

***Supporting Information***

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**Physicochemical Characterization of Diacyltetrol-Based Lipids  
consisting of both Diacylglycerol and Phospholipid headgroups**

*Narsimha Mamidi<sup>a,†</sup>, Sukhamoy Gorai<sup>a,†</sup>, Bolledu Ravi<sup>b</sup> and Debasis Manna<sup>a,\*</sup>*

<sup>a</sup>Department of Chemistry, Indian Institute of Technology Guwahati, Assam 781039, India

<sup>b</sup>Department of Chemical Engineering, Indian Institute of Technology Guwahati, Assam 781039, India

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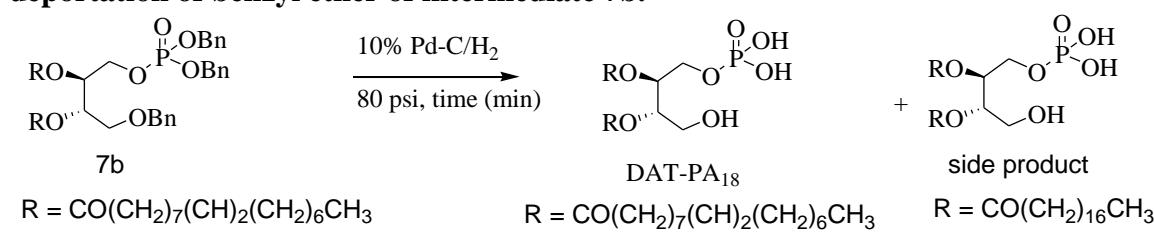
## (I) Synthesis of Hybrid Lipids

**General Procedure for the Deprotection of Isopropylidene Group (I)<sup>1,2</sup>:** To a stirring solution of isopropylidene protected compounds (1.0 equiv) in methanol (5 mL), p-TsOH (0.1 equiv) was added and stirring was continued at room temperature for 4 h. After completion of the reaction (monitored by TLC), the solvent was removed under reduced pressure to yield a residue. The residue was further dissolved in dichloromethane (10mL) and washed with saturated solution of sodium bicarbonate (3×). The organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. Purification by silica gel column chromatography and a gradient solvent system of 20–30% ethyl acetate to hexane yielded diol derivatives.

**General Procedure for the Preparation of Esters (II)<sup>1,2</sup>:** Palmitic acid/oleic acid (2.2 equiv.), dicyclohexylcarbodiimide (2.2 equiv.) and N,N-dimethylaminopyridine (0.1 equiv.) were added to a solution of protected alcohol (1.0 equiv.) in anhydrous dichloromethane (5 mL) under a N<sub>2</sub> atmosphere. Stirring was continued for 12 h at room temperature. After completion of the reaction (monitored by TLC), the reaction mixture was filtered and washed (3×) with dichloromethane. The filtrate was concentrated under reduced pressure and the column chromatography was performed with silica gel and a gradient solvent system of 2–5% ethyl acetate to hexane to yield corresponding esters.

**General Procedure for the Deprotection of Benzyl Groups (III)<sup>1,2</sup>:** The removal of benzyl ether group using 0.1 equivalents of 10% Pd-C, under 80 psi of H<sub>2</sub> gas for 3 h produced the desired compounds (yield ~ 90%) with saturated tail groups. Unfortunately, in case of oleoyl compounds reduction of oleic double was detected (NMR not shown). Removal of benzyl protecting groups in the presence of olefin double bond proved to be particularly challenging. To overcome this problem, the time dependent regioselective catalytic hydrogenation reaction conditions were optimized. Several trials were attempted with Pd-C catalyst concentrations, solvent systems and the reaction time. However, the reaction with 0.1 equivalents of 10% Pd-C under 80 psi of H<sub>2</sub> gas in EtOH/EtoAc (1:3) solvent system produced the targeted compound within 30 min. After completion of the reaction, the catalyst (Pd-C) was filtered off through a pad of Celite and washed with 30 ml of MeOH. Removal of solvent under reduced pressure yielded the targeted compounds.

**Table S1. Optimization of the catalytic hydrogenation reaction conditions for the deprotection of benzyl ether of intermediate 7b.**



Entry	Catalyst	Solvent system	Time(min)	% yield (DAT-PA <sub>18</sub> :side product)
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1	Pd-C/H <sub>2</sub> (10%)	EtOH/EtoAc (1:3)	180 min	10:90
2	Pd-C/H <sub>2</sub> (10%)	EtOH/EtoAc (1:3)	120 min	20:80
3	Pd-C/H <sub>2</sub> (10%)	EtOH/EtoAc (1:3)	60 min	35:65
4	Pd-C/H <sub>2</sub> (10%)	EtOH/EtoAc (1:3)	30 min	90:10
5	Pd-C/H <sub>2</sub> (10%)	EtOH/EtoAc (1:3)	15 min	60:40

**General Procedure for the Deprotection of TBDPS Group<sup>3,4</sup>:** To a stirring solution of TBDPS protected compound (1.0 equiv) in THF (5.0 mL) was added commercially available TBAF (2.0 equiv, 1.0 M solution in THF) at room temperature and stirring was continued for 1 h. After completion of the reaction (monitored by TLC), the solvent was removed under reduced pressure to yield a residue. The residue was dissolved in EtOAc (20 mL) and washed with saturated solution of sodium bicarbonate (3×). The organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. Purification by silica gel column chromatography and a gradient solvent system of 7–10% ethyl acetate to hexane yielded alcohol derivatives.

**General Procedure for the One-pot Phosphorylation of protected Alcohols to Prepare DAT-PS and DAT-PG derivatives (V)<sup>5</sup>:** To an ice-cooled stirring suspension of O-benzyl N,N,N',N'-tetraisopropyl phosphorodiamidite (1.1 equiv) and 1*H*-tetrazol (6.0 equiv), protected alcohol (1.0 equiv) in anhydrous dichloromethane (2 mL) was added under N<sub>2</sub> atmosphere. After continuous stirring for 30 min benzyl (S)-1-((benzyloxy)carbonyl)-2-hydroxyethylcarbamate or (2-phenyl-1,3-dioxan-4-yl)methanol (1.0 equiv) in anhydrous dichloromethane (2 mL) was added. The reaction mixture was stirred for another 5 h at room temperature and cooled to -20 °C and a solution of *meta*-chloroperbenzoic acid (1.5 equiv) in dichloromethane (2 mL) was added. Finally, the reaction mixture was stirred for 1 h at room temperature, diluted with dichloromethane (30 mL), washed (3×) with 10% aqueous NaHCO<sub>3</sub> (10 mL) and brine (10 mL). The organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. Column chromatography with silica gel and a gradient solvent system of 27–30% ethyl acetate to hexane yielded corresponding phosphates compound.

**((4*S*,5*S*)-diethyl 2,2-dimethyl-1,3-dioxane-4,5-dicarboxylate (2)<sup>1,2</sup>:** To a stirring solution of (+)-diethyl-L-tertrate (3.0 g, 14.56 mmol) in toluene (25 mL) p-toluenesulfonic acid (227 mg, 1.45 mmol) and 2,2-dimethoxypropane (3.56 mL, 29.13 mmol) were added respectively. The solution was refluxed for 8 h and the azeotrope was collected in a Dean–Stark trap. The reaction mixture was then cooled to room temperature and quenched by adding 20% solid sodium bicarbonate. After stirring for another 30 min at room temperature, the reaction mixture was filtered and concentrated under reduced pressure. The purification by silica gel column chromatography and a gradient solvent system of 20–30% ethyl acetate to hexanes yielded **2** (3.0 g, 84%) as a colorless oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ<sub>ppm</sub> 4.70 (s, 2H), 4.21 (q, 4H, J = 7.2 Hz), 1.43 (s, 6H), 1.25 (t, 6H, J = 7.2 Hz); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ<sub>ppm</sub> 169.3, 113.4, 76.9, 61.5, 26.1, 13.8; HRMS (ESI) Calcd for C<sub>11</sub>H<sub>19</sub>O<sub>6</sub> [M+H]<sup>+</sup>: 247.1182, Found: 247.1181.

**(4S,5S)-5-(hydroxymethyl)-2,2-dimethyl-1,3-dioxolan-4-yl]methanol (3)<sup>1,2</sup>:** Protected diester **2** (2.0 g, 8.13 mmol) in anhydrous THF (5 mL) was added drop-wise to a suspension of lithium aluminium hydride (679 mg, 17.89 mmol) in anhydrous THF (20 mL) at 0 °C under a N<sub>2</sub> atmosphere. Stirring was continued at room temperature for 1 h and then the solution was refluxed for additional 6 h. After completion of the reaction, the temperature was lowered to 0 °C and the reaction was cautiously quenched by addition of 2 mL of deionized water, followed by 2 mL of 10% NaOH and 4 mL of deionized water. The mixture was warmed to room temperature, and stirred until the gray colour disappeared. The reaction mixture was filtered in a sintered glass crucible using Celite. Resulting solution was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. Column chromatography with silica gel and a gradient solvent system of 50–60% ethyl acetate to hexane yielded **3** (1.29 g, 98%) as a colourless oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta_{\text{ppm}}$  3.90 (m, 2H) 3.63 (m, 2H), 3.21 (m, 2H), 1.25 (s, 6H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta_{\text{ppm}}$  109.1, 78.4, 62.2, 26.8; HRMS (ESI) Calcd for C<sub>7</sub>H<sub>14</sub>O<sub>4</sub>Na<sup>+</sup> [M+Na]<sup>+</sup>: 185.0790, Found: 185.0787.

**((4S,5S)-5-((benzyloxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol (4)<sup>6</sup>:** To a solution of compound **3** (1.0 g, 6.17 mmol) in anhydrous dichloromethane (20 mL), silver oxide (Ag<sub>2</sub>O, 2.14 g, 9.26 mmol) and benzyl bromide (806  $\mu$ L, 6.79 mmol) were added and stirred at room temperature for 8 h under a N<sub>2</sub> atmosphere. After completion of reaction (monitored by TLC) the reaction mixture was filtered off through a pad of celite and washed with 30 ml of dichloromethane. The solvent was removed under reduced pressure. The purification by silica gel column chromatography and a gradient solvent system of 15–20% ethyl acetate to hexane afforded **4** (1.3 g, 84%) as a colourless oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta_{\text{ppm}}$  7.37-7.28 (m, 5H), 4.58 (s, 2H), 4.08-4.03 (m, 1H), 3.96-3.92 (m, 1H), 3.79-3.74 (m, 1H), 3.70-3.64 (m, 2H), 3.58-3.54 (m, 1H), 2.43 (br s, 1H), 1.42 (s, 6H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta_{\text{ppm}}$  137.5, 128.2, 127.6, 127.5, 109.2, 79.3, 76.4, 73.4, 70.3, 62.2, 26.8, 26.7; HRMS (ESI) Calcd for C<sub>14</sub>H<sub>20</sub>O<sub>4</sub>Na<sup>+</sup> [M+Na]<sup>+</sup>: 275.1259, Found: 275.1257.

**Dibenzyl ((4S,5S)-5-((benzyloxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl phosphate (5)<sup>5</sup>:** To a stirring solution of compound **4** (252 mg, 1.0 mmol) in anhydrous dichloromethane (2.5 mL), a suspension of dibenzyldiisopropylphosphoramidite (518 mg, 1.5 mmol) and 1*H*-tetrazol (420 mg, 6.0 mmol) in anhydrous dichloromethane (2.5 mL) were added at room temperature under a N<sub>2</sub> atmosphere. Stirring was continued for another 4 h and cooled to -20 °C, and a solution of *meta*-chloroperbenzoic acid (259 mg, 1.5 mmol) was added. The reaction mixture was stirred for 1 h at room temperature, diluted with 30 mL of dichloromethane, washed (10% aqueous NaHCO<sub>3</sub>, brine). Resulting solution was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. Column chromatography with silica gel and a gradient solvent system of 25–30% ethyl acetate to hexane yielded **5** (470 mg, 92%) as a colorless oil.  $[\alpha]^{20}_{\text{D}} = -10.1$  (c 0.1, CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta_{\text{ppm}}$  7.36-7.30 (m, 15H), 5.11-5.00 (m, 4H), 4.54 (s, 2H), 4.16-4.11 (m, 2H), 4.08-3.97 (m, 2H), 3.59-3.50 (m, 2H), 1.39 (s, 3H), 1.37 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta_{\text{ppm}}$  137.9, 135.8, 135.6, 128.8, 128.6, 128.5, 128.1, 128.0, 127.8, 127.7, 110.1, 76.4, 73.6, 70.3, 69.5, 67.4, 67.3, 27.1, 26.9; <sup>31</sup>P NMR

(161.9 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{ppm}}$  0.59; HRMS (ESI) Calcd for  $\text{C}_{28}\text{H}_{33}\text{O}_7\text{PNa}^+ [\text{M}+\text{Na}]^+$ : 535.1862, Found: 535.1863.

**Dibenzyl (2S,3S)-4-(benzyloxy)-2,3-dihydroxubutyl phosphate (6):** Using the general procedure (I), starting from compound **5** (350 mg, 0.68 mmol) compound **6** (265 mg, 82%) was isolated as colorless oil.  $[\alpha]^{20}_{\text{D}} = -22.4$  (c 0.2,  $\text{CH}_2\text{Cl}_2$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{ppm}}$  7.23-7.16 (m, 15H), 4.91 (d, 4H,  $J = 8.4$  Hz), 4.39 (s, 2H), 4.00-3.95 (m, 2H), 3.74-3.68 (m, 2H), 3.45-3.43 (m, 2H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{ppm}}$  137.9, 135.7, 135.6, 128.6, 128.5, 128.0, 127.8, 73.5, 71.6, 70.5, 69.6, 69.4, 68.8;  $^{31}\text{P}$  NMR (161.9 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{ppm}}$  0.59; HRMS (ESI) Calcd for  $\text{C}_{25}\text{H}_{29}\text{O}_7\text{PNa}^+ [\text{M}+\text{Na}]^+$ : 495.1549, Found: 495.1546.

**(2S,3S)-4-(benzyloxy)-1-[[bis(benzyloxy)phosphoryl]oxy]-3-(hexadecanoyloxy)butan-2-yl hexadecanoate (7a):** Using the general procedure (II), starting from compound **6** (100 mg, 0.21 mmol) compound **7a** (173 mg, 86%) was isolated as colorless oil.  $[\alpha]^{20}_{\text{D}} = -15.4$  (c 0.2,  $\text{CH}_2\text{Cl}_2$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{ppm}}$  7.33-7.26 (m, 15H), 5.36-5.33 (m, 1H), 5.27-5.24 (m, 1H), 5.00 (t, 4H,  $J = 7.6$  Hz), 4.45 (d, 2H,  $J = 7.2$  Hz), 4.20-4.14 (m, 1H), 4.10-4.00 (m, 1H), 3.57-3.49 (m, 2H), 2.30 (t, 2H,  $J = 7.4$  Hz), 2.22 (t, 2H,  $J = 7.8$  Hz), 1.68-1.52 (m, 4H), 1.26 (br s, 48H), 0.88 (t, 6H,  $J = 6.8$  Hz);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{ppm}}$  172.9, 172.8, 137.6, 135.8, 128.6, 128.5, 128.1, 128.0, 127.9, 127.8, 73.4, 70.1, 70.0, 69.6, 68.0, 65.8, 34.3, 34.2, 32.0, 29.8, 29.6, 29.5, 29.4, 29.2, 25.0, 24.9, 22.8, 14.2;  $^{31}\text{P}$  NMR (161.9 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{ppm}}$  0.08; HRMS (ESI) Calcd for  $\text{C}_{57}\text{H}_{89}\text{O}_9\text{PNa}^+ [\text{M}+\text{Na}]^+$ : 971.6142, Found: 971.6142.

**(2S,3S)-4-(benzyloxy)-1-[[bis(benzyloxy)phosphoryl]oxy]-3-[(9Z)-octadec-9-enoyloxy]butan-2-yl (9Z)-octadec-9-enoate (7b):** Using the general procedure (II), starting from compound **6** (100 mg, 0.212 mmol) compound **7b** (170 mg, 80%) was isolated as yellow oil.  $[\alpha]^{20}_{\text{D}} = -11.6$  (c 0.1,  $\text{CH}_2\text{Cl}_2$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{ppm}}$  7.43-7.19 (m, 15H), 5.39-5.30 (m, 4H), 5.25-5.22 (m, 1H), 5.17-5.98 (m, 4H), 4.52 (s, 2H), 4.40-4.36 (m, 1H), 4.20-4.10 (m, 1H), 3.97-3.95 (m, 1H), 3.73-3.63 (m, 1H), 3.55-3.44 (m, 1H), 2.37-2.26 (m, 4H), 2.00 (m, 8H), 1.62-1.60 (m, 4H), 1.30 (br s, 40H), 0.88 (t, 6H,  $J = 6.8$  Hz);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{ppm}}$  173.4, 173.2, 137.6, 135.5, 135.4, 134.9, 130.0, 129.7, 129.3, 128.7, 128.4, 128.3, 128.2, 128.0, 127.8, 127.7, 127.6, 127.5, 127.3, 126.9, 73.5, 71.4, 70.9, 69.2, 68.8, 67.3, 64.7, 34.2, 34.1, 31.9, 29.8, 29.7, 29.5, 29.3, 29.2, 29.1, 27.2, 26.6, 24.9, 24.8, 22.7, 14.2;  $^{31}\text{P}$  NMR (161.9 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{ppm}}$  1.73; HRMS (ESI) Calcd for  $\text{C}_{61}\text{H}_{93}\text{O}_9\text{P} [\text{M}+\text{K}]^+$ : 1039.6194, Found: 1040.4760.

**[(2S,3S)-2,3-bis(hexadecanoyloxy)-4-hydroxybutoxy]phosphonic acid (DAT-PA<sub>16</sub>):** Using the general procedure (III), starting from compound **7a** (160 mg, 0.169 mmol) compound DAT-PA<sub>16</sub> (104 mg, 90%) was isolated as white solid. m.p: 45-46 °C;  $[\alpha]^{20}_{\text{D}} = -9.8$  (c 0.1,  $\text{EtOH}$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{ppm}}$  5.23-5.06 (m, 2H), 4.79 (br s, 2H), 4.31-3.59 (m, 2H), 2.28-2.19 (m, 4H), 1.53-1.51 (m, 4H), 1.18 (br s, 48H), 0.8 (t, 6H,  $J = 6.6$  Hz);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{ppm}}$  176.9, 173.9, 71.0, 69.0, 66.2, 63.3, 34.1, 31.9, 29.6, 29.3, 29.1, 24.9, 24.8, 22.6, 13.9;  $^{31}\text{P}$  NMR (161.9 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{ppm}}$  1.44; HRMS (ESI) Calcd for  $\text{C}_{36}\text{H}_{71}\text{O}_9\text{P Na}^+ [\text{M}+\text{Na}]^+$ : 701.4733, Found: 701.4733.

**[(2S,3S)-4-hydroxy-2,3-bis[(9Z)-octadec-9-enyloxy]butoxy]phosphonic acid (DAT-PA<sub>18</sub>):** Using the general procedure (III), starting from compound **7b** (150 mg, 0.15 mmol) compound DAT-PA<sub>18</sub> (99 mg, 90%) was isolated as a yellow oil.  $[\alpha]^{20}_D = -18.2$  (c 0.1, EtOH); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta_{\text{ppm}}$  5.26 (m, 4H), 4.22-4.19 (m, 1H), 4.10-4.40 (m, 2H), 3.86-3.84 (m, 1H), 3.72-3.67 (m, 1H), 3.62-3.58 (m, 1H), 3.10 (br s, 1H), 2.78-2.24 (m, 4H), 1.94-1.93 (m, 8H), 1.55 (m, 4H), 1.23 (br s, 40H), 0.81 (t, 6H, J = 6.7 Hz); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): 173.4, 129.8, 129.6, 78.0, 75.0, 64.0, 62.1, 36.6, 36.4, 34.0, 31.8, 29.7, 29.6, 29.5, 29.3, 29.1, 29.0, 27.1, 25.0, 24.8, 23.7, 23.6, 22.6, 14.0; <sup>31</sup>P NMR (161.9 MHz, CDCl<sub>3</sub>):  $\delta_{\text{ppm}}$  -1.59; HRMS (ESI) Calcd for C<sub>40</sub>H<sub>76</sub>O<sub>9</sub>P [M+H]<sup>+</sup>: 731.5227, Found: 731.5228.

**((4S,5S)-5-((benzyloxy)methyl)-2,2-dimethyl-1,3dioxolan-4-yl)methoxy)(tert-butyl)diphenylsilane (8):** To an ice-cooled stirring solution of *tert*-butylchlorodiphenylsilane (TBDPS-Cl) (340  $\mu$ L, 1.31 mmol) in anhydrous dichloromethane (5 mL) were added triethylamine (182  $\mu$ L, 1.31), catalytic amount of DMAP (15 mg, 0.12 mmol), and a solution of protected alcohol **4** (300 mg, 1.19 mmol) in dry dichloromethane (5 mL). The resulting mixture was allowed to warm up to room temperature and stirring was continued for 12 h at room temperature. After completion of the reaction, the solvent was removed under reduced pressure to yield a residue. The residue was dissolved in dichloromethane (20 mL) and washed with saturated solution of NaHCO<sub>3</sub>. The organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. Purification by silica gel column chromatography and a gradient solvent system of 3–5% ethyl acetate to hexane yielded **8** (572 mg, 98%) as a colourless oil.  $[\alpha]^{20}_D = -14.3$  (c 0.1, CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta_{\text{ppm}}$  7.68-7.63 (m, 5H), 7.44-7.28 (m, 10H), 4.59 (dd, 2H, J = 12.0 Hz, J = 12.0 Hz), 4.26-4.21 (m, 1H), 3.92-3.88 (m, 1H), 3.81-3.73 (m, 2H), 3.67-3.63 (m, 1H), 3.60-3.56 (m, 1H), 1.43 (s, 3H), 1.41 (s, 3H), 1.03 (s, 9H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta_{\text{ppm}}$  138.2, 135.7, 133.2, 129.9, 128.5, 127.8, 127.7, 109.5, 78.4, 76.9, 73.6, 71.1, 64.3, 27.3, 27.1, 26.9, 19.3; HRMS (ESI) Calcd for C<sub>30</sub>H<sub>38</sub>O<sub>4</sub>SiNa<sup>+</sup> [M+Na]<sup>+</sup>: 513.2437, Found: 513.2439.

**[(2S,3S)-4-(benzyloxy)-2,3-dihydroxybutoxy](tert-butyl)diphenylsilane (9):** Using the general procedure (I), starting from compound **8** (550 mg, 1.12 mmol) compound **9** (429 mg, 85%) was isolated as colorless oil.  $[\alpha]^{20}_D = -26.7$  (c 0.2, CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta_{\text{ppm}}$  7.60-7.55 (m, 5H), 7.35-7.14 (m, 10H), 4.41 (dd, 2H, J = 11.6 Hz, J = 11.2 Hz), 3.77-3.72 (m, 3H), 3.66-3.56 (m, 2H), 3.45-3.42 (m, 1H), 2.62 (br s, 2H), 0.97 (s, 9H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta_{\text{ppm}}$  138.1, 135.8, 135.7, 135.0, 133.2, 130.1, 129.9, 128.6, 128.5, 128.1, 128.0, 127.8, 79.7, 72.8, 72.7, 71.9, 63.9, 26.9, 19.4, 19.3; HRMS (ESI) Calcd for C<sub>27</sub>H<sub>35</sub>O<sub>4</sub>Si [M+H]<sup>+</sup>: 451.2305, Found: 451.2302.

**(2S,3S)-4-(benzyloxy)-1-[(tert-butyldiphenylsilyl)oxy]-3-(hexadecanoyloxy)butan-2-yl hexadecanoate (10a):** Using the general procedure (II), starting from compound **9** (200 mg, 0.44 mmol) compound **10a** (354 mg, 86%) was isolated as colorless oil.  $[\alpha]^{20}_D = -13.8$  (c 0.1, CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta_{\text{ppm}}$  7.67-7.63 (m, 5H), 7.43-7.25 (m, 10H), 5.40-5.36 (m, 1H), 5.21-5.17 (m, 1H), 4.58 (dd, 2H, J = 12.0 Hz, J = 12.0 Hz), 4.35-4.26 (m, 1H), 4.20-4.11 (m, 1H), 3.82-3.66 (m, 2H), 2.28-2.19 (m, 4H), 1.57-1.55 (m, 4H), 1.25 (br s, 48H), 1.05 (s, 9H), 0.88 (t, 6H, J = 6.8 Hz); <sup>13</sup>C NMR (100 MHz,

$\text{CDCl}_3$ ):  $\delta_{\text{ppm}}$  173.3, 173.1, 138.1, 135.8, 135.7, 135.6, 133.3, 133.1, 129.9, 128.4, 128.0, 127.9, 127.8, 78.0, 75.5, 73.2, 70.5, 62.7, 34.3, 34.2, 32.1, 29.8, 29.6, 29.5, 29.4, 29.3, 26.9, 25.1, 24.9, 22.8, 19.3, 19.2, 14.2; HRMS (ESI) Calcd for  $\text{C}_{59}\text{H}_{94}\text{O}_6\text{Si Na}^+ [\text{M}+\text{Na}]^+$ : 949.6717, Found: 949.6719.

**(2S,3S)-4-(benzyloxy)-1-[(tert-butyldiphenylsilyl)oxy]-3-[(9Z)-octadec-9-enoyloxy]butan-2-yl (9Z)-octadec-9-enoate (10b):** Using the general procedure (II), starting from compound **9** (200 mg, 0.44 mmol) compound **10b** (373 mg, 80%) was isolated as colorless oil.  $[\alpha]^{20}_D = -10.8$  (c 0.1,  $\text{CH}_2\text{Cl}_2$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{ppm}}$  7.63-7.60 (m, 3H), 7.43-7.25 (m, 12H), 5.44-5.41 (m, 1H), 5.37-5.33 (m, 4H), 5.31-5.27 (m, 1H), 4.46 (dd, 2H,  $J = 17.8$  Hz), 3.73 (d, 2H,  $J = 4.8$  Hz), 3.58 (d, 2H,  $J = 4.8$  Hz), 2.29-2.21 (m, 4H), 2.01-1.99 (m, 8H), 1.62-1.56 (m, 4H), 1.27 (br s, 40H), 1.02 (s, 9H), 0.88 (t, 6H,  $J = 6.8$  Hz);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{ppm}}$  173.1, 173.0, 137.9, 135.8, 135.7, 133.2, 133.1, 130.2, 130.0, 129.9, 128.5, 127.9, 73.4, 72.3, 70.5, 68.5, 62.4, 34.5, 32.1, 30.0, 29.9, 29.7, 29.5, 29.4, 29.3, 27.4, 27.3, 26.9, 25.1, 25.0, 22.9, 19.3, 14.3; HRMS (ESI) Calcd for  $\text{C}_{63}\text{H}_{98}\text{O}_6\text{Si} [\text{M}+\text{H}]^+$ : 979.7211, Found: 979.7212.

**(2S,3S)-4-(benzyloxy)-3-(hexadecanoyloxy)-1-hydroxybutan-2-yl hexadecanoate (11a):** Using the general procedure<sup>1,2</sup>, starting from compound **10a** (300 mg, 0.32 mmol) compound **11a** (216 mg, 98%) was isolated as a white solid. m.p: 50-51 °C;  $[\alpha]^{20}_D = -18.0$  (c 0.2,  $\text{CH}_2\text{Cl}_2$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{ppm}}$  7.26-7.19 (m, 5H), 4.57 (dd, 2H,  $J = 11.6$  Hz,  $J = 11.6$  Hz), 4.29-4.25 (m, 1H), 4.19-4.15 (m, 1H), 4.11-4.04 (m, 2H), 3.82-3.80 (m, 1H), 3.60-3.56 (m, 1H), 2.64 (br s, 1H), 1.24-2.16 (m, 4H), 1.53-1.50 (m, 4H), 1.18 (br s, 48H), 0.80 (t, 6H,  $J = 6.6$  Hz);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{ppm}}$  173.8, 173.6, 137.6, 128.6, 128.2, 76.4, 73.1, 69.6, 64.9, 62.7, 34.3, 34.2, 32.1, 29.8, 29.6, 29.5, 29.4, 29.3, 25.0, 22.8, 14.2; HRMS (ESI) Calcd for  $\text{C}_{43}\text{H}_{77}\text{O}_6 [\text{M}+\text{H}]^+$ : 689.5720, Found: 689.5717.

**(2S,3S)-4-(benzyloxy)-1-hydroxy-3-[(9Z)-octadec-9-enoyloxy]butan-2-yl (9Z)-octadec-9-enoate (11b):** Using the general procedure (II), starting from compound (300 mg, 0.31 mmol) compound **11b** (225 mg, 98%) was isolated as a yellow oil.  $[\alpha]^{20}_D = -16.0$  (c 0.2,  $\text{CH}_2\text{Cl}_2$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{ppm}}$  7.41-7.26 (m, 5H), 5.39-5.30 (m, 4H), 5.24-5.20 (m, 1H), 5.10-5.08 (m, 1H), 4.52 (s, 2H), 4.40-4.36 (m, 1H), 4.19-4.10 (m, 1H), 3.98-3.94 (m, 1H), 3.74-3.66 (m, 1H), 3.56-3.47 (m, 1H), 2.37-2.26 (m, 4H), 2.00 (m, 8H), 1.62-1.60 (m, 4H), 1.30 (br s, 40H), 0.88 (t, 6H,  $J = 6.8$  Hz);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{ppm}}$  173.5, 173.3, 137.6, 134.9, 130.0, 129.7, 129.5, 128.5, 127.9, 127.7, 127.6, 73.6, 71.4, 70.9, 69.4, 64.8, 34.3, 34.1, 32.0, 29.8, 29.7, 29.6, 29.4, 29.3, 29.2, 27.3, 27.2, 26.6, 25.0, 24.9, 22.8, 14.2; HRMS (ESI) Calcd for  $\text{C}_{47}\text{H}_{81}\text{O}_6 [\text{M}+\text{H}]^+$ : 741.6033, Found: 741.6032.

**2S,3S)-1-({[(2S)-2-amino-3-(benzyloxy)-3-oxopropoxy](benzyloxy)phosphoryl}oxy)-4-(benzyloxy)-3-(hexadecanoyloxy)butan-2-yl hexadecanoate (12a):** Using the general procedure (V), starting from O-benzyl N,N,N',N'-tetraisopropyl phosphorodiamidite (109 mg 0.33 mmol), benzyl (S)-1-((benzyloxy)carbonyl)-2-hydroxyethylcarbamate (100 mg, 0.30 mmol) and compound **11a** (210 mg, 0.30 mmol) compound **12a** (291 mg, 83%) isolated as a white solid. m.p: 70-71 °C;  $[\alpha]^{20}_D = -17.6$  (c 0.1,  $\text{EtOH}$ );  $^1\text{H}$  NMR (400

MHz, CDCl<sub>3</sub>):  $\delta_{\text{ppm}}$  7.32-7.25 (m, 20H), 5.90 (d, 1H, J = 7.6 Hz), 5.35-5.32 (m, 1H), 5.26-5.23 (m, 1H), 5.18 (s, 2H), 5.09 (s, 2H), 5.00-4.97 (m, 2H), 4.48-4.44 (m, 3H), 4.18-4.14 (m, 1H), 4.08-4.04 (m, 1H), 3.93 (dd, 2H, J = 11.2 Hz, J = 10.8 Hz), 3.55-3.48 (m, 2H), 2.32-2.19 (m, 4H), 1.60-1.51 (m, 4H), 1.25 (br s, 48 H), 0.88 (t, 6H, J = 6.8 Hz); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta_{\text{ppm}}$  172.9, 172.8, 170.6, 156.5, 137.5, 136.2, 135.5, 135.4, 135.3, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.8, 127.7, 73.3, 69.9, 69.7, 69.6, 67.9, 67.2, 67.0, 65.7, 62.8, 56.4, 34.2, 34.0, 31.9, 29.7, 29.5, 29.4, 29.3, 29.1, 24.9, 24.8, 22.7, 14.1; <sup>31</sup>P NMR (161.9 MHz, CDCl<sub>3</sub>):  $\delta_{\text{ppm}}$  0.14; HRMS (ESI) Calcd for C<sub>68</sub>H<sub>101</sub>NO<sub>13</sub>P [M+H]<sup>+</sup>: 1170.7011, Found: 1170.7010.

**(2S,3S)-1-(benzyloxy)-4-{{(benzyloxy)[(2S)-3-(benzyloxy)-2-[(benzyloxy)carbonyl]amino}-3-oxopropoxy]phosphoryl}oxy}-3-[(9Z)-octadec-9-enyloxy]butan-2-yl (9Z)-octadec-9-enoate (12b):** Using the general procedure (V), starting from compound **11b** (150 mg, 0.2 mmol) compound **12b** (202 mg, 83%) was isolated as a yellow oil.  $[\alpha]^{20}_{\text{D}} = -19.2$  (c 0.1, EtOH); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta_{\text{ppm}}$  7.41-7.25 (m, 20H), 5.76 (d, 1H, J = 8.0 Hz), 5.42-5.30 (m, 4H), 5.21 (s, 2H), 5.12 (s, 4H), 4.58-4.50 (m, 2H), 4.40-4.35 (m, 1H), 4.19-4.12 (m, 2H), 4.02-3.92 (m, 3H), 3.74-3.67 (m, 1H), 3.56-3.48 (m, 2H), 2.37-2.26 (m, 4H), 2.06-2.00 (m, 8H), 1.65-1.60 (m, 4H), 1.27 (br s, 40H), 0.88 (t, 6H, J = 6.8 Hz); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta_{\text{ppm}}$  173.5, 173.4, 170.6, 156.4, 137.6, 136.2, 135.5, 135.3, 135.0, 130.2, 130.0, 129.8, 128.8, 128.7, 128.6, 128.4, 128.3, 128.1, 128.0, 127.9, 73.7, 71.5, 71.3, 69.6, 69.1, 67.6, 67.4, 65.0, 63.4, 56.4, 34.4, 34.3, 32.1, 30.0, 29.9, 29.7, 29.5, 29.4, 29.3, 27.4, 27.3, 26.7, 25.1, 25.0, 22.9, 14.3; <sup>31</sup>P NMR (161.9 MHz, CDCl<sub>3</sub>):  $\delta_{\text{ppm}}$  2.23; HRMS (ESI) Calcd for C<sub>72</sub>H<sub>105</sub>NO<sub>13</sub>P [M+H]<sup>+</sup>: 1222.7318, Found: 1222.7319.

**(2S)-2-amino-3-{{(2S,3S)-2,3-bis(hexadecanoyloxy)-4-hydroxybutoxy}(hydroxy)phosphoryl}oxy}propanoic acid (DAT-PS<sub>16</sub>):** Using the general procedure (III), starting from compound **12a** (200 mg, 0.17 mmol) compound DAT-PS<sub>16</sub> (117 mg, 90%) was isolated as a white solid.m.p.: 140-141 °C;  $[\alpha]^{20}_{\text{D}} = -23.2$  (c 0.2, EtOH); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub> + DMSO-d<sub>6</sub>):  $\delta_{\text{ppm}}$  5.67 (d, 1H, J = 8.0 Hz), 4.88-4.84 (m, 1H), 4.02-3.92 (m, 2H), 3.86-3.81 (m, 1H), 3.77-3.72 (m, 1H), 3.66 (dd, 2H, J = 10.0 Hz, J = 10.0 Hz), 3.52-3.46 (m, 1H), 2.05 (t, 2H, J = 7.4 Hz), 1.99 (t, 2H, J = 7.4 Hz), 1.35-1.27 (m, 4H), 0.96 (br s, 48H), 0.58 (t, 6H, J = 6.8 Hz); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub> + DMSO-d<sub>6</sub>):  $\delta_{\text{ppm}}$  173.2, 173.0, 79.3, 74.1, 70.3, 65.3, 62.7, 62.5, 55.8, 34.1, 33.9, 31.7, 29.5, 29.3, 29.2, 29.1, 28.9, 28.8, 28.2, 26.0, 25.1, 24.8, 24.6, 22.5, 14.0; <sup>31</sup>P NMR (161.9 MHz, CDCl<sub>3</sub>):  $\delta_{\text{ppm}}$  0.60; HRMS (ESI) Calcd for C<sub>39</sub>H<sub>77</sub>NO<sub>11</sub>P [M+H]<sup>+</sup>: 766.5234, Found: 766.5234.

**(2S)-2-amino-3-{{hydroxy[(2S,3S)-4-hydroxy-2,3-bis[(9Z)-octadec-9-enyloxy]butoxy]phosphoryl}oxy}propanoic acid (DAT-PS<sub>18</sub>):** Using the general procedure (III), starting from compound **12b** (150 mg, 0.12 mmol) compound DAT-PS<sub>18</sub> (88 mg, 90%) was isolated as a yellow oil.  $[\alpha]^{20}_{\text{D}} = -17.8$  (c 0.1, EtOH); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta_{\text{ppm}}$  5.66 (d, 1H, J = 8.0 Hz), 4.95-4.87 (m, 4H), 3.79-3.73 (m, 2H), 3.62-3.58 (m, 2H), 3.51-3.48 (m, 1H), 3.38-3.31 (m, 2H), 3.19-3.12 (m, 2H), 1.85-1.81 (m, 4H), 1.61-1.59 (m, 8H), 1.73-1.14 (m, 4H), 1.02 (m, 40H), 0.47 (t, 6H, J = 6.6 Hz); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub> + DMSO-d<sub>6</sub>):  $\delta_{\text{ppm}}$  175.1, 172.1, 129.1, 128.9, 78.5, 75.7, 65.6, 62.1, 61.8, 55.2, 33.4, 31.1, 28.9, 28.7, 28.5, 28.4, 28.3, 27.6, 26.3, 26.0, 24.6, 24.1, 21.9, 13.4; <sup>31</sup>P NMR

(161.9 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{ppm}}$  0.69; HRMS (ESI) Calcd for  $\text{C}_{43}\text{H}_{80}\text{NO}_{11}\text{P}$   $[\text{M}+\text{Na}]^+$ : 840.5367, Found: 841.0718.

**(2S,3S)-4-(benzyloxy)-1-{[(benzyloxy)([(4S)-2-phenyl-1,3-dioxolan-4-yl]methoxy]phosphoryl]oxy}-3-(hexadecanoyloxy)butan-2-yl hexadecanoate (13a):** Using the general procedure (II), starting from compound **11a** (150 mg, 0.22 mmol) compound **13a** (186 mg, 83%) was isolated as a white solid. m.p: 126-127  $^{\circ}\text{C}$ ;  $[\alpha]^{20}_{\text{D}} = -25.7$  (c 0.1,  $\text{CH}_2\text{Cl}_2$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{ppm}}$  7.59-7.57 (m, 5H), 7.44-7.27 (m, 10H), 6.15 (s, 1H), 5.00-4.95 (m, 2H), 4.89-4.83 (m, 2H), 4.66 (s, 2H), 4.60-4.55 (m, 1H), 4.35-4.23 (m, 5H), 4.18-4.15 (m, 1H), 3.93-3.89 (m, 1H), 3.69-3.65 (m, 1H), 2.33 (t, 4H,  $J = 7.4$  Hz), 1.64-1.59 (m, 4H), 1.26 (br s, 48H), 0.88 (t, 6H,  $J = 6.6$  Hz);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{ppm}}$  173.8, 173.6, 140.9, 137.5, 135.5, 129.8, 128.4, 128.3, 128.2, 128.1, 127.9, 127.3, 127.2, 126.9, 107.5, 76.2, 72.9, 72.3, 70.5, 69.3, 67.5, 67.3, 64.7, 62.1, 34.1, 31.8, 29.6, 29.4, 29.3, 29.2, 29.1, 26.3, 24.8, 23.8, 23.7, 22.6, 14.0, 13.9;  $^{31}\text{P}$  NMR (161.9 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{ppm}}$  1.75, 1.28; HRMS (ESI) Calcd for  $\text{C}_{60}\text{H}_{94}\text{O}_{11}\text{P}$   $[\text{M}+\text{H}]^+$ : 1021.6534, Found: 1021.6536.

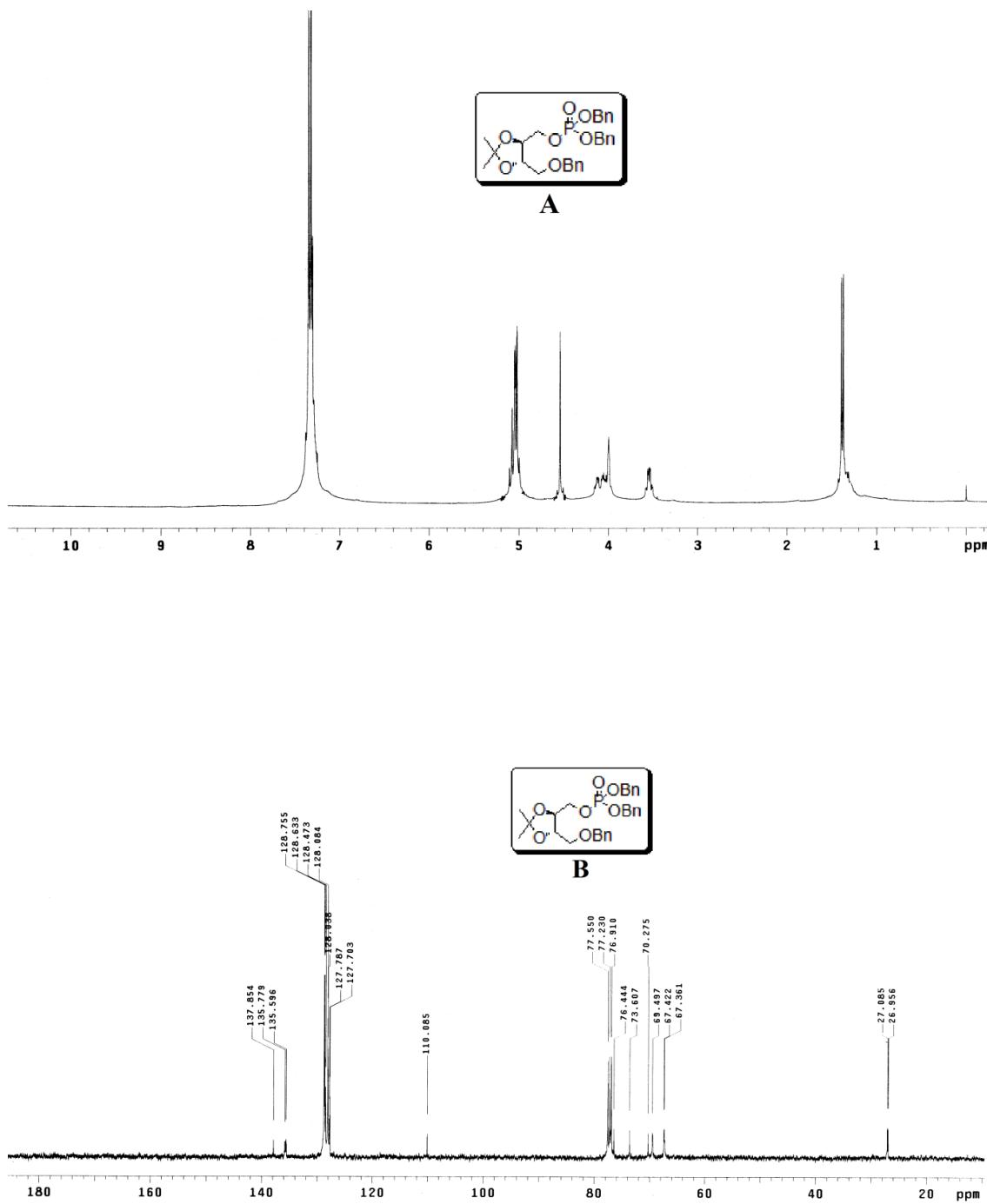
**(2S,3S)-4-(benzyloxy)-1-{[(benzyloxy)([(4S)-2-phenyl-1,3-dioxolan-4-yl]methoxy]phosphoryl]oxy}-3-[(9Z)-octadec-9-enoyloxy]butan-2-yl (9Z)-octadec-9-enoate (13b):** Using the general procedure (II), starting from compound **11b** (150 mg, 0.20 mmol) compound **13b** (178 mg, 83%) was isolated as a yellow oil.  $[\alpha]^{20}_{\text{D}} = -13.2$  (c 0.1,  $\text{CH}_2\text{Cl}_2$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{ppm}}$  7.40-7.26 (m, 15H), 6.16 (s, 1H), 5.40-5.30 (m, 4H), 5.24-5.20 (m, 1H), 5.10-5.08 (m, 1H), 4.98-4.83 (m, 1H), 4.52 (s, 2H), 4.40-4.25 (m, 3H), 4.20-4.12 (m, 3H), 3.98-3.95 (m, 1H), 3.74-3.66 (m, 1H), 3.56-3.46 (m, 2H), 2.37-2.26 (m, 4H), 2.00 (m, 8H), 1.61-1.59 (m, 4H), 1.27 (br s, 40H), 0.88 (t, 6H,  $J = 6.8$  Hz);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{ppm}}$  173.8, 173.5, 137.5, 135.6, 135.3, 130.1, 129.9, 129.8, 129.7, 129.1, 128.6, 128.5, 128.4, 128.0, 127.8, 127.7, 127.3, 106.8, 77.7, 77.6, 73.6, 71.4, 71.3, 70.8, 69.4, 64.8, 62.2, 34.3, 34.2, 32.0, 29.8, 29.6, 29.4, 29.3, 29.2, 27.3, 27.2, 26.6, 25.0, 24.9, 22.8, 14.2;  $^{31}\text{P}$  NMR (161.9 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{ppm}}$  2.14, 1.68; HRMS (ESI) Calcd for  $\text{C}_{64}\text{H}_{98}\text{O}_{11}\text{P}$   $[\text{M}+\text{H}]^+$ : 1073.6847, Found: 1073.6850.

**[(2S,3S)-2,3-bis(hexadecanoyloxy)-4-hydroxybutoxy][(2S)-2,3-dihydroxypropoxy]phosphinic acid (DAT-PG<sub>16</sub>):** Using the general procedure (III), starting from compound **13a** (150 mg, 0.15 mmol) compound DAT-PG<sub>16</sub> (102 mg, 90%) was isolated as a white solid. m.p: 80-81  $^{\circ}\text{C}$ ;  $[\alpha]^{20}_{\text{D}} = -25.7$  (c 0.1, EtOH);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{ppm}}$  7.16 (br s, 1H), 5.19-5.18 (m, 1H), 4.44-4.40 (m, 1H), 4.33-4.24 (m, 2H), 4.20-4.12 (m, 2H), 4.05-4.01 (m, 1H), 3.92-3.86 (m, 1H), 3.80-3.78 (m, 1H), 3.72-3.65 (m, 1H), 3.48-3.46 (m, 1H), 2.42-2.27 (m, 4H), 1.97-1.92 (m, 2H), 1.73-1.60 (m, 2H), 1.25 (br s, 48H), 0.88 (t, 6H,  $J = 6.6$  Hz);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{ppm}}$  173.7, 173.6, 74.5, 70.9, 70.7, 68.9, 65.6, 64.8, 62.9, 34.4, 34.3, 32.9, 31.0, 29.9, 29.6, 29.5, 29.4, 29.3, 26.5, 26.3, 25.8, 25.7, 25.5, 25.1, 25.0, 24.9, 22.9, 14.3;  $^{31}\text{P}$  NMR (161.9 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{ppm}}$  5.69, -0.22; HRMS (ESI) Calcd for  $\text{C}_{39}\text{H}_{78}\text{O}_{11}\text{P}$   $[\text{M}+\text{H}]^+$ : 753.5280, Found: 753.5281.

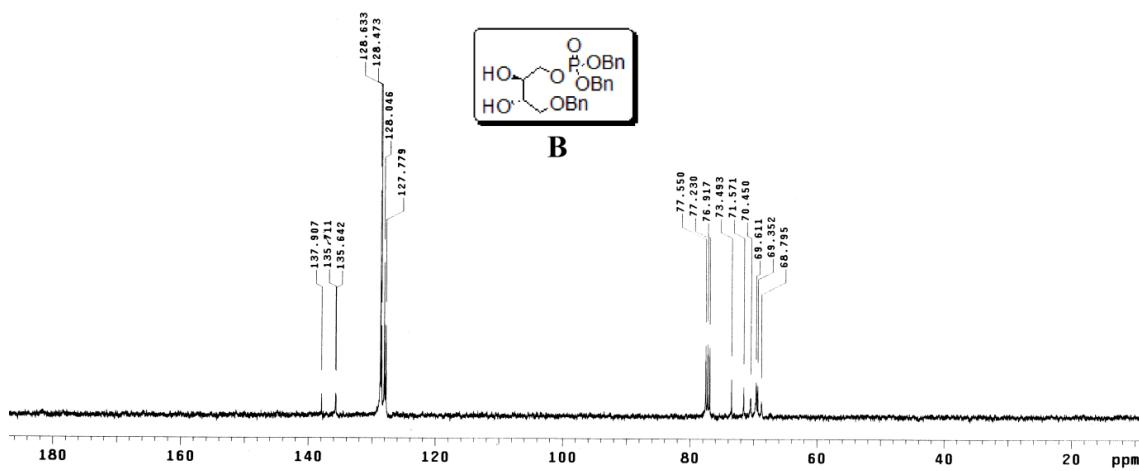
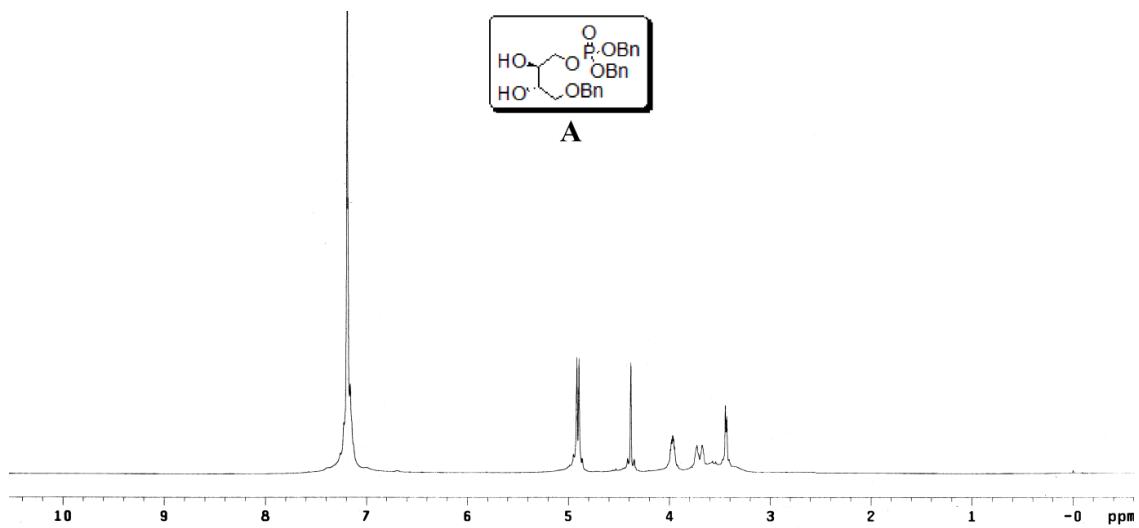
**[(2S)-2,3-dihydroxypropoxy][(2S,3S)-4-hydroxy-2,3-bis[(9Z)-octadec-9-enoyloxy]butoxy]phosphinic acid (DAT-PG<sub>18</sub>):** Using the general procedure (III), starting from

compound **13b** (140 mg, 0.13 mmol) compound DAT-PG<sub>18</sub> (94 mg, 90%) was isolated as a yellow oil.  $[\alpha]^{20}_D = -19.2$  (c 0.1, EtOH); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta_{\text{ppm}}$  7.27 (br s, 1H), 5.31-5.29 (m, 4H), 4.55-4.51 (m, 1H), 4.45-4.36 (m, 2H), 4.31-4.24 (m, 2H), 4.21-4.13 (m, 1H), 4.04-3.98 (m, 1H), 3.91-3.89 (m, 1H), 3.84-3.76 (m, 1H), 3.60-3.57 (m, 2H), 2.54-2.39 (m, 4H), 2.09-2.04 (m, 8H), 1.95-1.72 (m, 4H), 1.37 (br s, 40H), 0.99 (t, 6H,  $J = 6.8$  Hz); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta_{\text{ppm}}$  173.7, 173.6, 128.5, 126.8, 74.5, 70.7, 68.9, 65.6, 64.8, 62.9, 62.4, 34.2, 34.0, 32.9, 32.1, 31.0, 29.9, 29.6, 29.5, 29.4, 29.3, 26.5, 25.8, 25.7, 25.5, 25.4, 25.1, 25.0, 24.9, 22.9, 14.3; <sup>31</sup>P NMR (161.9 MHz, CDCl<sub>3</sub>):  $\delta_{\text{ppm}}$  0.81, -1.28; HRMS (ESI) Calcd for C<sub>43</sub>H<sub>82</sub>O<sub>11</sub>P [M+H]<sup>+</sup>: 805.5595, Found: 805.5594.

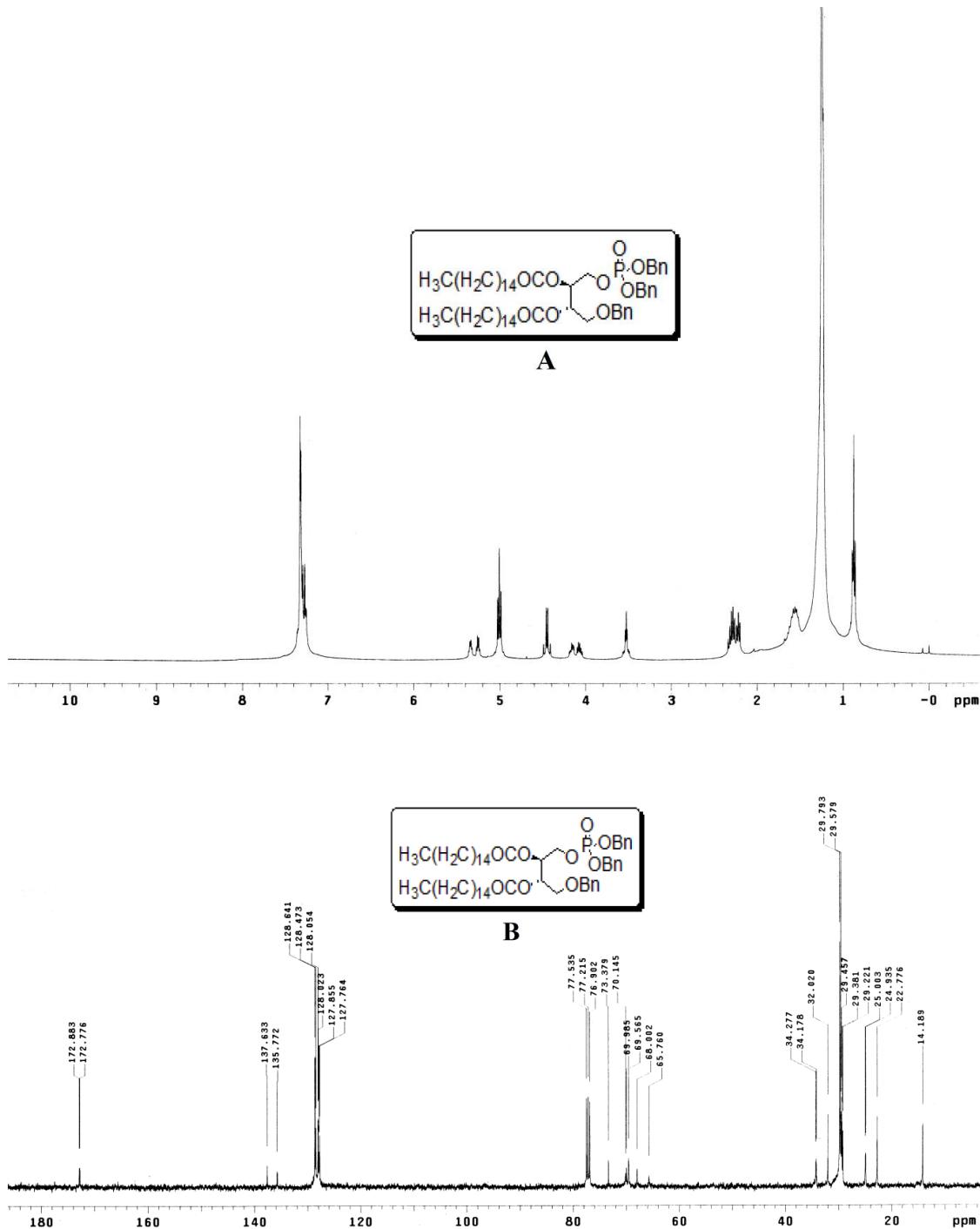
## (II) $^1\text{H}$ NMR and $^{13}\text{C}$ NMR Spectra of the New Compounds



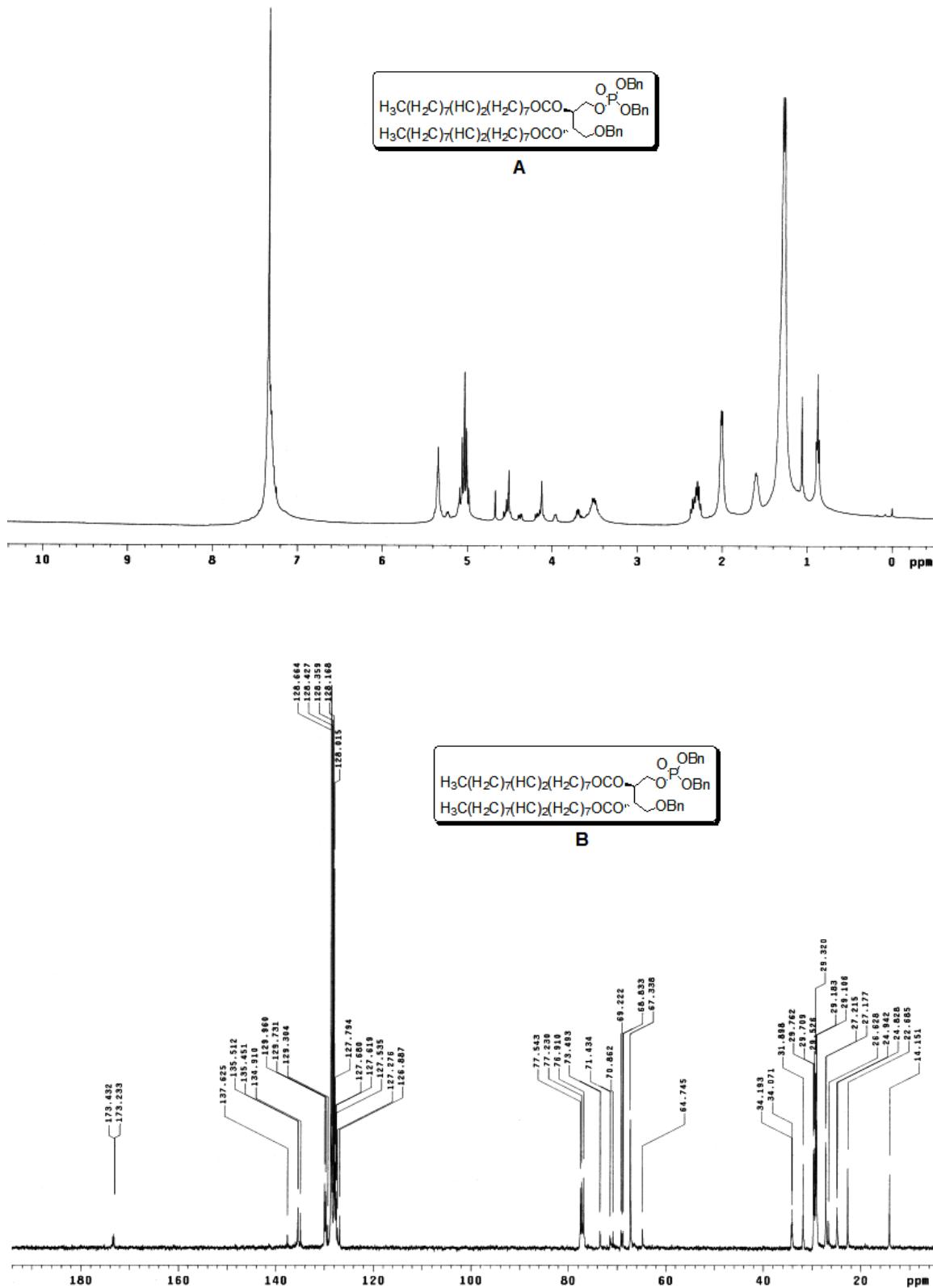
**Figure S1.**  $^1\text{H}$  NMR (A) and  $^{13}\text{C}$  NMR (B) spectra of compound 5.



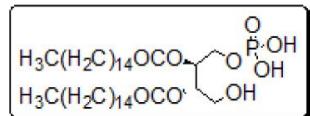
**Figure S2.**  $^1\text{H}$  NMR (A) and  $^{13}\text{C}$  NMR (B) spectra of compound 6.



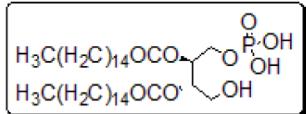
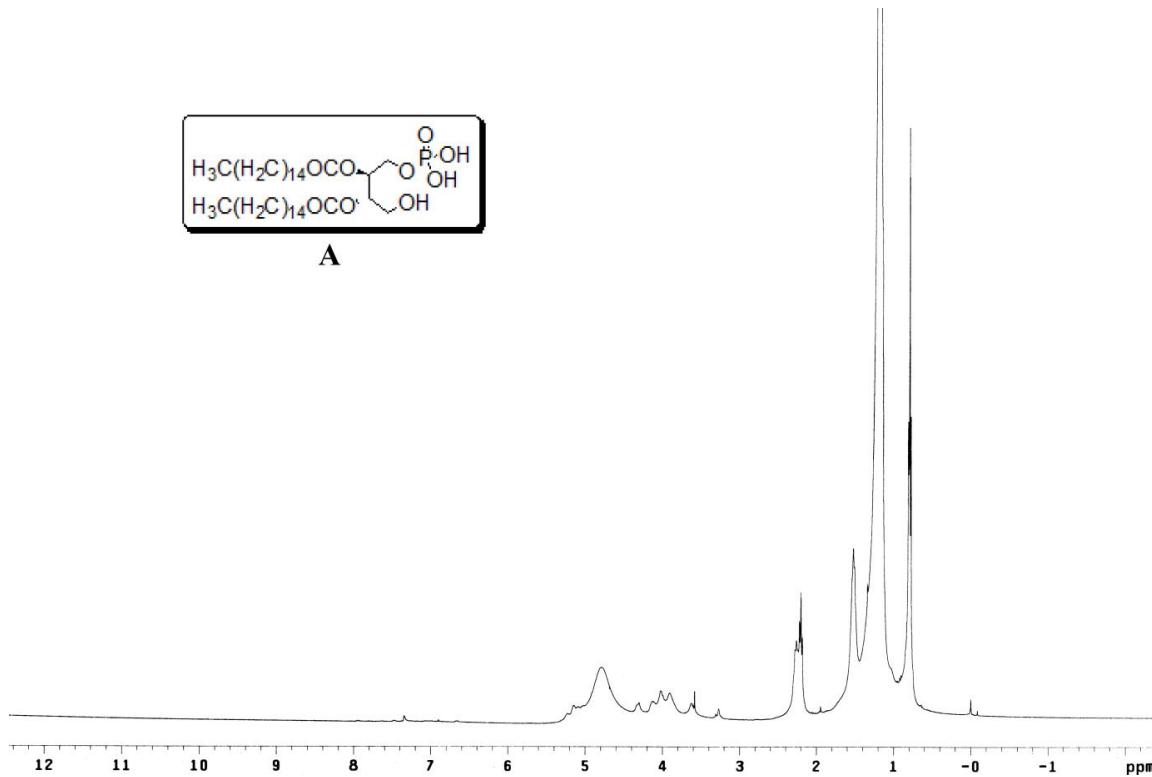
**Figure S3.**  $^1\text{H}$  NMR (A) and  $^{13}\text{C}$  NMR (B) spectra of compound **7a**.



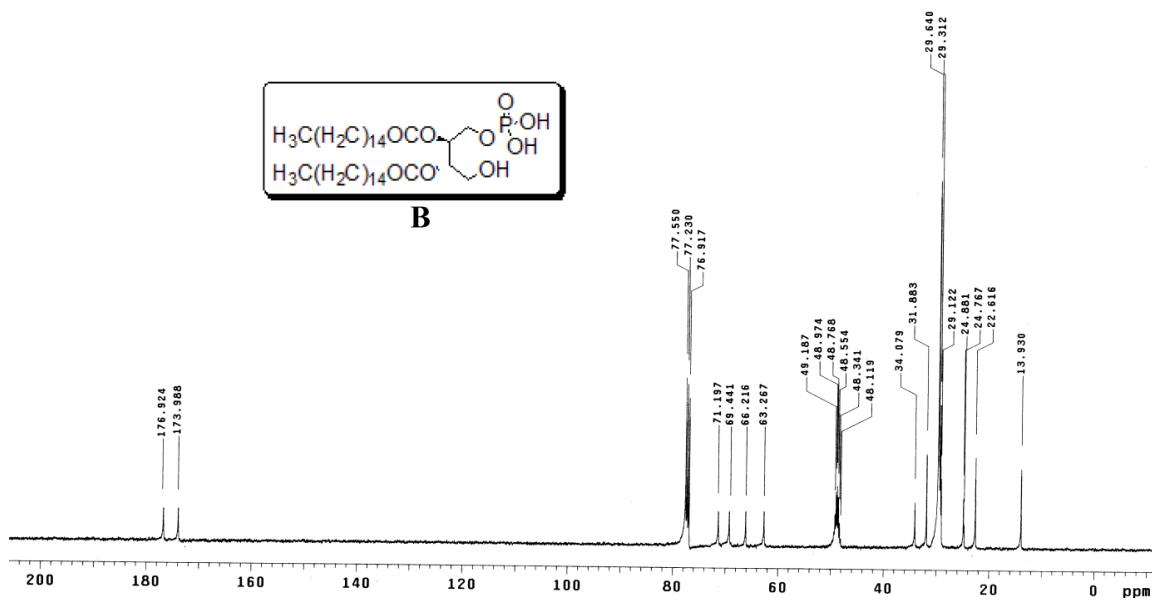
**Figure S4.**  $^1\text{H}$  NMR (A) and  $^{13}\text{C}$  NMR (B) spectra of compound **7b**.



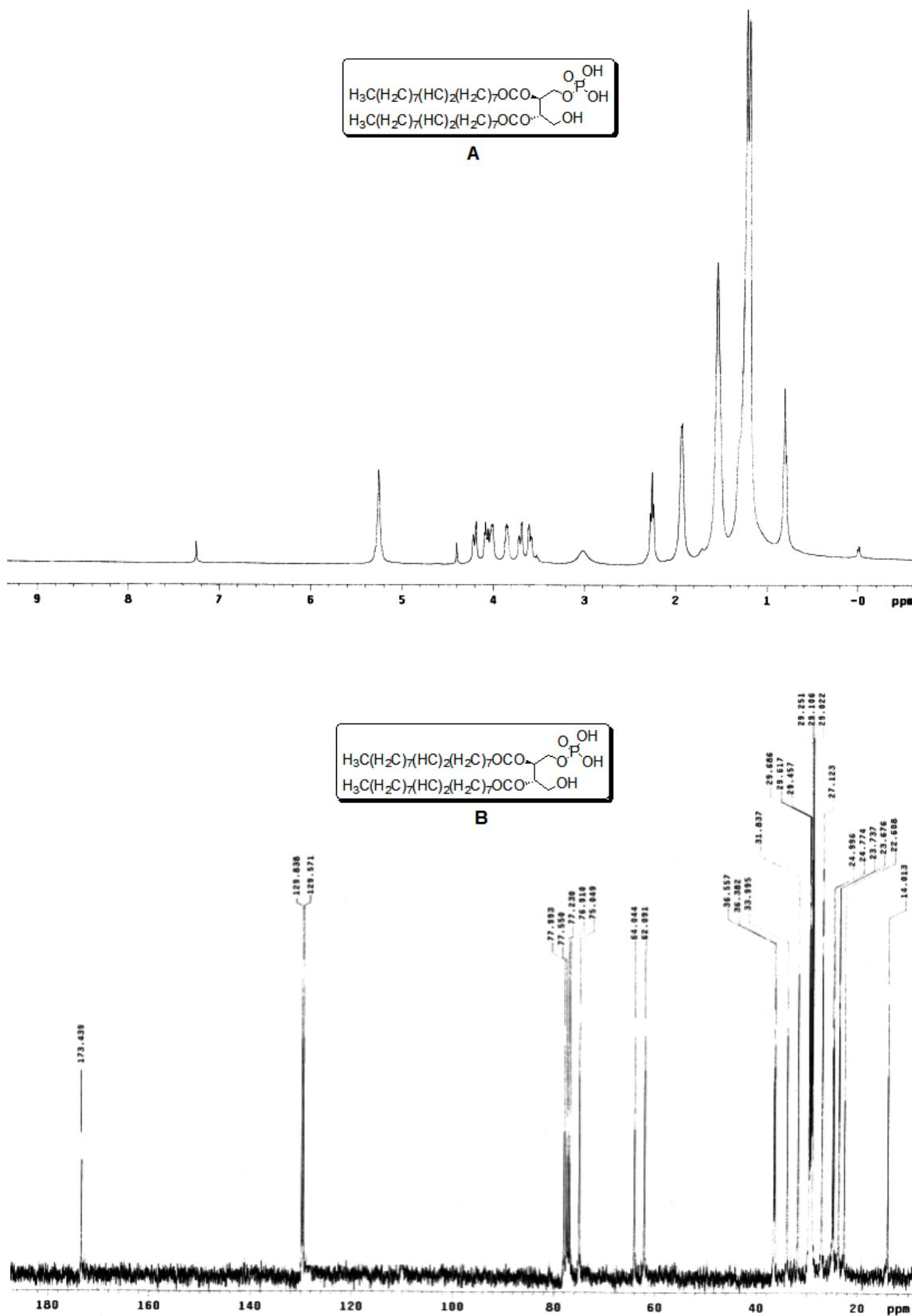
A



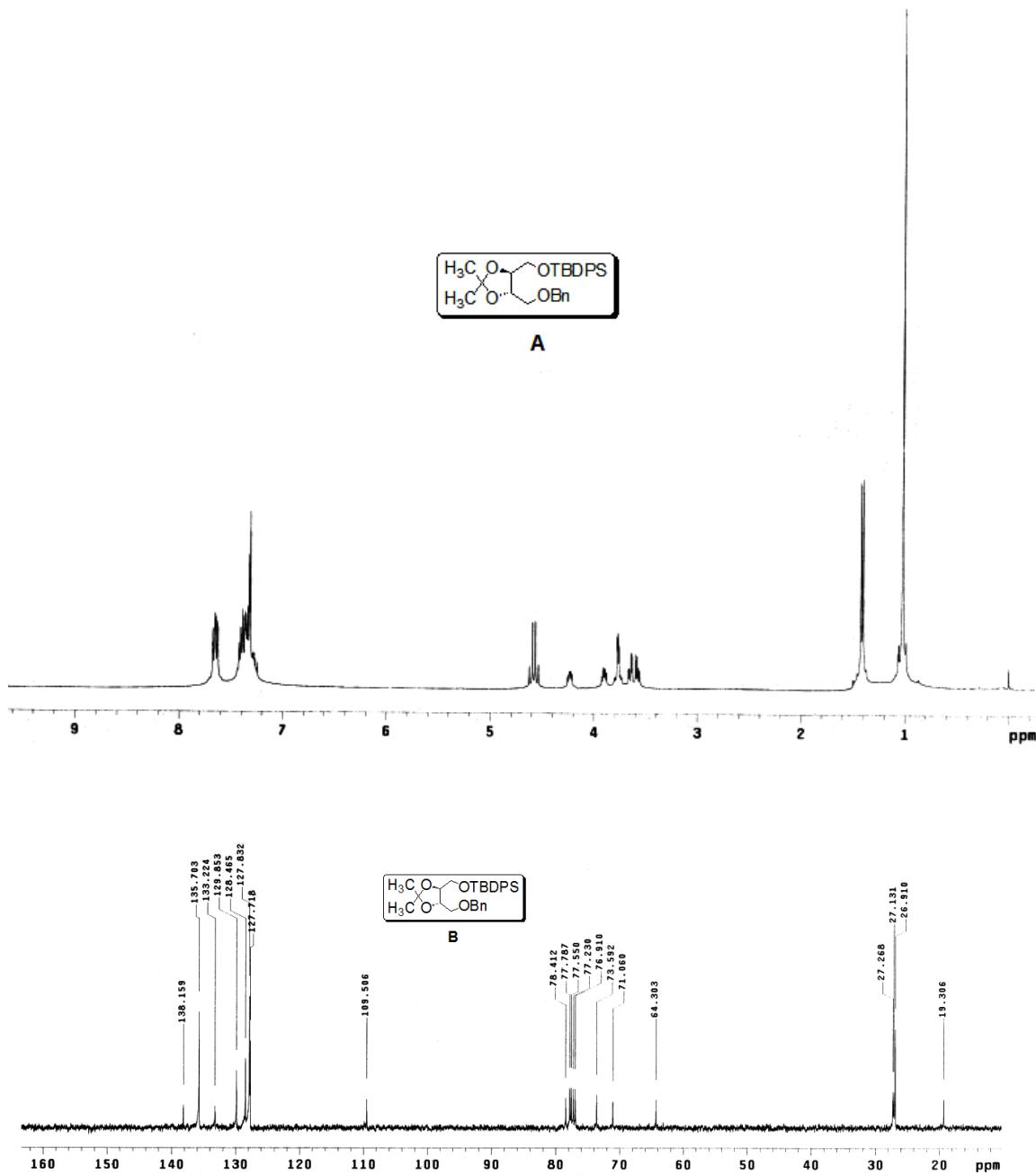
B



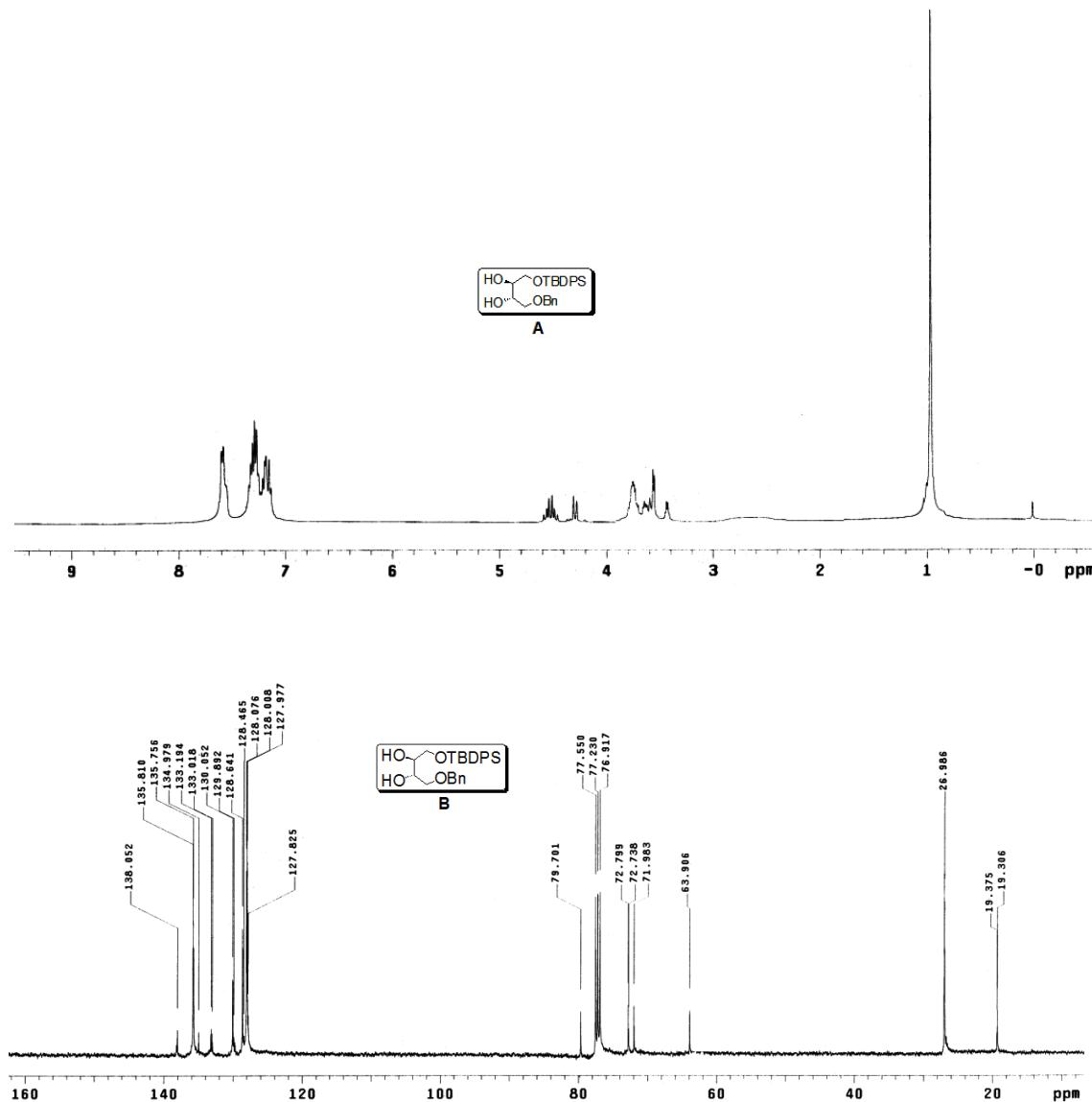
**Figure S5.** <sup>1</sup>H NMR (A) and <sup>13</sup>C NMR (B) spectra of DAT-PA<sub>16</sub>.



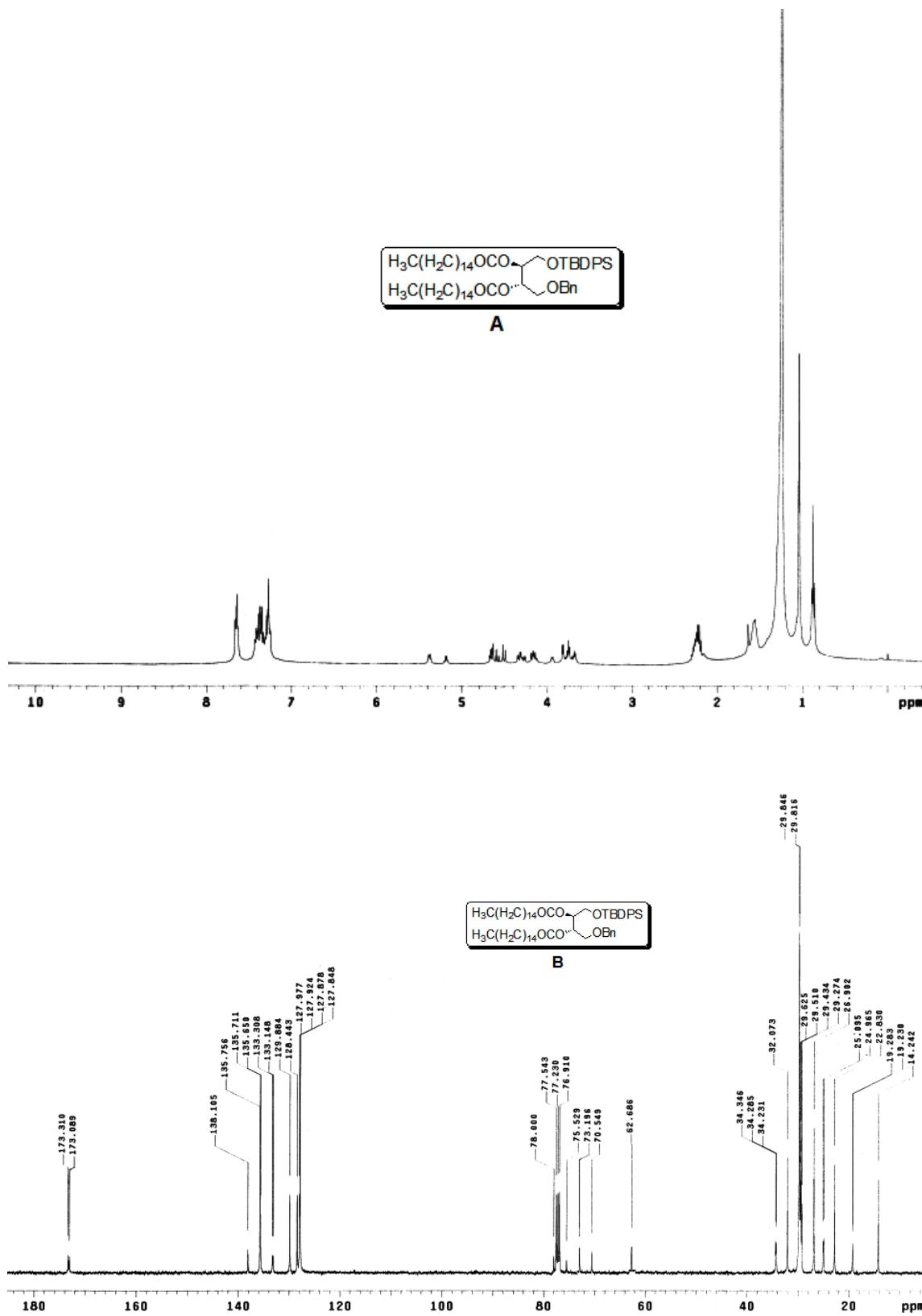
**Figure S6.**  $^1\text{H}$  NMR (A) and  $^{13}\text{C}$  NMR (B) spectra of DAT-PA<sub>18</sub>.



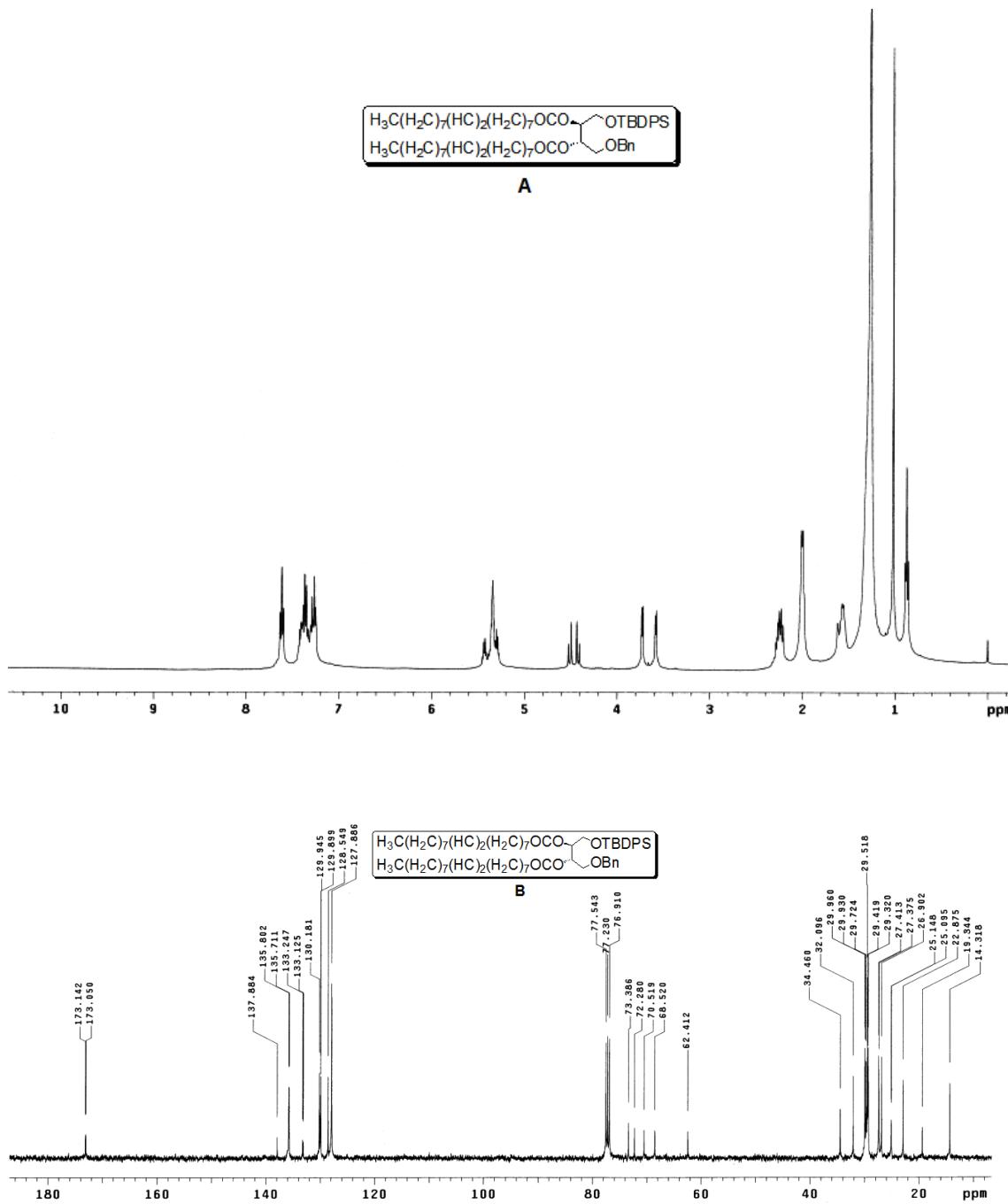
**Figure S7.**  $^1\text{H}$  NMR (A) and  $^{13}\text{C}$  NMR (B) spectra of compound 8.



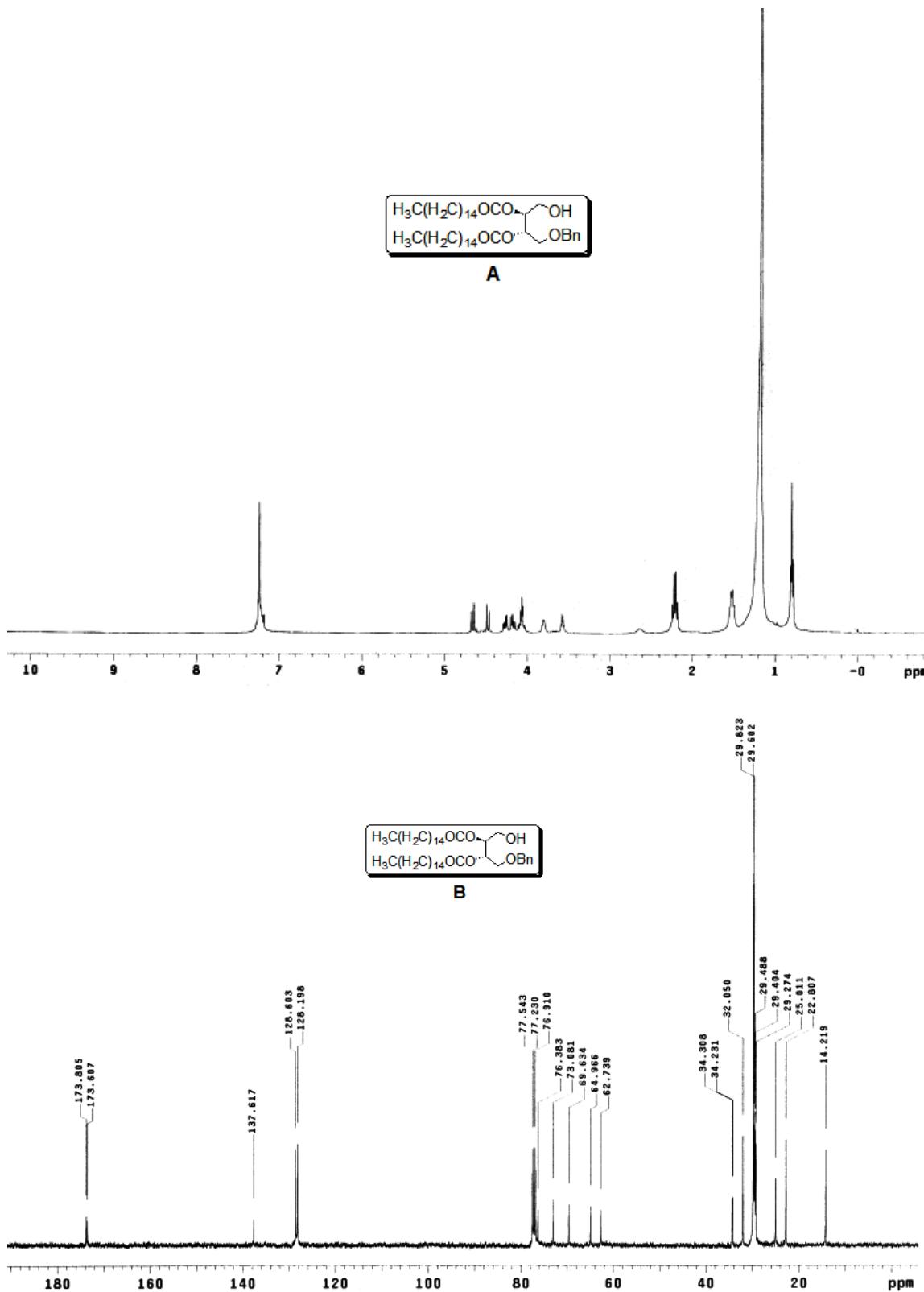
**Figure S8.**  $^1\text{H}$  NMR (A) and  $^{13}\text{C}$  NMR (B) spectra of compound 9.



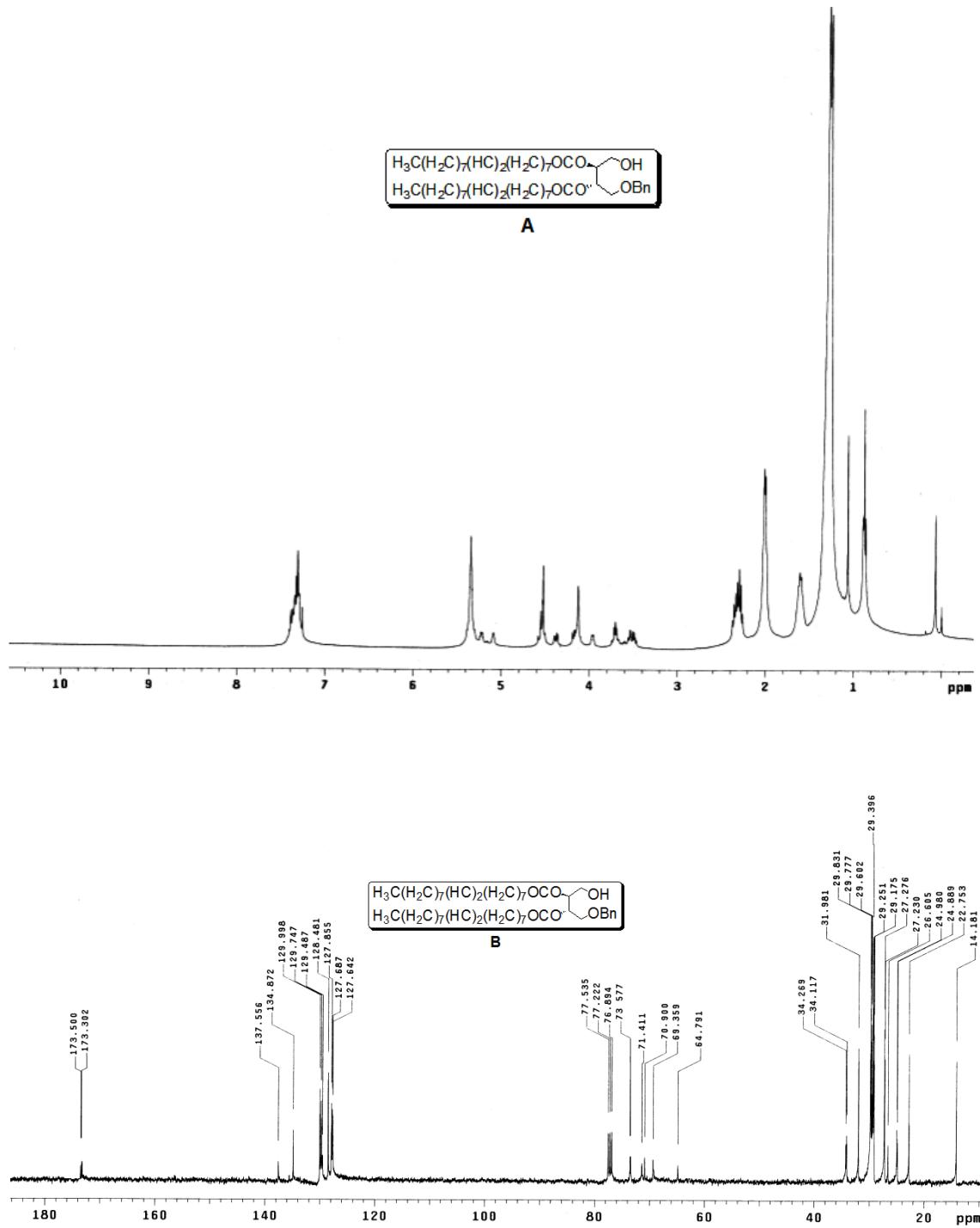
**Figure S9.**  $^1\text{H}$  NMR (A) and  $^{13}\text{C}$  NMR (B) spectra of compound **10a**.



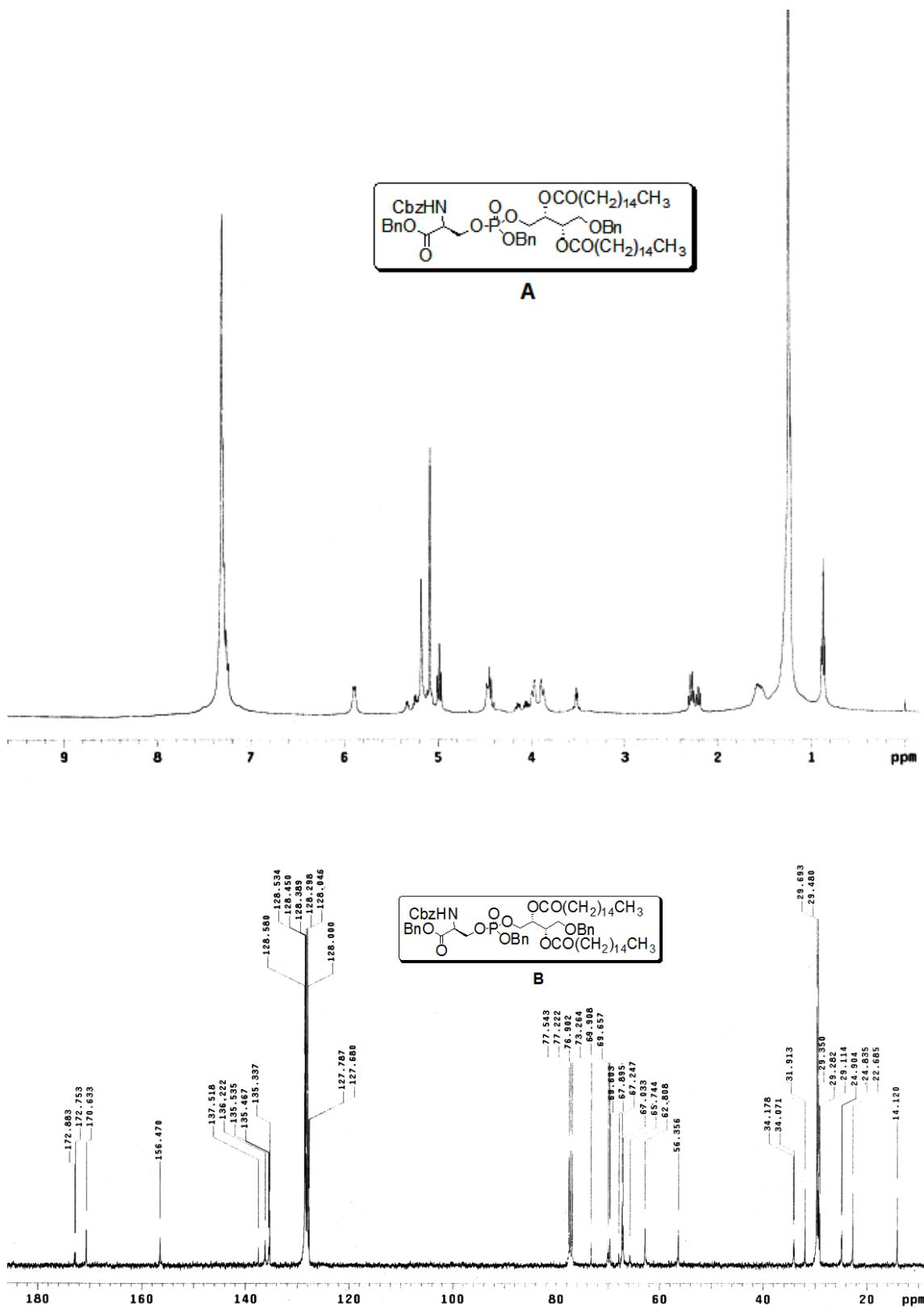
**Figure S10.**  $^1\text{H}$  NMR (A) and  $^{13}\text{C}$  NMR (B) spectra of compound **10b**.

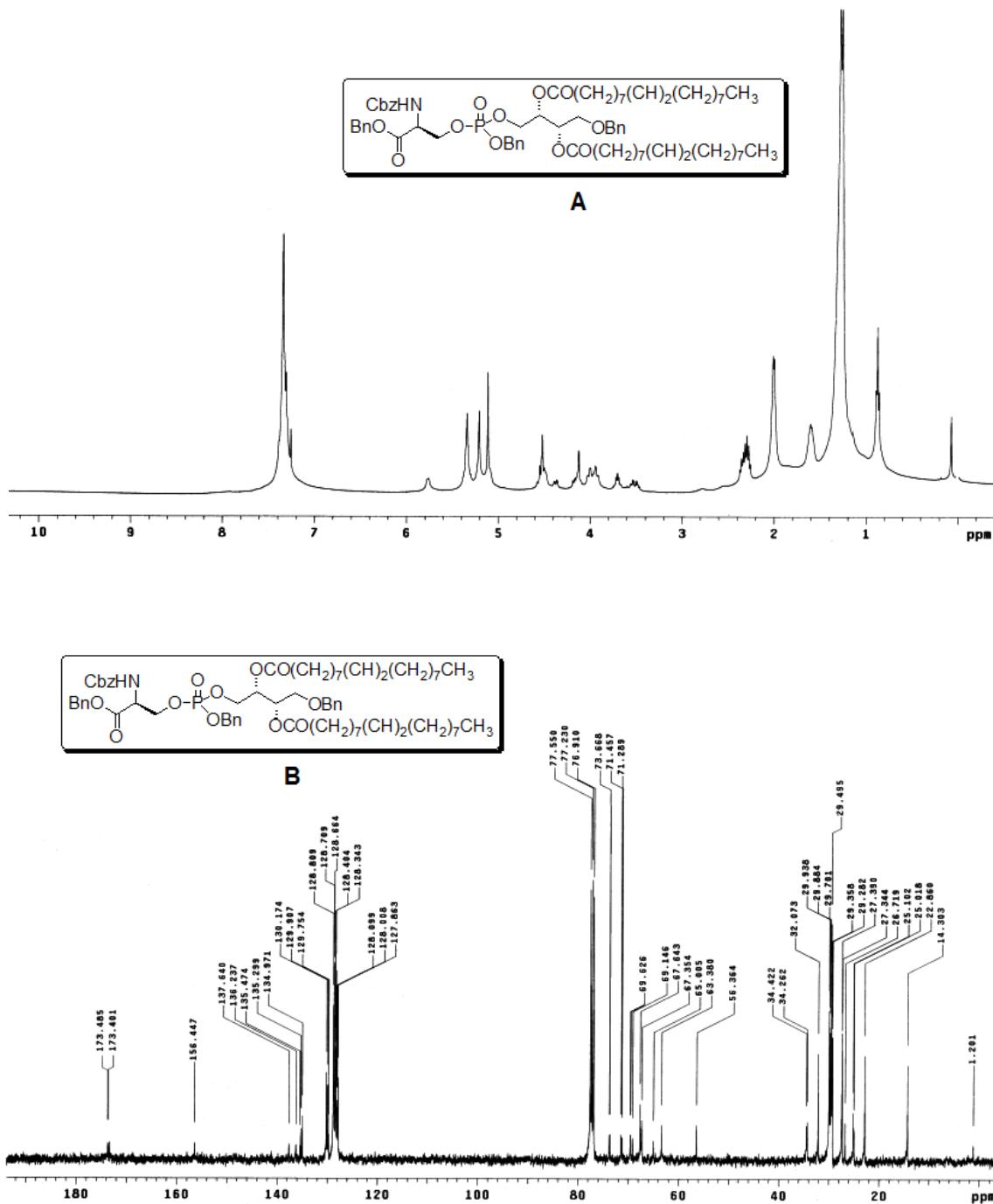


**Figure S11.**  $^1\text{H}$  NMR (A) and  $^{13}\text{C}$  NMR (B) spectra of compound **11a**.

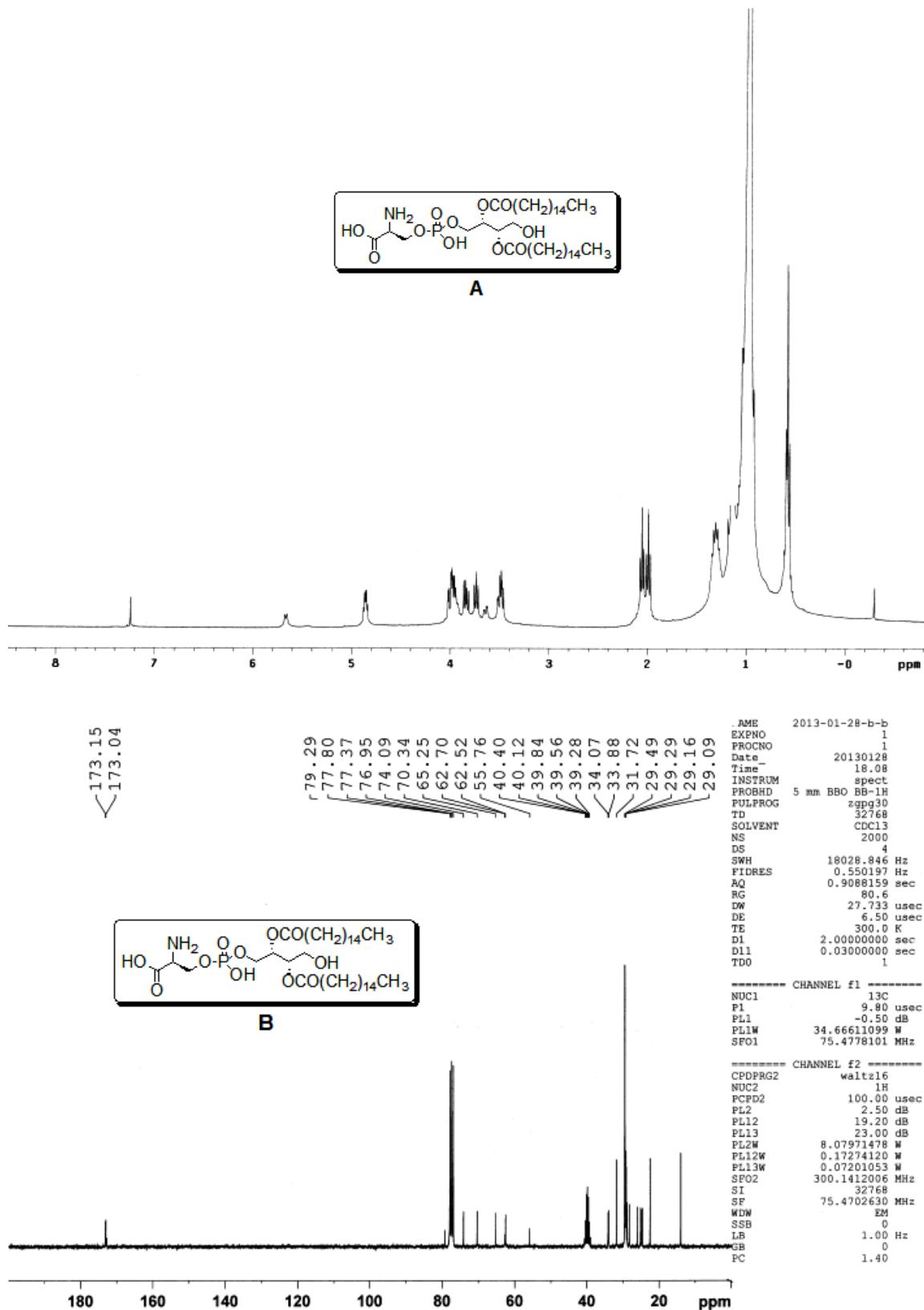


**Figure S12.**  $^1\text{H}$  NMR (A) and  $^{13}\text{C}$  NMR (B) spectra of compound **11b**.

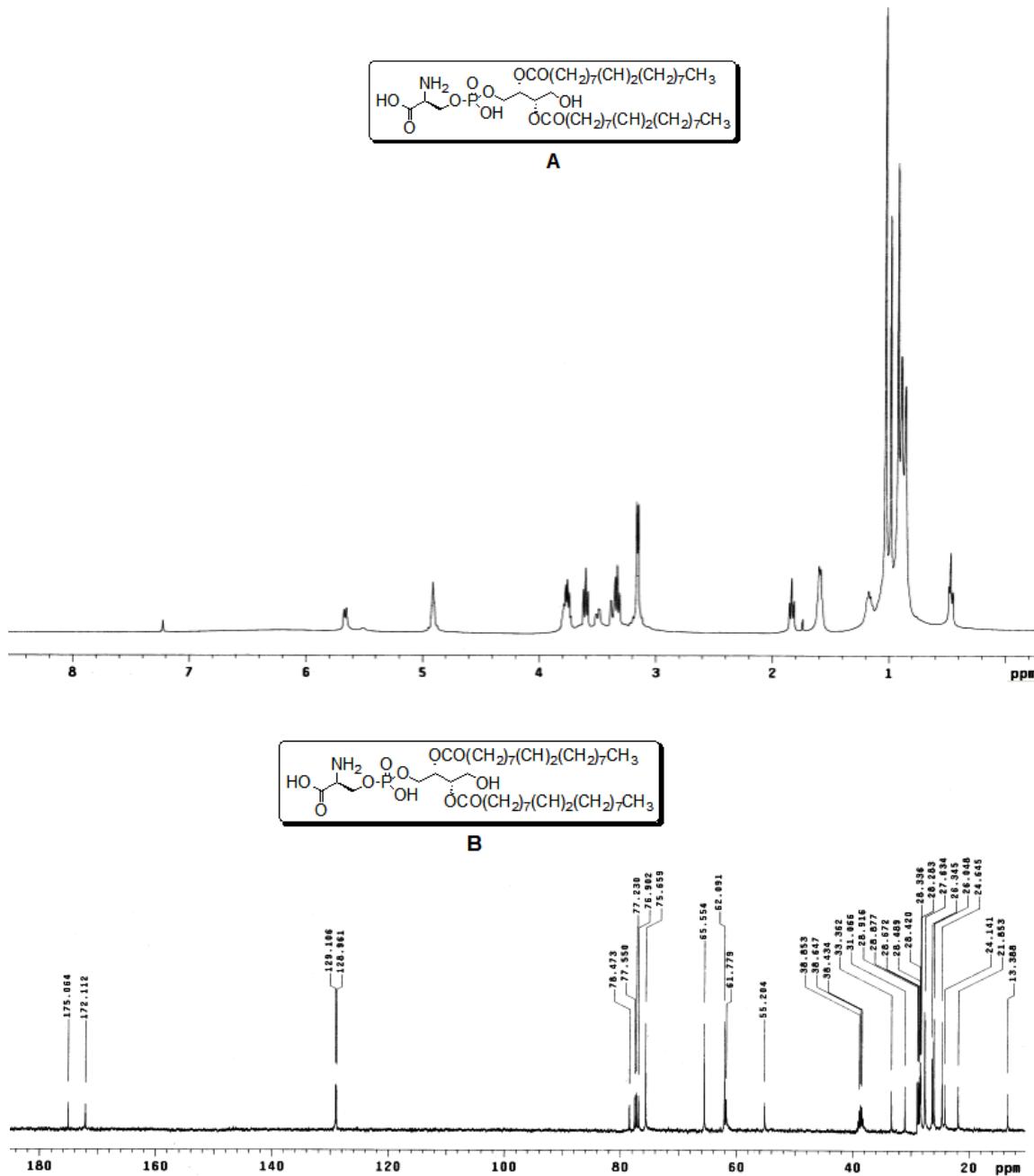




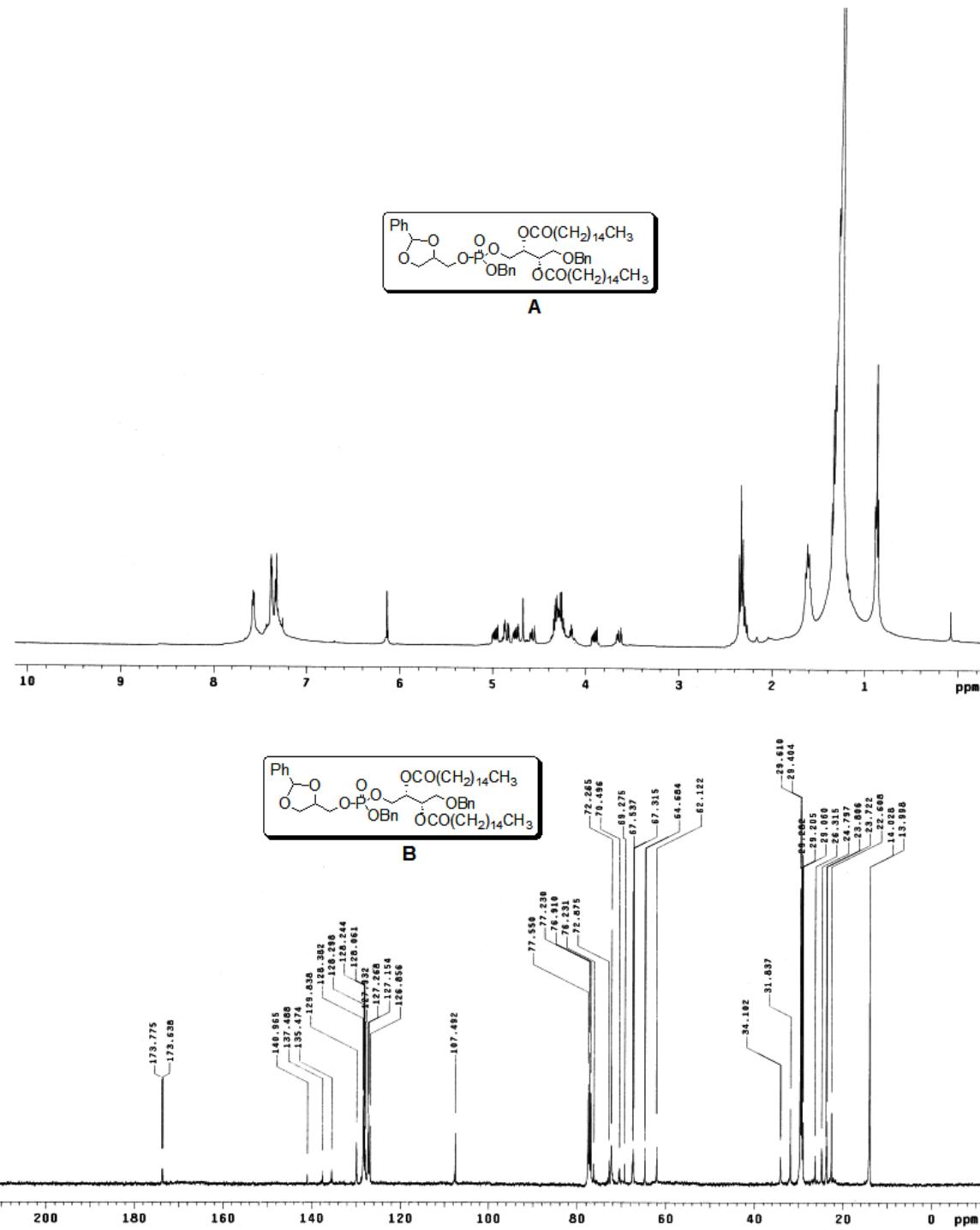
**Figure S14.**  $^1\text{H}$  NMR (A) and  $^{13}\text{C}$  NMR (B) spectra of compound **12b**.



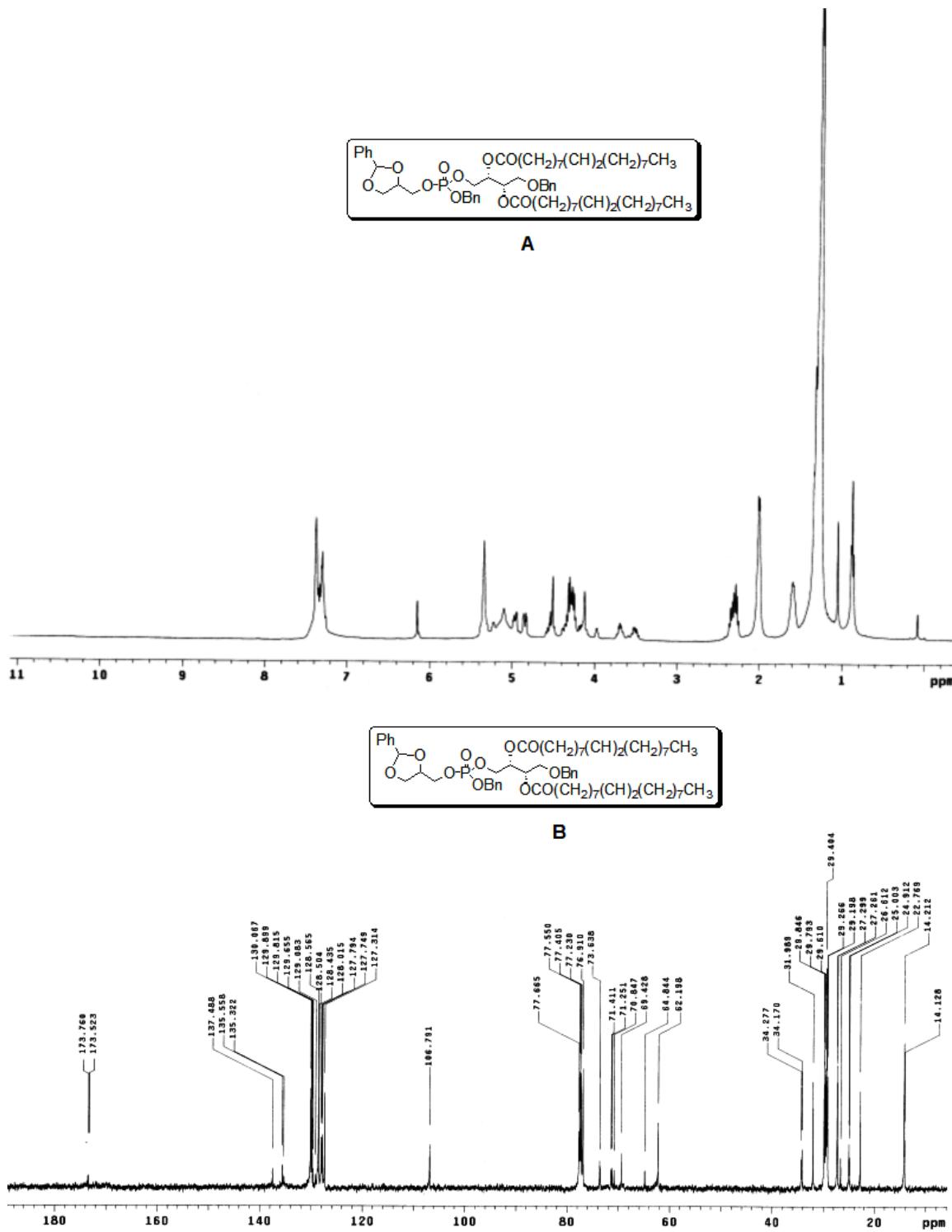
**Figure S15.**  $^1\text{H}$  NMR (A) and  $^{13}\text{C}$  NMR (B) spectra of DAT-PS<sub>16</sub>.



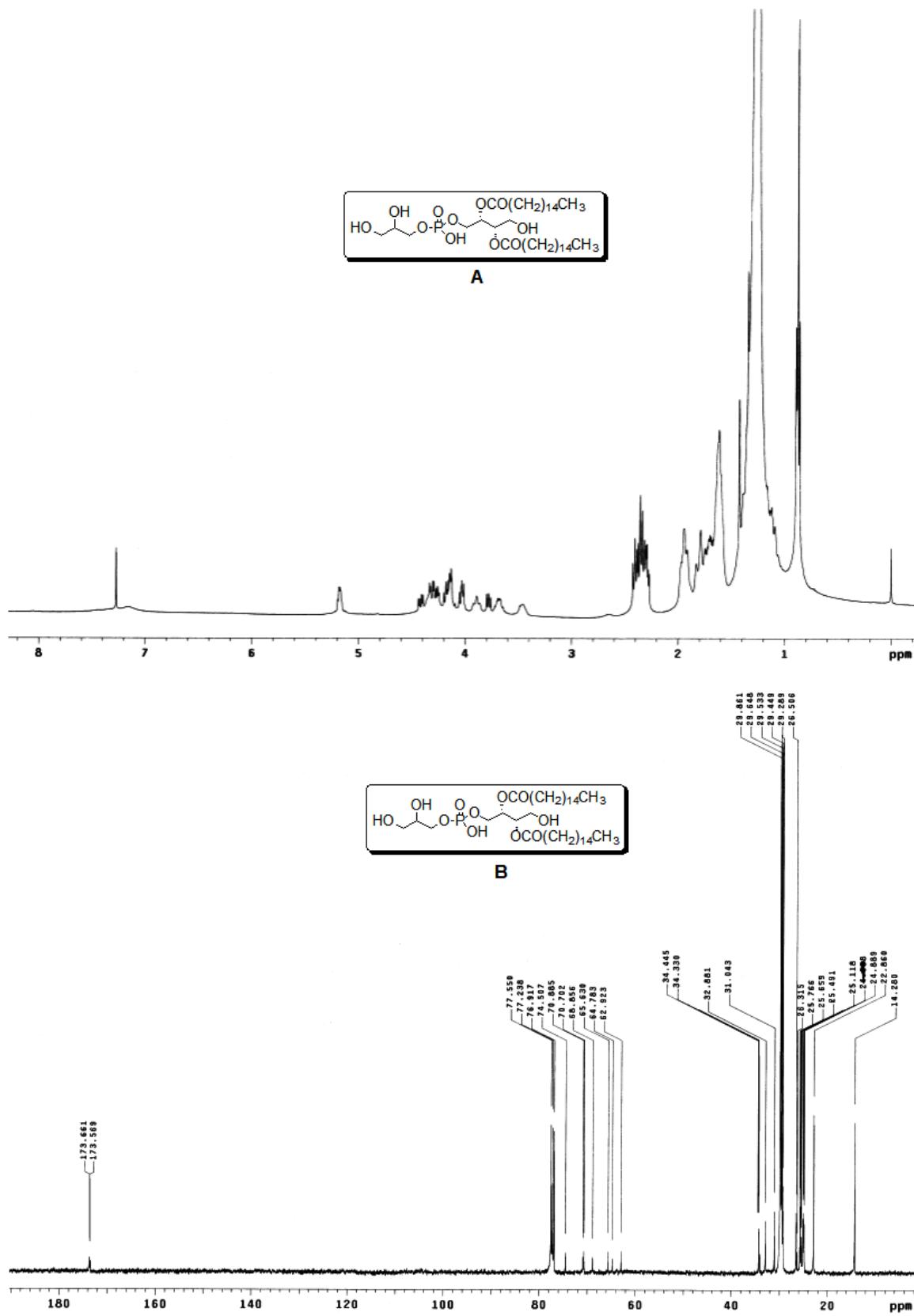
**Figure S16.**  $^1\text{H}$  NMR (A) and  $^{13}\text{C}$  NMR (B) spectra of DAT-PS<sub>18</sub>.



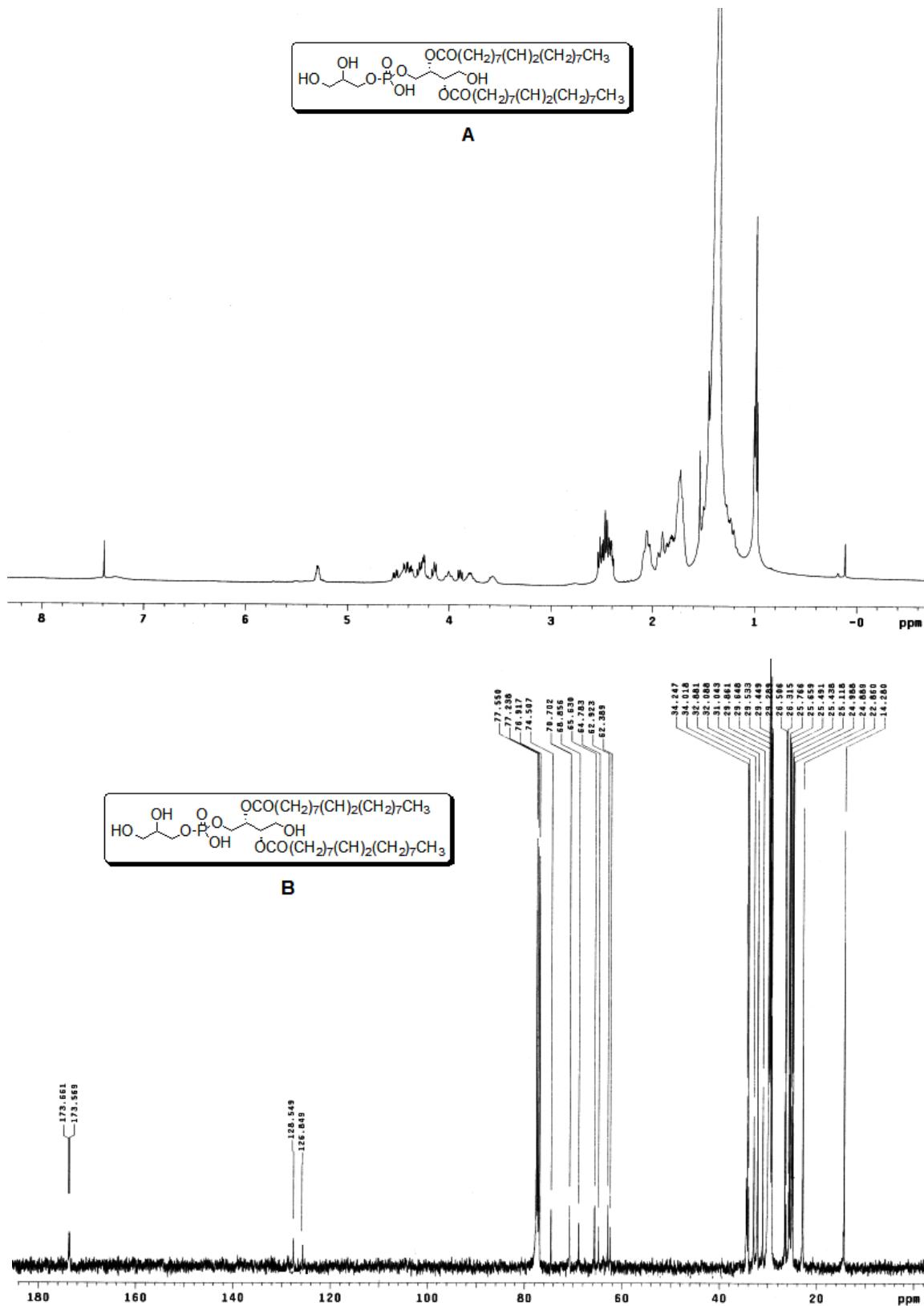
**Figure S17.**  $^1\text{H}$  NMR (A) and  $^{13}\text{C}$  NMR (B) spectra of compound **13a**.



**Figure S18.**  $^1\text{H}$  NMR (A) and  $^{13}\text{C}$  NMR (B) spectra of compound **13b**.

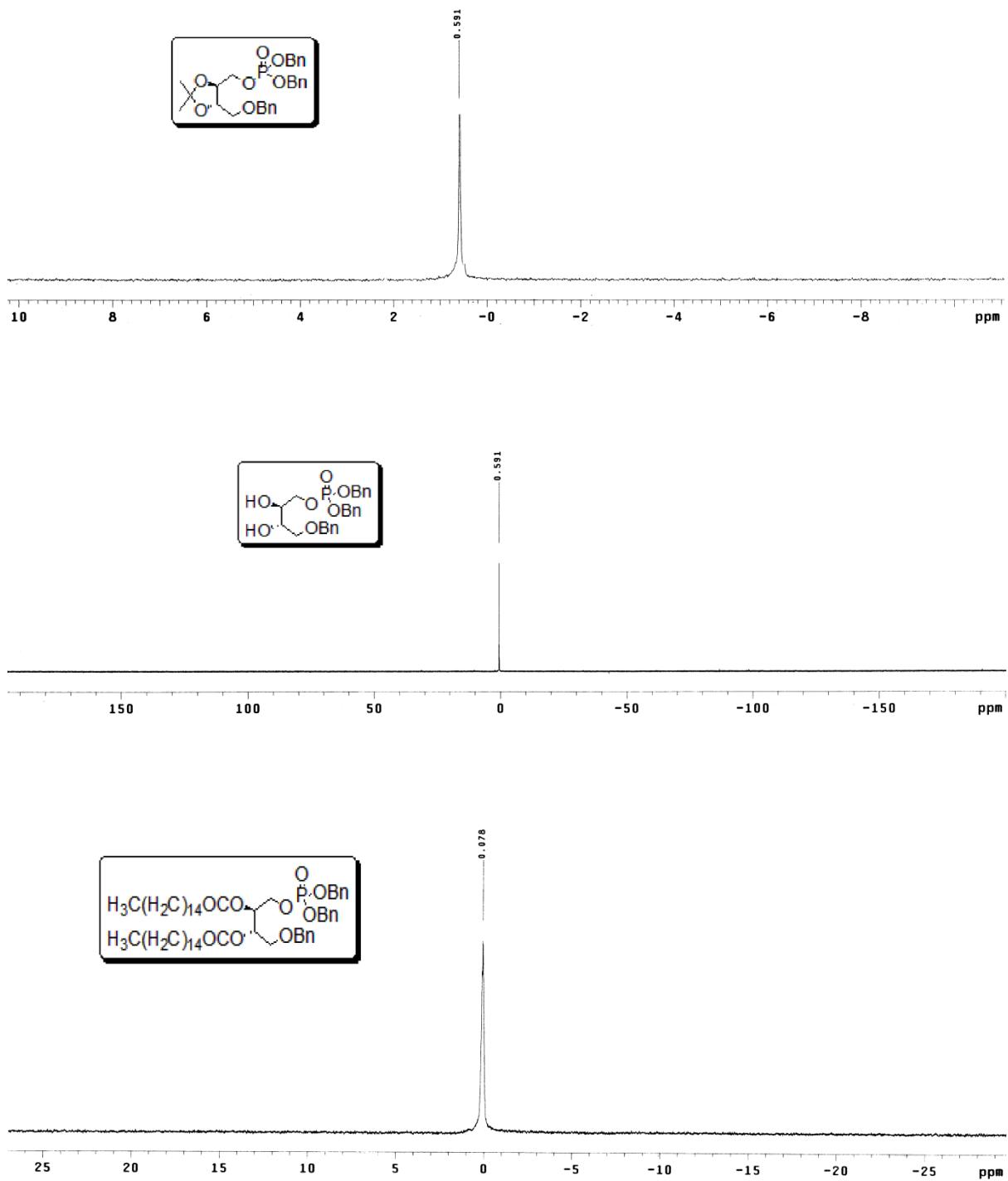


**Figure S19.**  $^1\text{H}$  NMR (A) and  $^{13}\text{C}$  NMR (B) spectra of DAT-PG<sub>16</sub>.

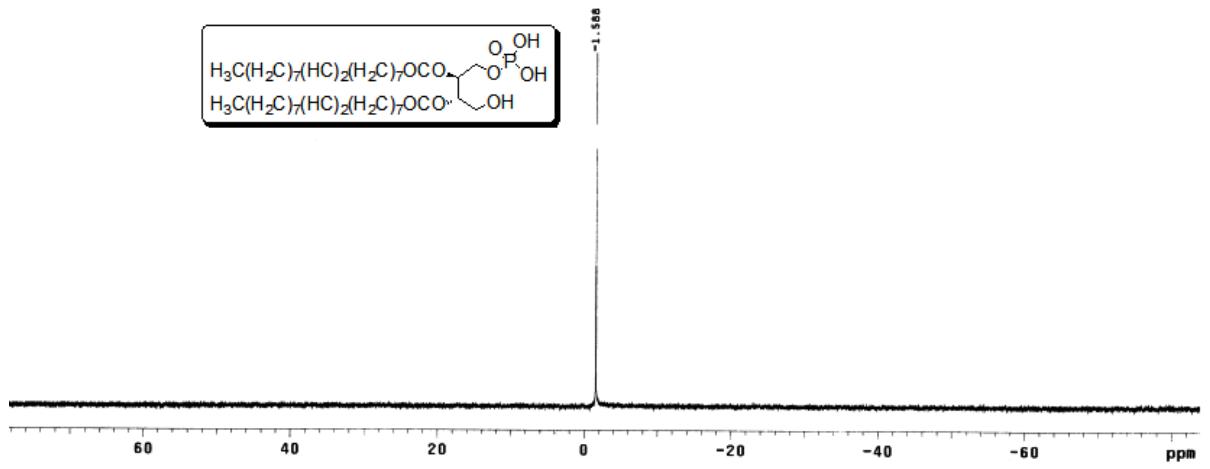
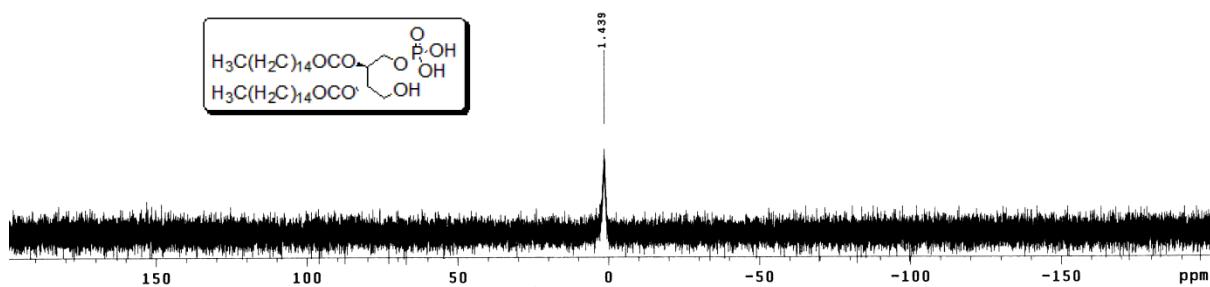
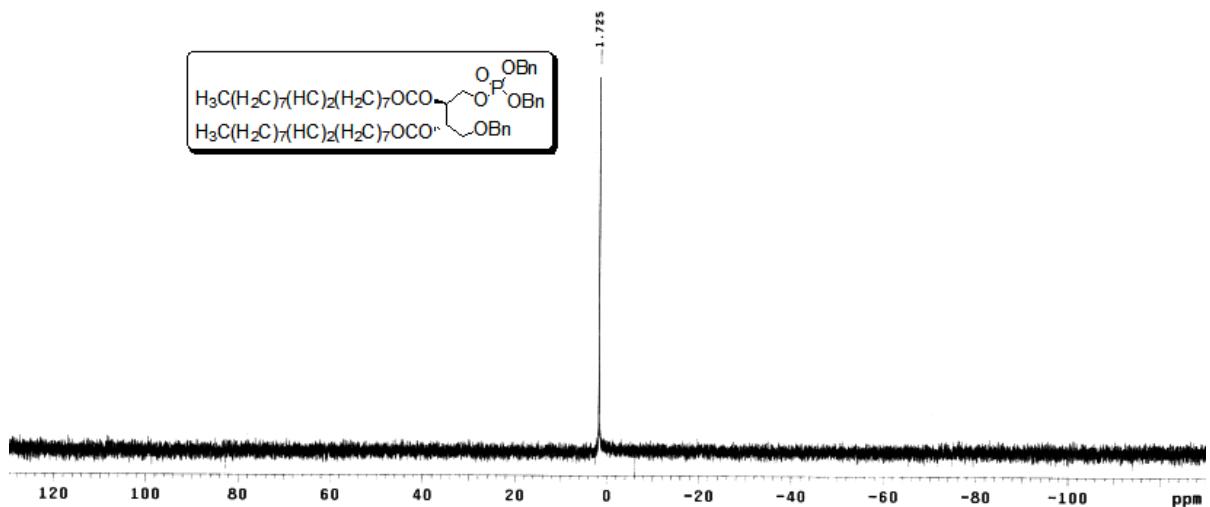


**Figure S20.**  $^1\text{H}$  NMR (A) and  $^{13}\text{C}$  NMR (B) spectra of DAT-PG<sub>18</sub>.

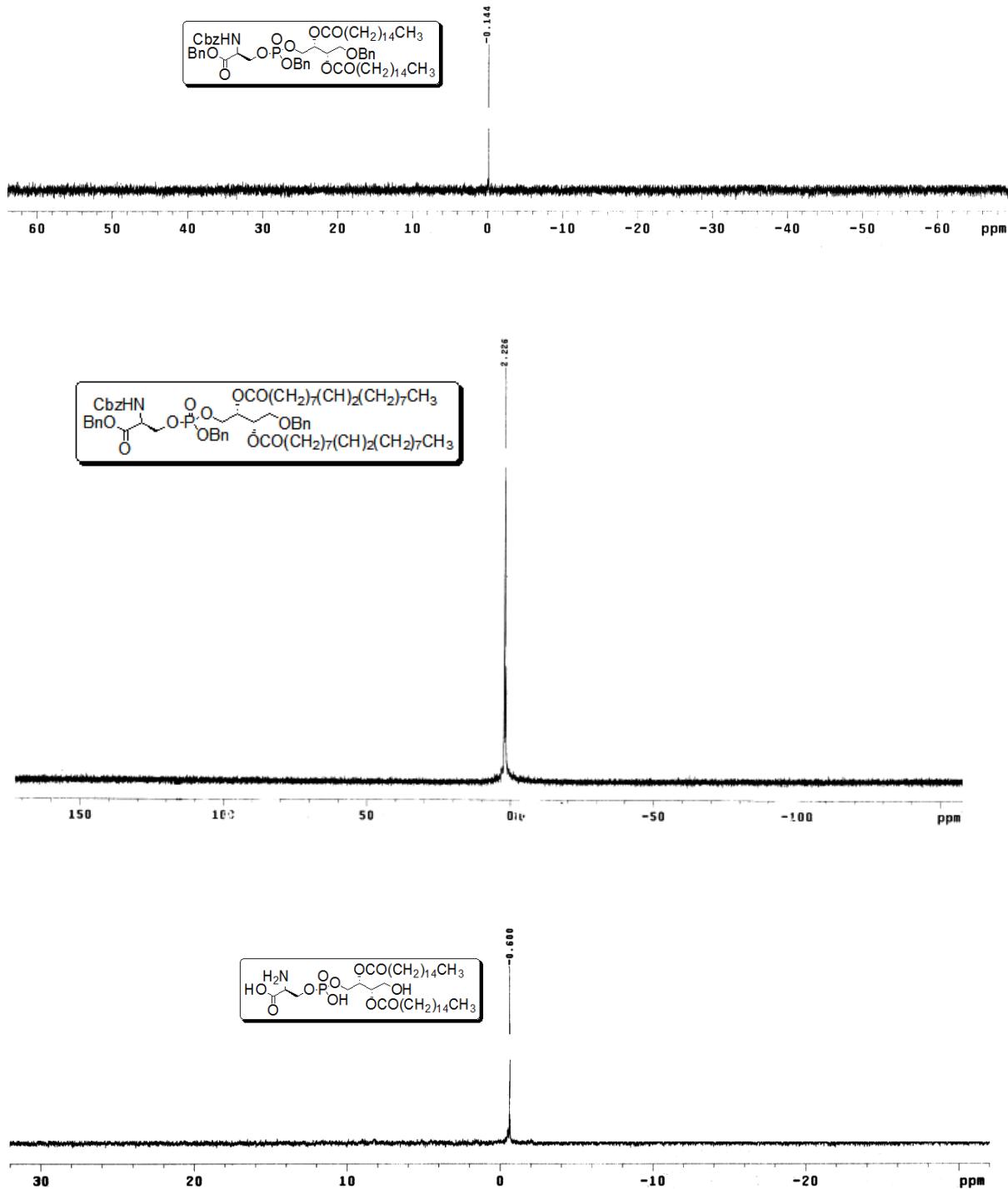
### (III) $^{31}\text{P}$ NMR Spectra of the New Compounds



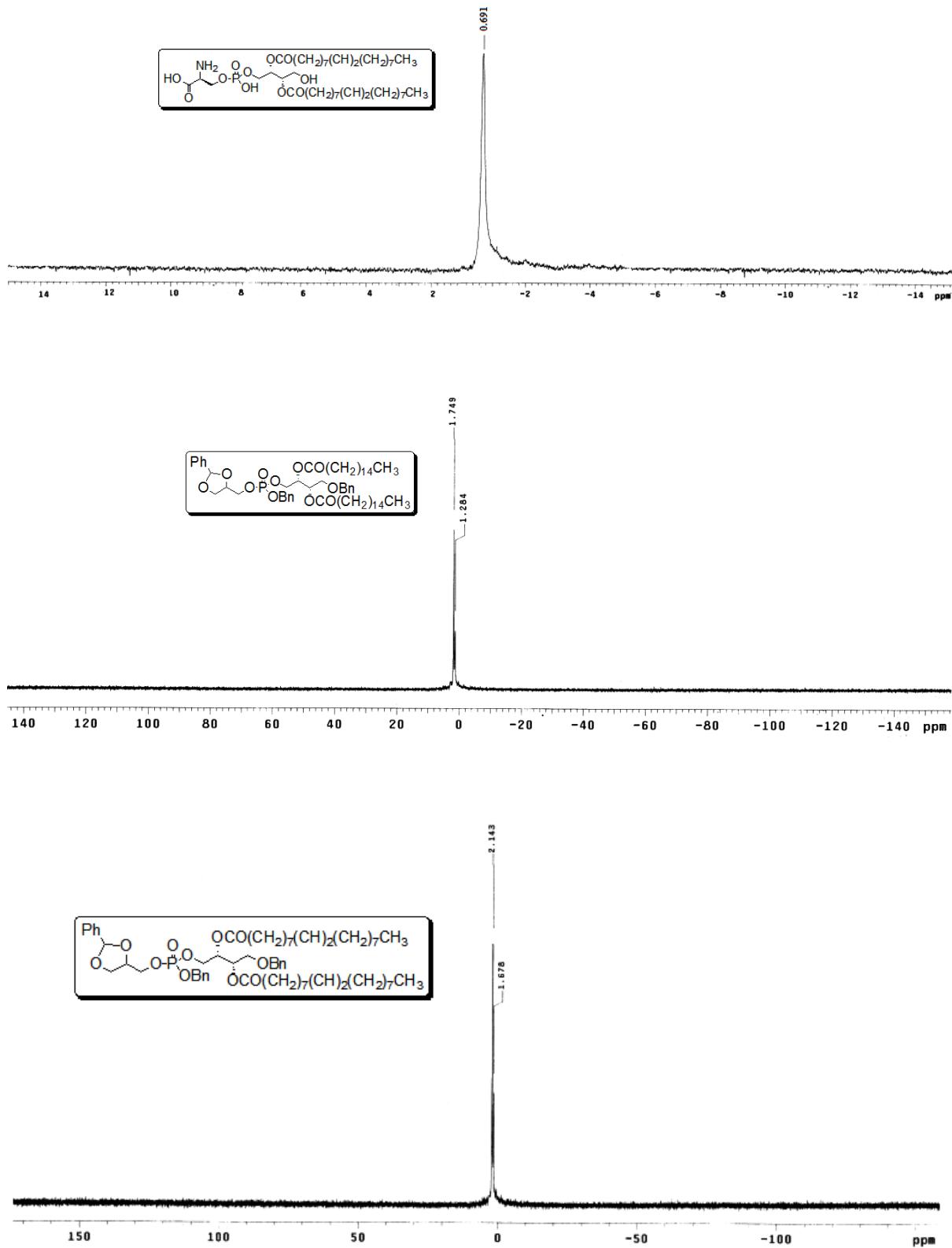
**Figure S21.**  $^{31}\text{P}$  NMR spectra of compound 5, 6, and 7a.



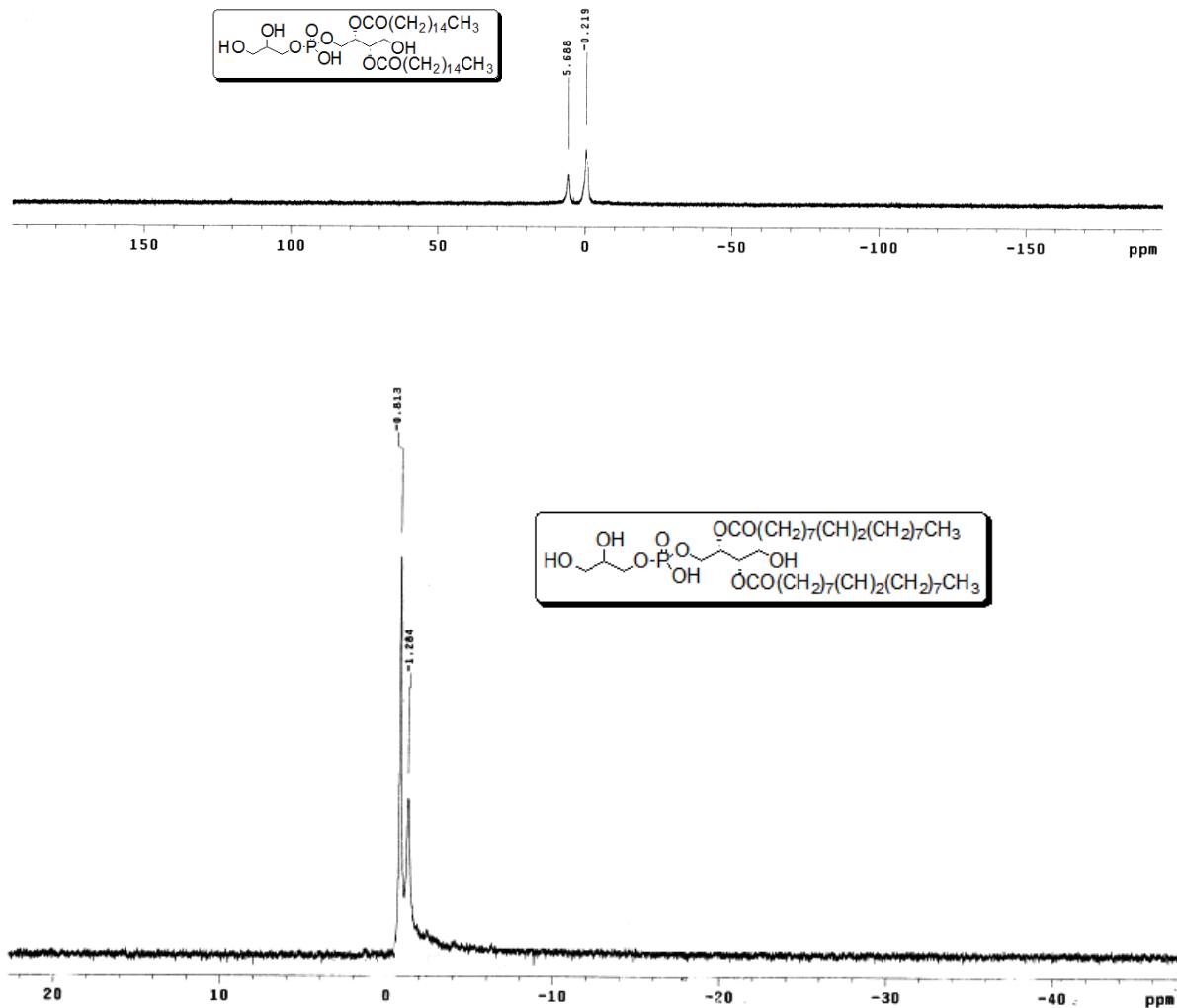
**Figure S22.**  $^{31}\text{P}$  NMR spectra of compound **7b**, DAT-PA<sub>16</sub>, and DAT-PA<sub>18</sub>.



**Figure S23.**  $^{31}\text{P}$  NMR spectra of compound **12a**, **12b**, and DAT-PS<sub>16</sub>.

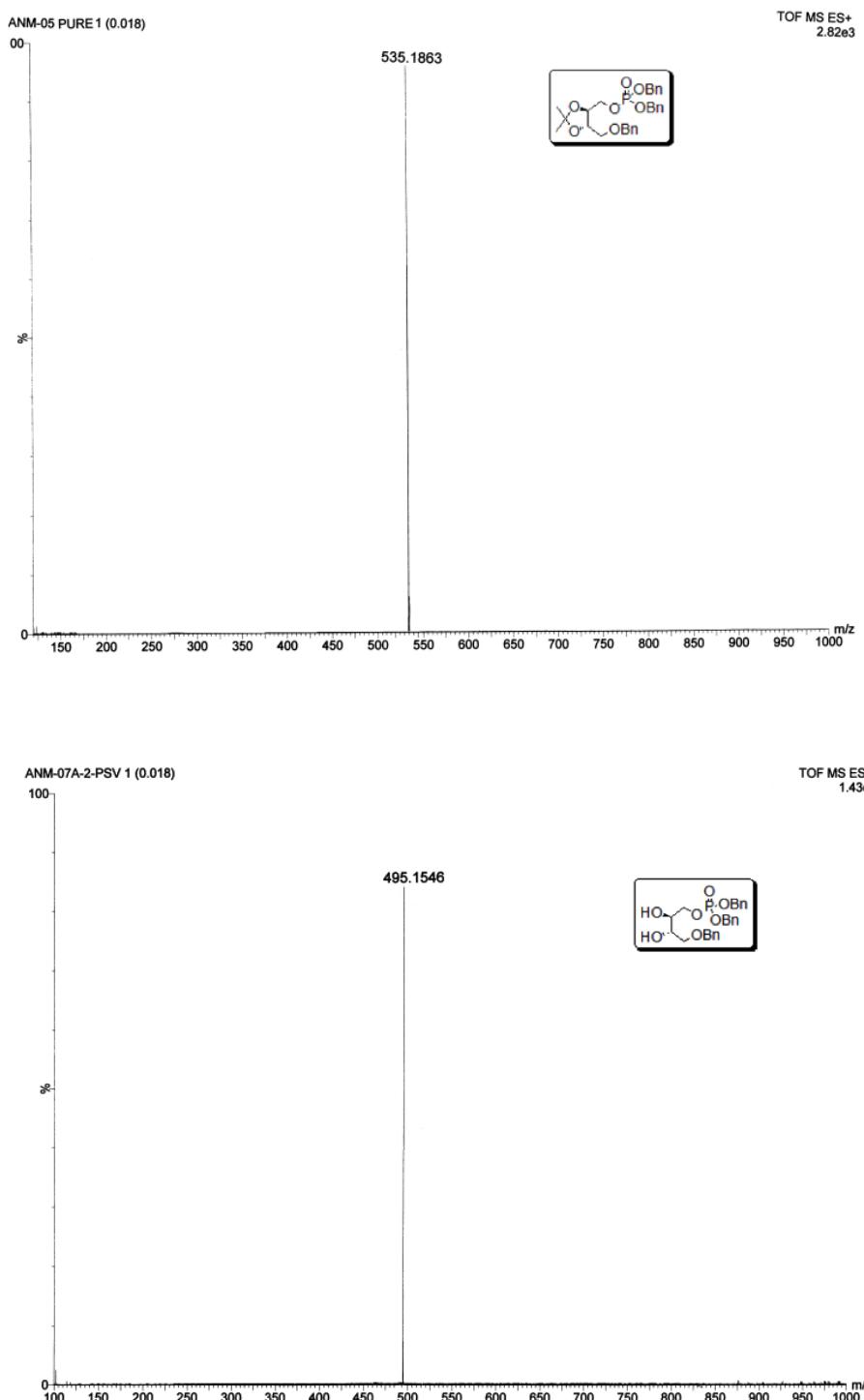


**Figure S24.** <sup>31</sup>P NMR spectra of compound DAT-PS<sub>18</sub>, **13a**, and **13b**.

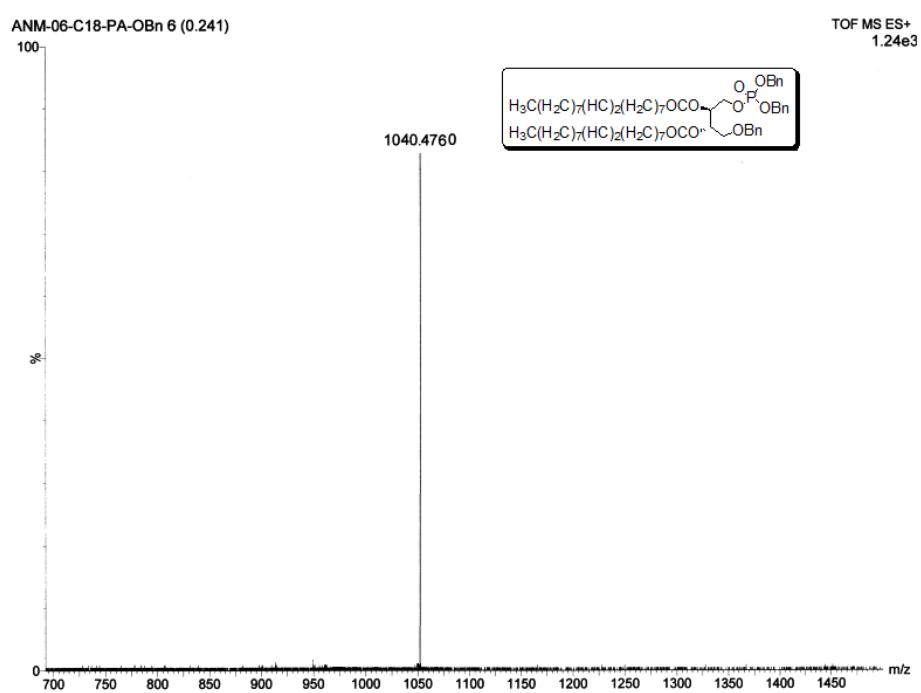
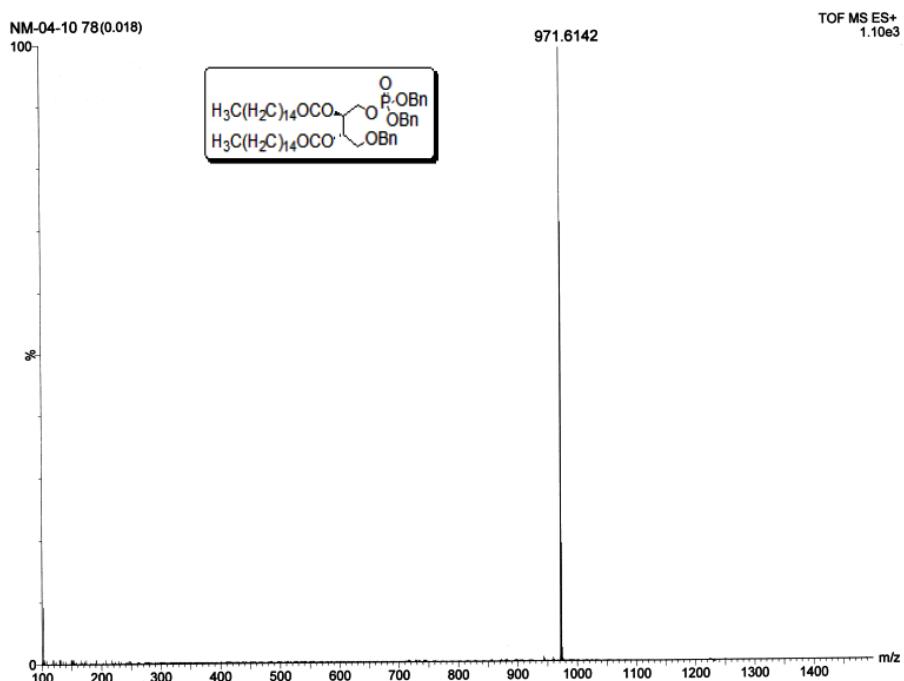


**Figure S25.**  $^{31}\text{P}$  NMR spectra of compound DAT-PG<sub>16</sub> and DAT-PG<sub>18</sub>.

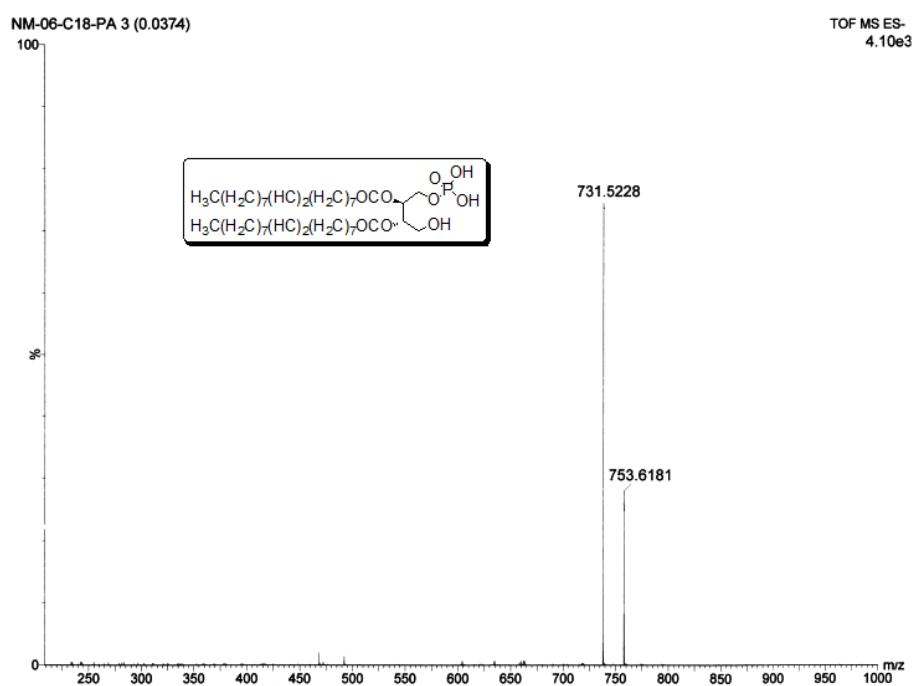
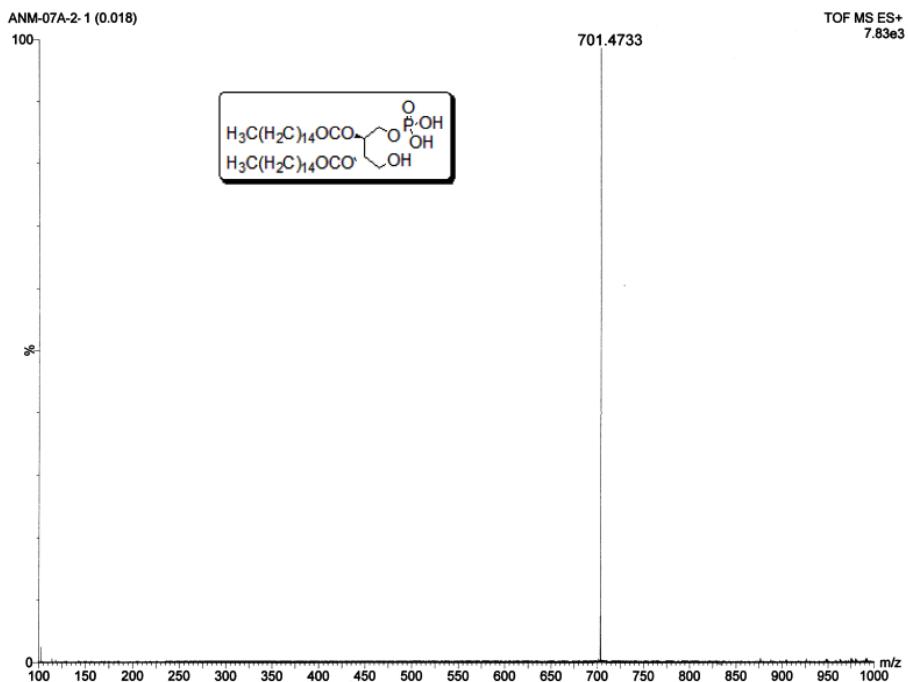
#### (IV) HRMS Spectra of the New Compounds



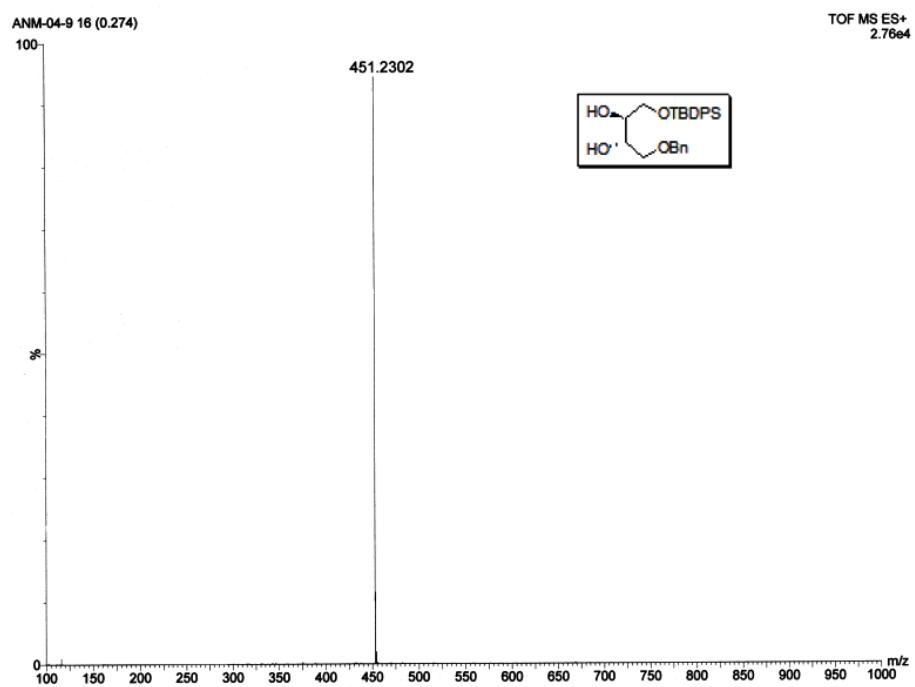
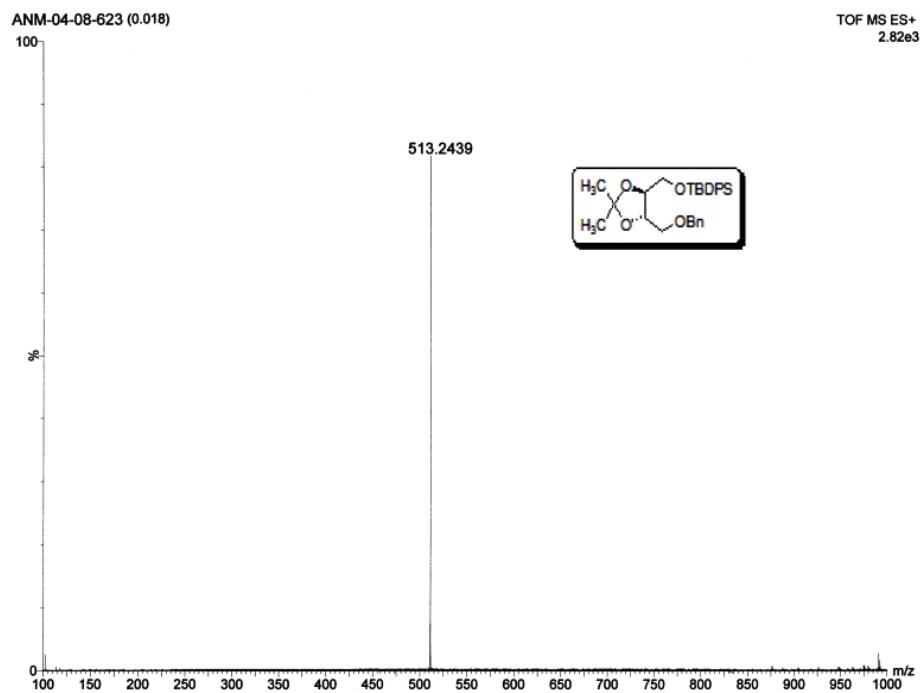
**Figure S26.** HRMS spectra of compound **5** and **6**.



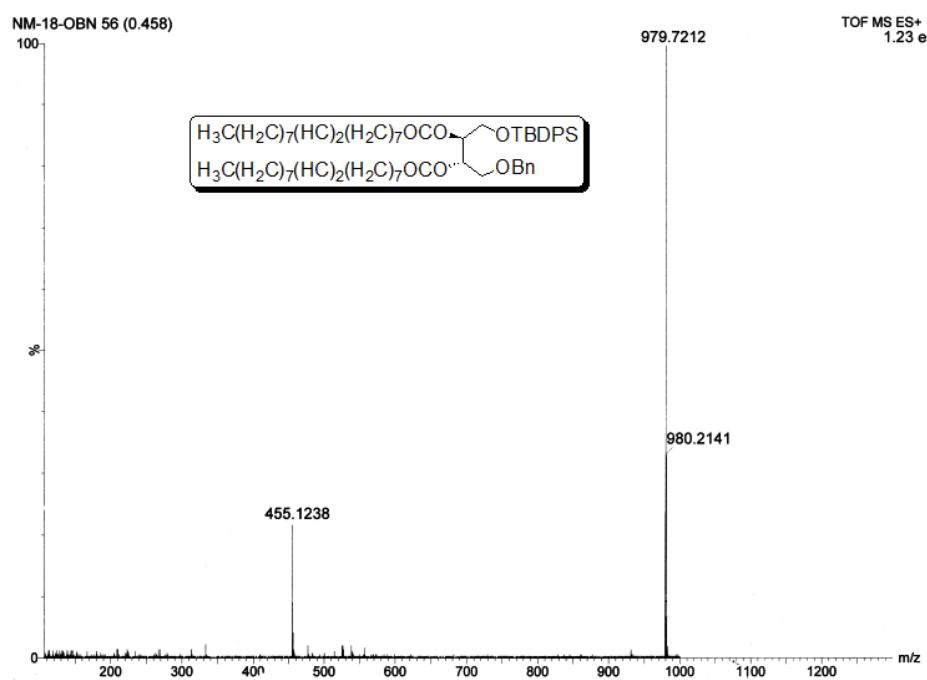
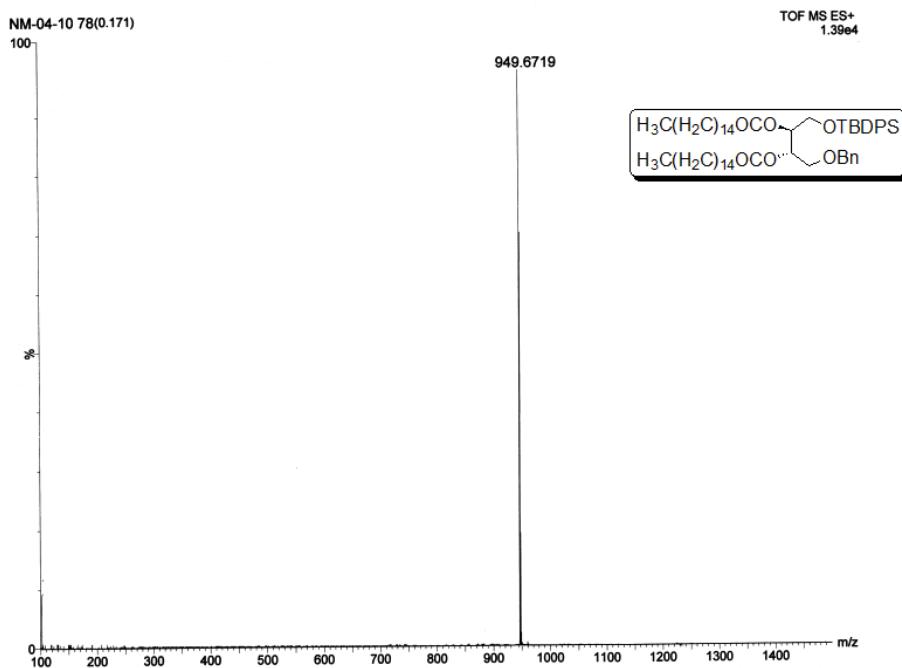
**Figure S27.** HRMS spectra of compound **7a** and **7b**.



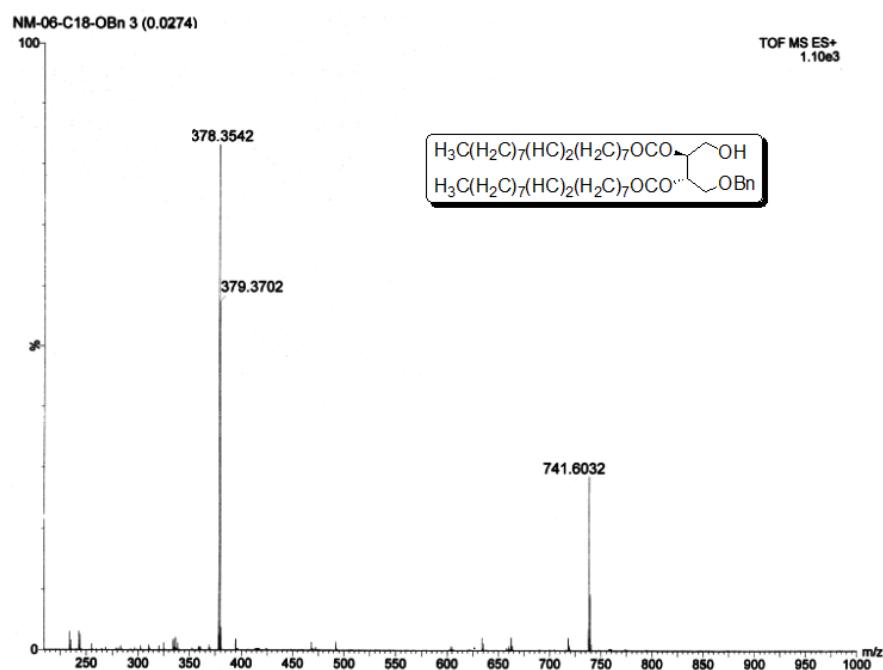
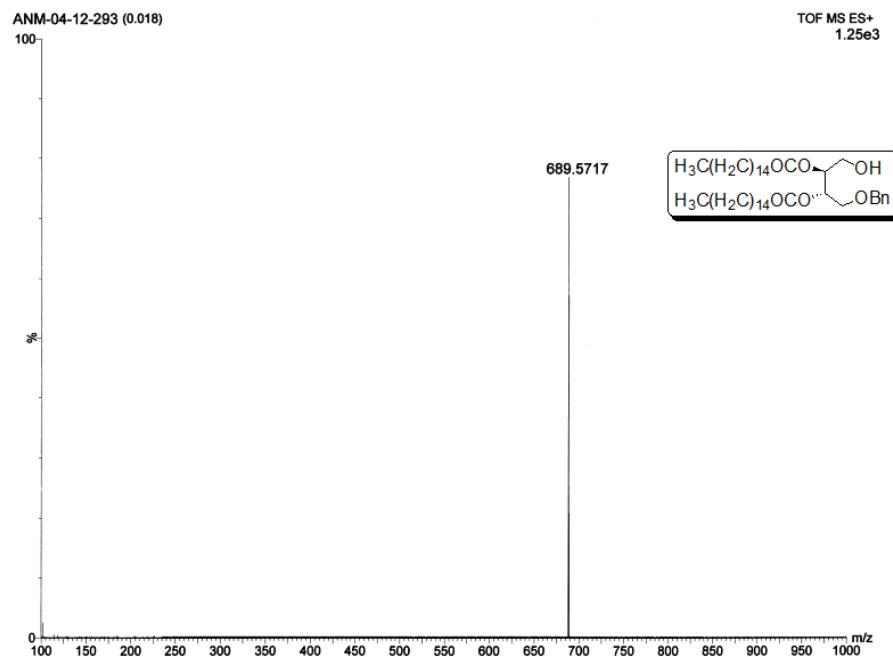
**Figure S28.** HRMS spectra of compound DAT-PA<sub>16</sub> and DAT-PA<sub>18</sub>.



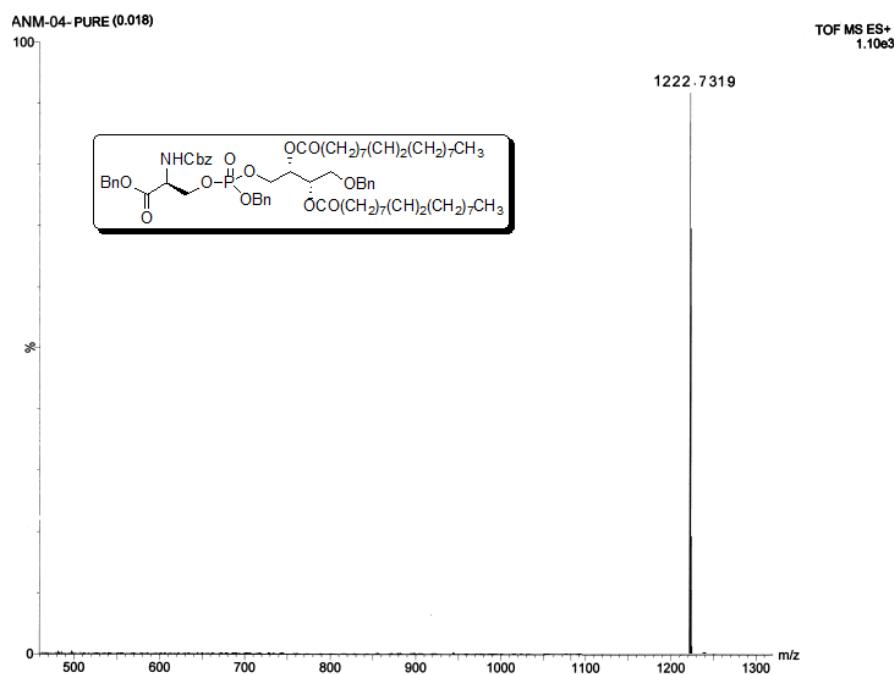
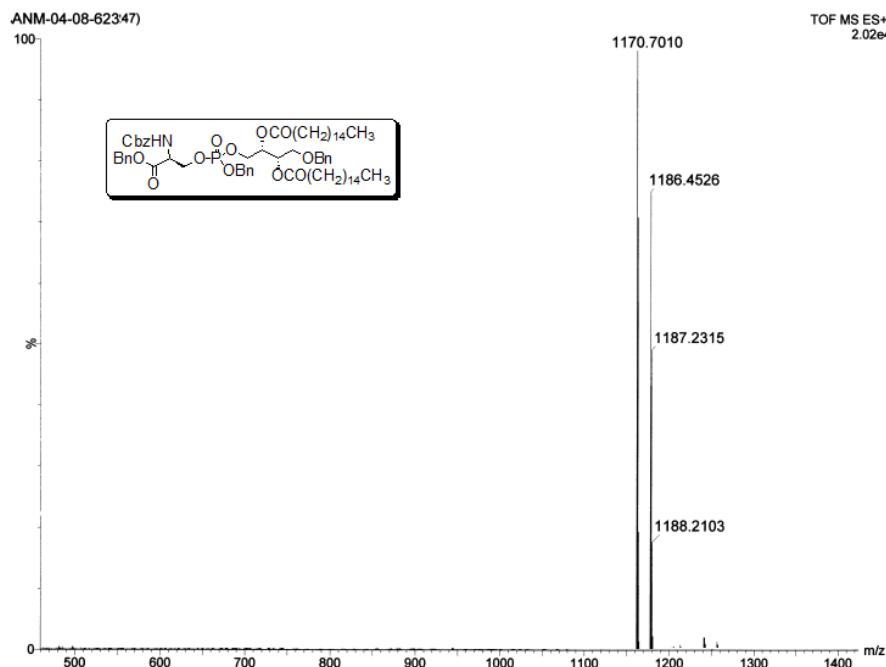
**Figure S29.** HRMS spectra of compound **8** and **9**.



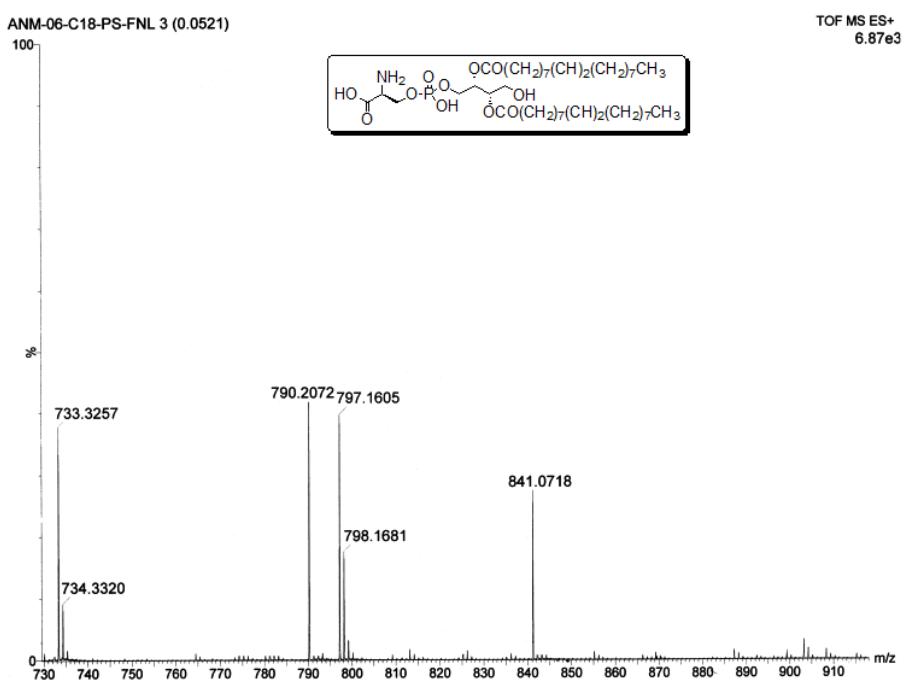
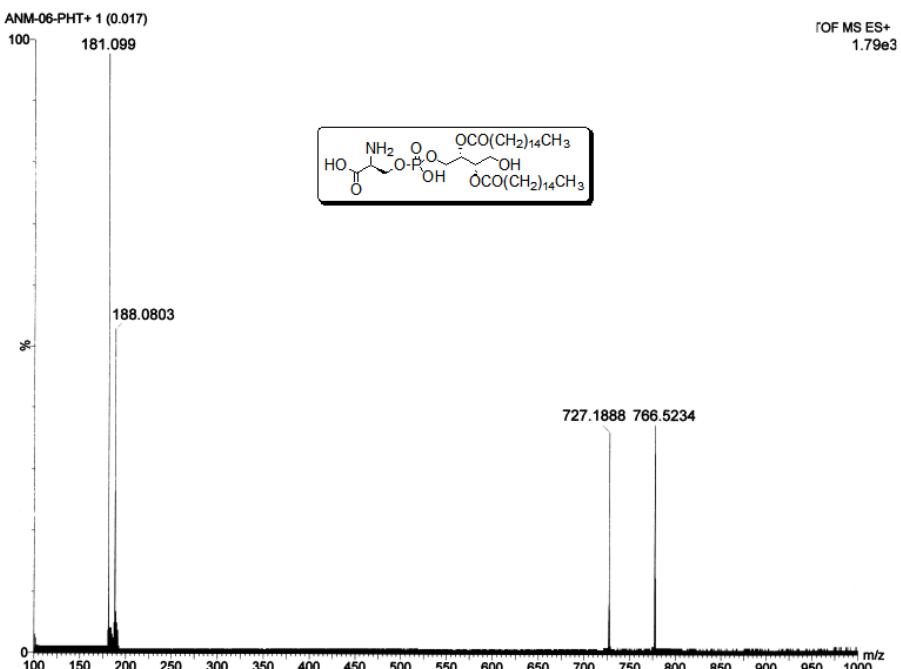
**Figure S30.** HRMS spectra of compound **10a** and **10b**.



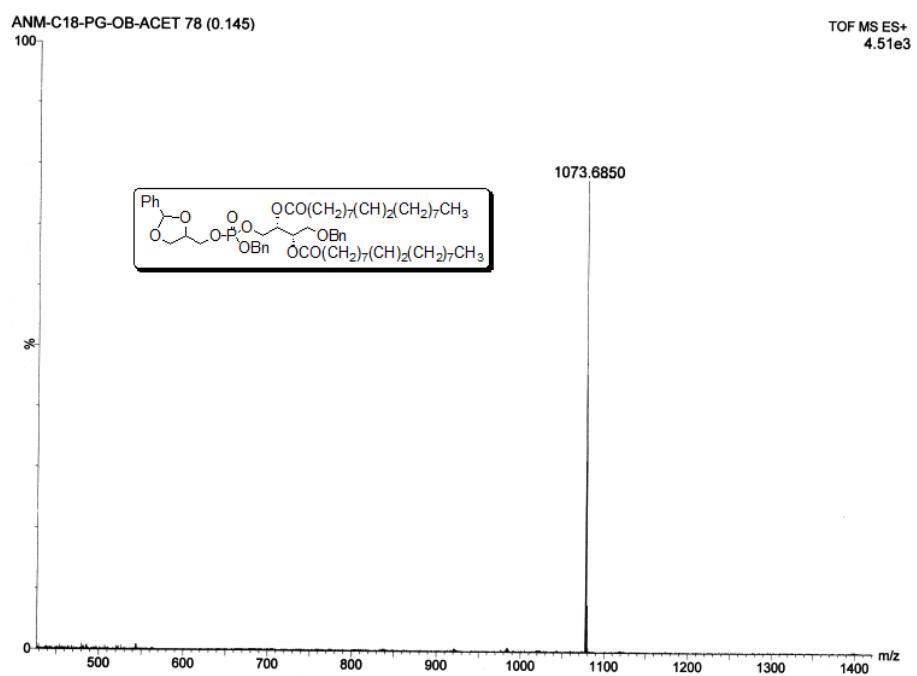
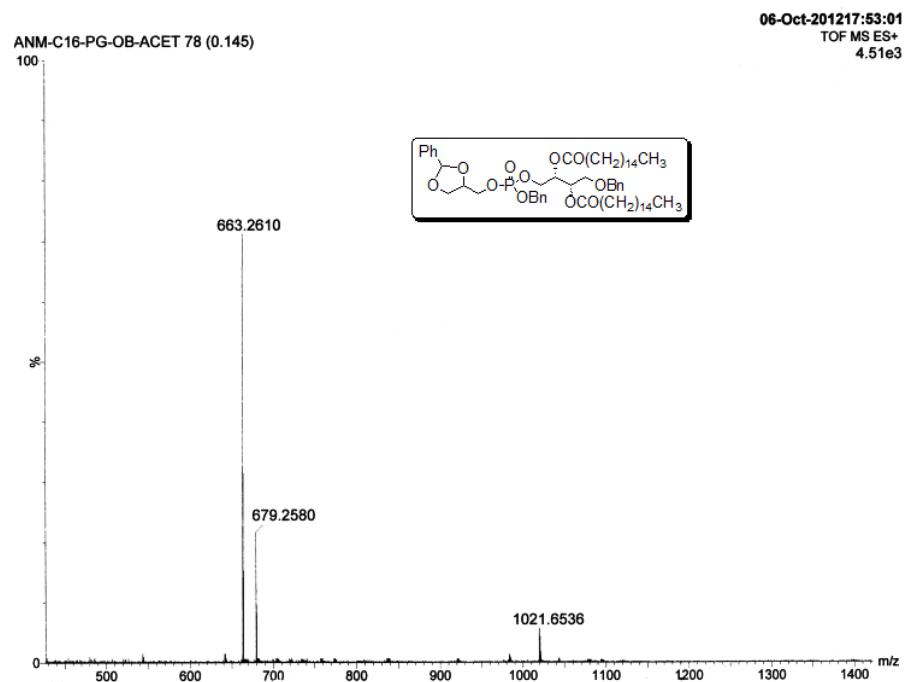
**Figure S31.** HRMS spectra of compound **11a** and **11b**.



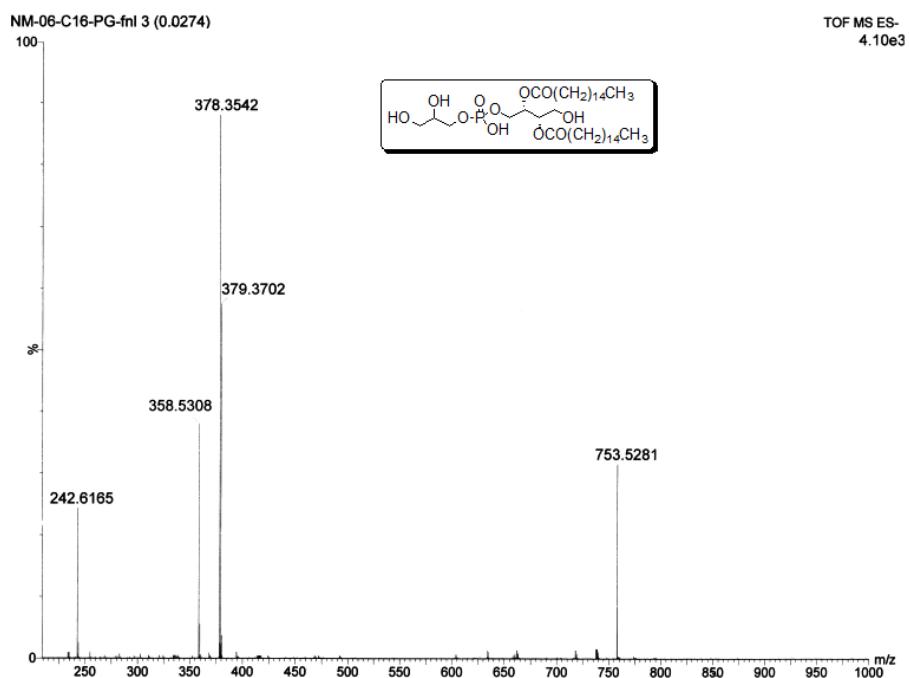
**Figure S32.** HRMS spectra of compound **12a** and **12b**.



**Figure S33.** HRMS spectra of compound DAT-PS<sub>16</sub> and DAT-PS<sub>18</sub>.



**Figure S34.** HRMS spectra of compound **13a** and **13b**.



**Figure S35.** HRMS spectra of compound DAT-PG<sub>16</sub> and DAT-PG<sub>18</sub>.

## (V) References

- (1) Mamidi, N.; Gorai, S.; Mukherjee, R.; Manna, D., Development of diacyltetrol lipids as activators for the C1 domain of protein kinase C. *Mol. Biosyst.* **2012**, 8, (4), 1275-1285.
- (2) Mamidi, N.; Manna, D., Zn(OTf)2-promoted chemoselective esterification of hydroxyl group bearing carboxylic acids. *J. Org. Chem.* **2013**, 78, (6), 2386-2396.
- (3) Prasad, K. R.; Swain, B., Enantioselective synthesis of possible diastereomers of heptadeca-1-ene-4,6-diyne-3,8,9,10-tetrol; putative structure of a conjugated diyne natural product isolated from Hydrocotyle leucocephala. *J. Org. Chem.* **2011**, 76, (7), 2029-2039.
- (4) Smith, M. D.; Sudhahar, C. G.; Gong, D.; Stahelin, R. V.; Best, M. D., Modular synthesis of biologically active phosphatidic acid probes using click chemistry. *Mol. Biosyst.* **2009**, 5, (9), 962-972.
- (5) Guanti, G.; Banfi, L.; Basso, A.; Bondanza, L.; Guglieri, G.; Powles, K.; Riva, R., Optimized synthesis of phosphatidylserine. *Amino Acids* **2010**, 39, (2), 367-373.
- (6) Zhu-Jun Yao , Y.-L. W., Synthetic Studies toward Mono-THF Annonaceous Acetogenins: A Diastereoselective and Convergent Approach to Corosolone and (10RS)-Corosoline. *J. Org. Chem.* **1995**; 60, 1170–1176.