Supplementary Data

Structural basis for the recognition of oxidized phospholipids in oxidized low density lipoproteins by class B scavenger receptors CD36 and SR-BI

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General methods

^{1}H NMR spectra were recorded on Varian Gemini spectrometers (200 MHz) and on a Varian Inova AS400 spectrometer (400 MHz). ^{13}C NMR spectra were recorded on a Varian Gemini spectrometer (50 MHz) or on a Varian Inova AS400 spectrometer (100 MHz). All high-resolution mass spectra were recorded on a Kratos AEI MS25 RFA high resolution mass spectrometer at 20 eV. Unless otherwise stated, the solvents and reagents were of commercially available analytical grade quality, all chemicals were obtained from Sigma-Aldrich or Fisher Scientific or Acros Organics.

Chemical synthesis of phospholipids

1-Palmitoyl-2-maleoyl-sn-glycero-3-phosphocholine (PMPC) (1a), 1-palmitoyl-2-phthalyl-sn-glycero-3-phosphocholine (PPPC)(1b), 1-palmitoyl-2-succinyl-sn-glycero-3-phosphocholine (PSuPC) (1c), 1-palmitoyl-2-glutaroyl-sn-glycero-3-phosphocholine (PGPC)(1d) and 1-palmitoyl-2-acetyl-sn-glycero-3-phosphocholine (PAcPC) (1e) were prepared with similar methods as shown in scheme S1 (1). The preparation of PMPC (1a) is presented as an example.

1-Palmitoyl-2-maleoyl-sn-glycero-3-phosphocholine (PMPC) (1a). Maleic anhydride (49 mg, 0.5 mmol) and 4-Dimethylaminopyridine (DMAP) (6 mg, 0.05 mmol) were added to a solution of L-α-Lysophosphatidylcholine (2-lysoPC) (25 mg, 0.05 mmol) in 3 ml dry CH_2Cl_2/THF (10/1 v/v) under argon. The mixture was stirred at 30 ^{o}C overnight, and then the solvent was removed under reduced pressure. The residue was applied to a 0.5 mm silica gel TLC plate, which was eluted with $CHCl_3$/MeOH/H_2O (65/35/7). The major band (R_f = 0.15) was extracted with $CHCl_3$/MeOH/H_2O (1/2/0.8). The extract was filtered and then washed by the Bligh/Dyer method (2), dried with anhydrous Na_2SO_4 and solvents were evaporated producing a white solid (10 mg, 33%). ^{1}H NMR (CD_3OD, 400 MHz): δ 0.89 (t, J = 6.8 Hz, 3H), 1.20-1.36 (24 H), 1.52-1.64 (2H), 2.33 (t, J = 7.6 Hz, 2H), 3.22 (s, 9 H), 3.64 (m, 2H) 4.06 (m, 2H), 4.20-4.30 (3H), 4.40 (dd, J = 12.4, 4.0 Hz, 1H), 5.31 (m, 1H), 6.29 (d, J = 12 Hz, 1H), 6.38 (d, J = 12 Hz, 1H). HRMS (FAB): m/z calcd for $C_{28}H_{53}NO_{10}P$ (MH^+) 594.3407, found 594.3406.

1-Palmitoyl-2-phthalyl-sn-glycero-3-phosphocholine (PPPC) (1b). A procedure analogous to that described above for **1a** was used to get **1b** (60%). ^{1}H NMR (CD_3OD, 400 MHz): δ 0.89 (t, J = 6.8 Hz, 3H), 1.20-1.35 (24H), 1.58 (m, 2H), 2.34 (t, J = 7.6 Hz, 2H), 3.17 (s, 9H), 3.58 (m, 2H), 4.15 (m, 2H), 4.27 (m, 2H), 4.37 (dd, J = 12.0, 6.8 Hz, 1H), 4.46 (dd, J = 12.0, 3.6 Hz, 1H), 5.45

(m, 1H), 7.56-7.61 (m, 2H), 7.70-7.75 (m, 2H). HRMS (FAB): m/z calcd for $C_{32}H_{55}NO_{10}P$ (MH^+) 644.3563, found 644.3569.

1-Palmitoyl-2-succinyl-sn-glycero-3-phosphocholine (PSuPC) (1c). A procedure analogous to that described above for **1a** was used to get **1c** (67%). ^{1}H NMR (CD_3OD, 400 MHz): δ 0.89 (t, *J* = 6.8 Hz, 3H), 1.25-1.35 (24H), 1.58 (m, 2H), 2.32 (t, *J* = 7.2 Hz, 2H), 2.48 (m, 2H), 2.58 (m, 2H), 3.23 (s, 9H), 3.66 (m, 2H), 4.01 (m, 2H), 4.22 (dd, *J* = 12.0, 6.4 Hz, 1H), 4.28 (m, 2H), 4.35 (dd, *J* = 12.0, 4.0 Hz, 1H), 5.23 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.48, 23.74, 25.95, 30.21, 30.45, 30.49, 30.65, 30.77, 30.80, 33.08, 34.80, 54.65, 60.60, 63.47, 64.94, 67.41, 71.90, 174.39, 174.98. HRMS (FAB): m/z calcd for $C_{28}H_{55}NO_{10}P$ (MH^+) 596.3563, found 596.3554.

1-Palmitoyl-2-glutaroyl-sn-glycero-3-phosphocholine (PGPC) (1d). A procedure analogous to that described above for **1a** was used to get **1d** (41%). ^{1}H NMR (CD_3OD, 400 MHz): δ 0.89 (t, *J* = 6.8 Hz, 3H), 1.25-1.35 (24H), 1.59 (m, 2H), 1.89 (m, 2H), 2.32 (t, *J* = 7.6 Hz, 2H), 2.36 (t, *J* = 7.2 Hz, 2H), 2.44 (t, *J* = 7.2 Hz, 2H), 3.23 (s, 9H), 3.65 (m, 2H), 4.01 (m, 2H), 4.20 (dd, *J* = 12.0, 6.8 Hz, 1H), 4.27 (m, 2H), 4.38 (dd, *J* = 12.0, 3.6 Hz,1H), 5.24 (m, 1H). HRMS (FAB): m/z calcd for $C_{29}H_{57}NO_{10}P$ (MH^+) 610.3720, found 610.3695.

1-Palmitoyl-2-acetyl-sn-glycero-3-phosphocholine (PAcPC) (1e). A procedure analogous to that described above for **1a** was used to get **1e** (75%). ^{1}H NMR (CD_3OD, 400 MHz): δ 0.89 (t, *J* = 6.8 Hz, 3H), 1.25-1.37 (24H), 1.60 (m, 2H), 2.08 (s, 3H), 2.33 (t, *J* =8.0 Hz, 2H), 3.23 (s, 9H), 3.63 (m, 2H), 4.01 (m, 2H), 4.20 (dd, *J* = 11.6, 6.8 Hz, 1H), 4.27 (m, 2H), 4.39 (dd, *J* = 12.0, 3.6 Hz, 1H), 5.22 (m, 1H). HRMS (FAB): m/z calcd for $C_{26}H_{53}NO_8P$ (MH^+) 538.3508, found 538.3526.

1-Palmitoyl-2-dodecanedioyl-sn-glycero-3-phosphocholine (PDPC) (4a), 1-palmitoyl-2-suberoyl-sn-glycero-3-phosphocholine (PSPC) (4b), and 1-palmitoyl-2-(3', 6'-dioxo)-suberoyl-sn-glycero-3-phosphocholine (PdiOSPC) (4c) were prepared with similar method, as shown in scheme S2. The preparation of PDPC (4a) is presented as an example.

12-(Benzyloxy)-12-oxododecanoic acid (2a). Dodecanedioic acid (1.0 g, 4.3 mmol) and triethylamine (Et_3N) (1.24 ml, 8.6 mmol) were dissolved in DMF (50 ml) and cooled to 0 ^{o}C. To this solution, benzyl bromide (0.34 g, 2 mmol) dissolved in DMF (50 ml) was added over a 1 h period. The reaction was stirred for an additional 4 h at 0 ^{o}C and allowed to slowly warm to room temperature overnight. The solvent was removed under reduced pressure. The obtained oily

residue was dissolved in aqueous 1 N HCl saturated with NaCl (80 ml) and extracted with Ethyl acetate (3 × 50 ml). The extracts were combined and concentrated under reduced pressure. The residue was purified by flash chromatography on a silica gel column, which was eluted with hexane / Ethyl acetate (2/1) to afford the monoester as white solid (980 mg, 70%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.22-1.38 (12H), 1.55-1.63 (4H), 2.30-2.42 (4H), 5.12 (s, 2H), 7.30-7.38 (5H); This spectrum agrees with that reported previously.(3)

8-(Benzyloxy)-8-oxooctanoic acid (2b). A procedure analogous to that described above for **2a** was used to get **2b** (65%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.35 (m, 2H), 1.65 (m, 2H), 2.35 (m, 2H), 5.12 (s, 2H), 7.3-7.4 (5H).

2-(Benzyloxycarbonylmethoxy-ethoxy)-acetic acid (2c). A procedure analogous to that described above for **2a** was used to get **2c** (51%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.78 (s, 4H), 4.18 (s, 2H), 4.21 (s, 2H), 5.20 (s, 2H), 7.37 (m, 5H). This spectrum agrees with that reported previously.(4)

1-Palmitoyl-2-(12'-benzyloxy-12'-oxododecanoyl)-sn-glycero-3-phosphocholine (3a) The obtained monoester 12-(benzyloxy)-12-oxododecanoic acid **2a** (64 mg, 0.2 mmol), 2-lysoPC (26 mg, 0.053 mmol) and DMAP (5.5 mg, 0.045 mmol) in dry CH_2Cl_2 (4 ml) were stirred at room temperature. Then dicyclohexylcarbodiimide (DCC) (28 mg, 0.14 mmol) in CH_2Cl_2 (0.4 ml) was added to the solution. The resulting mixture was stirred at room temperature for 24 h. The solution was then filtered, and solvent was removed with a rotary evaporator. The obtained residue was applied to a 0.5 mm silica gel TLC plate, which was eluted with $CHCl_3$/MeOH/NH_4OH (28%) (38/20/2). The major band (R_f = 0.2) was extracted with $CHCl_3$/MeOH/H_2O (1/2/0.8). The extract was filtered and then washed by Bligh/Dyer method, dried with anhydrous Na_2SO_4 and solvents were evaporated producing a white solid (30 mg, 71%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.83 (t, J = 6.8 Hz, 3H), 1.18-1.30 (36H), 1.48-1.60 (6H), 2.20-2.26 (4H), 2.30 (t, J = 7.6 Hz, 2H), 3.34 (s, 9H), 3.79 (m, 2H), 3.82-3.92 (2H), 4.05-4.12 (1H), 4.26 (m, 2H), 4.32-4.38 (1H), 5.06 (s, 2H), 5.12-5.20 (m, 1H), 7.22-7.34 (5 H).

1-Palmitoyl-2-(8'-benzyloxy-8'-oxooctanoyl)-sn-glycero-3-phosphocholine (3b). A procedure analogous to that described above for **3a** was used to get **3b** (45%). ^{1}H NMR (CD_3OD, 400 MHz): δ 0.87 (t, J = 6.8 Hz, 3H), 1.23-1.36 (28H), 1.60 (m, 6H), 2.28-2.40 (m, 6H), 3.22 (s, 9 H), 3.65 (m, 2 H), 3.98 (m, 2H), 4.18 (dd, J = 12.0, 6.8 Hz, 1H), 4.25 (m, 2H), 4.41 (dd, J = 12.0, 3.6 Hz, 1H), 5.12 (s, 2H), 5.23 (m, 1H), 7.30-7.37 (m, 5H).

1-Palmitoyl-2-(2-(benzyloxycarbonylmethoxy-ethoxy)-acetyl)-*sn*-glycero-3-phosphocholine (3c) A procedure analogous to that described above for **3a** was used to get **3c** (61%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.85 (t, *J* = 6.6 Hz, 3H), 1.18-1.32 (26 H), 1.51-1.58 (m, 2H), 2.25 (t, *J* = 7.8 Hz, 2H), 3.31 (s, 9 H), 3.68-3.80 (6 H), 3.94-4.36 (10 H), 5.15 (s, 2H), 5.26-5.32 (m, 1H), 7.28-7.38 (5 H).

1-Palmitoyl-2-dodecanedioyl-sn-glycero-3-phosphocholine (PDPC) (4a). 1-Palmitoyl-2-(12'-benzyloxy-12'-oxododecanoyl)-sn-glycero-3-phosphocholine (3a) (30 mg, 0.031 mmol) in 5 ml of $CHCl_3$/MeOH/H_2O (1/2/0.8) was hydrogenated over 10% Pd/C (10 mg) at atmospheric pressure for 3 h. The catalyst was removed by filtration, and the filtrate was concentrated. The obtained residue was applied to a 0.5 mm silica gel TLC plate, which was eluted with $CHCl_3$/MeOH/H_2O/CH_3COOH (90/26/4/1). The major band (R_f = 0.16) was extracted with $CHCl_3$/MeOH/H_2O (1/2/0.8). The extract was filtered and then washed by Bligh/Dyer method, dried with anhydrous Na_2SO_4 and solvents were evaporated producing a white solid (14.9 mg, 68%). ^{1}H NMR (CD_3OD, 400 MHz): δ 0.89 (t, *J* = 6.8 Hz, 3H), 1.25-1.37 (36 H), 1.55-1.64 (6H), 2.27 (t, *J* = 7.6 Hz, 2H), 2.29-2.36 (4H), 3.22 (s, 9 H), 3.64 (m, 2 H), 4.00 (m, 2H), 4.16 (dd, *J* = 11.6, 6.8 Hz, 1H), 4.27 (m, 2H), 4.42 (dd, *J* = 12.0, 3.2 Hz, 1H), 5.24 (m, 1H). HRMS (FAB): m/z calcd for $C_{36}H_{71}NO_{10}P$ (MH^+) 708.4816, found 708.4833.

1-Palmitoyl-2-suberoyl-sn-glycero-3-phosphocholine (PSPC) (4b). A procedure analogous to that described above for **4a** was used to get **4b** (71%). ^{1}H NMR (CD_3OD, 400 MHz): δ 0.89 (t, *J* = 6.8 Hz, 3H), 1.25-1.33 (24H), 1.33-1.38 (2H), 1.60 (m, 6H), 2.25 (t, *J* = 7.2 Hz, 2H), 2.32 (t, *J* = 7.6 Hz, 2H), 2.35 (t, *J* = 7.2 Hz, 2H), 3.23 (s, 9H), 3.65 (m, 2H), 4.01 (m, 2H), 4.20 (dd, *J* = 12.0, 6.8 Hz, 1H), 4.27 (m, 2H), 4.39 (dd, *J* = 12.0, 3.2 Hz, 1H), 5.23 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.35, 22.92, 24.70, 25.10, 28.26, 28.49, 29.40, 29.56, 29.59, 29.77, 29.89, 29.93, 32.15, 34.18, 34.30, 54.50, 59.59, 62.97, 64.14, 66.44, 70.93, 173.47, 173.76. HRMS (FAB): m/z calcd for $C_{32}H_{63}NO_{10}P$ (MH^+) 652.4189, found 652.4183.

1-Palmitoyl-2-(3', 6'-dioxo)-suberoyl-sn-glycero-3-phosphocholine (PdiOSPC) (4c). A procedure analogous to that described above for **4a** was used to get **4c** (68%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 0.87 (t, *J* = 7.0 Hz, 3H), 1.18-1.36 (24 H), 1.50-1.65 (m, 2H), 2.28 (t, *J* = 7.2 Hz, 2H), 3.31 (s, 9 H), 3.60-3.85 (6 H), 3.92-4.40 (10 H), 5.28-5.40 (m, 1H). HRMS (FAB): calcd for $C_{30}H_{59}NO_{12}P$ (MH^+) 656.3775, found 656.3767.

1-Palmitoyl-2-(6'-hydroxy)-hexanoyl-sn-glycero-3-phosphocholine (P6HHPC) (7a) and 1-palmitoyl-2-(8'-hydroxy)-octanoyl-sn-glycero-3-phosphocholine (P8HOPC) (7b) were prepared

with similar method, as shown in scheme S3. The preparation of P6HHPC (7a) is presented as an example.

6-(*tert*-Butyldimethylsilyloxy)-hexanoic acid (5a). 6-Hydroxyhexanoic acid (528 mg, 4mmol) and imidazole (653mg, 9.6mmol) were dissolved in 10ml DMF, tert-Butyldimethylsilyl chloride (TBDMSCl) (660mg, 4.4mmol) was added at 0 ^{o}C, after 30min, the reaction temperature rise to room temperature and continue to react overnight at room temperature. Then 20ml ethyl ether and 20ml saturated NaCl solution were added and the resulted solution was acidified with H_3PO_4 to pH 3. The ethyl ether layer was separated and concentrated under reduced pressure. The obtained pale yellow oil was purified by flash chromatography on silica gel (Acetone/hexanes, 1/4, TLC: R*f* = 0.3) to afford the 6-(*tert*-Butyldimethylsilyloxy)-hexanoic acid (5a) **(**440 mg, 45%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.04 (s, 6H), 0.89 (s, 9H), 1.39 (m, 2H), 1.53 (m, 2H), 1.66 (m, 2H), 2.36 (t, *J* = 7.6 Hz, 2H), 3.61 (t, *J* = 6.4 Hz, 2H). The ^{1}H NMR spectra was identical with that reported previously (5).

8-(tert-Butyldimethylsilyloxy)-octanoic acid (5b). A procedure analogous to that described above for **5a** was used to get **5b** (57%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.05 (s, 6H), 0.87 (s, 9H), 1.21-1.32 (6H), 1.45 (m, 2H), 1.57 (m, 2H), 2.29 (t, *J* = 7.4 Hz, 2H), 3.55 (t, *J* = 6.6 Hz, 2H).

1-Palmitoyl-2-(6'-(*tert*-butyldimethylsilyloxy)-hexanoyl)-sn-glycero-3-phosphocholine (6a). The obtained compound 5a (103 mg, 0.42 mmol), 2-lysoPC (30 mg, 0.06 mmol) and DMAP (6 mg, 0.048 mmol) were dissolved in dry $CHCl_3$ (3 ml) and stirred at room temperature under the protection of argon, then DCC (139 mg, 0.67 mmol) in $CHCl_3$ (0.4 ml) was added to the solution. The resulting mixture was stirred at room temperature for 48 h. The solution was then filtered, and solvent was removed with a rotary evaporator. The obtained residue was applied to a 0.5 mm silica gel TLC plate, which was eluted with $CHCl_3$/MeOH/CH_3COOH/H_2O (75/15/14/3). The product band (R_f = 0.6) was extracted with $CHCl_3$/MeOH/H_2O (1/2/0.8). The extract was filtered and then washed by Bligh/Dyer method, dried by with anhydrous Na_2SO_4 and solvents were evaporated producing a white solid (17.4 mg, 40%). ^{1}H NMR (CD_3OD, 400 MHz): δ 0.00 (s, 6H), 0.81-0.87 (12H), 1.20-1.30 (24 H), 1.30-1.38 (2H), 1.44-1.62 (6H), 2.26 (t, *J* = 7.2 Hz, 2H), 2.29 (t, *J* = 7.4 Hz, 2H), 3.17 (s, 9 H), 3.56-3.61 (4H), 3.94 (t, 2H), 4.12 (dd, *J* = 12.0, 6.8 Hz, 1H), 4.22 (m, 2H), 4.35 (dd, *J* = 12.0, 3.6 Hz, 1H), 5.18 (m, 1H).

1-Palmitoyl-2-(6'-hydroxyhexanoyl)-sn-glycero-3-phosphocholine (P6HHPC) (7a). The obtained 6a compound was dissolved in 2 ml THF. To the mixture, 100μl tetra-n-butylammonium fluoride (TBAF) (1M in THF) was added. The resulted mixture was stirred at room temperature. 5 hours later, the solvent was removed with a rotary evaporator. The obtained residue was applied to a 0.5 mm silica gel TLC plate, which was eluted with $CHCl_3$/MeOH/CH_3COOH/H_2O (50/15/14/3). The product band (R_f = 0.4) was extracted with $CHCl_3$/MeOH/H_2O (1/2/0.8). The extract was filtered and then washed by Bligh/Dyer method, dried with anhydrous Na_2SO_4 and solvents were evaporated producing a white solid (10.9 mg, 75%). ^{1}H NMR (CD_3OD, 400 MHz): δ 0.90 (t, *J* = 6.8 Hz, 3H), 1.25-1.35 (24 H), 1.35-1.45 (2H), 1.50-1.70 (6H), 2.32 (t, *J* = 7.2 Hz, 2H), 2.36 (t, *J* = 7.2 Hz, 2H), 3.22 (s, 9 H), 3.54 (t, *J* = 6.8 Hz, 2H), 3.62-3.66 (2H), 3.97-4.02 (2H), 4.16 (dd, *J* = 12.0, 6.4 Hz, 1H), 4.27 (m, 2H), 4.40 (dd, *J* = 12.0, 3.6 Hz, 1H), 5.23 (m, 1H). HRMS (FAB): m/z calcd for $C_{30}H_{61}NO_9P$ (MH^+) 610.4084, found 610.4097.

1-Palmitoyl-2-(8'-hydroxy)-octanoyl sn-glycero-3-phosphocholine (P8HOPC) (7b). A procedure analogous to that described above for **7a** was used to get **7b** (50%). ^{1}H NMR (CD_3OD, 400 MHz): δ 0.90 (t, *J* = 6.8 Hz, 3H), 1.25-1.39 (30 H), 1.50-1.55 (2H), 1.55-1.65 (4H), 2.32 (t, *J* = 7.6 Hz, 2H), 2.35 (t, *J* = 7.6 Hz, 2H), 3.22 (s, 9 H), 3.54 (t, *J* = 6.8 Hz, 2H), 3.64 (m, 2H), 3.99 (m, 2H), 4.16 (dd, *J* = 12.0, 6.8 Hz, 1H), 4.27 (m, 2H), 4.41 (dd, *J* = 12.0, 3.2 Hz, 1H), 5.23 (m, 1H). HRMS (FAB): m/z calcd for $C_{32}H_{65}NO_9P$ (MH^+) 638.4397, found 638.4398.

1-Acetyl-2-suberoyl-sn-3-phosphocholine (AcSPC) (15a), 1-palmitoyl -2-suberoyl-sn-glycero-3-phosphatidyl-(N,N,N-trimethylamino)-propanol (PSPP) (15b), 1-palmitoyl-2-suberoyl-sn-glycero-3-phosphatidyl-(N,N,N-trimethylamino)-hexanol (PSPH) (15c), 1-palmitoyl-2-suberoyl-sn-glycerol (PSG) (13) and 1-palmitoyl-2- suberoyl-sn-glycero-3-phosphatidic acid (PSPA) (17) were prepared with similar method, as shown in scheme S4. The preparation of AcSPC (15a) is presented as an example.

1,2-O-isopropylideneglycerol acetate (8a). 1,2-O-isopropylideneglycerol (3.0g, 23mmol) and triethylamine (3.0g, 30mmol) were dissolved in 20 ml methylene chloride. Acetyl chloride (2.4g, 30mmol, in 10ml methylene chloride) was added dropwise at room temperature in 30min. The mixture was stirred at room temperature for 5 hours and then filtered to remove the precipitate. The filtrate was washed with water 3 times and concentrated under reduced pressure to remove the solvent. 3.5g colorless oil was obtained. ^{1}H NMR (CD_3OD, 400 MHz): δ 1.32 (s, 3 H), 1.37 (s, 3 H), 2.05 (s, 3 H), 3.73 (m, 1 H), 4.08 (m, 3 H), 4.30(m, 1 H). The ^{1}H NMR spectra was

identical with that reported previously (6). The crude product was used directly in the next step without further purification.

1, 2-O-isopropylideneglycerol palmitate (8b). A procedure analogous to that described above for **8a** was used to get **8b**. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.88 (t, *J* = 6.8 Hz, 3H), 1.20-1.37 (24H), 1.37 (s, 3H), 1.44 (s, 3H), 1.63 (m, 2H), 2.34 (t, *J* = 7.2 Hz, 2H), 3.74 (dd, *J* = 8.4, 6.0 Hz, 1H), 4.05-4.12 (m, 2H), 4.16 (dd, *J* = 11.6, 4.8 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.36, 22.92, 25.12, 25.62, 26.91, 29.35, 29.48, 29.59, 29.68, 29.83, 29.88, 29.92, 32.15, 34.34, 64.74, 66.56, 73.89, 173.90.

1-O-acetylglycerol (9a). Compound 8a (3.3g, 19mmol) was dissolved in 15ml 80% acetic acid solution. The mixture was stirred at room temperature for 16 hours and then concentrated under reduced pressure to remove the solvent. 2.4 g pale yellow oil was obtained. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.08 (s, 3 H), 3.60 (dd, *J* = 11.6, 6.0 Hz, 1H), 3.70 (dd, *J* = 11.6, 3.6 Hz, 1H), 3.96 (m, 1 H), 4.14 (m, 2 H). The ^{1}H NMR spectra was identical with that reported previously(7). The crude product was used directly in the next step without further purification.

1-O-palmitoyl glycerol (9b). A procedure analogous to that described above for **9a** was used to get **9b**. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.87 (t, *J* = 6.8 Hz, 3H), 1.20-1.35 (24H), 1.61 (m, 2H), 2.34 (t, *J* = 7.6 Hz, 2H), 2.39 (t, *J* = 4.6 Hz, 1H), 2.78 (d, *J* = 4.8 Hz, 1H), 3.57-3.70 (2H), 3.92 (m, 1H), 4.14 (dd, *J* = 11.6, 6.0 Hz, 1H), 4.19 (dd, *J* = 11.6, 4.8 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.34, 22.92, 25.12, 29.35, 29.48, 29.59, 29.68, 29.83, 29.88, 29.92, 32.15, 34.38, 63.57, 65.36, 70.49, 174.63.

1-Acetoxy-3-(tert-butyldimethylsilyl)-oxypropan-2-ol (10a). Compound 9a (2.0g, 14.9mmol) and triethylamine (1.8g, 17.9mmol) was dissolved in 7ml DMF. To the mixture, tert-butyldimethylsilyl chloride (2.7g, 17.9mmol, in 10ml DMF) was added dropwise in 30min at room temperature. The mixture was stirred at room temperature for 1 day and then filtered to remove the precipitate. The filtrate was concentrated under reduced pressure to remove the solvent. The obtained residue was purified by flash chromatography on silica gel with Hexanes/Ethyl acetate (6/1, TLC: R*f* = 0.2) to give **10a** (1.6 g, 44%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.0 (s, 6H), 0.82 (s, 9H), 2.02 (s, 3H), 2.49 (d, *J* = 5.6 Hz, 1H), 3.54 (dd, *J* = 10.0, 5.2 Hz, 1H), 3.59 (dd, *J* = 10.0, 5.6 Hz, 1H), 3.80 (m, 1H), 4.03 (dd, *J* = 11.6, 6.0 Hz, 1H), 4.07 (dd, *J* = 11.2, 4.4 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ -5.24, 18.48, 21.10, 26.04, 63.87, 65.50, 70.11, 171.38.

1-Palmitoxy-3-(tert-butyldimethylsilyl)-oxypropan-2-ol (10b). A procedure analogous to that described above for **10a** was used to get **10b** (46%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.06 (s, 6H), 0.85-0.89 (12H), 1.20-1.35 (24H), 1.61 (m, 2H), 2.32 (t, *J* = 7.6 Hz, 2H), 2.51 (d, *J* = 5.2 Hz, 2H), 3.60 (dd, *J* = 10.0, 5.6 Hz, 1H), 3.65 (dd, *J* = 10.0, 4.4 Hz, 1H), 3.86 (m, 1H), 4.10 (dd, *J* = 11.6, 6.0 Hz, 1H), 4.13 (dd, *J* = 11.6, 4.8 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ -5.47, 14.10, 18.25, 22.67, 24.92, 25.81, 29.12, 29.25, 29.35, 29.44, 29.59, 29.64, 29.68, 31.90, 34.18, 63.66, 64.96, 69.97, 173.97.

1-(1-Acetoxy-3-(tert-butyldimethylsilyloxy)-propan-2-yl)-8-benzyl octanedioate (11a). Compound 10a (0.6g, 2.4mmol) and 0.23g pyridine were dissolved in 6ml methylene chloride. To the mixture, 7-benzyloxycarbonylheptanoyl chloride (0.82g, 2.9mmol, in 6ml methylene chloride) was added dropwise at room temperature. The resulted mixture was stirred at room temperature for 6 hours and then filtered to remove the precipitate. The filtrate was concentrated under reduced pressure to remove the solvent. The obtained residue was purified by flash chromatography on silica gel with Hexanes/Ethyl acetate (5/1, TLC: R*f* = 0.5) to give 11a (pale yellow oil, 1.0 g, 83%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.05 (s, 6H), 0.88 (s, 9H), 1.34 (m, 4H), 1.63 (m, 4H), 2.06 (s, 3H), 2.30 (t, *J* = 7.2 Hz, 2H), 2.35 (t, *J* = 7.2 Hz, 2H), 3.70-3.72 (2H), 4.16 (dd, *J* = 12.0, 6.4Hz, 1H), 4.32 (dd, *J* = 12.0, 3.6 Hz, 1H), 5.06 (m, 1H), 5.11 (s, 2H), 7.33-7.37 (m, 5H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 0.0, 23.7, 26.3, 30.2, 31.2, 34.2, 39.7, 66.9, 68.2, 71.6, 133.7, 134.0, 141.5, 176.2, 178.5, 179.0.

1-(1-Palmitoxy-3-(tert-butyldimethylsilyloxy)-propan-2-yl)-8-benzyl octanedioate (11b). A procedure analogous to that described above for **11a** was used to get **11b** (90%). ^{1}H NMR (CD_3OD, 400 MHz): δ 0.07 (s, 6H), 0.87-0.92 (12H), 1.20-1.38 (28H), 1.61 (m, 6H), 2.30 (t, *J* = 7.6 Hz, 4H), 2.35 (t, *J* = 7.6 Hz, 2H), 3.76 (d, *J* = 5.2 Hz, 2H), 4.13 (dd, *J* = 12.0, 6.4 Hz, 1H), 4.35 (dd, *J* = 12.0, 3.6 Hz, 1H), 5.05 (m, 1H), 5.10 (s, 2H), 7.30-7.37 (5H).

1-(1-Acetoxy-3-hydroxypropan-2-yl)-8-benzyl octanedioate (12a). Compound 11a (0.9g, 1.8mmol) was mixed with 22ml DMSO, 2.3ml THF, 2.3ml H_2O in 50ml flask covered with aluminum foil to protect the reaction from light. Then N-Bromosuccinimide (NBS) (1.5g, 8.4mmol) was added to the mixture at room temperature. 1 hour later, 50ml 1% sodium thiosulfate solution was added to quench the reaction. The mixture was extracted with ethyl acetate and the obtained crude product was purified by flash chromatography on silica gel with

Hexanes/Ethyl acetate (1/1, TLC: R*f* = 0.4) to give 12a (colorless oil, 0.51 g, 74%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.32 (m, 4H), 1.62 (m, 4H), 2.06 (s, 3H), 2.32 (m, 4H), 3.72 (m, 2H), 4.22 (dd, *J* = 12.0, 6.0 Hz, 1H), 4.34 (dd, *J* = 12.0, 4.4 Hz, 1H), 5.06 (m, 1H), 5.10 (s, 2H), 7.30-7.36 (m, 5H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.97, 24.87, 24.90, 28.81, 28.86, 34.33, 34.38, 61.61, 62.60, 66.37, 72.27, 128.42, 128.77, 136.2, 171.20, 173.53, 173.81.

1-(1-Palmitoxy-3-hydroxypropan-2-yl)-8-benzyl octanedioate (12b). A procedure analogous to that described above for **12a** was used to get **12b** (78%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.87 (t, *J* = 6.8 Hz, 3H), 1.20-1.37 (28H), 1.62 (m, 6H), 2.10 (t, *J* = 6.4 Hz, 1H), 2.33 (m, 6H), 3.72 (m, 2H), 4.24 (dd, *J* = 12.0, 4.8 Hz, 1H), 4.33 (dd, *J* = 12.0, 3.6 Hz, 1H), 5.07 (m, 1H), 5.11 (s, 2H) 7.30-7.38 (5H).

1-Acetyl-2-(8'-benzyloxy-8'-oxooctanoyl)-sn-3-phosphocholine (14a). Phosphorus chloride oxide (136mg, 0.89mmol) and triethylamine (98mg, 0.97mmol) were dissolved in 2.8ml methylene chloride. To the mixture, compound 12a (269mg, 0.71mmol, in 2.6ml methylene chloride) was added dropwise in 10 min at room temperature. 1.5 hours later, choline tosylate (311mg, 1.13mmol) and 0.9ml pyridine were added. The mixture was stirred at room temperature for 1 day. Then 0.6 ml water was added. 1 hour later, the reaction mixture was concentrated under reduced pressure to remove the solvent. The residue was dissolved in THF/H2O (3/1) and passed through an IWT TMD-8 (H^+, OH^-) ion exchange resin column. The obtained crude product was purified further by flash chromatography on silica gel with CH_3CN / H_2O (2/1, TLC: R*f* = 0.3) to give 14a (colorless oil, 230mg, 60%). ^{1}H NMR (CD_3OD, 400 MHz): δ 1.31 (m, 4H), 1.61 (m, 4H), 2.02 (s, 3H), 2.32 (t, *J* = 7.6 Hz, 2H), 2.36 (t, *J* = 7.6 Hz, 2H), 3.22 (s, 9H), 3.63 (m, 2H), 3.99 (m, 2H), 4.19 (dd, *J* = 12.0, 6.4 Hz, 1H), 4.27 (m, 2H), 4.37 (dd, *J* = 12.0, 3.6 Hz, 1H), 5.10 (s, 2H), 5.21 (m, 1H), 7.30-7.35 (m, 5H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 19.49, 24.57, 24.68, 28.50, 28.53, 33.71, 33.76, 53.50, 59.25, 62.55, 63.67, 65.94, 70.05, 128.03, 128.39, 136.20, 171.20, 173.40, 173.96.

1-Palmitoyl-2-(8'-benzyloxy-8'-oxooctanoyl)-sn-3-phosphatidyl-(N,N,N-trimethyl- amino)-propanol (14b). A procedure analogous to that described above for **14a** was used to get **14b** (46%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.86 (t, *J* = 6.8 Hz, 3H), 1.19-1.35 (28H), 1.50-1.67 (m, 6H), 2.10 (m, 2H), 2.27 (m, 4H), 2.33 (t, *J* = 7.6 Hz, 2H), 3.26 (s, 9H), 3.70 (m, 2H), 3.94 (m, 4H), 4.08-4.40 (2H), 5.09 (s, 2H), 5.18 (m, 1H), 7.27-7.38 (5H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.04, 22.60, 24.58, 24.62, 24.80, 28.61, 28.65, 29.08, 29.24, 29.28, 29.45, 29.58, 29.62, 31.83,

34.03, 34.07, 53.24, 61.61, 63.00, 64.00, 65.99, 70.62, 128.04, 128.10, 128.46, 135.98, 172.90, 173.36, 173.47.

1-Palmitoyl-2-(8'-benzyloxy-8'-oxooctanoyl)-sn-3-phosphatidyl-(N,N,N-trimethyl- amino)-hexanol (14c). A procedure analogous to that described above for **14a** was used to get **14c** (48%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.86 (t, *J* = 6.8 Hz, 3H), 1.19-1.38 (28H), 1.49 (m, 4H), 1.58 (m, 8H), 1.77 (m, 2H), 2.28 (m, 4H), 2.33 (t, *J* = 7.6 Hz, 2H), 3.21 (s, 9H), 3.42 (m, 2H), 3.78-3.92 (m, 4H), 4.08-4.30 (5H), 4.37 (dd, *J* = 12.0, 2.8 Hz, 1H), 5.10 (s, 2H), 5.18 (m, 1H), 7.27-7.38 (5H).

1-Palmitoyl-2-(8'-benzyloxy-8'-oxooctanoyl)-sn-3-phosphatidic acid (16). A procedure analogous to that described above for **14a** was used to get **16** (70%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.88 (t, *J* = 7.2 Hz, 3H), 1.19-1.40 (28H), 1.49-1.70 (6H), 2.24-2.40 (6H), 4.08-4.40 (4H), 5.10 (s, 2H), 5.24 (m, 1H), 7.27-7.38 (5H).

1-Acetyl-2-suberoyl-sn-3-phosphocholine (AcSPC) (15a). Compound 14a (73mg, 0.13mmol) in 7 ml of methylene chloride was hydrogenated over 10% Pd/C (10 mg) at atmospheric pressure for 1 hour. The catalyst was removed by filtration, and the filtrate was concentrated. The crude product was purified by 0.5 mm preparative silica gel TLC plate with CH_3OH/H_2O (3/1, TLC: R*f* = 0.3) to give 15a (43mg, 70%). ^{1}H NMR (D_2O, 400 MHz): δ 1.18 (m, 4H), 1.45 (m, 4H), 1.94 (s, 3H), 2.22 (t, *J* = 7.2 Hz, 2H), 2.27 (t, *J* = 7.2 Hz, 2H), 3.06 (s, 9H), 3.50 (m, 2H), 3.90 (m, 2H), 4.10-4.18 (m, 3H), 4.20 (dd, *J* = 12.0, 3.2 Hz, 1H), 5.14 (m, 1H). ^{13}C NMR (D_2O, 100 MHz): δ 21.22, 25.13, 28.76, 28.80, 34.74, 34.78, 54.97, 60.50, 63.81, 64.84, 67.03, 71.67, 174.75, 176.89, 179.94.

1-Palmitoyl-2-suberoyl-sn-glycero-3-phosphatidyl-(N,N,N-trimethylamino)-propanol (PSPP) (15b). A procedure analogous to that described above for **15a** was used to get **15b** (61%). ^{1}H NMR (CD_3OD, 400 MHz): δ 0.89 (t, *J* = 6.8 Hz, 3H), 1.25-1.47 (28H), 1.60 (m, 6H), 2.11 (m, 2H), 2.24 (m, 2H), 2.32 (t, *J* = 7.6 Hz, 2H), 2.35 (t, *J* = 7.2 Hz, 2H), 3.15 (s, 9H), 3.48 (m, 2H), 3.95 (m, 4H), 4.14 (dd, *J* = 12.0, 6.8 Hz, 1H), 4.43 (dd, *J* = 12.0, 3.2 Hz, 1H), 5.22 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.36, 18.95, 22.92, 24.77, 25.11, 28.33, 28.62, 29.41, 29.58, 29.60, 29.78, 29.90, 29.94, 32.15, 34.32, 53.55, 62.13, 63.07, 64.00, 64.28, 71.02, 173.54, 173.79. HRMS (FAB): m/z calcd for $C_{33}H_{65}NO_{10}P$ (MH^+) 666.4346, found 666.4346.

1-Palmitoyl-2-suberoyl-sn-glycero-3-phosphatidyl-(N,N,N-trimethylamino)-hexanol (PSPH) (15c). A procedure analogous to that described above for **15a** was used to get **15c** (72%). ^{1}H NMR (CD_3OD, 400 MHz): δ 0.89 (t, *J* = 6.4 Hz, 3H), 1.19-1.38 (28H), 1.40-1.55 (m, 4H), 1.62 (m, 8H), 1.81 (m, 2H), 2.28- 2.37 (m, 6H), 3.13 (s, 9H), 3.33 (m, 6H), 3.87 (m, 2H), 3.98 (m, 2H), 4.17 (dd, *J* = 12.0, 6.4 Hz, 1H), 4.45 (dd, *J* = 12.0, 2.8 Hz, 1H), 5.21 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.35, 22.45, 22.91, 24.90, 25.10, 25.36, 28.07, 28.48, 29.38, 29.54, 29.59, 29.74, 29.88, 29.93, 32.15, 34.32, 53.47, 62.97, 63.90, 65.18, 66.62, 71.00, 173.40, 173.74. HRMS (FAB): m/z calcd for $C_{36}H_{71}NO_{10}P$ (MH^+) 708.4816, found 708.4791.

1-Palmitoyl-2-suberoyl-sn-glycerol (PSG) (13). A procedure analogous to that described above for **15a** was used to get **13** (81%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.89 (t, *J* = 6.8 Hz, 3H), 1.24-1.40 (28H), 1.65 (m, 6H), 2.35 (m, 6H), 3.74 (m, 2H), 4.20 (dd, *J* = 12.0, 5.6 Hz, 1H), 4.35 (dd, *J* = 12.0, 4.6 Hz, 1H), 5.09 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.35, 22.91, 24.64, 24.83, 25.10, 28.77, 29.34, 29.49, 29.59, 29.70, 29.84, 29.88, 29.92, 32.14, 34.30, 34.32, 61.68, 62.22, 72.36, 173.54, 174.09. HRMS (FAB): m/z calcd for $C_{27}H_{51}O_7$ (MH^+) 487.3635, found 487.3637.

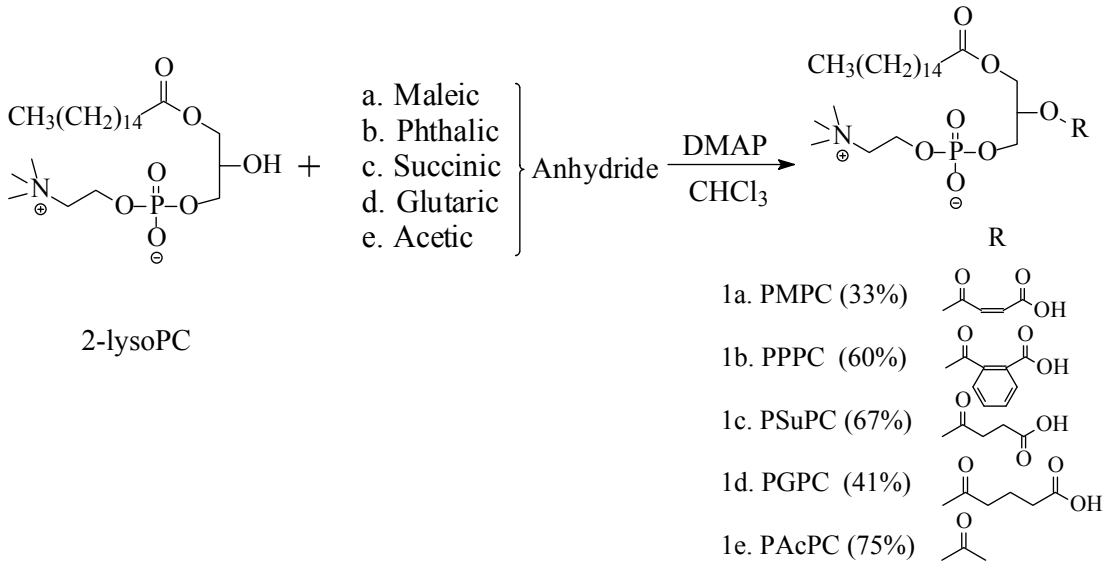
1-Palmitoyl-2-suberoyl-sn-glycero-3-phosphatidic acid (PSPA) (17). A procedure analogous to that described above for **15a** was used to get **17** (60%). ^{1}H NMR (CD_3OD, 400 MHz): δ 0.89 (t, *J* = 6.8 Hz, 3H), 1.26-1.47 (28H), 1.60 (m, 6H), 2.18-2.40 (6H), 3.90-4.02 (1H), 4.15-4.28 (1H), 4.35-4.60 (2H), 5.27 (m, 1H). HRMS (FAB): m/z calcd for $C_{27}H_{51}NaO_{10}P$ (MNa^+) 589.3118, found 589.3122.

The preparation of 1-palmitoyl-2-(9'-methoxyl-9'-oxo-nonanoyl)-sn-glycero-3-phosphocholine (P9MNPC) (18) and 1-palmitoyl-2-(8'-amino-8'-oxo)-cctanoyl-sn-glycero-3-phosphocholine (P8AOPC) (19) is presented in Scheme S5.

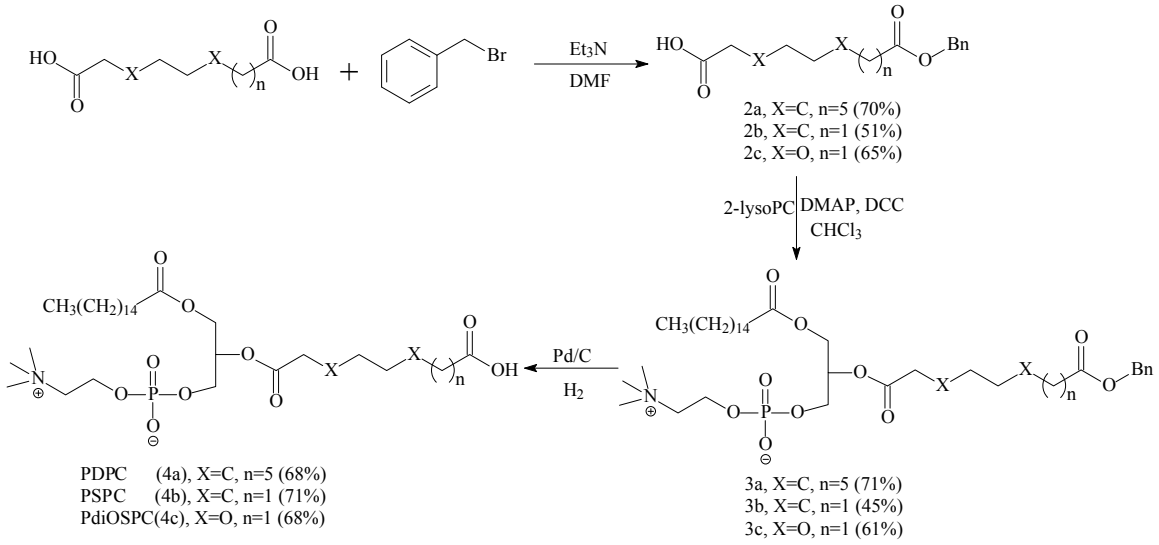
1-Palmitoyl-2-(9'-methoxyl-9'-oxo-nonanoyl)-sn-glycero-3-phosphocholine (P9MNPC) (18). A procedure analogous to that described above for **6a** was used to get **18** (38%). ^{1}H NMR (CD_3OD, 400 MHz): δ 0.89 (t, *J* = 6.8 Hz, 3H), 1.25-1.37 (30H), 1.60 (m, 6H), 1.81 (m, 2H), 2.29- 2.36 (6H), 3.22 (s, 9H), 3.65 (m, 5H), 3.98 (m, 2H), 4.15 (dd, *J* = 12.0, 6.8 Hz, 1H), 4.27 (m, 2H), 4.45 (dd, *J* = 12.0, 3.6 Hz, 1H), 5.23 (m, 1H). HRMS (FAB): m/z calcd for $C_{34}H_{67}NO_{10}P$ (MH^+) 680.4502, found 680.4485.

1-Palmitoyl-2-(8'-amino-8'-oxo)-octanoyl-sn-glycero-3-phosphocholine (P8AOPC) (19). Octanedioyl dichloride (105mg, 0.5mmol) was dissolved in 15ml anhydrous chloroform. To the

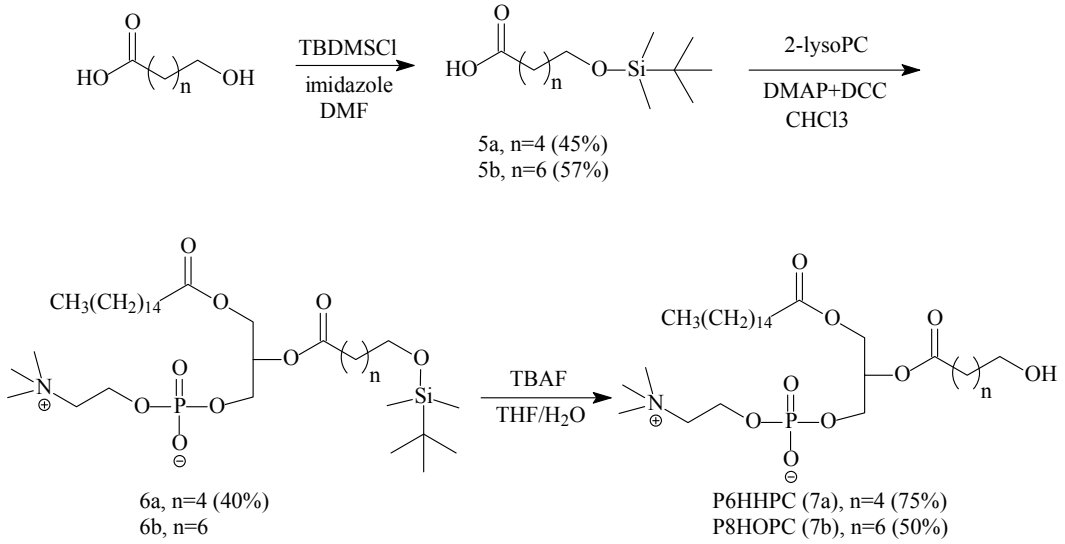
mixture, 184mg 4-dimethylaminopyridine was added at room temperature. 10 min later, 2-lysoPC (25mg, 0.05mmol, in 1ml anhydrous chloroform) was added. After 1 hour of stirring, ammonia gas was bubbled into the solution. 25min later, the mixture was concentrated to remove the solvent. The obtained residue was purified by 0.5 mm preparative silica gel TLC plate with $CHCl_3/CH_3OH/NH_3{\cdot}H_2O$ (29%) (65/35/8, TLC: R*f* = 0.28) to give **19** (10.8 mg, 34%). ^{1}H NMR (CD_3OD, 400 MHz): δ 0.89 (t, J = 6.8 Hz, 3H), 1.25-1.35 (22H), 1.36 (m, 6H), 1.61 (m, 6H), 2.21 (t, J = 7.6 Hz, 2H), 2.31 (t, J = 7.4 Hz, 2H), 2.35 (t, J = 7.4 Hz, 2H), 3.22 (s, 9H), 3.64 (m, 2H), 4.00 (m, 2H), 4.17 (dd, *J* = 12.0, 6.8 Hz, 1H), 4.26 (m, 2H), 4.40 (dd, *J* = 12.0, 3.4 Hz, 1H), 5.23 (m, 2H). HRMS (FAB): m/z calcd for $C_{32}H_{64}N_2O_9P$ (MH^+) 651.4349, found 651.4347.



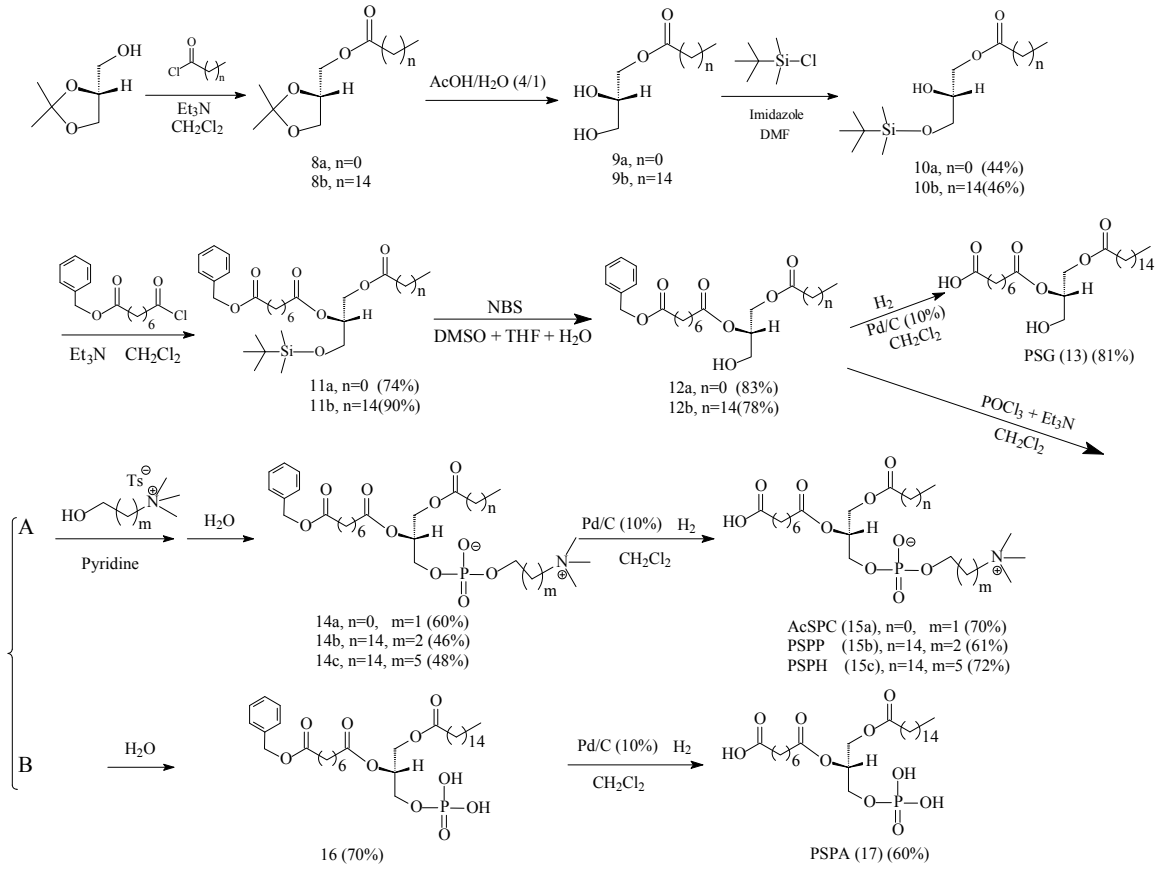
Scheme S1. The synthetic route of PMPC, PPPC, PSuPC, PGPC and PAcPC.



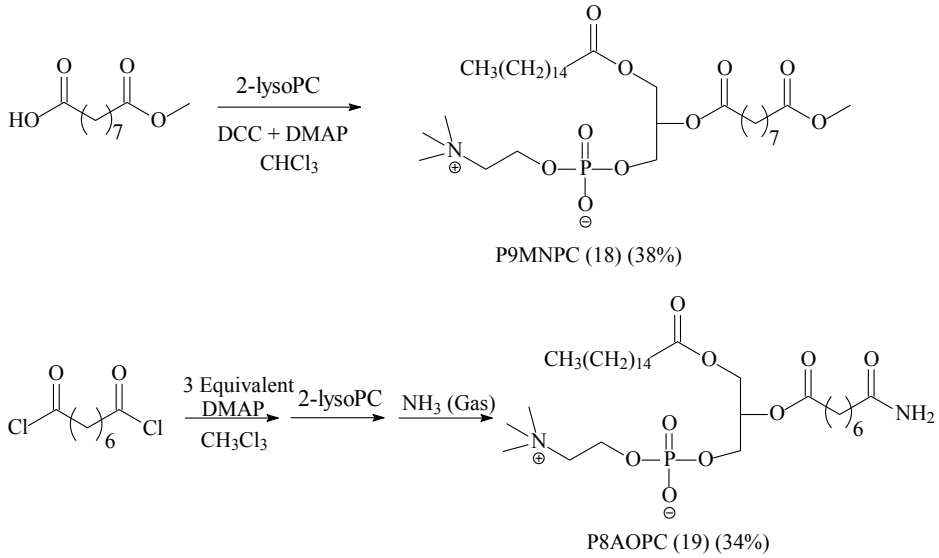
Scheme S2. The synthetic route of PDPC, PSPC and PdiOSPC.



Scheme S3. The synthetic route of P6HHPC and P8HOPC.



Scheme S4. The synthetic route of AcSPC, PSPP, PSPH, PSPA and PSG.



Scheme S5. The synthetic route of P9MNPC and P8AOPC.

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