Synthesis of a Small Library of Mixed-Acid Phospholipids from D-Mannitol as a Homochiral Starting Material

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Synthesis of a series of mixed-acid phospholipids containing a polyunsaturated fatty acid using a newly protecting strategy are described. Thus, benzyl and methyl α-(2,4-dinitrophenyl)acetic acid which were respectively removed by BCl_3 and 354 nm light are used as protecting groups.

Key words synthesis; library; phospholipid; D-mannitol; polyunsaturated fatty acid

Phospholipids constitute the main structural component of cell membranes. Due to their amphiphilic nature, they associate into aggregate structures such as vesicles, micelles and bilayers. In biological phospholipid assemblies, the nature of the lipid components affects the function and dynamics of the membrane.[1] At the same time, since their discovery, liposomes have been widely employed as models of biological membranes. Especially, this membrane model is studied for application for drug delivery system. Therefore, current investigation for the structure of biological membranes and liposomes requires efficient methods for preparation of phospholipids.[2] Phospholipids with defined fatty acid composition[3] are widely used as components of artificial membranes for physiochemical studies.[4] Phospholipids with defined fatty acid composition are widely used as fluorescent,[5] radiolabelled,[6] and spin-labeled probes[7] for study of membrane motion and as photoactivatable probes for investigation of protein–lipid interaction.[8] Phospholipids with defined fatty acid composition are also involved in signal transduction in the enzymatic processing of phospholipid.[9] A commonly employed method for synthesis involves specific deacylation of phospholipase A_2 and reacylation of the resulting 2-lysophospholipids with the desired acid. The drawback of this strategy is the difficulty for the preparation of large scale of desired compound. Therefore, efficient synthetic methods for the preparation of mixed diacyl phospholipids have to be developed. Here, we wish to report the synthesis of a small library of mixed diacyl phospholipids (Chart 1) starting from D-mannitol as the chiral starting material.

Results and Discussion

Our synthetic strategy is outlined in Chart 1, for the natural mixed acid diacylglycerol (DAG) or phospholipids are in gereral compounds with optical activity. D-Mannitol was chosen as the homochiral starting material. Preparation of (*S*)-2,3-isopropylideneglycerol **1** was first performed from D-mannitol according to the literature. Having the desired (*S*)-2,3-isopropylideneglycerol in hand, we are able to construct the intermediate **6**. Coupling of the 1,2-diacylglycerol **6** with chloroethylphosphoryl dichloride with weak base[3b] as catalyst was performed in this strategy. Compared with the standard methodology, this strategy has several advantages. Firstly, the use of a mild base as catalyst for the coupling reaction at low temperature prevents acyl group migration in the 1,2-diacylglycerol. Secondly, the intermediate phosphate diester is neutral and can be purified at this stage using normal-phase flash chromatography. Finally, this strategy is useful for synthesis of varied analogues of DAG which is an activator of protein kinase C (PKC). Thus, **1** was treated with KOH (powered) in tetrahydrofuran (THF) in the presence of 18-crown-6 as phase transfer catalyst at room temperature and followed by benzyl bromide to give compound **2** in excellent yield. Compound **2** was then treated with 60% acetic acid aqueous solution at 60 to 65 °C resulting in the removal of the 1,2-isopropylidene protecting group. The primary hydroxyl group of 1-benzylglycerol could be selectively acylated in the presence of the secondary hydroxyl group. Compound **3** was treated with desired free fatty acid in the presence of dicyclohexylcarbodiimide (DCC) and 4-dimethylaminopyridine (DMAP) at 0 °C to give compound **4** in reasonable yield. Subsequent acylation of the monoester **4** with a second carboxylic acid in the presence of DCC and DMAP proceeded without deleterious 1,2-acyl migration to furnish the mixed diacyl glycerol **5**. The 3,4-dimethoxylbenzyl,[8b] *tert*-butyldimethylsilyl (TBDMS),[11] 9-phenylxanthen-9-ol (pxOH),[12] 2,2,2-trichloroethoxycarbonyl,[13] and trityl[14] protecting groups are widely employed as protecting groups for preparation of diacylglycerols with polyunsaturated fatty acids chain instead of the benzyl group because of the lack of an efficient method for removal of the benzyl protecting group without affecting the double bonds.[15] Although there are several methods in which dimethylboron bromide has been used at low temperature to deprotect an acyl glycerol bearing benzyl, trityl, 4-methoxybenzyl or isopropylidene groups, dimethylboron bromide was not an efficient reagent for the removal of the benzyl group from glycerol. Therefore,

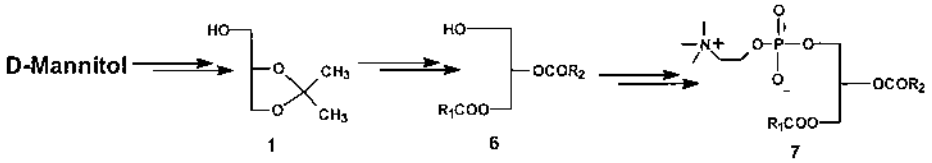


Chart 1. The Strategy for Synthesis of Mixed-Acid DAG or Phospholipid

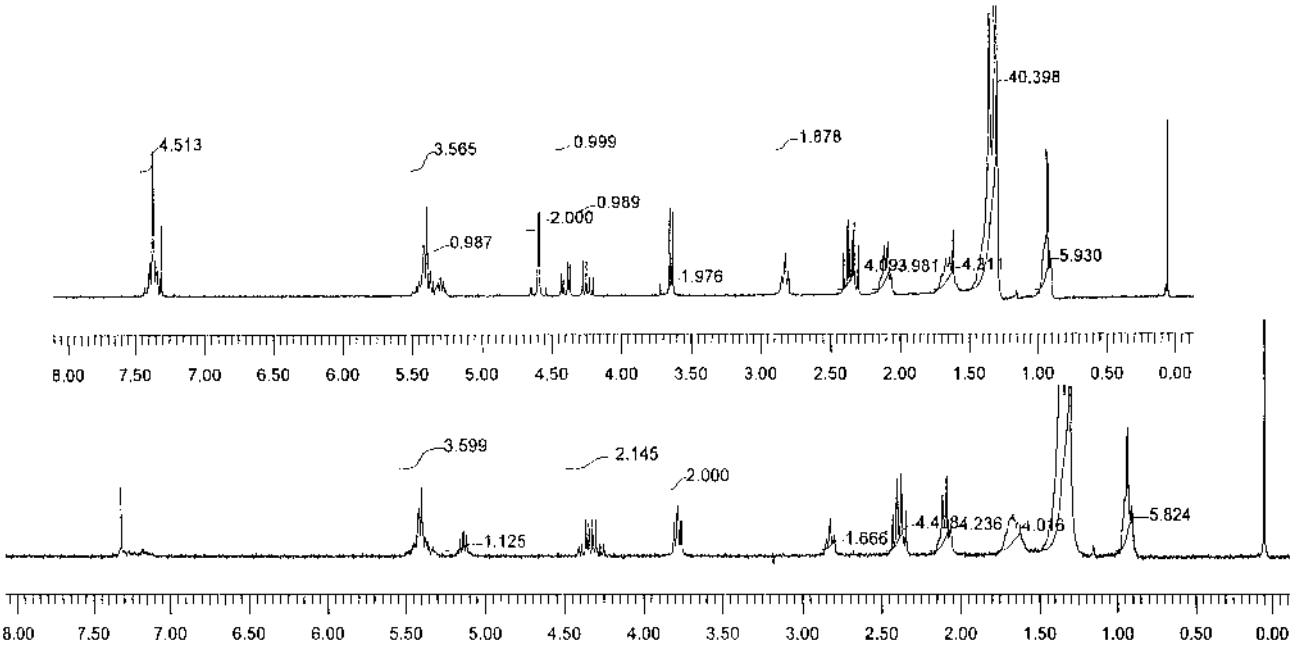


Fig. 1. The 300 MHz ^{1}H-NMR Spectra Indicated Debenzylation of Compound **5d**

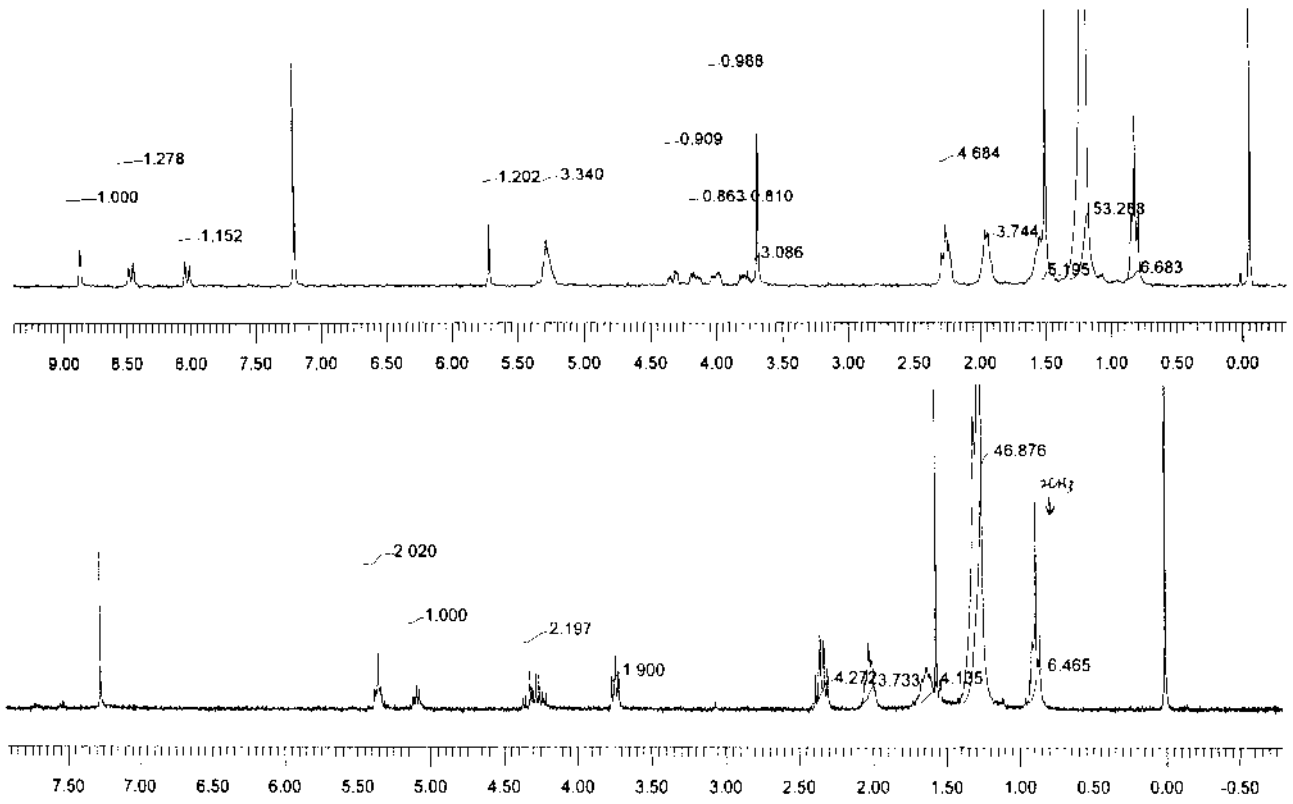
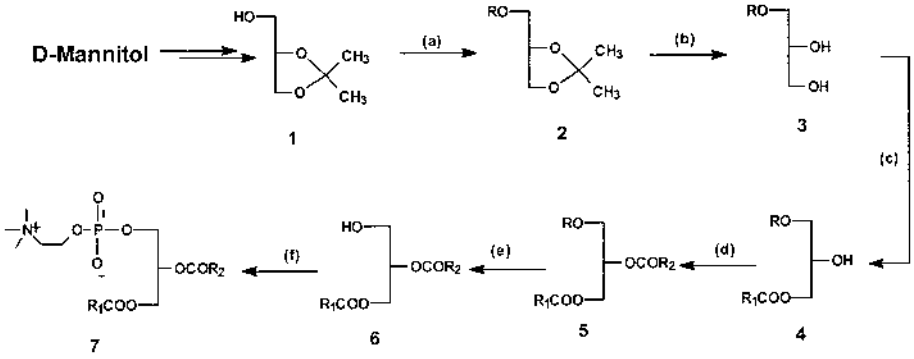


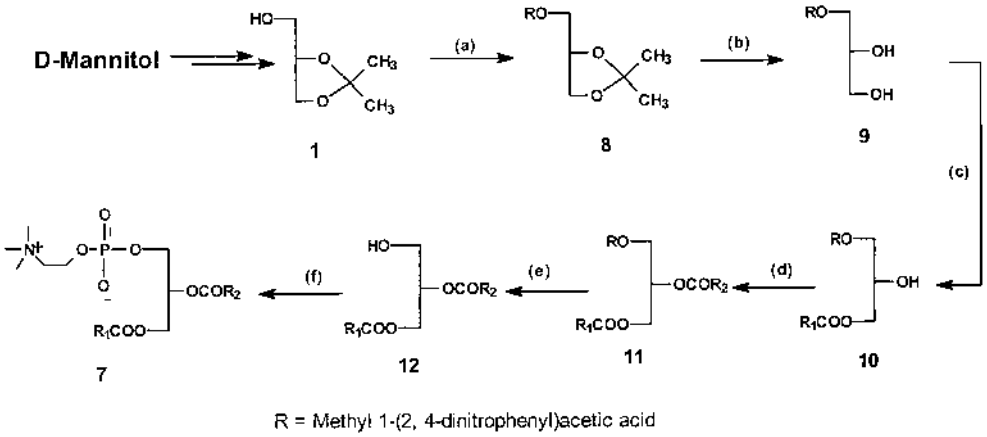
Fig. 2. The 300 MHz ^{1}H-NMR Spectra Indicated Removal of Methyl α-(2,4-Dinitrophenyl)acetate **11a**

an efficient method for removal of the benzyl group from glycerol without affecting double bonds in polyunsaturated fatty acids needed to be developed. Fortunately, when 1-benzyl-2,3-diacylglycerol **5** was exposed to boron trichloride in dry dichloromethane at low temperature, the benzyl group of 1-benzyl-2,3-diacylglycerol **5** was efficiently removed without affecting the double bonds in the polyunsaturated fatty acid and without any acyl group migration, which was confirmed by ^{1}H-NMR (Fig.1), TLC and HPLC experiments. Finally, key intermediate **6** was converted into mixed diacyl phospholipids under the standard procedure shown in Chart 2. Alternatively, methyl α-(2,4-dinitrophenyl) acetate was used as a photolabile protecting group for preparation of compound **11** from (*S*)-2,3-isopropylideneglycerol. Thus, compound **12** (see ^{1}H-NMR in Fig. 2) was obtained after compound **11** was exposed to 354 nm light in 6 h. Unfortu-



a) BnBr-KOH, 18-crown-6/THF, r.t., 3—4 h, yield 100%; b) 60% HOAc, 60—65 °C, 15 h, yield 100%; c) R_1COOH/DCC-DMAP/CH_2Cl_2, 0 °C, 6—8 h, yield 78.5—85.5%; d) R_2COOH/DCC-DMAP/CH_2Cl_2, r.t., 24 h, 65.5—69.5%; e) BCl_3/CH_2Cl_2, −78 °C to −40 °C, 6 h, yield 69.5—96.0%; f) $ClCH_2CH_2OP(O)Cl_2/Et_3N$-$CH_2Cl_2$, 0 °C to r.t., 12 h, then, $(CH_3)_3N$-EtOH, 70—80 °C, 72 h, yield 58.9—64.0%.

Chart 2



R = Methyl 1-(2, 4-dinitrophenyl)acetic acid

a) ref. 16; b) 60% HOAc, 80—65 °C, 1.5 h, yield 95—100%; c) $C_{15}H_{31}COOH$/DCC-DMAP/CH_2Cl_2, 0 °C, 6—8 h, yield 75.3%; d) R_2COOH/DCC-DMAP/CH_2Cl_2, r.t., 24 h, yield 60—65%; e) 354 nm, CH_2Cl_2, 6 h, yield 85.6—86.8%; f) $ClCH_2CH_2OP(O)Cl_2/Et_3N$-$CH_2Cl_2$, 0 °C to r.t., 12 h, then, $(CH_3)_3N$-EtOH, 70—80 °C, 72 h, yield 63.5—66.6%.

Chart 3

nately, this protocol was inefficient because it was very difficult to prepare larger amounts of precusor **12** for construction of the desired phospholipids.

In summary, we describe an efficient pathway for construction of a small library of DAGs and phospholipids from D-mannitol through developing a strategy of efficient de-protecting of the benzyl group.

Experimental

Dichloromethane was distilled from calcium hydride, triethylamine was distilled from calcium hydride, and dimethylformamide (DMF) was distilled from calcium hydride under reduced pressure. Glass-backed silica gel TLC plates were used (Silica gel F_{254}, 0.2 mm thickness). Chromatography was performed on Silical gel H (400 mesh). ^{1}H-NMR spectra were measured on a Bruker AMX-300 MHz spectrometer with tetramethylsilane as internal standard, hexadeuteroacetone and deuterochloroform as solvent. FAB and EI mass spectra were obtained on a VGQ Quattro-MS/MS spectrometer. IR was measured on Shimadzu IR-400. Optical rotations were measured on a Perkin-Elmer 241 C polarimeter.

1-*O*-Benzyl-2,3-isopropylideneglycerol 2 To a solution of 2,3-isopropylideneglycerol (500 mg, 3.79 mmol), 18-crown-6 (50 mg) in dry THF (20 ml), KOH (powered) (1.06 g, 18.95 mmol) was added and stirred at room temperature for 40 min. BnBr (967 mg, 5.69 mmol) was then added dropwise and the stirring was continued at the same temperature for 3—4 h. The solid was filtered off and the filtrate was concentrated. The residue was passed through a column of silica gel and eluted with hexane : ethyl acetate 10 : 1 to give compound **2** in quantitative yield. $[\alpha]_D^{20} = +15.5°$ (c=0.5 $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 300 MHz) 7.50—7.00 (m, 5H, ArH), 4.80—4.50 (m, 2H, OBn), 4.50—4.30 (m, 1H), 4.15—4.00 (t, 1H), 3.90—3.70 (t, 1H), 3.65—3.50 (m, 3H), 1.50 (s, 3H), 1.45 (s, 3H). EIMS (m/z): 223 (M^++1), 91(Bn^+) (100%).

1-Benzylglycerol 3 A solution of compound **2** (500 mg, 2.25 mmol) in 60% acetic acid aqueous solution (20 ml) was stirred at 60 to 65 °C for 1.5 h. The mixture was concentrated and co-evaportaed with toluene three times. The residue was then passed through a short column of silica gel and eluted with dichloromethane : methanol 20 : 1 to give compound **3** as a clear oil in quantitative yield. $[\alpha]_D^{20} = +16.5°$ (c=0.5 $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 300 MHz) 7.50—7.30 (m, 5H, ArH), 4.80—4.65 (m, 2H, OBn), 3.50—3.45 (m, 2H), 3.40—3.30 (m, 2H), 3.30—3.15 (m, 2H). EIMS (m/z): 164 (M^+-H_2O), 91 (Bn^+) (100%).

General Procedure for Selectivel Esterification of Primary Hydroxyl Group of Glycerol Derivatives with DCC and Fatty Acid To a solution of 1-benzylglycerol (1.00 mmol), fatty acid (1.5 mmol) and DMAP (0.1 mmol) in dry dichloromethane (10 ml), DCC (1.5 mmol) was added and stirred at 0 °C for 6—8 h. The solid was filtered off and the filtrate was concentrated under reduced pressure. The residue was then passed through a column of silica gel and eluted with petroleum ether : ethyl acetate (100 : 1) to give a clear oil.

1-*O*-Palmitoyl-3-Benzylglycerol 4a Yield 78.5%. $[\alpha]_D^{20} = +14.5°$ (c= 1.0 $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 7.50—7.35 (m, 5H, ArH), 4.60—4.50 (m, 2H, OBn), 4.40—4.30 (m, 3H), 3.70—3.50 (m, 2H), 2.40—2.30 (t, 2H, J=7.6 Hz, CH_2CO), 1.70—1.50 (m, 4H), 1.40—1.20 (s, 22H), 0.90 (t, 3H, J=6.8, 7.6 Hz, CH_3). EIMS (m/z): 420 (M^+), 265 ($C_{15}H_{31}CO^+$), 91 (Bn^+) (100%). *Anal*. Calcd for $C_{26}H_{44}O_4$: C, 74.25; H, 10.54. Found: C, 74.85; H, 10.90.

1-*O*-(9*z*)-Octadenyl-3-benzylglycerol 4b Yield 85.5%. $[\alpha]_D^{20} = +15.9°$

(c=1.2 $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 300 MHz) 7.55—7.35 (m, 5H, ArH), 5.40—5.30 (t, 2H, CH=CH), 4.70—4.60 (m, 2H, J=12.6 Hz, OBn), 4.30—4.20 (m, 3H), 3.70—3.65 (m, 2H), 2.40—2.20 (t, 2H, J=7.6 Hz, CH_2CO), 2.10—1.90 (m, 4H), 1.70—1.40 (t, 4H), 1.30—1.20 (s, 18H), 0.90 (t, 3H, J=6.8, 7.6 Hz, CH_3). EIMS (m/z): 446 (M^+), 279 ($C_{17}H_{33}CO^+$), 91 (Bn^+) (100%). *Anal*. Calcd for $C_{26}H_{46}O_4$: C, 75.30; H, 10.38. Found: C, 75.95; H, 10.40.

General Procedure of Esterification of Secondary Hydroxyl Group of 1-Benzyl-3-acylglycerol Derivatives with DCC and Fatty Acids To a solution of 1-benzyl-3-acylglycerol **4** (1.0 mmol), fatty acid (0.52 mmol) and DMAP (0.15 mmol) in dry dichloromethane (10 ml), DCC (0.52 mmol) was added and stirred for 24 h at room temperature. The solid was filtered off and solvent was evaporated under vacuum. The residue was purified by a column of silica gel and eluted with petroleum ether : ethyl acetate (100 : 1) to give the pure product as a clear oil.

1-*O*-Palmitoyl-2-[(9*z*)-octadenoyl]-3-benzylglycerol 5a Yield 65.5%. $[\alpha]_D^{20}$=+17.5° (c=1.0 $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 300 MHz) 7.55—7.35 (m, 5H, ArH), 5.50—5.45 (t, 2H, CH=CH), 5.45—5.25 (m, 1H, CHOCO), 4.65—4.55 (m, 2H, J=12.6 Hz, OBn, ABq), 4.50—4.40 (dd, 1H, J=7.6, 11.8 Hz, CHOCOR), 4.35—4.25 (dd, 1H, J=6.8, 12.4 Hz, CHOCOR, ABq), 3.65—3.60 (d, 2H, J=7.8 Hz, CH_2O), 2.45—2.40 (dt, 4H, CH_2CO, CH_2CO'), 2.15—2.00 (m, 4H, CH_2C=), 1.65—1.60 (m, 4H), 1.50—1.30 (s, 47H), 1.00—0.90 (t, 6H, J=7.8, 7.6 Hz, $2CH_3$). *Anal*. Calcd for $C_{43}H_{74}O_4$: C, 78.84; H, 11.38. Found: C, 78.60; H, 11.58.

1,2-*O*-Dipalmitoyl-3-benzylglycerol 5b Yield 69.5%. $[\alpha]_D^{20}$=+15.5° (c=1.0 $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 7.45—7.35 (m, 5H, ArH), 5.45—5.25 (m, 1H, CHOCO), 4.65—4.55 (d, 2H, J=12.6 Hz, OBn, ABq), 4.45—4.35 (dd, 1H, J=7.6, 11.8 Hz, CHOCOR, ABq), 4.35—4.15 (dd, 1H, J=6.8, 12.4 Hz, CHOCOR, ABq), 3.65—3.60 (d, 2H, J=7.6 Hz, CH_2O), 2.45—2.40 (dt, 4H, CH_2CO, CH_2CO'), 1.65—1.60 (m, 8H), 1.50—1.30 (s, 50H), 1.00—0.90 (t, 6H, J=7.8, 7.6 Hz, $2CH_3$). *Anal*. Calcd for $C_{41}H_{72}O_4$: C, 78.29; H, 11.54. Found: C, 78.59; H, 12.00.

1-*O*-Palmitoyl-2-archidonoyl-3-benzylglycerol 5c Yield 65.5%. $[\alpha]_D^{20}$=+17.5° (c=1.2 $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 300 MHz) 7.45—7.35 (m, 5H, ArH), 5.50—5.45 (m, 8H, 4CH=CH), 5.30—5.20 (m, 1H, CHOCO), 4.60—4.50 (m, 2H, J=12.8 Hz, Obn, ABq), 4.45—4.35 (dd, 1H, J=7.6, 11.8 Hz, CHOCOR), 4.30—4.25 (dd, 1H, J=6.8, 12.4 Hz, CHOCOR, ABq), 3.65—3.55 (d, 2H, J=7.8 Hz, CH_2O), 2.90—2.80 (m, 6H, $=CCH_2C=$), 2.45—2.40 (dt, 4H, CH_2CO, CH_2CO'), 2.15—2.00 (m, 4H, CH_2C=), 1.75—1.65 (m, 2H), 1.65—1.50 (m, 4H), 1.50—1.30 (s, 31H), 0.95—0.90 (t, 6H, J=7.8, 7.6 Hz, $2CH_3$). *Anal*. Calcd for $C_{46}H_{74}O_4$: C, 79.95; H, 10.29. Found: C, 75.35; H, 11.01.

1-*O*-Palmitoyl-2-[(9*z*,12*z*)-octadenoyl]-3-benzylglycerol 5d Yield 65.5%. $[\alpha]_D^{20}$=+17.5° (c=1.2 $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 7.45—7.30 (m, 5H, ArH), 5.50—5.45 (m, 4H, 2CH=CH), 5.30—5.20 (m, 1H, CHOCO), 4.65—4.50 (m, 2H, J=12.4 Hz, OBn, ABq), 4.45—4.00 (dd, 1H, J=7.6, 11.8 Hz, CHOCOR), 4.25—4.20 (dd, 1H, J=6.8, 12.4 Hz, CHOCOR, ABq), 3.70—3.60 (d, 2H, J=7.8 Hz, CH_2O), 2.85—2.75 (m, 2H, $=CCH_2C=$), 2.40—2.30 (dt, 4H, CH_2CO, CH_2CO'), 2.15—2.00 (m, 4H, CH_2C=), 1.75—1.60 (m, 4H), 1.50—1.30 (m, 40H), 0.95—0.90 (t, 6H, J=7.7, 7.6 Hz, $2CH_3$). HREIMS (m/z) Calcd for $C_{41}H_{70}O_4$: 652.9948. Found 652.9900.

General Procedure for Removal of the Benzyl Protecting Group from 1,2-*O*-Diacyl-3-benzylglycerol by BCl_3 at Low Temperature To a solution of 1,2-*O*-diacyl-3-benzylglycerol **5** (1.0 mmol) in dry dichloromethane (6—8 ml), trichloroborane (2.2 mmol) (1.0 M in dichloromethane) was added dropwise at −78 °C to −40 °C over 10 min. The reaction mixture was stirred at the same temperature for another 30—40 min under the protection of nitrogen. The mixture was then poured into ice water. The dichloromethane was separated and washed with ice water, dried with anhydrous sodium sulfate and concentrated at room temperature. The residue was passed through a column of silica gel and eluted with light petroleum ether : ethyl acetate 10 : 1 and 4 : 1 to give the pure compound as a clear oil.

1-*O*-Palmitoyl-2-[(9*z*)-octadenoyl]-glycerol 6a Yield 96.0%. $[\alpha]_D^{20}$=+17.5° (c=1.2 $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 300 MHz) 5.50—5.45 (t, 2H, CH=CH), 5.45—5.25 (m, 1H, CHOCO), 4.40—4.35 (dd, 1H, J=7.6, 11.8 Hz, CHOCOR, ABq), 4.35—4.20 (dd, 1H, J=6.8, 12.4 Hz, CHOCOR, ABq), 3.65—3.60 (d, 2H, J=7.8, 7.6 Hz, CH_2O), 2.45—2.40 (dt, 4H, CH_2CO, CH_2CO'), 2.15—2.00 (m, 4H, CH_2C=), 1.65—1.60 (m, 4H), 1.50—1.30 (s, 47H), 1.00—0.90 (t, 6H, J=7.8, 7.6 Hz, $2CH_3$). HREIMS (m/z) Calcd for $C_{36}H_{68}O_4$: 564.8932. Found 564.8968.

1,2-*O*-Dipalmitoyl-glycerol 6b Yield 69.5%. $[\alpha]_D^{20}$=+15.5° (c=1.0 $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 300 MHz) 5.45—5.30 (m, 1H, CHOCO), 4.45—4.35 (dd, 1H, J=7.6, 11.8 Hz, CHOCOR, ABq), 4.35—4.15 (dd, 1H, J=6.8, 12.4 Hz, CHOCOR, ABq), 3.65—3.60 (d, 2H, J=7.6 Hz, CH_2O), 2.45—2.40 (dt, 4H, CH_2CO, CH_2CO'), 1.65—1.60 (m, 8H), 1.50—1.30 (s, 50H), 1.00—0.90 (t, 6H, J=7.8, 7.6 Hz, $2CH_3$). HREIMS (m/z) Calcd for $C_{34}H_{66}O_4$: 520.8426 (M^+-H_2O). Found 520.8420.

1-*O*-Palmitoyl-2-archidonoyl-glycerol 6c Yield 88.0%. $[\alpha]_D^{20}$=+17.5° (c=1.2 $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 5.50—5.45 (m, 8H, 4CH=CH), 5.30—5.20 (m, 1H, CHOCO), 4.35—4.25 (dd, 1H, J=7.6, 11.8 Hz, CHOCOR), 4.25—4.15 (dd, 1H, J=6.8, 12.4 Hz, CHOCOR, ABq), 3.65—3.55 (d, 2H, J=7.8 Hz, CH_2O), 2.90—2.80 (m, 6H, $=CCH_2C=$), 2.45—2.40 (dt, 4H, CH_2CO, CH_2CO'), 2.15—2.00 (m, 4H, CH_2C=), 1.75—1.65 (m, 2H), 1.65—1.50 (m, 4H), 1.50—1.30 (s, 31H), 0.95—0.90 (t, 6H, J=7.8, 7.6 Hz, $2CH_3$). HREIMS (m/z) Calcd for $C_{39}H_{68}O_4$: 600.9232 Found 600.9250.

1-*O*-Palmitoyl-2-[(9*z*,12*z*)-octadenoyl]-glycerol 6d Yield 88.0%. $[\alpha]_D^{20}$=+17.5° (c=1.2 $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 5.50—5.45 (m, 4H, 2CH=CH), 5.30—5.20 (m, 1H, CHOCO), 4.45—4.40 (dd, 1H, J=7.6, 11.8 Hz, CHOCOR), 4.25—4.20 (dd, 1H, J=6.8, 12.4 Hz, CHOCOR, ABq), 3.70—3.60 (d, 2H, J=7.8 Hz, CH_2O), 2.85—2.75 (m, 2H, $=CCH_2C=$), 2.40—2.30 (dt, 4H, CH_2CO, CH_2CO'), 2.15—2.00 (m, 4H, CH_2C=), 1.70—1.60 (m, 4H), 1.50—1.30 (m, 40H), 0.95—0.90 (t, 6H, J=7.7, 7.6 Hz, $2CH_3$). HREIMS (m/z) Calcd for $C_{34}H_{64}O_4$: 562.8774. Found 562.8764.

General Procedure for Phosphorylation and Amination of 1,2-Diacylglycerol Derivatives To a solution of compound **6** (0.25 mmol) and triethylamine (1 ml) in dry dichloromethane (5 ml), β-chloroethylphosphoryl dichloride[$ClCH_2CH_2OP(O)Cl_2$] (0.5 ml) was added at 0—5 °C. The reaction mixture was then stirred at room temperature under the protection of nitrogen overnight. The reaction was then quenched with water and the organic layer was dried with Na_2SO_4, concentrated under reduced pressure. The residue was purified by silica gel chromatography eluting with trichloromethane : methanol: 60 : 35 to give a yellow oil which was treated with trimethylamine in ethanol (2 ml) in a sealed tube at 70 to 80 °C for 72 h. The solvent was evaporated under reduced pressure. The residue was then passed through a short column of silica gel and eluted with trichloromethane : methanol : water: 65 : 30 : 4 to give a yellow oil.

1-*O*-Palmitoyl-2-[(9*z*)-octadenoyl]-*sn*-glycerophosphocholine 7a Yield 64.0%. $[\alpha]_D^{20}$=+15.3° (c=0.5 $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 5.50—5.40 (t, 2H, CH=CH), 5.35—5.25 (m, 1 H, CHOCO), 4.45—4.30 (m, 4H, $2CH_2O$), 4.25—4.10 (m, 4H, CH_2CH_2N), 3.20—3.10 (s, 9H, NMe_3), 2.45—2.40 (dt, 4H, CH_2CO, CH_2CO'), 2.15—2.00 (m, 4H, CH_2C=), 1.65—1.60 (m, 4H), 1.50—1.30 (s, 47H), 1.00—0.90 (t, 6H, J=7.8, 7.6 Hz, $2CH_3$). ^{31}P ($CDCl_3$): −0.59 ppm. FABMS (m/z) (positive ion mode) 962 (M^++Na).

1,2-*O*-Dipalmitoyl-*sn*-glycerophosphocholine 7b Yield 60.5%. $[\alpha]_D^{20}$=+10.5° (c=1.0 $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 5.45—5.30 (m, 1H, CHOCO), 4.50—4.45 (m, 4H, $2CH_2O$), 4.30—4.20 (m, 4H, CH_2CH_2N), 3.20—3.10 (s, 9H, NM_3), 2.45—2.40 (dt, 4H, CH_2CO, CH_2CO'), 1.65—1.60 (m, 8H), 1.50—1.30 (s, 50H), 1.00—0.90 (t, 6H, J=7.8, 7.6 Hz, $2CH_3$). ^{31}P ($CDCl_3$): 0.50 ppm.

1-*O*-Palmitoyl-2-archidonoyl-*sn*-glycerophosphocholine 7c Yield 63.5%. $[\alpha]_D^{20}$=+16.5° (c=0.78 $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 5.50—5.45 (m, 8H, 4CH=CH), 5.30—5.20 (m, 1H, CHOCO), 4.50—4.45 (m, 4H, CH_2OCH_2), 4.30—4.20 (m, 4H, CH_2CH_2N), 3.20—3.10 (s, 9H, NMe_3), 2.90—2.80 (m, 6H, $=CCH_2C=$), 2.45—2.40 (dt, 4H, CH_2CO, CH_2CO'), 2.15—2.00 (m, 4H, CH_2C=), 1.75—1.65 (m, 2H), 1.65—1.50 (m, 4H), 1.50—1.30 (s, 31H), 0.95—0.90 (t, 6H, J=7.8, 7.6 Hz, $2CH_3$). ^{31}P ($CDCl_3$): −0.30 ppm.

1-*O*-Palmitoyl-2-[(9*z*,12*z*)-octadenoyl]-*sn*-glycerophosphocholine 7d Yield 58.9%. $[\alpha]_D^{20}$=+10.5° (c=1.5 $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 5.50—5.45 (m, 4H, 2CH=CH), 5.35—5.20 (m, 1H, CHOCO), 4.50—4.45 (m, 4H, CH_2CH_2O), 4.30—4.20 (m, 4H, CH_2CH_2N), 3.20—3.10 (s, 9H, NMe_3), 2.85—2.75 (m, 2H, $=CCH_2C=$), 2.40—2.30 (dt, 4H, CH_2CO, CH_2CO'), 2.15—2.00 (m, 4H, CH_2C=), 1.70—1.60 (m, 4H), 1.50—1.30 (m, 40H), 0.95—0.90 (t, 6H, J=7.7, 7.6 Hz, $2CH_3$). ^{31}P ($CDCl_3$): −0.25 ppm. HRFABMS (m/z) Calcd for $C_{49}H_{76}O_7NP$: 562.8774. Found: 562.8764. Preparation of **8** was carried out according to the literature.[16)]

1-*O*-Palimoyl-3-[methyl α-(2,4-dinitrophenyl)acetate]glycerol 10 $[\alpha]_D^{20}$=+10.5° (c=1.5 $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 9.00—8.90 (d, 1H, ArH), 8.60—8.50 (dd, 1H, ArH), 8.15—8.00 (dd, 1H, ArH), 5.90—5.85 (s, 1H, CHCOOMe), 4.40—4.10 (m, 4H, CH_2O), 4.00—3.85 (m, 1H, CHOH), 3.80—3.70 (s, 3H, $COOCH_3$), 2.40—2.30 (t, 2H, J=7.6, 7.8 Hz, CH_2CO), 1.75—1.60 (m, 2H), 1.40—1.30 (s, 20H), 1.00—0.90 (t, 3H, J=8.3, 7.8 Hz, CH_3). *Anal*. Calcd for $C_{28}H_{44}O_9$: C, 60.85; H, 8.02. Found: C, 60.25; H, 8.05.

1-*O*-Palimoyl-2-[(9*z*)-octadenoyl]-3-[methyl α-(2,4-dinitrophenyl)acetate]glycerol 11a $[\alpha]_D^{20}$=+10.5° (c=1.5 $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 300

MHz) δ 8.90—8.85 (d, 1H, ArH), 8.50—8.40 (dd, 1H, ArH), 8.10—8.00 (dd, 1H, ArH), 5.75—5.65 (s, 1H, CHCOOMe), 5.40—5.25 (m, 2H, CH=CH), 4.35—4.25 (dd, 1H), 4.20—4.10 (dd, 1H), 4.05—3.95 (m, 1H), 3.85—3.70 (m, 1H), 3.65 (s, 3H, $COOCH_3$), 2.30—2.15 (m, 4H, CH_2CO, CH_2CO'), 2.00—1.90 (dd, 4H, $2CH_2C=$), 1.60—1.50 (m, 4H), 1.30—1.15 (s, 54H), 0.90—0.85 (t, 6H, $2CH_3$). *Anal*. Calcd for $C_{46}H_{76}O_{10}$: C, 67.66; H, 9.38. Found: C, 67.76; H, 9.58.

1-*O*-Palimoyl-2-arachidonoyl-3-[methyl α-(2,4-dinitrophenyl)acetate]-glycerol 11b $[\alpha]_D^{20}=+10.5°$ (c=1.5 $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 8.90—8.85 (d, 1H, ArH), 8.50—8.40 (dd, 1H, ArH), 8.10—8.00 (dd, 1H, ArH), 5.80—5.70 (s, 1H, CHCOOMe), 5.50—5.20 (m, 8H, 4CH=CH), 4.45—4.35 (dd, 1H), 4.25—4.15 (dd, 1H), 4.10—4.00 (m, 1H), 3.90—3.80 (m, 1H), 3.80—3.75 (s, 3H, $COOCH_3$), 2.85—2.75 (t, 6H, $=CCH_2C=$), 2.40—2.35 (m, 4H), 2.15—2.00 (m, 4H, CH_2CO, CH_2CO'), 2.00—1.90 (dd, 4H, $2CH_2C=$), 1.60—1.50 (m, 4H), 1.30—1.15 (s, 54H), 0.90—0.85 (t, 6H, $2CH_3$). *Anal*. Calcd for $C_{48}H_{74}O_{10}$: C, 68.70; H, 8.89. Found: C, 68.85; H, 9.50.

General Procedure for Removal of the Methyl α-(2,4-Dinitrophenyl)-acetate Group from 11a and 11b Compound **11** (2 mg) in ethanol (2 ml) was photoirradiated at room temperature for 6 h. The mixture was concentrated. The residue was then passed through a short column of silica gel and eluted with petroleum ether : ethyl acetate 10 : 1 and 4 : 1 to give the pure compound **12** in 85.6—86.8% yield.

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