{-}p}$ = 1Hz), 80.5, 69.8 (t, $J_{c\text{-}p}$ = 5 Hz), 69.1 (d, $J_{c\text{-}p}$ = 8 Hz), 68.5 (m), 67.7 (t, $J_{c\text{-}p}$ = 4 Hz), 64.8, 54.0 (d, $J_{c\text{-}p}$ = 7 Hz), 52.9, 34.3, 32.1, 29.8, 29.7, 29.6, 29.5, 29.4, 29.3, 28.4, 25.8, 25.0, 22.8, 18.1, 14.2, -4.7, -4.8; DEPT-135 NMR (100 MHz, $CDCl_3$) δ 128.8 (CH), 128.7 (CH), 128.1 (d, $J_{c\text{-}p}$ = 1Hz, CH), 69.7 (t, $J_{c\text{-}p}$ = 5 Hz, CH_2), 69.0 (d, $J_{c\text{-}p}$ = 9 Hz, CH), 68.4 (m, CH_2), 67.6 (t, $J_{c\text{-}p}$ = 4 Hz, CH_2), 64.7 (CH_2), 53.9 (d, $J_{c\text{-}p}$ = 7 Hz, CH), 52.7 (CH_3), 34.1 (CH_2), 31.9 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 28.3 (CH_3), 25.6 (CH_3), 24.9 (CH_2), 22.7 (CH_2), 14.1 (CH_3), -4.8 (CH_3), -4.9 (CH_3); MALDI (ESI-TOF) for $C_{45}H_{82}NO_{11}PSi$ $[M+K]^+$: calcd., 910.50; found, 910.52; $[M+Na]^+$: calcd., 894.52; found, 894.53.



(2*S*)-3-(((benzyloxy)((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)phosphoryl)oxy)-2-((*tert*-butyldimethylsilyl)oxy)propyl docosanoate (Compound (*S*)-**8g**): Following the general procedure (**A2**), (*S*)-**6** (80 mg, 0.139 mmol), **7g**

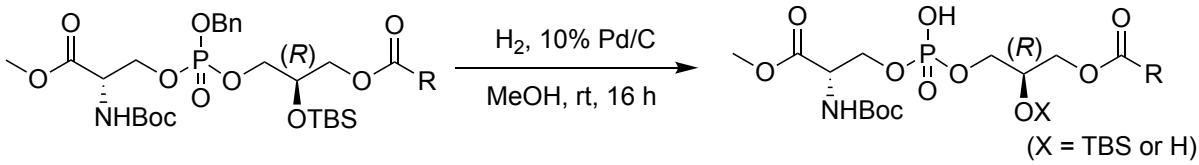
(Behenic acid, C22:0) (38 mg, 0.125 mmol), EDC·HCl (24 mg, 0.125 mmol), DMAP (4 mg, 0.0348 mmol) and CH_2Cl_2 (5 mL) were used. The crude mixture was purified by silica gel (100-200 mesh) column chromatography using 25% EtOAc in *n*-hexane as an eluent to afford the desired product (*S*)-**8g** (57 mg, 0.0633 mmol, 45% yield) as a colourless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.30 (m, 5H), 5.47 (t, J = 9.7 Hz, 1H), 5.06 (t, J = 8.0 Hz, 2H), 4.54-4.34 (m, 2H), 4.29-4.19 (m, 1H), 4.14-4.04 (m, 1H), 4.03-3.85 (m, 4H), 3.73 (2s, 3H), 2.29 (t, J = 7.5 Hz, 2H), 1.60 (quint, J = 7.0 Hz, 2H), 1.44 (s, 9H), 1.33-1.21 (m, 36H), 0.90-0.84 (m, 12H), 0.07 (2s, 6H); ^{31}P NMR (400 MHz, $CDCl_3$) δ -1.06, -1.09; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6, 169.8, 155.3, 135.6 (d, $J_{c\text{-}p}$ = 6 Hz), 128.9, 128.8, 128.1 (d, J = 2 Hz), 80.5, 69.8 (t, $J_{c\text{-}p}$ = 5 Hz), 69.2 (d, $J_{c\text{-}p}$ = 8 Hz), 68.5 (m), 67.7 (t, $J_{c\text{-}p}$ = 4 Hz), 64.8, 54.1 (d, $J_{c\text{-}p}$ = 8 Hz), 52.9, 34.3, 32.1, 29.8, 29.7, 29.6, 29.5, 29.4, 29.3, 28.4, 25.8, 25.0, 22.8, 18.2, 14.2, -4.7, -4.8; DEPT-135 NMR (100 MHz, $CDCl_3$) δ 128.8 (CH), 128.7 (CH), 128.1 (d, $J_{c\text{-}p}$ = 2 Hz, CH), 69.7 (t, $J_{c\text{-}p}$ = 5 Hz, CH_2), 69.0 (d, $J_{c\text{-}p}$ = 9 Hz, CH), 68.4 (m, CH_2), 67.6 (t, $J_{c\text{-}p}$ = 4 Hz, CH_2), 64.7 (CH_2), 53.9 (d, $J_{c\text{-}p}$ = 6 Hz, CH), 52.7 (CH_3), 34.1 (CH_2), 31.9 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 28.3 (CH_3), 25.6 (CH_3), 24.9 (CH_2), 22.7 (CH_2), 14.1 (CH_3), -4.8 (CH_3), -4.9 (CH_3); MALDI (ESI-TOF) for $C_{47}H_{86}NO_{11}PSi$ $[M+K]^+$: calcd., 938.53; found, 938.55; $[M+Na]^+$: calcd., 922.56; found, 922.58.



(2*S*)-3-(((benzyloxy)((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)phosphoryl)oxy)-2-((*tert*-butyldimethylsilyl)oxy)propyl tetracosanoate (Compound (*S*)-**8h**): Following the general procedure (**A2**), (*S*)-**6** (90 mg, 0.156 mmol), **7h** (Lignoceric acid, C24:0) (42 mg, 0.140 mmol), EDC·HCl (27 mg, 0.140 mmol), DMAP (5 mg, 0.039 mmol) and CH_2Cl_2 (5 mL) were used. The crude mixture was purified by silica gel (100-200 mesh) column chromatography using 25% EtOAc in *n*-hexane as an eluent to afford the desired product (*S*)-**8h** (68 mg, 0.0589 mmol, 47% yield) as a colourless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.30 (m, 5H), 5.47 (t, J = 9.8 Hz, 1H), 5.05 (t, J = 8.0 Hz, 2H), 4.54-4.35 (m, 2H), 4.28-4.18 (m, 1H), 4.14-4.05 (m, 1H), 4.02-3.85 (m, 4H), 3.73 (2s, 3H), 2.29 (t, J = 7.5 Hz, 2H), 1.60 (quint, J = 7.0 Hz, 2H), 1.44 (s, 9H), 1.33-1.20 (m, 40H), 0.90-0.82 (m, 12H), 0.07 (2s, 6H); ^{31}P NMR (400 MHz, $CDCl_3$) δ -1.06, -1.10; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6, 169.8, 155.3, 135.6 (d, $J_{c\text{-}p}$ = 6 Hz), 128.9, 128.8, 128.1 (d, $J_{c\text{-}p}$ = 1 Hz), 80.4, 69.8 (t, $J_{c\text{-}p}$ = 5 Hz), 69.1 (d, $J_{c\text{-}p}$ = 9 Hz), 68.5 (m), 67.7 (t, $J_{c\text{-}p}$ = 4 Hz), 64.8, 54.0 (d, $J_{c\text{-}p}$

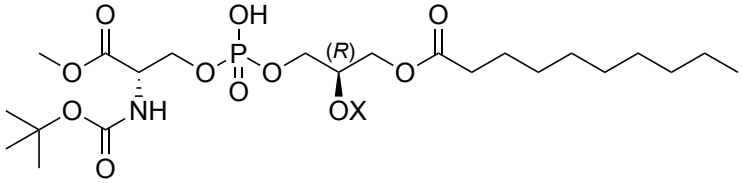
= 7 Hz), 52.8, 34.2, 32.0, 29.8, 29.7, 29.6, 29.5, 29.4, 29.3, 28.4, 25.7, 25.0, 22.8, 18.1, 14.2, -4.7, -4.8; DEPT-135 NMR (100 MHz, $CDCl_3$) δ 128.8 (CH), 128.7 (CH), 128.0 (d, $J_{c\text{-}p}$ = 1 Hz, CH), 69.7 (t, $J_{c\text{-}p}$ = 5 Hz, CH_2), 69.0 (d, $J_{c\text{-}p}$ = 8 Hz, CH), 68.4 (m, CH_2), 67.6 (t, $J_{c\text{-}p}$ = 4 Hz, CH_2), 64.7 (CH_2), 53.9 (d, $J_{c\text{-}p}$ = 7 Hz, CH), 52.7 (CH_3), 34.1 (CH_2), 31.9 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 28.3 (CH_3), 25.6 (CH_3), 24.9 (CH_2), 22.7 (CH_2), 14.1 (CH_3), -4.8 (CH_3), -4.9 (CH_3); MALDI (ESI-TOF) for $C_{49}H_{90}NO_{11}PSi$ $[M+K]^+$: calcd., 966.57; found, 966.57; $[M+Na]^+$: calcd., 950.59; found, 950.60.

General procedure (B1) for the synthesis of intermediates (*R*)-9a-h (debenzylation): The intermediates (*R*)-**9a-h** described in this section were synthesized using a previously reported methodology in literature(Ikubo et al., 2015).



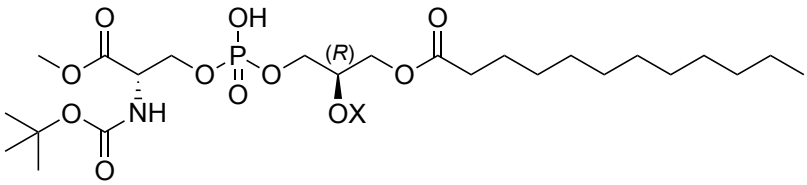
(*R*)-**8a-h** (*R*)-**9a-h**

The benzylated compound (*R*)-**8** was dissolved in dry MeOH in a two-neck round bottom flask, following which, Pd/C (10%) was added to this solution under N_2 atmosphere, and the round bottom flask was subsequently equipped with hydrogen filled rubber bladder. The reaction mixture was stirred for next 12 to 16 h at room temperature. The reaction solution was filtered through a celite pad, and washed with MeOH (3 × 10 mL). The filtrate was then concentrated under reduced pressure at 25 °C to yield (*R*)-**9** intermediates (> 95% pure, > 80% yield), which were used as such, without any further purification for the next step. The debenzylated (*R*)-**9** intermediates consisted of a mixture of two compounds where the *sn*-2 hydroxyl was either TBS protected or deprotected because of solvent methanolysis as per literature precedence(Ikawa et al., 2004). As per our reaction scheme (**Supplementary Fig. 1**), both compounds would yield the final desired products, hence we did not try to purify or isolate them separately, and proceeded with the intermediate to the next step.

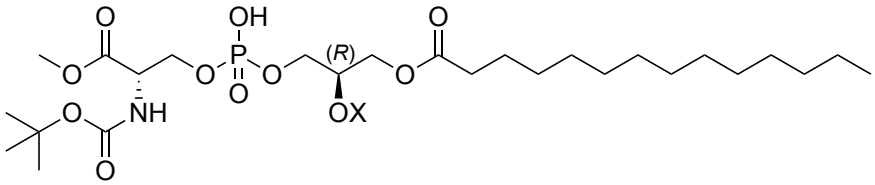


Intermediate (*R*)-**9a**: **TBS protected**: (2*R*)-3-((((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-((*tert*-butyldimethylsilyl)oxy)propyl decanoate + **TBS deprotected**: (2*R*)-3-((((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-

oxopropoxy)(hydroxy)phosphoryl)oxy)-2-hydroxypropyl decanoate: Following the general procedure (**B1**), (*R*)-**8a** (49 mg, 0.0669 mmol), Pd/C (25 mg), and MeOH (5 mL) were used. The intermediate (*R*)-**9a** (30 mg) was obtained in a ratio of 39:61 (TBS protected: TBS deprotected; based the percentage abundant is calculated based on the ^{1}H NMR integration under (-$SiMe_2$) peak from δ 0.15-0.09) as a colourless oil: ^{1}H NMR (400 MHz, MeOH-d_4) δ 4.37 (m, 1H), 4.30-4.14 (m, 2H), 4.13-3.92 (m, 3H), 3.91-3.77 (m, 2H), 3.75 (s, 3H), 2.40-2.31 (m, 2H), 1.62 (q, *J* = 7.0 Hz, 2H), 1.45 (s, 9H), 1.37-1.23 (m, 12H), 0.94-0.86 (m, 7H), 0.15-0.09 (m, 2H); ^{31}P NMR (400 MHz, MeOH-d_4) δ -0.19, -0.46.

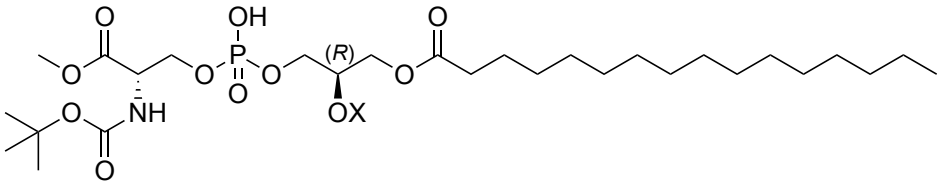


Intermediate (*R*)-**9b: TBS protected**: (2*R*)-3-((((*S*)-2-((tert-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-((*tert*-butyldimethylsilyl)oxy)propyl dodecanoate + **TBS deprotected**: (2*R*)-3-((((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-hydroxypropyl dodecanoate: Following the general procedure (**B1**), (*R*)-**8b** (45 mg, 0.0592 mmol), Pd/C (23 mg), and MeOH (4.5 mL) were used. The intermediate (*R*)-**9b** (32 mg) was obtained in a ratio of 54:46 (TBS protected: TBS deprotected; based the percentage abundant is calculated based on the ^{1}H NMR integration under (-$SiMe_2$) peak from δ 0.16-0.10) as a colourless oil: ^{1}H NMR (400 MHz, MeOH-d_4) δ 4.39-4.33 (m, 1H), 4.30-4.14 (m, 2H), 4.13-3.92 (m, 3H), 3.91-3.76 (m, 2H), 3.74 (s, 3H), 2.38-2.33 (m, 2H), 1.62 (q, *J* = 7.0 Hz, 2H), 1.45 (s, 9H), 1.36-1.23 (m, 16H); 0.94-0.86 (m, 8H), 0.16-0.10 (m, 3H); ^{31}P NMR (400 MHz, MeOH-d_4) δ 0.14, -0.22.

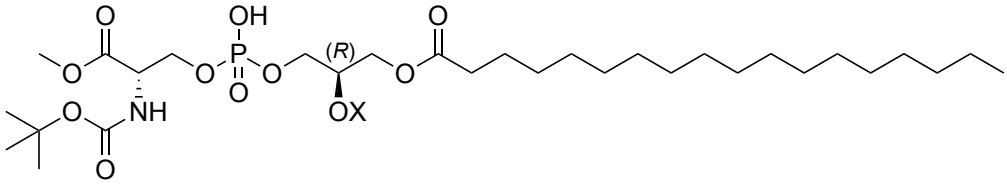


Intermediate (*R*)-**9c**: **TBS protected**: (2*R*)-3-((((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-((*tert*-butyldimethylsilyl)oxy)propyl tetradecanoate + **TBS deprotected**: (2*R*)-3-((((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-hydroxypropyl tetradecanoate: Following the general procedure (**B1**), (*R*)-**8c** (44 mg, 0.0558 mmol), Pd/C (22 mg), and MeOH (4.4 mL) were used. The intermediate (*R*)-**9c** (28 mg) was obtained in a ratio of 67:33 (TBS protected: TBS deprotected; based the percentage abundant is calculated based on the ^{1}H NMR integration under (-$SiMe_2$) peak from δ 0.17-0.08) as a colourless oil: ^{1}H NMR (400 MHz,

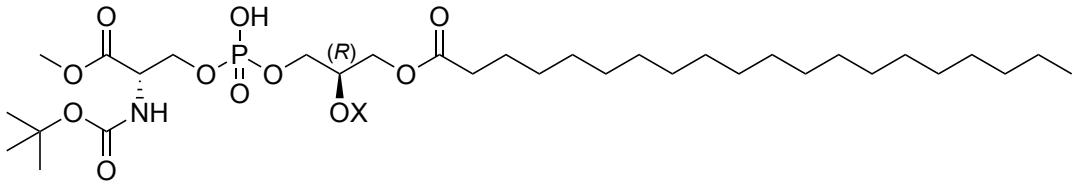
MeOH-d_4) δ 4.39-4.33 (m, 1H), 4.30-4.14 (m, 2H), 4.13-3.92 (m, 3H), 3.91-3.76 (m, 2H), 3.74 (s, 3H), 2.41-2.29 (m, 2H), 1.62 (q, J = 6.9 Hz, 2H), 1.45 (s, 9H), 1.36-1.22 (m, 20H), 0.93-0.86 (m, 9H), 0.17-0.08 (m, 4H); ^{31}P NMR (400 MHz, MeOH-d_4) δ 0.22, -0.16.



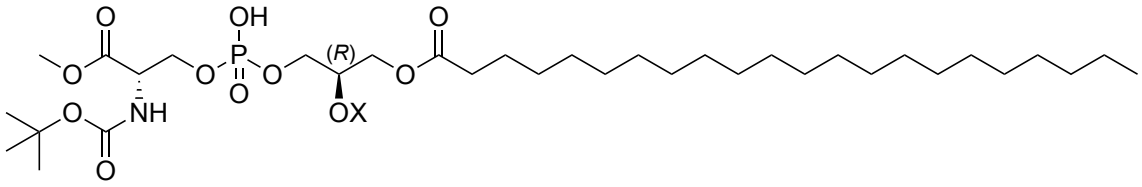
Intermediate (*R*)-**9d**: **TBS protected**: (2*R*)-3-((((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-((*tert*-butyldimethylsilyl)oxy)propyl palmitate + **TBS deprotected**: (2*R*)-3-((((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-hydroxypropyl palmitate: Following the general procedure (**B1**), (*R*)-**8d** (55 mg, 0.0674 mmol), Pd/C (28 mg), and MeOH (5.5 mL) were used. The intermediate (*R*)-**9d** (36 mg) was obtained in a ratio of 60:40 (TBS protected: TBS deprotected; based the percentage abundant is calculated based on the ^{1}H NMR integration under (-$SiMe_2$) peak from δ 0.17-0.08) as a colourless oil: ^{1}H NMR (400 MHz, MeOH-d_4) δ 4.40-4.33 (m, 1H), 4.30-4.14 (m, 2H), 4.13-3.92 (m, 3H), 3.90-3.76 (m, 2H), 3.75 (m, 3H), 2.39-2.30 (m, 2H), 1.62 (q, J = 7.0 Hz, 2H), 1.45 (s, 9H), 1.37-1.24 (m, 24H), 0.93-0.86 (m, 8H), 0.17-0.09 (m, 4H); ^{31}P NMR (400 MHz, MeOH-d_4) δ 0.28, -0.12.



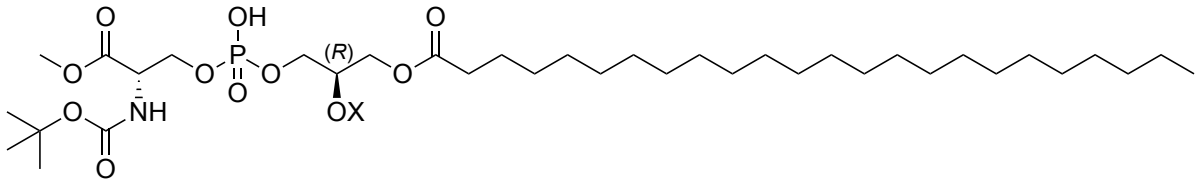
Intermediate (*R*)-**9e**: **TBS protected**: (2*R*)-3-((((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-((*tert*-butyldimethylsilyl)oxy)propyl stearate + **TBS deprotected**: (2*R*)-3-((((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-hydroxypropyl stearate: Following the general procedure (**B1**), (*R*)-**8e** (45 mg, 0.0533 mmol), Pd/C (22 mg), and MeOH (4.5 mL) were used. The intermediate (*R*)-**9e** (30 mg) was obtained in a ratio of 65:35 (TBS protected: TBS deprotected; based the percentage abundant is calculated based on the ^{1}H NMR integration under (-$SiMe_2$) peak from δ 0.17-0.08) as a colourless oil: ^{1}H NMR (400 MHz, MeOH-d_4) δ 4.40-4.32 (m 1H), 4.30-4.14 (m, 2H), 4.13-3.92 (m, 3H), 3.92-3.76 (m, 2H), 3.74 (s, 3H), 2.40-2.30 (m, 2H), 1.62 (q, J = 7.0 Hz, 2H), 1.45 (s, 9H), 1.36-1.24 (m, 28H), 0.93-0.86 (m, 9H), 0.17-0.09 (m, 4H); ^{31}P NMR (400 MHz, MeOH-d_4) δ 0.24, -0.14.



Intermediate (*R*)-**9f**: **TBS protected**: (2*R*)-3-((((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-((*tert*-butyldimethylsilyl)oxy)propyl icosanoate + **TBS deprotected**: (2*R*)-3-((((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-hydroxypropyl icosanoate: Following the general procedure (**B1**), (*R*)-**8f** (65 mg, 0.0745 mmol), Pd/C (33 mg), and MeOH (6.5 mL) were used. The intermediate (*R*)-**9f** (49 mg) was obtained in a ratio of 58:42 (TBS protected: TBS deprotected based the percentage abundant is calculated based on the ^{1}H NMR integration under (-$SiMe_2$) peak from δ 0.17-0.09) as a colourless oil: ^{1}H NMR (400 MHz, MeOH-d_4) δ 4.40-4.34 (m, 1H), 4.30-4.14 (m, 2H), 4.13-3.92 (m, 3H), 3.91-3.76 (m, 2H), 3.75 (s, 3H), 2.38-2.27 (m, 2H), (q, *J* = 7.0 Hz, 2H), 1.45 (s, 9H), 1.37-1.24 (m, 32H), 0.95-0.85 (m, 9H), 0.17-0.09 (m, 4H); ^{31}P NMR (400 MHz, MeOH-d_4) δ -0.79, -0.93.

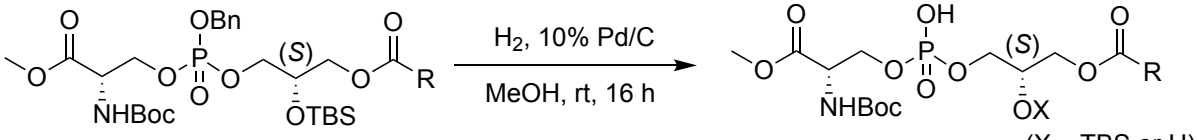


Intermediate (*R*)-**9g**: **TBS protected**: (2*R*)-3-((((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-((*tert*-butyldimethylsilyl)oxy)propyl docosanoate + **TBS deprotected**: (2*R*)-3-((((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-hydroxypropyl docosanoate: Following the general procedure (**B1**), (*R*)-**8g** (52 mg, 0.0578 mmol), Pd/C (26 mg), and MeOH (5.2 mL) were used. The intermediate (*R*)-**9g** (35 mg) was obtained in a ratio of 63:37 (TBS protected: TBS deprotected based the percentage abundant is calculated based on the ^{1}H NMR integration under (-$SiMe_2$) peak from δ 0.17-0.09) as a colourless oil: ^{1}H NMR (400 MHz, MeOH-d_4) δ 4.40-4.32 (m, 1H), 4.31-4.14 (m, 2H), 4.13-3.92 (m, 3H), 3.90-3.77 (m, 2H), 3.74 (s, 3H), 2.42-2.28 (m, 2H), 1.62 (q, *J* = 7.0 Hz, 2H), 1.45 (s, 9H), 1.37-1.21 (m, 36H), 0.96-0.84 (m, 10H), 0.17-0.09 (m, 4H); ^{31}P NMR (400 MHz, MeOH-d_4) δ -0.57.



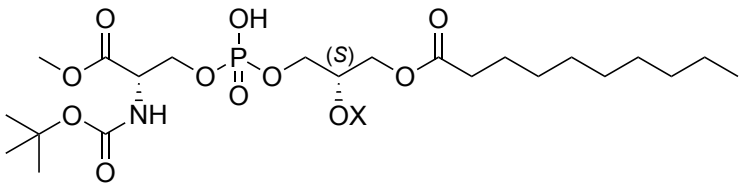
Intermediate (*R*)-**9h**: **TBS protected**: (2*R*)-3-((((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-((*tert*-butyldimethylsilyl)oxy)propyl tetracosanoate + **TBS deprotected**: (2*R*)-3-((((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-hydroxypropyl tetracosanoate: Following the general procedure (**B1**), (*R*)-**8h** (59 mg, 0.0589 mmol), Pd/C (30 mg), and MeOH (5.9 mL) were used. The intermediate (*R*)-**9h** (40 mg) was obtained in a ratio of 46:54 (TBS protected: TBS deprotected based the percentage abundant is calculated based on the ^{1}H NMR integration under (-$SiMe_2$) peak from δ 0.17-0.06) as a colourless oil: ^{1}H NMR (400 MHz, MeOH-d_4 + $CDCl_3$) δ 4.45-4.36 (m, 1H), 4.33-4.03 (m, 4H), 4.02-3.83 (m, 3H), 3.75 (s, 3H), 2.41-2.23 (m, 2H), 1.62 (m, 2H), 1.45 (s, 9H), 1.36-1.18 (m, 40H), 0.96-0.80 (m, 9H), 0.17-0.06 (m, 3H); ^{31}P NMR (400 MHz, MeOH-d_4 + $CDCl_3$) δ -0.50, -0.91.

General procedure (B2) for the synthesis of intermediates (*S*)-9a-h (debenzylation): The intermediates (*S*)-**9a-h** described in this section were synthesized using a previously reported methodology in literature(Ikubo et al., 2015).

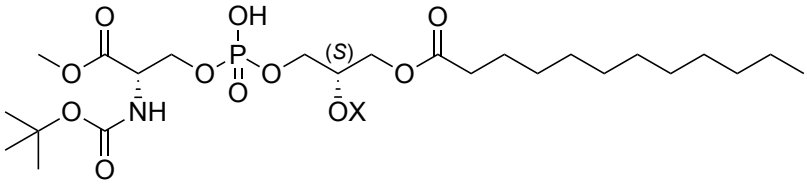


(*S*)-**8a-h** (*S*)-**9a-h**

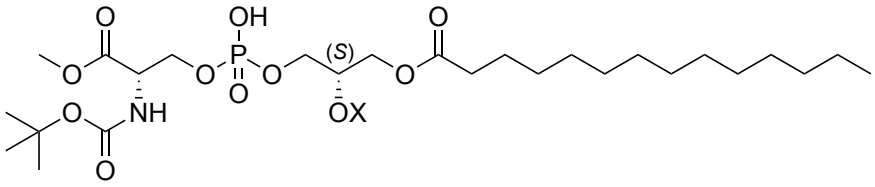
The benzylated compound (*S*)-**8** was dissolved in dry MeOH in a two-neck round bottom flask, following which, Pd/C (10%) was added to this solution under N_2 atmosphere, and the round bottom flask was subsequently equipped with hydrogen filled rubber bladder. The reaction mixture was stirred for next 12 to 16 h at room temperature. The reaction solution was filtered through a celite pad, and washed with MeOH (3 × 10 mL). The filtrate was then concentrated under reduced pressure at 25 °C to yield (*S*)-**9** intermediates (> 95% pure, > 80% yield), which were used as such, without any further purification for the next step. The debenzylated (*S*)-**9** intermediate consisted of a mixture of two compounds where the *sn*-2 hydroxyl was either TBS protected or deprotected because of solvent methanolysis as per literature precedence(Ikawa et al., 2004). As per our reaction scheme (**Supplementary Fig. 2**), both compounds would yield the final desired products, hence we did not try to purify or isolate them separately, and proceeded with the intermediate to the next step.



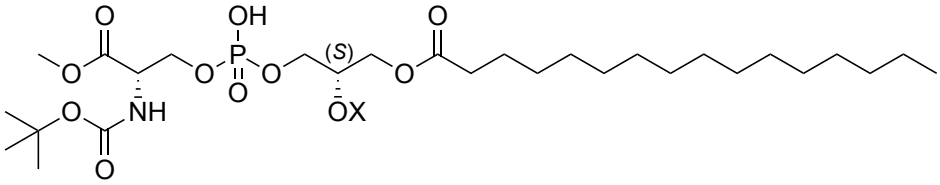
Intermediate (*S*)-**9a**: **TBS protected**: (2*S*)-3-((((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-((*tert*-butyldimethylsilyl)oxy)propyl decanoate + **TBS deprotected**: (2*S*)-3-((((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-hydroxypropyl decanoate: Following the general procedure (**B2**), (*S*)-**8a** (50 mg, 0.0683 mmol), Pd/C (25 mg), and MeOH (5.0 mL) were used. The intermediate (*S*)-**9a** (36 mg) was obtained in a ratio of 50:50 (TBS protected: TBS deprotected based the percentage abundant is calculated based on the ^{1}H NMR integration under (-$SiMe_2$) peak from δ 0.16-0.07) as a colourless oil: ^{1}H NMR (400 MHz, MeOH-d_4) δ 4.39-4.33 (m, 1H), 4.30-4.14 (m, 2H), 4.13-3.92 (m, 3H), 3.89-3.77 (m, 2H), 3.75 (s, 3H), 2.40-2.31 (m, 2H), 1.62 (q, *J* = 7.0 Hz, 2H), 1.45 (s, 9H), 1.37-1.23 (m, 12H), 0.94-0.86 (m, 8H), 0.16-0.07 (m, 3H); ^{31}P NMR (400 MHz, MeOH-d_4) δ 0.22, -0.17.



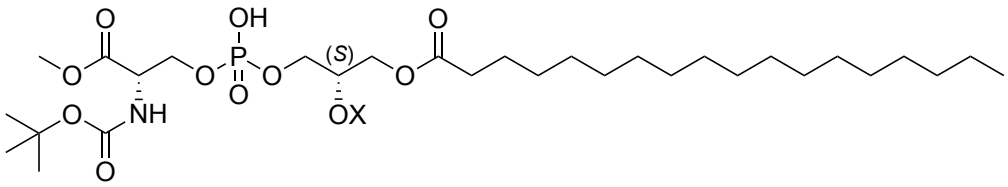
Intermediate (*S*)-**9b**: **TBS protected**: (2*S*)-3-((((*S*)-2-((tert-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-((*tert*-butyldimethylsilyl)oxy)propyl dodecanoate + **TBS deprotected**: (2*S*)-3-((((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-hydroxypropyl dodecanoate: Following the general procedure (**B2**), (*S*)-**8b** (42 mg, 0.0553 mmol), Pd/C (21 mg), and MeOH (4.2 mL) were used. The intermediate (*S*)-**9b** (30 mg) was obtained in a ratio of 58:42 (TBS protected: TBS deprotected based the percentage abundant is calculated based on the ^{1}H NMR integration under (-$SiMe_2$) peak from δ 0.16-0.09) as a colourless oil: ^{1}H NMR (400 MHz, MeOH-d_4) δ 4.39-4.33 (m, 1H), 4.30-4.14 (m, 2H), 4.13-3.92 (m, 3H), 3.89-3.76 (m, 2H), 3.74 (s, 3H), 2.39-2.30 (m, 2H), 1.62 (q, *J* = 7.0 Hz, 2H), 1.45 (s, 9H), 1.36-1.23 (m, 16H); 0.94-0.86 (m, 8H), 0.16-0.09 (m, 3H); ^{31}P NMR (400 MHz, MeOH-d_4) δ 0.16, -0.21.



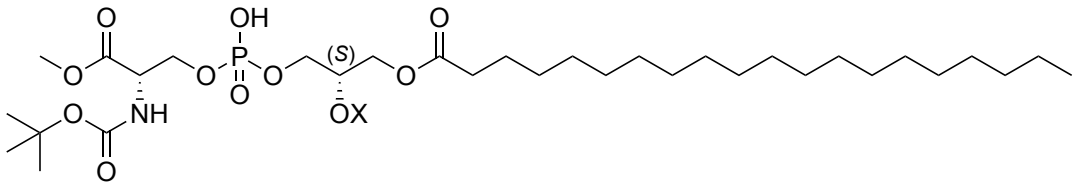
Intermediate (*S*)-**9c**: **TBS protected**: (2*S*)-3-((((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-((*tert*-butyldimethylsilyl)oxy)propyl tetradecanoate + **TBS deprotected**: (2*S*)-3-((((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-hydroxypropyl tetradecanoate: Following the general procedure (**B2**), (*S*)-**8c** (54 mg, 0.0686 mmol), Pd/C (27 mg), and MeOH (5.4 mL) were used. The intermediate (*S*)-**9c** (40 mg) was obtained in a ratio of 79:21 (TBS protected: TBS deprotected based the percentage abundant is calculated based on the ^{1}H NMR integration under (-$SiMe_2$) peak from δ 0.17-0.08) as a colourless oil: ^{1}H NMR (400 MHz, MeOH-d_4) δ 4.39-4.32 (m, 1H), 4.30-4.14 (m, 2H), 4.13-3.92 (m, 3H), 3.91-3.76 (m, 2H), 3.74 (s, 3H), 2.41-2.29 (m, 2H), 1.62 (q, *J* = 7.0 Hz, 2H), 1.45 (s, 9H), 1.36-1.22 (m, 20H), 0.93-0.85 (m, 10H), 0.17-0.08 (m , 5H); ^{31}P NMR (400 MHz, MeOH-d_4) δ 0.16, -0.22.



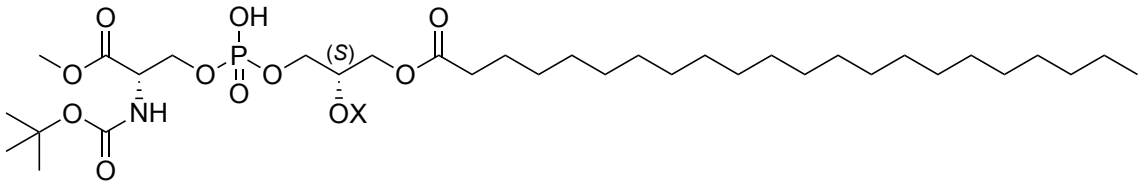
Intermediate (*S*)-**9d**: **TBS protected**: (2*S*)-3-((((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-((*tert*-butyldimethylsilyl)oxy)propyl palmitate + **TBS deprotected**: (2*S*)-3-((((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-hydroxypropyl palmitate: Following the general procedure (**B2**), (*S*)-**8d** (53 mg, 0.0649 mmol), Pd/C (27 mg), and MeOH (5.3 mL) were used. The intermediate (*S*)-**9d** (38 mg) was obtained in a ratio of 62:38 (TBS protected: TBS deprotected based the percentage abundant is calculated based on the ^{1}H NMR integration under (-$SiMe_2$) peak from δ 0.17-0.09) as a colourless oil: ^{1}H NMR (400 MHz, MeOH-d_4) δ 4.40-4.32 (m, 1H), 4.30-4.14 (m, 2H), 4.13-3.92 (m, 3H), 3.90-3.76 (m, 2H), 3.74 (s, 3H), 2.39-2.30 (m, 2H), 1.62 (q, *J* = 7.0 Hz, 2H), 1.45 (s, 9H), 1.37-1.24 (m, 24H), 0.93-0.86 (m, 9H), 0.17-0.09 (m, 4H); ^{31}P NMR (400 MHz, MeOH-d_4) δ 0.23, -0.16.



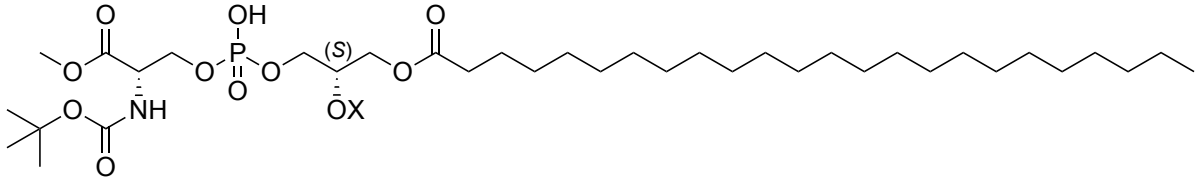
Intermediate (*S*)-**9e**: **TBS protected**: (2*S*)-3-((((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-((*tert*-butyldimethylsilyl)oxy)propyl stearate + **TBS deprotected**: (2*S*)-3-((((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-hydroxypropyl stearate: Following the general procedure (**B2**), (*S*)-**8e** (55 mg, 0.0652 mmol), Pd/C (28 mg), and MeOH (5.5 mL) were used. The intermediate (*S*)-**9e** (43 mg) was obtained in a ratio of 65:35 (TBS protected: TBS deprotected based the percentage abundant is calculated based on the ^{1}H NMR integration under (-SiMe$_2$) peak from δ 0.17-0.09) as a colourless oil: ^{1}H NMR (400 MHz, MeOH-d$_4$) δ 4.40-4.32 (m 1H), 4.30-4.14 (m, 2H), 4.13-3.92 (m, 3H), 3.91-3.76 (m, 2H), 3.74 (s, 3H), 2.40-2.31 (m, 2H), 1.62 (q, *J* = 7.0 Hz, 2H), 1.45 (s, 9H), 1.36-1.24 (m, 28H), 0.93-0.86 (m, 9H), 0.17-0.09 (m, 4H); ^{31}P NMR (400 MHz, MeOH-d$_4$) δ 0.22, -0.17.



Intermediate (*S*)-**9f**: **TBS protected**: (2*S*)-3-((((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-((*tert*-butyldimethylsilyl)oxy)propyl icosanoate + **TBS deprotected**: (2*S*)-3-((((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-hydroxypropyl icosanoate: Following the general procedure (**B2**), (*S*)-**8f** (62 mg, 0.0711 mmol), Pd/C (31 mg), and MeOH (6.2 mL) were used. The intermediate (*S*)-**9f** (48 mg) was obtained in a ratio of 45:55 (TBS protected: TBS deprotected based the percentage abundant is calculated based on the ^{1}H NMR integration under (-SiMe$_2$) peak from δ 0.17-0.09) as a colourless oil: ^{1}H NMR (400 MHz, MeOH-d$_4$) δ 4.41-4.33 (m, 1H), 4.31-4.25 (m, 1H), 4.24-4.00 (m, 4H), 3.98-3.80 (m, 2H), 3.75 (s, 3H), 2.42-2.29 (m, 2H), 1.62 (q, *J* = 7.0 Hz, 2H), 1.45 (s, 9H), 1.35-1.26 (m, 32H), 0.94-0.85 (m, 8H), 0.17-0.09 (m, 3H); ^{31}P NMR (400 MHz, MeOH-d$_4$) δ 0.05, -0.39.

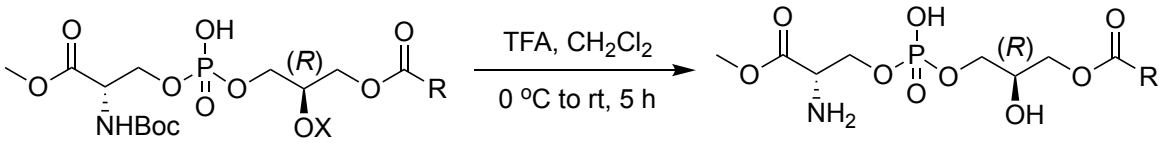


Intermediate (*S*)-**9g**: **TBS protected**: (2*S*)-3-((((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-((*tert*-butyldimethylsilyl)oxy)propyl docosanoate + **TBS deprotected**: (2*S*)-3-((((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-hydroxypropyl docosanoate: Following the general procedure (**B2**), (*S*)-**8g** (57 mg, 0.0633 mmol), Pd/C (28 mg), and MeOH (5.7 mL) were used. The intermediate (*S*)-**9g** (40 mg) was obtained in a ratio of 75:25 (TBS protected: TBS deprotected based the percentage abundant is calculated based on the ^{1}H NMR integration under (-$SiMe_2$) peak from δ 0.17-0.08) as a colourless oil: ^{1}H NMR (400 MHz, MeOH-d_4) δ 4.40-4.32 (m, 1H), 4.30-4.25 (m, 1H), 4.24-4.00 (m, 4H), 3.98-3.80 (m, 2H), 3.74 (s, 3H), 2.42-2.29 (m, 2H), 1.62 (m, 2H), 1.45 (s, 9H), 1.38-1.24 (m, 36H), 0.94-0.85 (m, 10H), 0.17-0.08 (m, 5H); ^{31}P NMR (400 MHz, MeOH-d_4) δ -0.44.



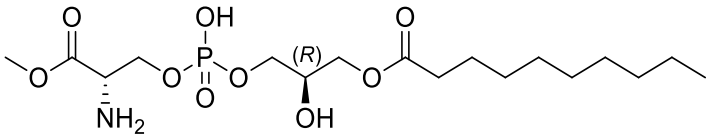
Intermediate (*S*)-**9h**: **TBS protected**: (2*S*)-3-((((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-((*tert*-butyldimethylsilyl)oxy)propyl tetracosanoate + **TBS deprotected**: (2*S*)-3-((((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-hydroxypropyl tetracosanoate: Following the general procedure (**B2**), (*S*)-**8h** (68 mg, 0.0589 mmol), Pd/C (34 mg), and MeOH (6.8 mL) were used. The intermediate (*S*)-**9h** (30 mg) was obtained in a ratio of 49:51 (TBS protected: TBS deprotected based the percentage abundant is calculated based on the ^{1}H NMR integration under (-$SiMe_2$) peak from δ 0.18-0.06) as a colourless oil: ^{1}H NMR (400 MHz, MeOH-d_4 + $CDCl_3$) δ 4.62-4.44 (m, 1H), 4.40-3.91 (m, 6H), 3.89-3.80 (m, 1H), 3.75 (s, 3H), 2.42-2.27 (m, 2H), 1.62 (m, 2H), 1.44 (s, 9H), 1.37-1.21 (m, 40H), 0.95-0.81 (m, 9H), 0.18-0.06 (m, 3H); ^{31}P NMR (400 MHz, MeOH-d_4) δ 0.32, -0.14.

General procedure (C1) for the synthesis of the final compounds (*R*)-2a-h (TBS and *t*-BOC deprotection):

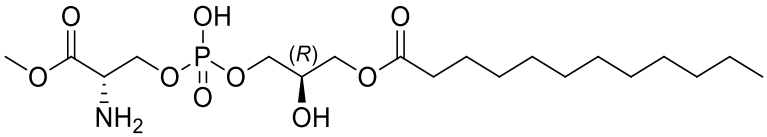


(*R*)-**9a-h** (*R*)-**2a-h**

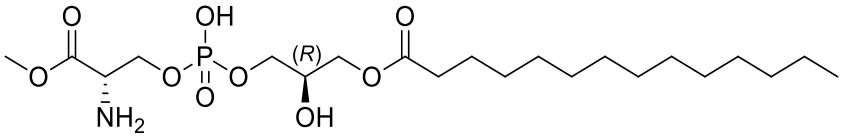
The intermediate (*R*)-**9** in dry CH_2Cl_2 was charged into a two-neck round bottom flask, which was equipped with a N_2 balloon. The solution was cooled to -10 °C, following which the solution of trifluoroacetic acid (TFA) was added dropwise. After TFA addition, the reaction temperature and stirring time was different, depending on the compound that was synthesized. For the intermediates (*R*)-**9a-d**, the reaction mixture was stirred at 0 °C for 1 h and then at room temperature for another 4 h. For intermediate (*R*)-**9e** the reaction solution was stirred at 0 °C for 4 h and then at room temperature for 1 h. For the intermediates (*R*)-**9f-h,** the reaction mixture was stirred only at 0 °C for 5 h. The rationale for using different temperatures, was to minimize hydrolysis of the fatty acid moiety. Our observation was that as the fatty acid chain length of this moiety increases, temperatures of the reaction mixture had to be maintained at 0 °C. After completion the deprotection reaction, the remaining solution was concentrated under reduced pressure at 25 °C. The resultant residue was washed three times with *n*-Pentane: Et_2O (3:1), and then dried under high vacuum to afford the desired final product (*R*)-**2**. The purity of the final compounds (*R*)-**2a-h** was determined based on the NMR analysis, and LC-MS analysis, and found to be ≥ 95% for all compounds.



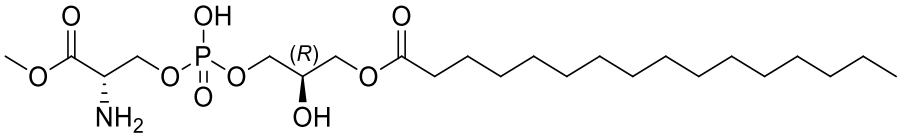
(2*R*)-3-((((*S*)-2-amino-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-hydroxypropyl decanoate (Compound (*R*)-**2a**): Following the general procedure (**C1**), (*R*)-**9a** (30 mg), TFA (0.300 mL) and CH_2Cl_2 (0.170 mL) were used. The product was washed with *n*-pentane: Et_2O (4:1) (3 x 2 mL) to yield desired final compound (*R*)-**2a** (21 mg, 0.0491 mmol, 72% yield relative to (*R*)-**8a**) as a white solid: ^{1}H NMR (400 MHz, MeOH-d_4) δ 4.60 (m, 1H), 4.40-4.07 (m, 4H), 4.05-3.89 (m, 3H), 3.86 (2s, 3H), 3.79-3.64 (m, 1H), 2.36 (t, J = 7.4 Hz, 2H), 1.61 (q, J = 7.0 Hz, 2H), 1.40-1.22 (m, 12H), 0.90 (t, J = 6.8 Hz, 3H); ^{31}P NMR (400 MHz, MeOH-d_4) δ 0.44; HRMS (ESI): m/z calcd. for ($C_{17}H_{35}NO_9P$) $[M + H]^+$ 428.2049; found, 428.2048.



(2*R*)-3-((((*S*)-2-amino-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-hydroxypropyl dodecanoate (Compound (*R*)-**2b**): Following the general procedure (**C1**), (*R*)-**9b** (32 mg), TFA (0.320 mL) and CH_2Cl_2 (0.180 mL) were used. The product was washed with *n*-pentane: Et_2O (4:1) (3 x 2 mL) to yield desired final compound (*R*)-**2b** (21 mg, 0.0461 mmol, 78% yield relative to (*R*)-**8b**) as a white solid: ^{1}H NMR (400 MHz, MeOH-d_4) δ 4.60 (m, 1H), 4.40-4.07 (m, 4H), 4.06-3.88 (m, 3H), 3.86 (2s, 3H), 3.77-3.64 (m, 1H), 2.36 (td, J = 7.4, 3.4 Hz, 2H), 1.62 (q, J = 7.0 Hz, 2H), 1.38-1.23 (m, 16H), 0.90 (t, J = 6.8 Hz, 3H); ^{31}P NMR (400 MHz, MeOH-d_4) δ 0.44; HRMS (ESI): m/z calcd. for ($C_{19}H_{39}NO_9P$) $[M + H]^+$ 456.2362; found, 456.2363.

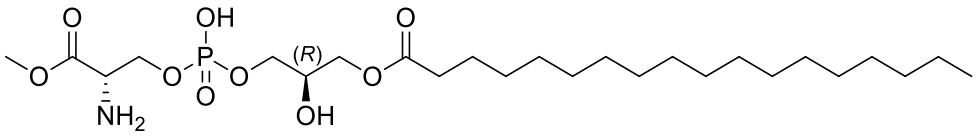


(2*R*)-3-((((*S*)-2-amino-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-hydroxypropyl tetradecanoate (Compound (*R*)-**2c**): Following the general procedure (**C1**), (*R*)-**9c** (28 mg), TFA (0.280 mL) and CH_2Cl_2 (0.160 mL) were used. The product was washed with *n*-pentane: Et_2O (4:1) (3 x 2 mL) to yield desired final compound (*R*)-**2c** (20 mg, 0.0414 mmol, 67% yield relative to (*R*)-**8c**) as a white solid: ^{1}H NMR (400 MHz, MeOH-d_4) δ 4.49-4.30 (m, 1H), 4.28-4.00 (m, 4H), 3.98-3.82 (m, 3H), 3.79 (s, 3H), 3.73-3.55 (m, 1H), 2.30 (m, 2H), 1.56 (m, 2H), 1.33-1.15 (m, 20H), 0.83 (t, J = 6.3 Hz, 3H); ^{31}P NMR (400 MHz, MeOH-d_4) δ 0.44; HRMS (ESI): m/z calcd. for ($C_{21}H_{43}NO_9P$) $[M + H]^+$ 484.2675; found, 484.2677.

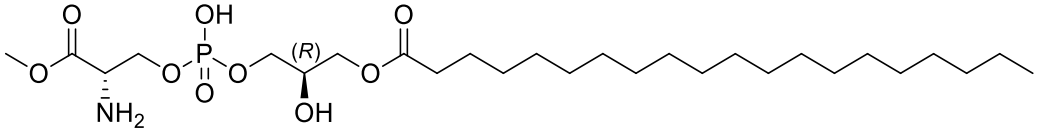


(2*R*)-3-((((*S*)-2-amino-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-hydroxypropyl palmitate (Compound (*R*)-**2d**): Following the general procedure (**C1**), (*R*)-**9d** (36 mg), TFA (0.360 mL) and CH_2Cl_2 (0.210 mL) were used. The product was washed with *n*-pentane: Et_2O (4:1) (3 x 2 mL) to yield desired final compound (*R*)-**2d** (26 mg, 0.0508 mmol, 74% yield relative to (*R*)-**8d**) as a white solid: ^{1}H NMR (400 MHz, MeOH-d_4) δ 4.61(m, 1H), 4.37-4.07 (m, 4H), 4.06-3.89 (m, 3H), 3.86 (2s, 3H), 3.77-3.64 (m, 1H), 2.36 (td, J = 7.4, 2.5 Hz, 2H), 1.62 (q, J = 7.0 Hz, 2H), 1.38-1.21 (m, 24H), 0.90 (t, J = 6.8 Hz, 3H); ^{31}P NMR

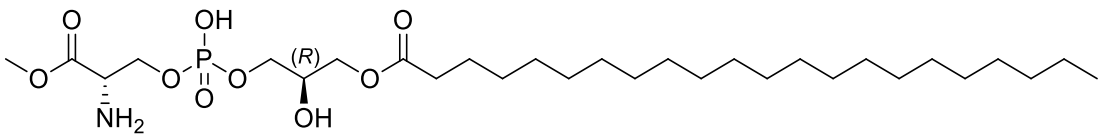
(400 MHz, MeOH-d_4) δ 0.44; HRMS (ESI): m/z calcd. for ($C_{23}H_{47}NO_9P$) $[M + H]^+$ 512.2988; found, 512.2988.



(2*R*)-3-((((*S*)-2-amino-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-hydroxypropyl stearate (Compound (*R*)-**2e**): Following the general procedure (**C1**), (*R*)-**9e** (18 mg), TFA (0.180 mL) and CH_2Cl_2 (0.110 mL) were used. The product was washed with *n*-pentane: Et_2O (4:1) (3 x 1 mL) to yield desired final compound (*R*)-**2e** (13 mg, 0.0241 mmol, 76% yield relative to (*R*)-**8e**) as a white solid: ^{1}H NMR (400 MHz, MeOH-d_4 + $CDCl_3$ (1:2 ratio)) δ 4.30-4.23 (m, 3H), 4.22-4.04 (m, 2H), 4.02-3.89 (m, 2H), 3.86 (s, 3H), 3.75-3.65 (m, 1H), 2.34 (t, *J* = 6.6 Hz, 2H), 1.61 (m, 2H), 1.36-1.19 (m, 28H), 0.88 (m, 3H); ^{31}P NMR (400 MHz, MeOH-d_4) δ 0.44; HRMS (ESI): m/z calcd. for ($C_{25}H_{51}NO_9P$) $[M + H]^+$ 540.3296; found, 540.3297.

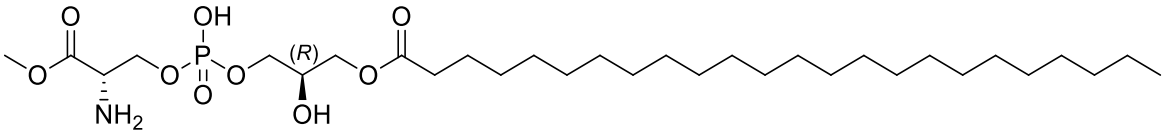


(2*R*)-3-((((*S*)-2-amino-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-hydroxypropyl icosanoate (Compound (*R*)-**2f**): Following the general procedure (**C1**), (*R*)-**9f** (25 mg), TFA (0.200 mL) and CH_2Cl_2 (0.350 mL) were used. The product was washed with *n*-pentane: Et_2O (4:1) (3 x 2 mL) to yield desired final compound (*R*)-**2f** (17 mg, 0.0299 mmol, 79% yield relative to (*R*)-**8f**) as a white solid: ^{1}H NMR (400 MHz, MeOH-d_4 + $CDCl_3$ (1:2 ratio)) δ4.37-4.14 (m, 3H), 4.13-4.04 (m, 2H), 4.03-3.88 (m, 2H), 3.84 (s, 3H), 3.75-3.55 (m, 1H), 2.32 (t, *J* = 7.3 Hz, 2H), 1.58 (m, 2H), 1.32-1.20 (m, 32H), 0.85 (t, *J* = 6.6 Hz, 3H); ^{31}P NMR (400 MHz, MeOH-d_4) δ 0.45; HRMS (ESI): m/z calcd. for ($C_{27}H_{55}NO_9P$) $[M + H]^+$ 568.3609; found, 568.3610.



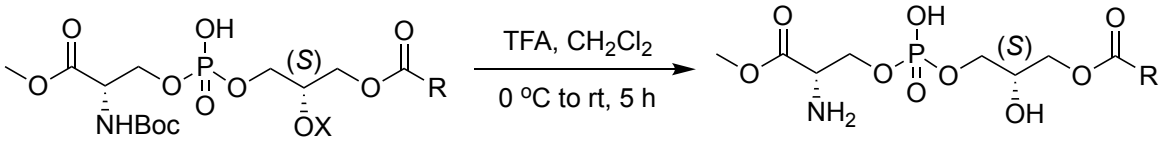
(2*R*)-3-((((*S*)-2-amino-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-hydroxypropyl docosanoate (Compound (*R*)-**2g**): Following the general procedure (**C1**), (*R*)-**9g** (28 mg), TFA (0.225 mL) and CH_2Cl_2 (0.390 mL) were used. The product was washed with *n*-pentane: Et_2O (4:1) (3 x 2 mL) to yield desired final compound (*R*)-**2g** (22 mg,

0.0369 mmol, 79% yield relative to (*R*)-**8g**) as a white solid: ^{1}H NMR (400 MHz, MeOH-d_4 + $CDCl_3$ (1:2 ratio)) *δ*4.33-4.05 (m, 5H), 4.04-3.90 (m, 2H), 3.83 (s, 3H), 3.77-3.55 (m, 1H), 2.31 (m, 2H), 1.58 (m, 2H), 1.32-1.19 (m, 36H), 0.84 (t, *J* = 6.3 Hz, 3H); ^{31}P NMR (400 MHz, MeOH-d_4) *δ* 0.44; HRMS (ESI): m/z calcd. for ($C_{29}H_{59}NO_9P$) $[M + H]^+$ 596.3922; found, 596.3923.



(2*R*)-3-((((*S*)-2-amino-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-hydroxypropyl tetracosanoate (Compound (*R*)-**2h**): Following the general procedure (**C1**), (*R*)-**9h** (25 mg), TFA (0.200 mL) and CH_2Cl_2 (0.350 mL) were used. The product was washed with *n*-pentane: Et_2O (4:1) (3 x 2 mL) to yield desired final compound (*R*)-**2h** (18 mg, 0.0289 mmol, 78% yield relative to (*R*)-**8h**) as a white solid: ^{1}H NMR (400 MHz, MeOH-d_4 + $CDCl_3$ (1:2 ratio)) *δ* 4.33-4.05 (m, 5H), 4.04-3.88 (m, 3H), 3.83 (s, 3H), 3.72-3.52 (m, 1H), 2.31 (m, 2H), 1.58 (m, 2H), 1.34-1.14 (m, 40H), 0.84 (m, 3H); ^{31}P NMR (400 MHz, MeOH-d_4) *δ* 0.44; ; HRMS (ESI): m/z calcd. for ($C_{31}H_{63}NO_9P$) $[M + H]^+$ 624.4235; found, 624.4236.

General procedure (C2) for the synthesis of compounds (*S*)-2a-h (TBS and *t*-BOC deprotection):



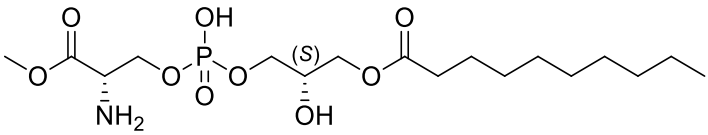
(*S*)-**9a-h**

(X = TBS or H)

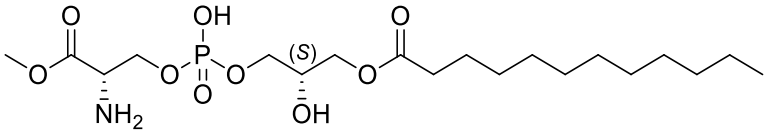
(*S*)-**2a-h**

The intermediate (*S*)-**9** in dry CH_2Cl_2 was charged into a two-neck round bottom flask, which was equipped with a N_2 balloon. The solution was cooled to -10 °C, following which the solution of trifluoroacetic acid (TFA) was added dropwise. After TFA addition, the reaction temperature and stirring time was different, depending on the compound that was synthesized. For the intermediates (*S*)-**9a-d**, the reaction mixture was stirred at 0 °C for 1 h and then at room temperature for another 4 h. For intermediate (*S*)-**9e** the reaction solution was stirred at 0 °C for 4 h and then at room temperature for 1 h. For the intermediates (*S*)-**9f-h,** the reaction mixture was stirred only at 0 °C for 5 h. The rationale for using different temperatures, was to minimize hydrolysis of the fatty acid moiety. Our observation was that as the fatty acid chain length of this moiety increases, temperatures of the reaction mixture had to be maintained at 0 °C. After completion the deprotection reaction, the remaining solution was concentrated under reduced pressure at 25 °C. The resultant residue was

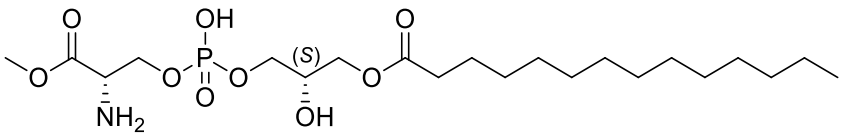
washed three times with *n*-Pentane: Et_2O (3:1), and then dried under high vacuum to afford the desired final product (*S*)-**2**. The purity of the final compounds (*S*)-**2a-h** was determined based on the NMR analysis, and LC-MS analysis, and found to be ≥ 95% for all compounds.



(2*S*)-3-((((*S*)-2-amino-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-hydroxypropyl decanoate (Compound (*S*)-**2a**): Following the general procedure (**C2**), (*S*)-**9a** (36 mg), TFA (0.360 mL) and CH_2Cl_2 (0.210 mL) were used. The product was washed with *n*-pentane: Et_2O (4:1) (3 x 2 mL) to yield the desired final compound (*S*)-**2a** (22 mg, 0.0515 mmol, 75% yield relative to (*S*)-**8a**) as a white solid: ^{1}H NMR (400 MHz, MeOH-d_4) δ 4.41-4.05 (m, 4H), 4.04-3.85 (m, 4H), 3.82 (s, 3H), 3.75-3.58 (m, 1H), 2.40-2.29 (m, 2H), 1.66-1.51 (m, 2H), 1.36-1.19 (m, 12H), 0.87 (t, *J* = 6.4 Hz, 3H); ^{31}P NMR (400 MHz, MeOH-d_4) δ 0.44; HRMS (ESI): m/z calcd. for ($C_{17}H_{35}NO_9P$) $[M + H]^+$ 428.2049; found, 428.2048.

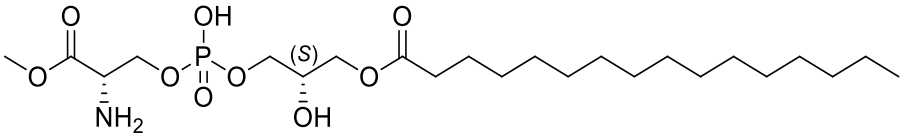


(2*S*)-3-((((*S*)-2-amino-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-hydroxypropyl dodecanoate (Compound (*S*)-**2b**): Following the general procedure (**C2**), (*S*)-**9b** (30 mg), TFA (0.300 mL) and CH_2Cl_2 (0.170 mL) were used. The product was washed with *n*-pentane: Et_2O (4:1) (3 x 2 mL) to yield the desired final compound (*S*)-**2b** (17 mg, 0.0373 mmol, 67% yield relative to (*S*)-**8b**) as a white solid: ^{1}H NMR (400 MHz, MeOH-d_4) δ 4.59 (m, 1H), 4.40-4.07 (m, 4H), 4.06-3.88 (m, 3H), 3.86 (2s, 3H), 3.78-3.61 (m, 1H), 2.36 (t, *J* = 7.4 Hz, 2H), 1.62 (q, *J* = 7.0 Hz, 2H), 1.38-1.23 (m, 16H), 0.90 (t, *J* = 6.7 Hz, 3H); ^{31}P NMR (400 MHz, MeOH-d_4) δ 0.44; HRMS (ESI): m/z calcd. for ($C_{19}H_{39}NO_9P$) $[M + H]^+$ 456.2362; found, 456.2361.

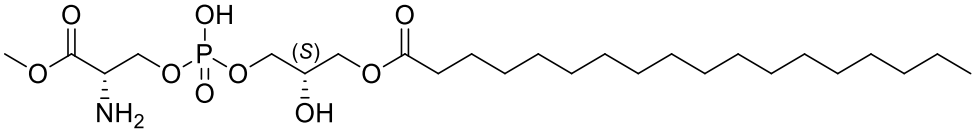


(2*S*)-3-((((*S*)-2-amino-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-hydroxypropyl tetradecanoate (Compound (*S*)-**2c**): Following the general procedure (**C2**), (*S*)-**9c** (40 mg), TFA (0.400 mL) and CH_2Cl_2 (0.230 mL) were used. The product was washed with *n*-pentane: Et_2O (4:1) (3 x 2 mL) to yield the desired final compound (*S*)-**2c** (26 mg,

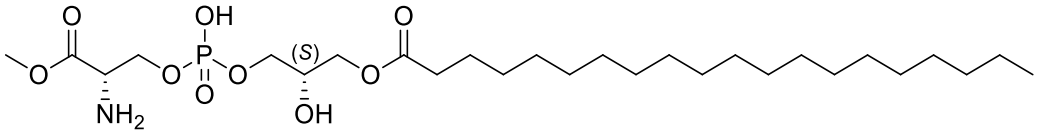
0.0538 mmol, 78% yield relative to (*S*)-**8c**) as a white solid: ^{1}H NMR (400 MHz, MeOH-d_4) δ 4.60 (m, 1H), 4.40-4.07 (m, 4H), 4.06-3.89 (m, 3H), 3.85 (2s, 3H), 3.76-3.65 (m, 1H), 2.36 (t, J = 7.4 Hz, 2H), 1.62 (m, 2H), 1.38-1.23 (m, 20H), 0.90 (t, J = 6.7 Hz, 3H); ^{31}P NMR (400 MHz, MeOH-d_4) δ 0.44; HRMS (ESI): m/z calcd. for ($C_{21}H_{43}NO_9P$) $[M + H]^+$ 484.2675; found, 484.2676.



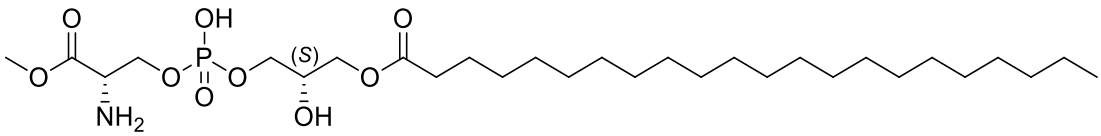
(2*S*)-3-((((*S*)-2-amino-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-hydroxypropyl palmitate (Compound (*S*)-**2d**): Following the general procedure (**C2**), (*S*)-**9d** (38 mg), TFA (0.380 mL) and CH_2Cl_2 (0.220 mL) were used. The product was washed with *n*-pentane: Et_2O (4:1) (3 x 2 mL) to yield the desired final compound (*S*)-**2d** (24 mg, 0.0469 mmol, 73% yield relative to (*S*)-**8d**) as a white solid: ^{1}H NMR (400 MHz, MeOH-d_4) δ 4.62 (m, 1H), 4.40-4.08 (m, 4H), 4.04-3.89 (m, 3H), 3.86 (2s, 3H), 3.76-3.65 (m, 1H), 2.36 (td, J = 7.4, 2.8 Hz, 2H), 1.62 (q, J = 7.0 Hz, 2H), 1.37-1.24 (m, 24H), 0.90 (t, J = 6.9 Hz, 3H); ^{31}P NMR (400 MHz, MeOH-d_4) δ 0.43; HRMS (ESI): m/z calcd. for ($C_{23}H_{47}NO_9P$) $[M + H]^+$ 512.2988; found, 512.2989.



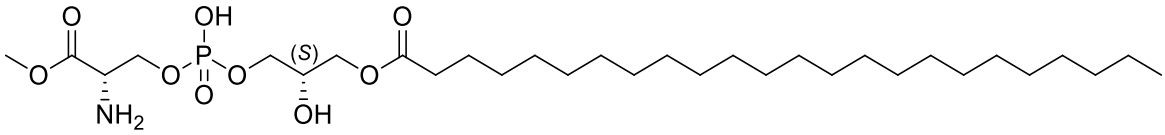
(2*S*)-3-((((*S*)-2-amino-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-hydroxypropyl stearate (Compound (*S*)-**2e**): Following the general procedure (**C2**), (*S*)-**9e** (43 mg), TFA (0.430 mL) and CH_2Cl_2 (0.250 mL) were used. The product was washed with *n*-pentane: Et_2O (4:1) (3 x 2 mL) to yield the desired final compound (*S*)-**2e** (26 mg, 0.0482 mmol, 74% yield relative to (*S*)-**8e**) as a white solid: ^{1}H NMR (400 MHz, MeOH-d_4) δ 4.61 (m, 1H), 4.37-4.07 (m, 5H), 4.06-3.88 (m, 2H), 3,86 (2s, 3H), 3.77-3.65 (m, 1H), 2.36 (td, J = 7.4, 2.5 Hz, 2H), 1.62 (q, J = 7.0 Hz, 2H), 1.37-1.24 (m, 28H), 0.90 (t, J = 6.9 Hz, 3H); ^{31}P NMR (400 MHz, MeOH-d_4) δ 0.43; HRMS (ESI): m/z calcd. for ($C_{25}H_{51}NO_9P$) $[M + H]^+$ 540.3296; found, 540.3298.



(2*S*)-3-((((*S*)-2-amino-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-hydroxypropyl icosanoate (Compound (*S*)-**2f**): Following the general procedure (**C2**), (*S*)-**9f** (25 mg), TFA (0.200 mL) and CH_2Cl_2 (0.350 mL) were used. The product was washed with *n*-pentane: Et_2O (4:1) (3 x 2 mL) to yield the desired final compound (*S*)-**2f** (16 mg, 0.0282 mmol, 76% yield relative to (*S*)-**8f**) as a white solid: ^{1}H NMR (400 MHz, MeOH-d_4 + $CDCl_3$ (1:2 ratio)) δ 4.37-4.14 (m, 3H), 4.13-4.04 (m, 2H), 4.03-3.89 (m, 2H), 3.84 (s, 3H), 3.75-3.54 (m, 1H), 2.32 (m, 2H), 1.58 (m, 2H), 1.32-1.17 (m, 32H), 0.84 (m, 3H); ^{31}P NMR (400 MHz, MeOH-d_4) δ 0.43; HRMS (ESI): m/z calcd. for ($C_{27}H_{55}NO_9P$) $[M + H]^+$ 568.3609; found, 568.3610.



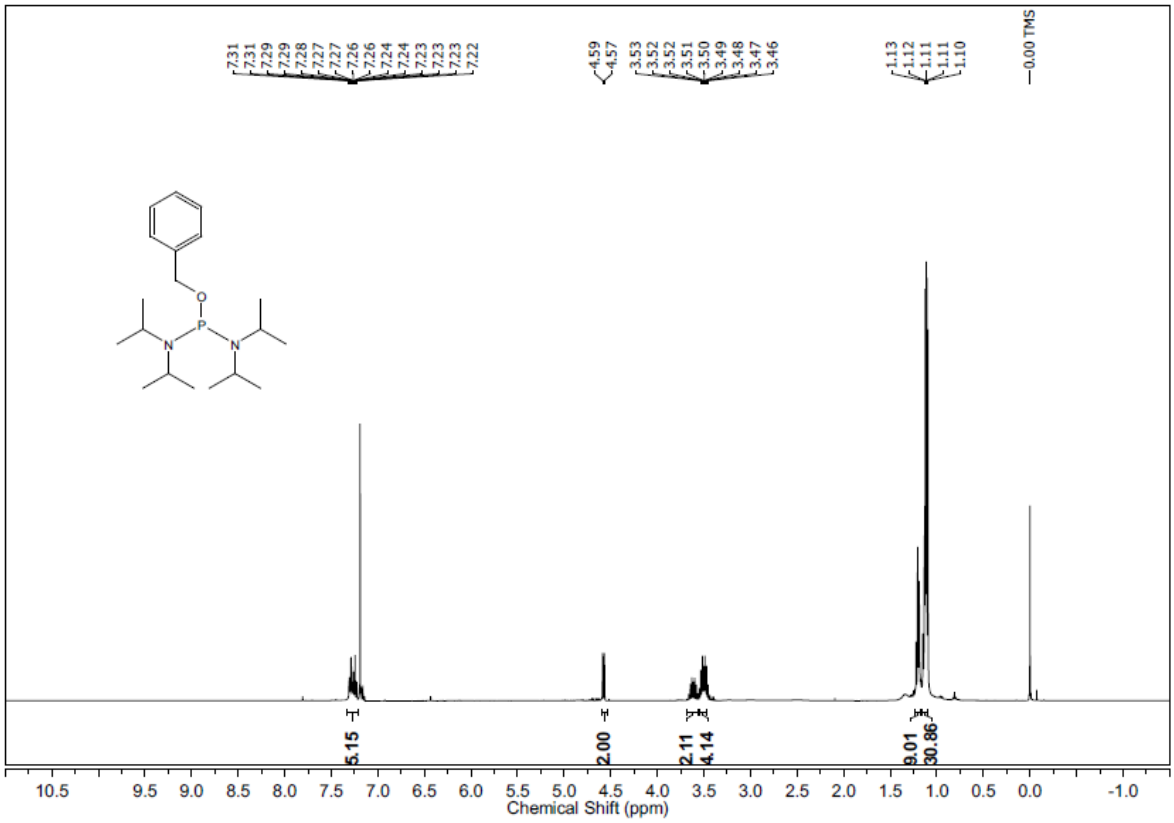
(2*S*)-3-((((*S*)-2-amino-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-hydroxypropyl docosanoate (Compound (*S*)-**2g**): Following the general procedure (**C2**), (*S*)-**9g** (30 mg), TFA (0.240 mL) and CH_2Cl_2 (0.420 mL) were used. The product was washed with *n*-pentane: Et_2O (4:1) (3 x 2 mL) to yield the desired final compound (*S*)-**2g** (21 mg, 0.0352 mmol, 74% yield relative to (*S*)-**8g**) as a white solid: ^{1}H NMR (400 MHz, MeOH-d_4 + $CDCl_3$ (1:2 ratio)) δ 4.36-4.15 (m, 3H), 4.14-4.04 (m, 2H), 4.03-3.90 (m, 2H), 3.84 (s, 3H), 3.77-3.55 (m, 1H), 2.32 (t, *J* = 7.4Hz, 2H), 1.59 (m, 2H), 1.33-1.19 (m, 36H), 0.85 (t, *J* = 6.3 Hz, 3H); ^{31}P NMR (400 MHz, MeOH-d_4) δ 0.45; HRMS (ESI): m/z calcd. for ($C_{29}H_{59}NO_9P$) $[M + H]^+$ 596.3922; found, 596.3924.



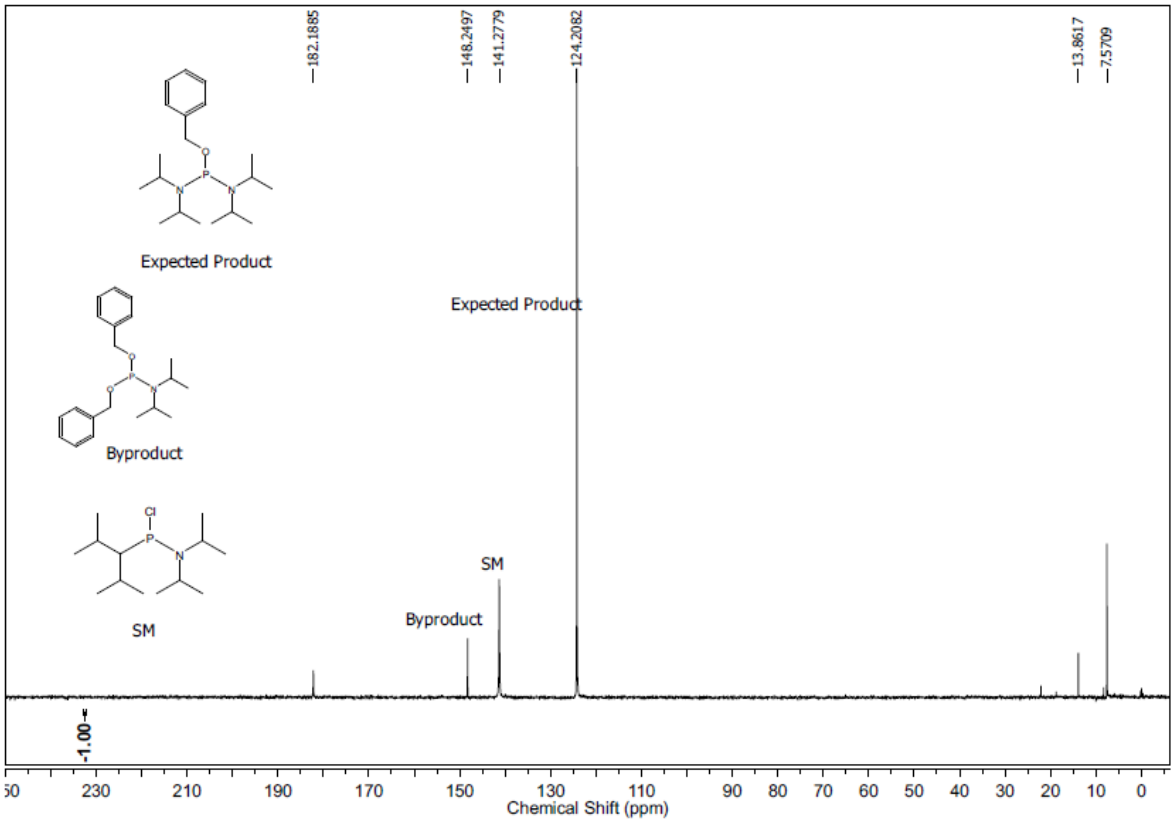
(2*S*)-3-((((*S*)-2-amino-3-methoxy-3-oxopropoxy)(hydroxy)phosphoryl)oxy)-2-hydroxypropyl tetracosanoate (Compound (*S*)-**2h**): Following the general procedure (**C2**), (*S*)-**9h** (26 mg), TFA (0.210 mL) and CH_2Cl_2 (0.360 mL) were used. The product was washed with *n*-pentane: Et_2O (4:1) (3 x 2 mL) to yield the desired final compound (*S*)-**2h** (15 mg, 0.0240 mmol, 81% yield relative to (*S*)-**8h**) as a white solid: ^{1}H NMR (400 MHz, MeOH-

d_4 + $CDCl_3$ (1:2 ratio)) δ 4.34-4.05 (m, 5H), 4.03-3.88 (m, 3H), 3.84 (s, 3H), 3.72-3.53 (m, 1H), 2.31 (m, 2H), 1.58 (m, 2H), 1.33-1.14 (m, 40H), 0.85 (m, 3H); ^{31}P NMR (400 MHz, MeOH-d_4) δ 0.44; HRMS (ESI): m/z calcd. for ($C_{31}H_{63}NO_9P$) $[M + H]^+$ 624.4235; found, 634.4233.

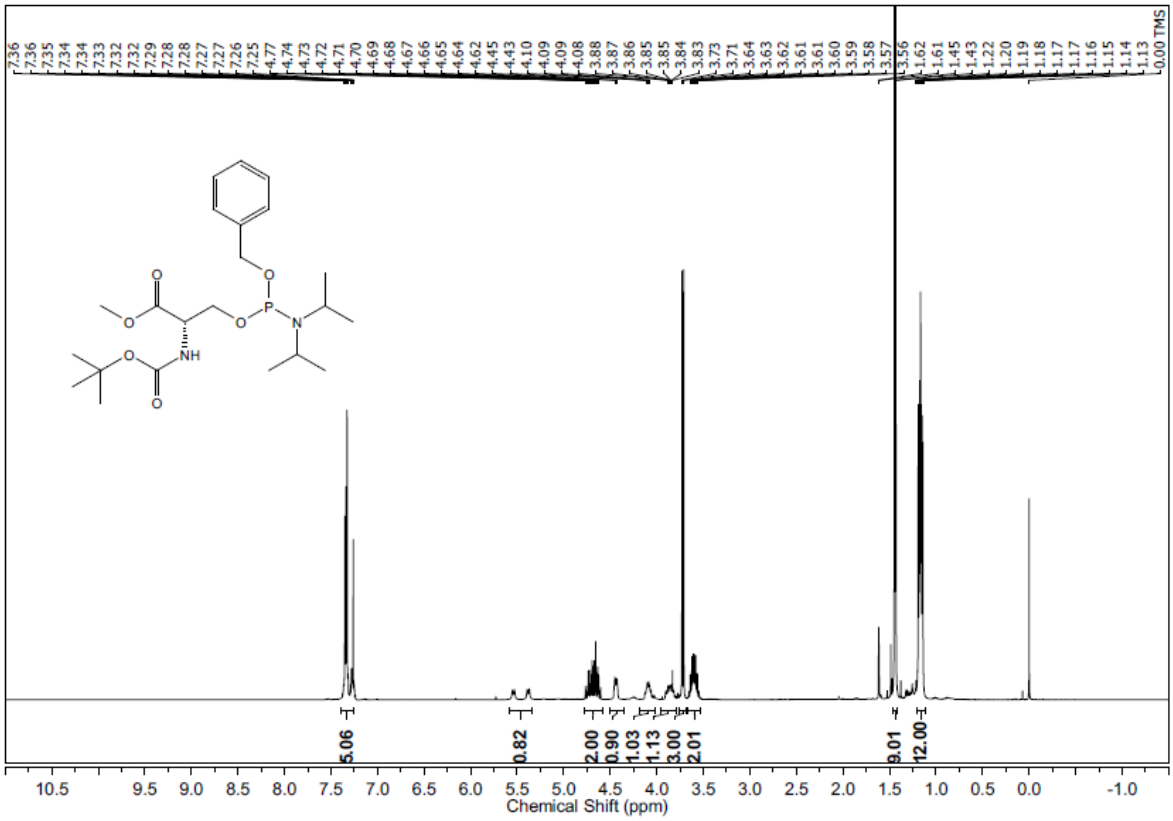
^{1}H NMR of compound **10**



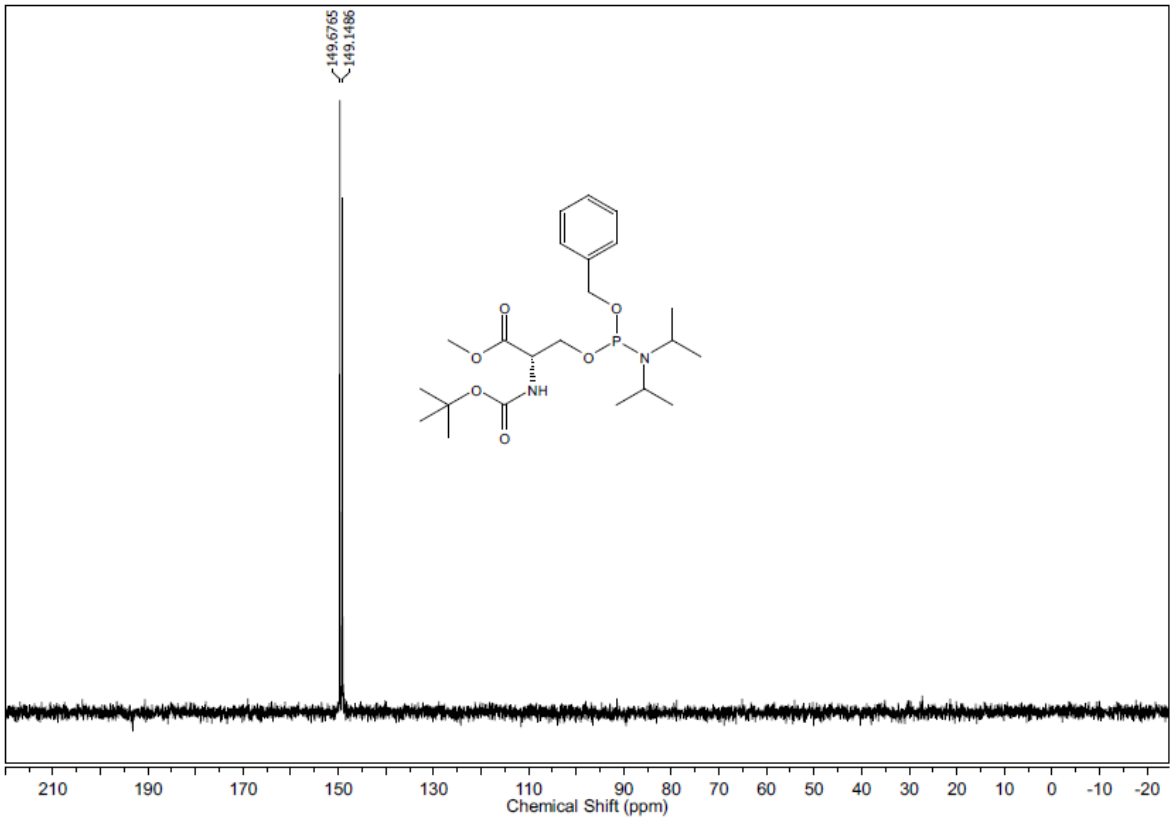
^{31}P NMR of compound **10**



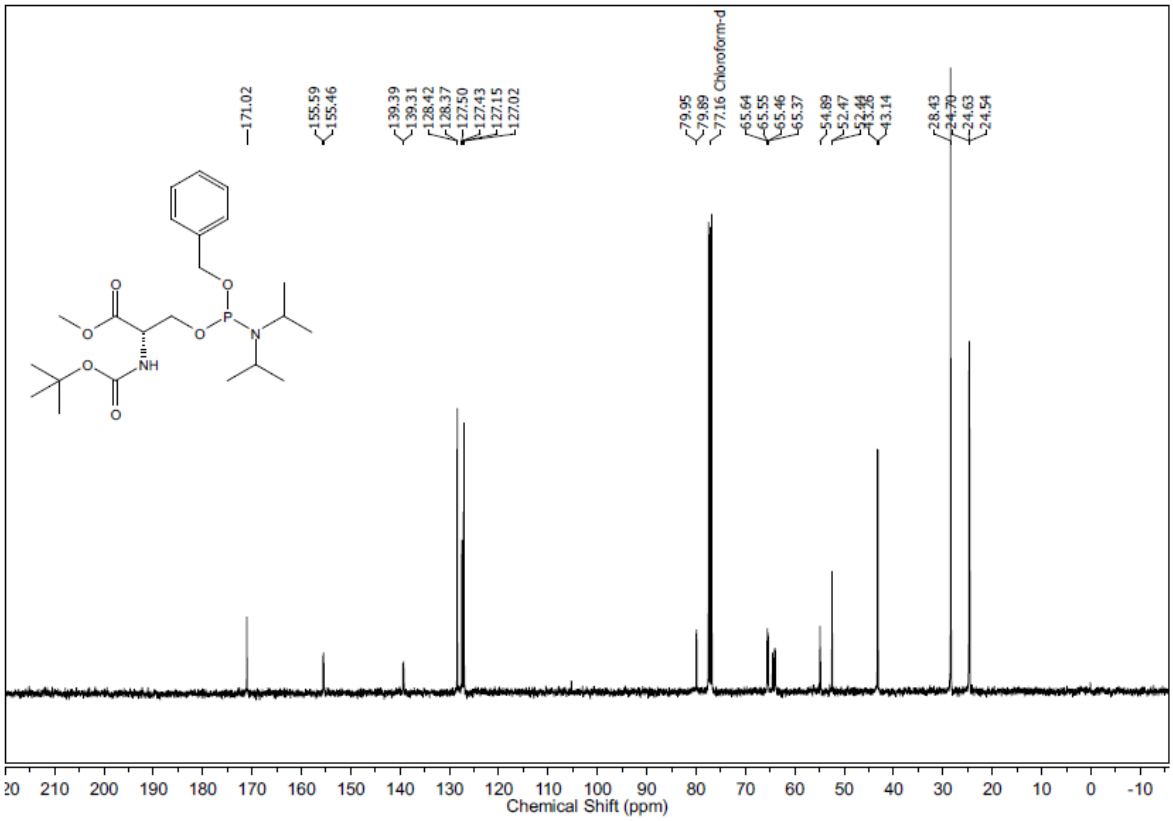
^{1}H NMR of compound **3**



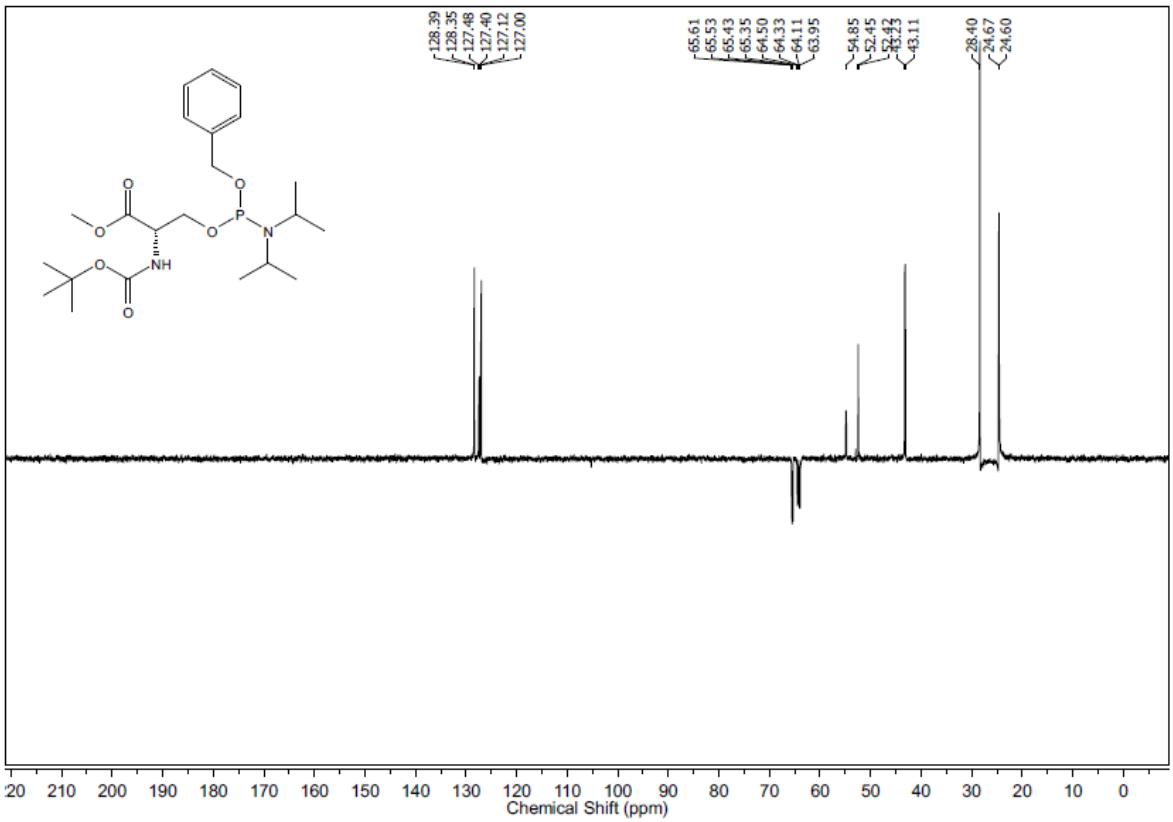
^{31}P NMR of compound **3**



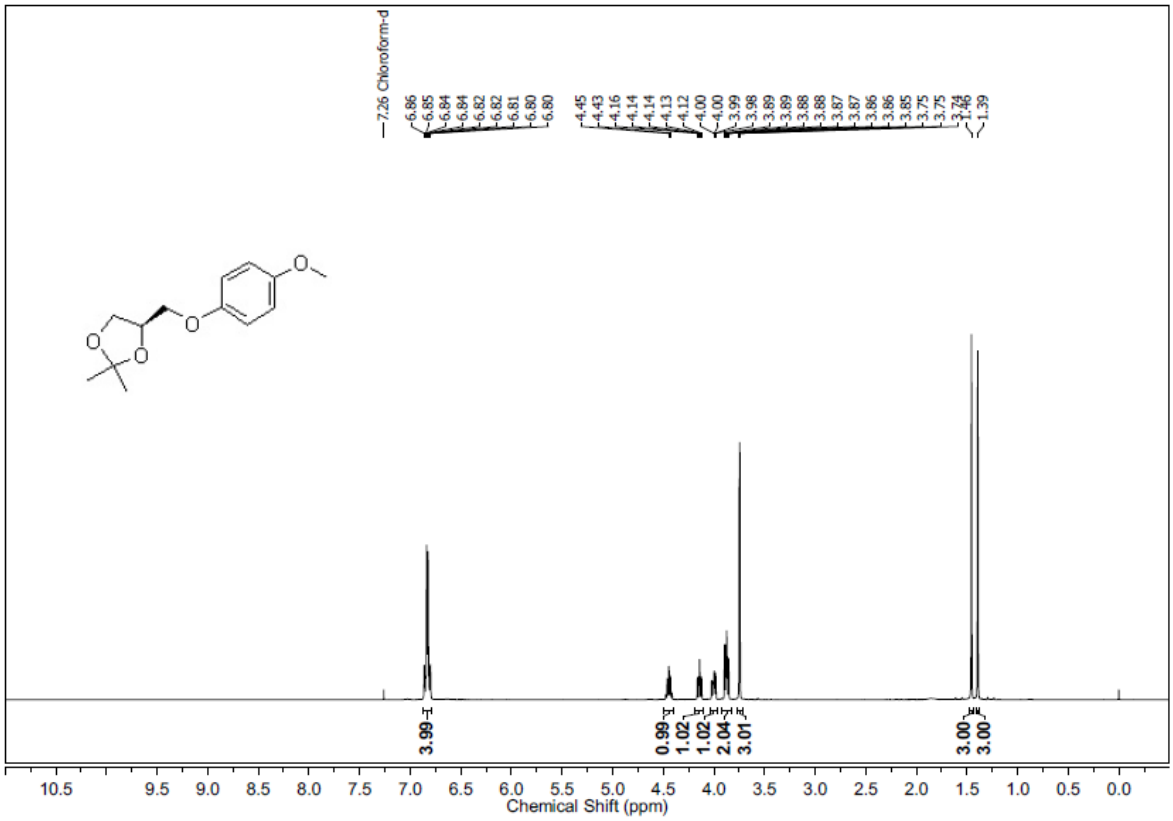
^{13}C NMR of compound **3**



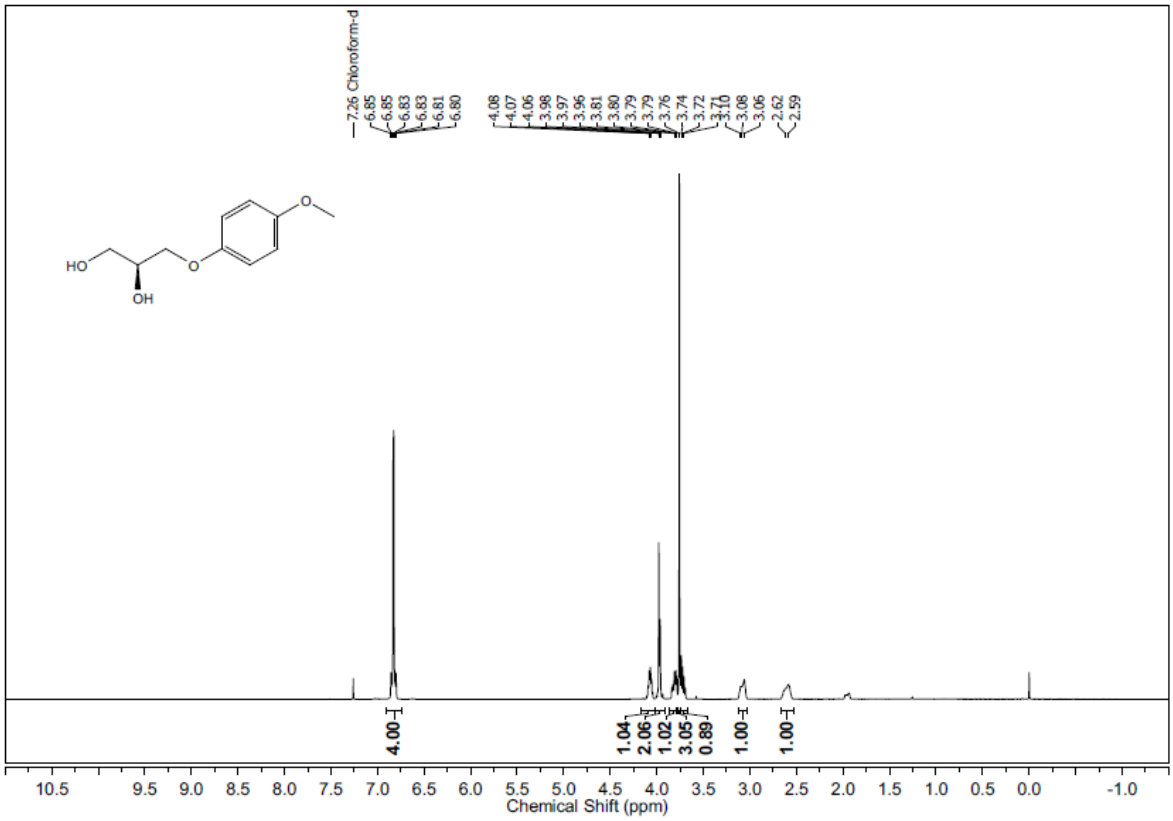
DEPT-135 NMR of compound **3**



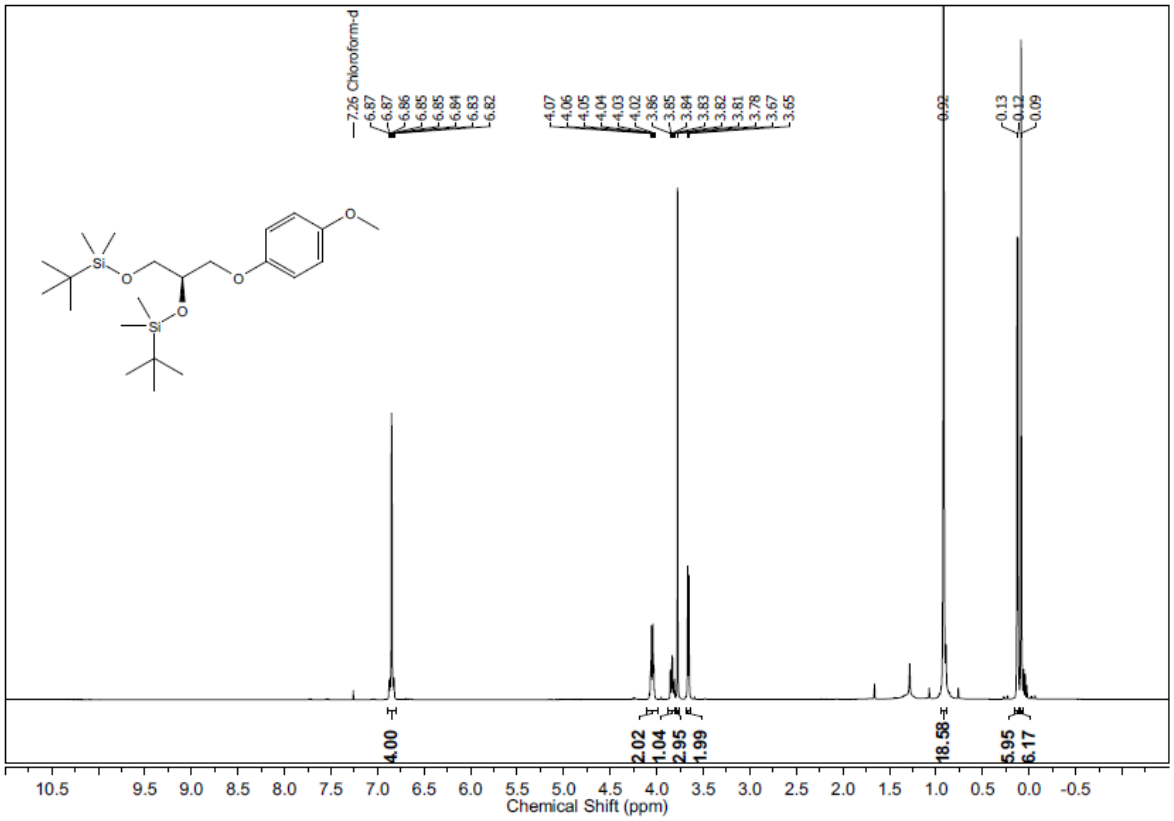
^{1}H NMR of compound (*R*)-**11**



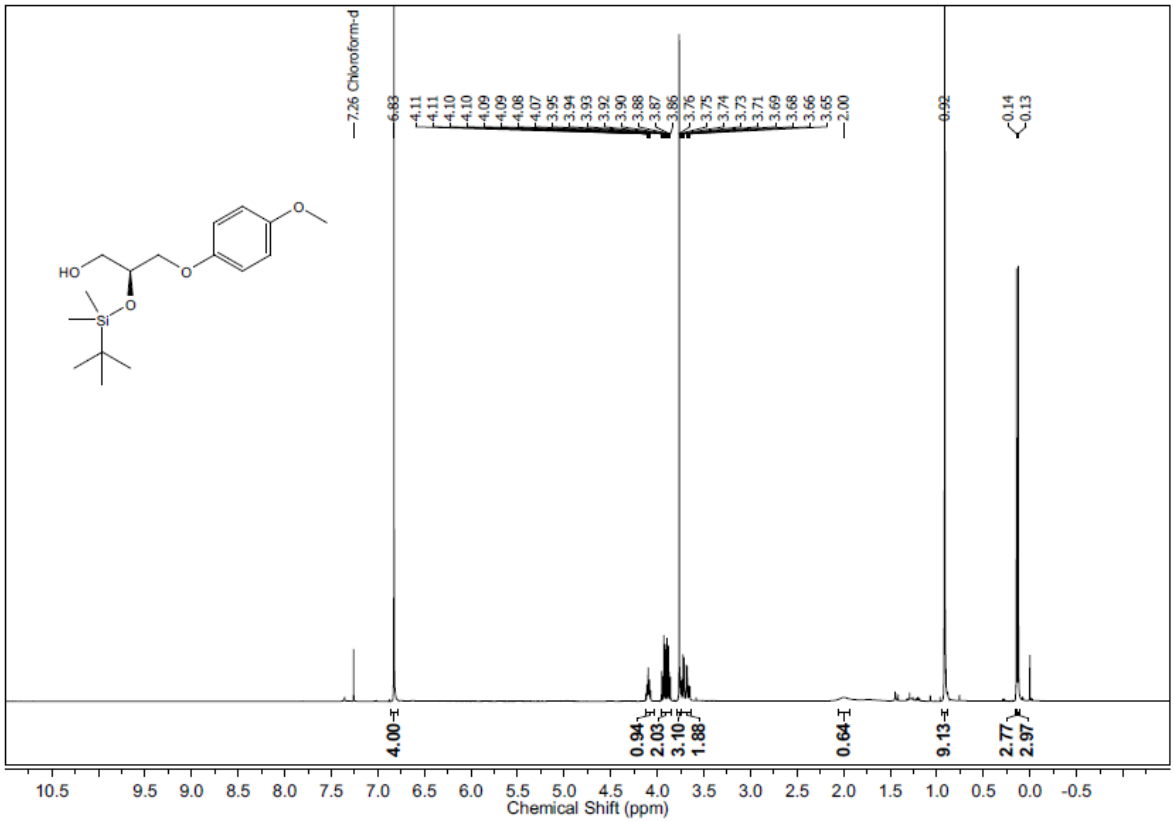
^{1}H NMR of compound (*R*)-**12**



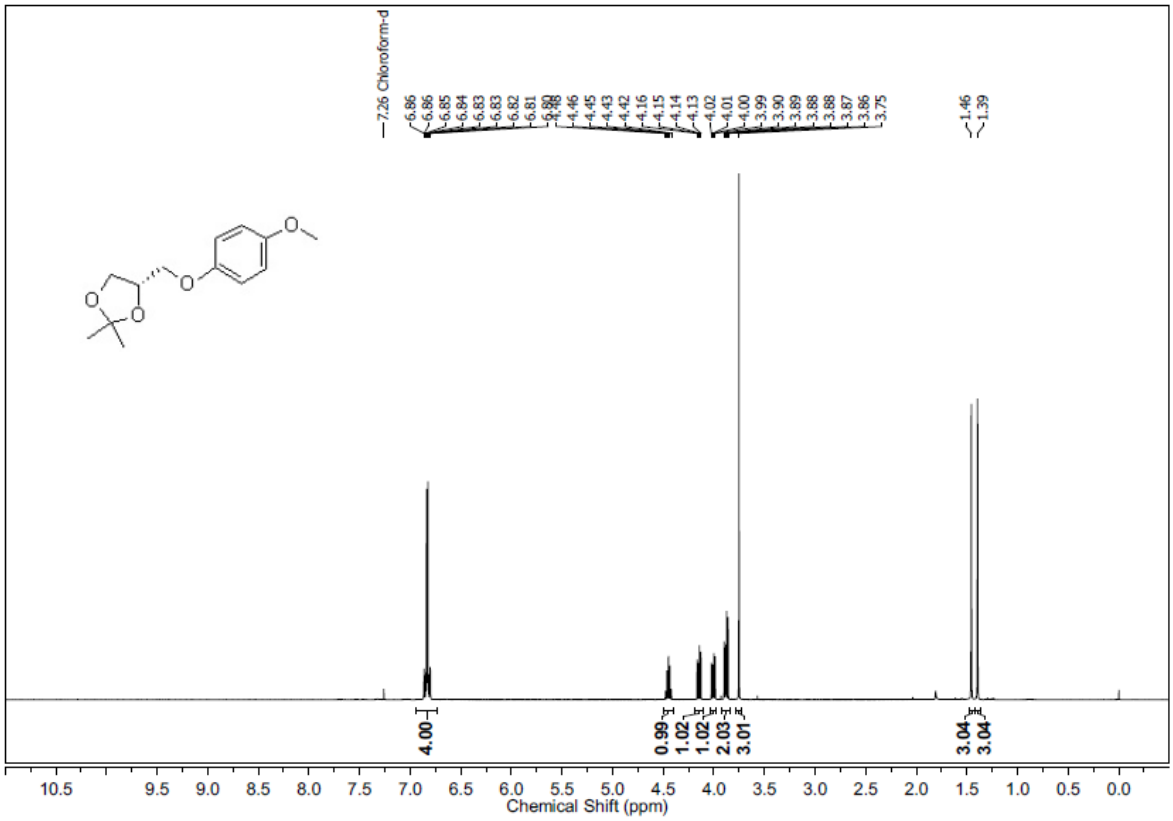
^{1}H NMR of compound (*R*)-**13**



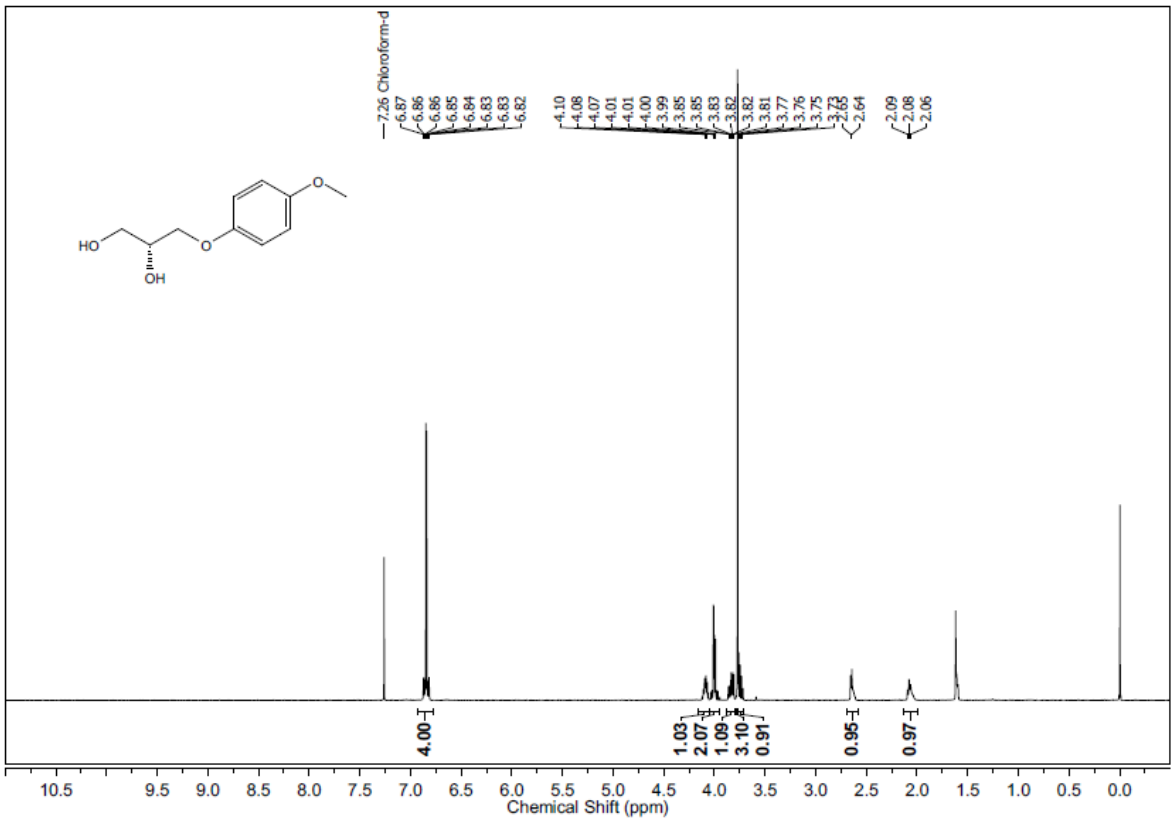
^{1}H NMR of compound (*R*)-**4**



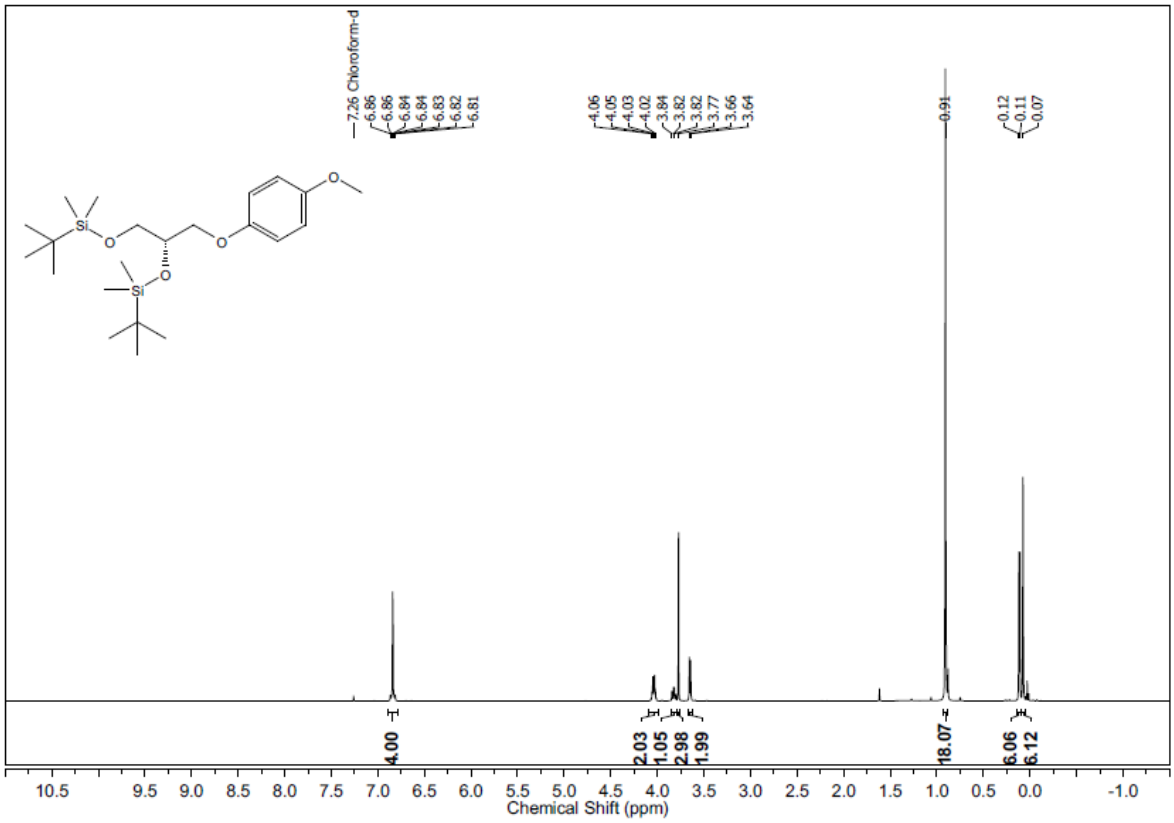
^{1}H NMR of compound (*S*)-**11**



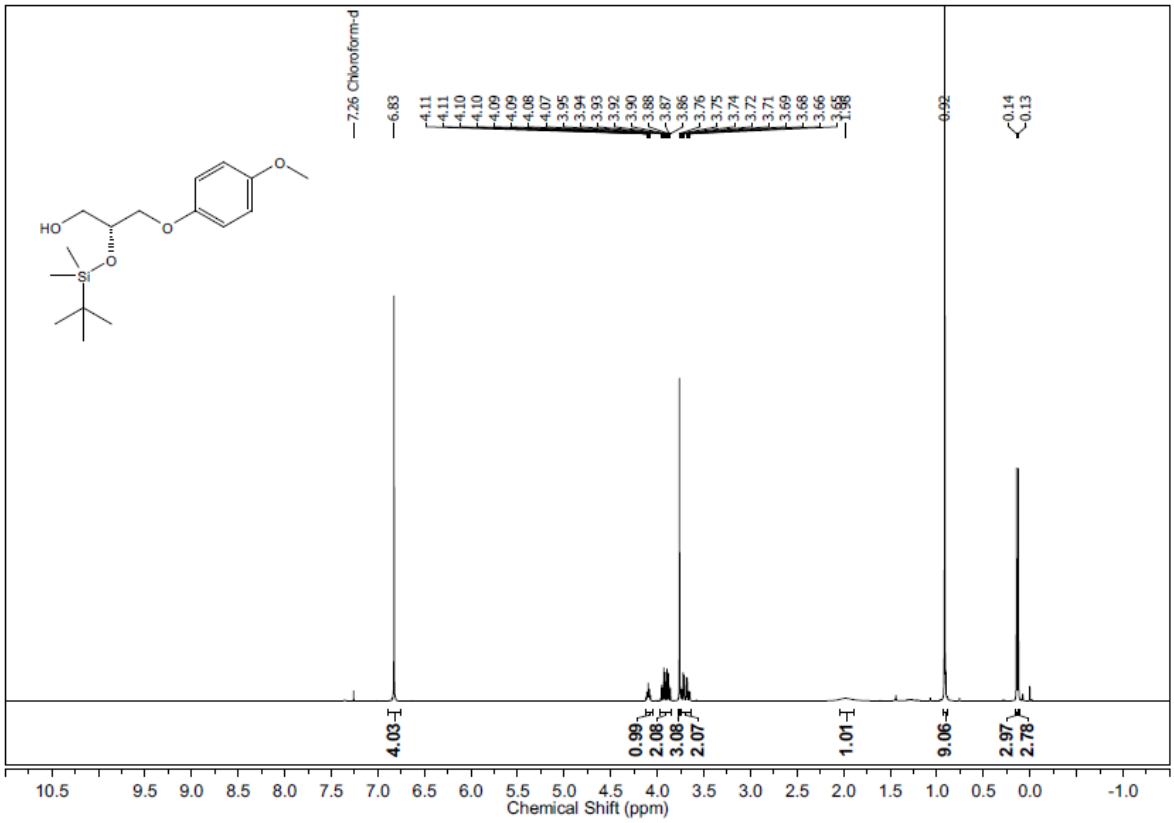
^{1}H NMR of compound (*S*)-**12**



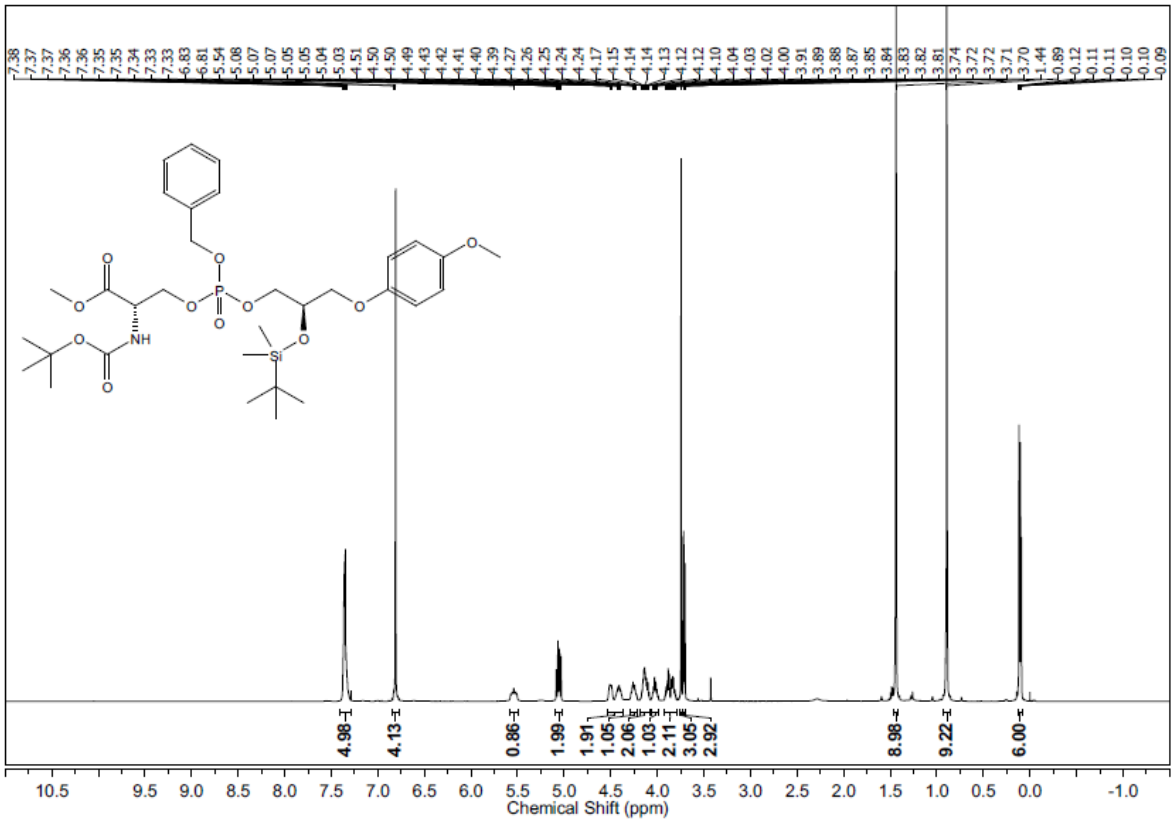
^{1}H NMR of compound (*S*)-**13**



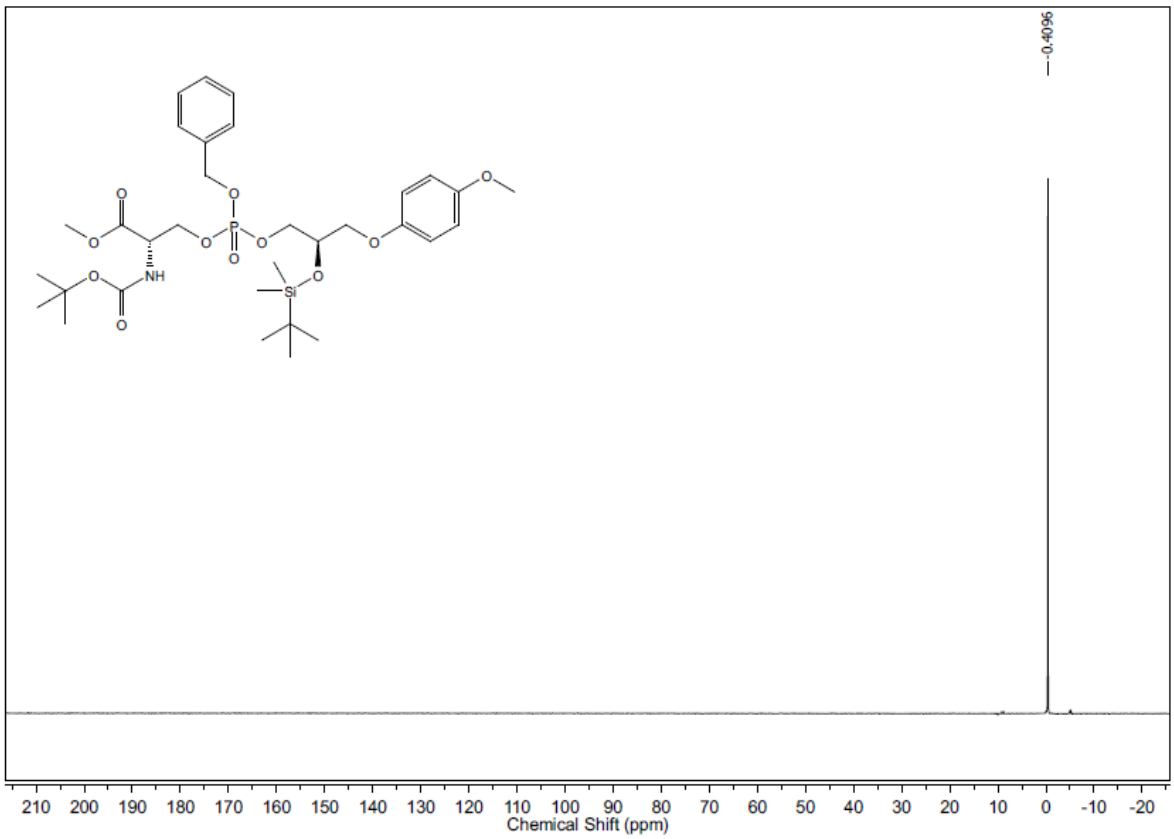
^{1}H NMR of compound (*S*)-**4**



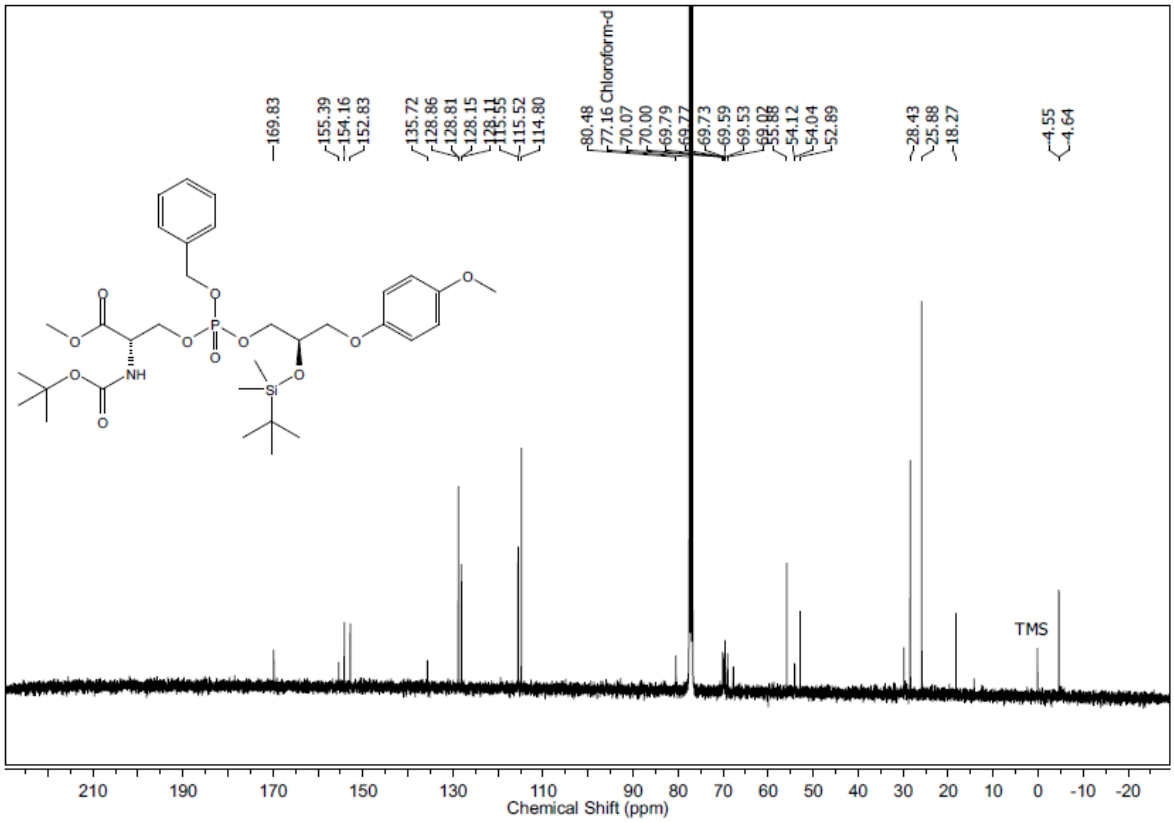
^{1}H NMR of compound (*R*)-**5**



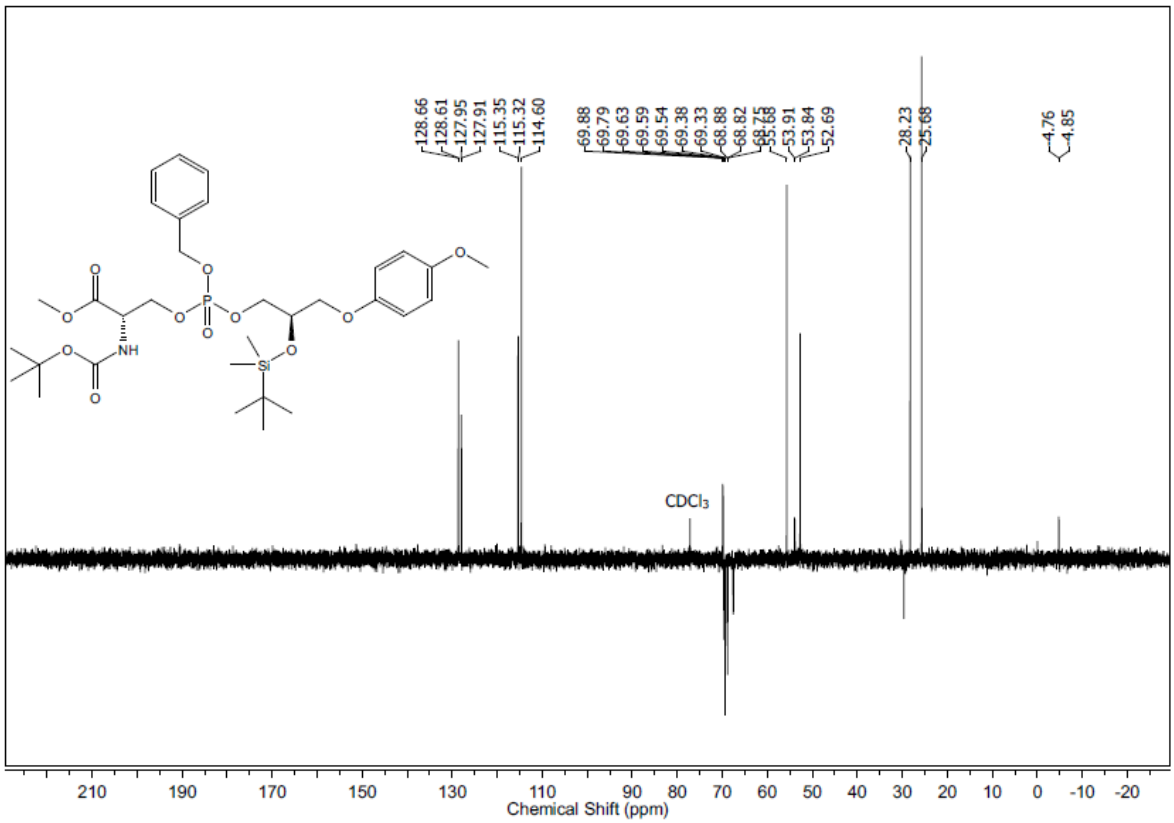
^{31}P NMR of compound (*R*)-**5**



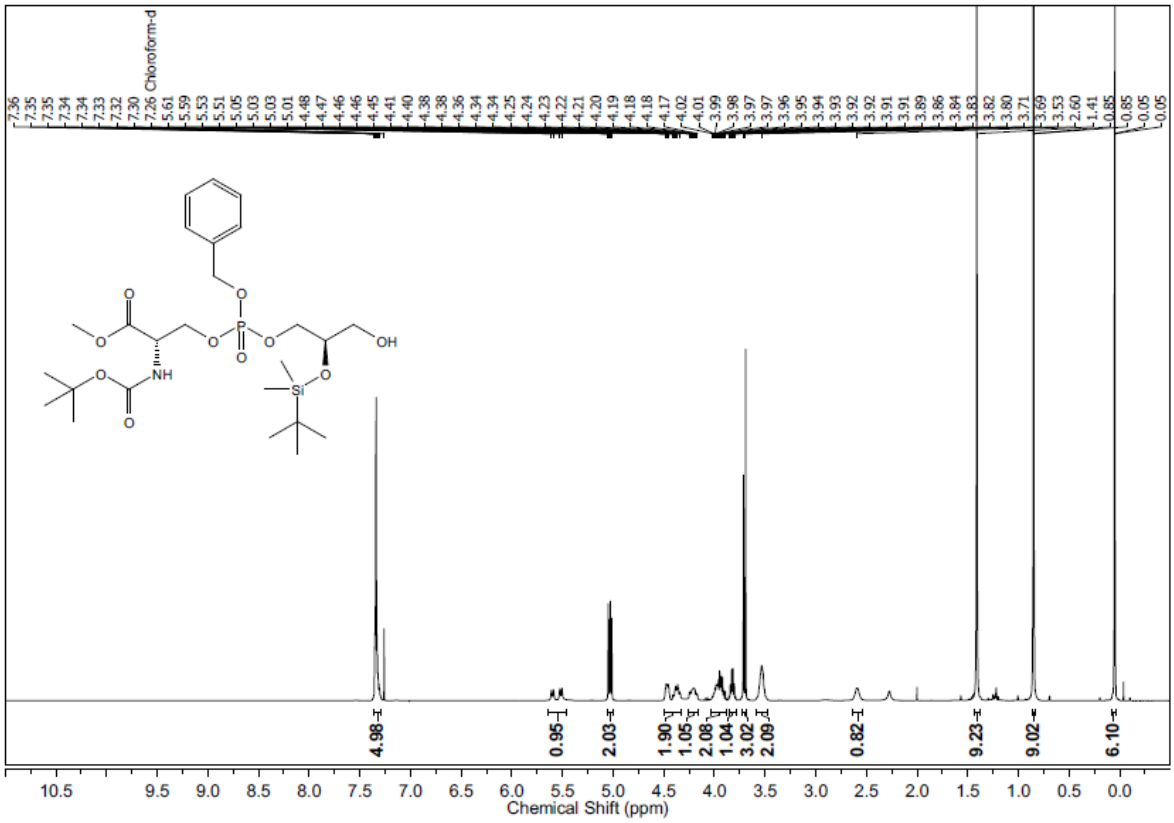
^{13}C NMR of compound (*R*)-**5**



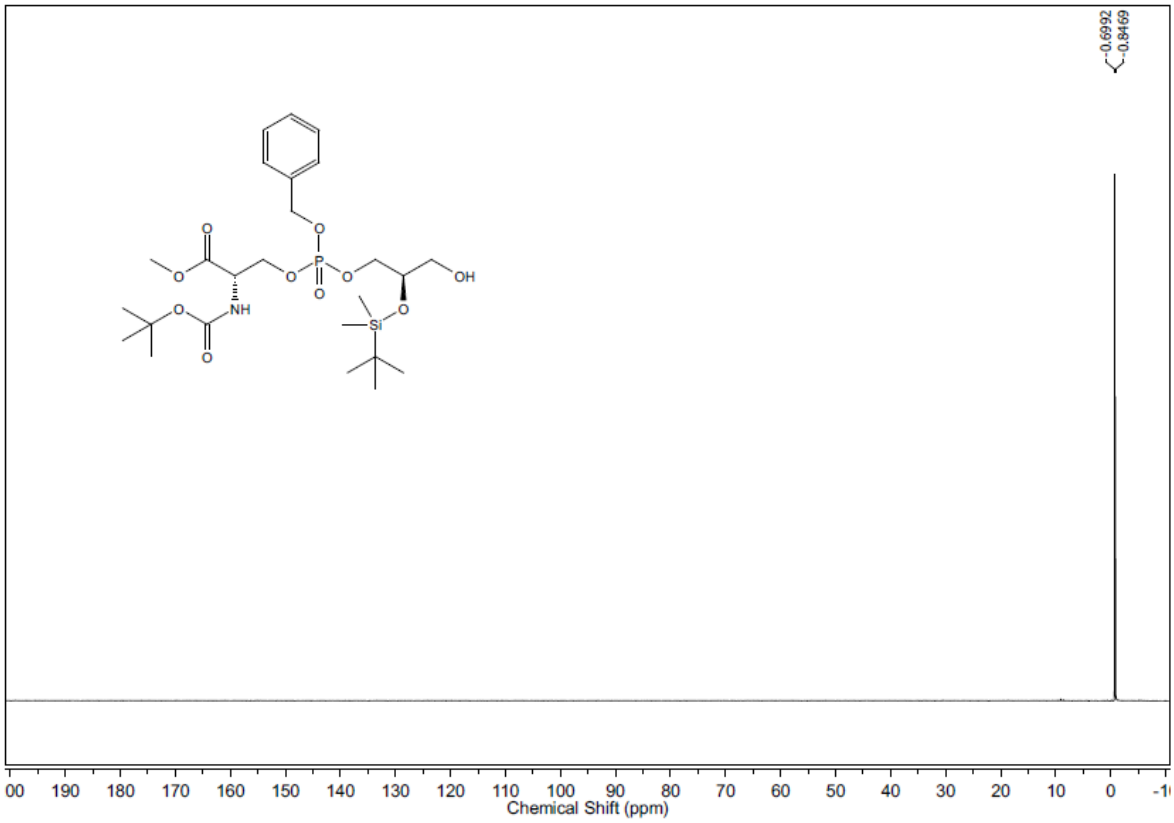
DEPT-135 NMR of compound (*R*)-**5**



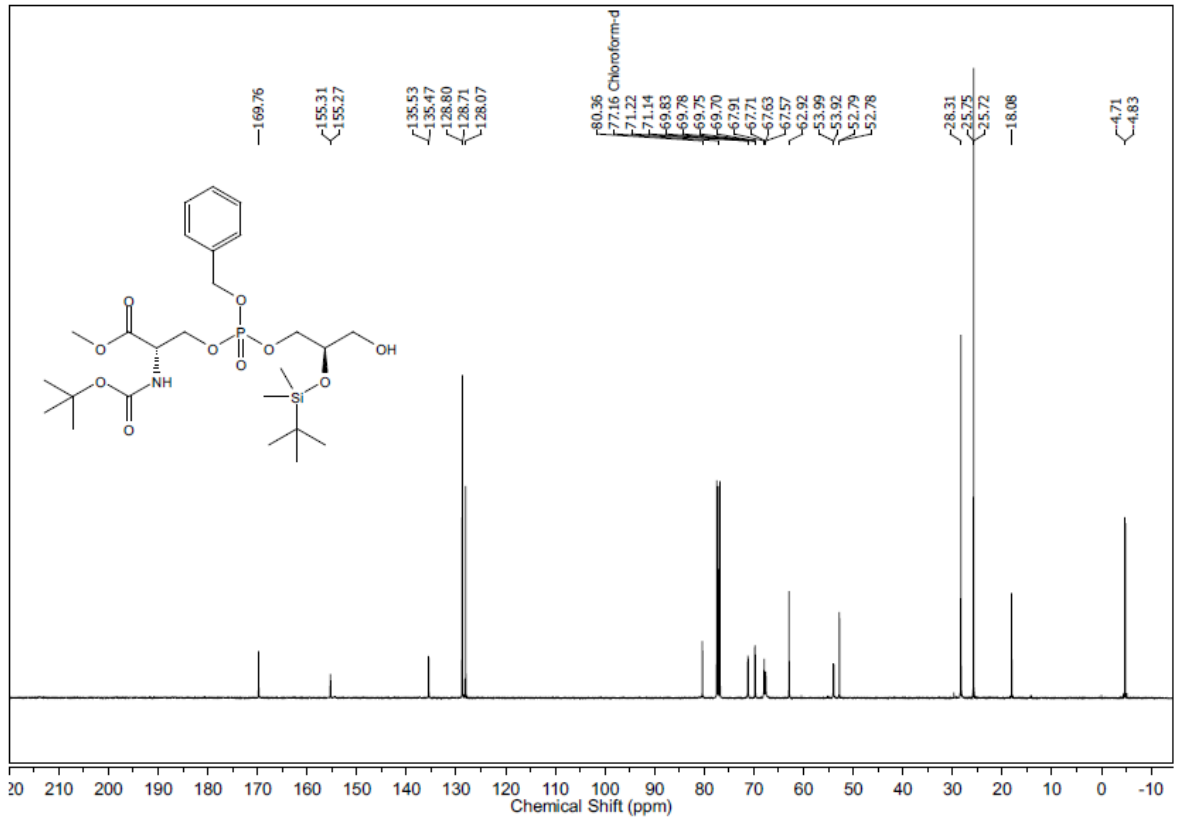
^{1}H NMR of compound (*R*)-**6**



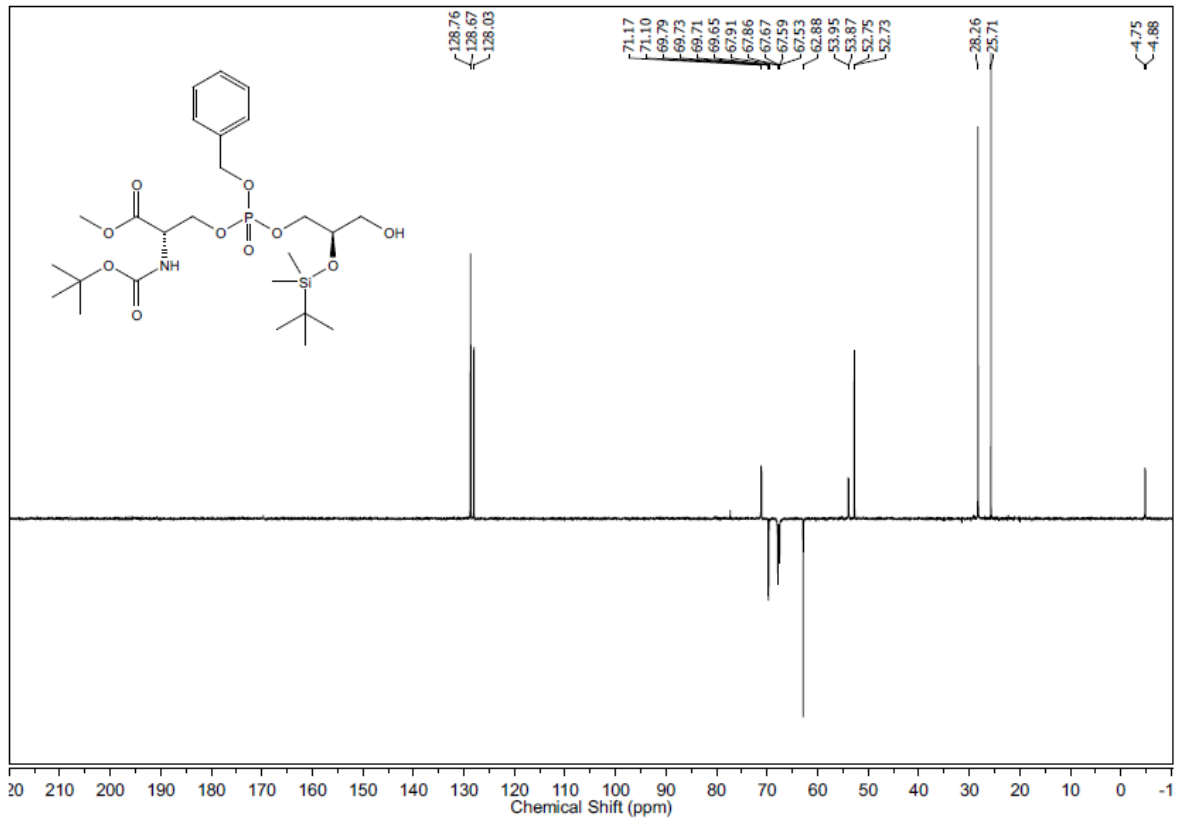
^{31}P NMR of compound (*R*)-**6**



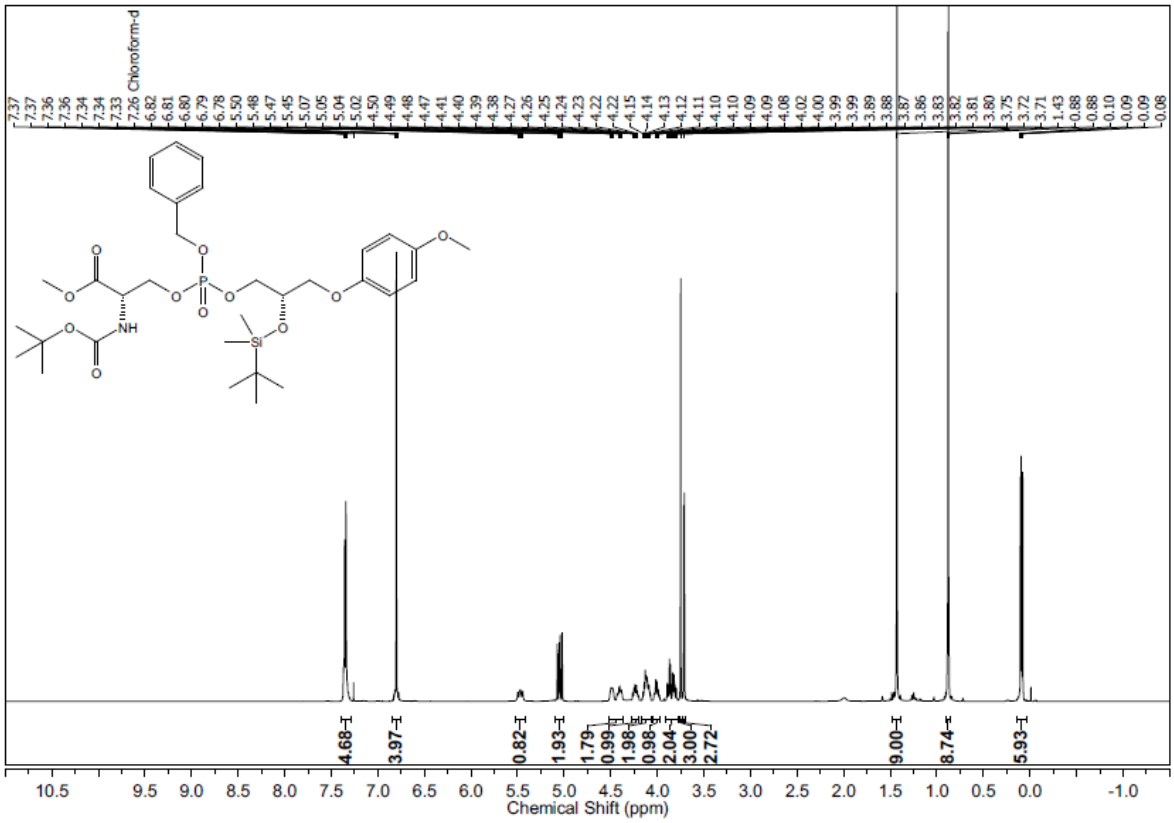
^{13}C NMR of compound (*R*)-**6**



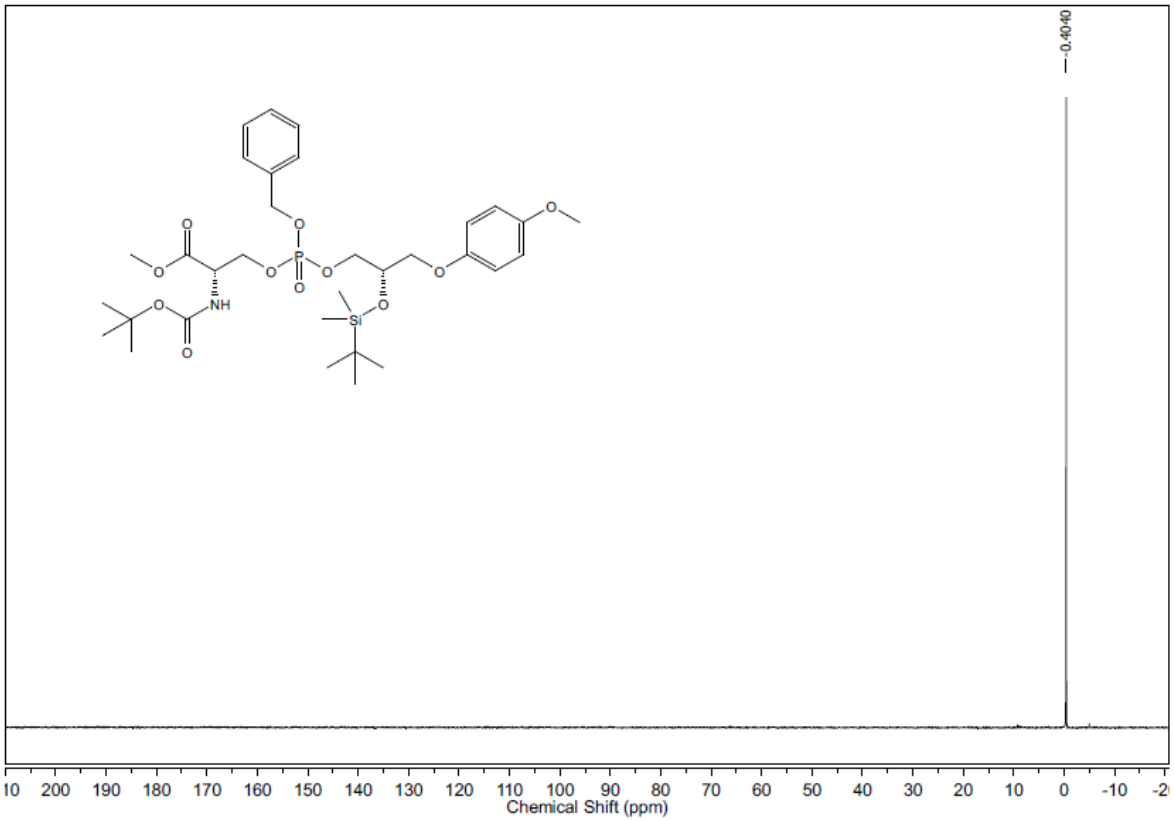
DEPT-135 NMR of compound (*R*)-**6**



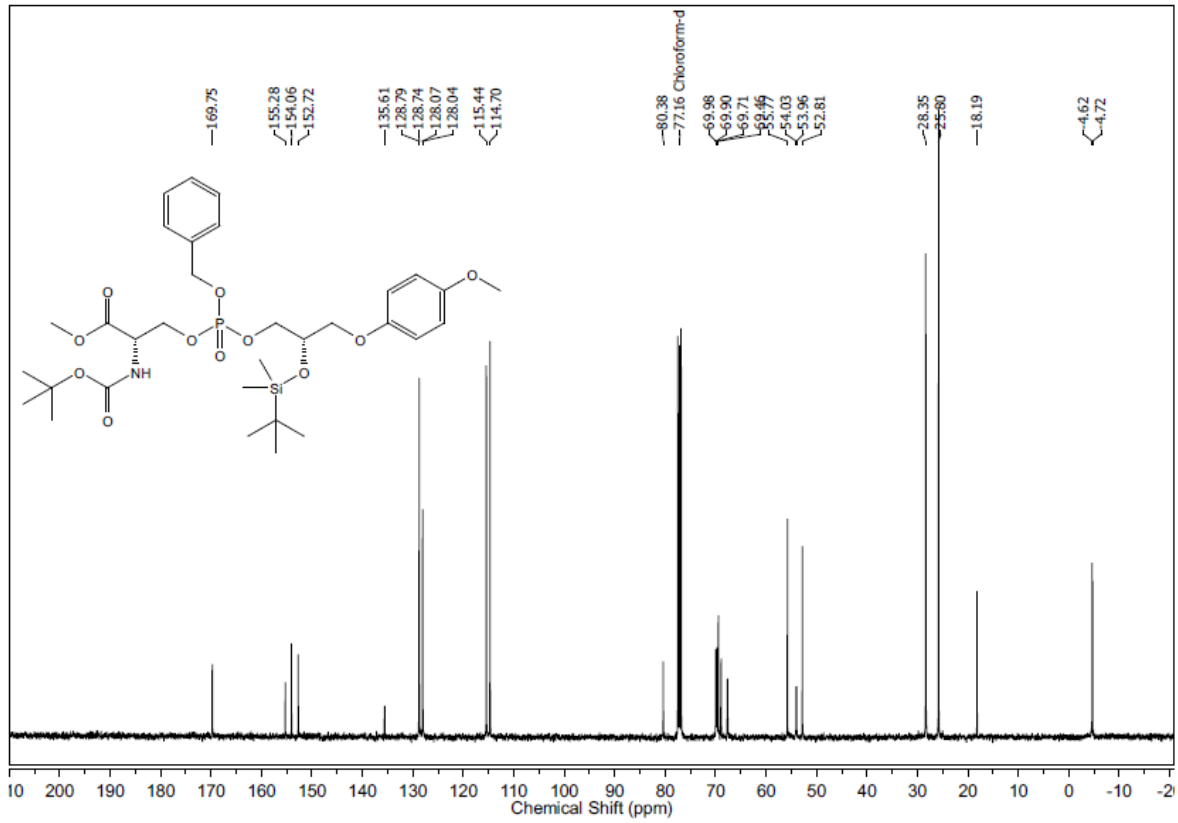
^{1}H NMR of compound (*S*)-**5**



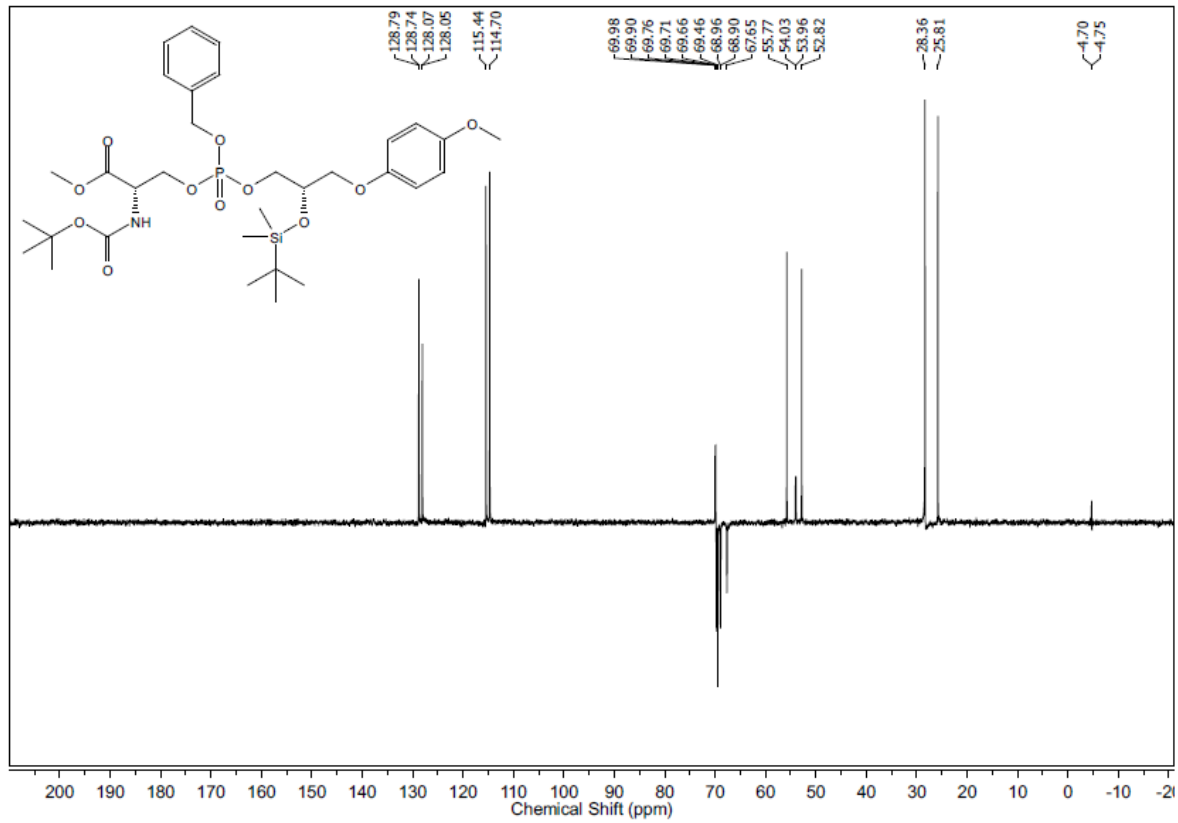
^{31}P NMR of compound (*S*)-**5**



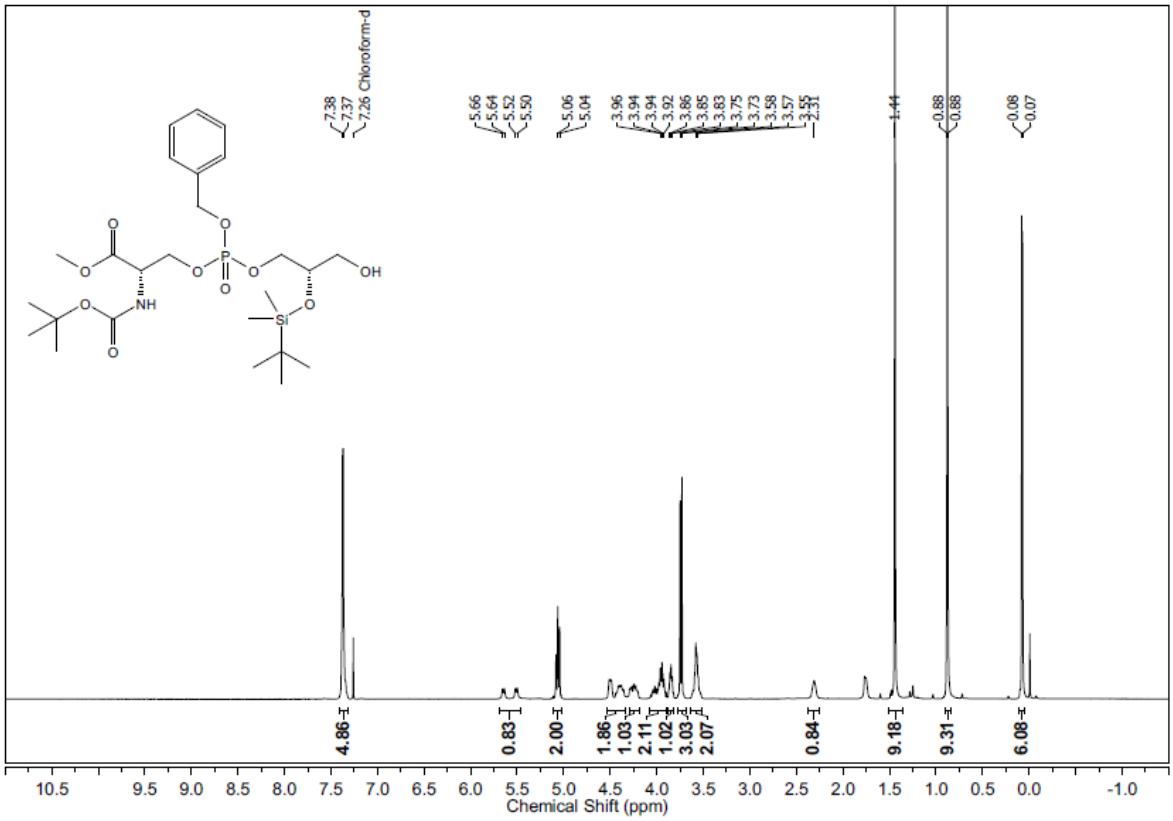
^{13}C NMR of compound (*S*)-**5**



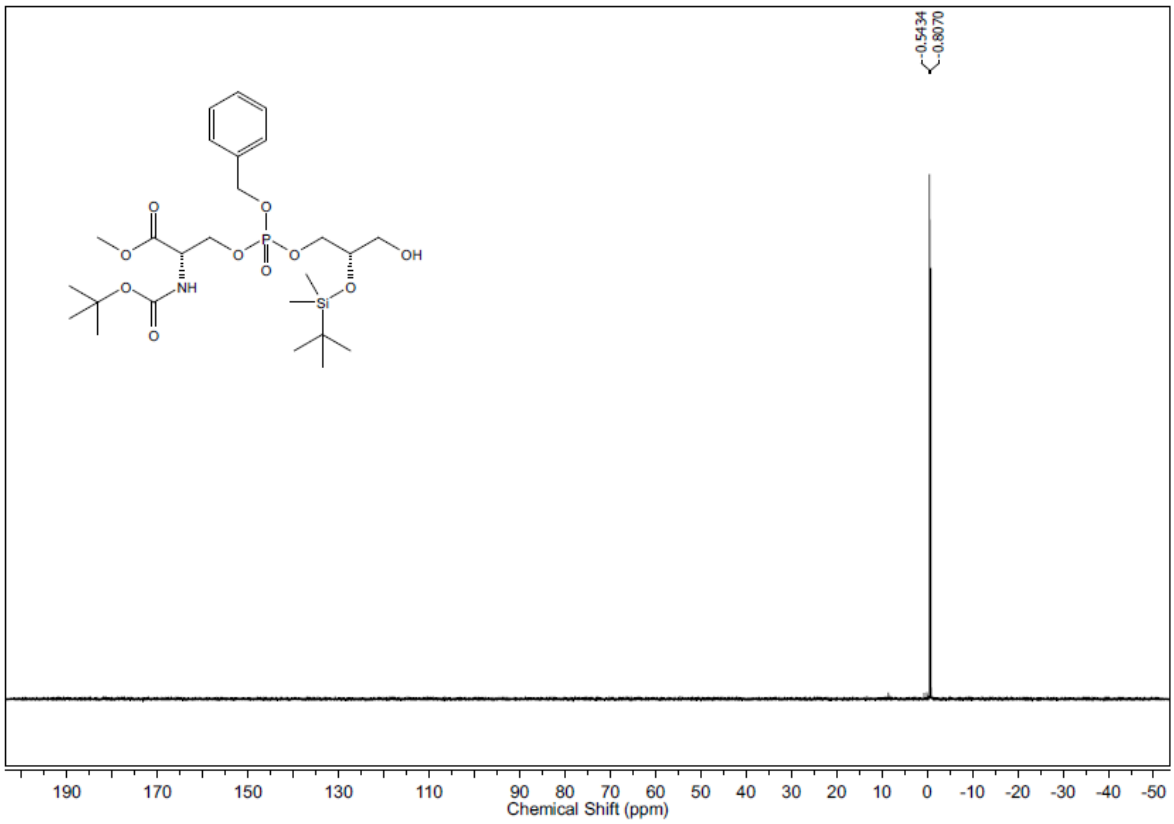
DEPT-135 NMR of compound (*S*)-**5**



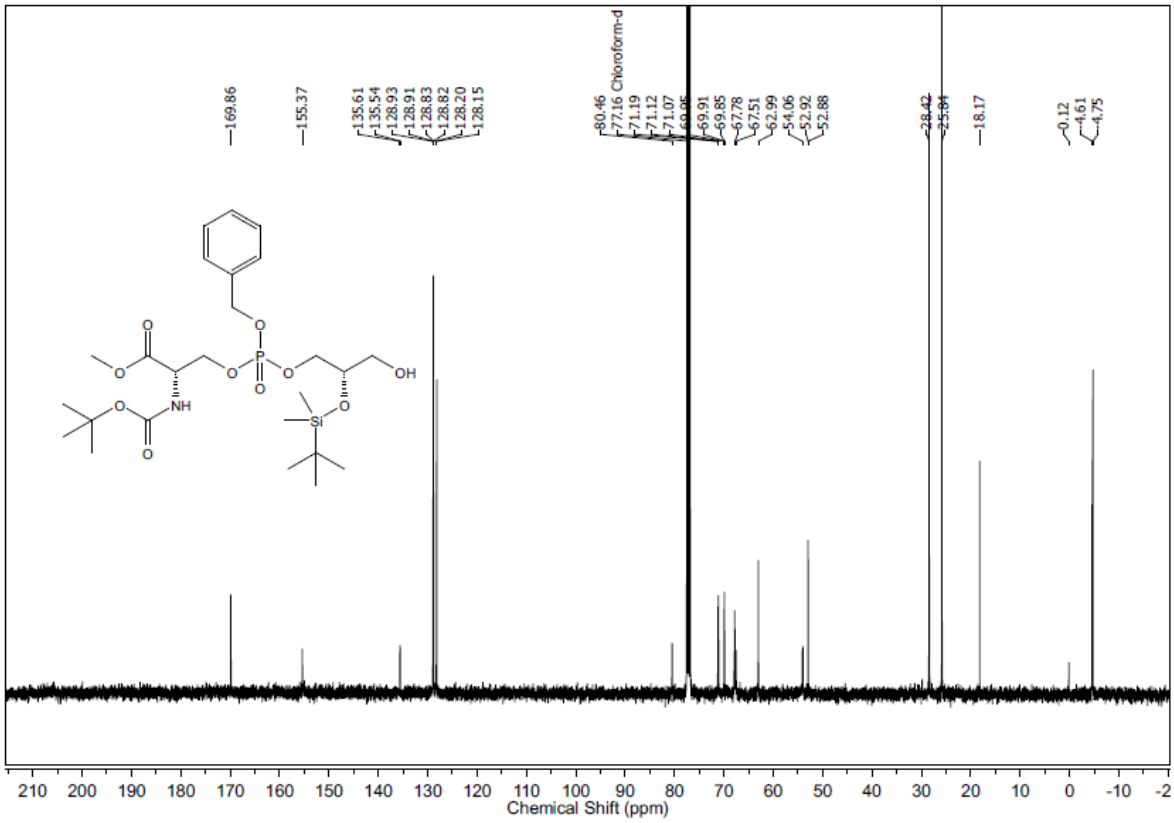
^{1}H NMR of compound (*S*)-**6**



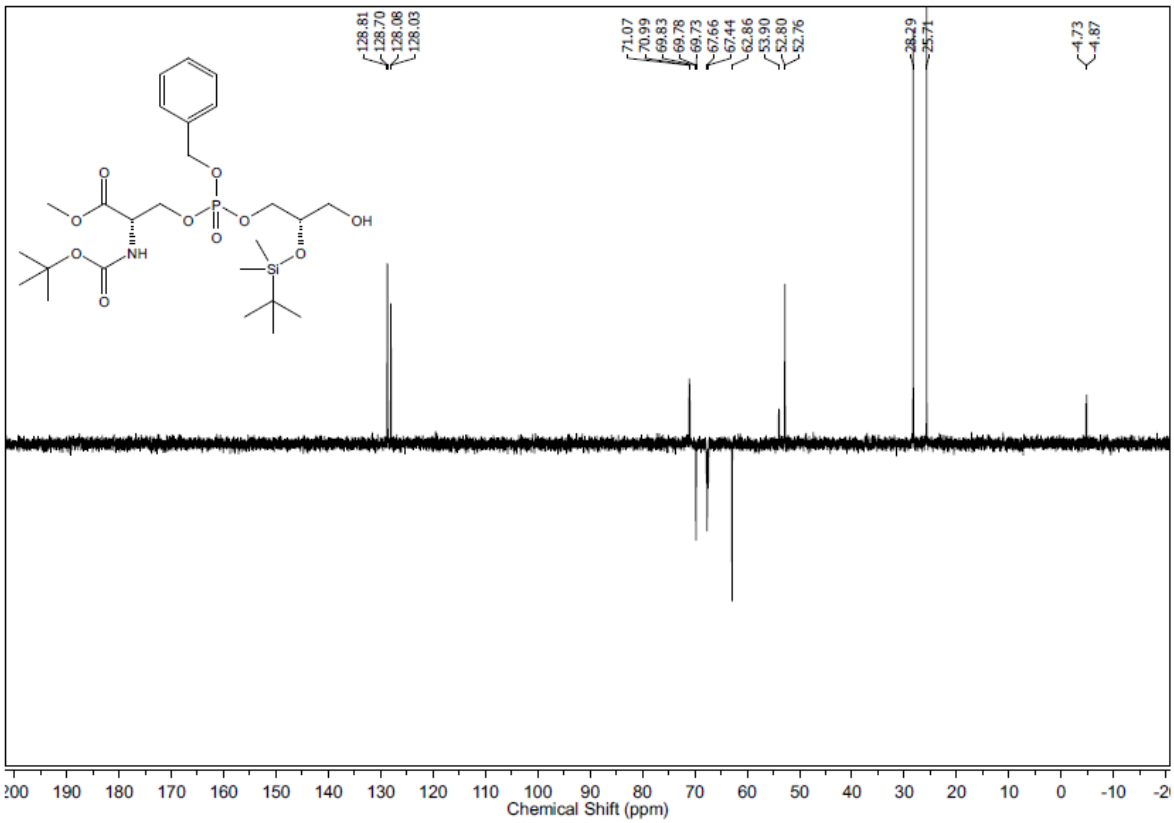
^{31}P NMR of compound (*S*)-**6**



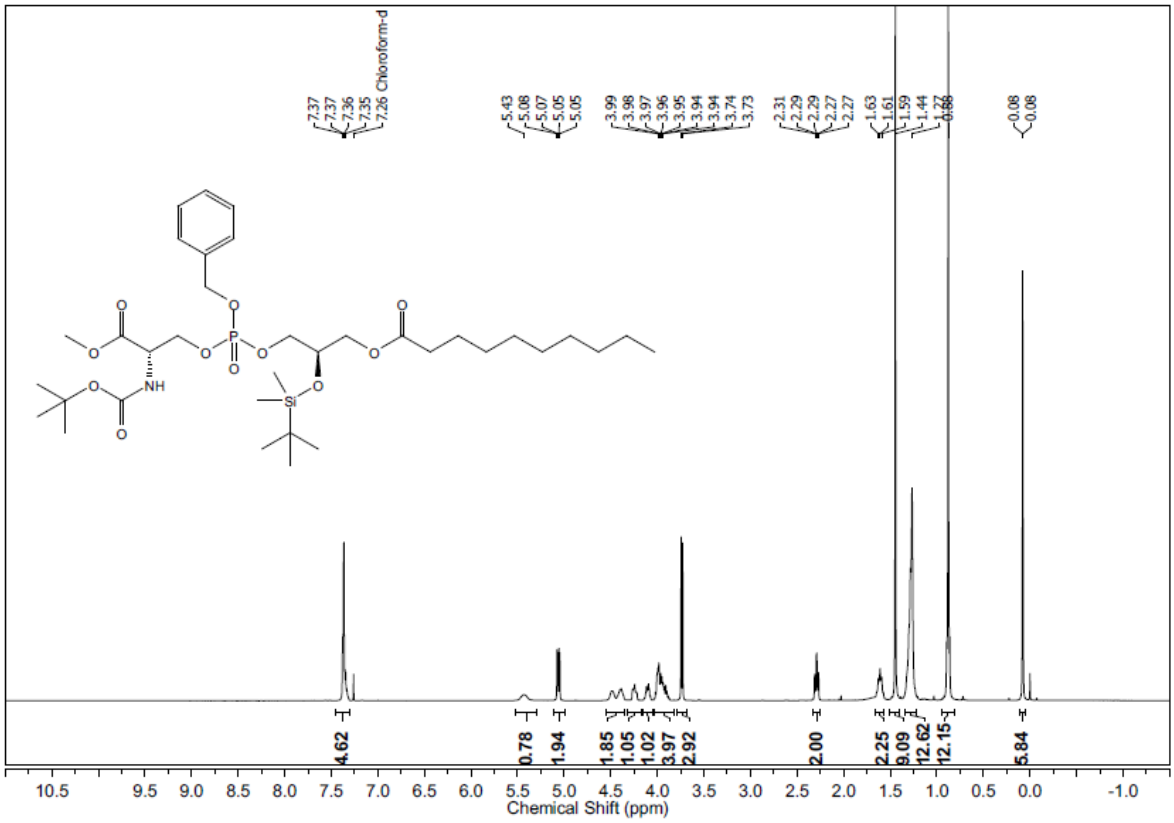
^{13}C NMR of compound (*S*)-**6**



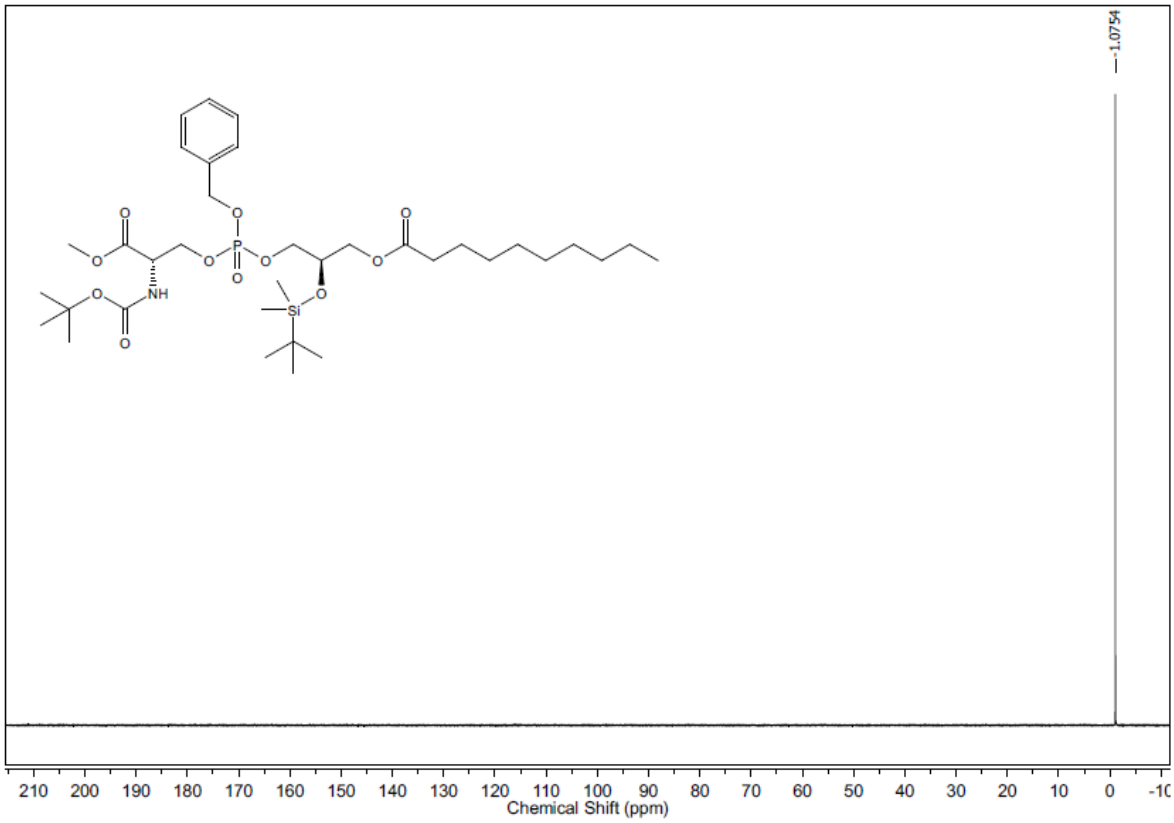
DEPT-135 NMR of compound (*S*)-**6**



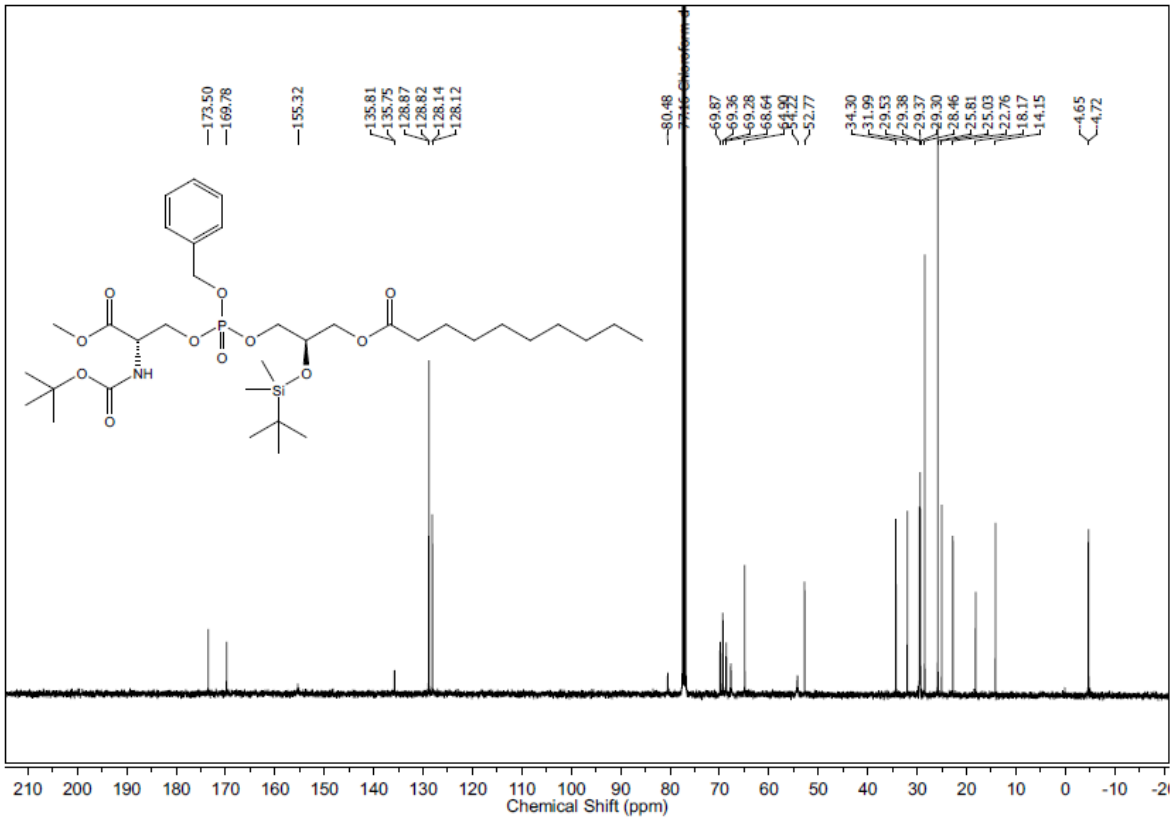
^{1}H NMR of compound (*R*)-**8a**



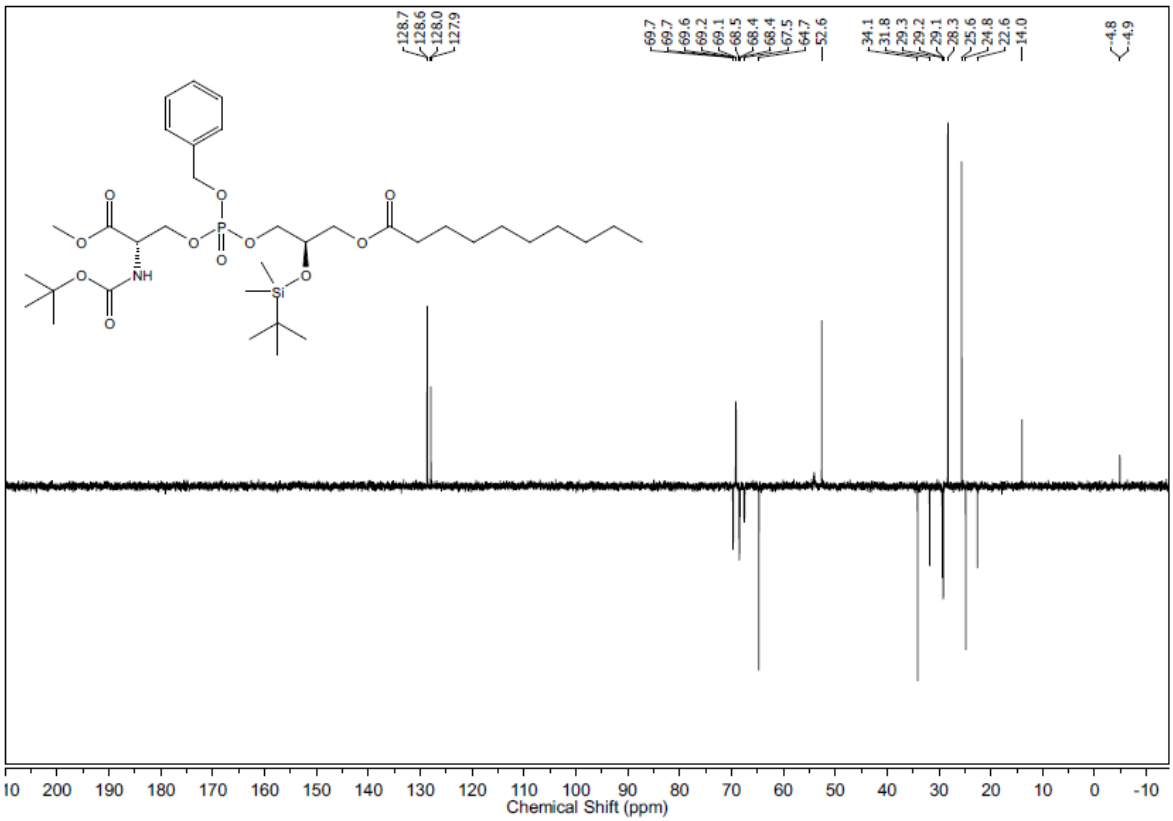
^{31}P NMR of compound (*R*)-**8a**



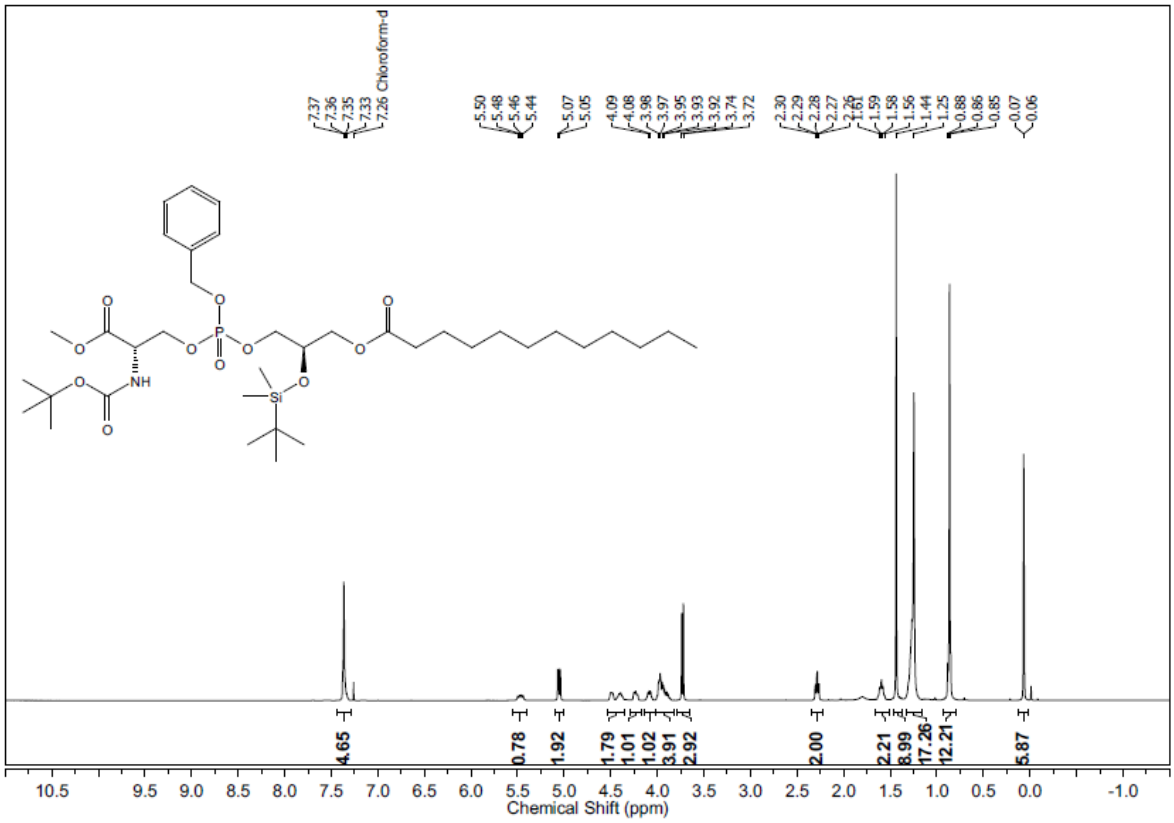
^{13}C NMR of compound (*R*)-**8a**



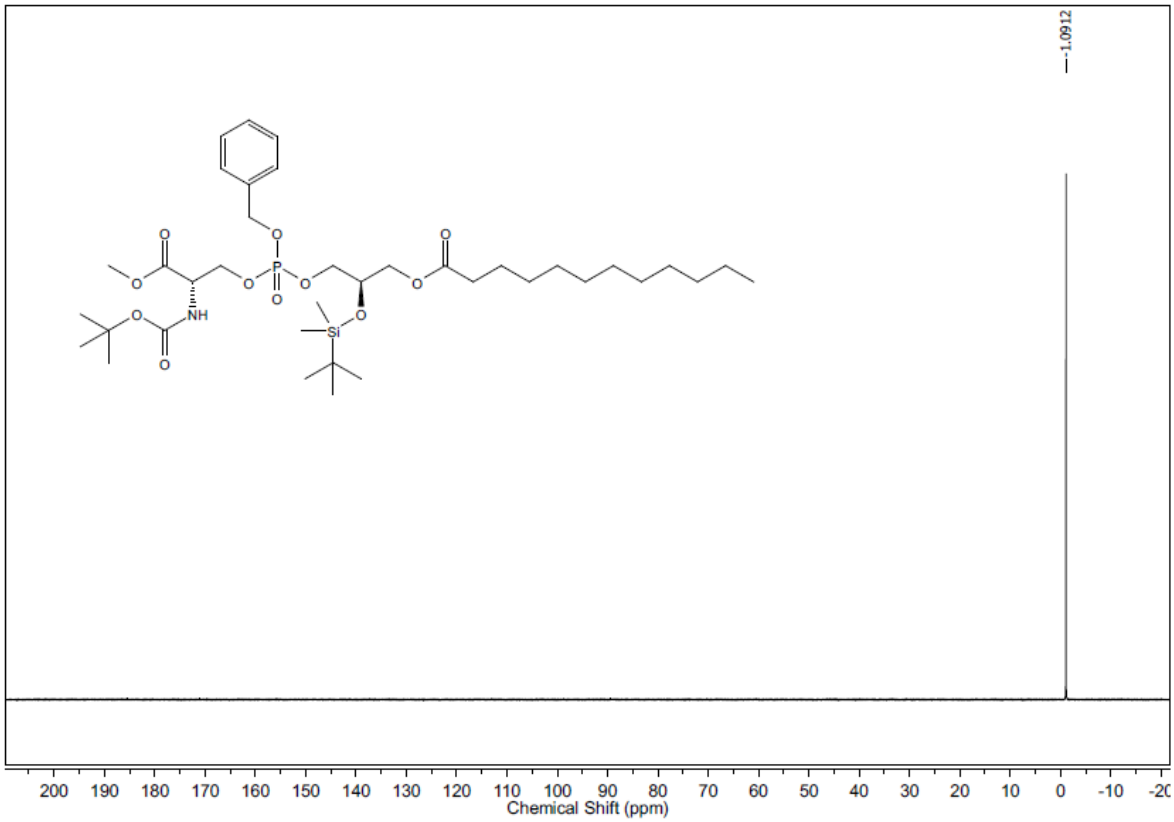
DEPT-135 NMR of compound (*R*)-**8a**



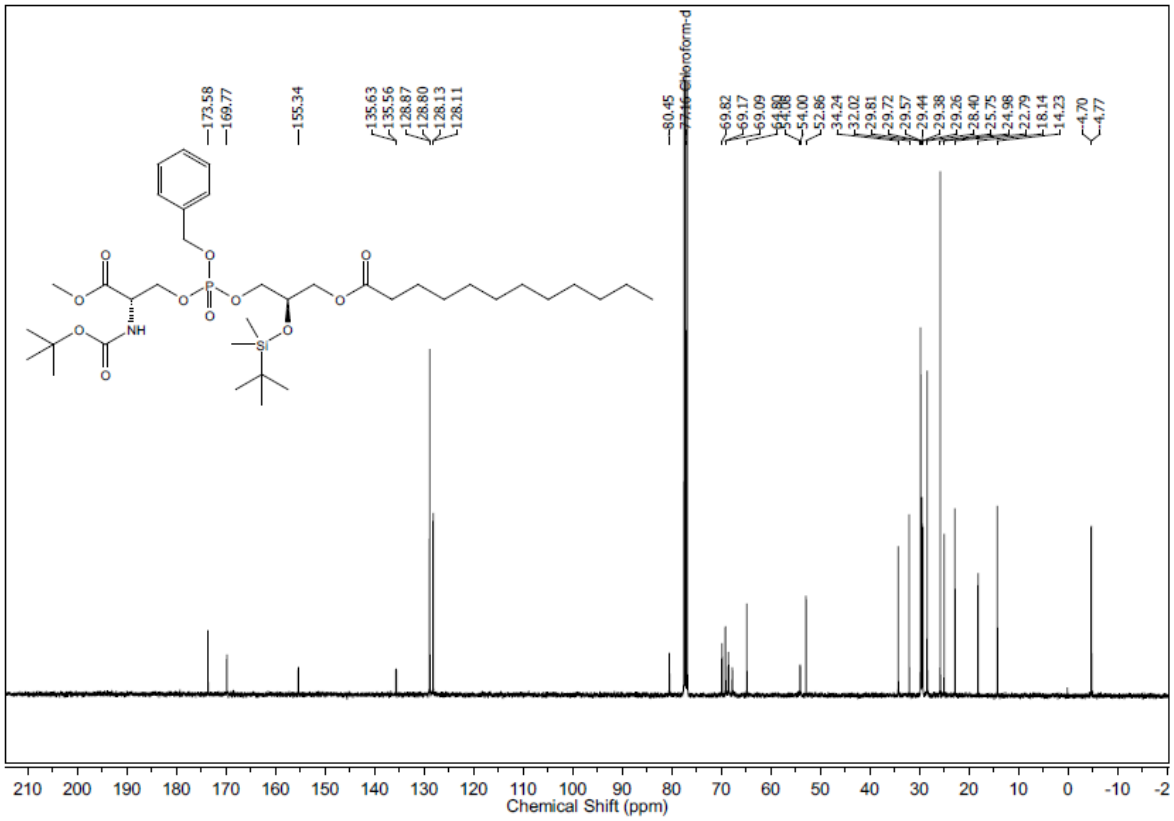
^{1}H NMR of compound (*R*)-**8b**



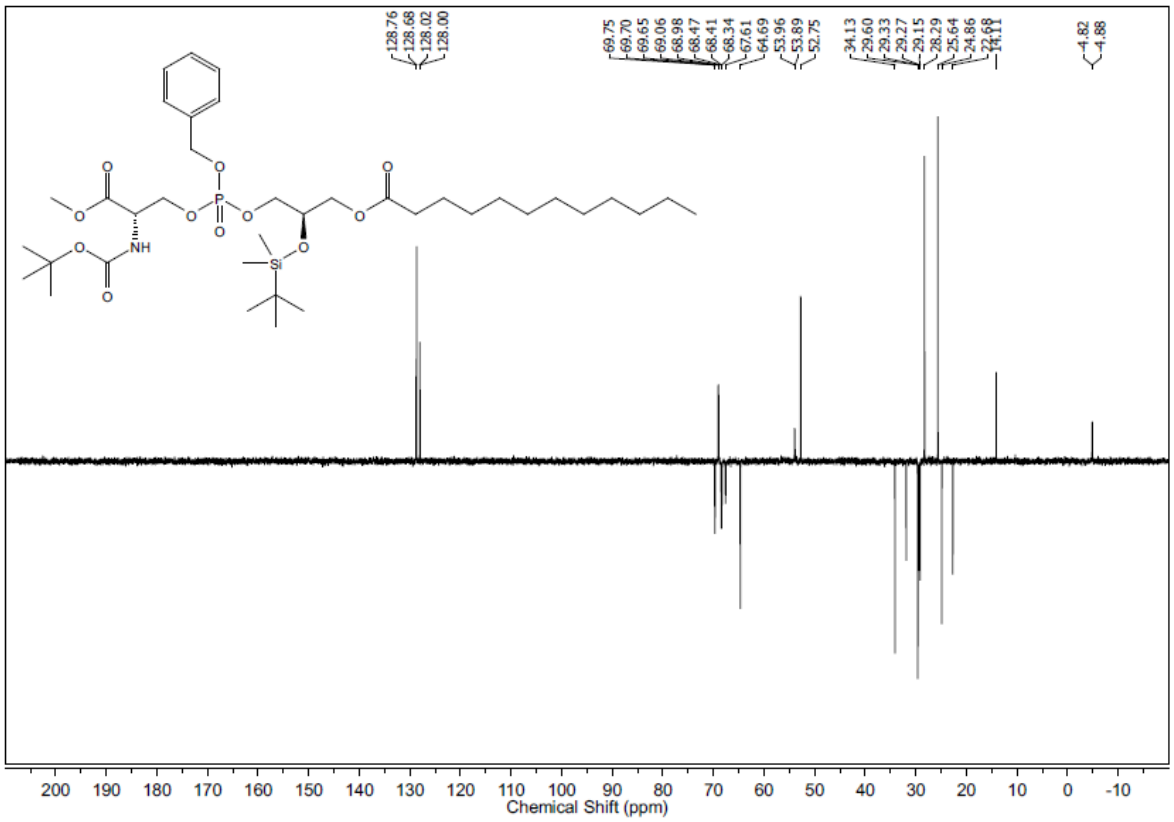
^{31}P NMR of compound (*R*)-**8b**



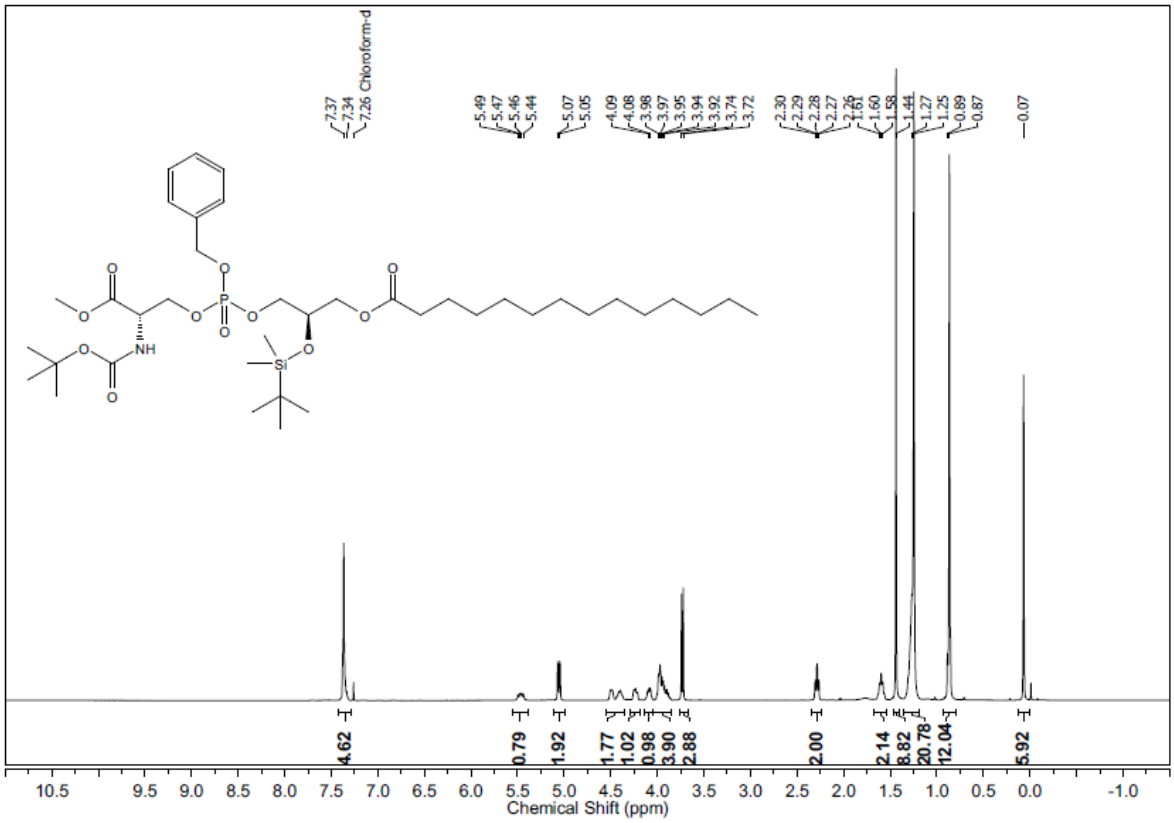
^{13}C NMR of compound (*R*)-**8b**



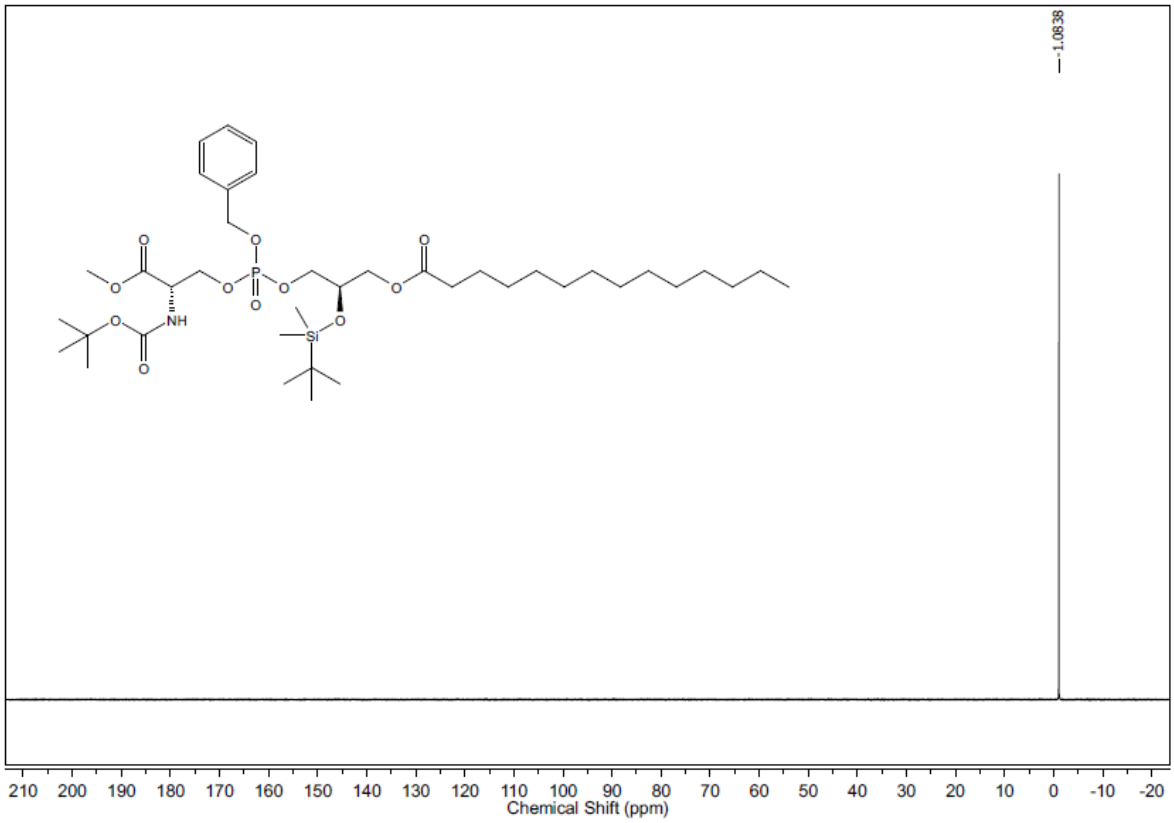
DEPT-135 NMR of compound (*R*)-**8b**



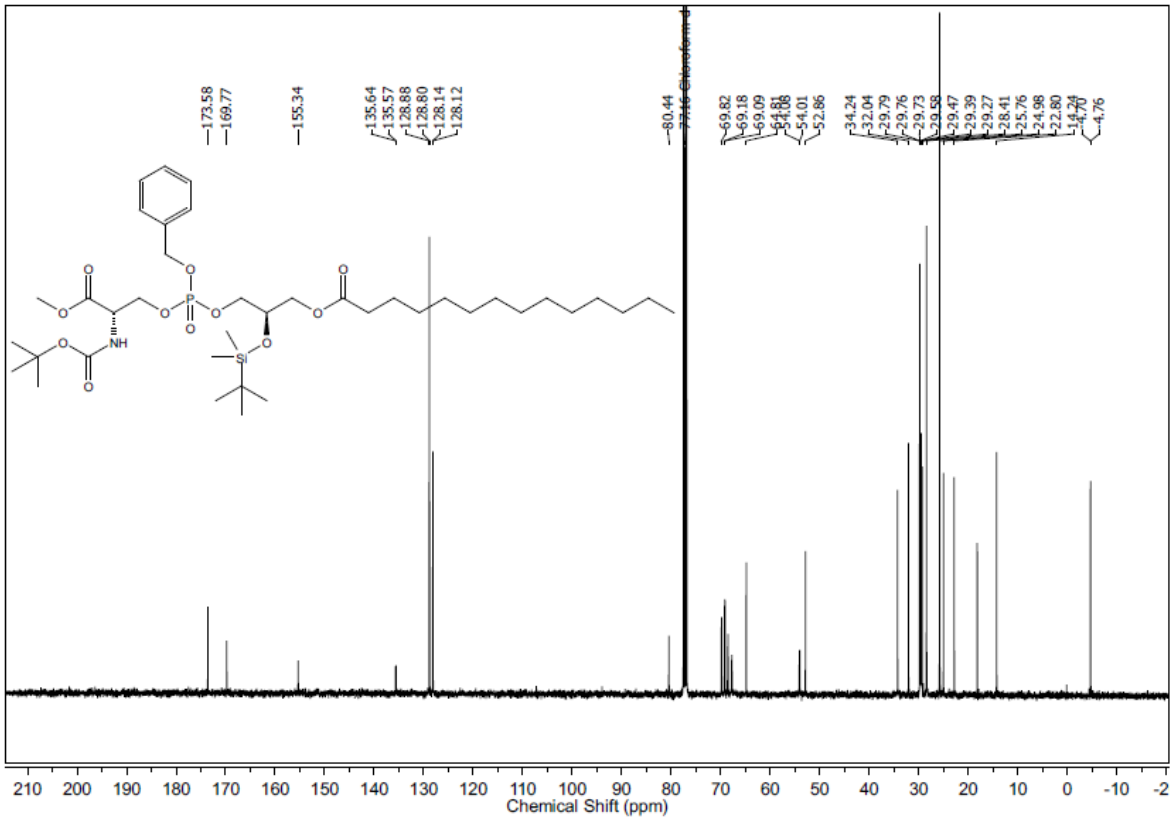
^{1}H NMR of compound (*R*)-**8c**



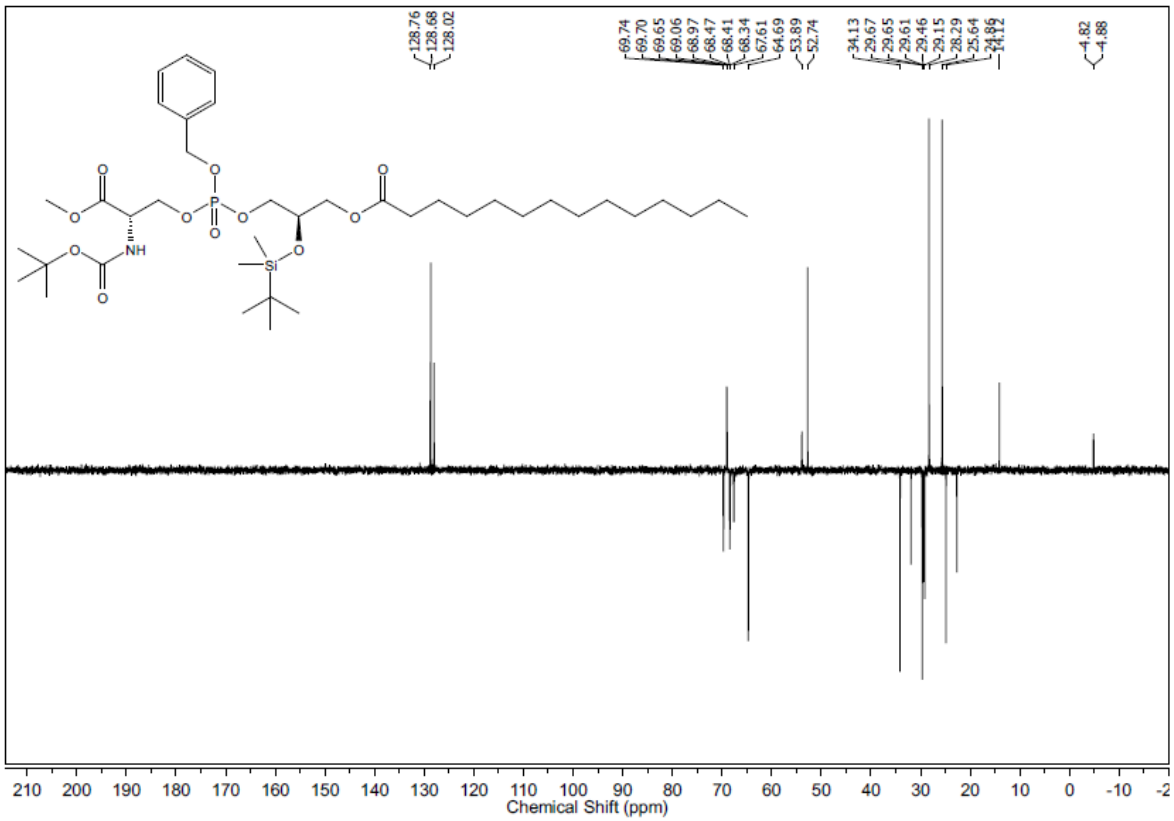
^{31}P NMR of compound (*R*)-**8c**



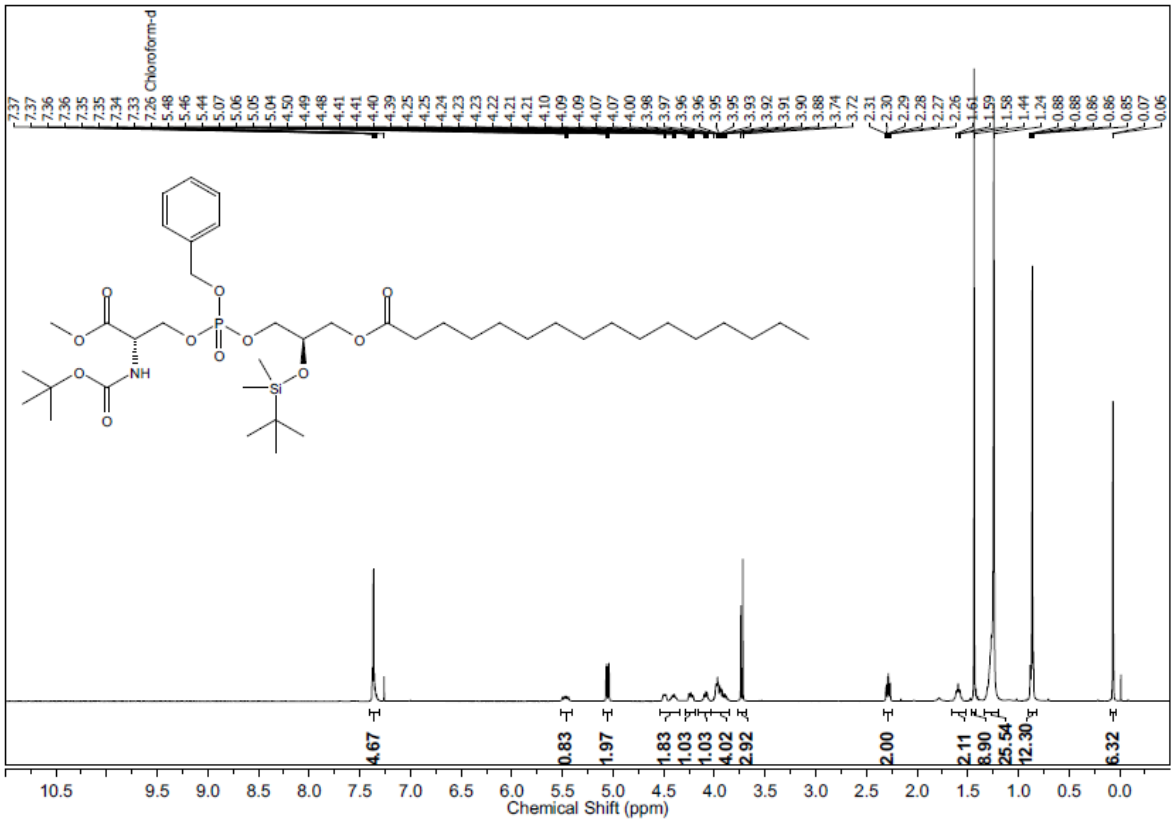
^{13}C NMR of compound (*R*)-**8c**



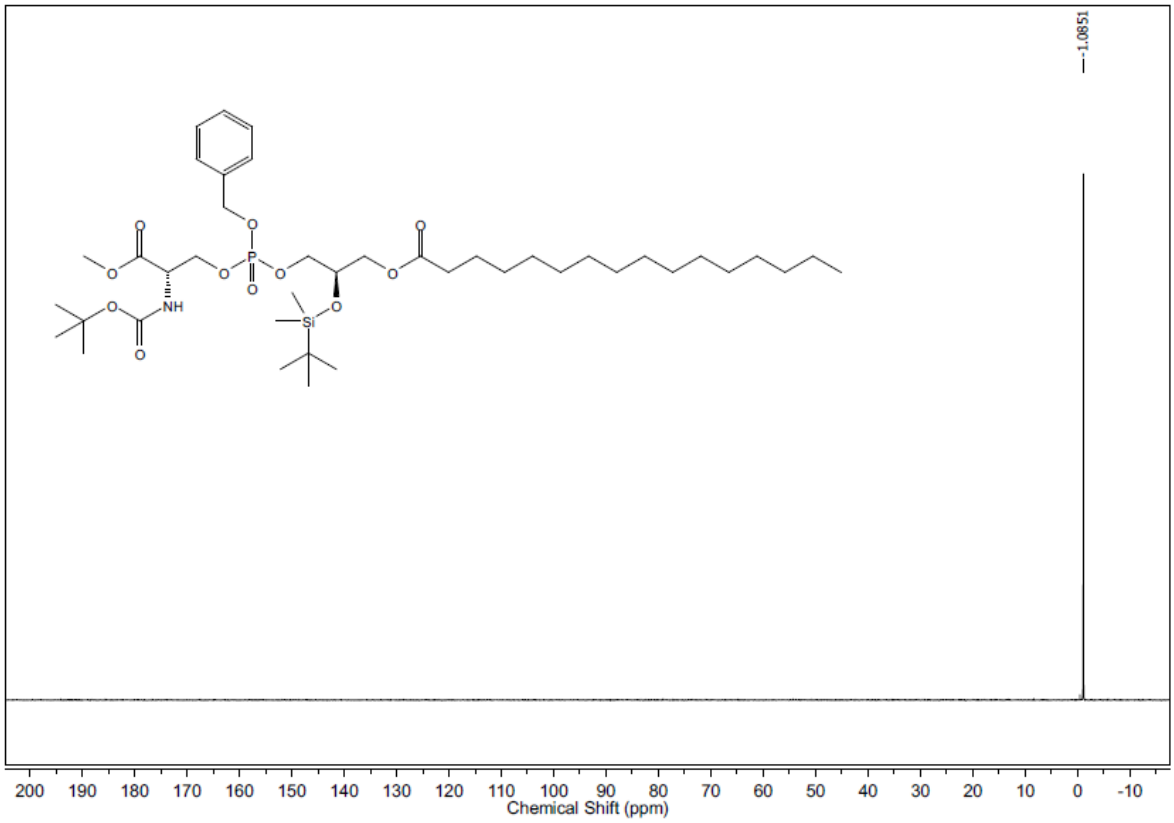
DEPT-135 NMR of compound (*R*)-**8c**



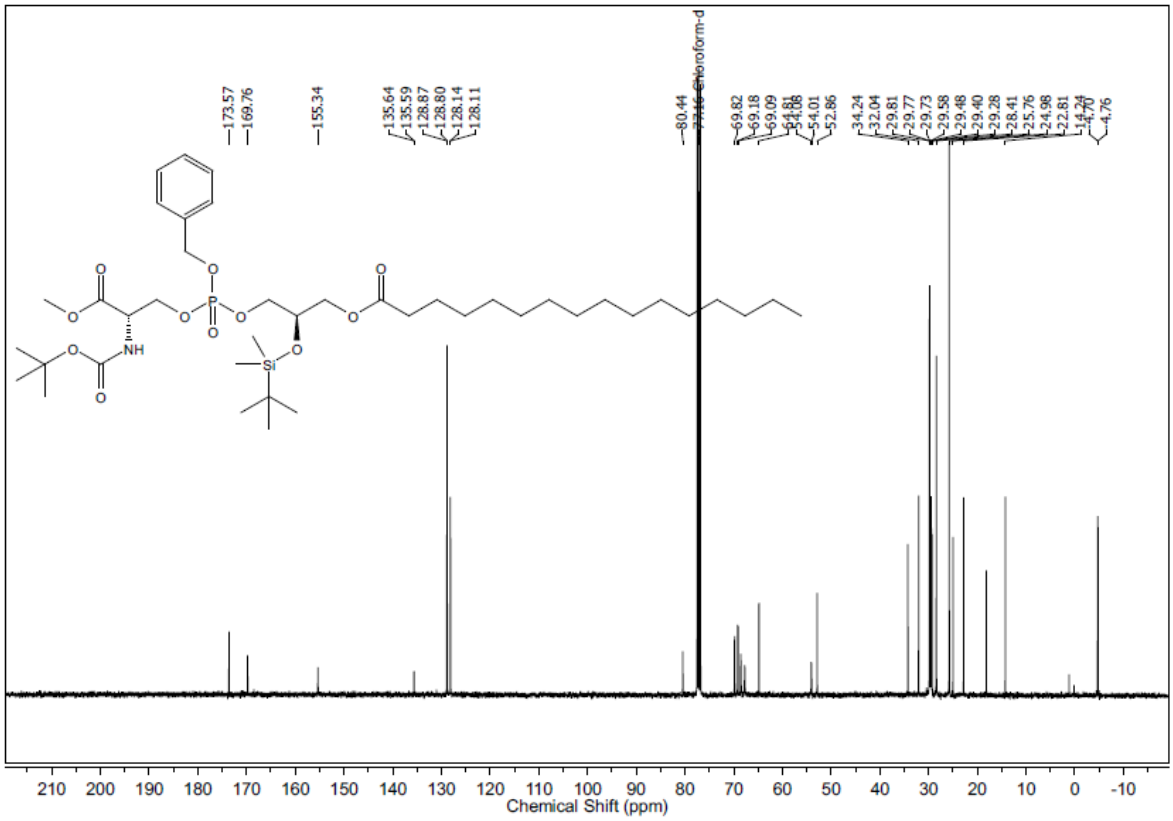
^{1}H NMR of compound (*R*)-**8d**



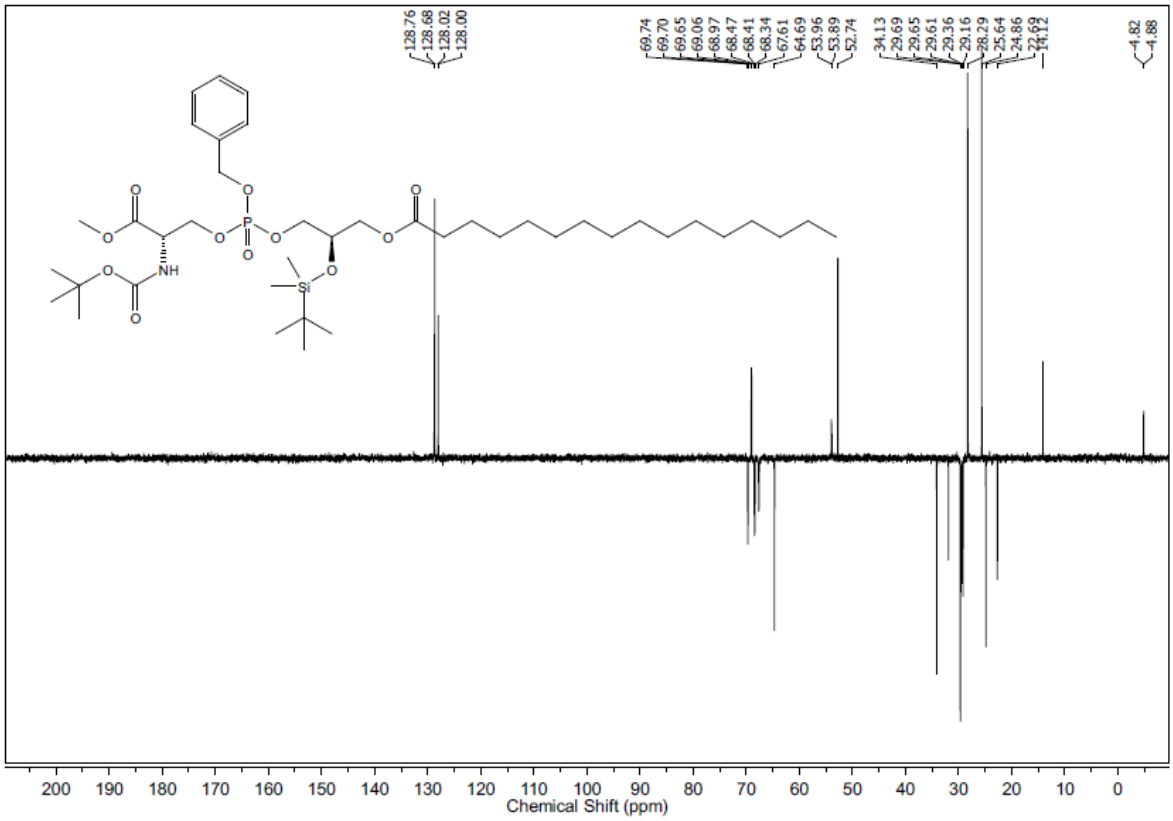
^{31}P NMR of compound (*R*)-**8d**



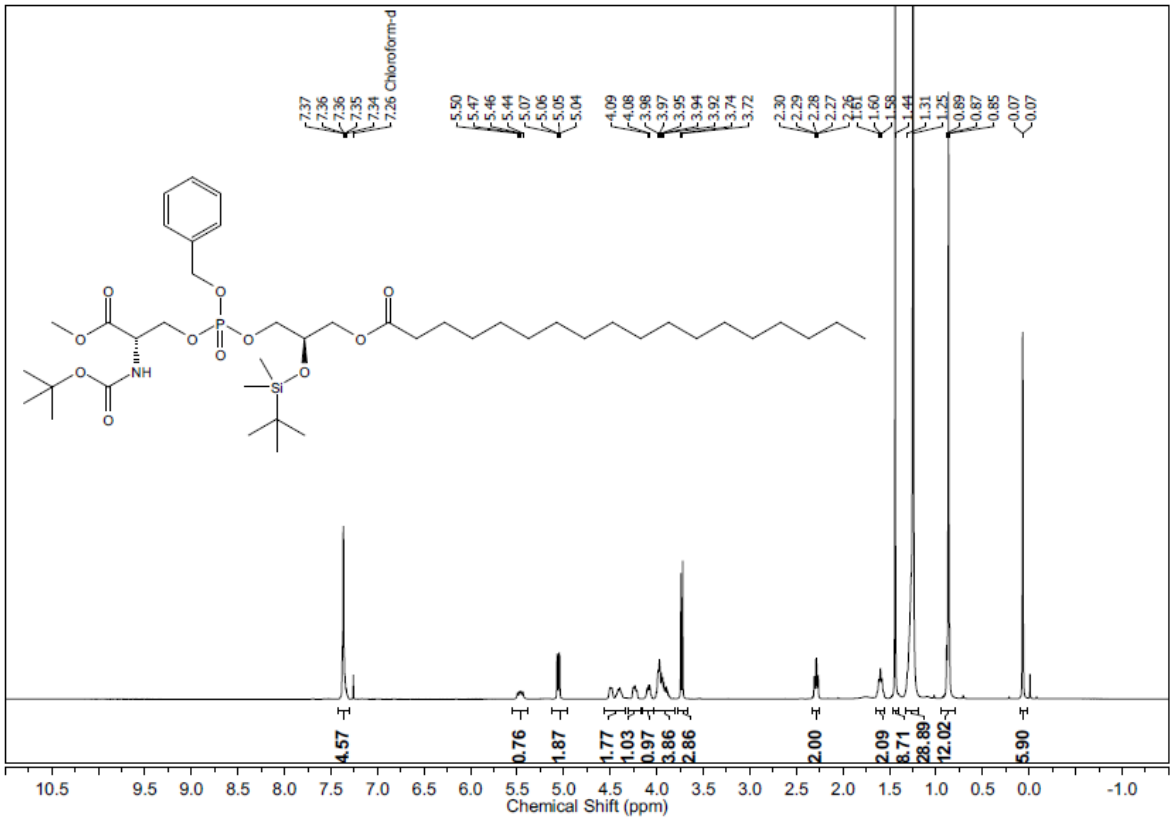
^{13}C NMR of compound (*R*)-**8d**



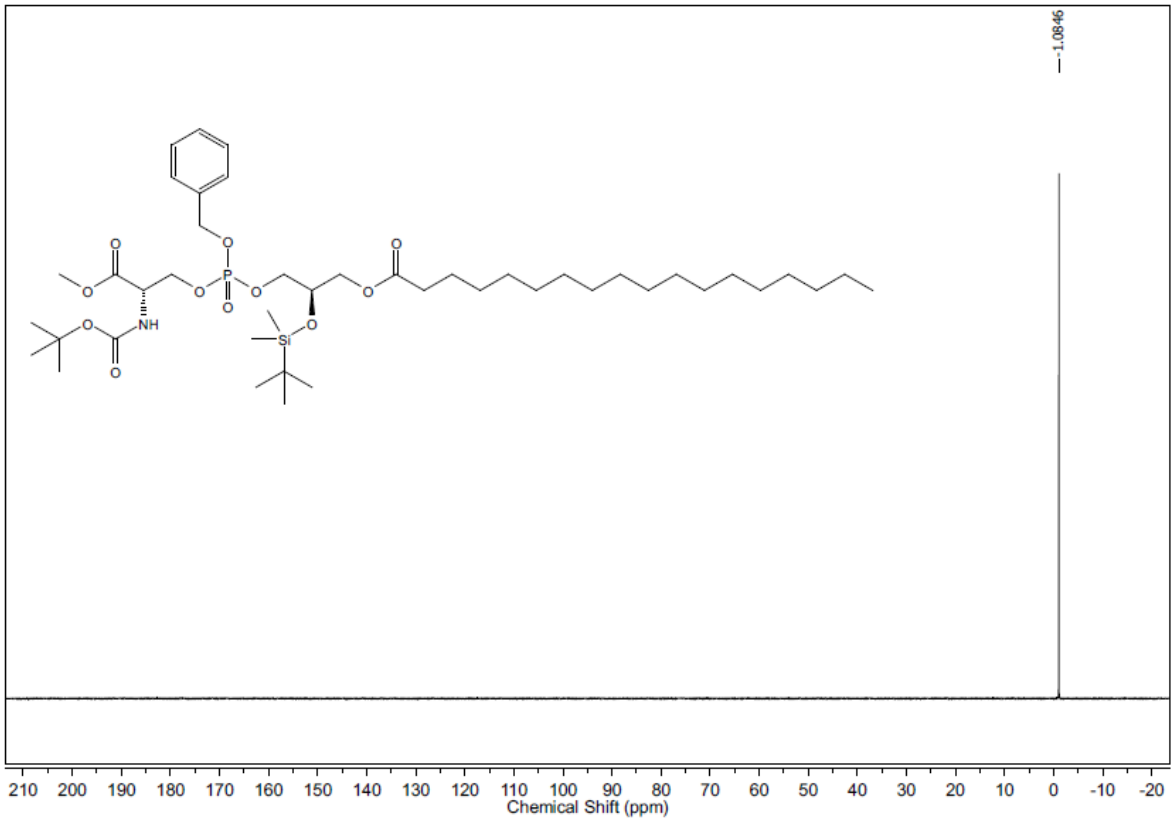
DEPT-135 NMR of compound (*R*)-**8d**



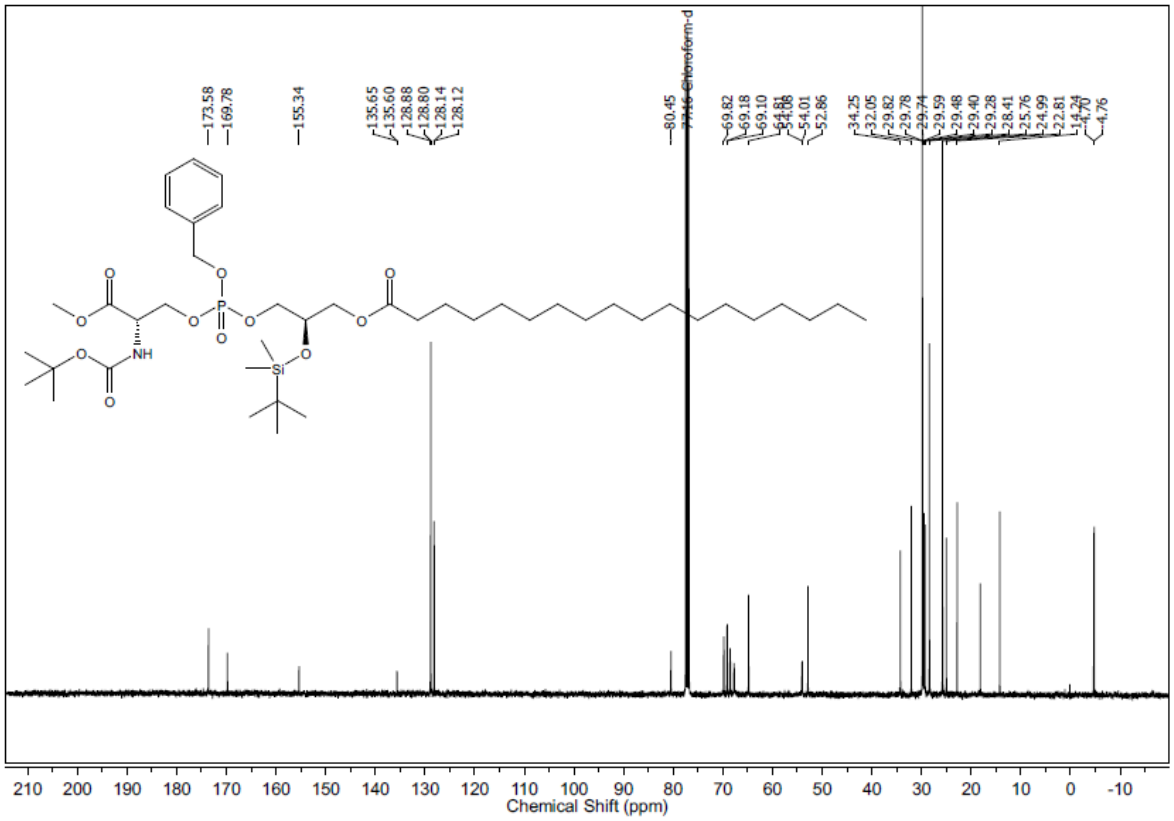
^{1}H NMR of compound (*R*)-**8e**



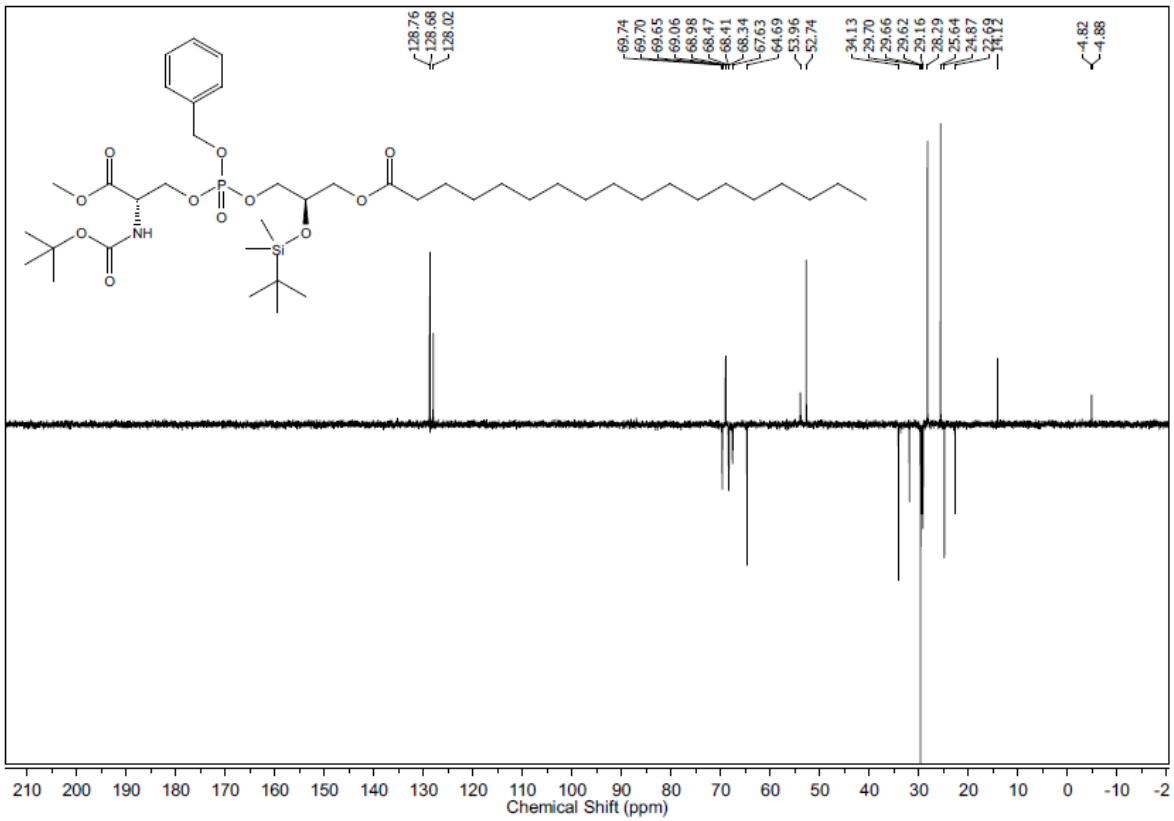
^{31}P NMR of compound (*R*)-**8e**



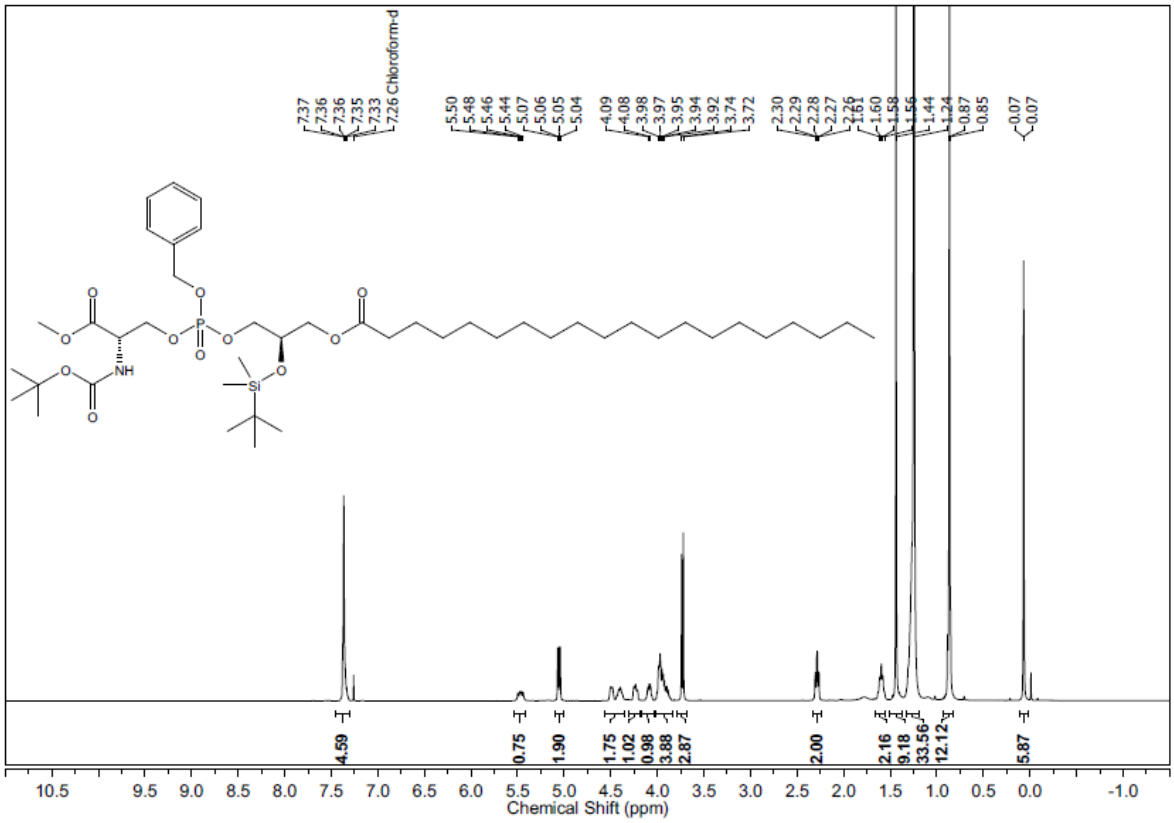
^{13}C NMR of compound (*R*)-**8e**



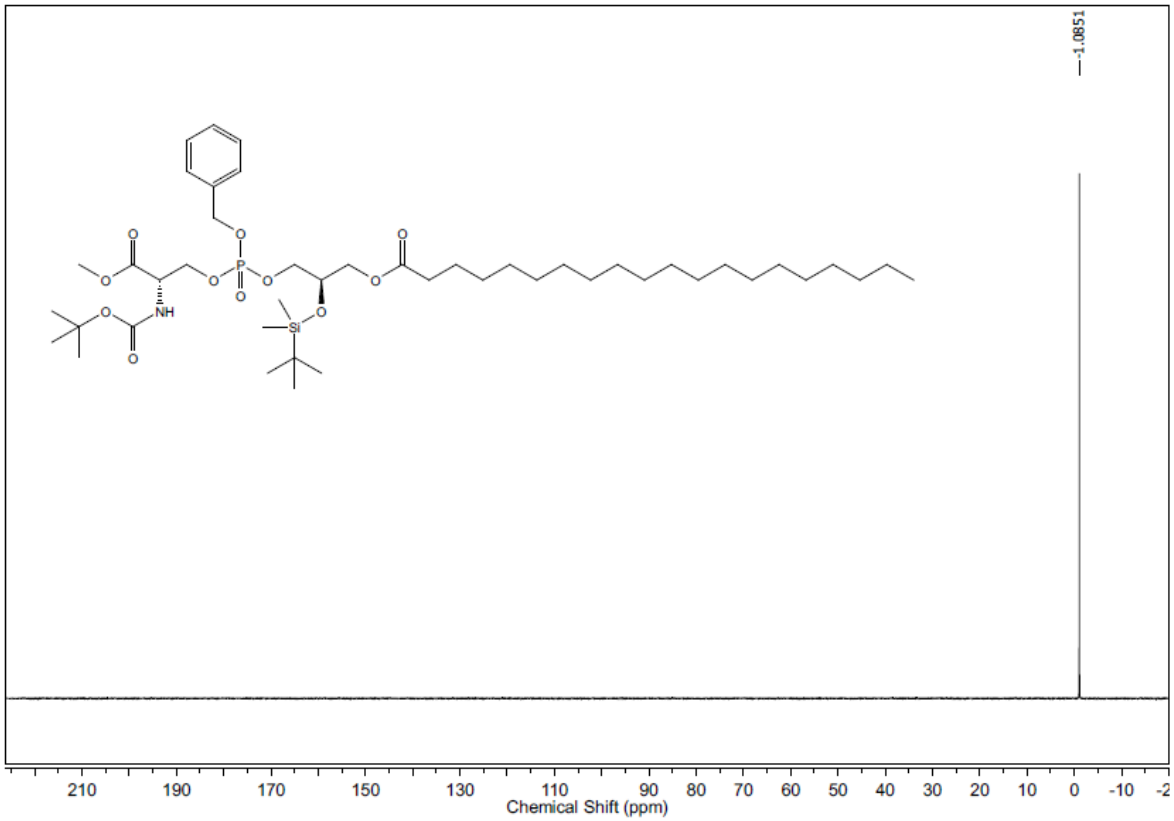
DEPT-135 NMR of compound (*R*)-**8e**



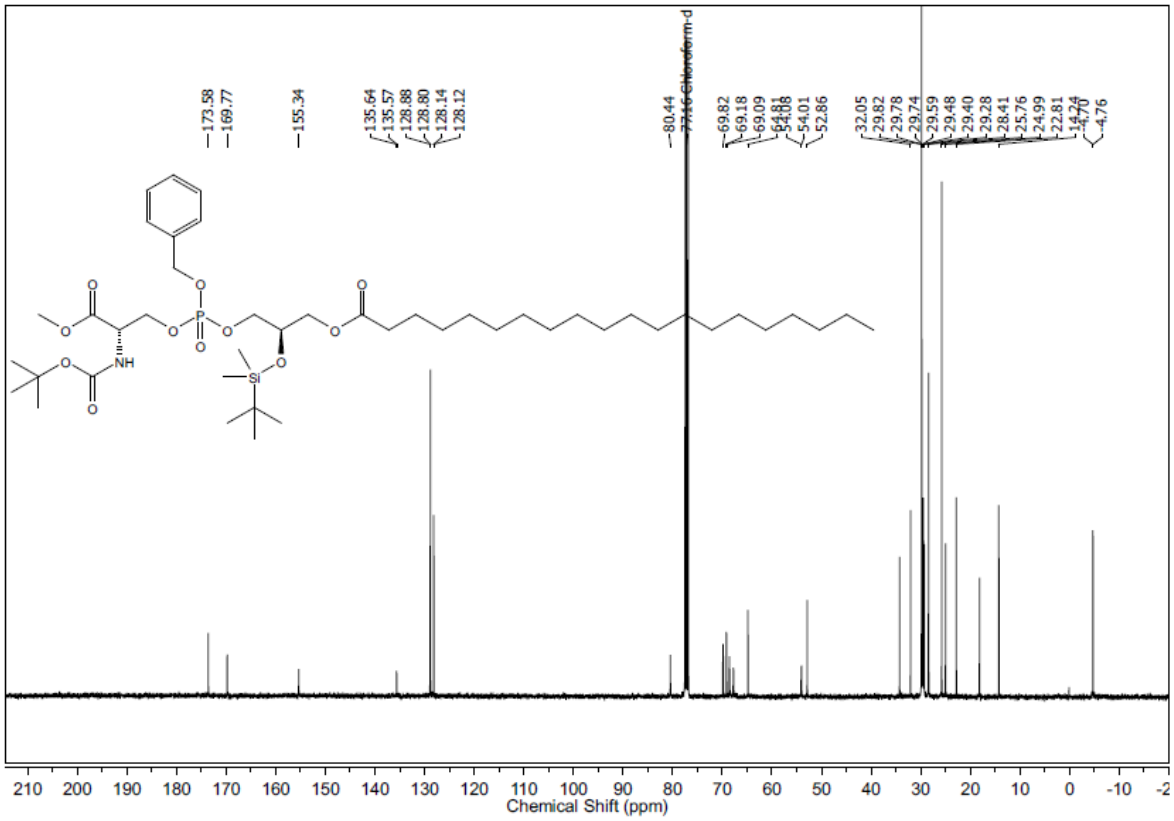
^{1}H NMR of compound (*R*)-**8f**



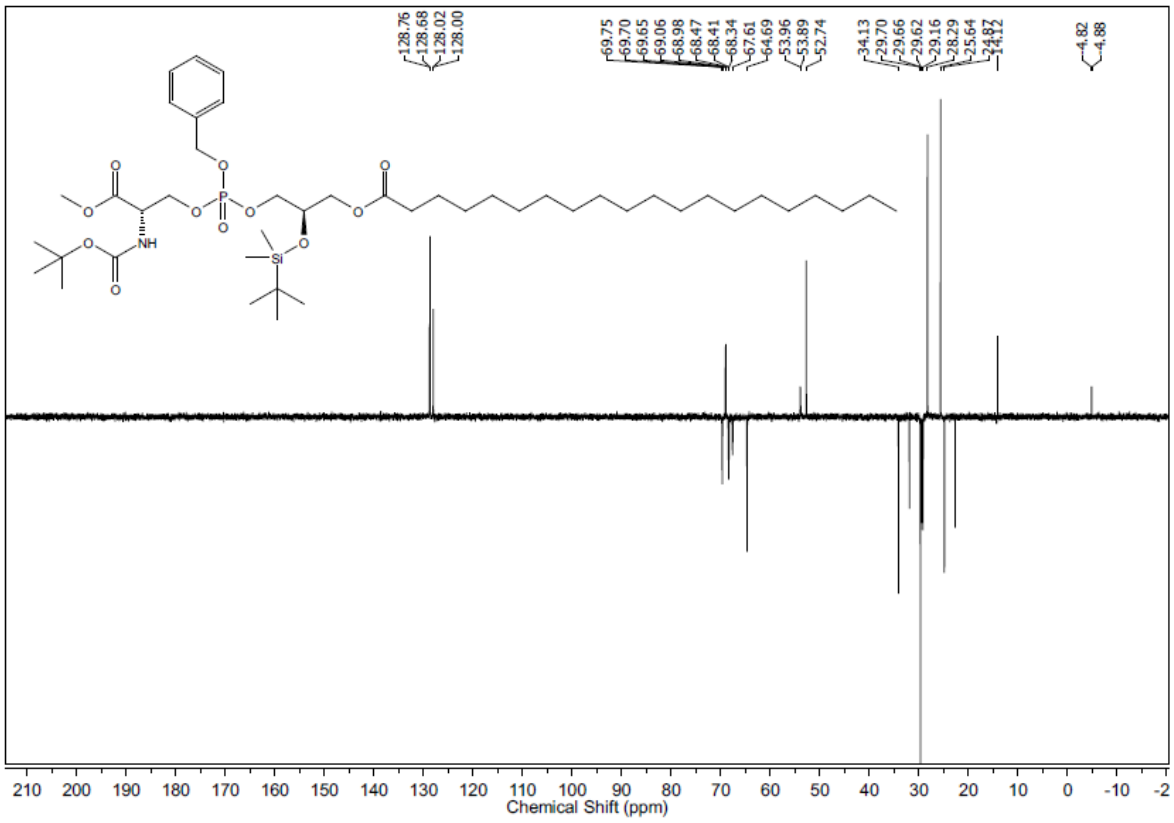
^{31}P NMR of compound (*R*)-**8f**



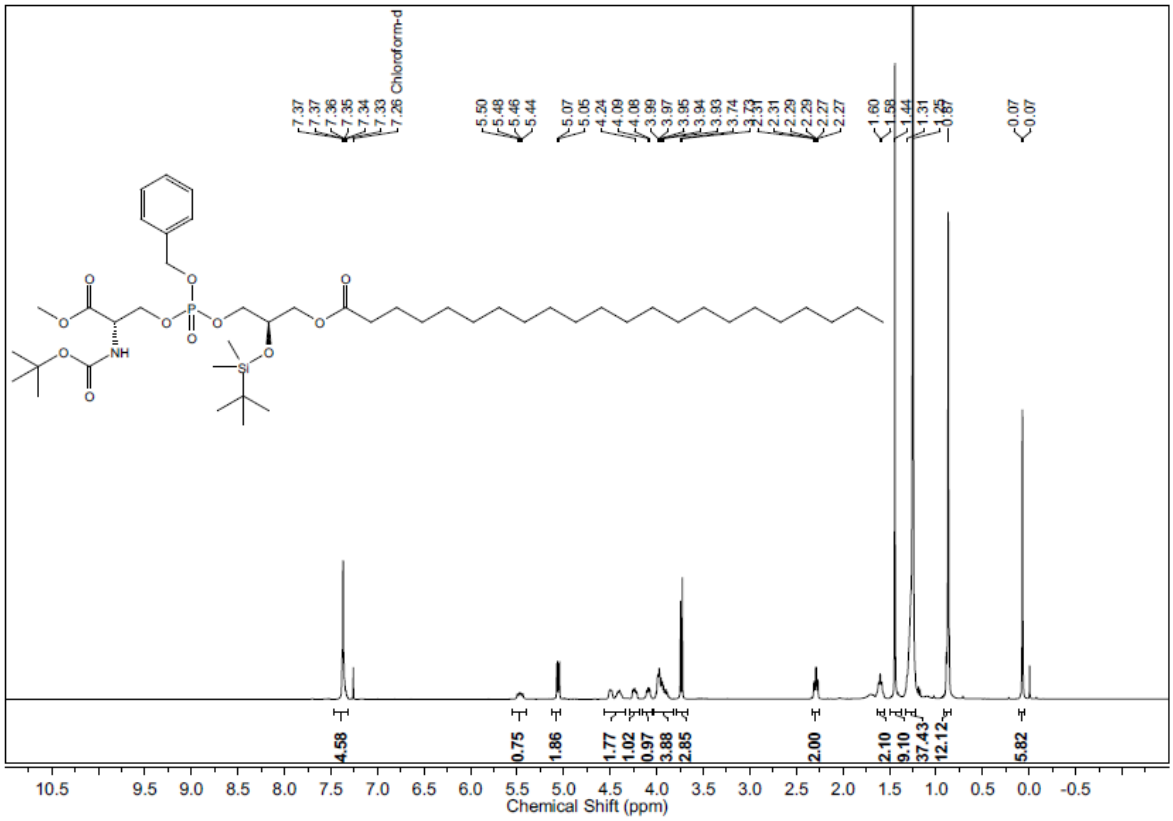
^{13}C NMR of compound (*R*)-**8f**



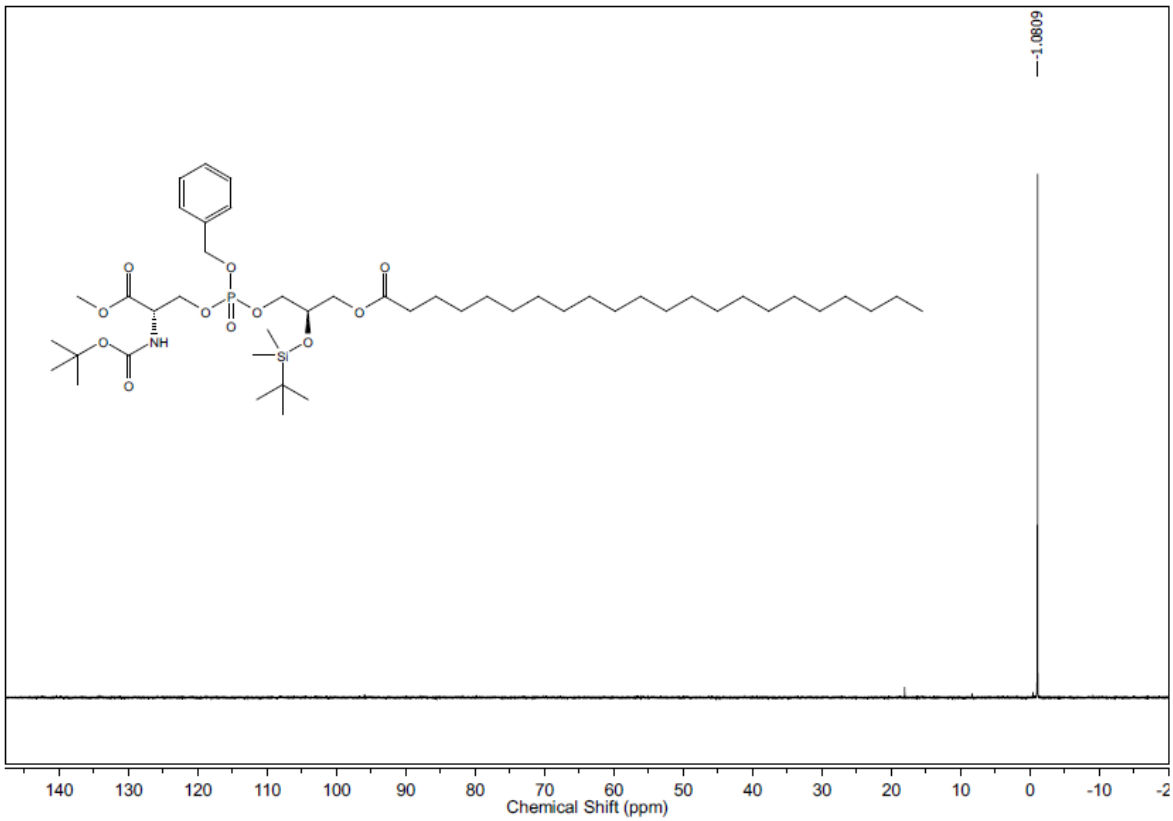
DEPT-135 NMR of compound (*R*)-**8f**



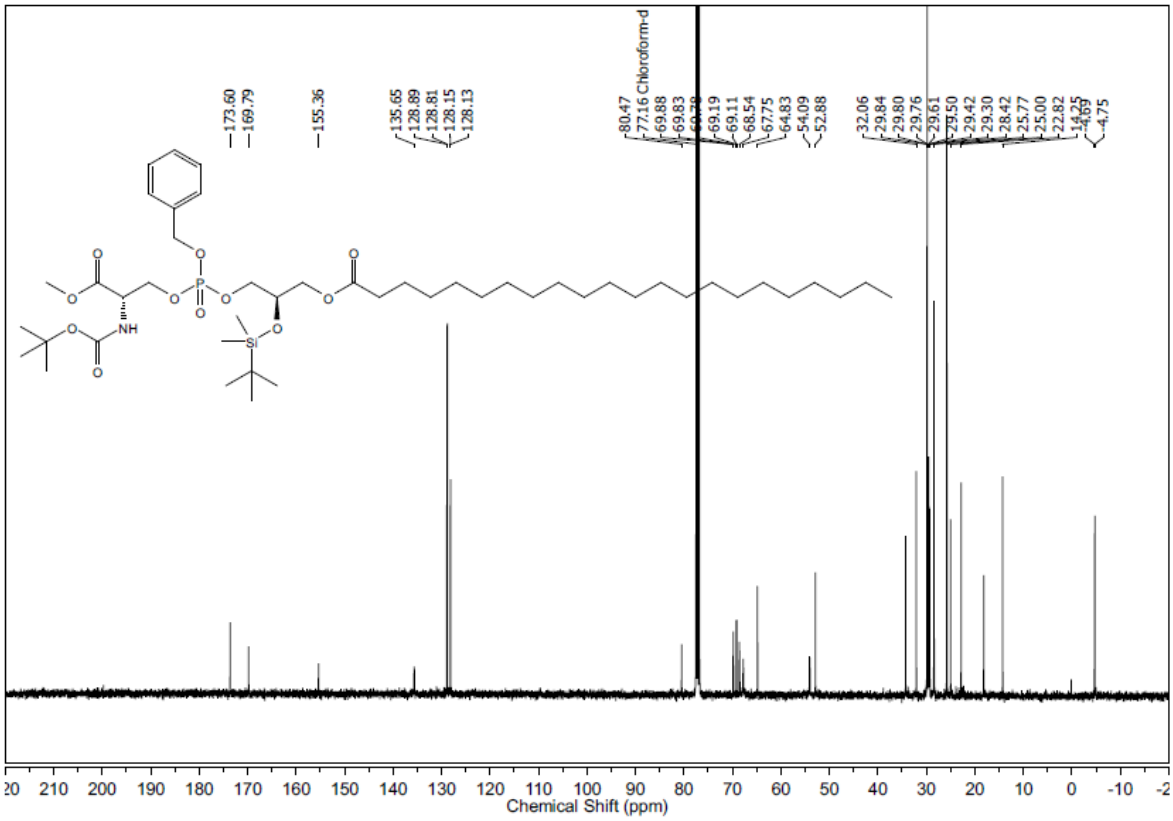
^{1}H NMR of compound (*R*)-**8g**



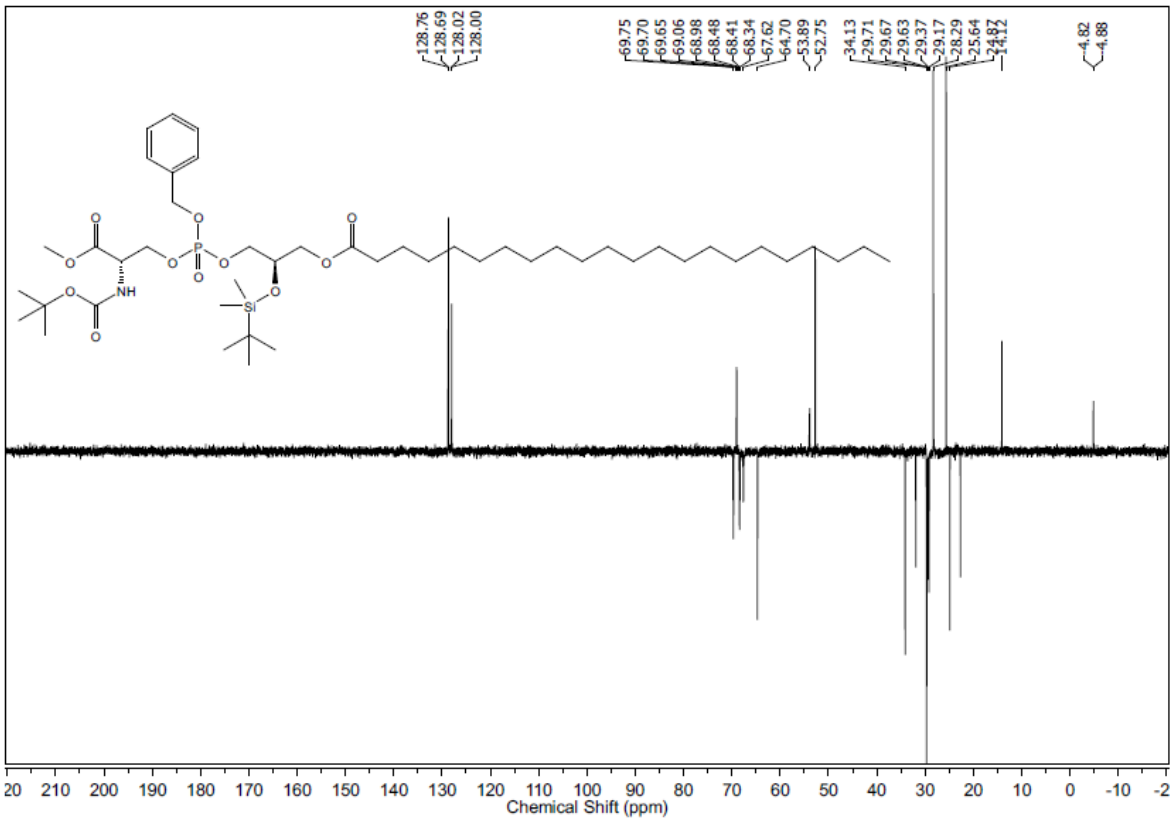
^{31}P NMR of compound (*R*)-**8g**



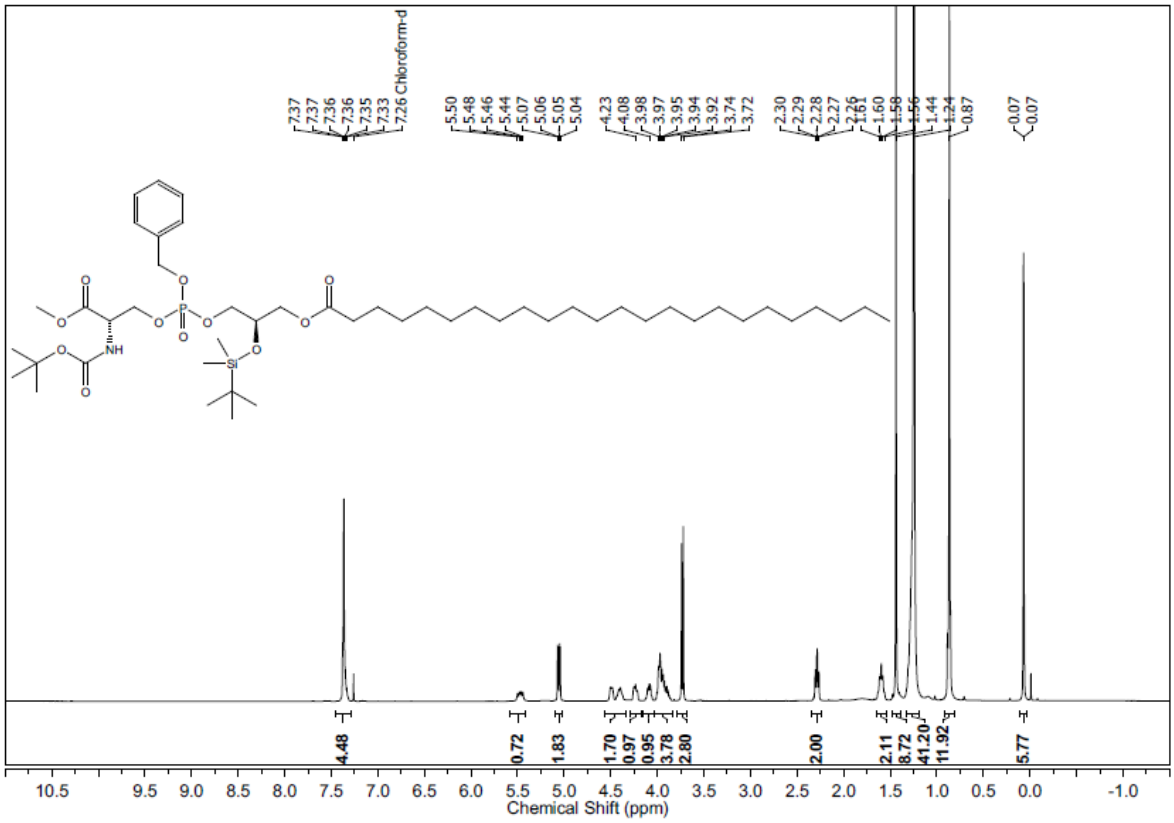
^{13}C NMR of compound (*R*)-**8g**



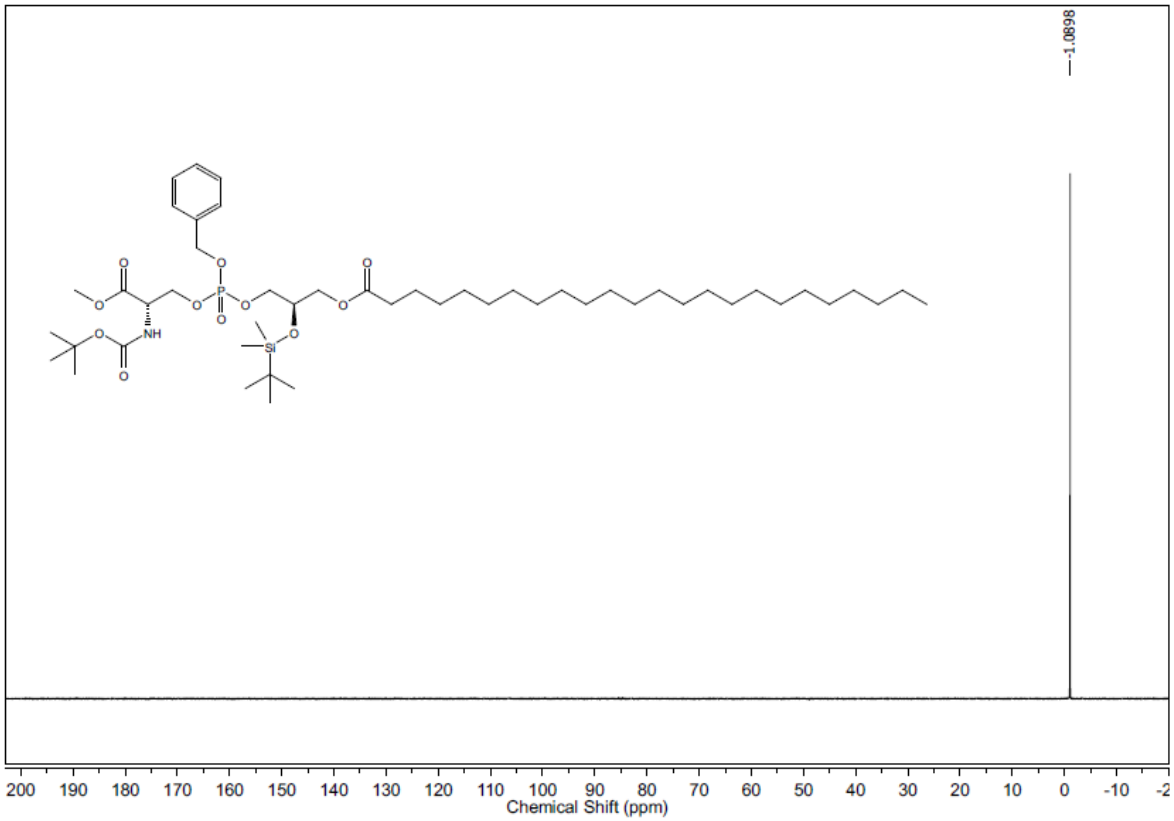
DEPT-135 NMR of compound (*R*)-**8g**



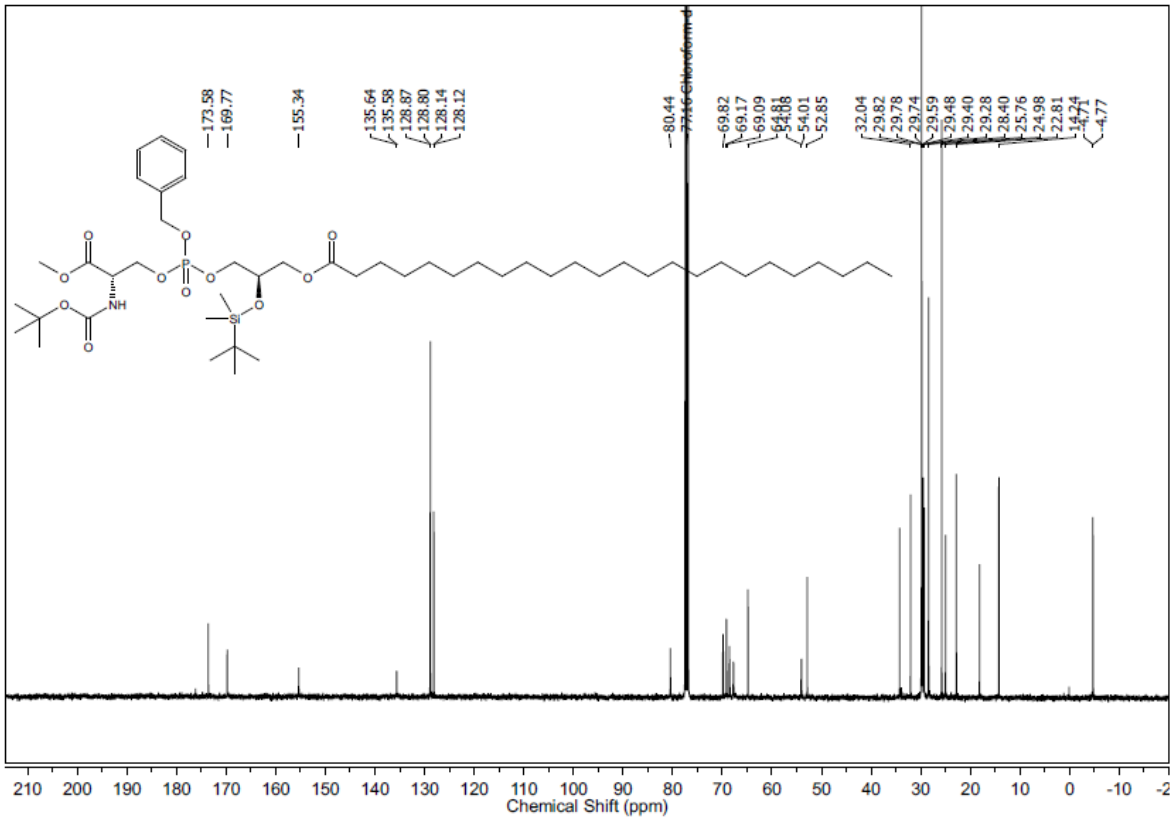
^{1}H NMR of compound (*R*)-**8h**



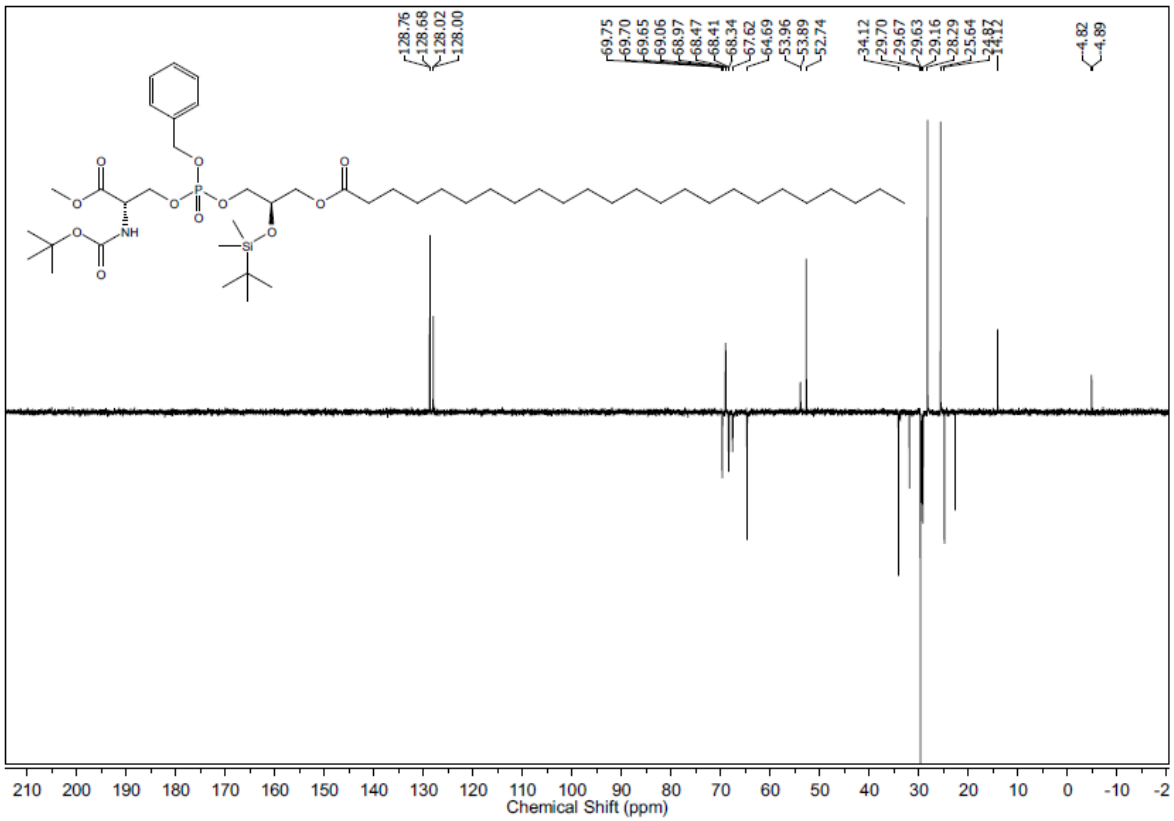
^{31}P NMR of compound (*R*)-**8h**



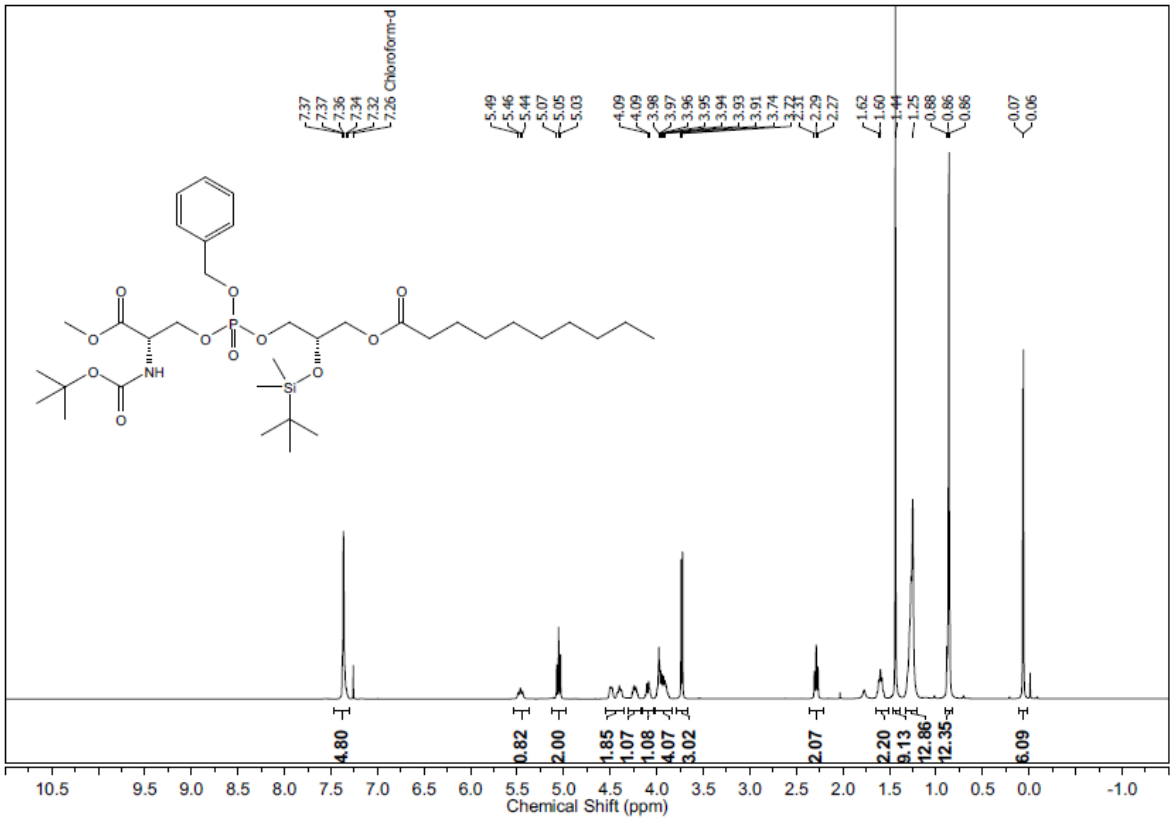
^{13}C NMR of compound (*R*)-**8h**



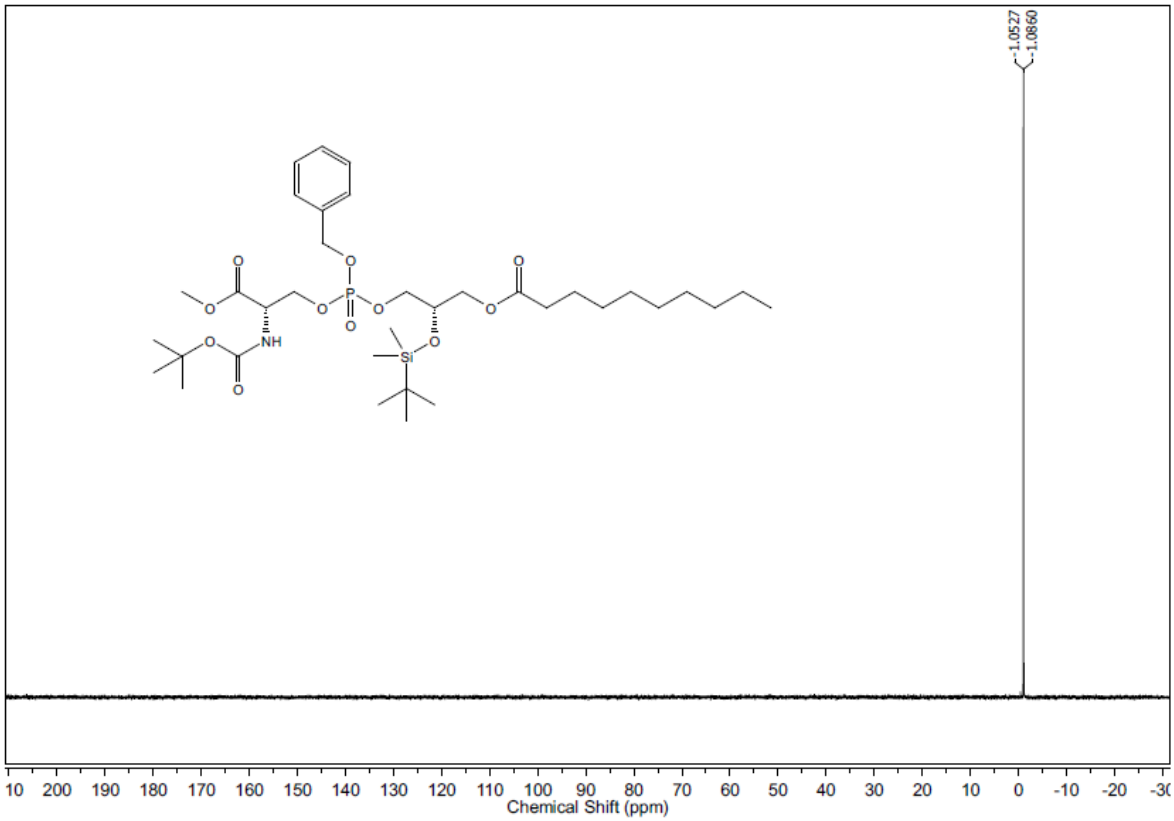
DEPT-135 NMR of compound (*R*)-**8h**



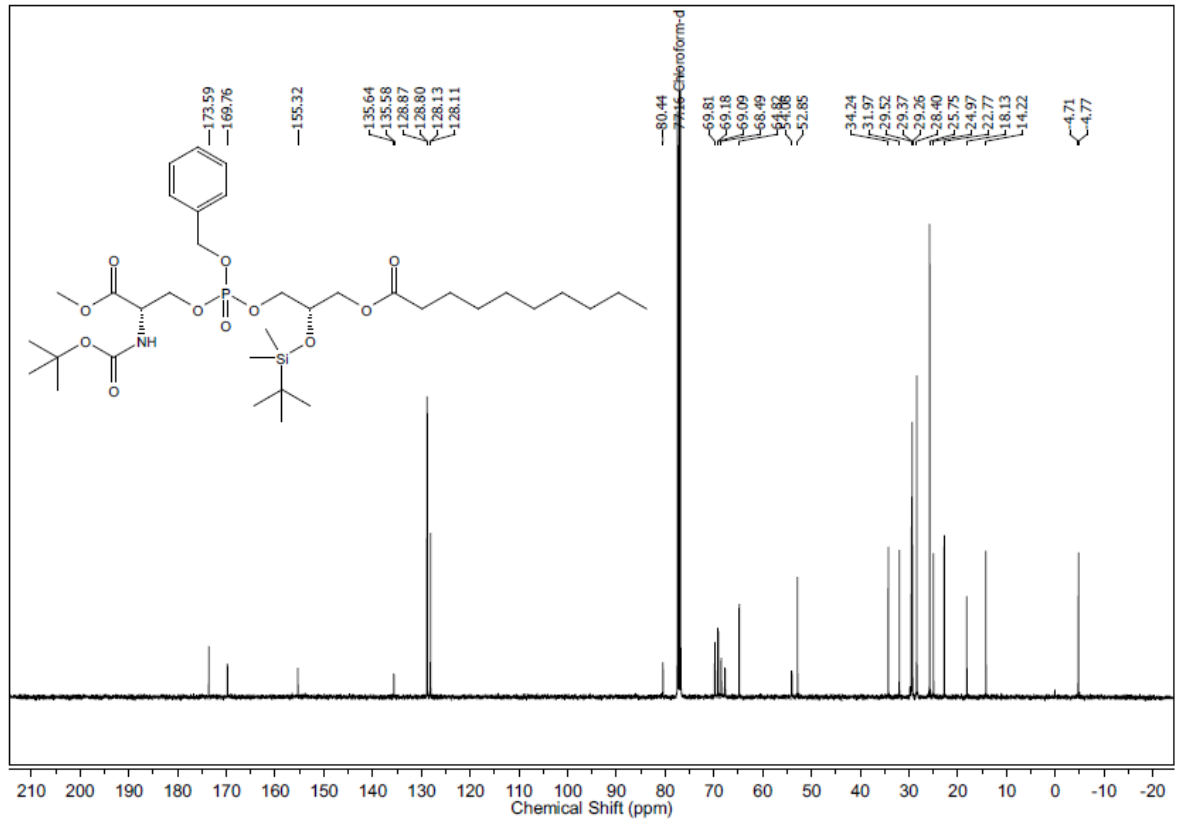
^{1}H NMR of compound (*S*)-**8a**



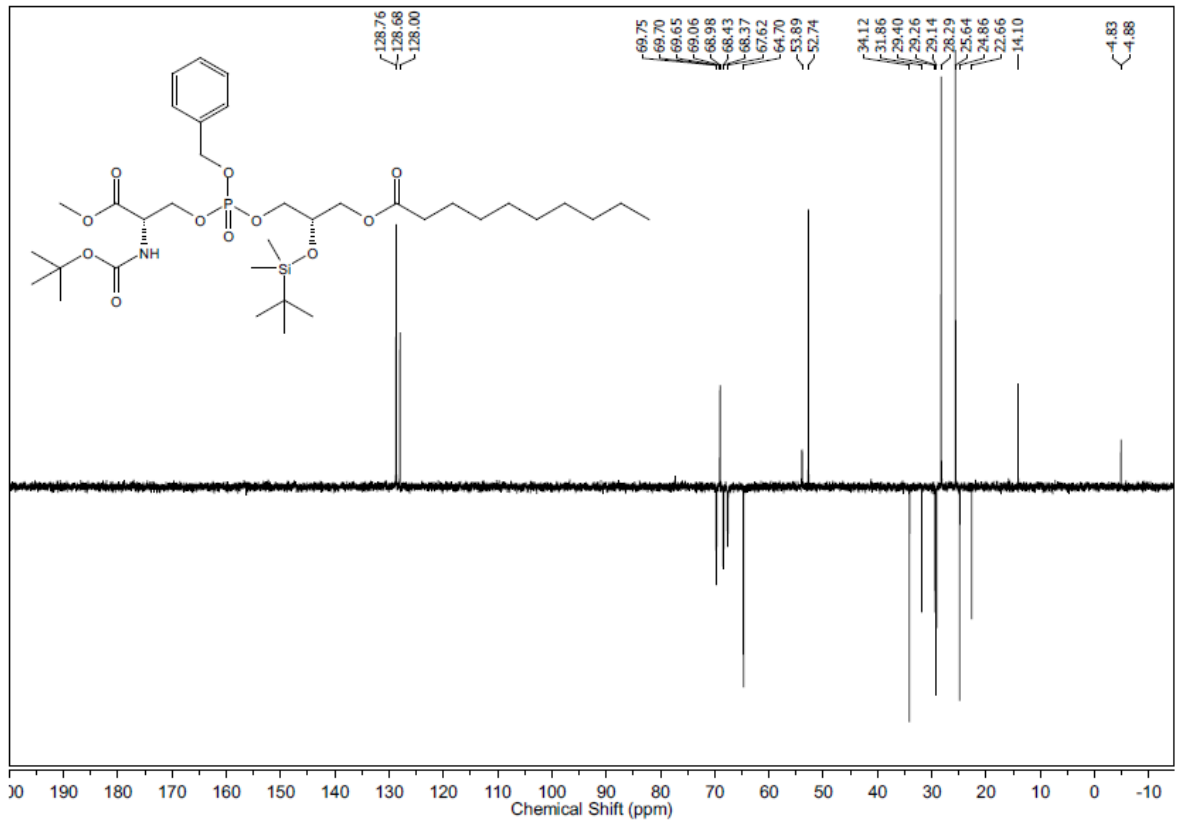
^{31}P NMR of compound (*S*)-**8a**



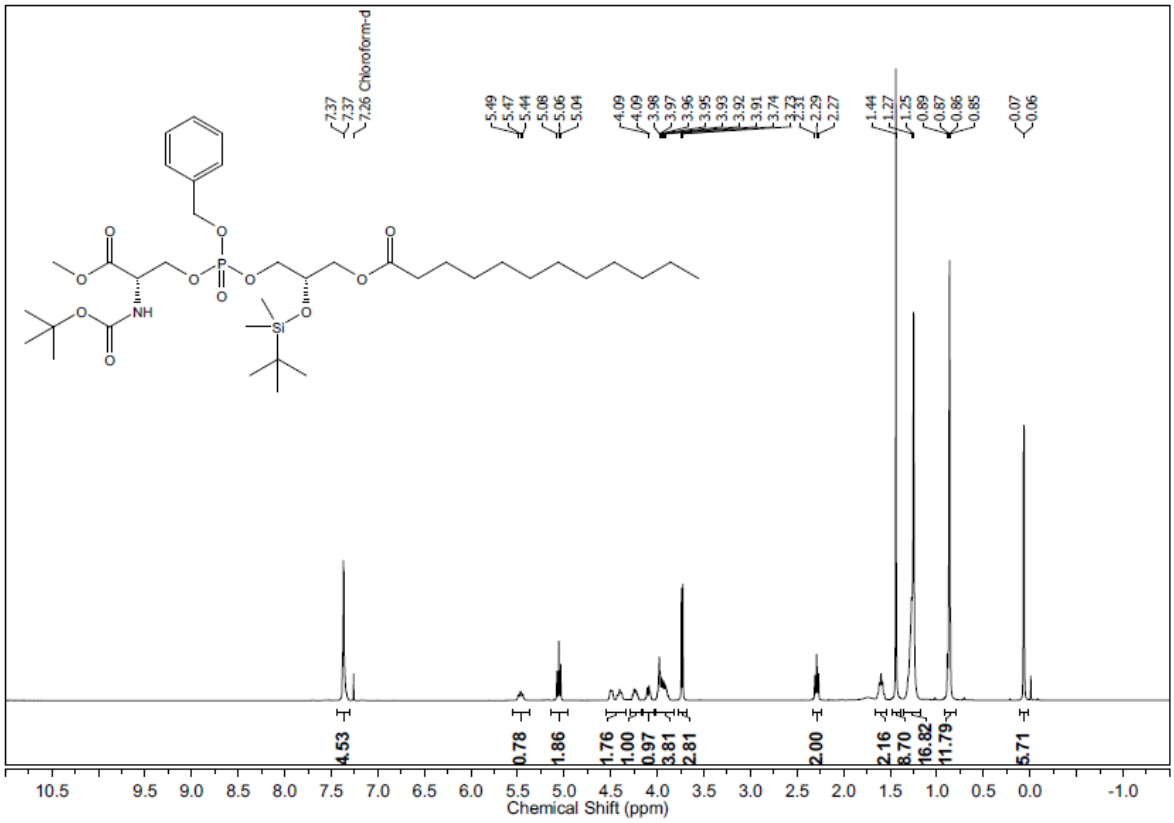
^{13}C NMR of compound (*S*)-**8a**



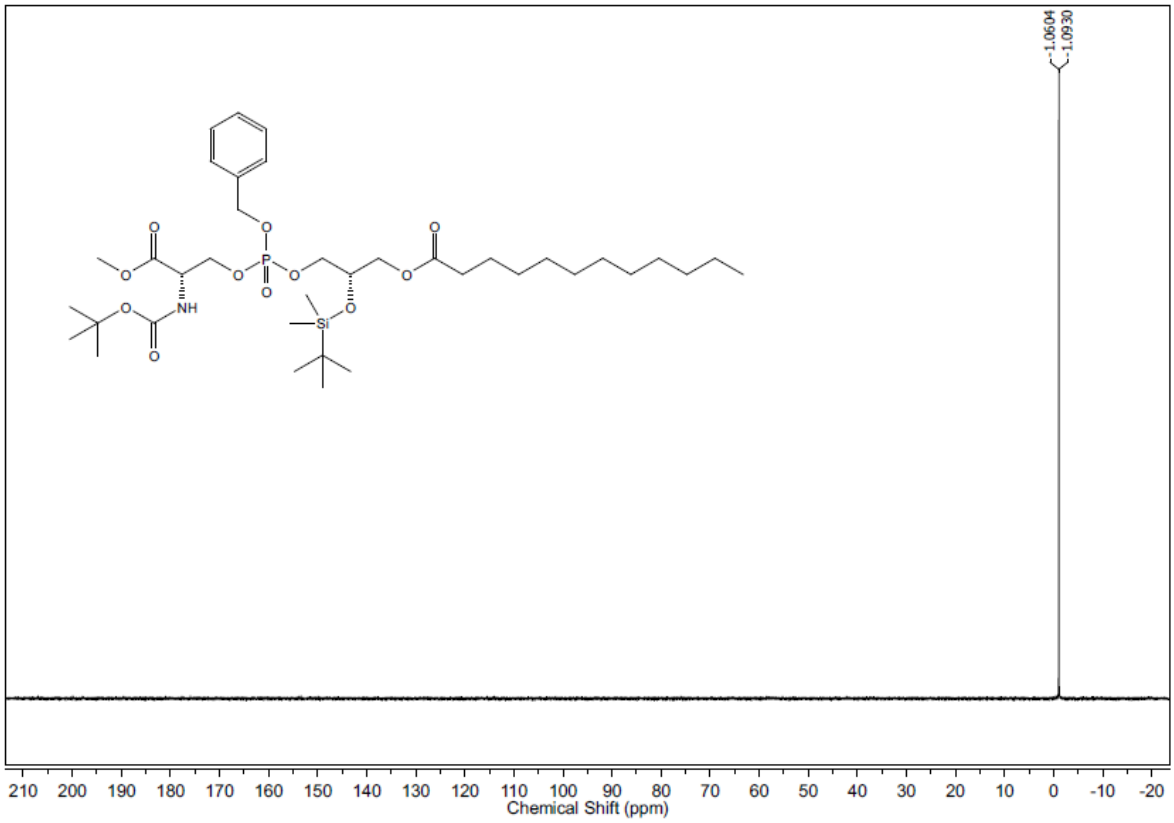
DEPT-135 NMR of compound (*S*)-**8a**



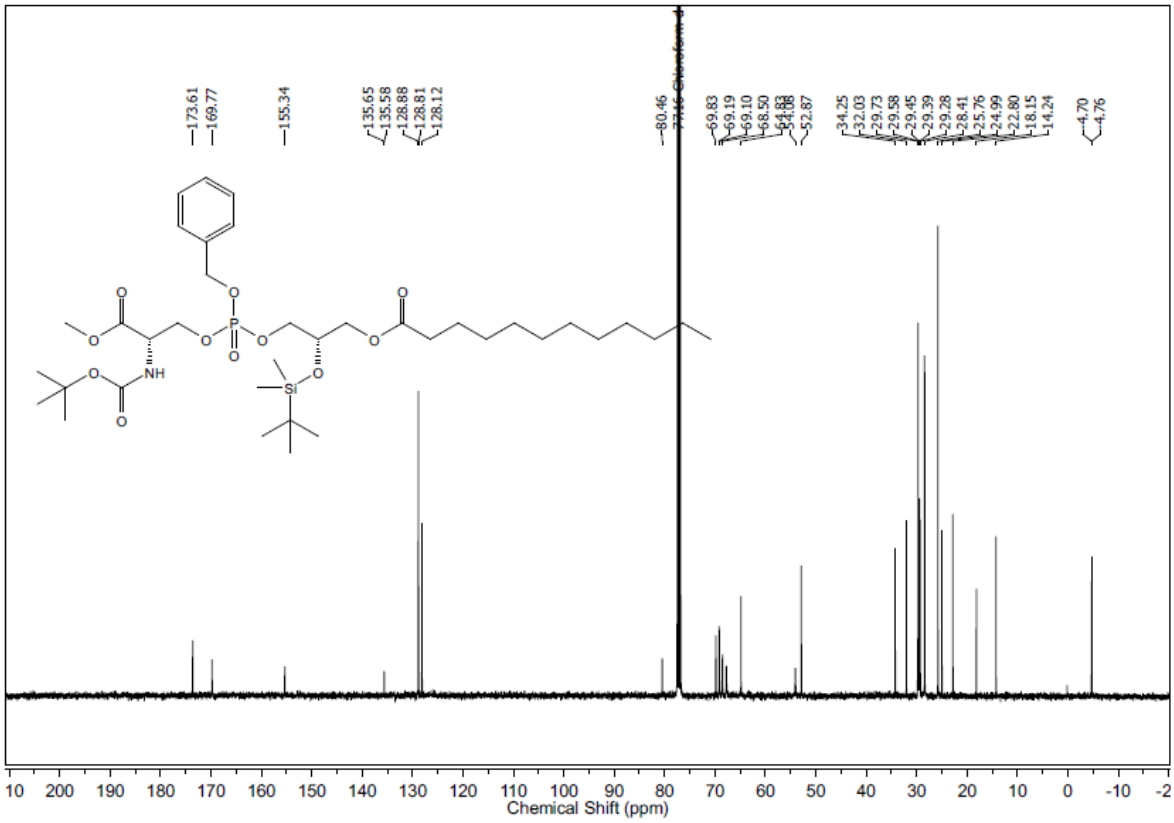
^{1}H NMR of compound (S)-**8b**



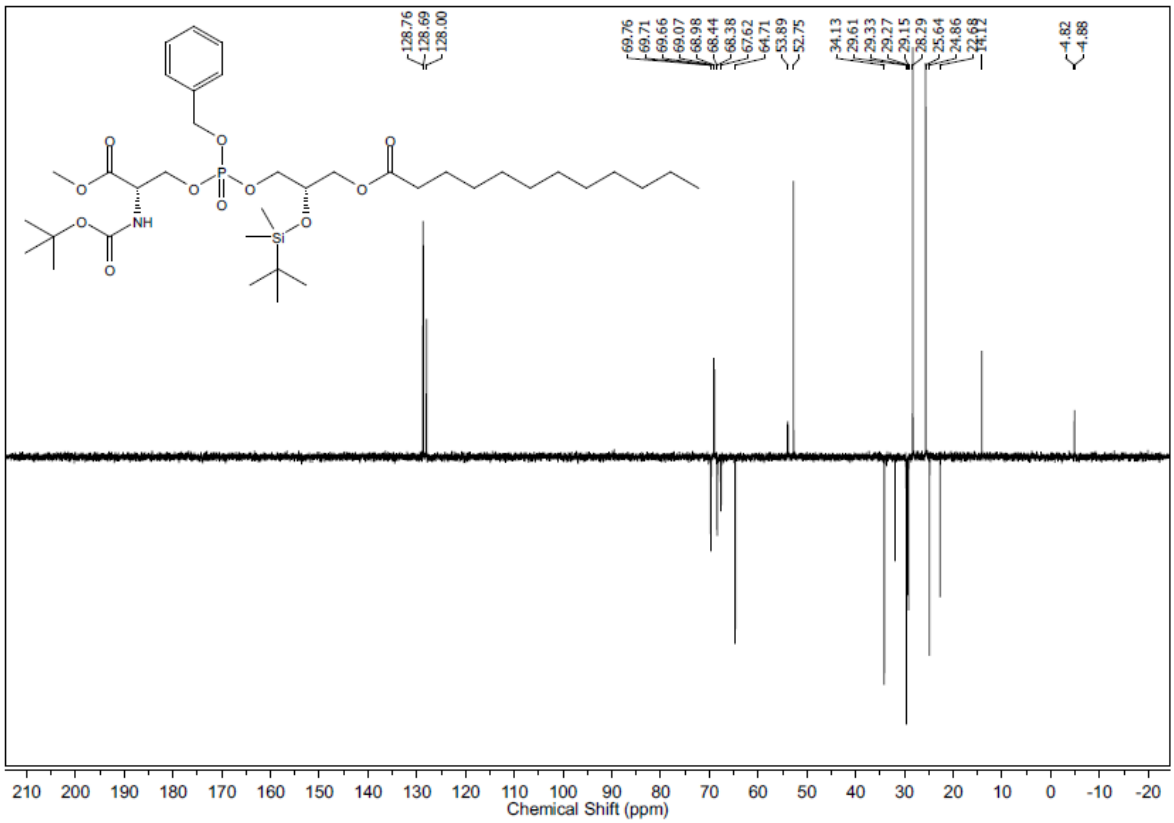
^{31}P NMR of compound (*S*)-**8b**



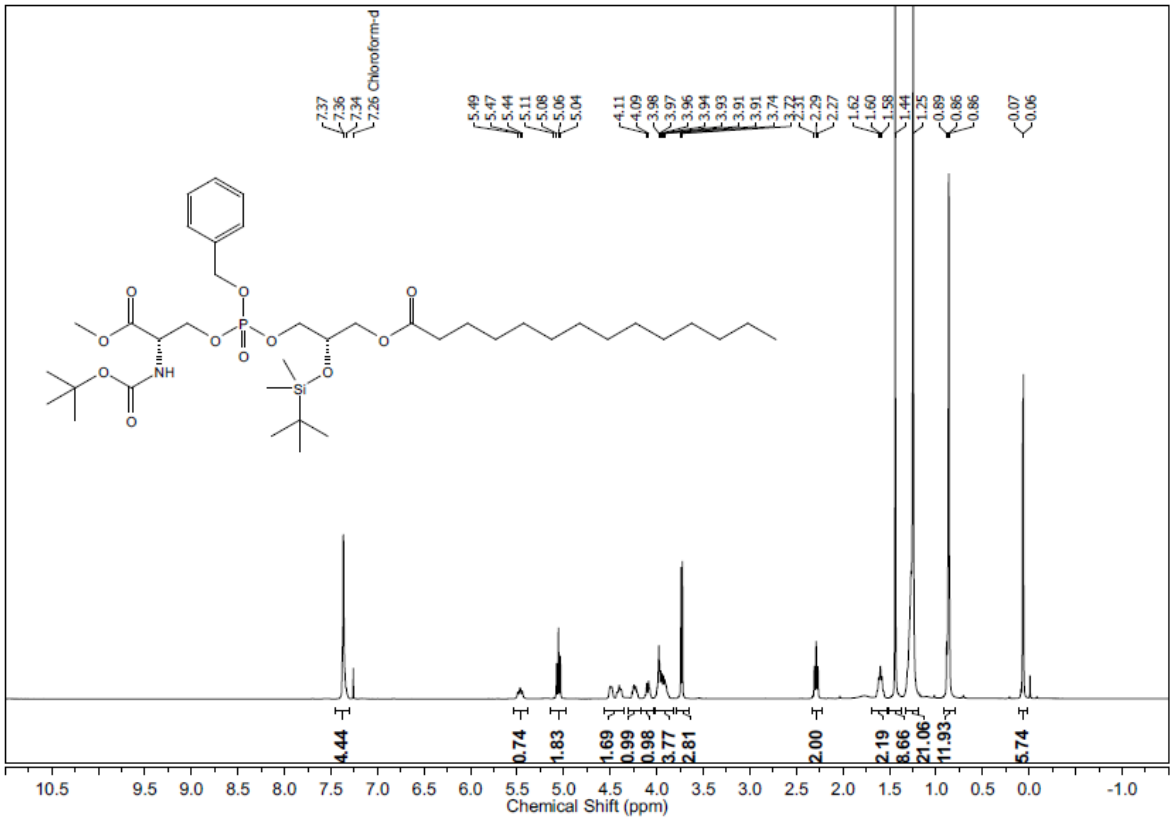
^{13}C NMR of compound (*S*)-**8b**



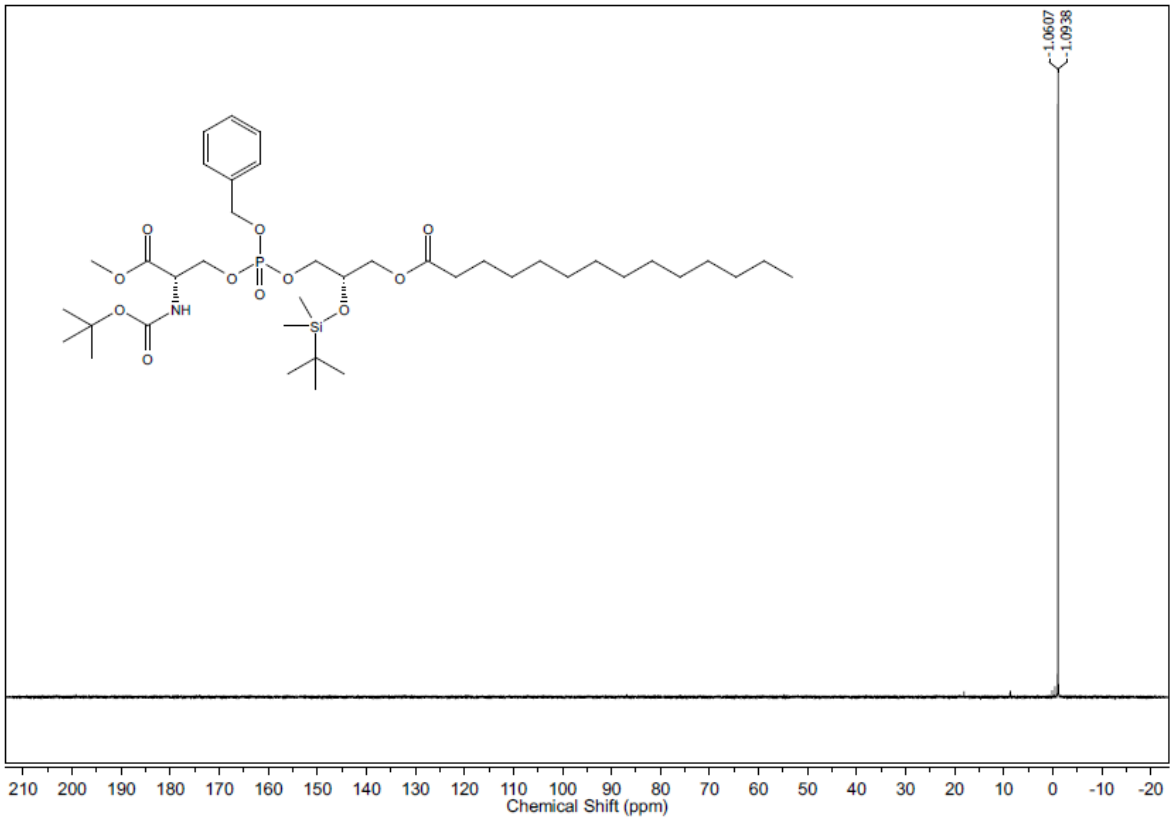
DEPT-135 NMR of compound (*S*)-**8b**



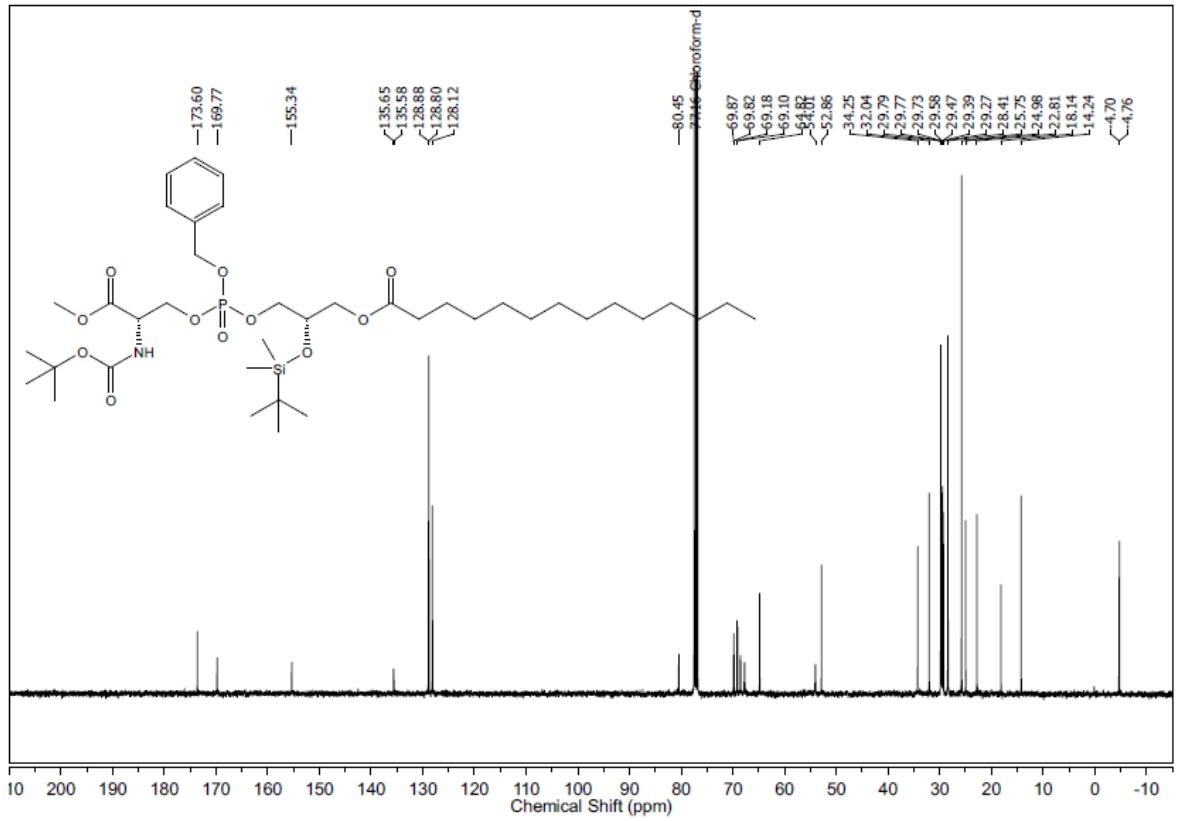
^{1}H NMR of compound (*S*)-**8c**



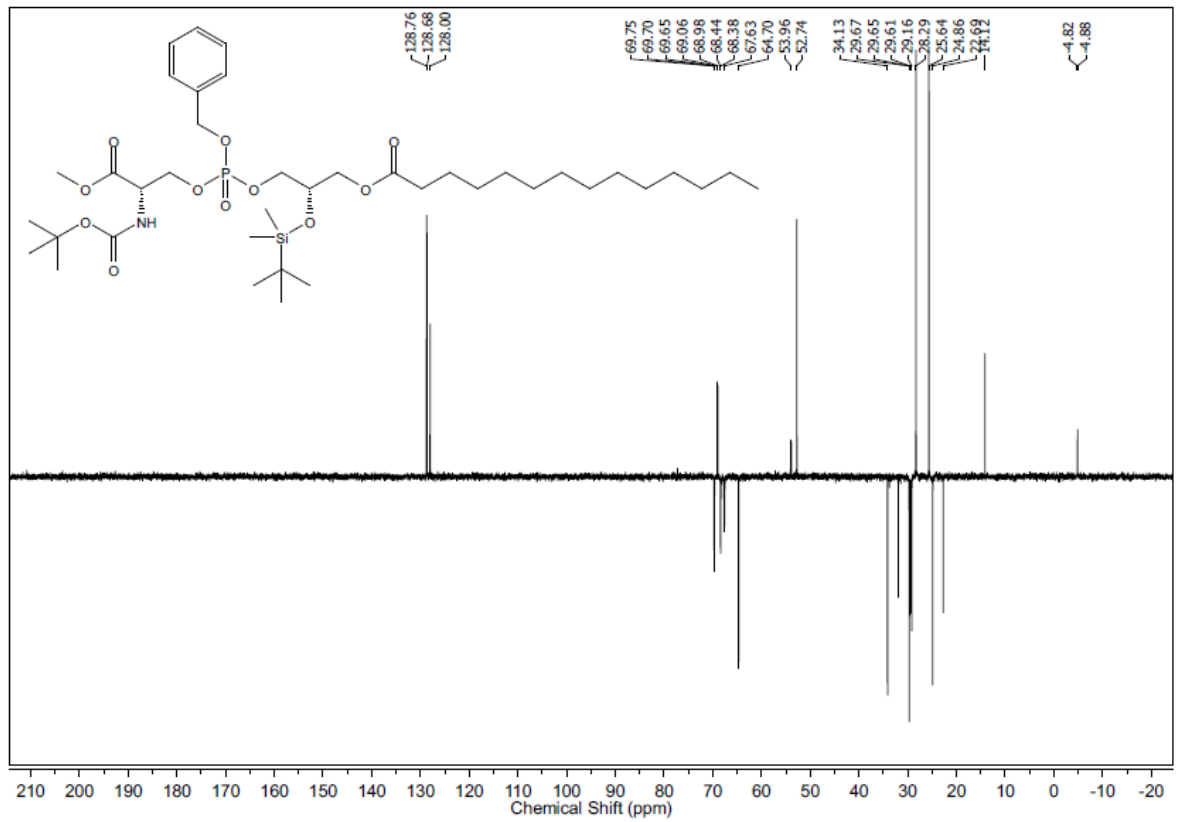
^{31}P NMR of compound (*S*)-**8c**



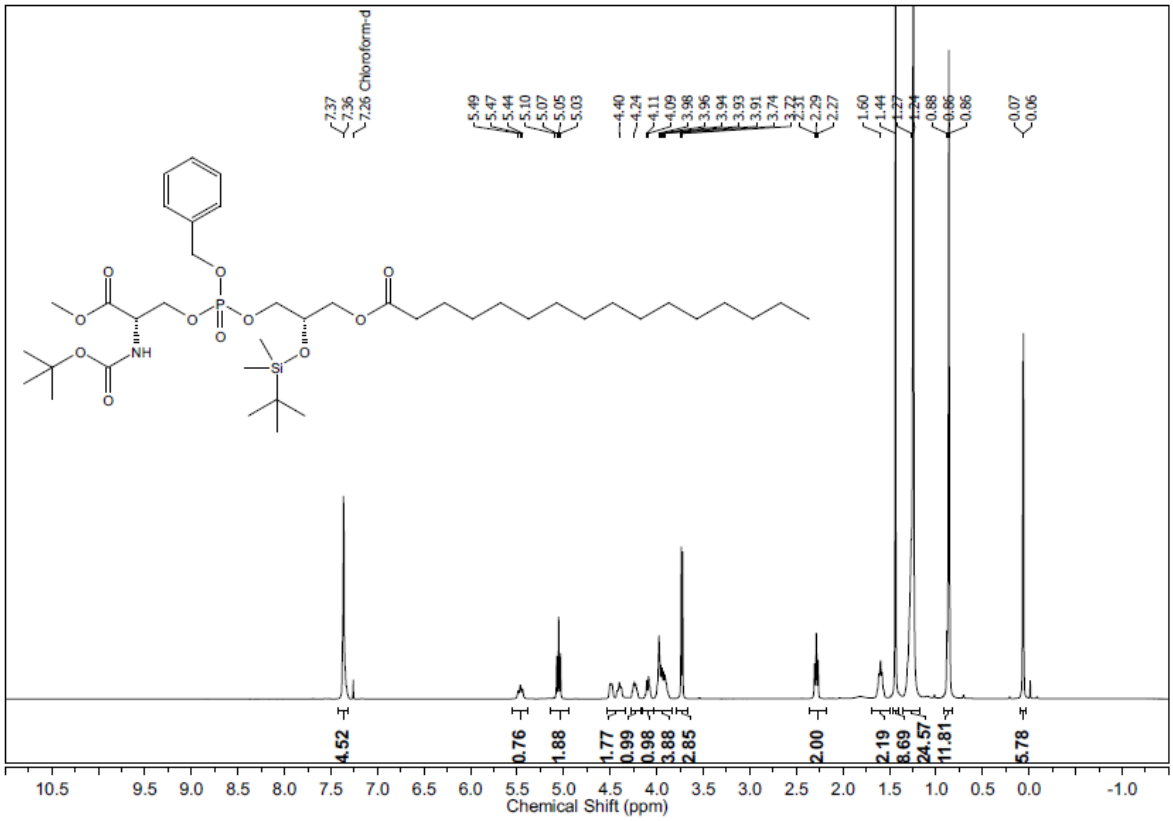
^{13}C NMR of compound (*S*)-**8c**



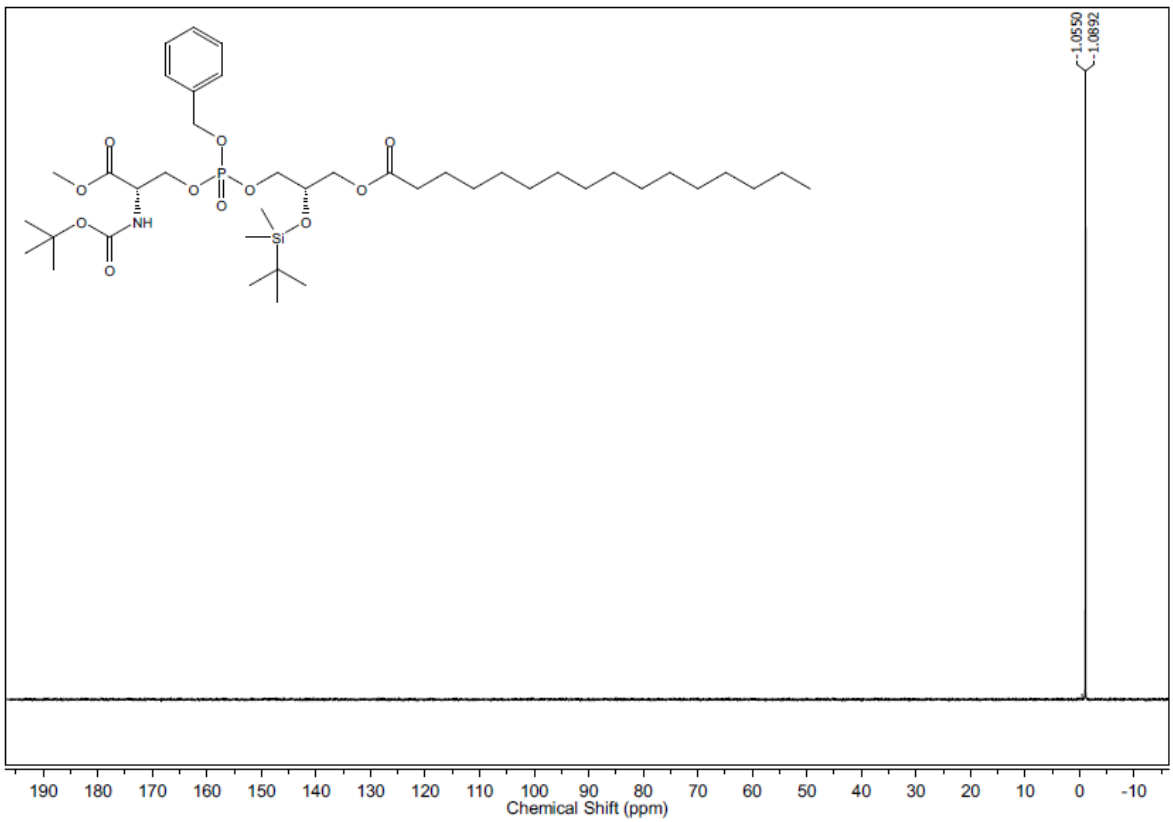
DEPT-135 NMR of compound (*S*)-**8c**



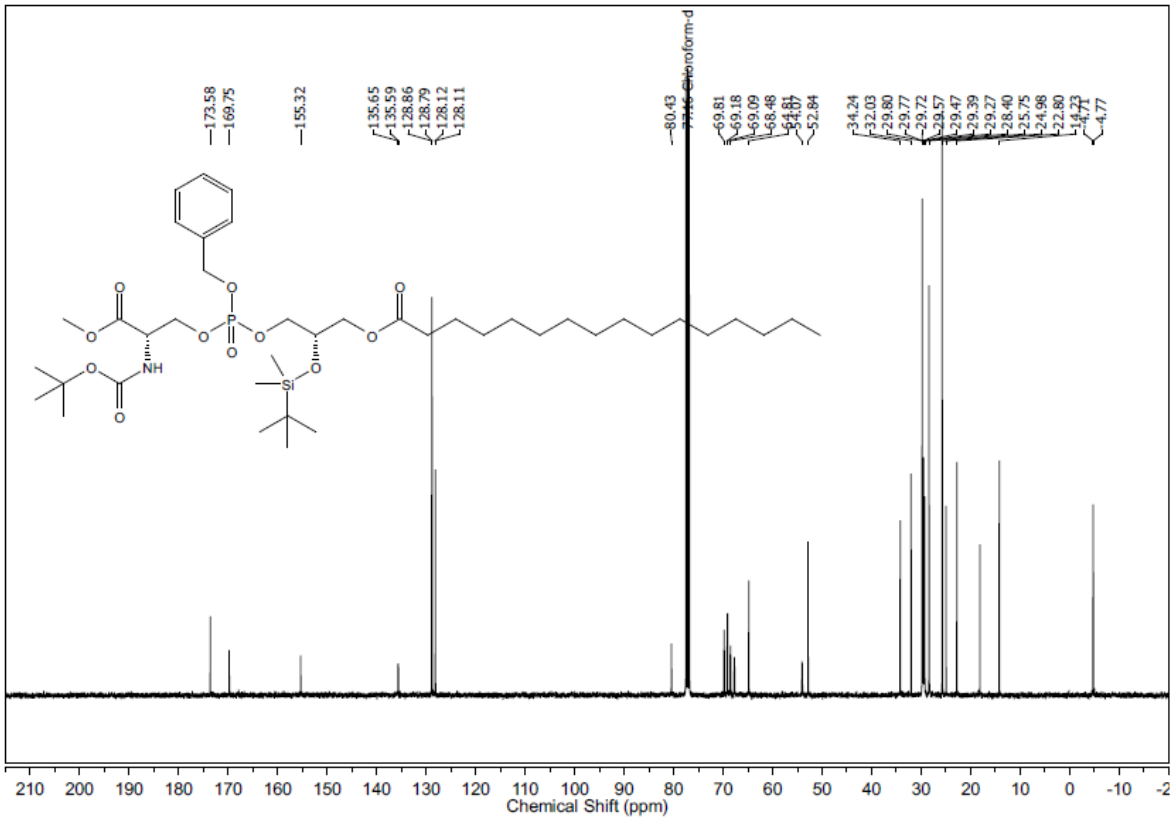
^{1}H NMR of compound (*S*)-**8d**



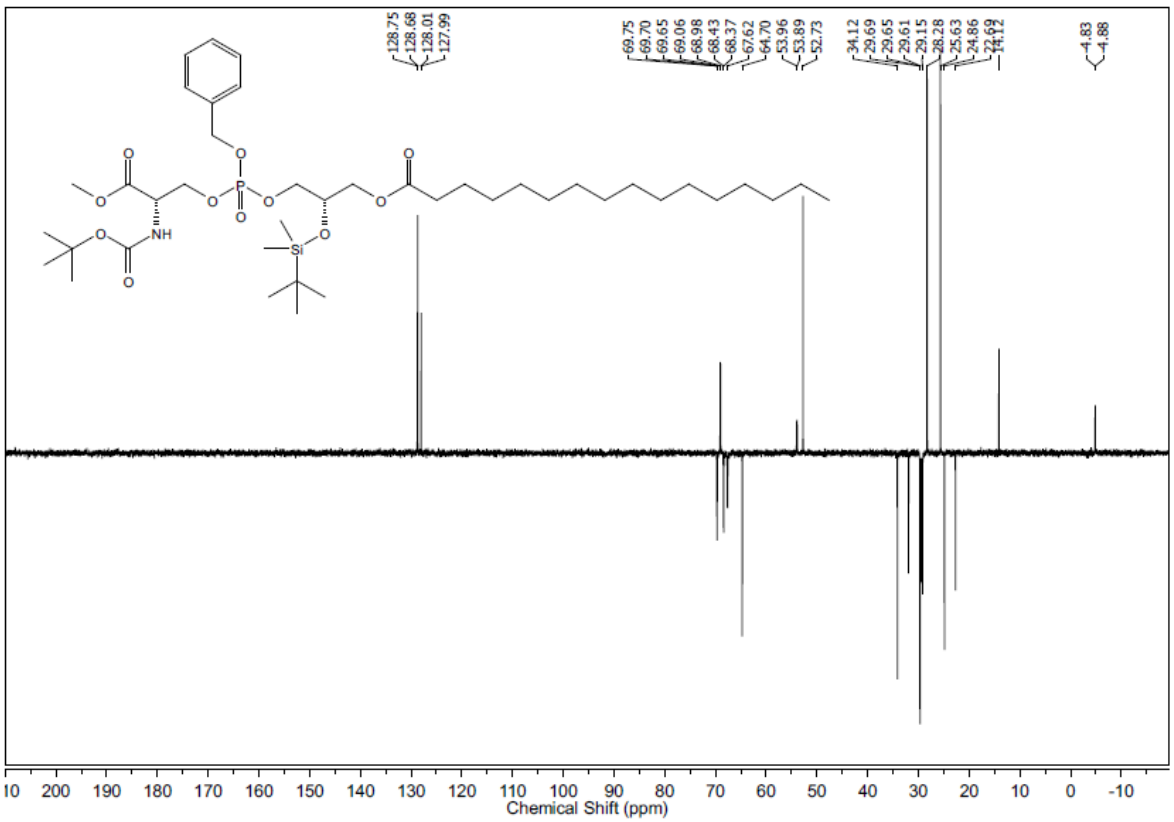
^{31}P NMR of compound (*S*)-**8d**



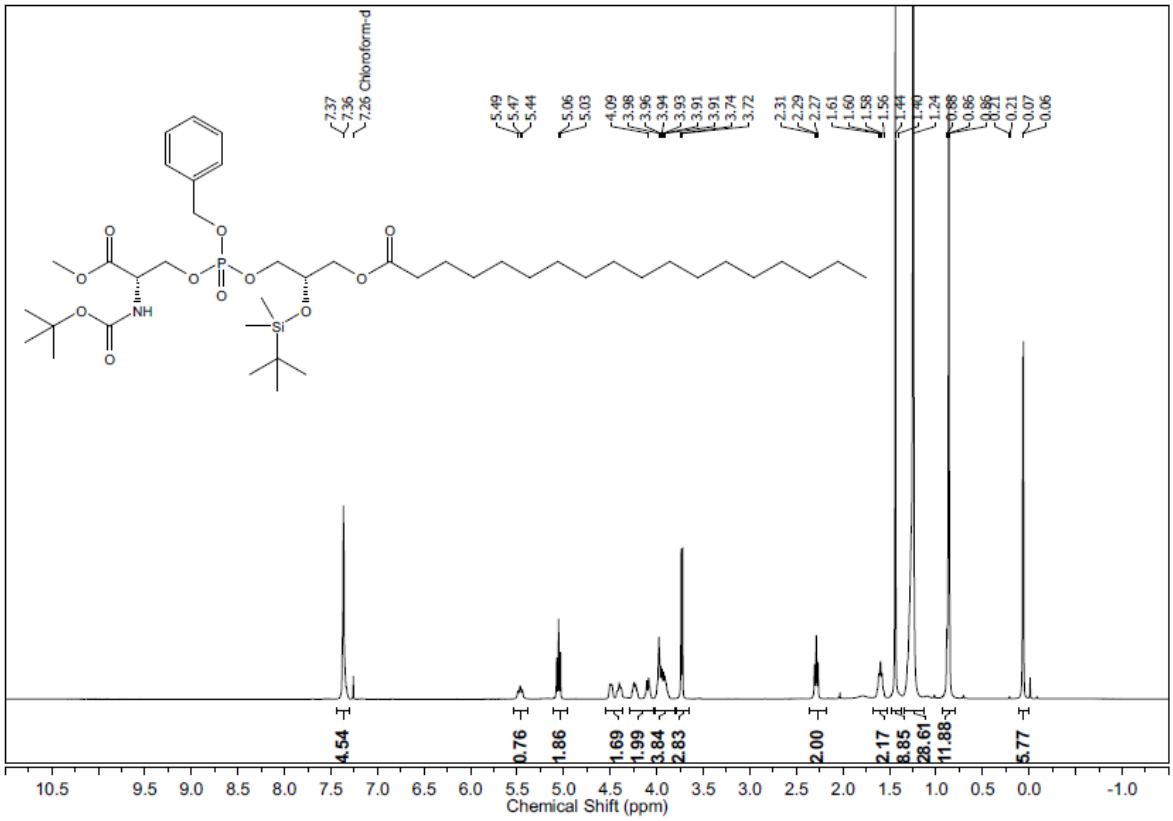
^{13}C NMR of compound (*S*)-**8d**



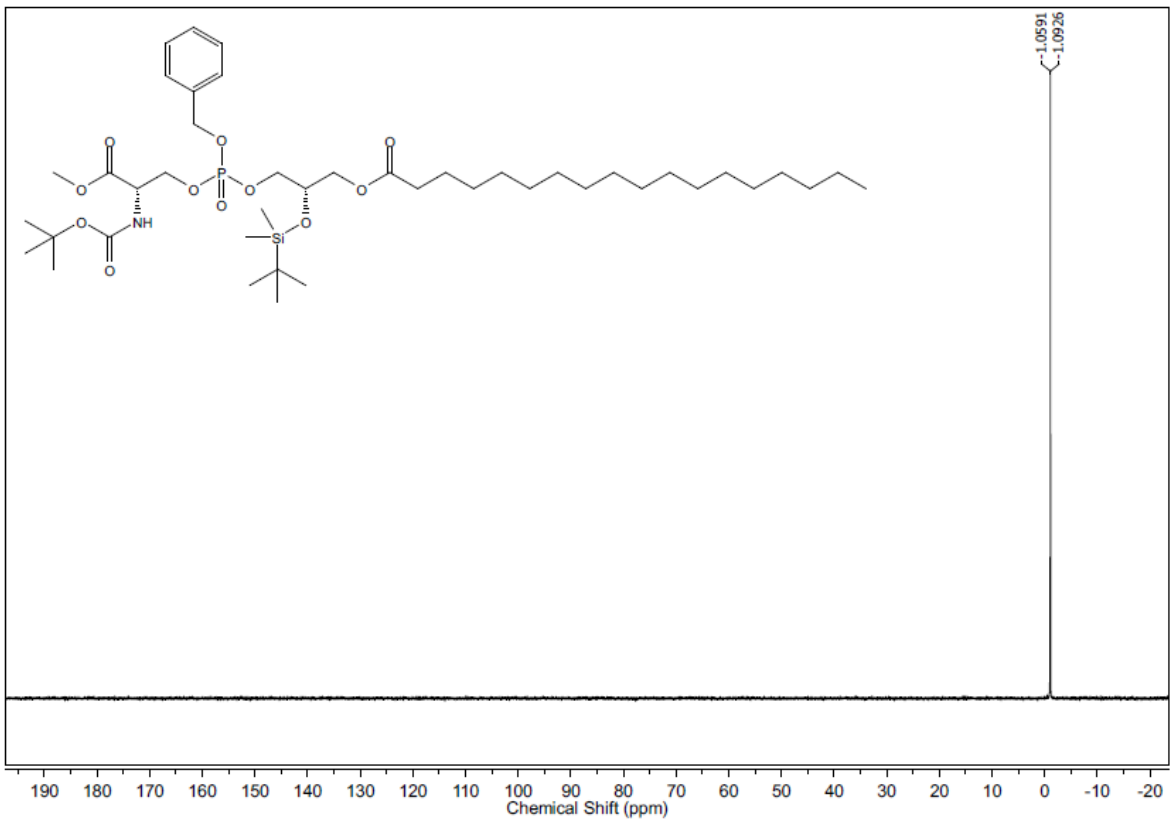
DEPT-135 NMR of compound (*S*)-**8d**



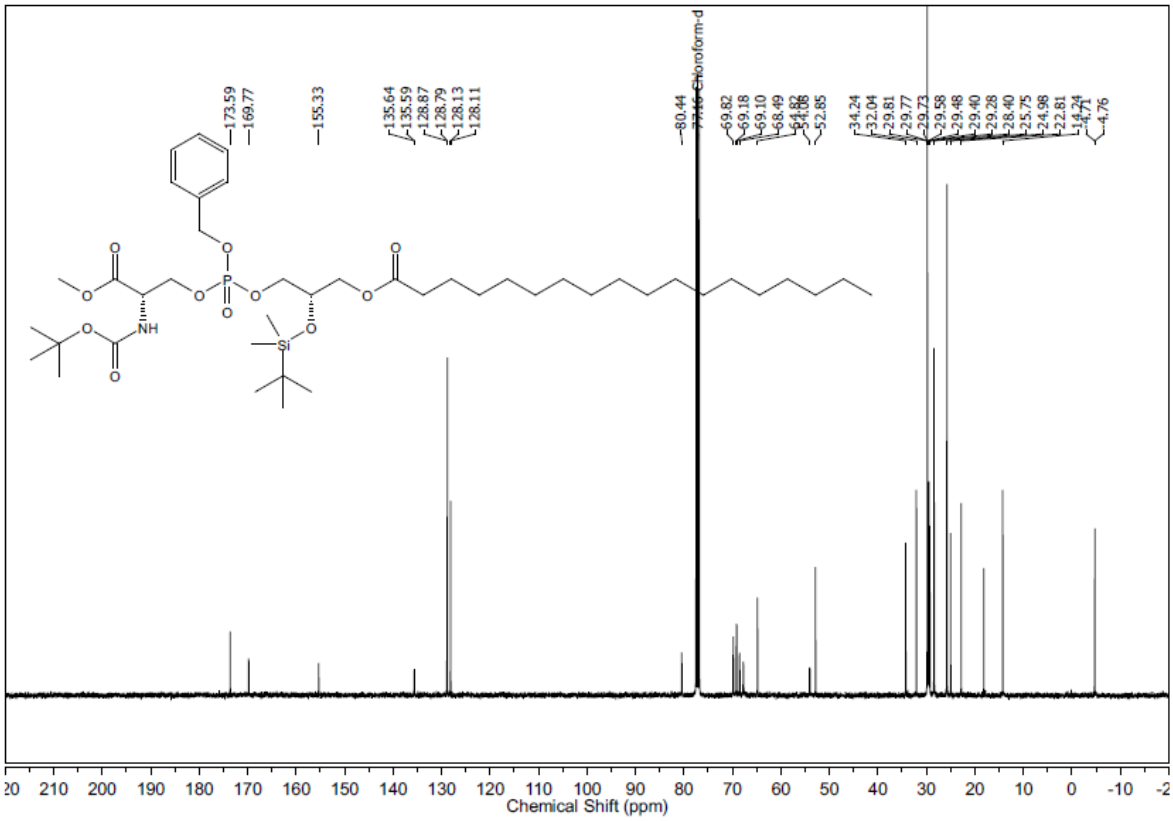
^{1}H NMR of compound (*S*)-**8e**



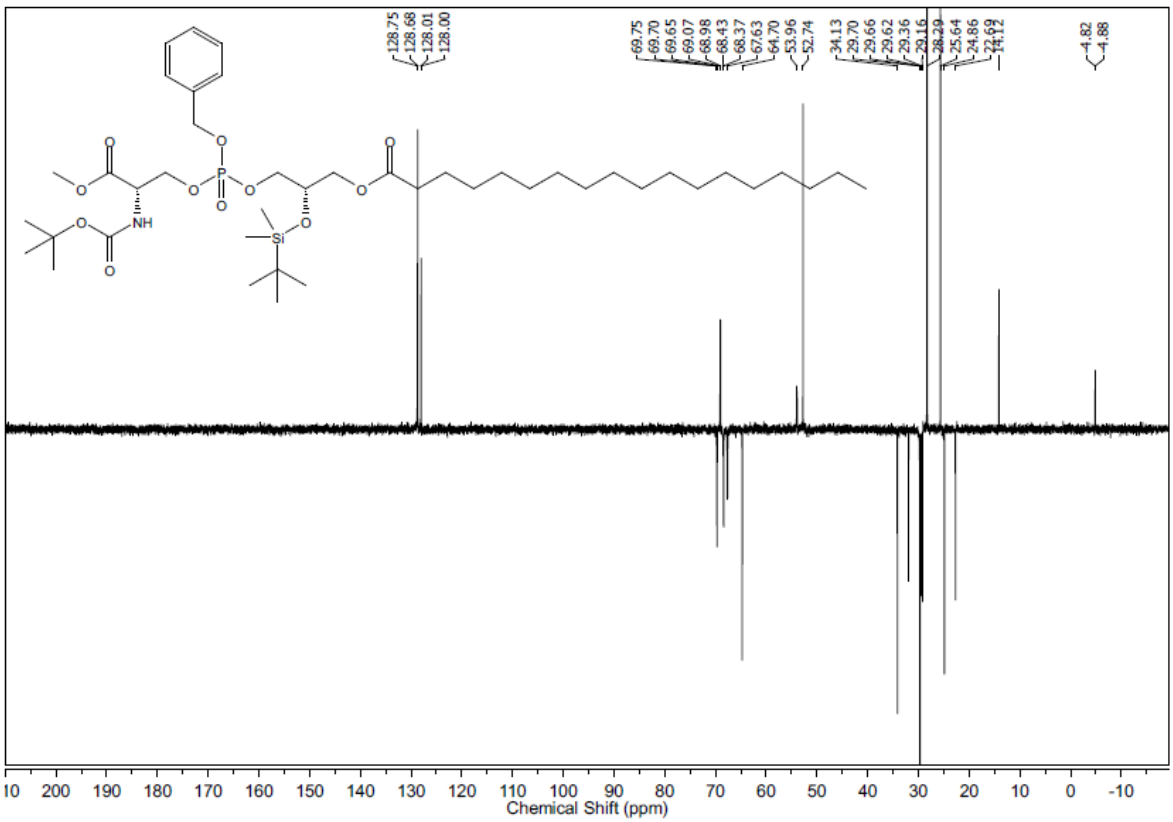
^{31}P NMR of compound (*S*)-**8e**



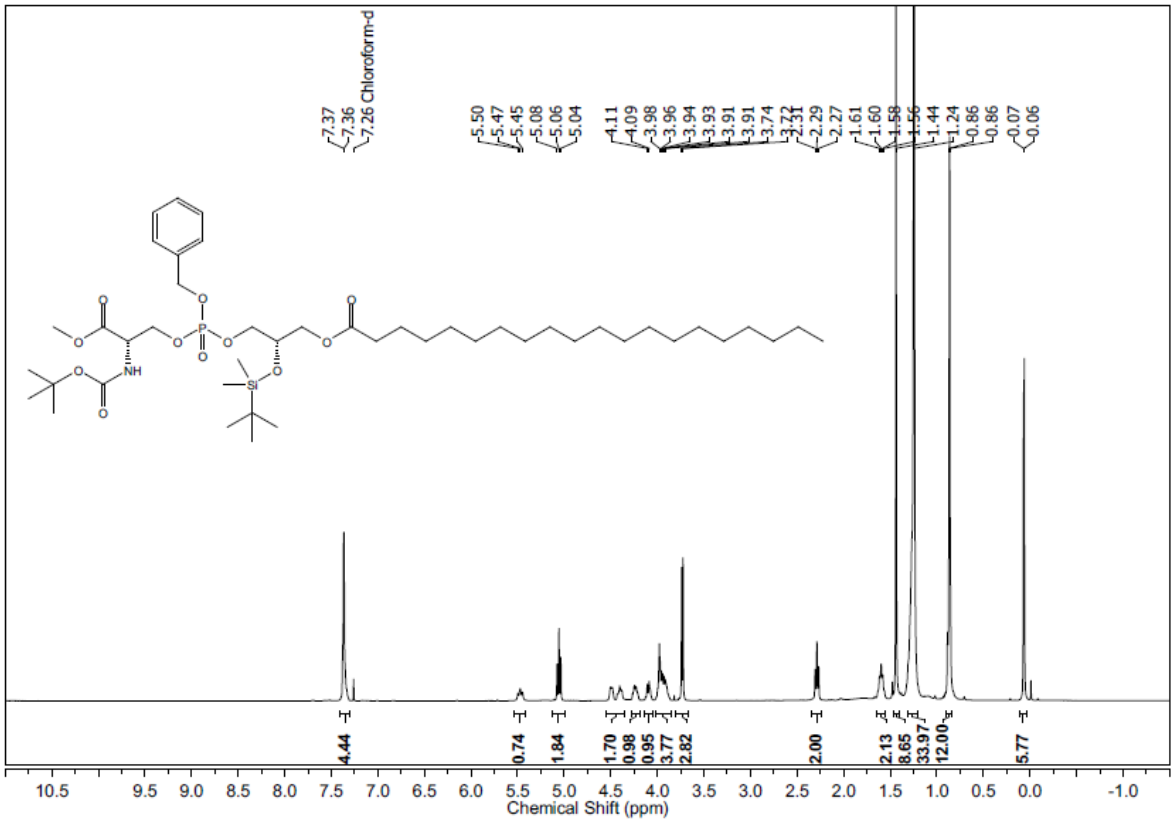
^{13}C NMR of compound (*S*)-**8e**



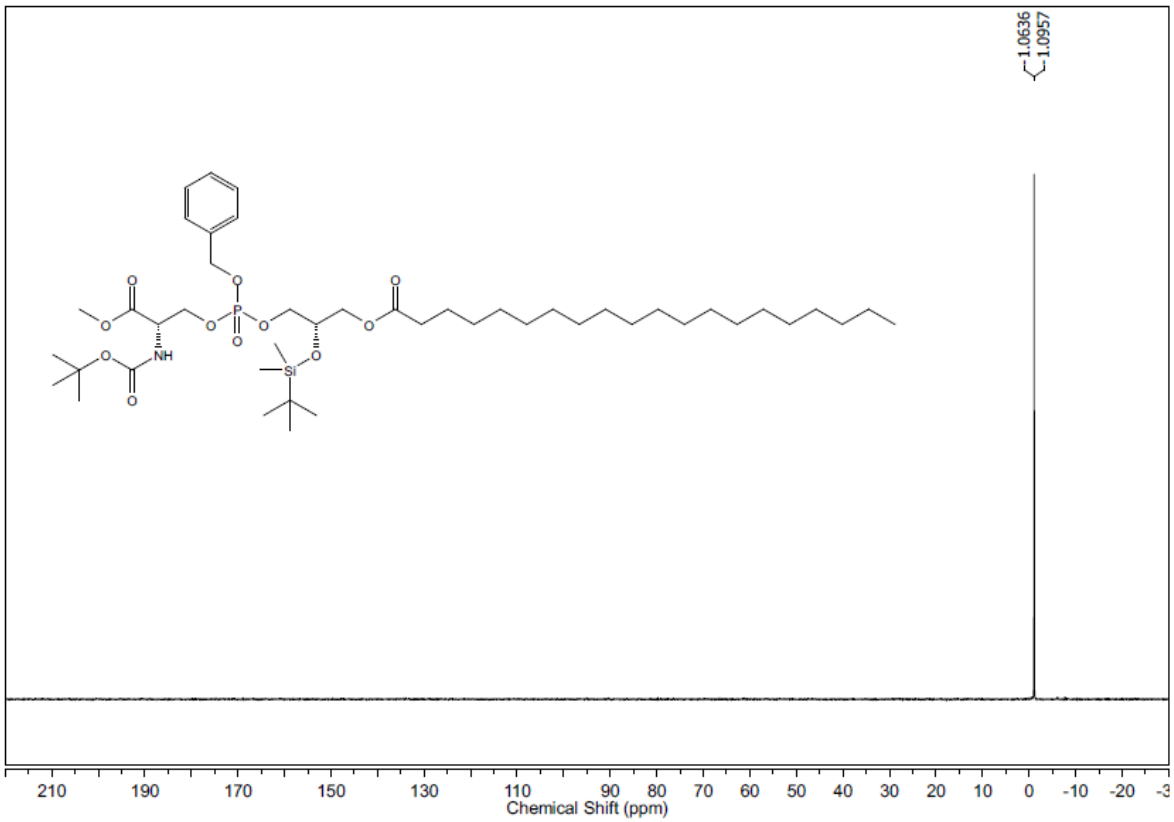
DEPT-135 NMR of compound (*S*)-**8e**



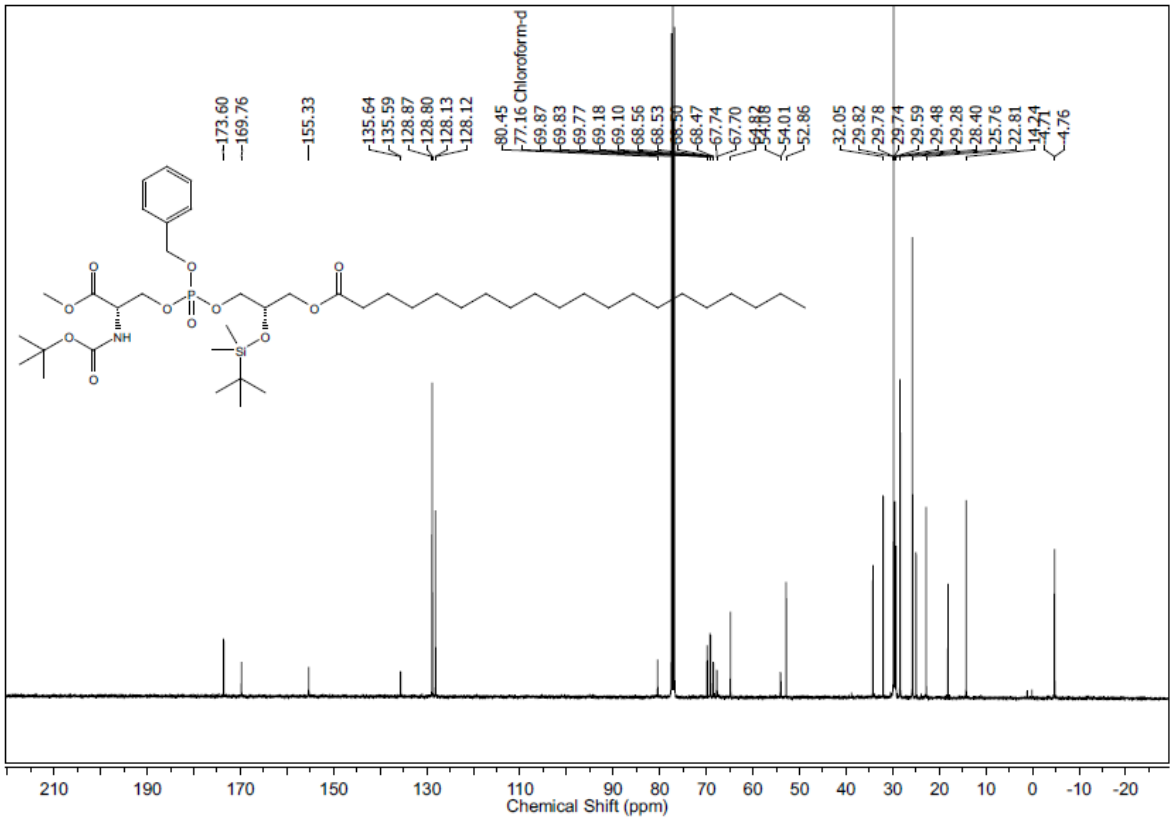
^{1}H NMR of compound (*S*)-**8f**



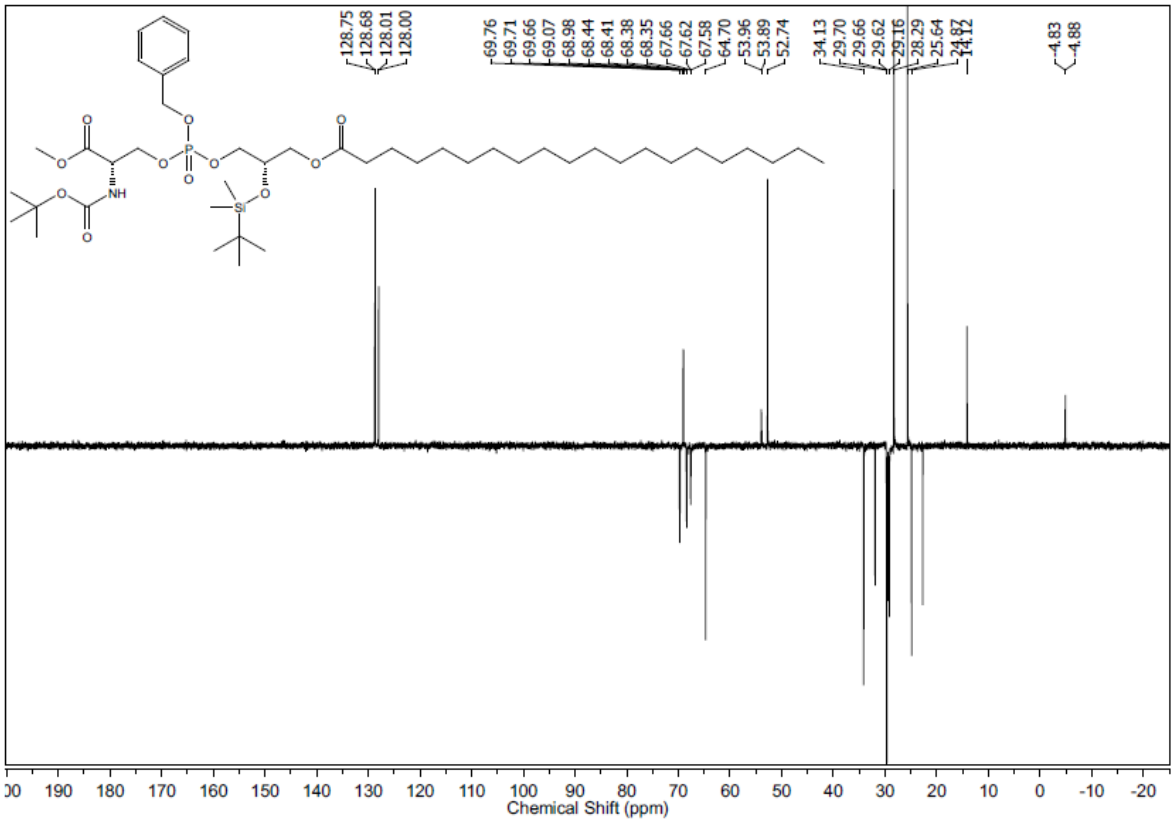
^{31}P NMR of compound (*S*)-**8f**



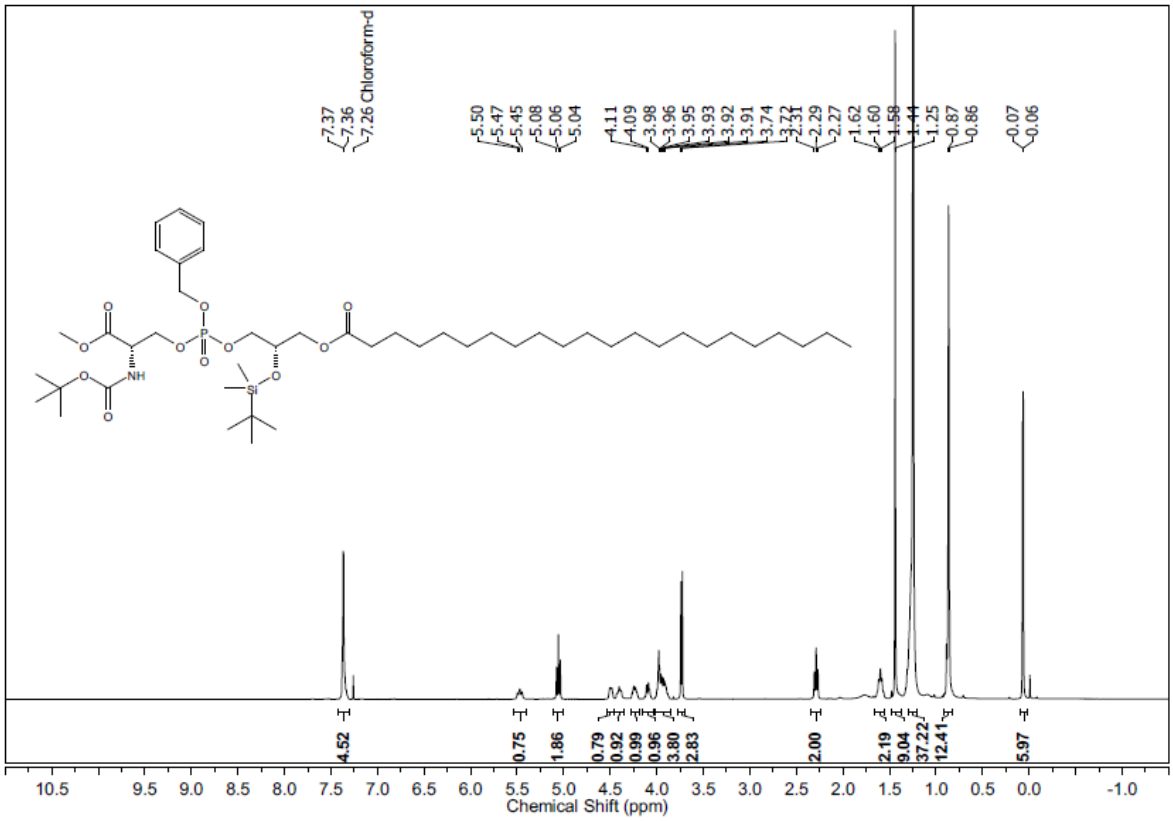
^{13}C NMR of compound (*S*)-**8f**



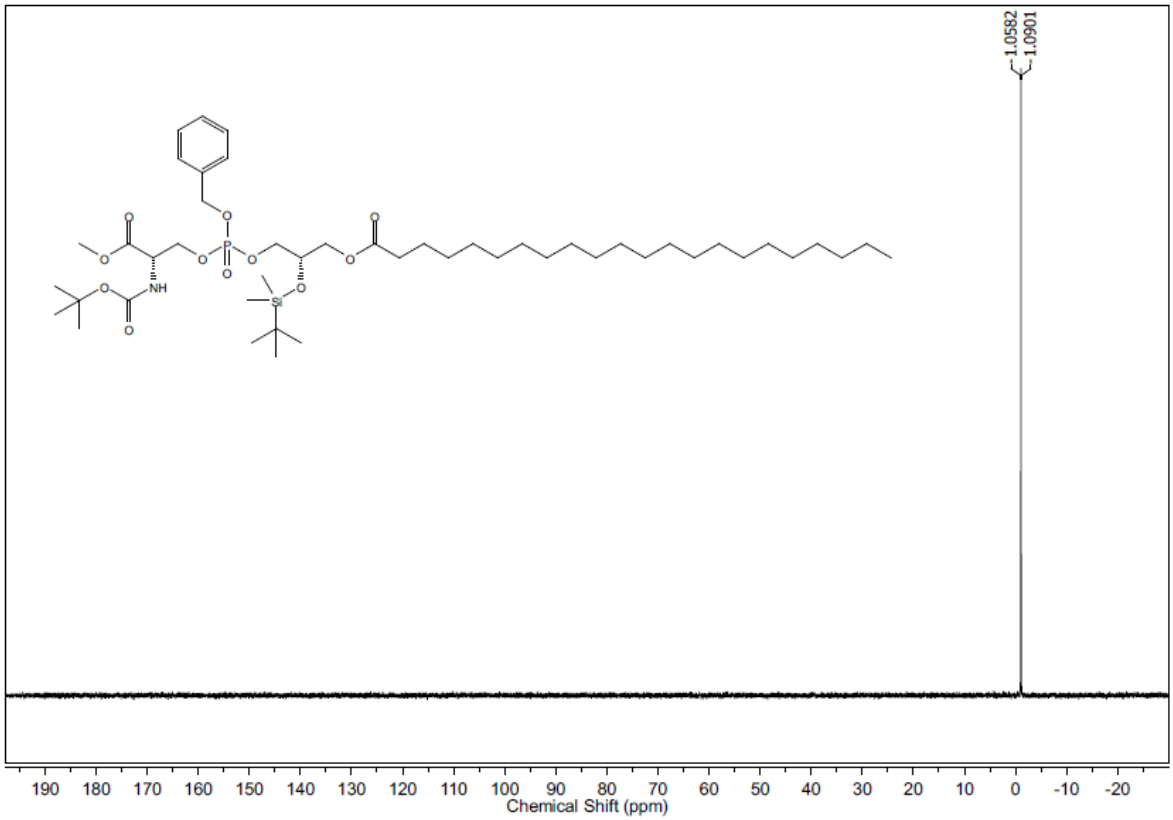
DEPT-135 NMR of compound (*S*)-**8f**



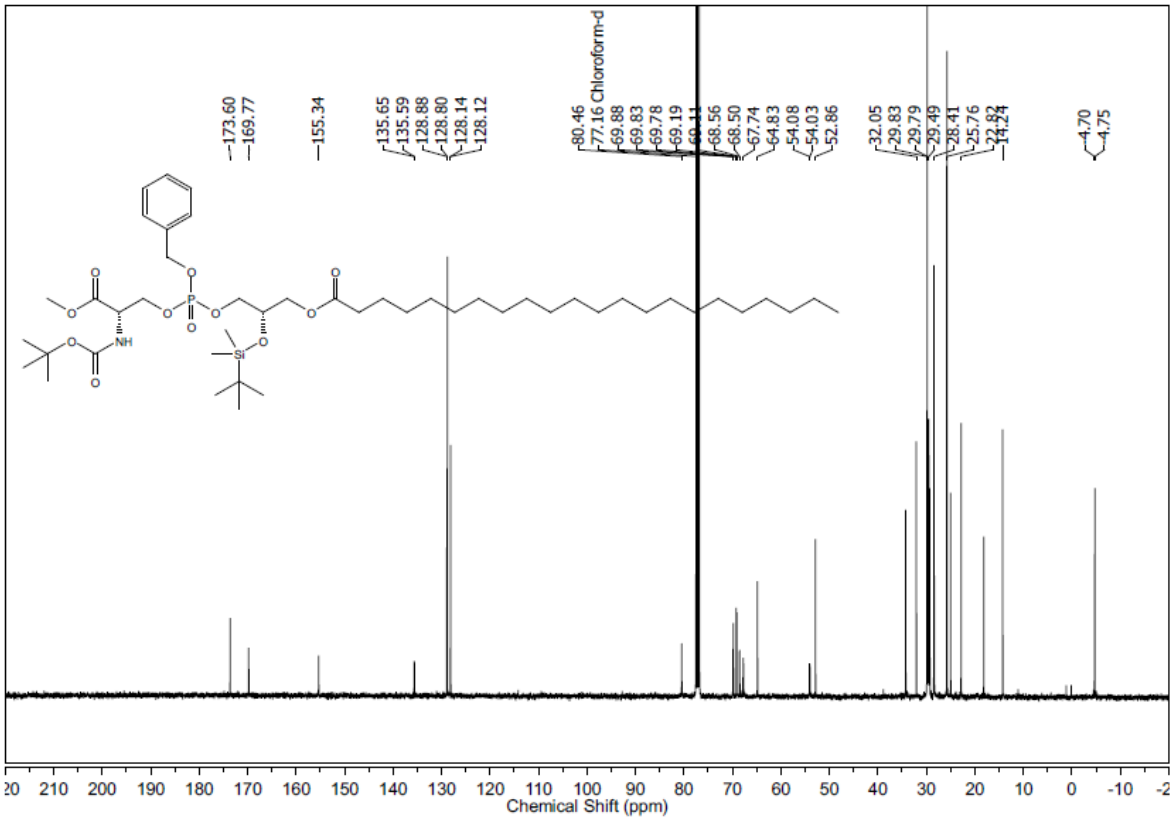
^{1}H NMR of compound (*S*)-**8g**



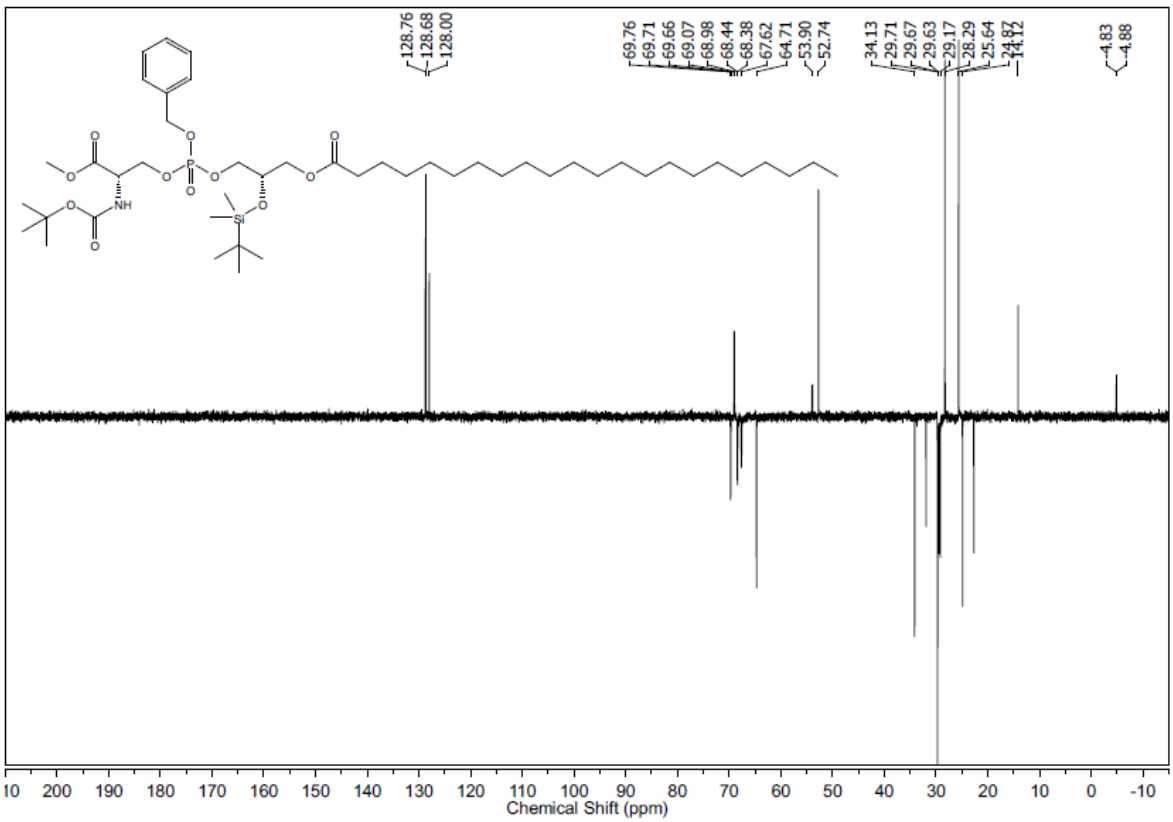
^{31}P NMR of compound (*S*)-**8g**



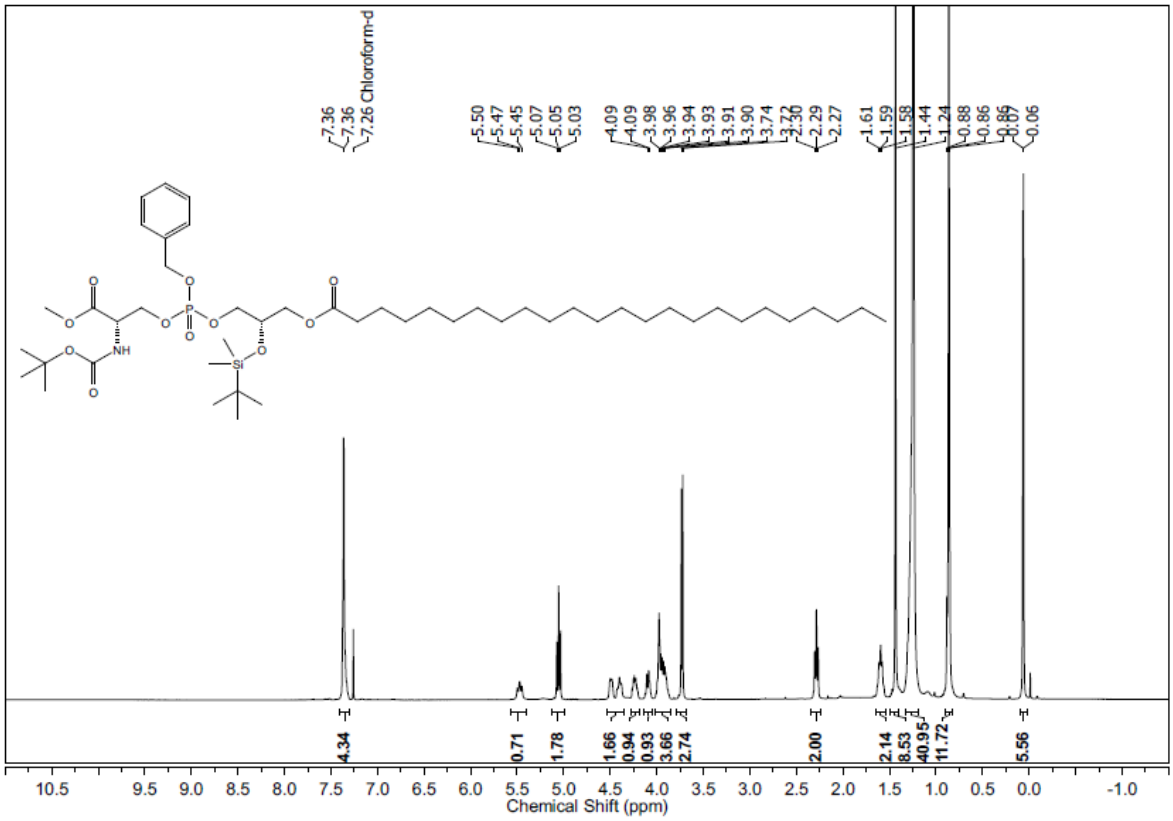
^{13}C NMR of compound (*S*)-**8g**



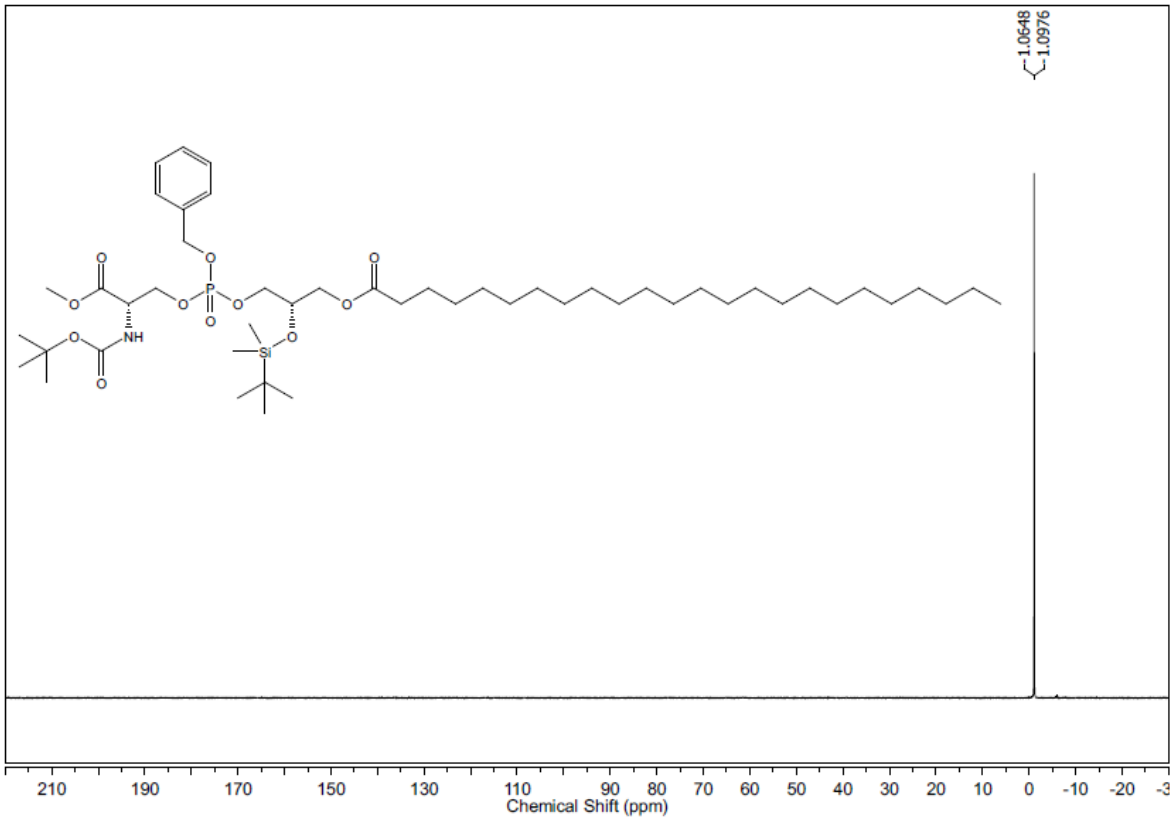
DEPT-135 NMR of compound (*S*)-**8g**



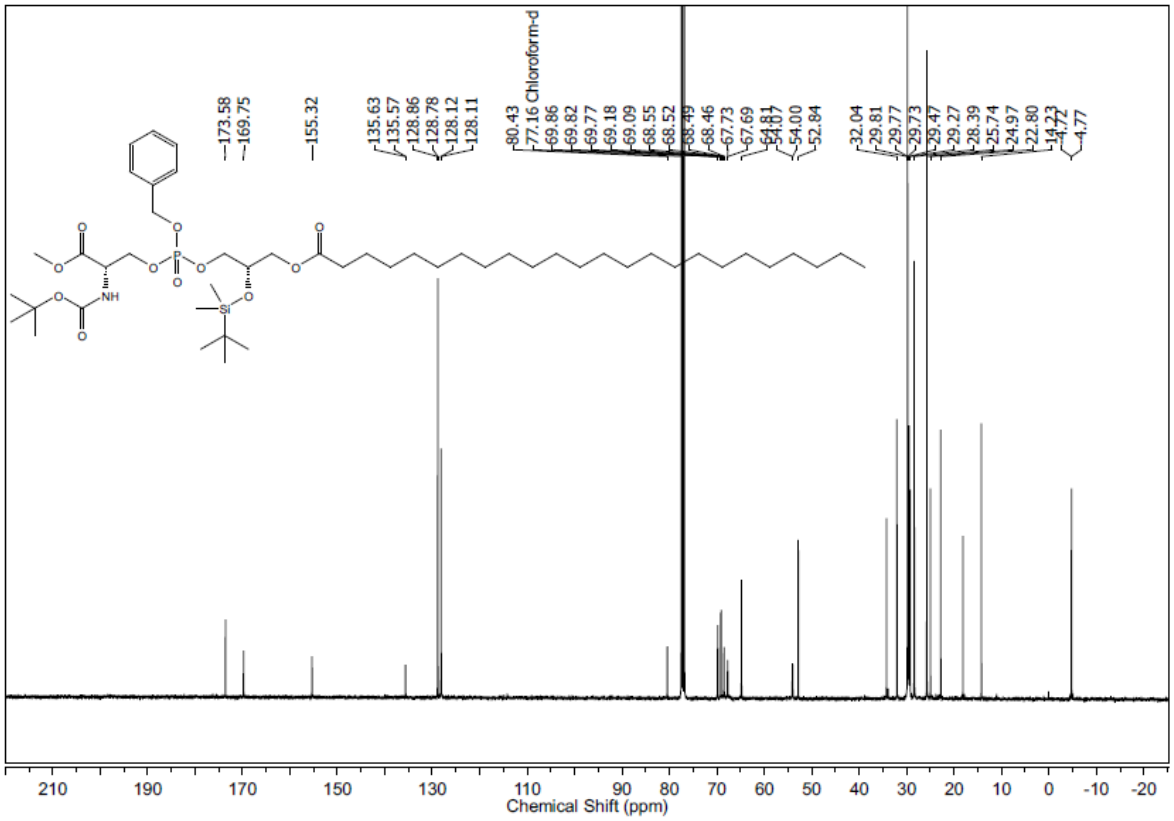
^{1}H NMR of compound (*S*)-**8h**



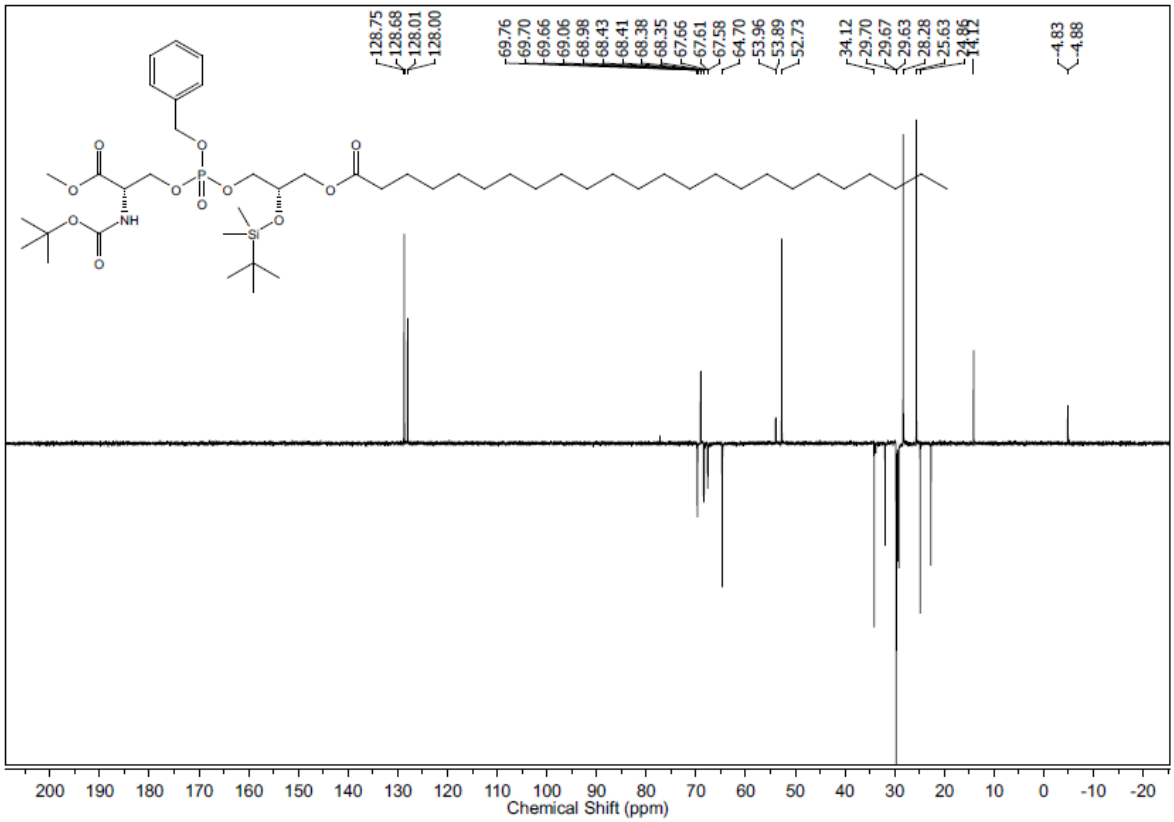
^{31}P NMR of compound (*S*)-**8h**



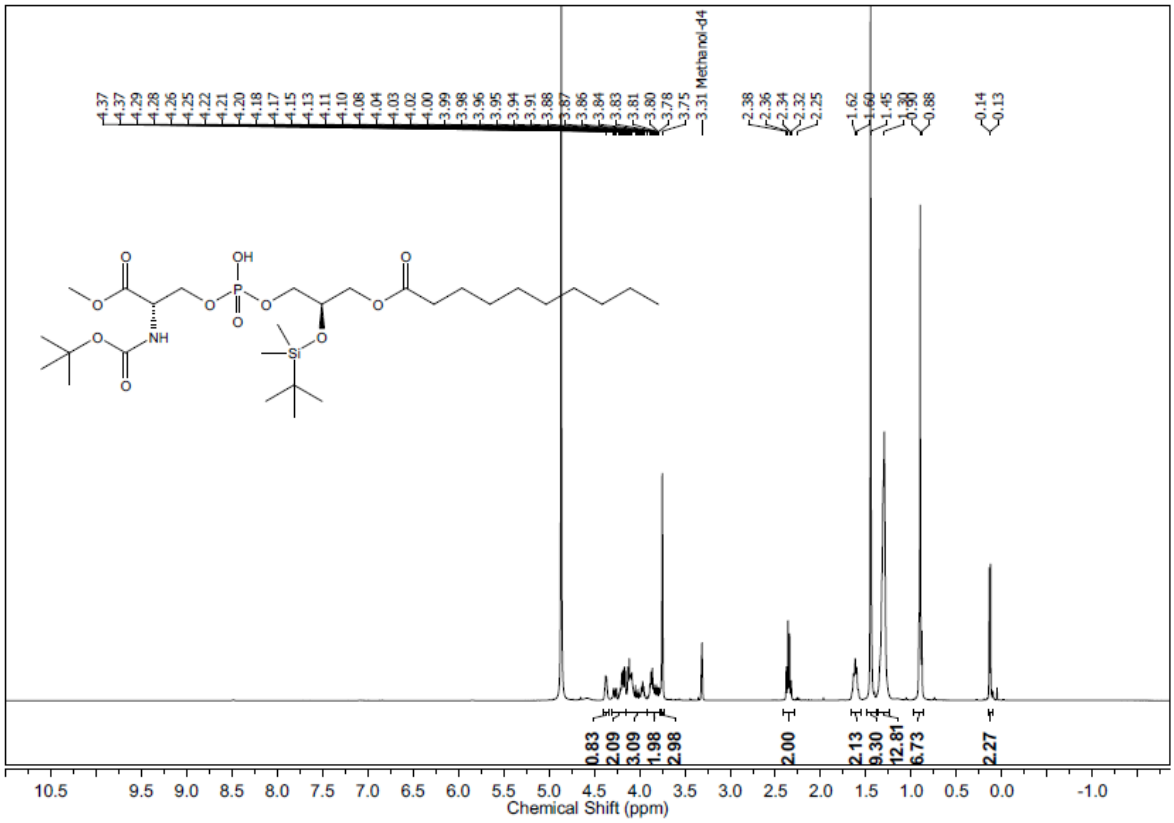
^{13}C NMR of compound (*S*)-**8h**



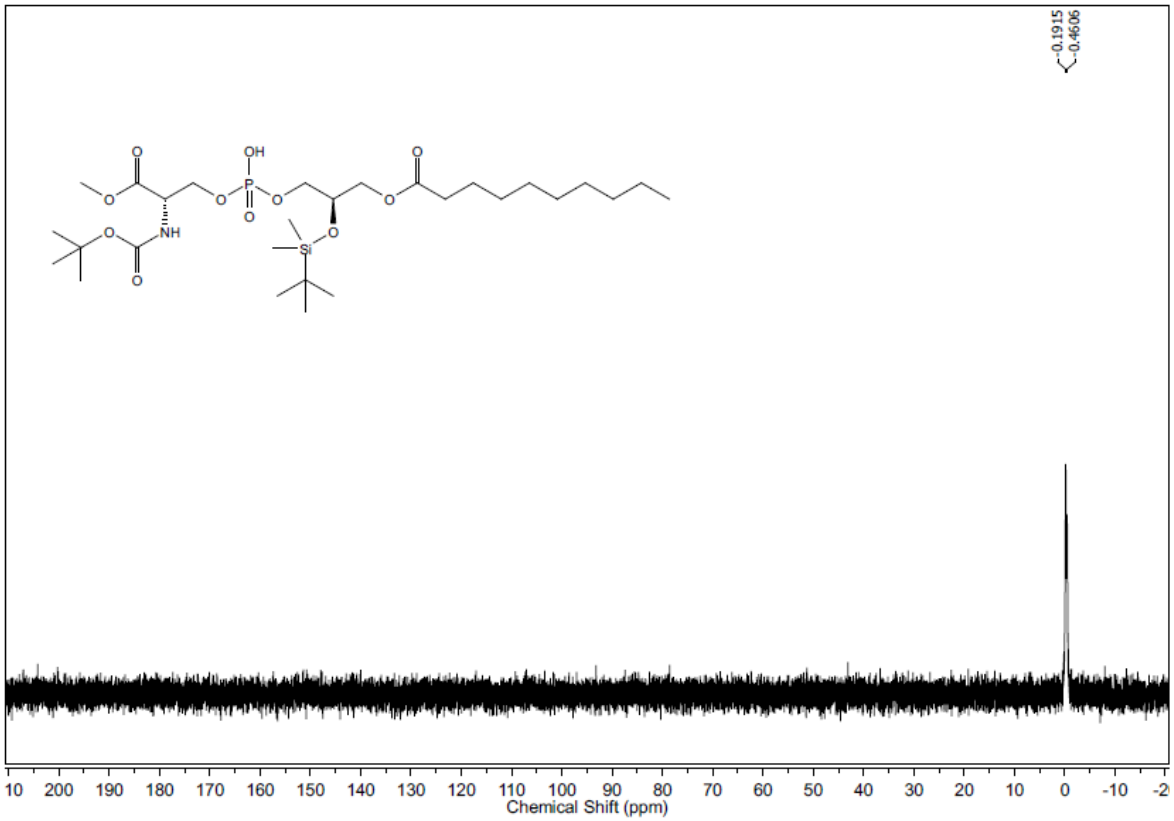
DEPT-135 NMR of compound (*S*)-**8h**



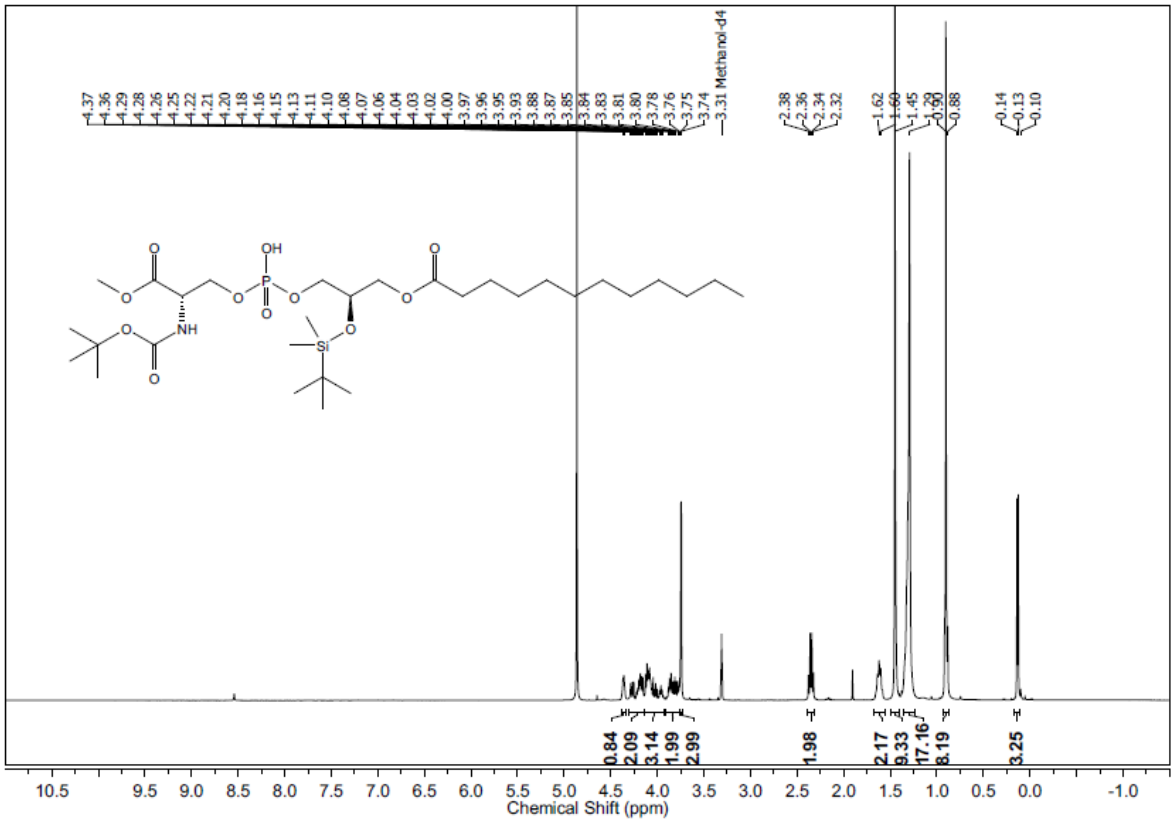
^{1}H NMR of intermediate (*R*)-**9a**



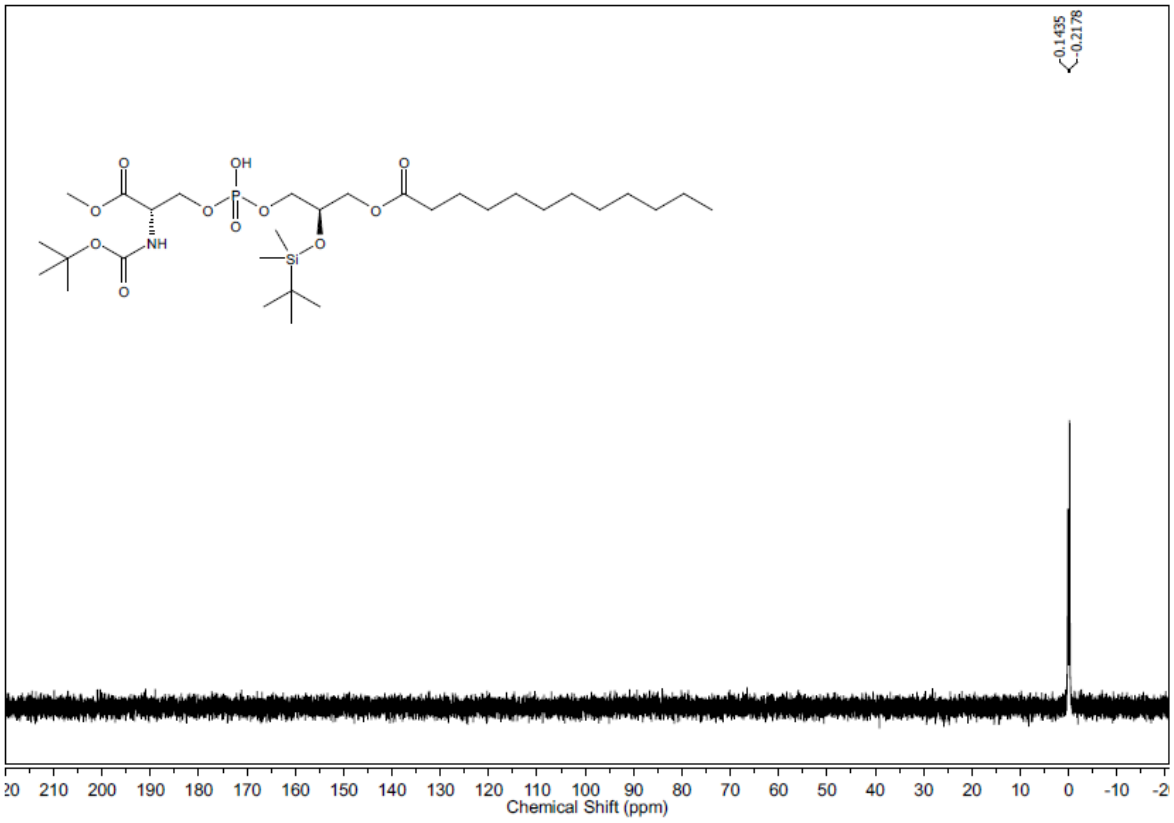
^{31}P NMR of intermediate (*R*)-**9a**



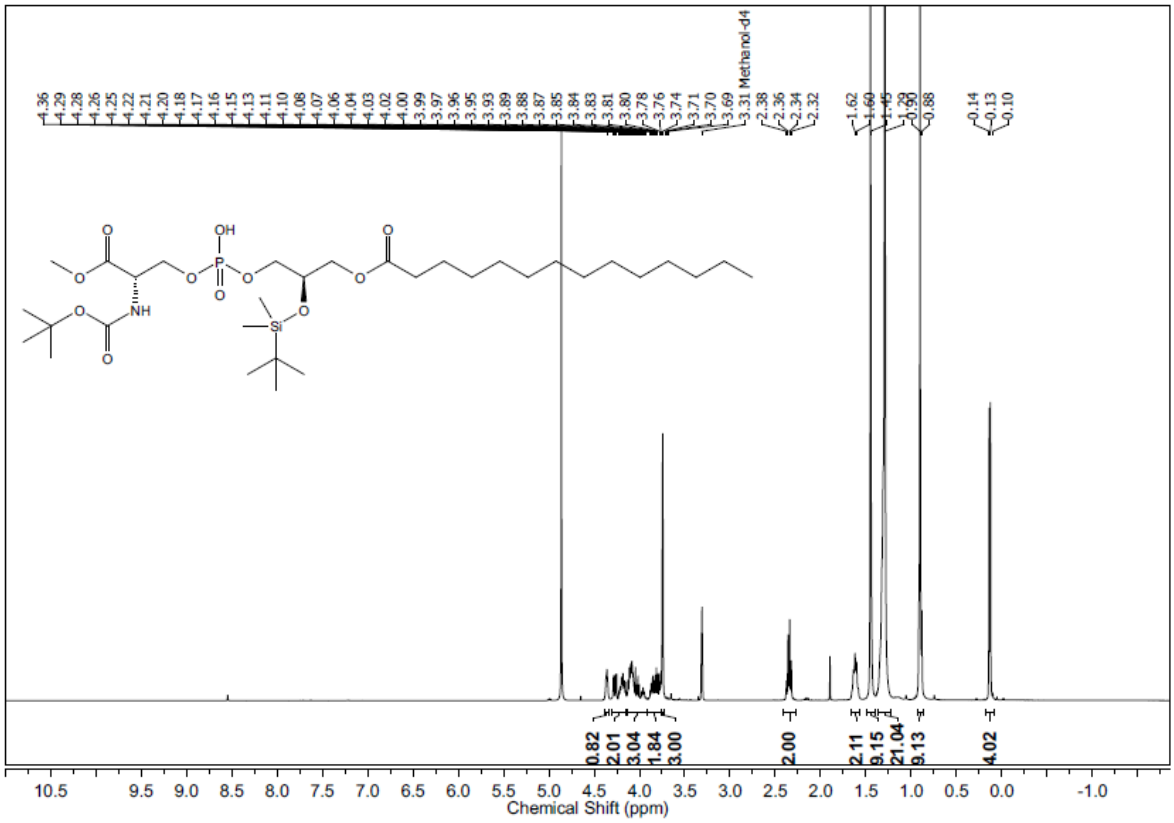
^{1}H NMR of intermediate (*R*)-**9b**



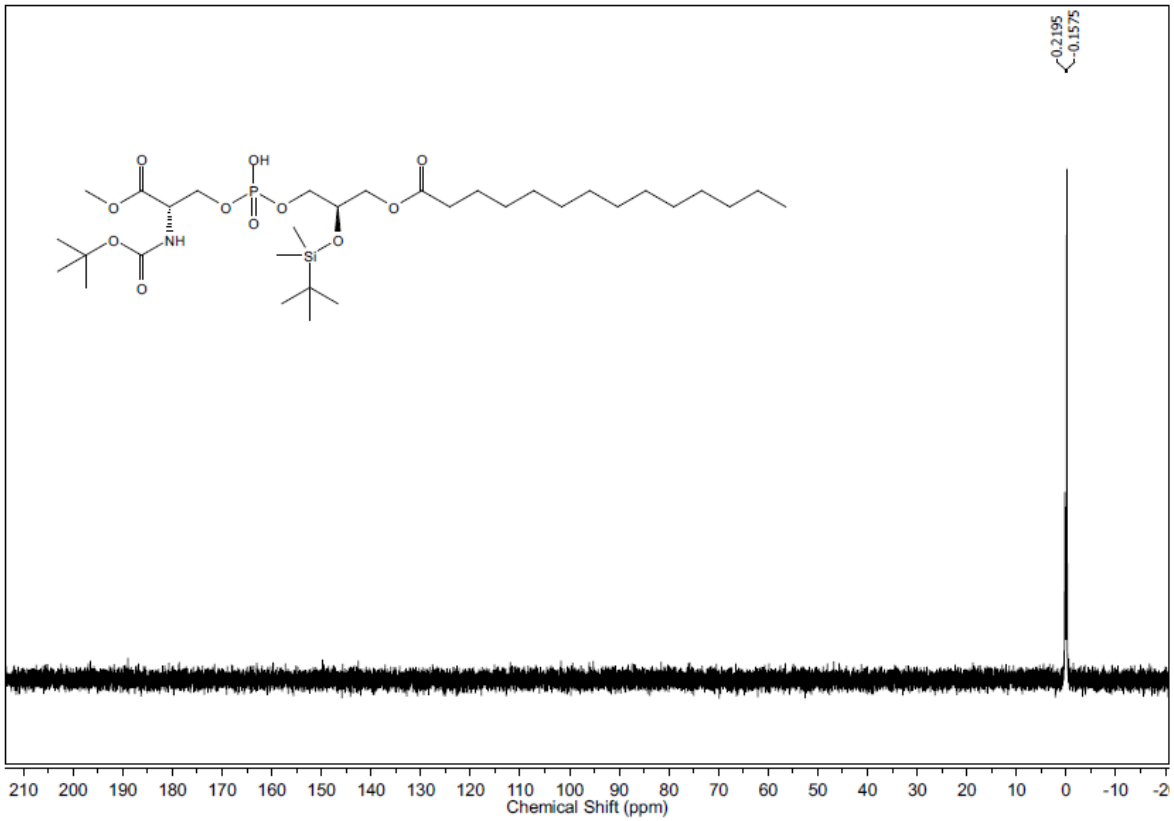
^{31}P NMR of intermediate (*R*)-**9b**



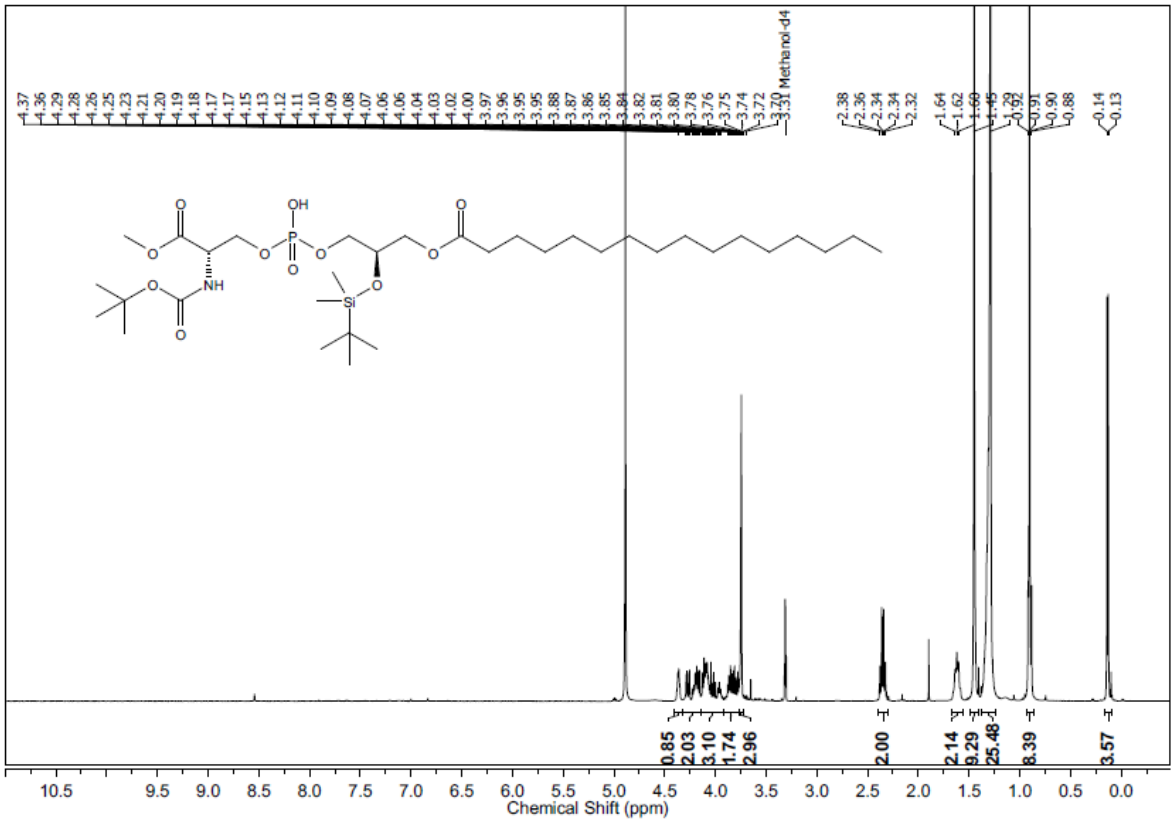
^{1}H NMR of intermediate (*R*)-**9c**



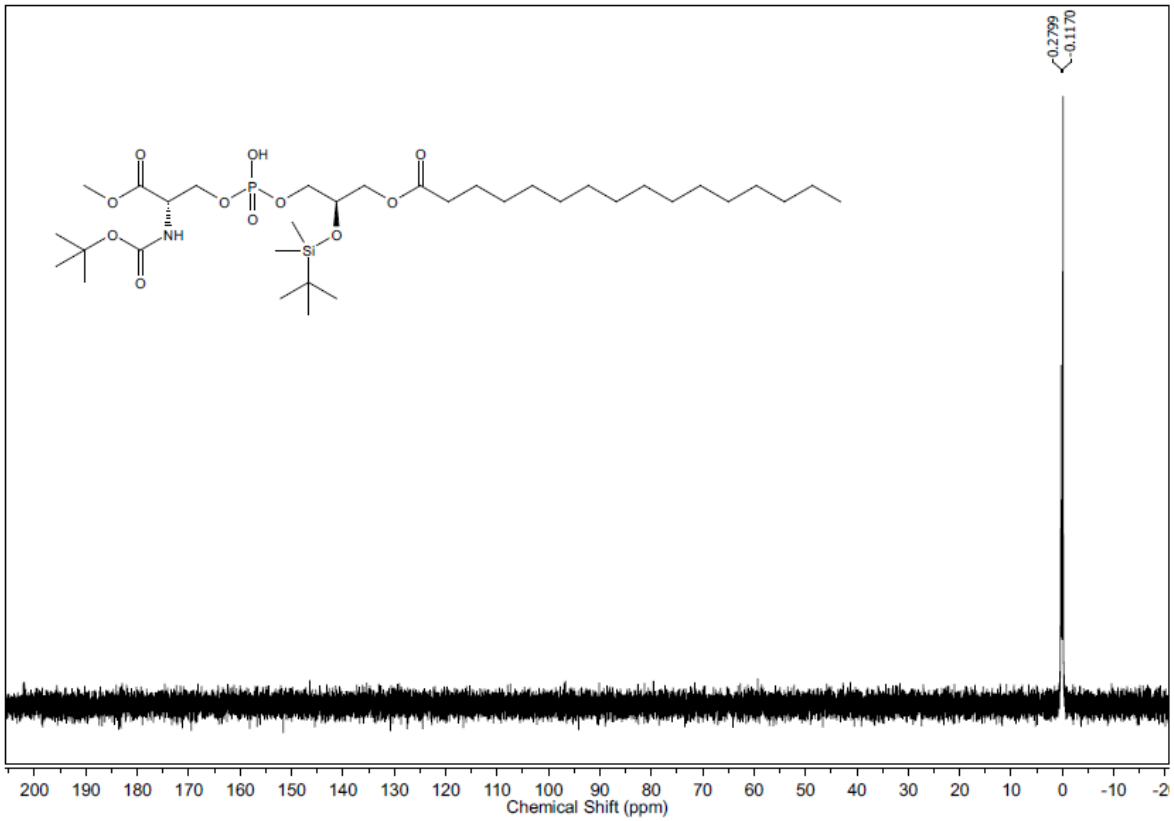
^{31}P NMR of intermediate (*R*)-**9c**



^{1}H NMR of intermediate (*R*)-**9d**



^{31}P NMR of intermediate (*R*)-**9d**



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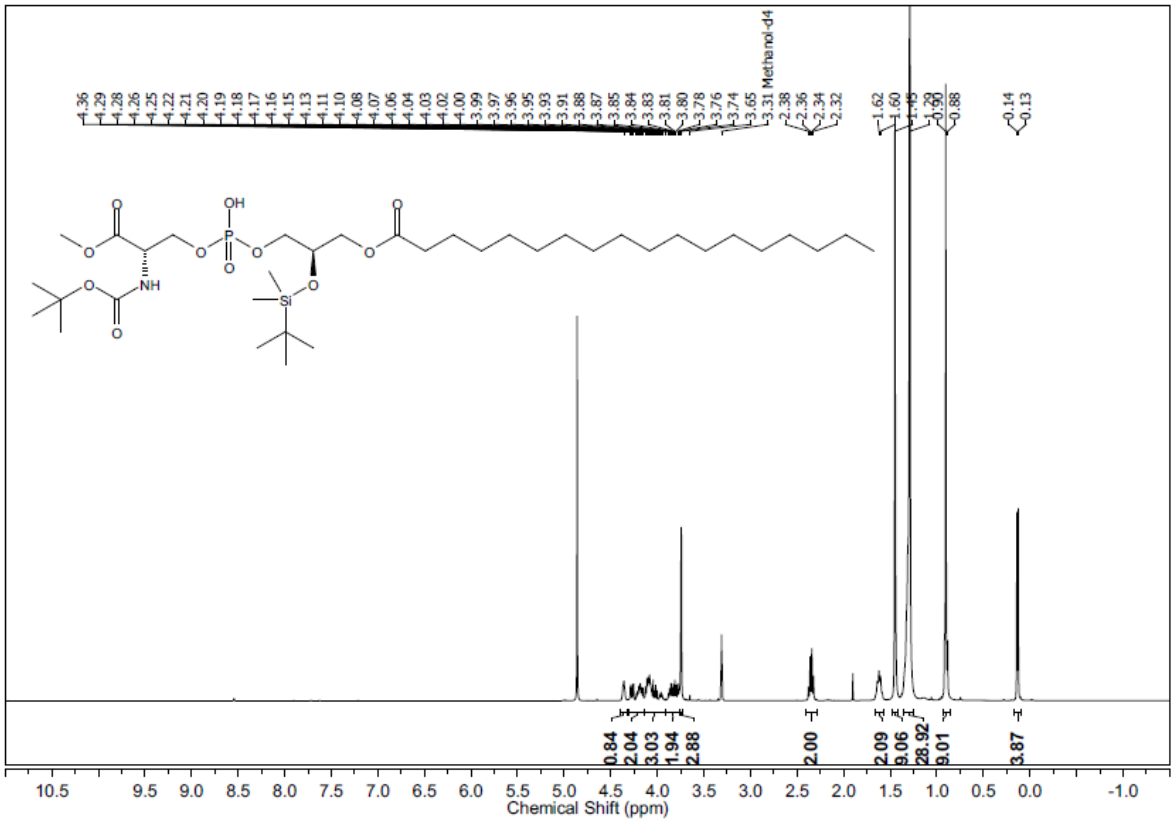
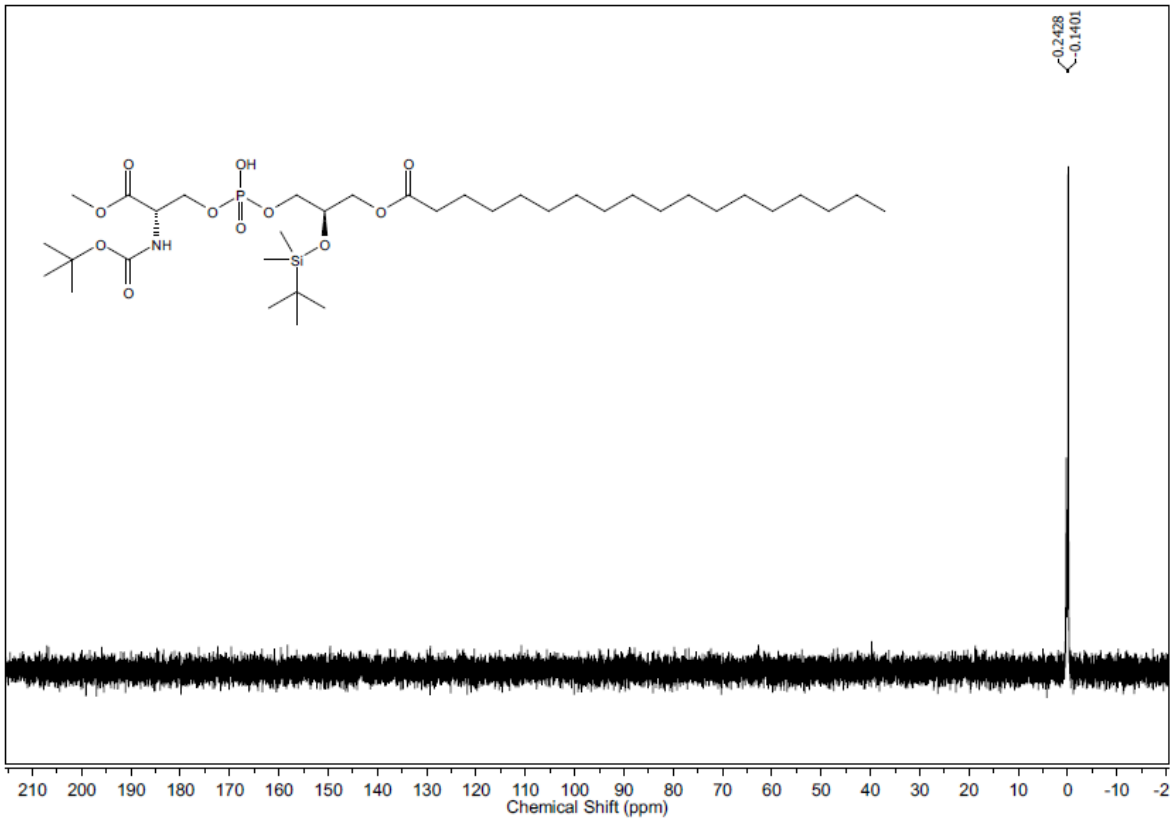
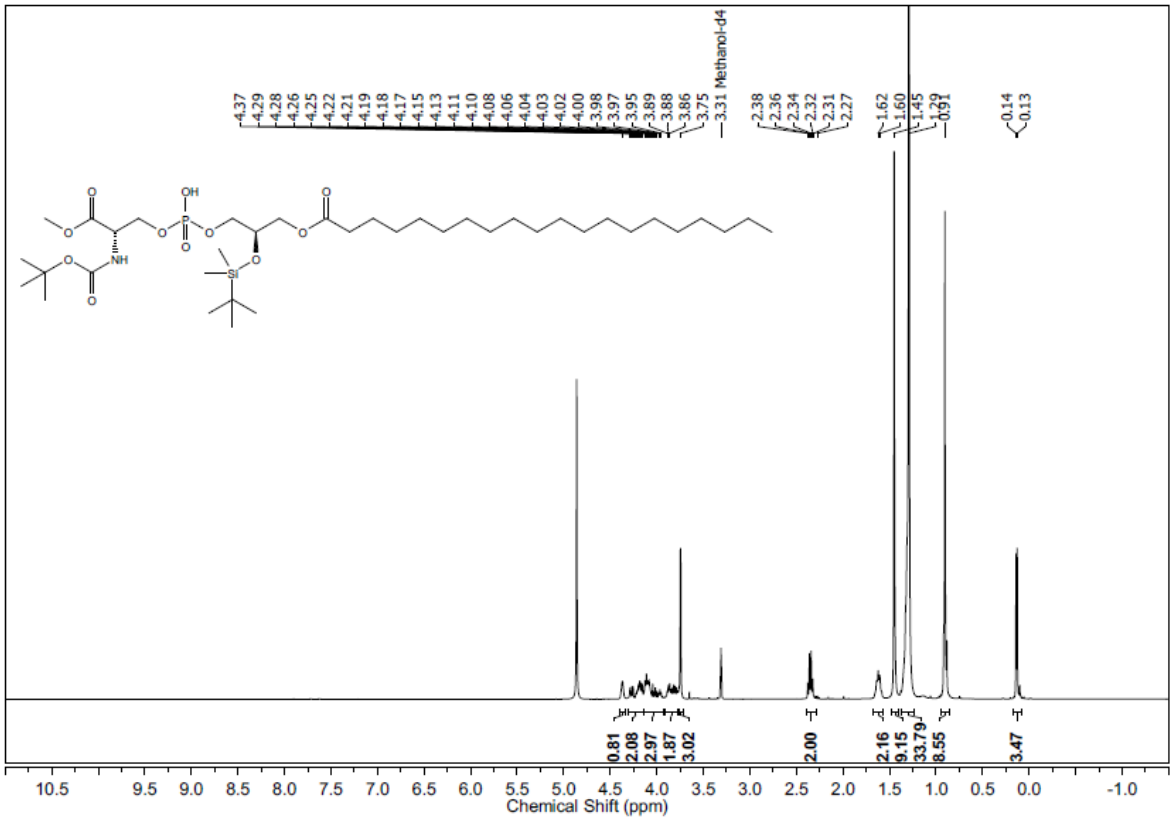


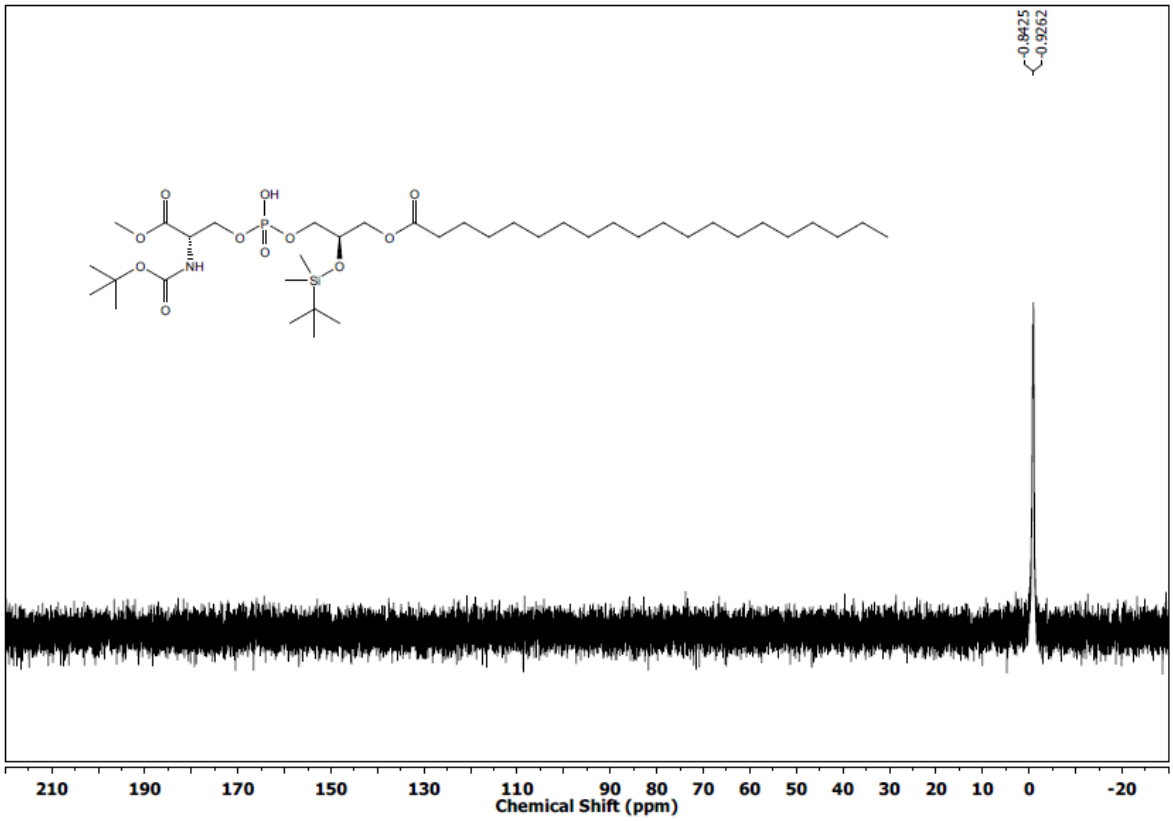
^{31}P NMR of intermediate (*R*)-**9e**



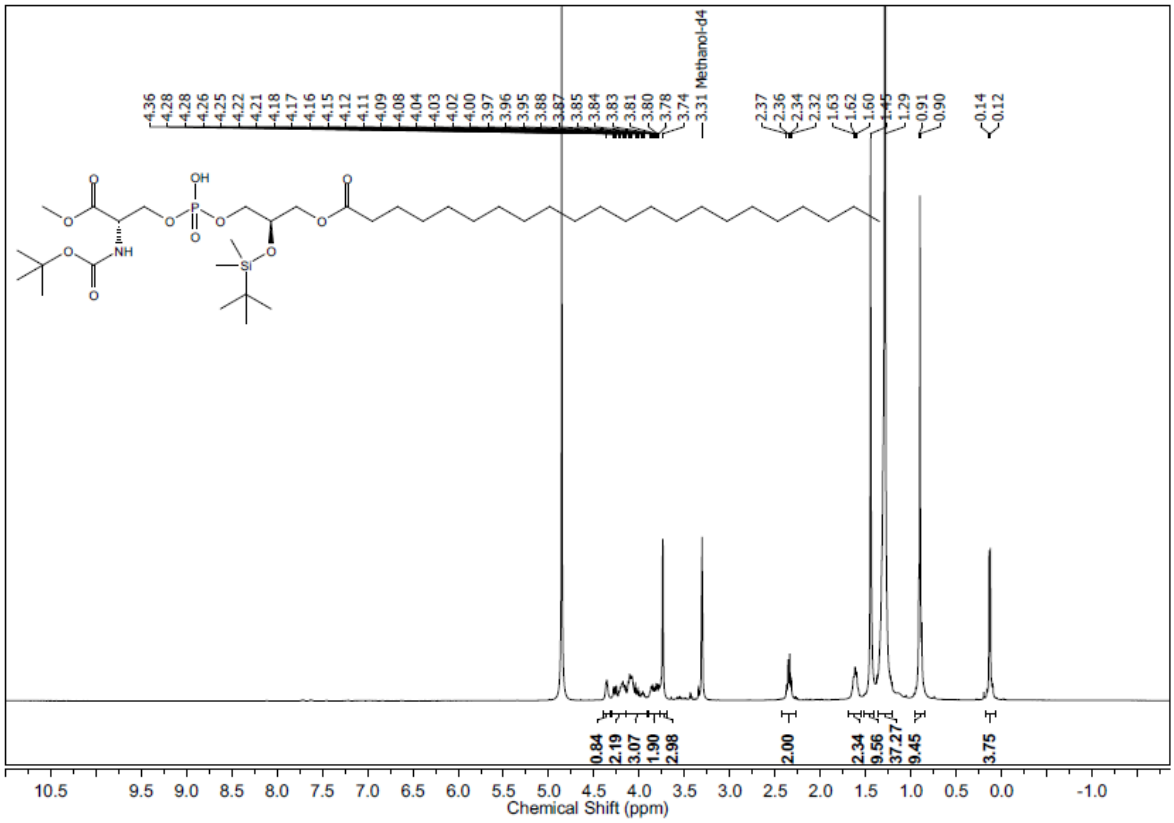
^{1}H NMR of intermediate (*R*)-**9f**



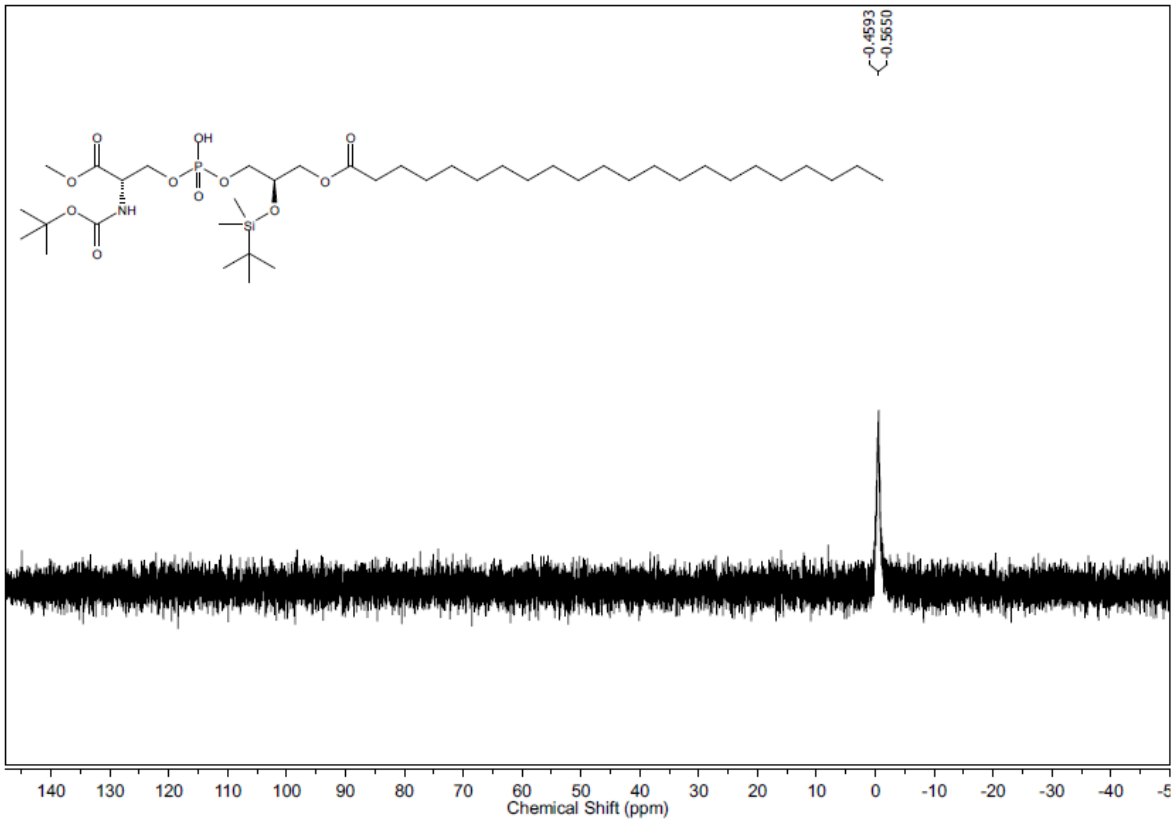
^{31}P NMR of intermediate (*R*)-**9f**



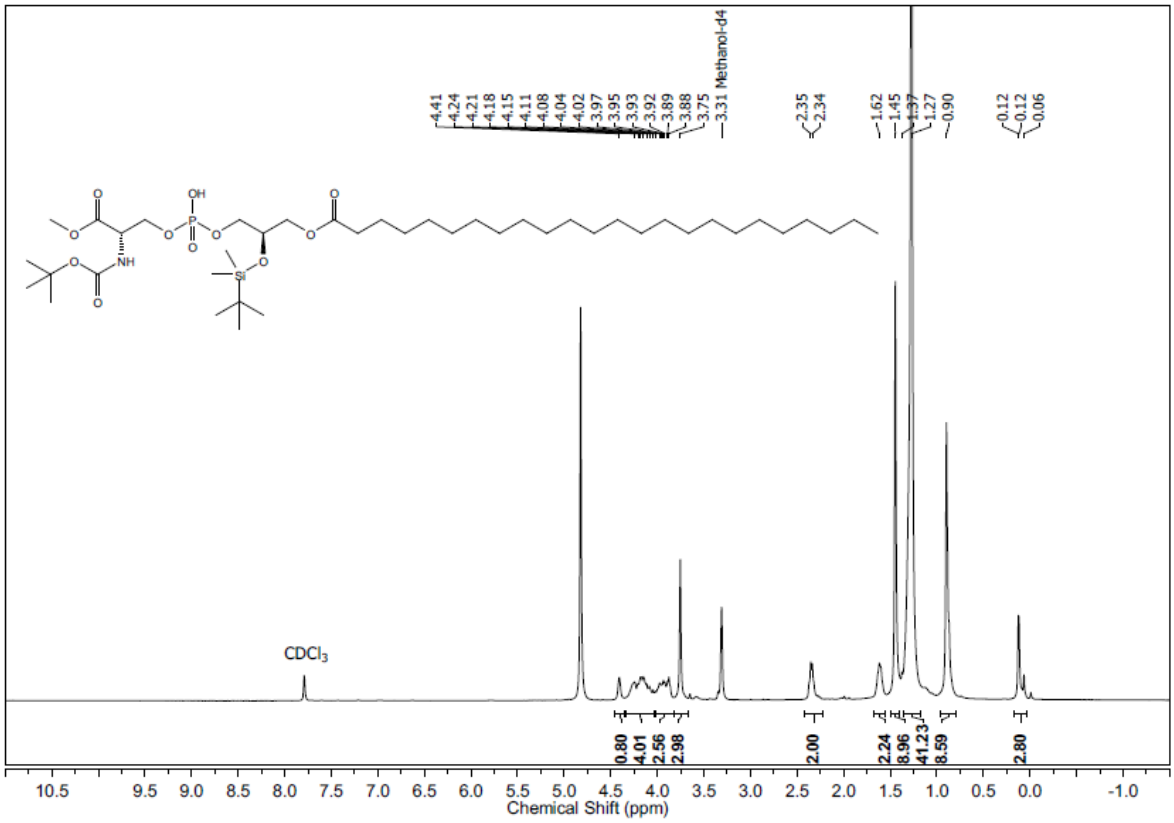
^{1}H NMR of intermediate (*R*)-**9g**



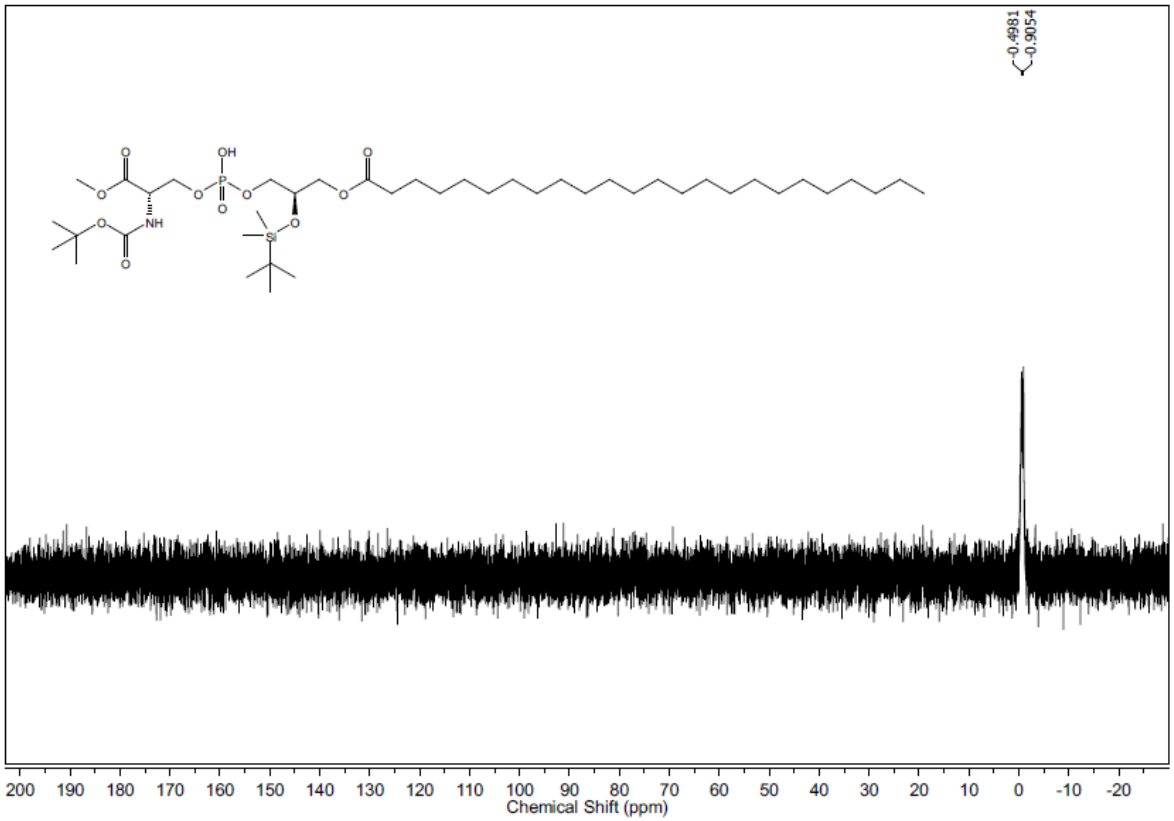
^{31}P NMR of intermediate (*R*)-**9g**



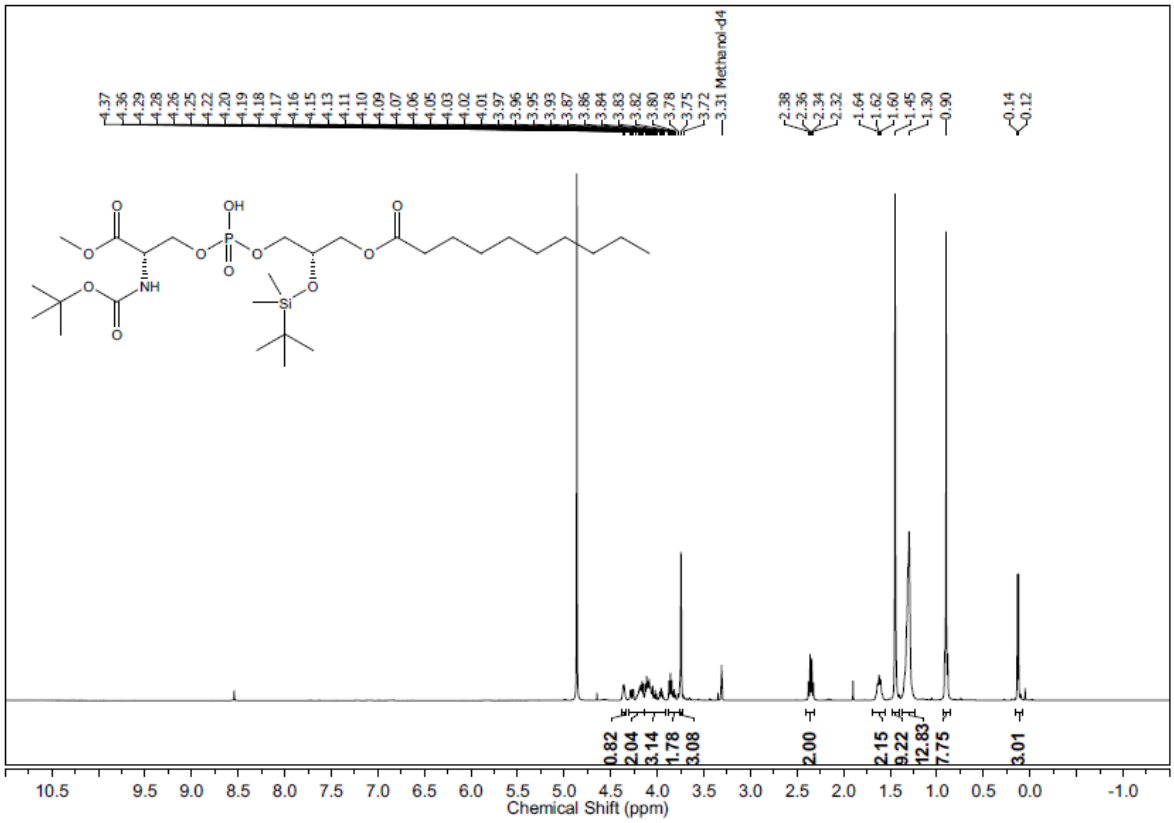
^{1}H NMR of intermediate (*R*)-**9h**



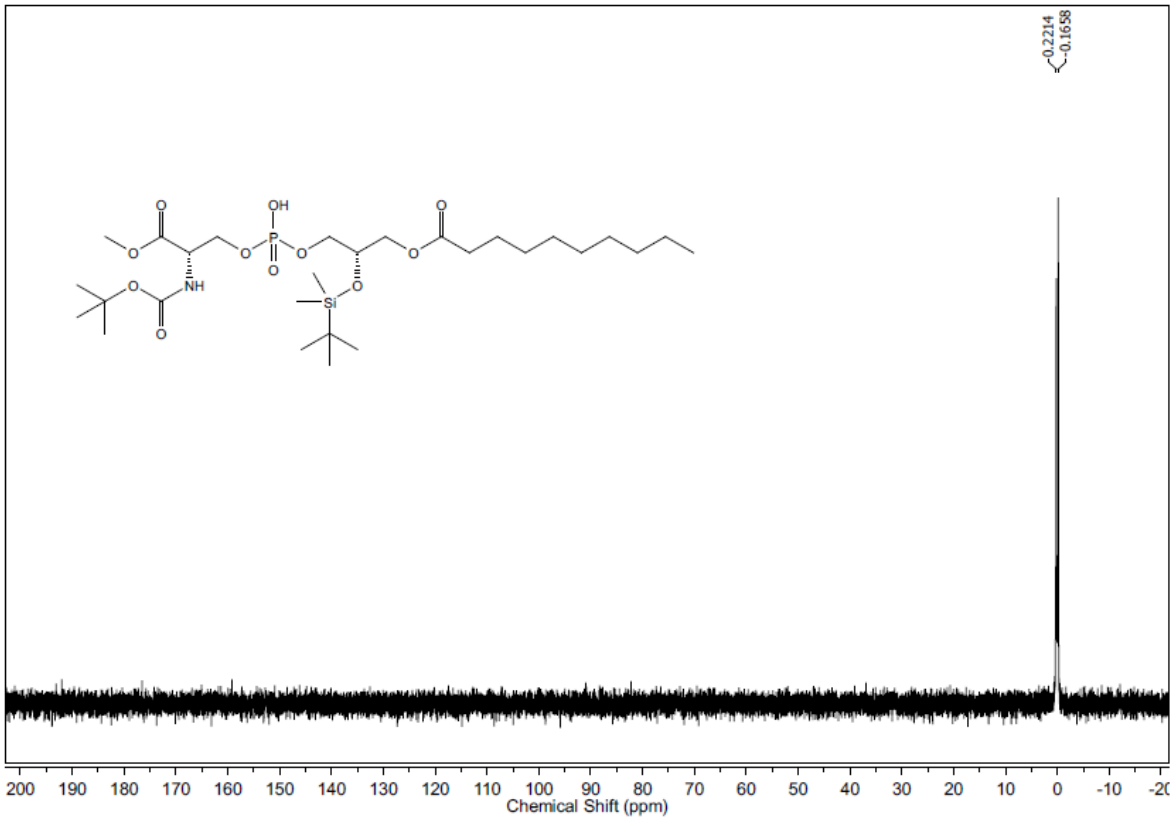
^{31}P NMR of intermediate (*R*)-**9h**



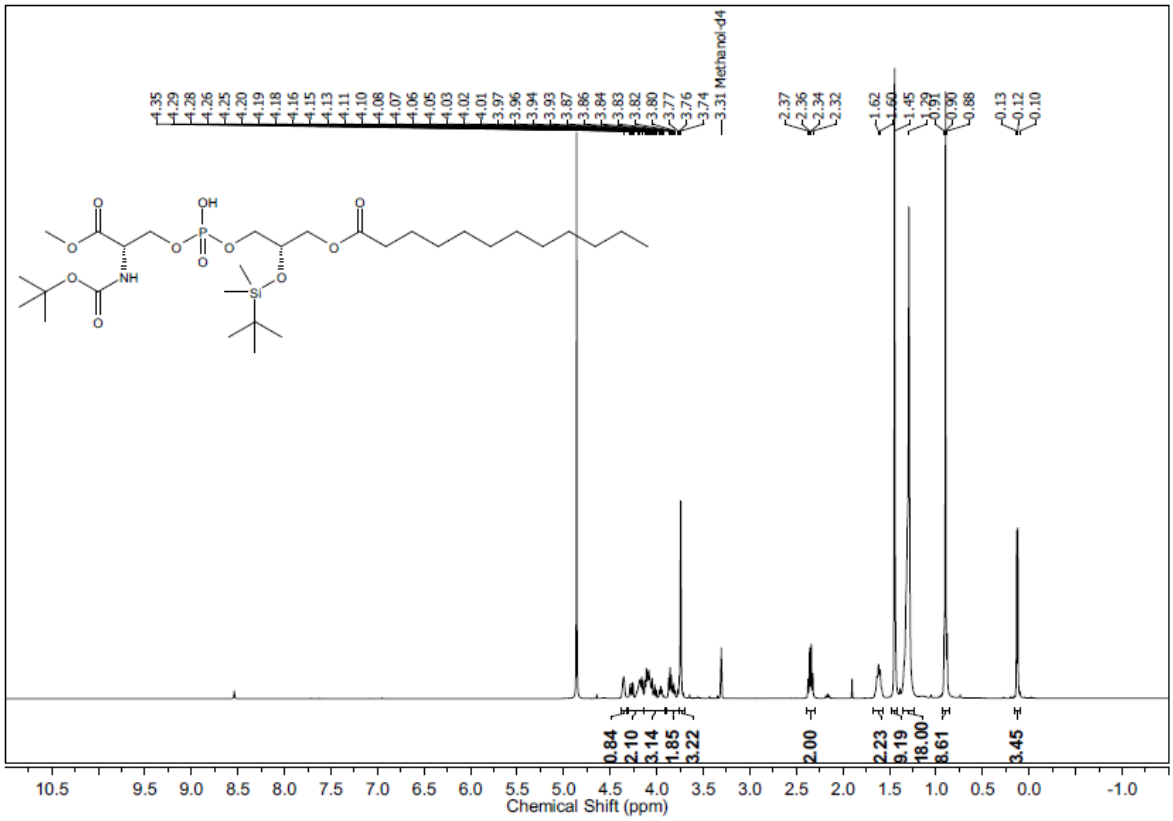
^{1}H NMR of intermediate (*S*)-**9a**



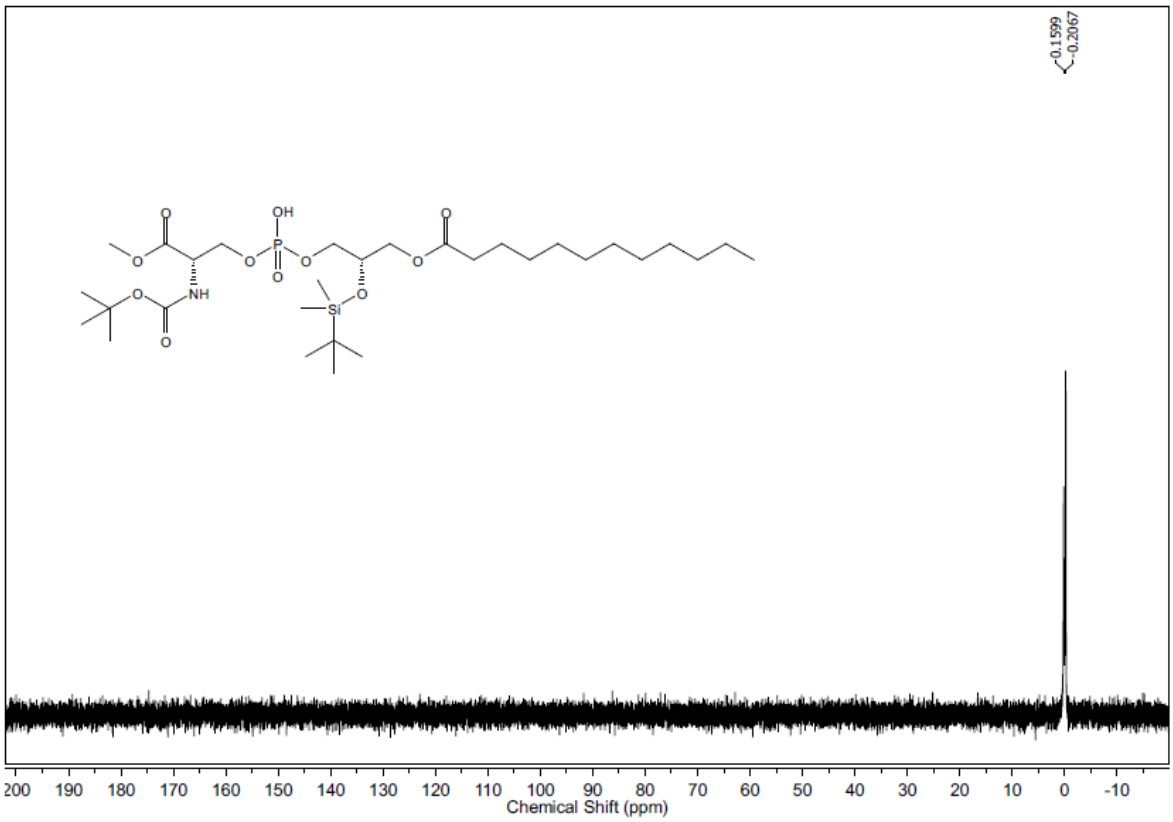
^{31}P NMR of intermediate (*S*)-**9a**



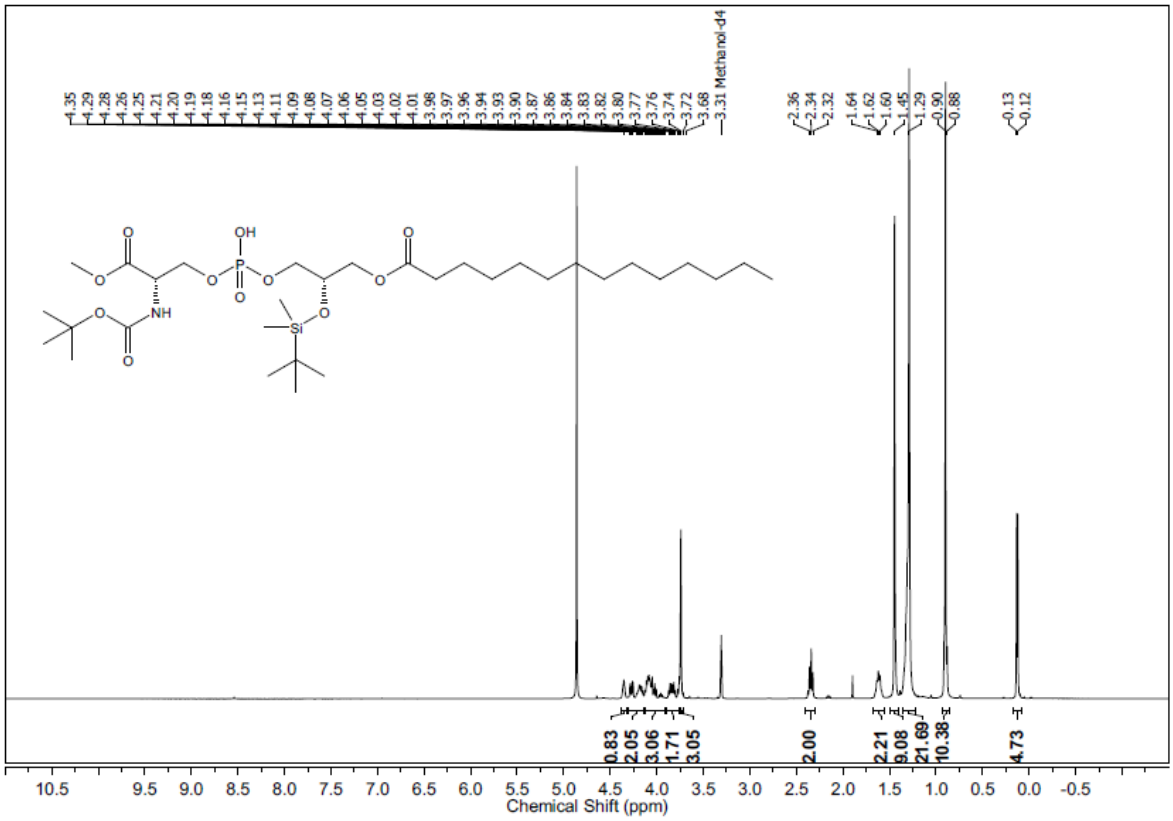
^{1}H NMR of intermediate (*S*)-**9b**



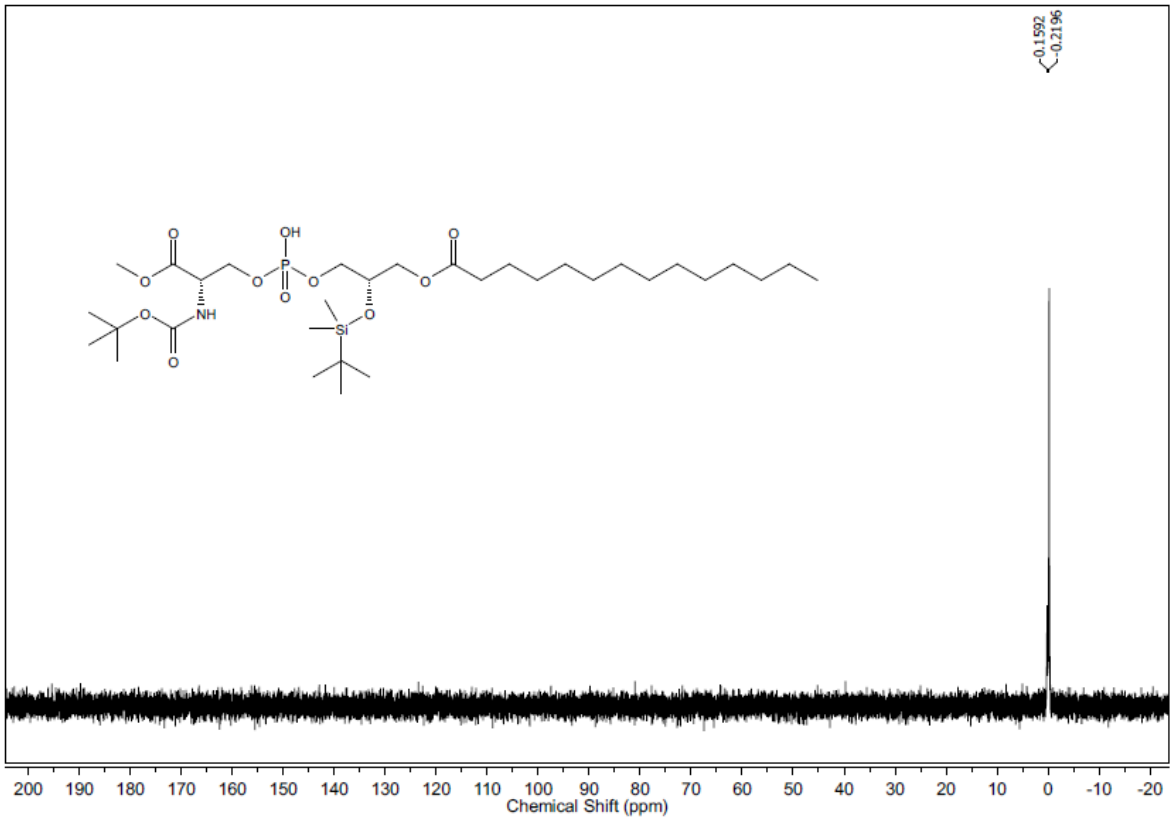
^{31}P NMR of intermediate (*S*)-**9b**



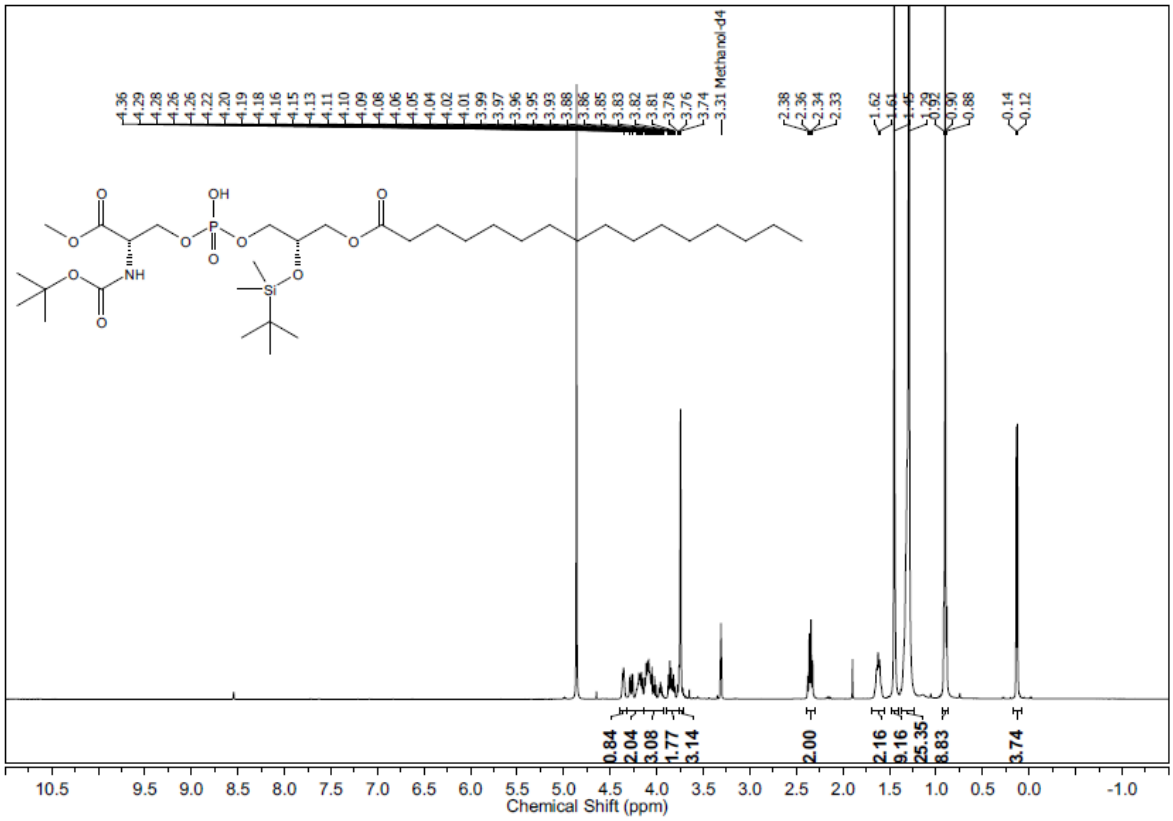
^{1}H NMR of intermediate (*S*)-**9c**



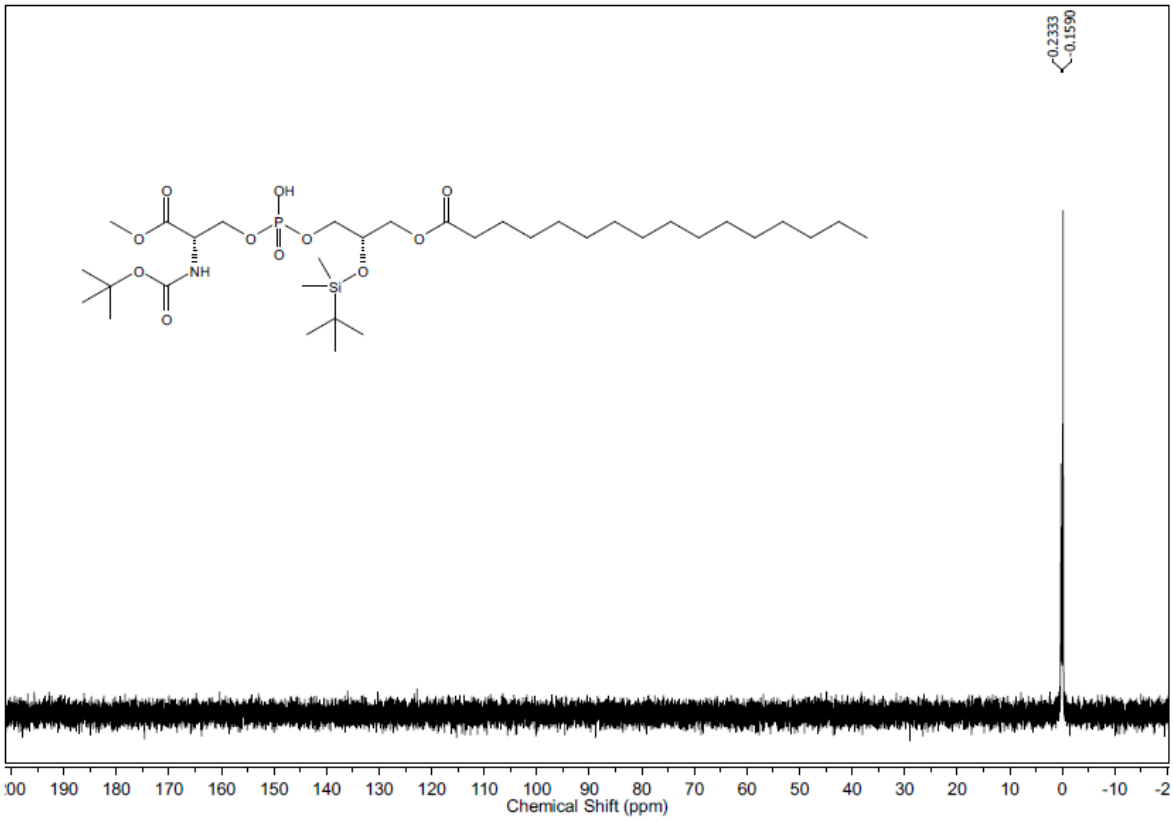
^{31}P NMR of intermediate (*S*)-**9c**



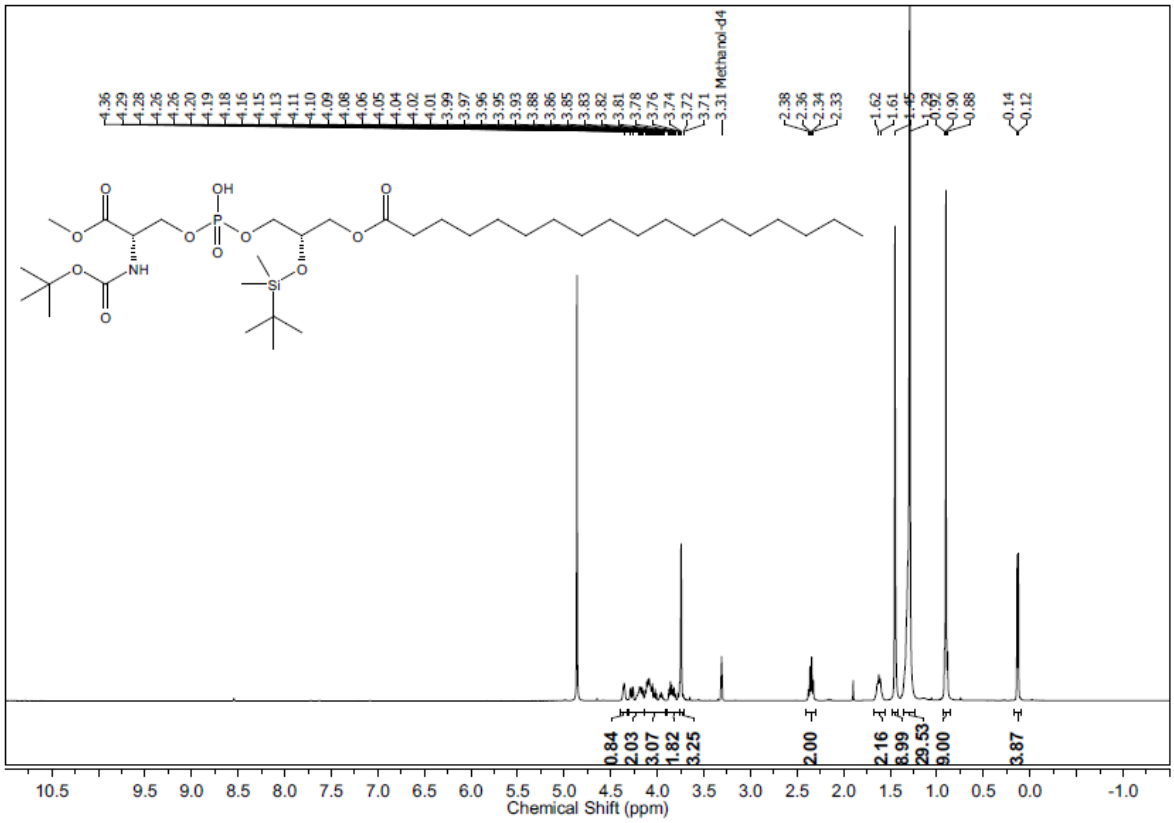
^{1}H NMR of intermediate (*S*)-**9d**



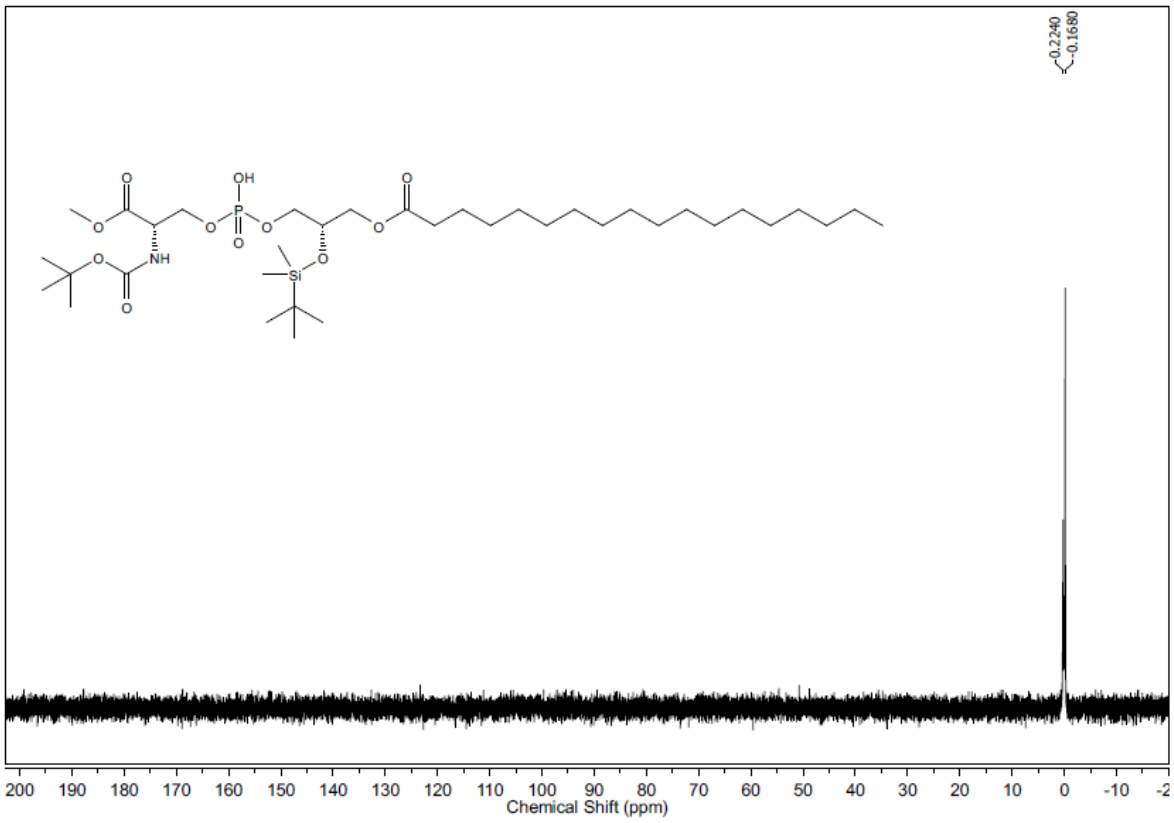
^{31}P NMR of intermediate (*S*)-**9d**



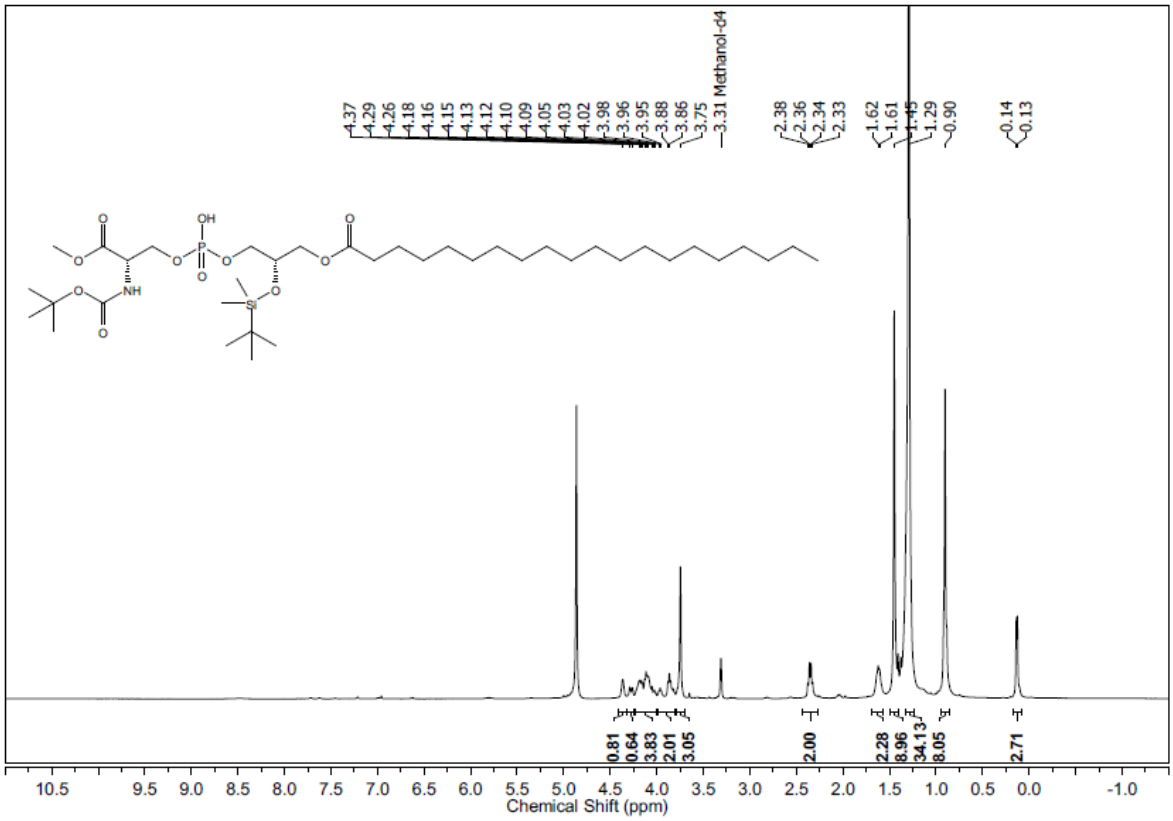
^{1}H NMR of intermediate (*S*)-**9e**



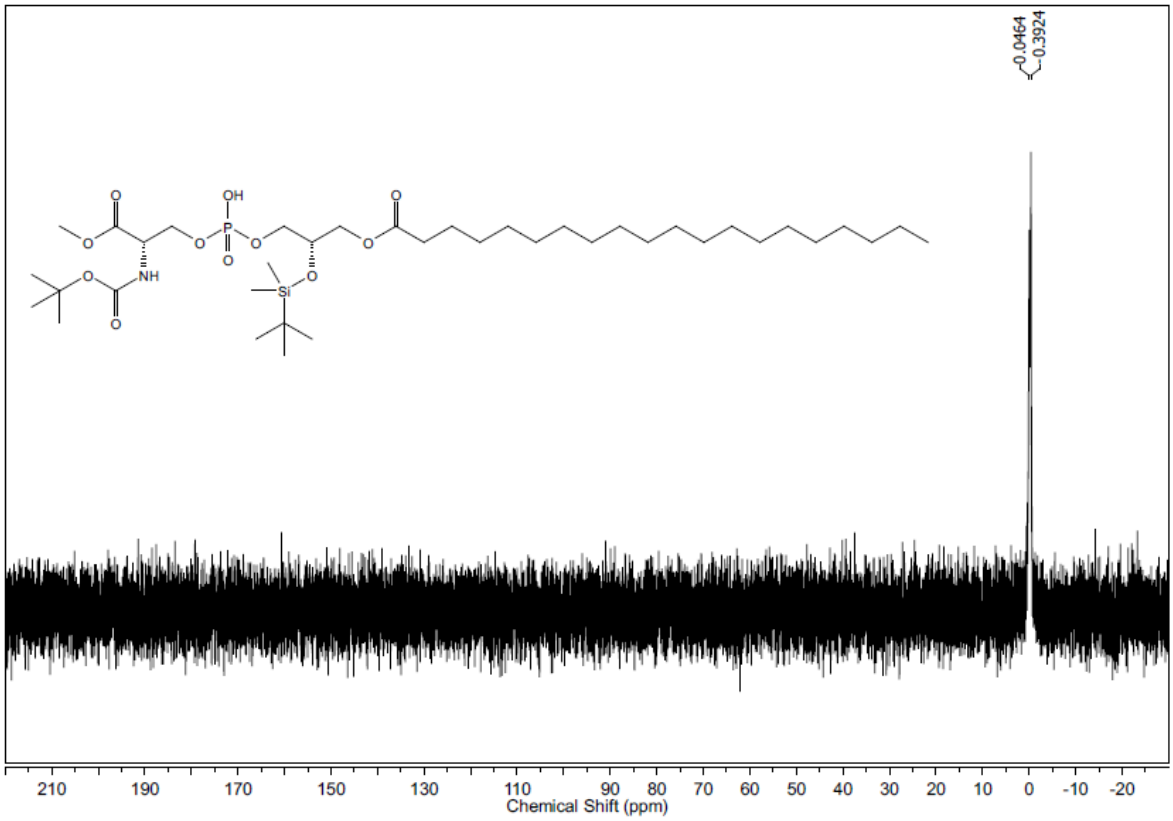
^{31}P NMR of intermediate (*S*)-**9e**



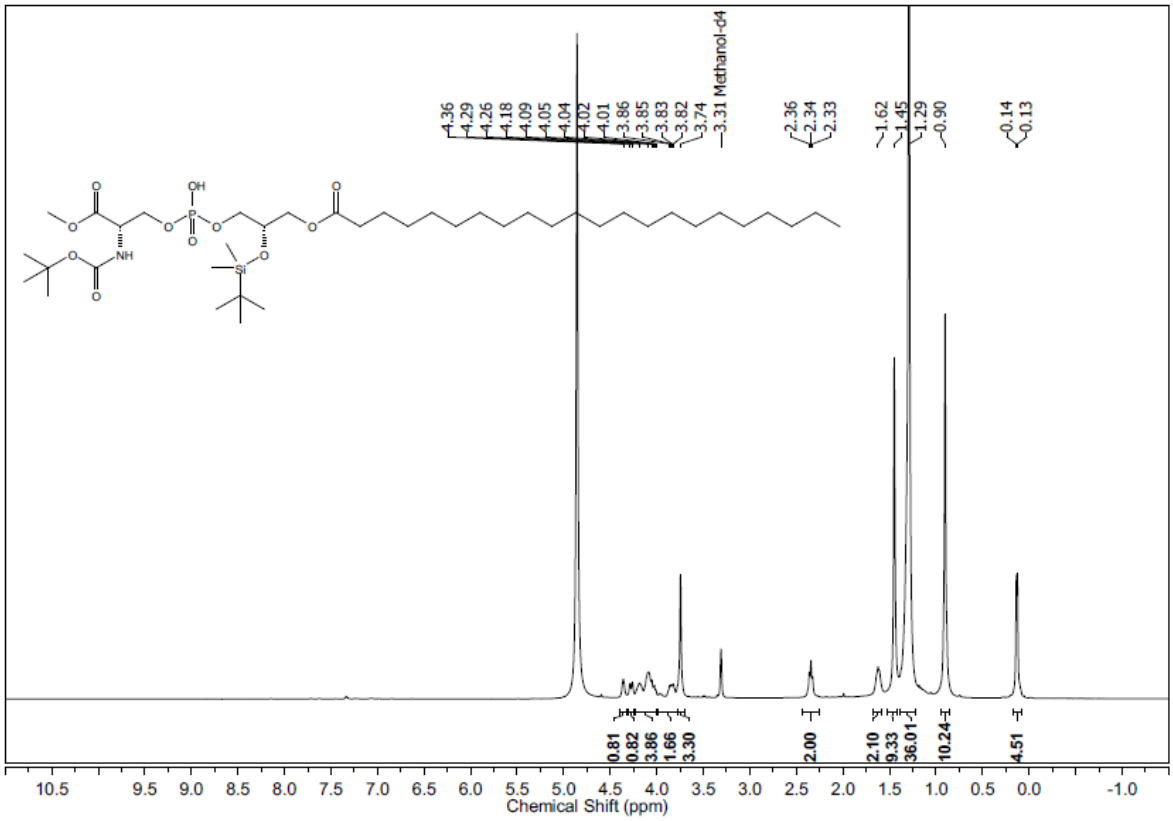
^{1}H NMR of intermediate (*S*)-**9f**



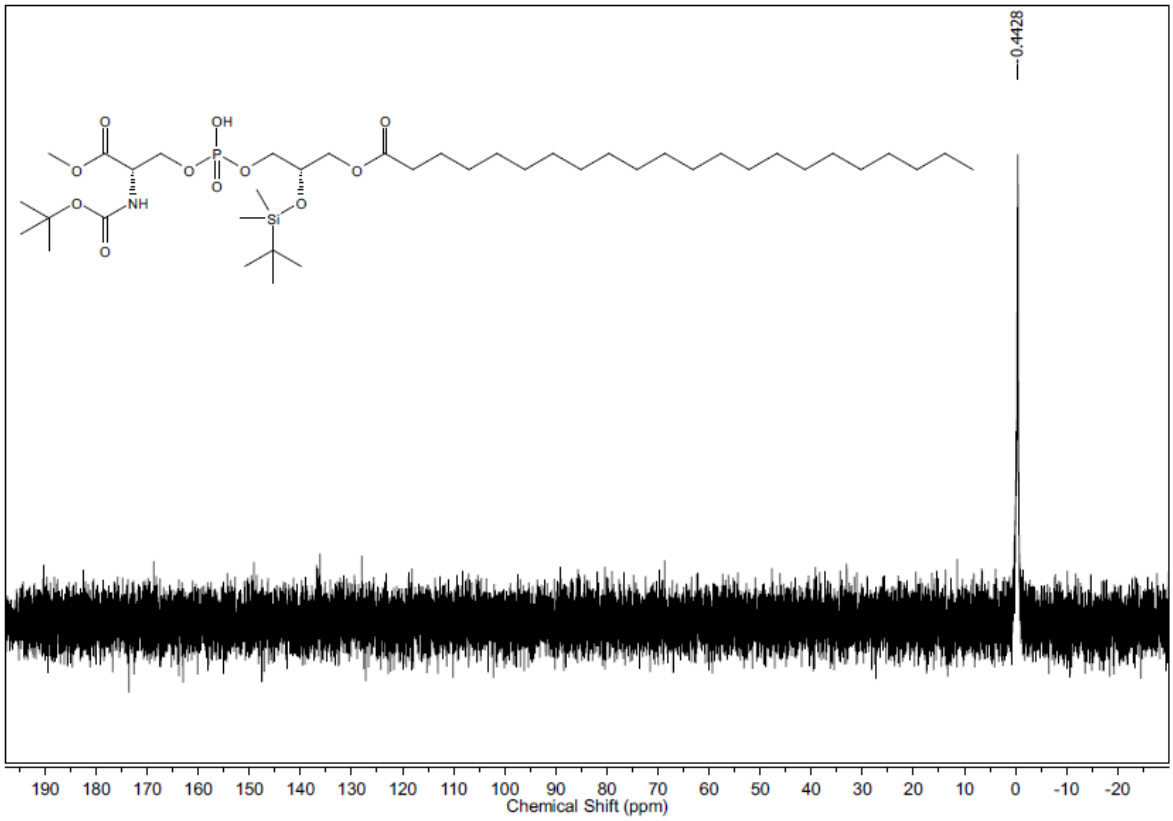
^{31}P NMR of intermediate (*S*)-**9f**



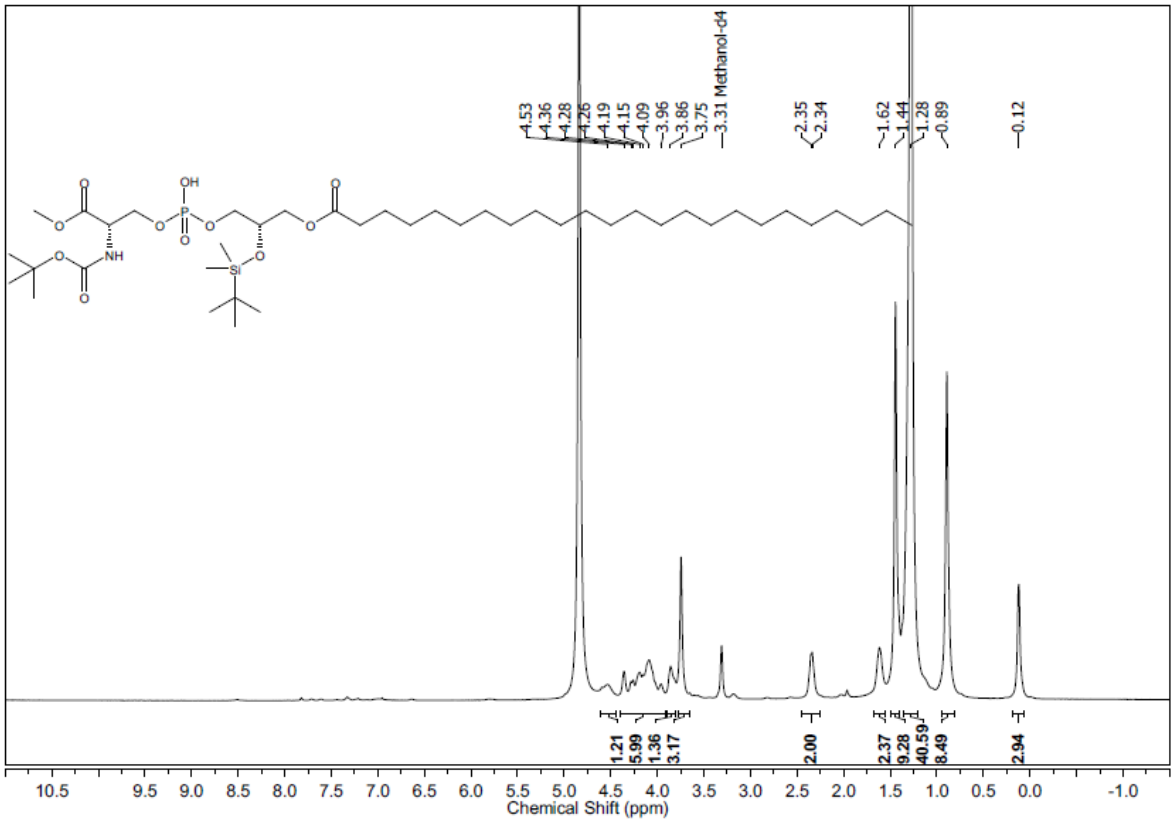
^{1}H NMR of intermediate (*S*)-**9g**



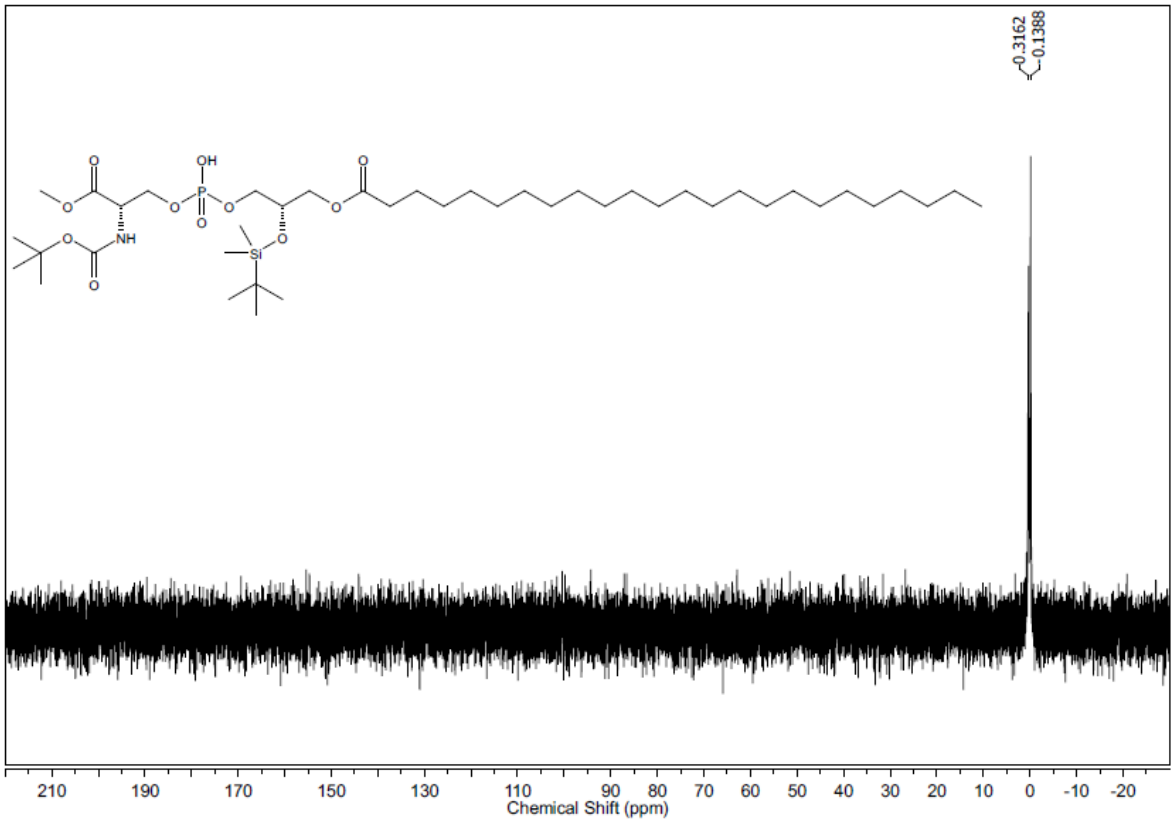
^{31}P NMR of intermediate (*S*)-**9g**



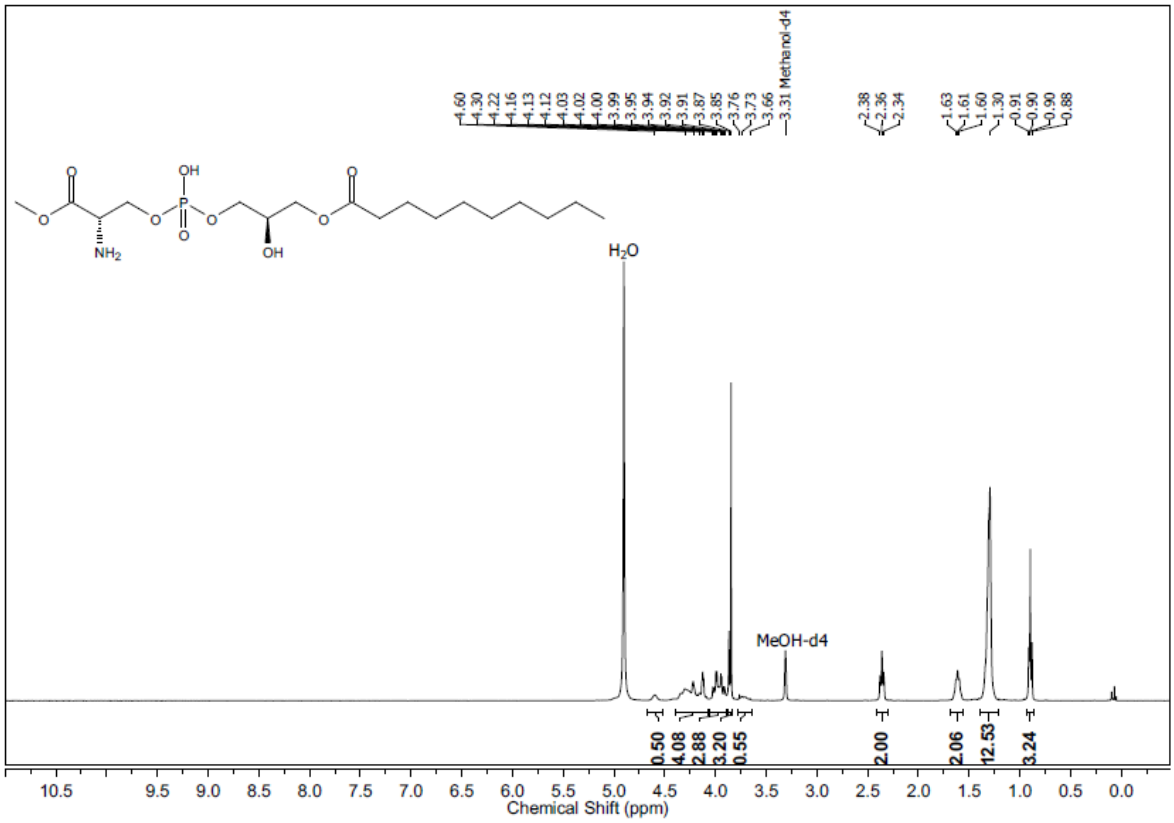
^{1}H NMR of intermediate (*S*)-**9h**



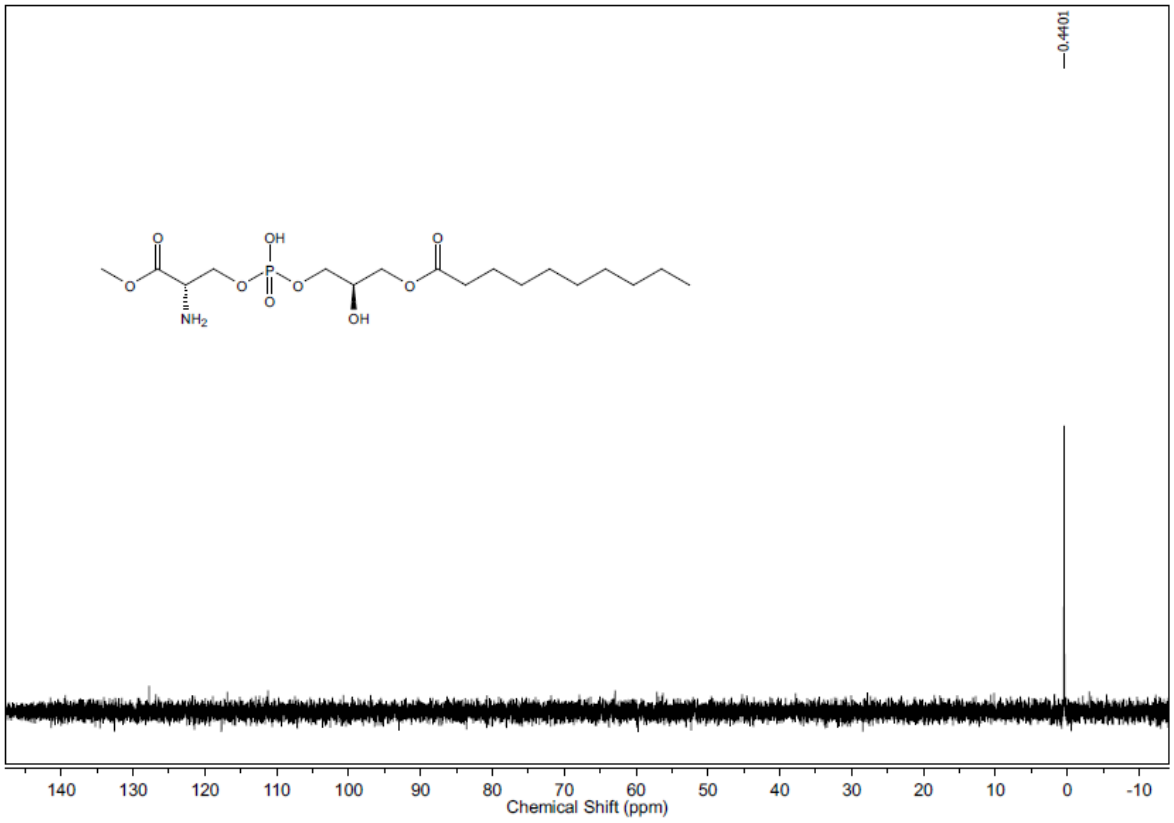
^{31}P NMR of intermediate (*S*)-**9h**



^{1}H NMR of final compound (*R*)-**2a**



^{31}P NMR of final compound (*R*)-**2a**



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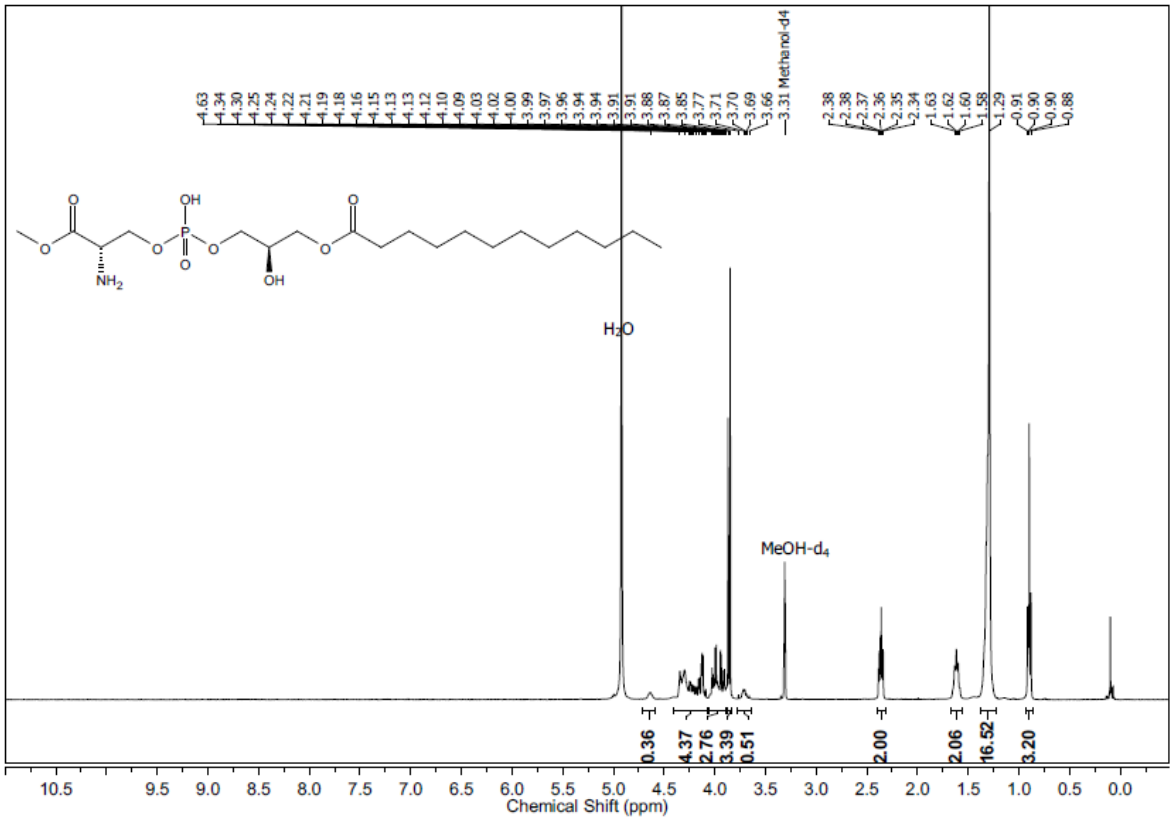
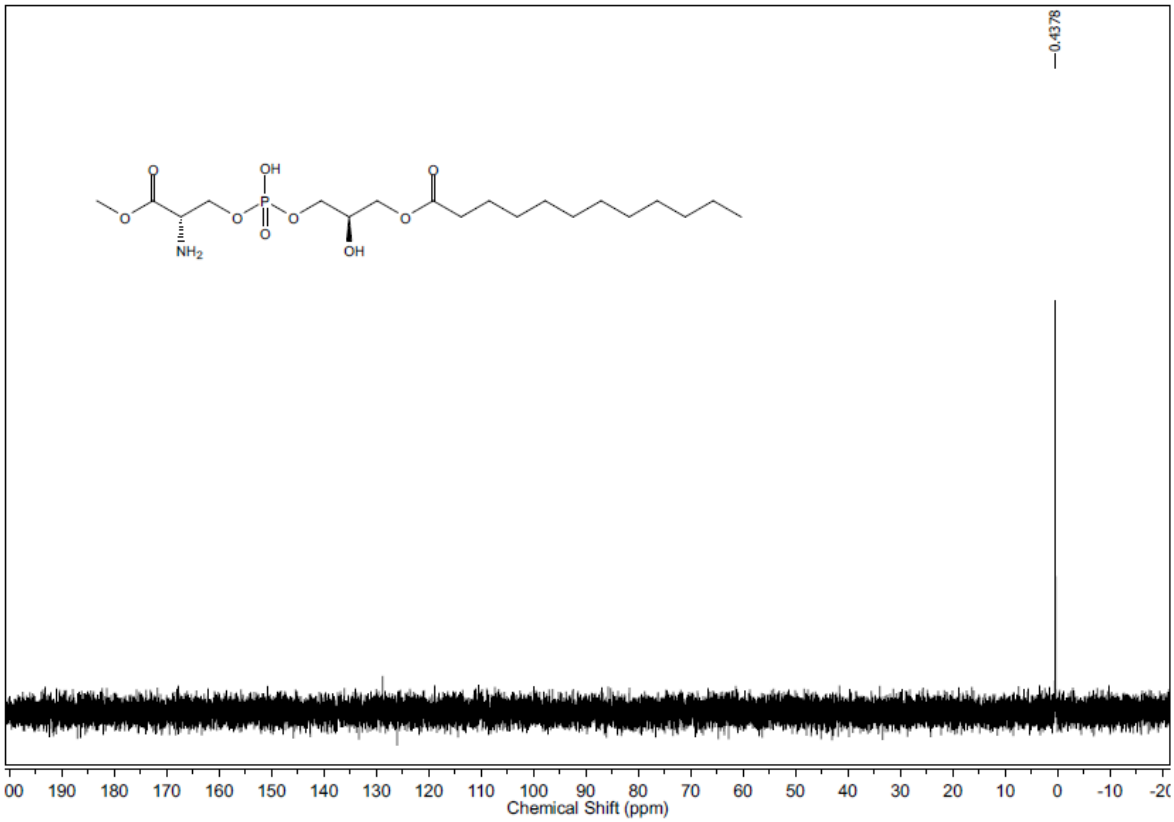


^{31}P NMR of final compound (*R*)-**2b**



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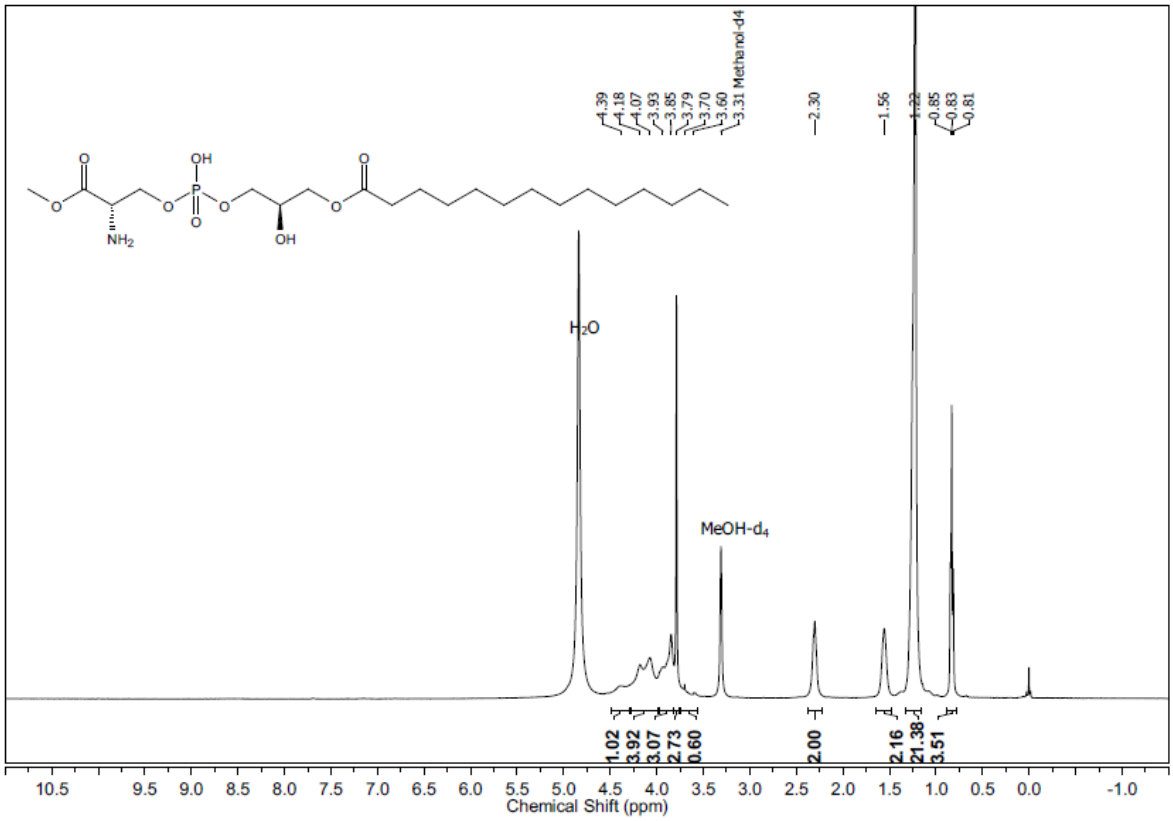
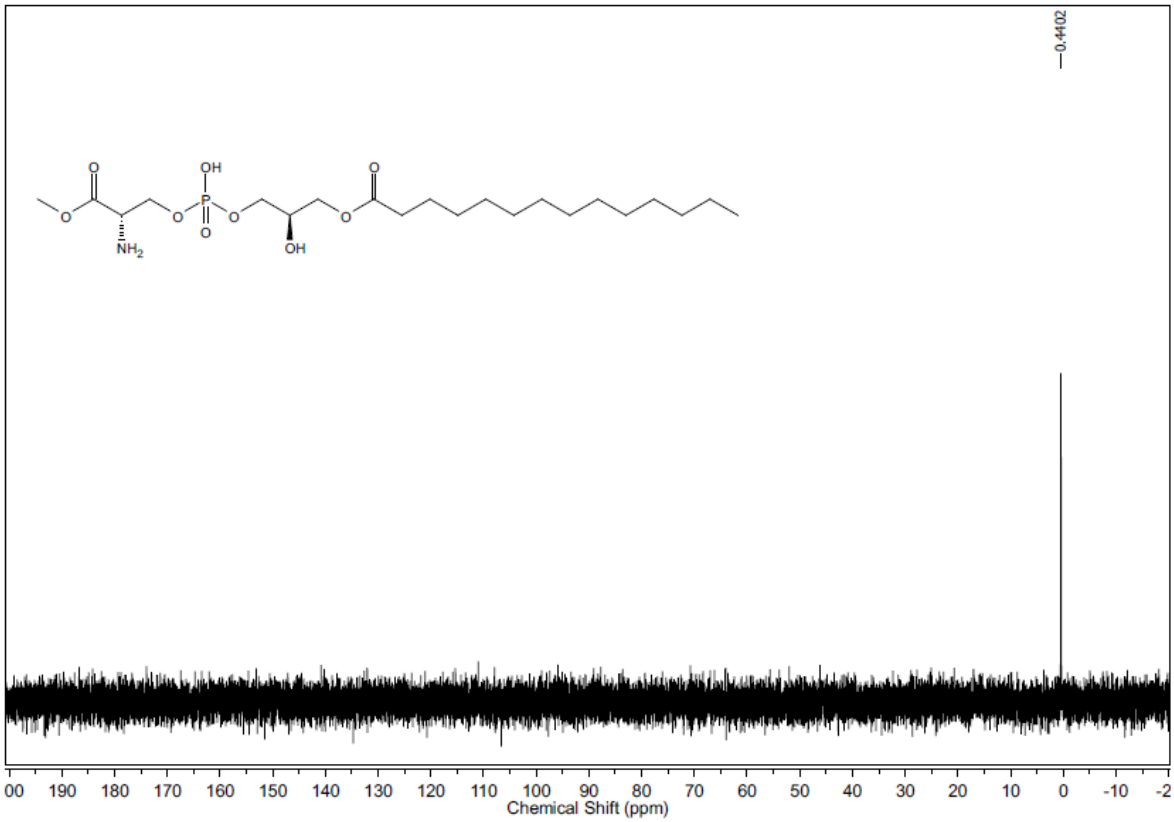


^{31}P NMR of final compound (*R*)-**2c**



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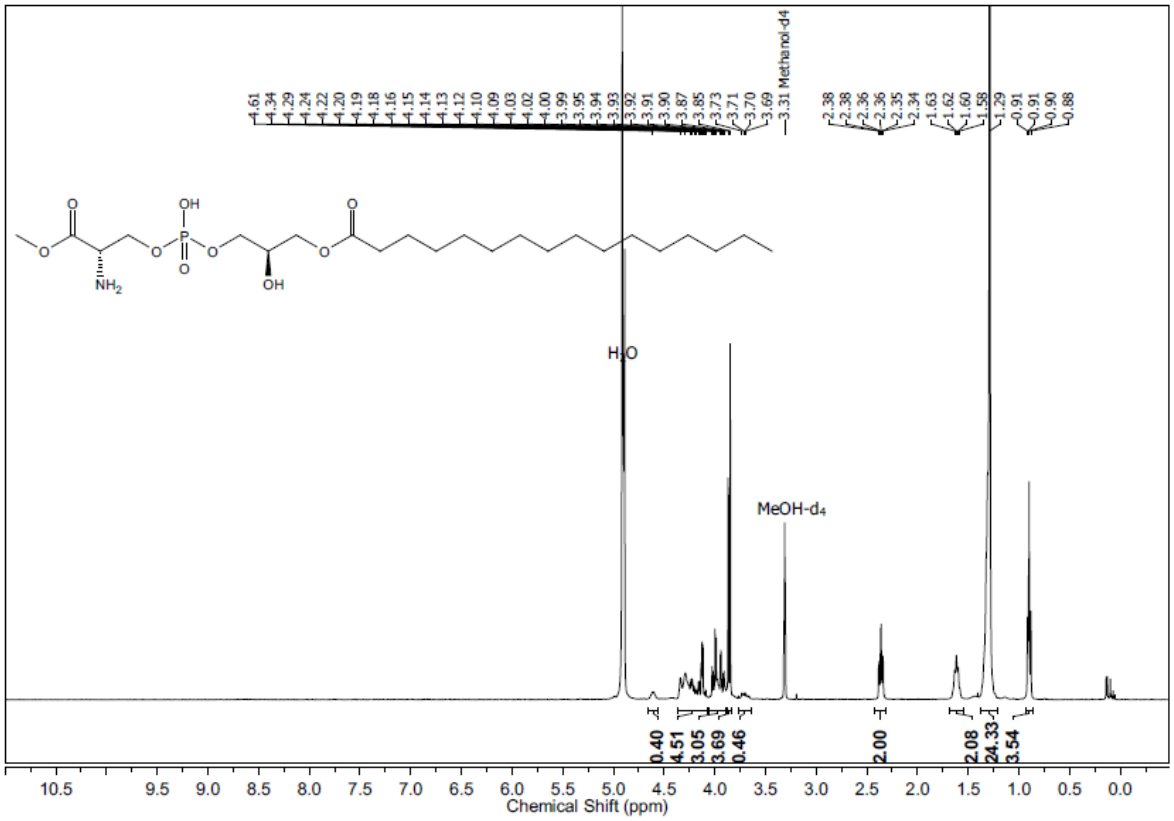

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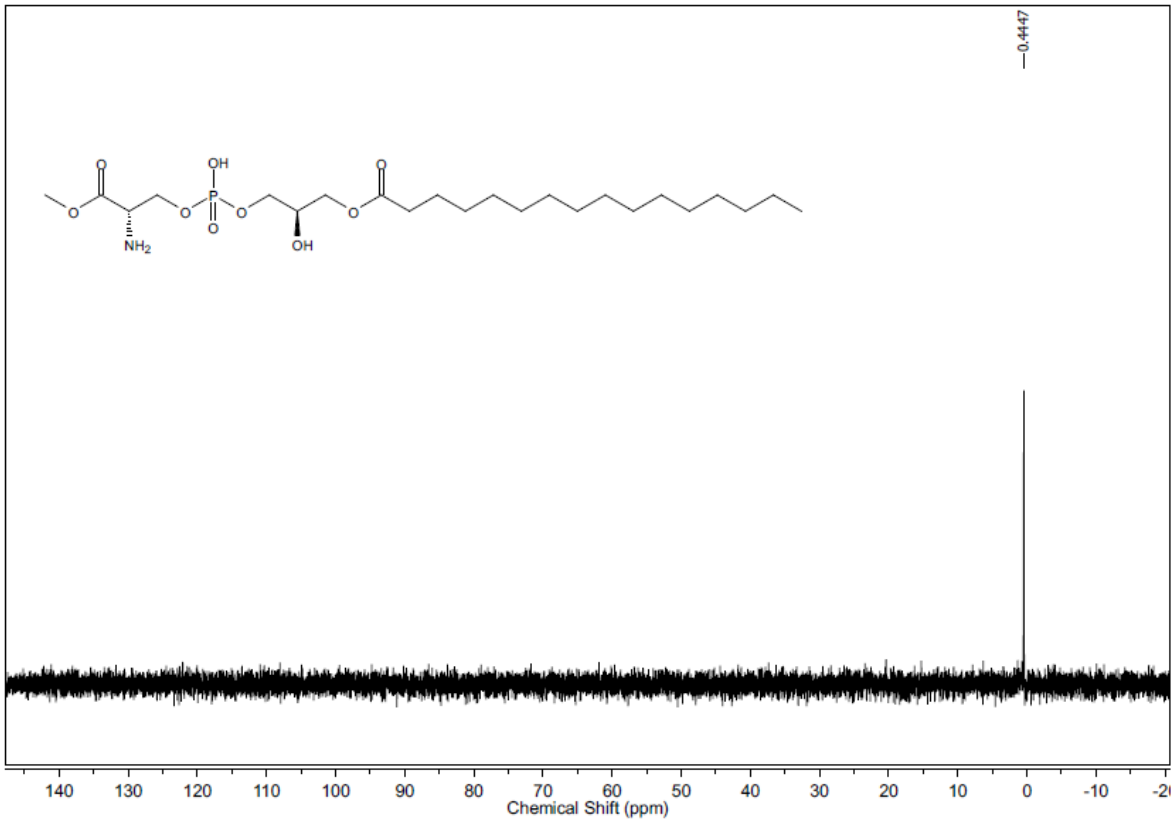

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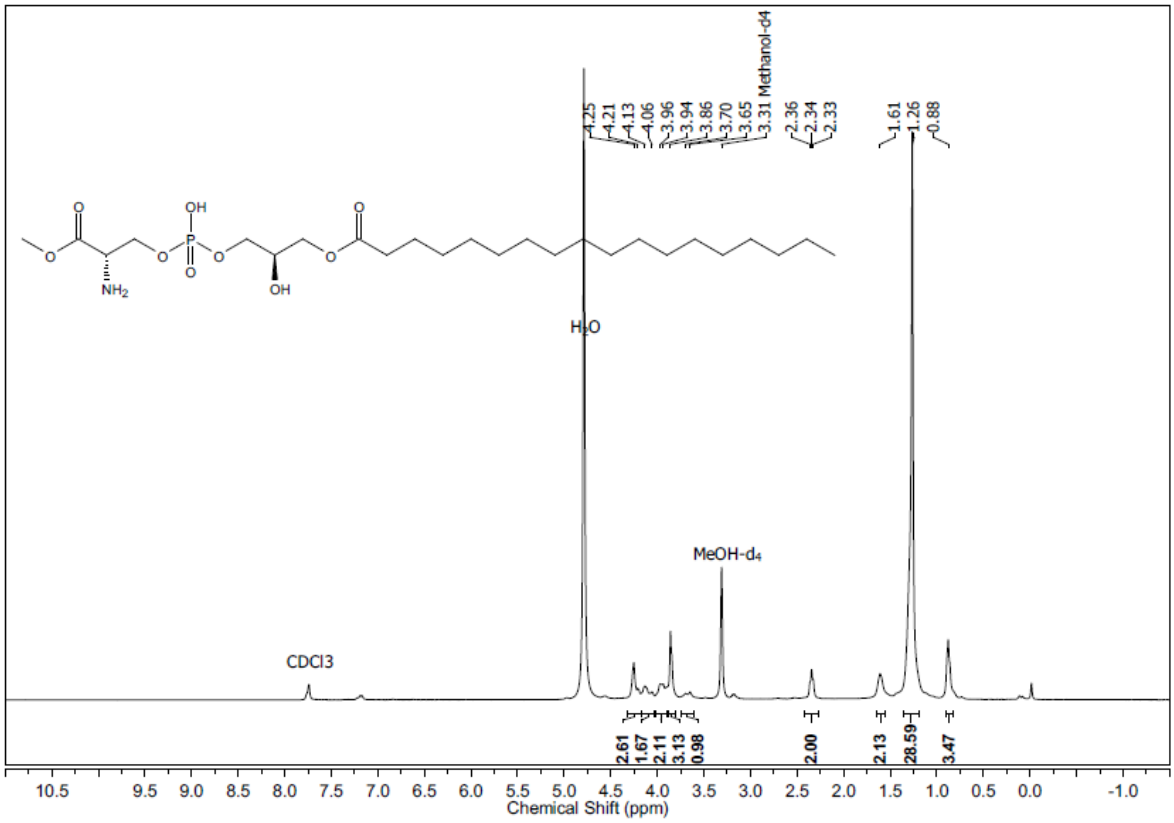

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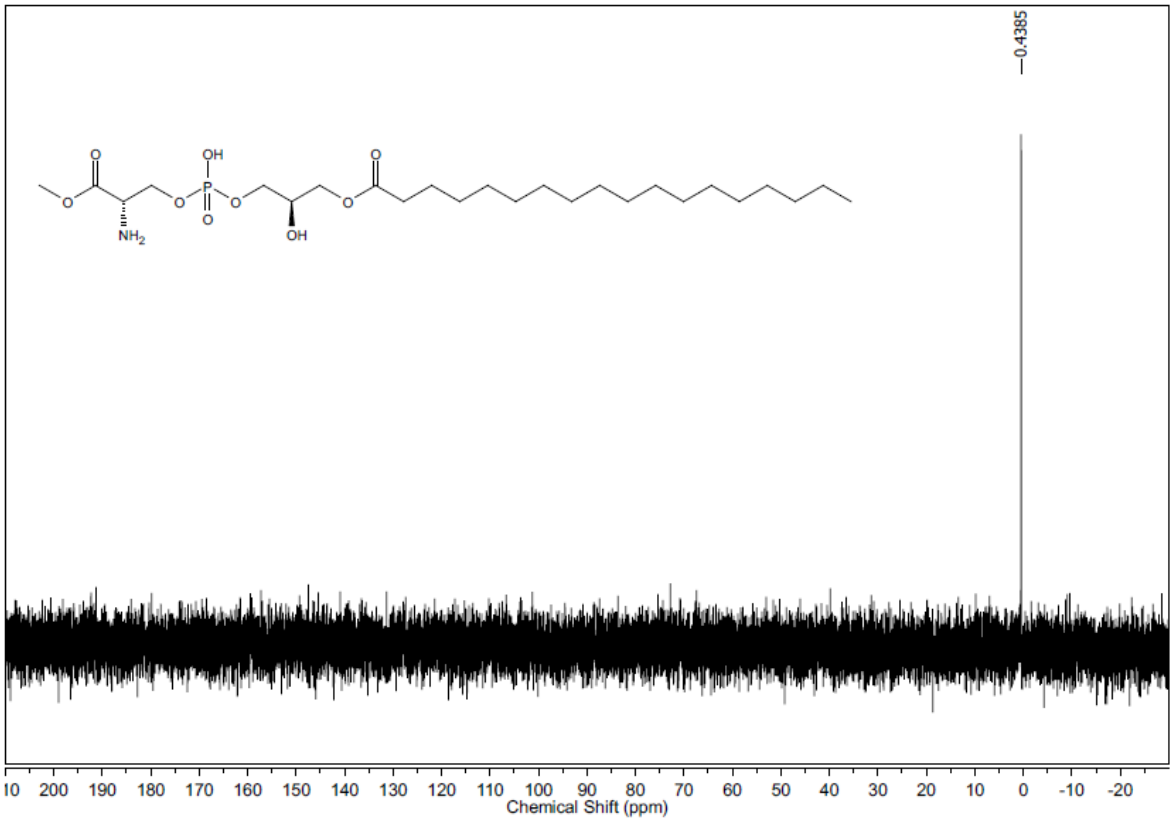

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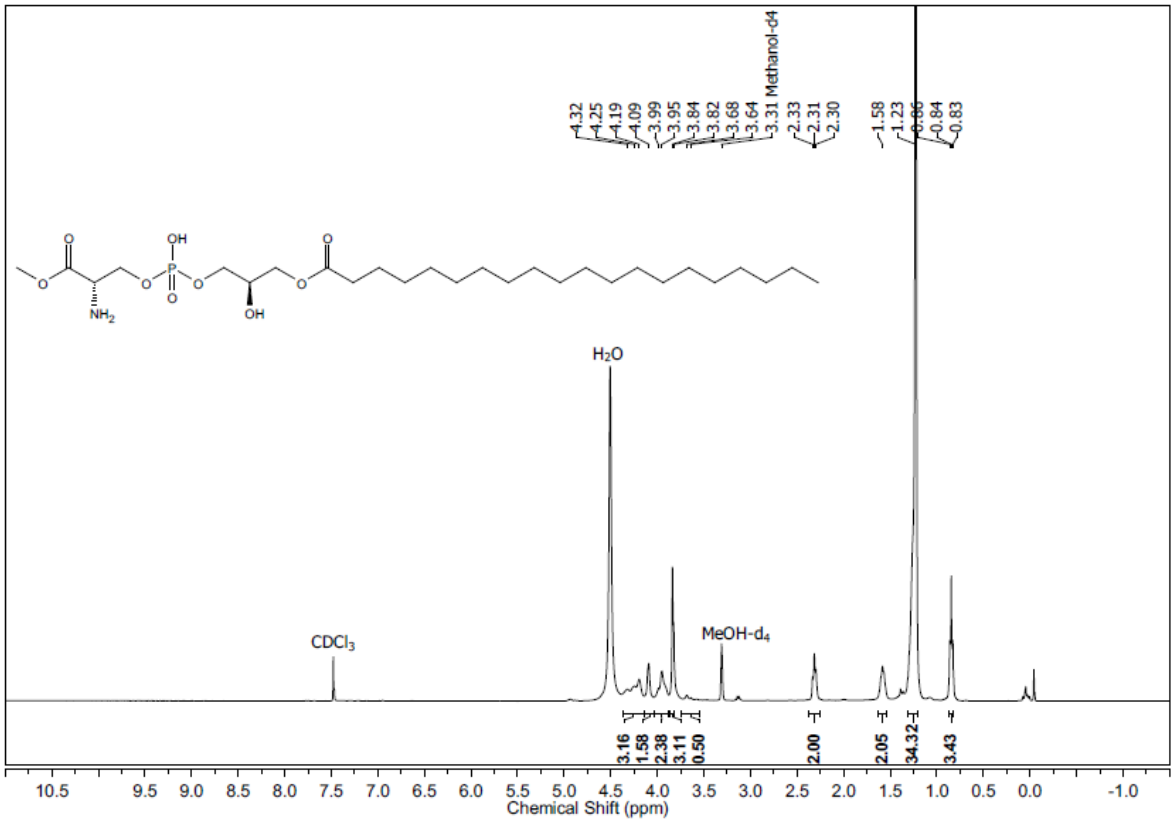

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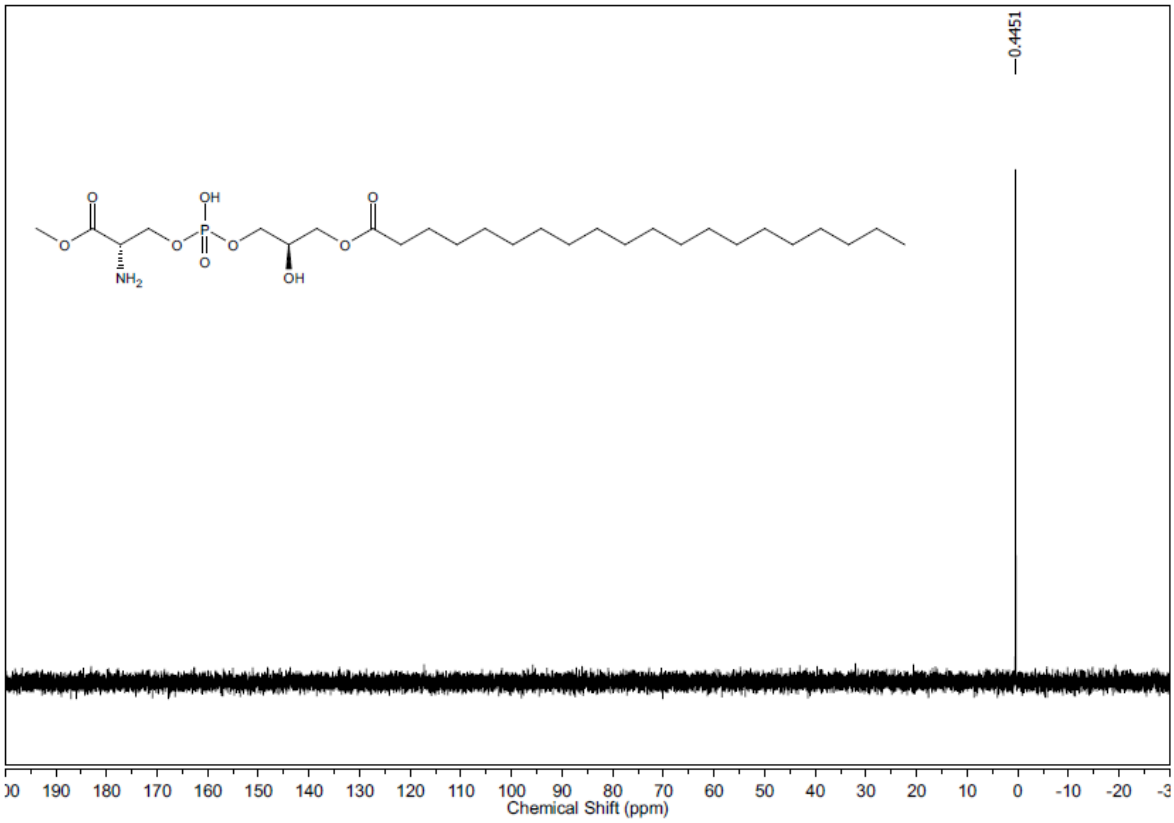

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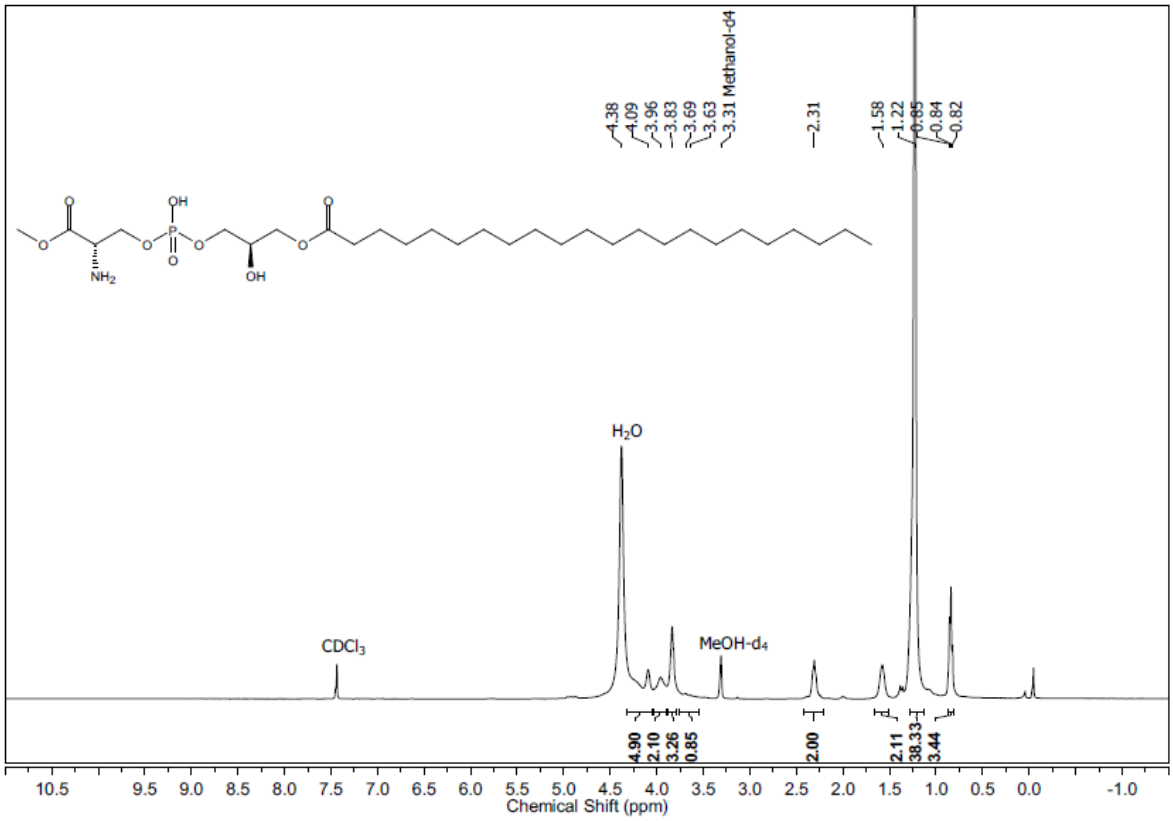

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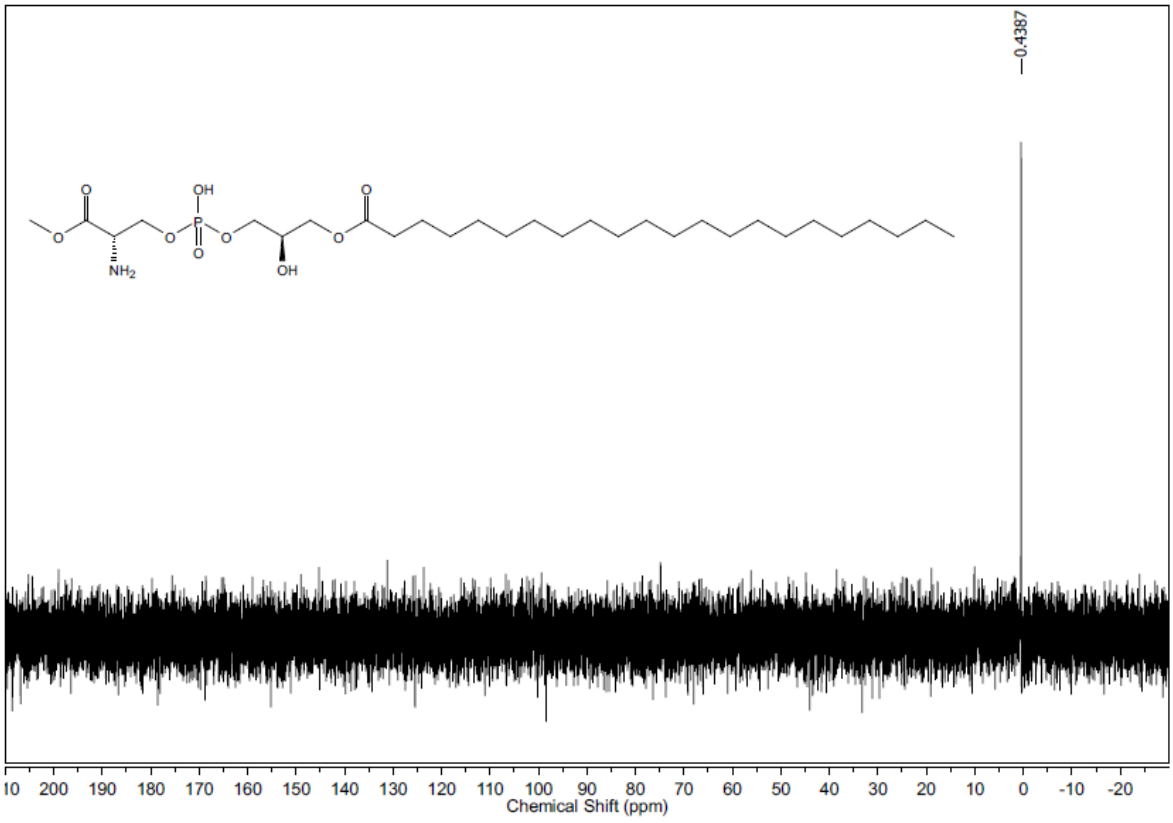

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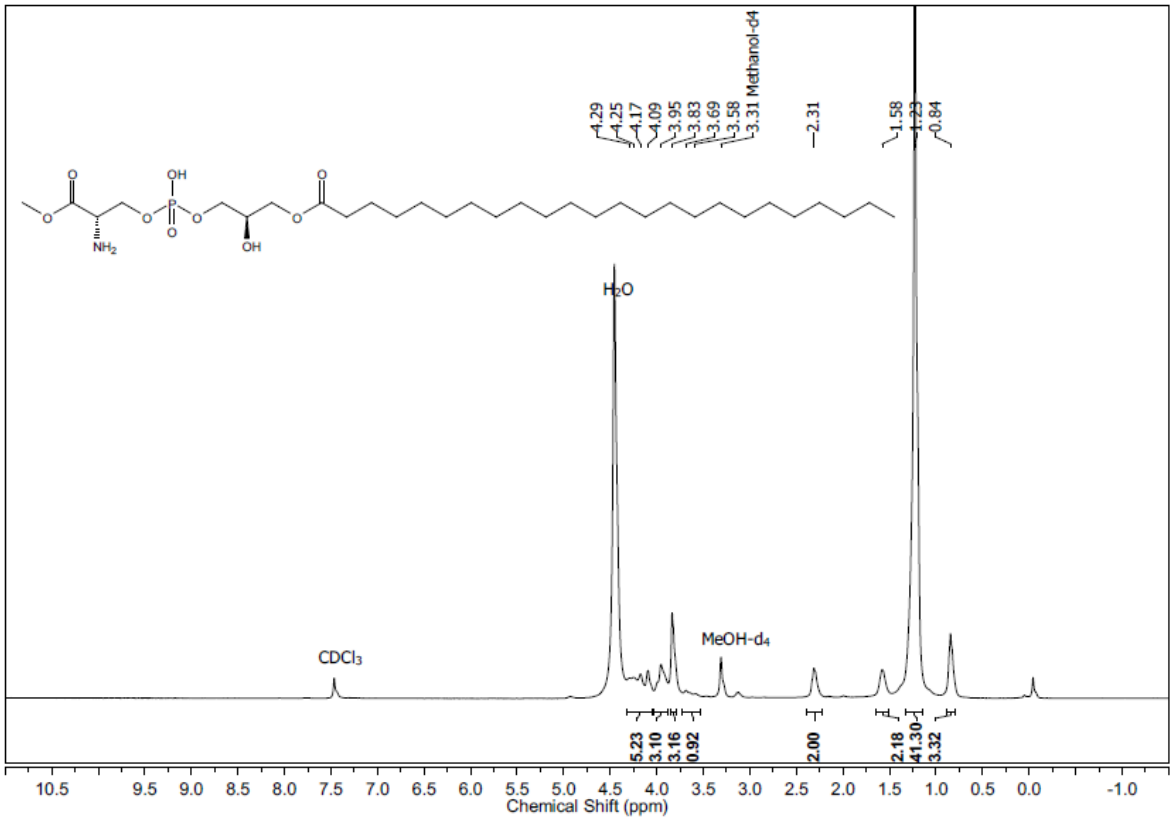

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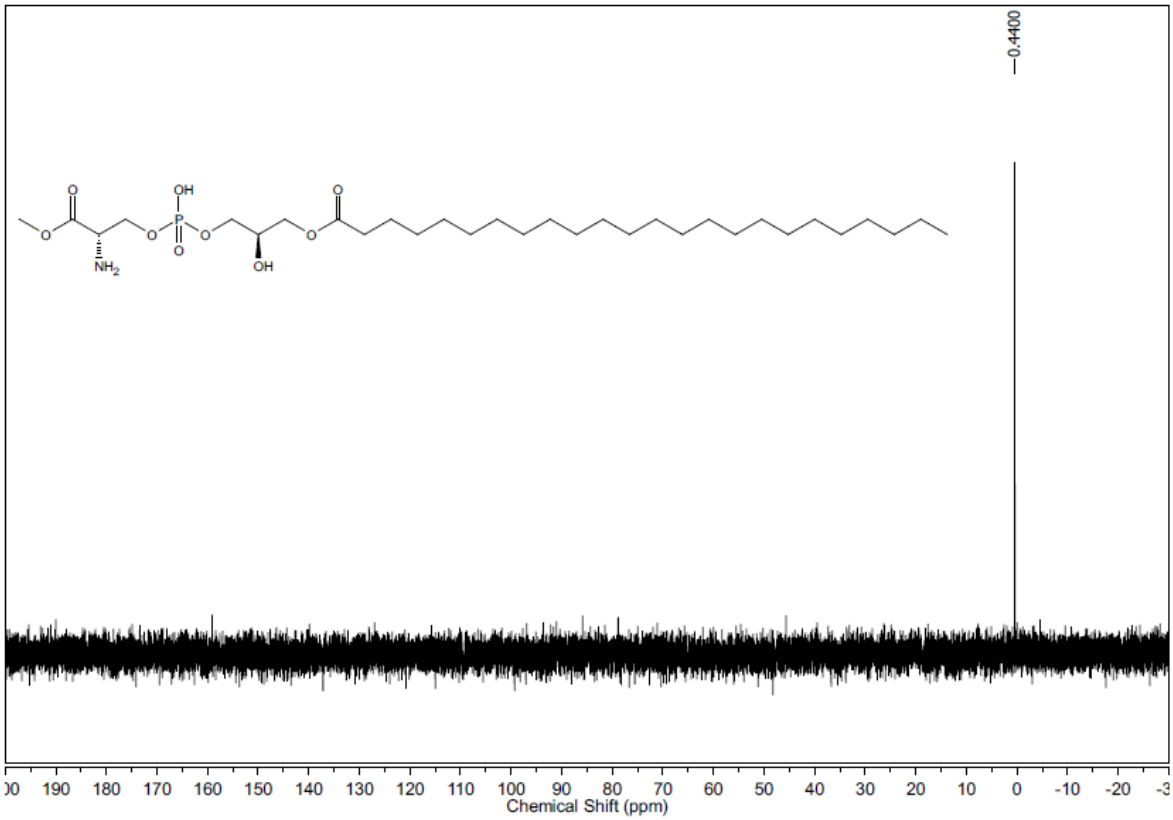

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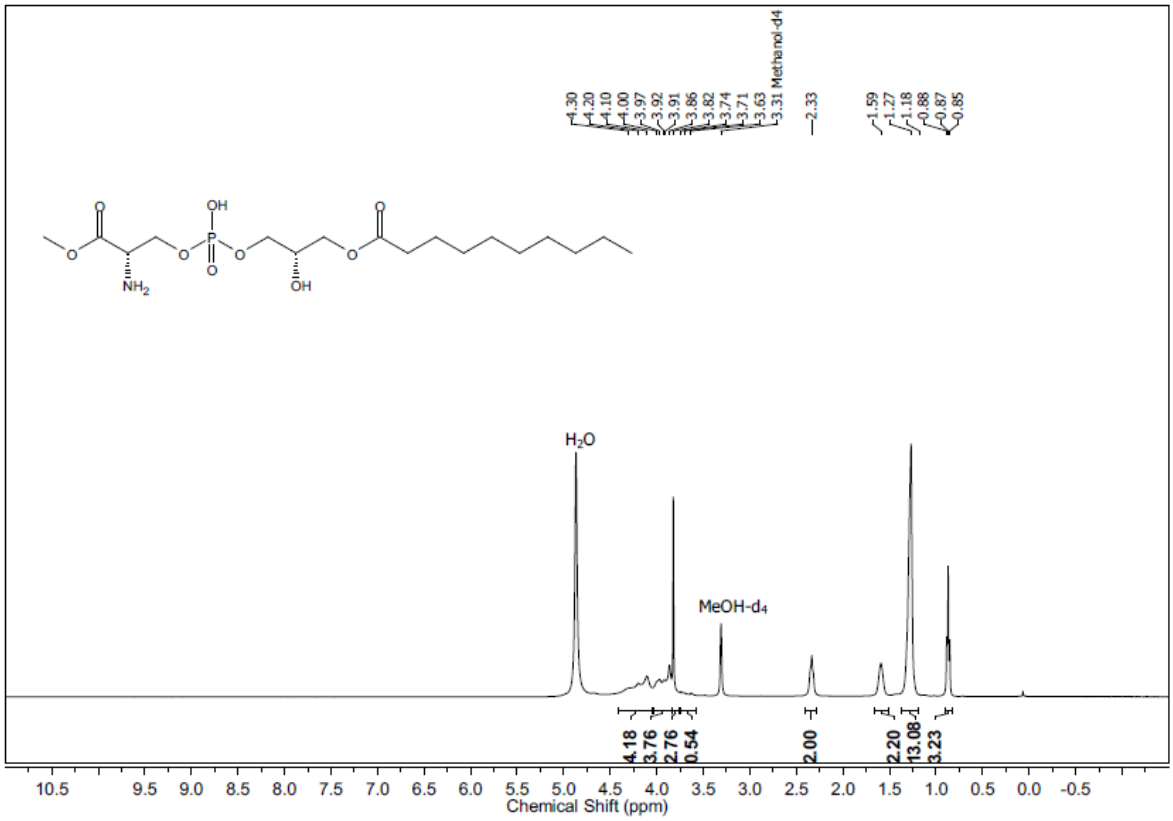

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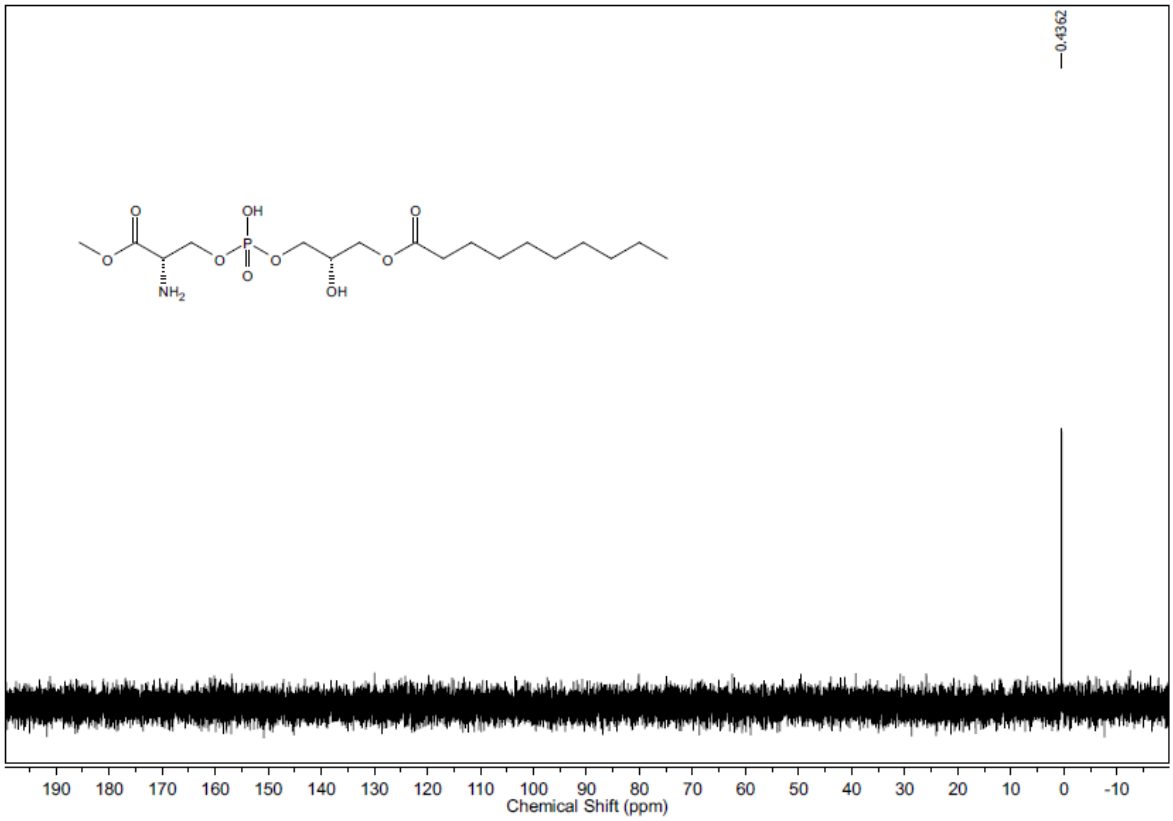

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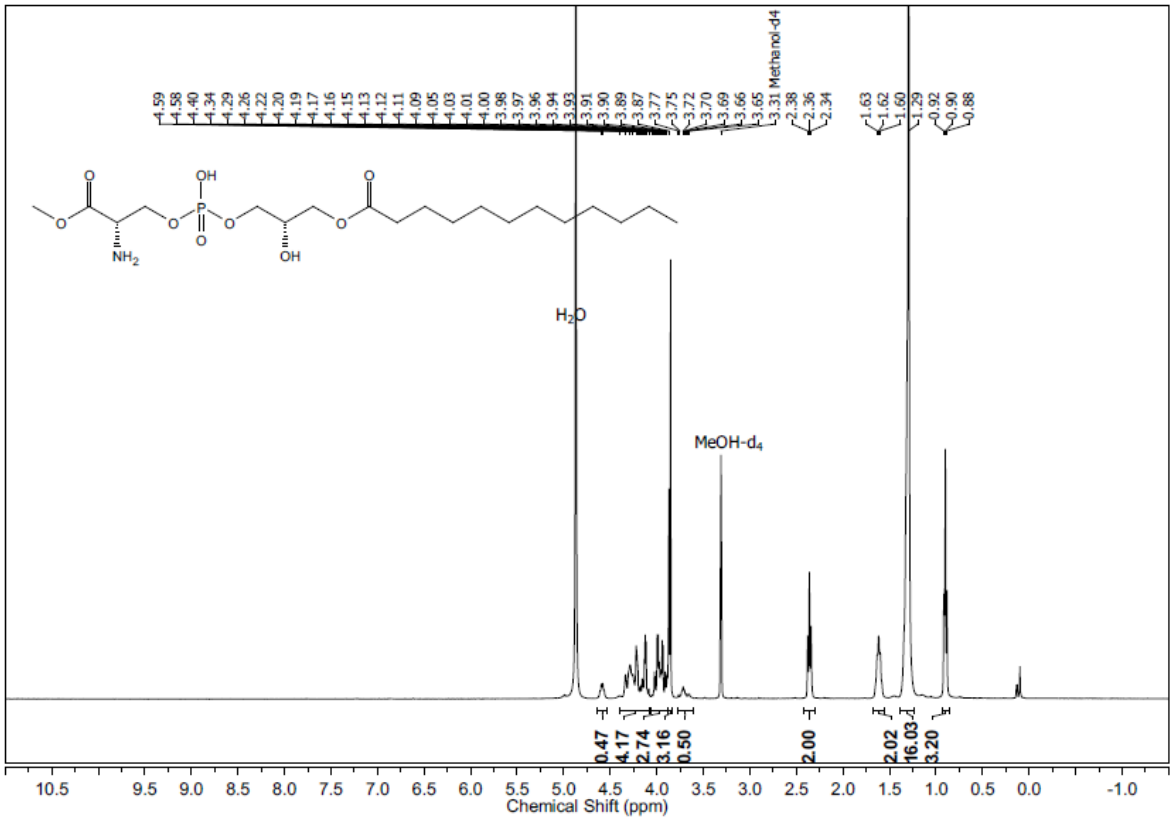

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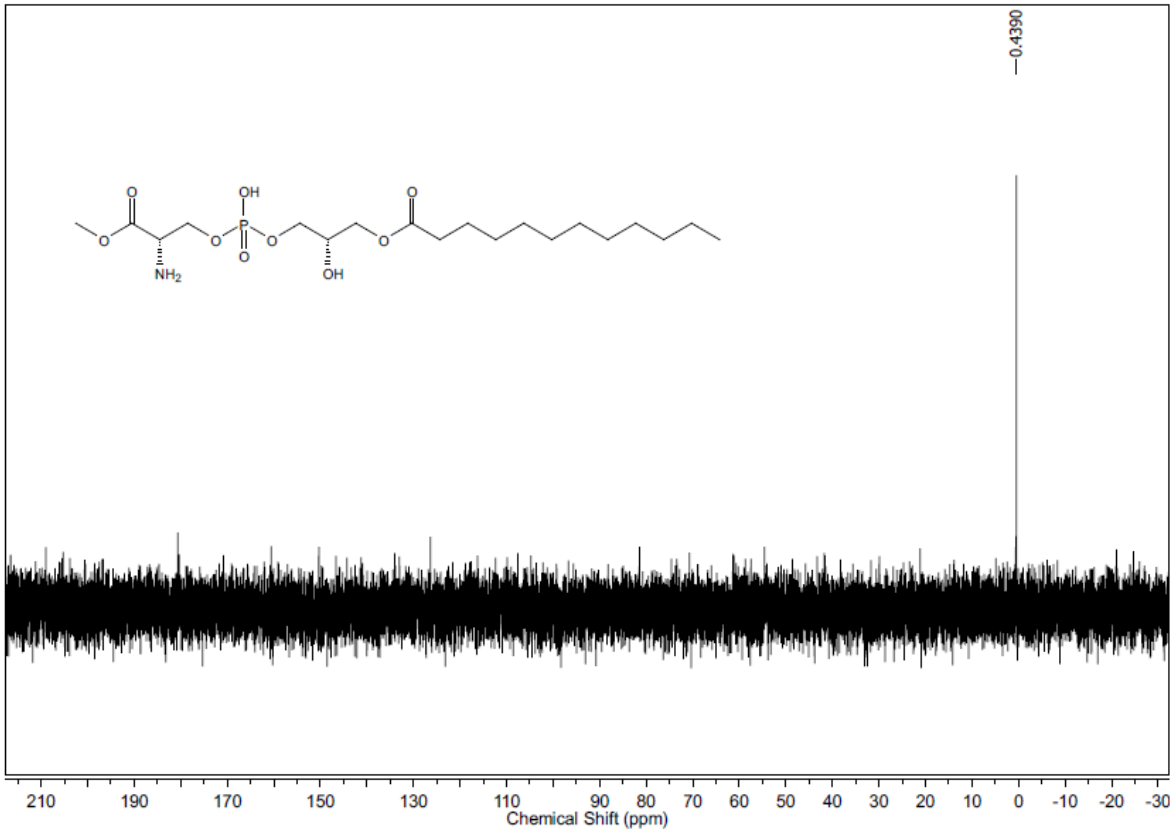

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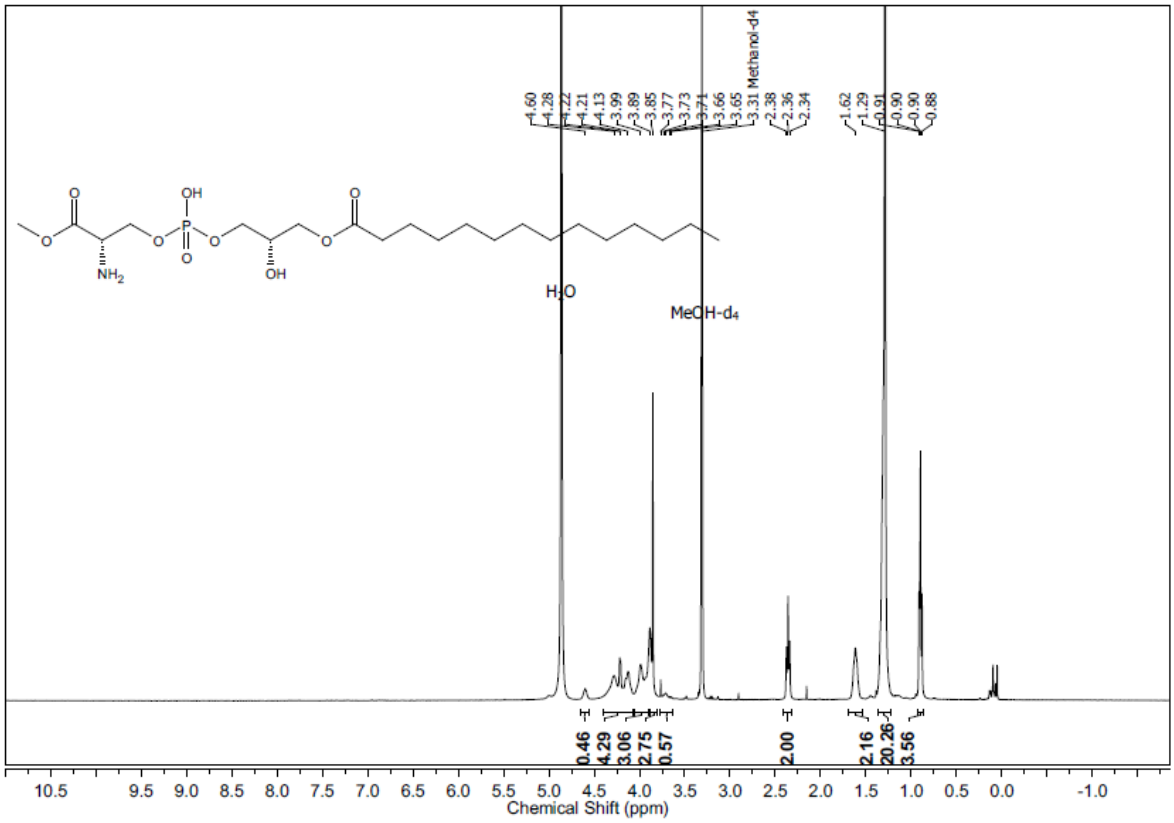

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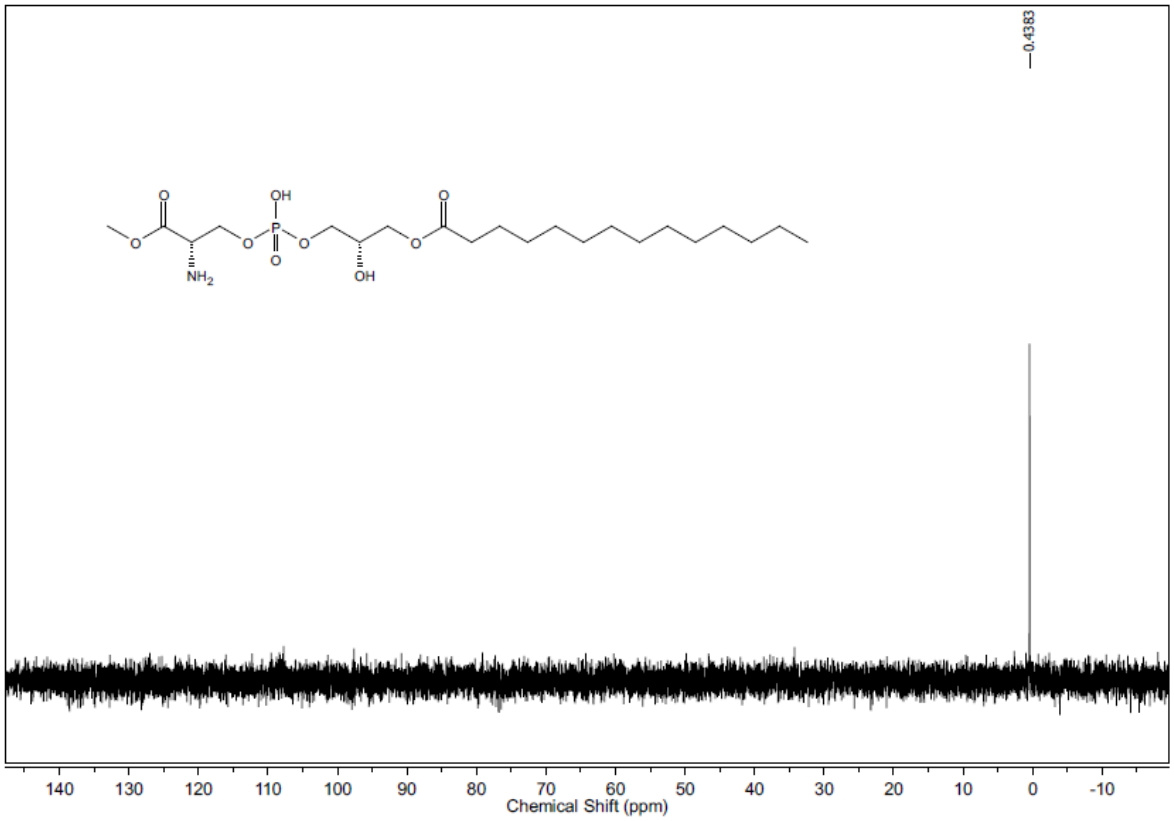

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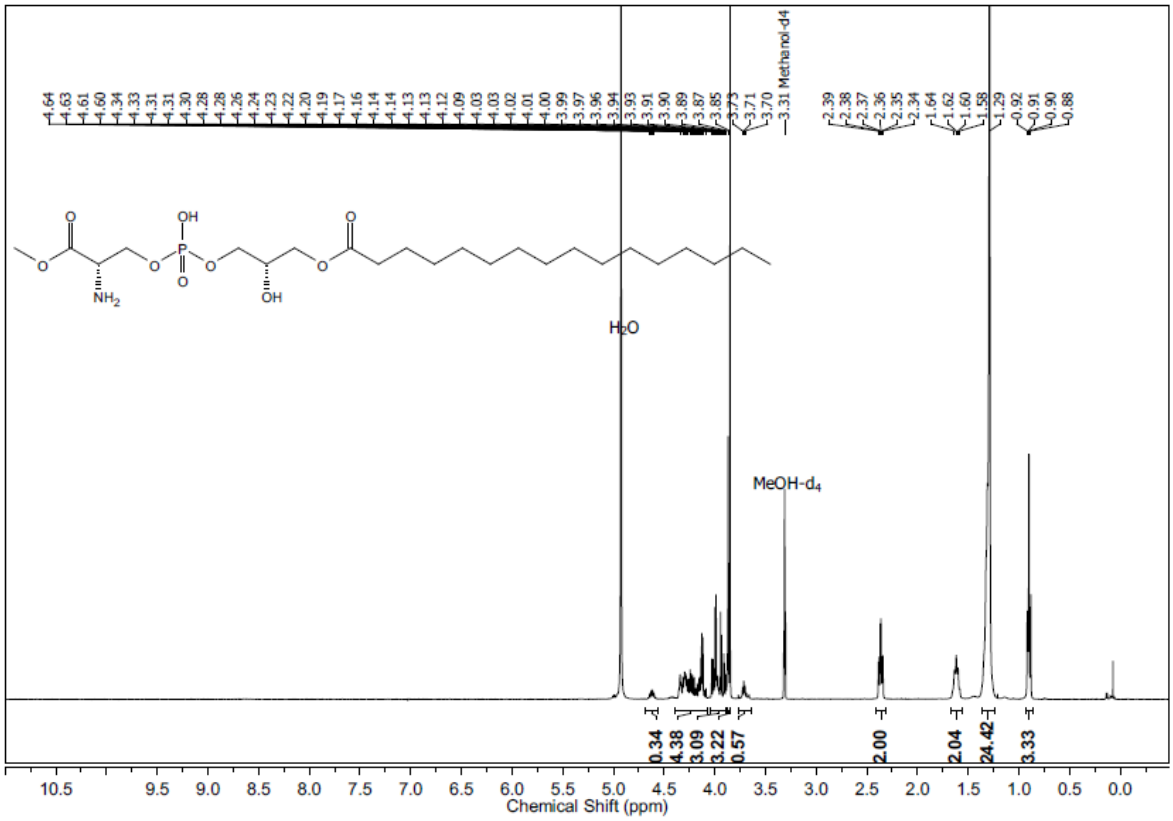

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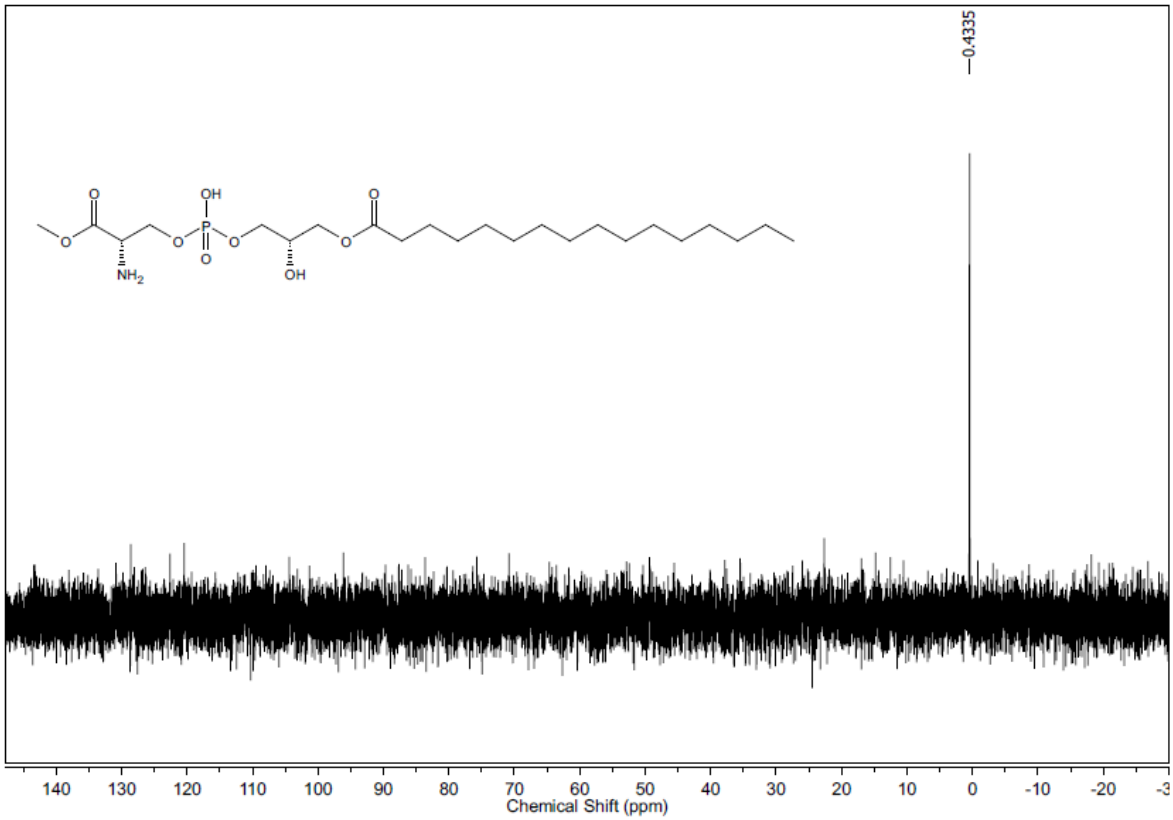

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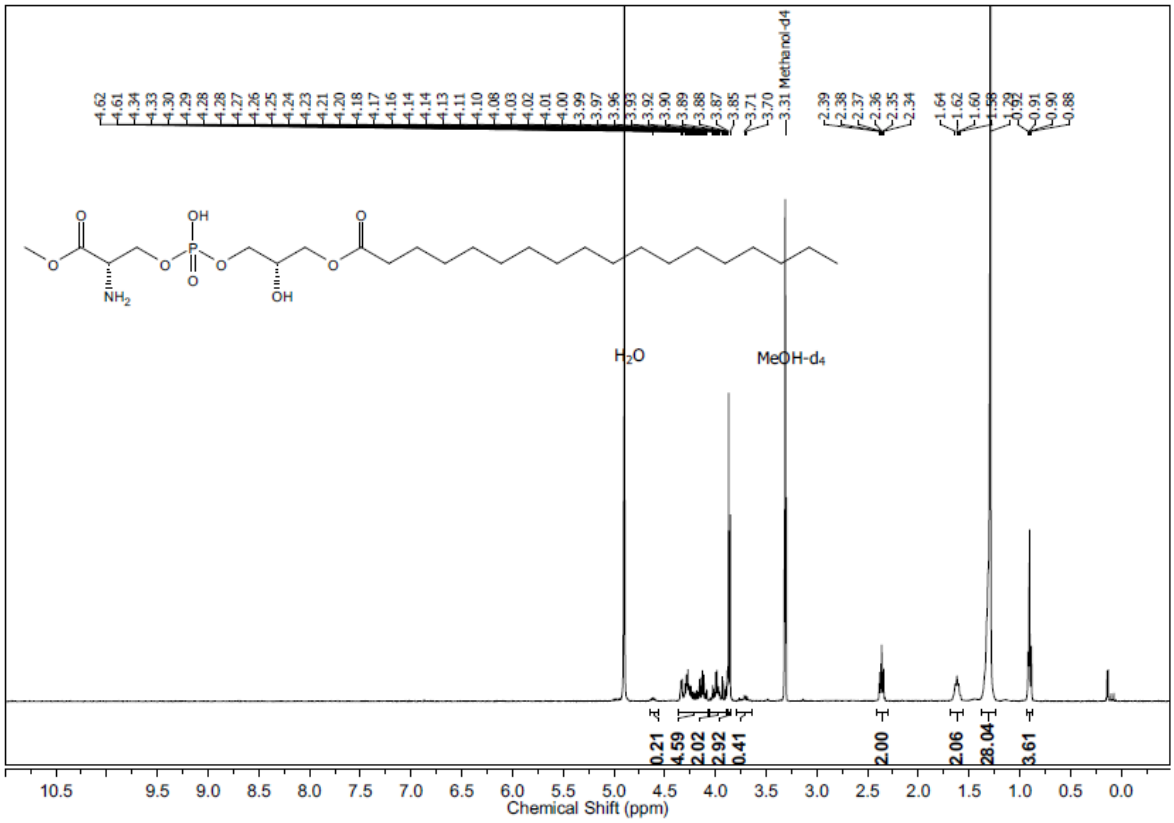

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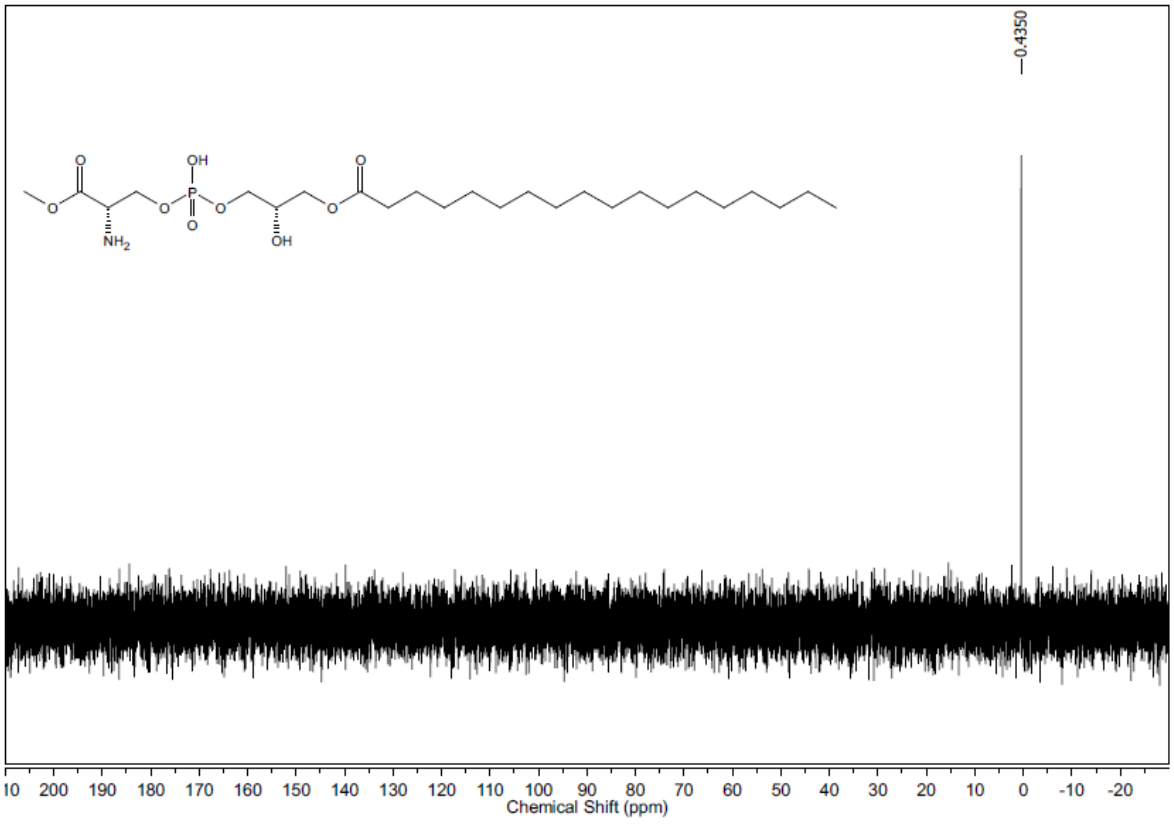

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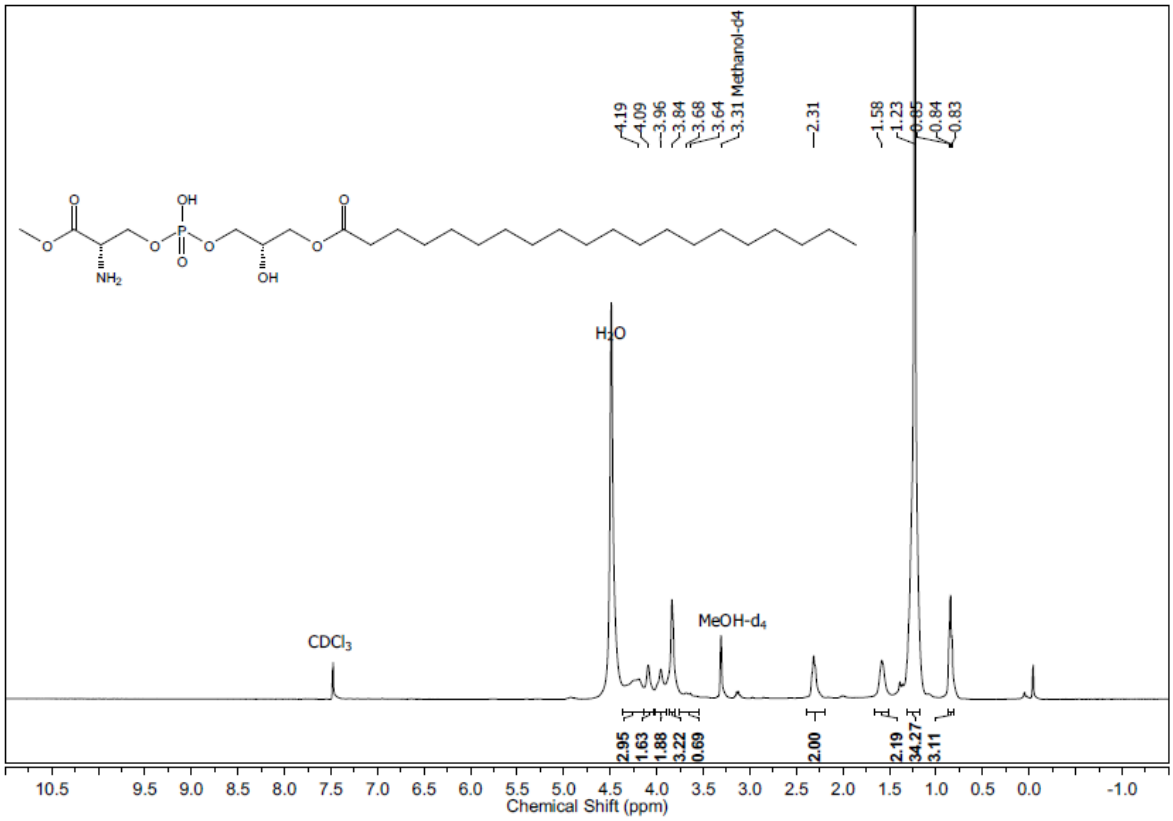
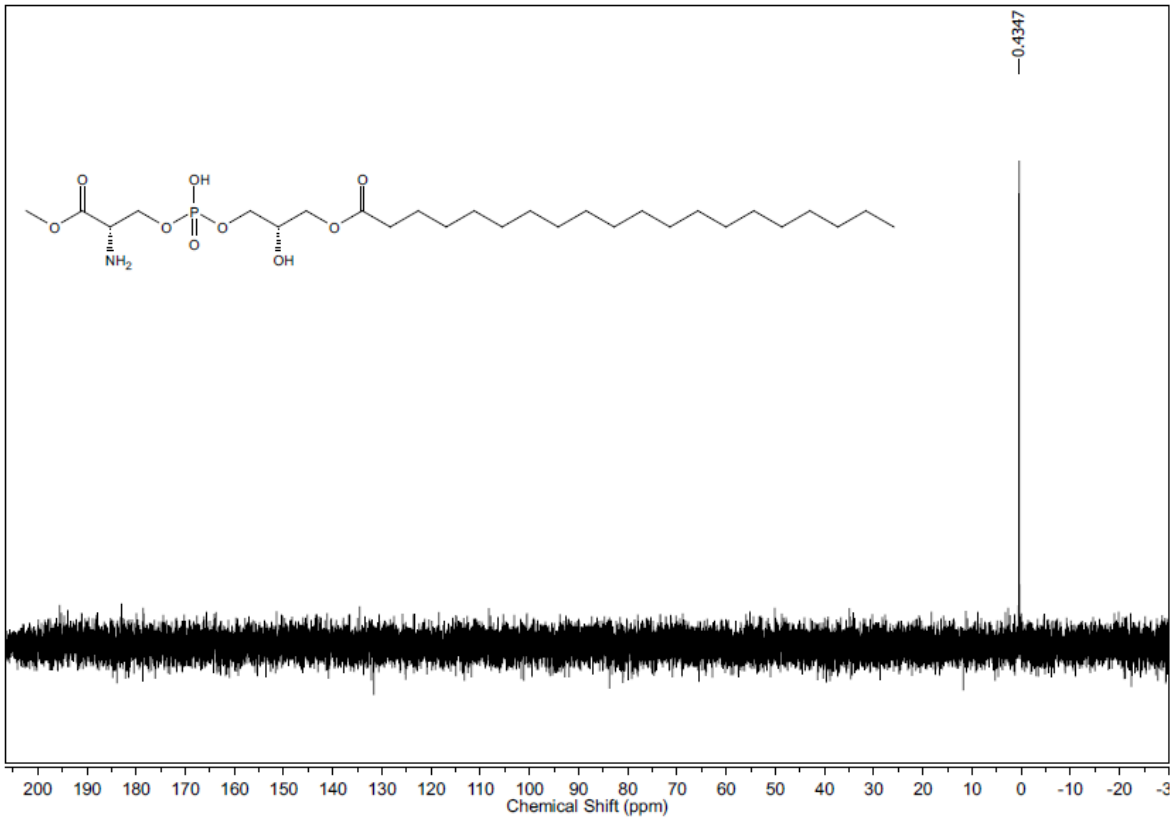


^{31}P NMR of final compound (*S*)-**2f**



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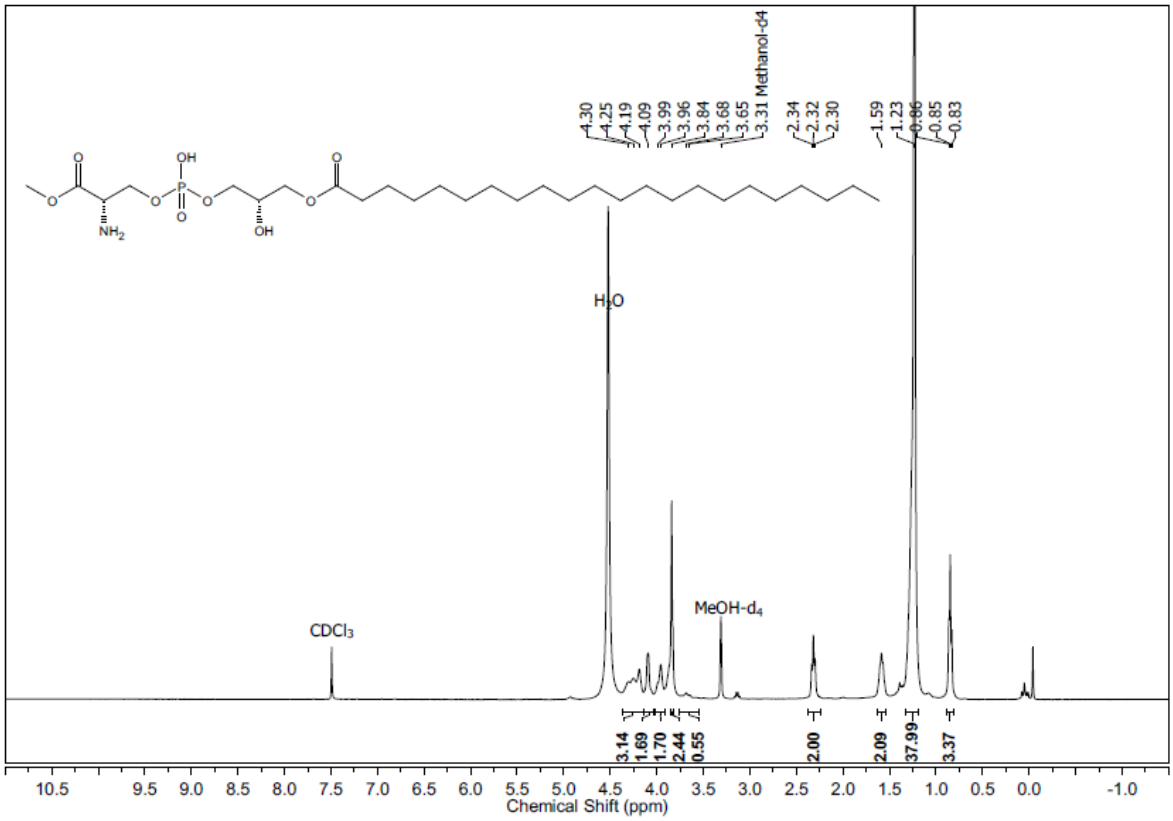

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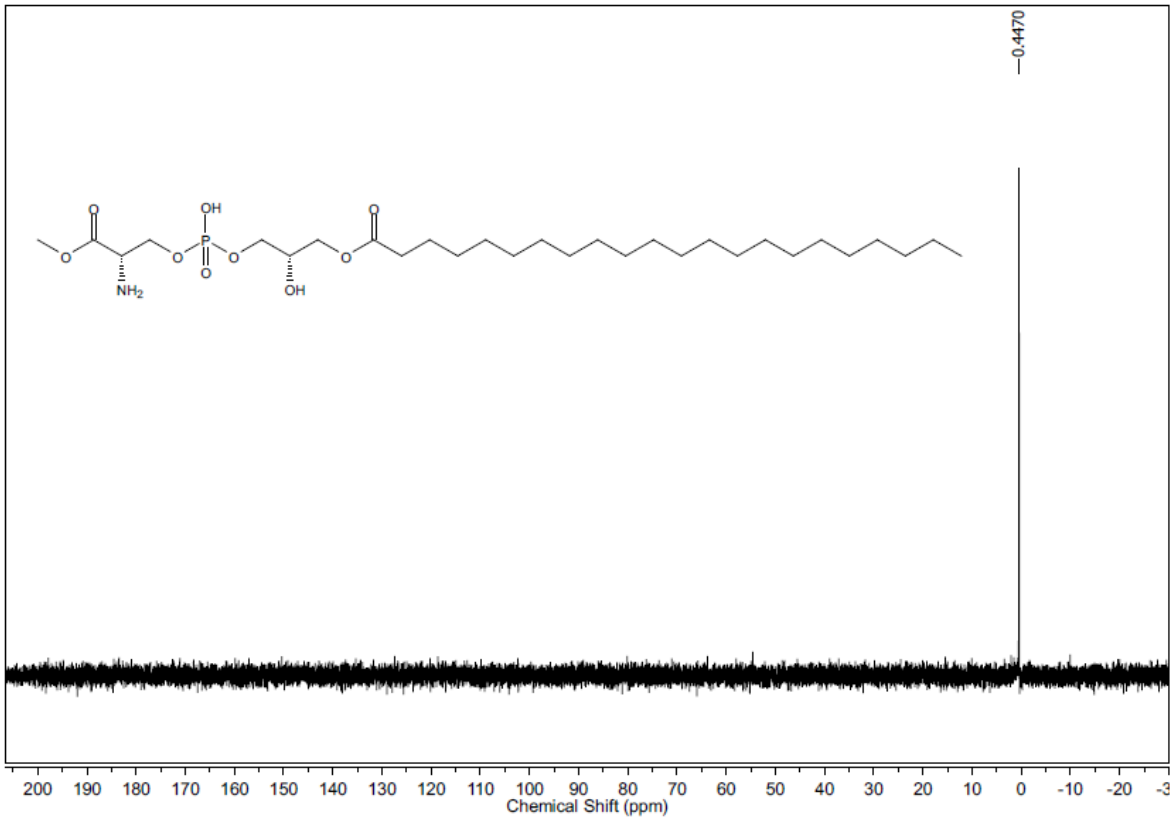

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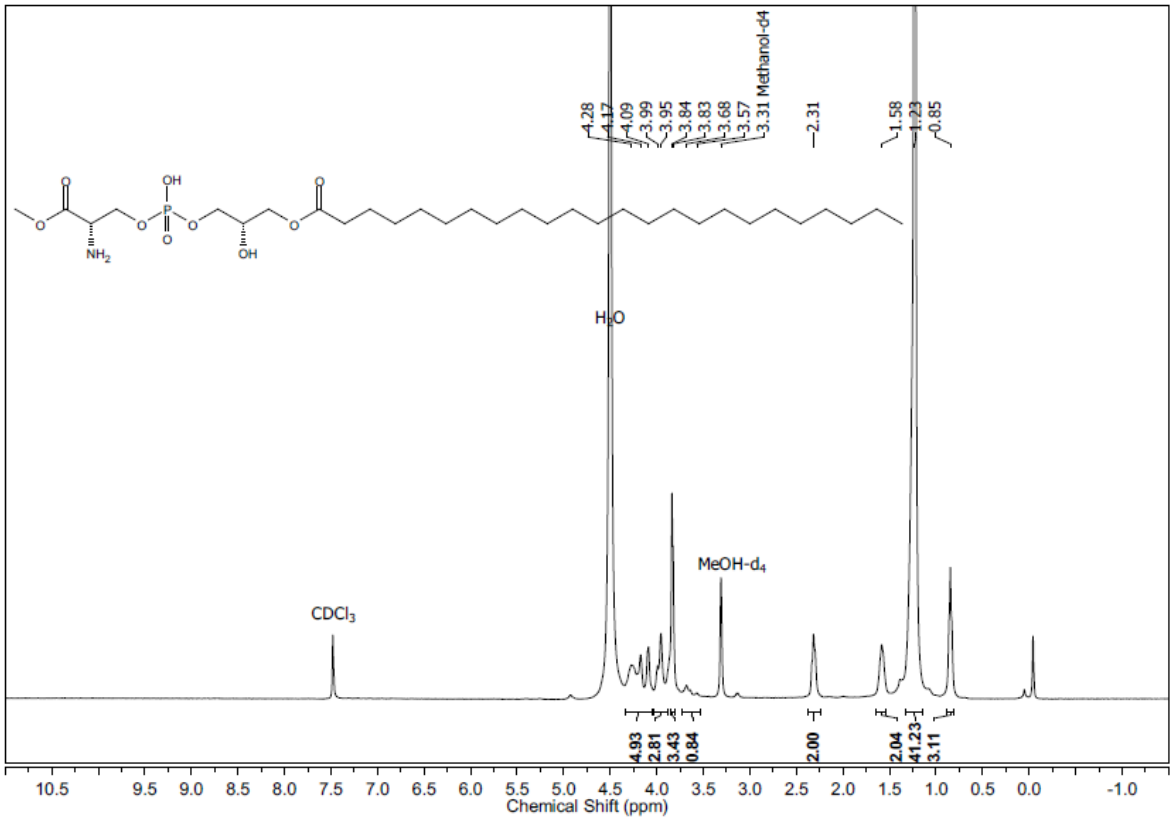

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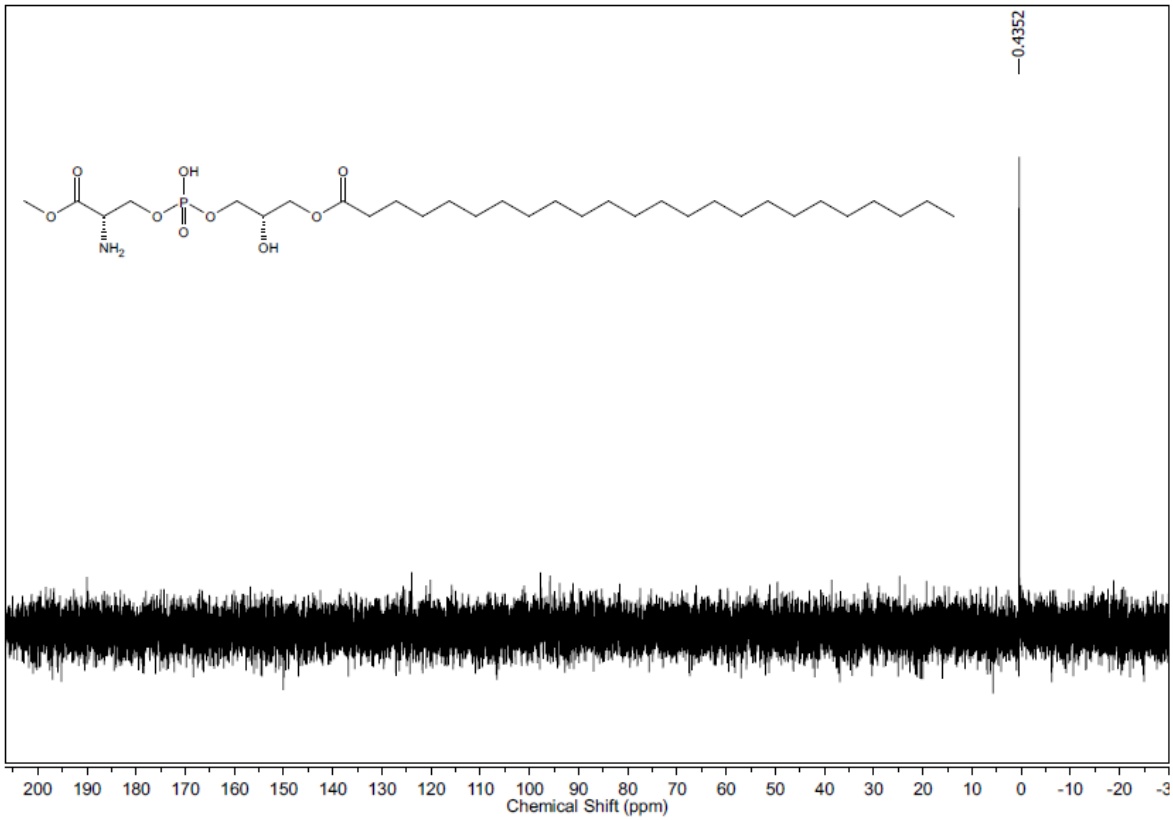

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