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The chemical synthesis of a series of ether phospholipids from D-mannitol and their properties

Jie Xia and Yong-Zheng Hui *

State Key Laboratory of Bio-organic and Natural Products of Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, China

Abstract: The synthesis of the novel ether phospholipids from D-mannitol as homochiral material using a new method for the removal of a tert-butyldimethylsilyl group for hydroxyl protection without acyl migration and their properties including bioactivity are described.
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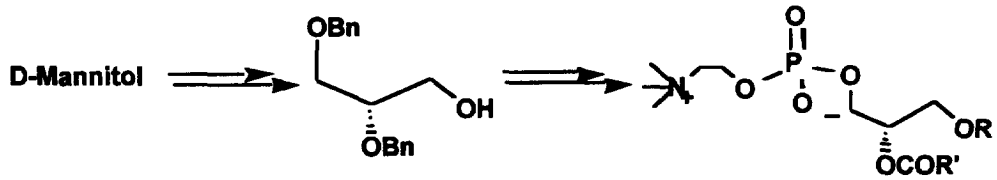
Introduction

Antitumor active ether phospholipids occupy a particularly important position as they represent a new class of chemotherapeutic agents with potent and selective anticancer activity *in vitro* or *in vivo*.[1–4] For example, the platelet-activating factor, PAF (1-octadecyl-2-acetyl-sn-glycerophosphocholine) and its analogues have been shown to exhibit a broad spectrum of biological activities.[5–9] Replacement of the sn-2-acetyl-moiety of PAF by a short alkyl (methyl or ethyl) group or introduction of a 2-acetamido function resulted in a series of highly potent and selective tumor-cytotoxic ether phospholipids.[10] The importance of these and related PAF derivatives is best illustrated by the fact that three such analogues have entered clinical trials as potential antileukemic and anticancer drugs.[11] Therefore, the development of efficient methods for the preparation of biologically active structural analogues of platelet activating factor has continued to be one of the most timely problems. Here, we describe a convenient method for the synthesis of the novel analogues of PAF, 1-alkyl-2-acyl-sn-glycerophosphocholine starting from D-mannitol[12] using a new method for the removal of a tert-butyldimethylsilyl group for hydroxyl protection without acyl migration and describe their properties.

Results and discussion

As the natural ether phospholipids are in general chiral enantiomerically pure compounds, our synthetic strategy is outlined in Scheme 1.

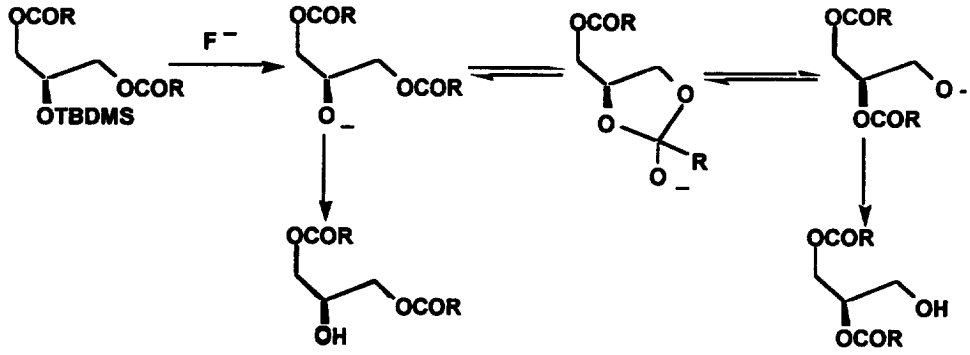


Scheme 1.

2,3-Di-O-benzylglycerol **1** as a starting material was prepared from D-mannitol according to literature.[13] Thus, the alkoxide of compound **1** prepared using sodium hydride (60% dispersion) in dry THF was alkylated with alkyl-1-ol-O-methanesulfonate to afford 1-alkyl-2,3-di-O-benzylglycerol **2a,b**. Catalytic hydrogenolysis of compounds **2a,b** in chloroform–methanol with Pd–C (10%) led to the removal of the benzyl group and formation of 1-alkylglycerols **3a,b**. The next step in the synthetic sequence was a reaction selective for the primary hydroxyl over the secondary hydroxyl group in

* Corresponding author.

the compounds **3a,b**. The trityl group had frequently been used as a selective protecting group in phospholipid synthesis,[14] but as an alternative method, we have re-examined a silylation–desilylation sequence. Silylation of compounds **3a,b** with tert-butyldimethylchlorosilane was very selective, giving the monosilyl ethers **4a,b** in nearly quantitative yield. Esterification of the compounds **4a,b** with a series of fatty acids under esterification conditions afforded the compounds **5a–h**. The tert-butyldimethylsilyl group had been considered unsuitable as a protecting group for diacylglycerol because of the standard methods for the removal of the tert-butyldimethylsilyl group accompanied by extensive acyl migration[15] shown in Scheme 2, and 1–3 and 1–2 acyl migration in the intramolecular backbone of glycerol are general problems in lipid chemistry; the intramolecular migration mainly depends on the length of the fatty acids side chains, it occurs more slowly with long linear fatty acid.[16] However, we had found that pyridinium para-toluenesulfonate (PPTS) which was a weaker acid (pH=3.0 in 1.0 M aqueous solution) than acetic acid (pH=2.4 in 1.0 M aqueous solution)[17] in dichloromethane–methanol might be mild enough to be used for this deprotection without any acyl migration under carefully controlled conditions. Therefore, by using PPTS with compounds **5a–h**, we were able to obtain key intermediate compounds **6a–h**, 1-alkyl-2-acylglycerol **6a–h**, without any acyl migration as shown in Table 1.



Scheme 2.

The ^{1}H NMR spectrum of intermediate compounds **6a–h** showed a single methylene signal (δ 2.40–2.20 ppm). For example, the part of the ^{1}H NMR spectrum of intermediate compound **6g**, showed a single triplet signal for two protons of methylene from fatty acid chain (R**CH**$_2$COOCH) at 2.4–2.2 ppm in Figure 1. In contrast to 2—3 acyl migrated product, there was always a double triplet signal of two different kinds of methylene (R**CH**$_2$COOCH and R**CH**′$_2$COOCH) at 2.4–2.2 ppm because of formation of two different esters. One is the primary alcohol ester, the other is

Table 1. The removal of t-butyldimethylsilyl group from 1-alkyl-2-acyl-3-t-butyldimethylsilylglycerol **5a–h**

No	Reagent	Temp (°C)	Time (days)	Yield (%)
6a	PPTS	0 - -5	4-7	86.1
6b	PPTS	0 - -5	4-7	75.0
6c	PPTS	0 - -5	4-7	66.7
6d	PPTS	0 - -5	4-7	80.0
6e	PPTS	0 - -5	7-14	75.0
6f	PPTS	0 - -5	7-14	70.0
6g	PPTS	0 - -5	7-14	85.3
6h	PPTS	0 - -5	7-14	81.0

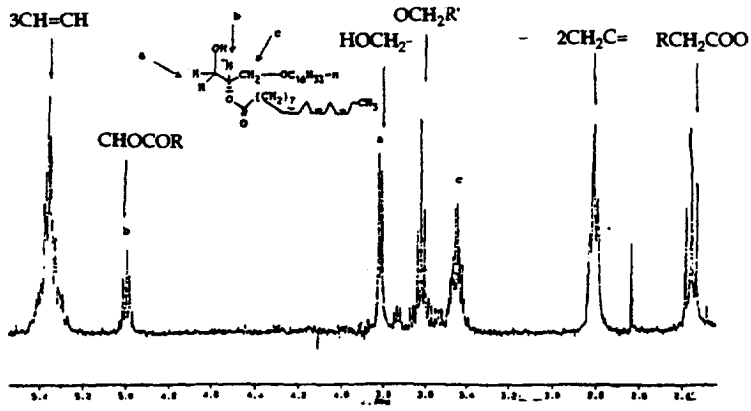


Figure 1. The part ^{1}H NMR spectrum of intermediate compound **6g**.

the secondary alcohol ester. To further verify that no 2→3 acyl migration occurred, 1-hexadecyl-2-[(9z,12z,15z)-octadecatrienoyl]-3-trimethylsilylglycerol was prepared and analyzed as its silylated derivative by using capillary gas chromatography (GC). The result revealed that 1-hexadecyl-2-[(9z,12z,15z)-octadecatrienoyl]-3-trimethylsilylglycerol was >99% pure on the basis of the limits of the method. Alcohols **6a–h** were converted to optically active phosphocholine ether-esters by using the standard procedure shown in Scheme 3.

In water, phospholipids spontaneously assemble into higher molecular aggregates if their concentration surpasses a critical level, called the critical miceller concentration (CMC). The type of aggregates formed depends not only on the chemical structure of the lipid but also physical parameters such as the surface charge, temperature, and ionic environment. For typical membrane lipids such as 1-palmitoyl-2-oleoyl-sn-glycerophosphocholine, the CMC values are smaller than 10^{-10} M. Therefore, the concentration of lipid actually dissolved in the water is negligibly small and the phospholipids are true membrane components. The decisive parameter is the ratio of the surface requirement of the apolar and the polar regions of the molecule. The most important types of organized structures formed by phospholipids are micelles, lamellar bilayer structures, vesicles, and hexagonal structures. When the ratio of the surface requirement of the apolar and the polar regions of the molecules is near 1, they form spheres enclosing water, called vesicles or liposomes with extended lamellar bilayer as shown in Figure 2.

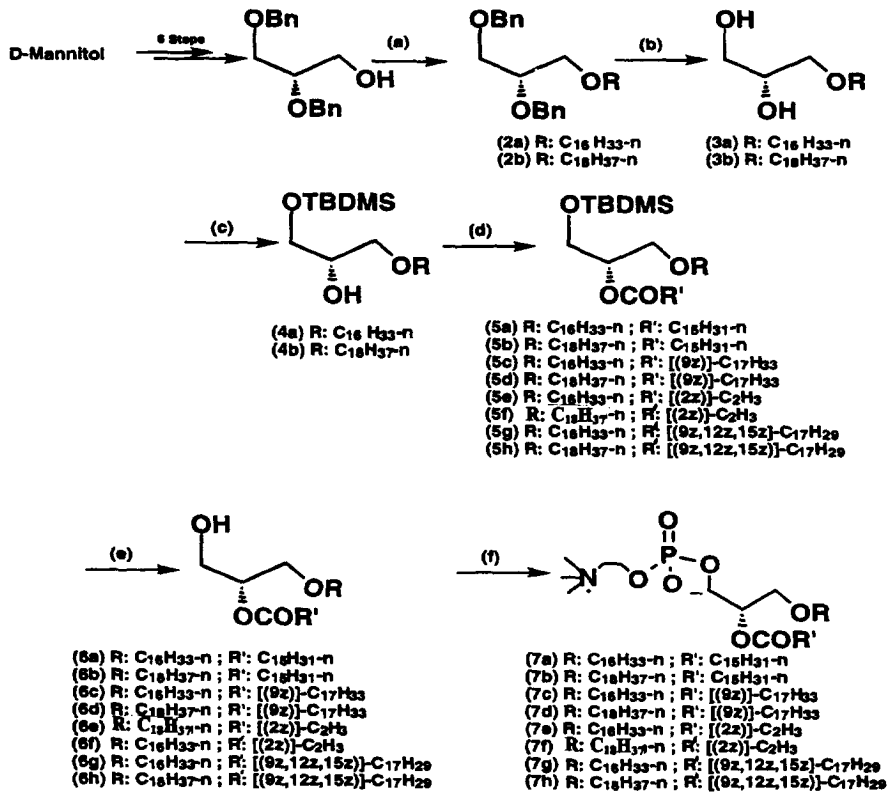
The bilayer forming properties[18] of phospholipids **7a–d**, **7g,h** were studied by coating the lipid onto the wall of a round-bottomed flask (dichloromethane evaporation), dispersing the lipid onto doubly distilled water, and irradiating the dispersion with ultrasound at 50°C for about 10–20 minutes. TLC indicated that no lipid decomposition occurred during sonication. Opalescent derived from phospholipids **7a–d** and **7g,h** are shown in Figure 3. The average diameter of vesicles derived from phospholipids **7a–d** and **7g,h** are shown in Table 2.

The phase transition of phospholipids shown in Table 3 was obtained by changes in absorbance at 400 nm as a function of temperature which were used to monitor phase-transition behavior in the vesicular state.[18]

Finally, studies were completed on the bioactivity of 1-hexadecyl-2-acyl-sn-glycerophosphocholines **7g**. The experimental results showed that the ether phospholipid **7g** had weakly inhibitory aggregation, only 4.3% (1.2×10^{-6} M), of rabbit platelets induced by platelet-activating factor (PAF).

Conclusion

The synthesis of the novel ether phospholipids from D-mannitol as homochiral material using a new method for the removal of a tert-butyldimethylsilyl group for hydroxyl protection without any acyl



Scheme 3.

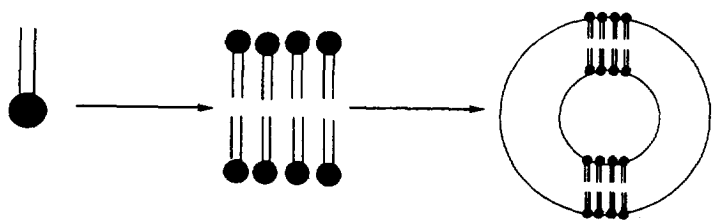


Figure 2. The organization of phospholipids in water.

migration has been described. In addition, some of the physical properties and the biological activities of the novel ether phospholipids have been characterized.

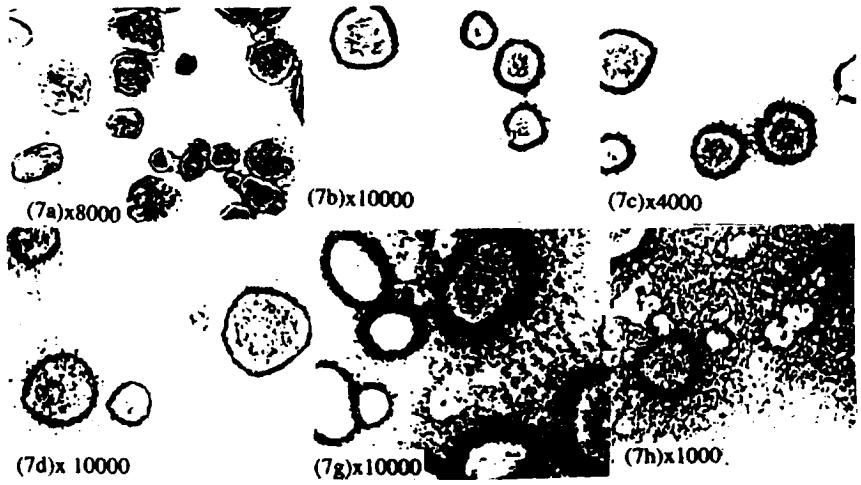


Figure 3. The electron micrographs of vesicles of phospholipids (**7a–d, 7g,h**).

Table 2. The average diameter of vesicles derived from phospholipids (**7a–d, 7g,h**)

Phospholipids	Diameter (nm)	Thickness (A)
7a	1100-1900	100-150
7b	1200-1800	100-160
7c	1250-2750	100-100
7d	1300-2700	100-120
7g	1000-2300	100-150
7h	700-1500	100-130

Table 3. The phase transition of phospholipids (**7a–d, 7g,h**)

Phospholipids	Temperature (°C)
7a	36.5
7b	37
7c	34
7d	36
7g	35
7h	37

Experimental

General methods and materials

Dichloromethane was distilled from calcium hydride; triethylamine was distilled from calcium hydride; DMF was distilled from calcium hydride under reduced pressure; PPTS (pyridinium p-toluenesulfonate) was prepared according to the literature.[17] Glass-backed silica gel TLC plate (silica gel F254, 0.2 mm thickness) were supplied by Qing Dao, China. Chromatography was performed on silica gel H, 400 mesh, from Qing Dao, China. ^{1}H NMR spectra were measured on a Bruker AMX-300M Hz spectrometer with tetramethysilane as internal standard, hexadeuterioacetone and

deuteriochloroform as solvent. EI mass spectra were obtained on a VGQuattro-MS/MS spectrometer. IR were measured on a Shimadzu IR-440. Optical rotations were measured on a Perkin–Elmer 241c Polarimeter. Quantitative gas chromatographic analysis (GC) of the 1-hexadecyl-2-[(9z,12z,15z)-octadecatrienoyl]-3-trimethylglycerol was performed using a capillary DB-1 column (25 m, 0.25 i.d. 1 μm film) at 250°C (oven temperature). Turbidity was measured on a Perkin–Elmer Lambda 5 UV-Vis spectrometer at 400 nm. The bilayer formation of lipid was obtained by coating the lipid (1.8 mg) onto a double bottom flask (dichloromethane evaporated under vacuum 3–10 mmHg for 6–8 hours), dispersing the lipid into double distilled water (5 ml), irradiating the dispersion with ultrasound at 50°C for 20 min, and keeping for stablization in a refrigerator for half an hour.

Inhibition of PAF-induced platelet aggregation assay[19]

About 100 ml of blood was collected and platelet-rich plasma (PRP) was recovered from 20 ml blood centrifuged at 800–900 rpm $-\times$ 15 min at room temperature. Dilutions (1:3000) of PRP in Isoton diluent were made and the platelet count was determined to be from 340,000 to 560,000 per μl. The incubation mixture consisted of 350 μl of PRP, 50 μl test compound and 45 μl of L-PAF agonist. Briefly, 400 μl of PRP was stablized for 1–2 min at 37°C to achieve a stable baseline. Fifty microliters of test compound (final concentration ranging from 10^{-8} to 10^{-5}) was added and incubated for 6 min and the challenge concentration (5×10^{-8} or 1×10^{-7} of PAF) was added. The percent of inhibitory aggregration and the concentration needed to inhibit platelet aggregation were determined.

General procedure for alkylation of 1,2-dibenzylglycerol

To a solution of 2,3-dibenzylglycerol (1 mmol) in dry THF (25 ml), sodium hydride (3.6–3.75 mmol) (60% dispersion) was added. The temperature was raised to 50–55°C and maintained for 30 min. Alkylmethanesulfonate (1.1–1.7 mmol) was then added and the temperatue raised to refluxing temperature and continued for 8 hours. The reaction was complete as shown by TLC and ended by pouring the solution into ice water. It was then extracted with dichloromethane and the organic phase separated and washed with water three times. The combined organic phase was dried with anhydrous sodium sulfate. The solution was concentrated under reduced pressure to give crude oil and purified by silica gel chromatography eluting with petroleum ether–ethyl acetate (100:1 and 20:1) resulting in pure product.

1-Hexadecyl-2,3-dibenzylglycerol ***2a***

Yield: 88%; $[\alpha]^{20}_D$=+3.3 [c=0.11 $CHCl_3$]; EIMS (m/e): 405 (M^+-CH_2Ph), 91 (CH_2Ph) (100%), 57; ^1H NMR (acetone-d_6) δ 7.40–7.20 (m, 10H, Ar), 4.80–4.60 (s, 2H, CH_2Ph), 4.60–4.50 (s, 2H, CH_2Ph), 3.90–3.75 (m, 1H, CHO), 3.70–3.50 (m, 4H, CH_2OCH_2), 3.50–3.40 (t, 2H, J=6.4 Hz, J=6.3 Hz, CH_2O), 1.60–1.50 (m, 2H), 1.40–1.20 (s, 26H), 0.90–0.80 (t, 3H, J=6.4 Hz, J=7.0 Hz, CH_3); Anal. calcd for $C_{33}H_{52}O_3$: 79.49 (C%), 10.55 (H%). Found: 79.02 (C%), 10.45 (H%).

1-Octadecyl-2,3-dibenzylglycerol ***2b***

Yield: 85.5%; $[\alpha]^{20}_D$=+4.08 [c=0.76 $CHCl_3$]; EIMS (m/e): 433 (M^+-CH_2Ph), 91 (CH_2Ph) (100%), 57, 43; ^1H NMR (acetone-d_6) δ 7.40–7.20 (m, 10H, Ar), 4.80–4.60 (s, 2H, CH_2Ph), 4.60–4.50 (s, 2H, CH_2Ph), 3.90–3.75 (m, 1H, CHO), 3.70–3.50 (m, 4H, CH_2OCH_2), 3.50–3.40 (t, 2H, J=6.4 Hz, J=6.3 Hz, CH_2O), 1.60–1.50 (m, 2H), 1.40–1.20 (s, 30H), 0.90–0.80 (t, 3H, J=6.4 Hz, J=7.0 Hz, CH_3); Anal. calcd for $C_{35}H_{56}O_3$: 80.10 (C%), 10.76 (H%). Found: 80.50 (C%), 11.07 (H%).

General procedure for debenzylation of 1-alkyl-2,3-dibenzylglycerol

To a solution of 1-alkyl-2,3-dibenzylglycerol (1 mmol) in a mixed solvent of methanol and chloroform, Pd–C (10%) (64 mg) was added and hydrogenated overnight at room temperature. The solution was then filtered and the organic phase was concentrated under reduced pressure to give a crude product which was purified on silica gel chromatography eluting with petroleum ether–ethyl acetate (4:1 and 2:1) resulting in a white solid.

1-Hexadecylglycerol ***3a***

Yield: 86%; $[\alpha]^{20}_D$=+4.33 [c=0.15 $CHCl_3$]; EIMS (m/e): 317 (M^++1), 57 (100%), 43; ^{1}H NMR (acetone-d_6) δ 3.98–3.80 (m, 1H, CHO), 3.75–3.70 (dd, 1H, J=3.6 Hz, J=11.3 Hz, CH_2O), 3.50–3.40 (t, 2H, J=6.4 Hz, J=6.3 Hz, CH_2O), 1.60–1.50 (m, 2H), 1.40–1.20 (s, 26H), 0.90–0.80 (t, 3H, J=6.4 Hz, J=7.0 Hz, CH_3); Anal. calcd for $C_{19}H_{40}O_3$: 72.09 (C%), 12.73 (H%). Found: 72.59 (C%), 12.27 (H%).

1-Octadecylglycerol ***3b***

Yield: 82%; $[\alpha]^{20}_D$=+2.5 [c=0.15 $CHCl_3$]; EIMS (m/e): 345 (M^++1), 327 (M^+−OH), 57 (100%), 43; ^{1}H NMR (acetone-d_6) δ 4.00–3.85 (m, 1H, CHO), 3.80–3.70 (dd, 1H, J=3.3 Hz, J=11.3 Hz, CH_2O), 3.70–3.60 (t, 2H, J=4.9 Hz, J=11.3 Hz, CHO), 3.60–3.40 (m, 4H, CH_2OCH_2), 1.70–1.50 (t, 2H), 1.40–1.30 (s, 30H), 0.90–0.80 (t, 3H, J=6.4 Hz, J=7.0 Hz, CH_3); Anal. calcd for $C_{21}H_{44}O_3$: 73.19 (C%), 12.87 (H%). Found: 73.57 (C%), 12.27 (H%).

General procedure for monosilylation of 1-alkylglycerol

To a solution of 1-alkylglycerol (1.38 mmol) in dry dichloromethane (10 ml) and dry DMF (1 ml), t-butyldimethylsilylchloride (1.66 mmol), triethylamine (3.21 mmol) and 4-(N,N-dimethylamino)pyridine (1.1 mmol) were added. The solution was stirred for 24 hours at room temperature and completion shown by TLC. The solvent was removed under reduced pressure to give a crude product which was purified on silica gel chromatography eluting with petroleum ether–ethyl acetate (10:1) resulting in an oil.

*1-Hexadecyl-3-t-butyldimethylsilyl-*D*-glycerol* ***4a***

Yield: 95.5%; $[\alpha]^{20}_D$=+2.3 [c=1.5 $CHCl_3$]. IR (film): 3500–3400 cm^{-1}; EIMS (m/e): 431 (M^++1), 13 (t-$BuSiMe_2$) (100%), 57, 43; ^{1}H NMR (acetone-d_6) δ 3.80–3.60 (m, 3H, OCH_2CHO), 3.50–3.40 (m, 4H, CH_2OCH_2), 1.60–1.50 (t, 2H), 1.40–1.30 (s, 26H), 1.00–0.80 (m, 12H, $4CH_3$), 0.10–0.00 [s, 6H, $(CH_3)_2Si$]; HREIMS (m/e): 373.3137 ($M^+-C_4H_9$). Calcd: 373.3136.

*1-Octadecyl-3-t-butyldimethylsilyl-*D*-glycerol* ***4b***

Yield: 93.5%; $[\alpha]^{20}_D$=+1.88 [c=0.78 $CHCl_3$]; IR(film): 3500–3400 cm^{-1}; EIMS (m/e): 459 (M^++1), 131 (t-$BuSiMe_2$) (100%), 57, 43; ^{1}H NMR (acetone-d_6) δ 3.80–3.60 (m, 3H, OCH_2CHO), 3.50–3.40 (m, 4H, CH_2OCH_2), 1.60–1.50 (t, 2H), 1.30–1.20 (s, 30H), 1.00–0.80 (m, 12H, $4CH_3$), 0.10–0.00 [s, 6H, $(CH_3)_2Si$]; HREIMS (m/e): 401.3458 ($M^+-C_4H_9$). Calcd: 401.3465.

General procedure for esterification of protected glycerol derivatives with DCC and fatty acids

To a solution of 1-alkyl-3-t-butyldimethylglycerol (0.15 mmol), fatty acid (0.52 mmol) and 4-(N,N-dimethylamino)pyridine (0.15 mmol) in dry dichloromethane (10 ml), DCC (0.52 mmol) were added and stirred for three to four days at room temperature. The reaction was completed as shown by TLC. The solution was filtered and the solvent was removed under reduced pressure to give a crude product. The crude product was then purified on silica gel chromatography eluting with petroleum ether–ethyl acetate (100:1) resulting in an oil.

1-Hexadecyl-2-palmitoyl-3-t-butyldimethylsilylglycerol ***5a***

Yield: 60.9%; $[\alpha]^{20}_D$=+5.5 [c=0.54 $CHCl_3$]; IR (film): 1750 cm^{-1}; EIMS (m/e): 314, 239 ($C_{15}H_{31}CO^+$), 131 (t-$BuSiMe_2$), 57 (100%), 43; ^{1}H NMR ($CDCl_3$) δ 5.10–4.90 (m, 1H, CHOCO), 3.90–3.75 (m, 2H, CH_2O), 3.70–3.50 (m, 2H, CH_2O), 3.50–3.40 (m, 2H), 2.40–2.20 (t, 2H, CH_2CO), 1.70–1.50 (dt, 4H), 1.50–1.20 (s, 50H), 1.00–0.90 (m, 15H, $5CH_3$), 0.10–0.00 [s, 6H, $(CH_3)_2Si$]; HREIMS (m/e): 611.5665 ($M^+-C_4H_9$). Calcd: 611.5660.

1-Octadecyl-2-palmitoyl-3-t-butyldimethylsilylglycerol ***5b***

Yield: 60.0%; $[\alpha]^{20}_D$=+2.3 [c=1.34 $CHCl_3$]; IR (film): 1750–1740 cm^{-1}; EIMS (m/e): 698 (M^++2), 313 (100%), 239 ($C_{15}H_{31}CO^+$), 131 (t-$BuSiMe_2$), 57, 43; ^{1}H NMR ($CDCl_3$): δ 5.10–4.90 (m, 1H,

CHOCO), 3.80–3.60 (dd, 1H, CH_2O), 3.50–3.40 (dd, 1H, CHO), 3.40–3.30 (m, 2H, CH_2O), 2.30–2.10 (t, 2H, CH_2CO), 1.50–1.40 (dt, 2H), 1.30–1.10 (s, 56H), 0.90–0.80 (m, 15H, $5CH_3$), 0.10–0.00 [s, 6H, $(CH_3)_2Si$]; Anal. calcd for $C_{43}H_{88}O_3$: 74.09 (C%), 12.72 (H%). Found: 74.56 (C%), 12.90 (H%).

1-Hexadecyl-2-[(z)-9-octadecenoyl]-3-t-butyldimethylsilylglycerol ***5c***

Yield: 60.9%; $[\alpha]^{20}_D$=+7.4 [c=1.14 $CHCl_3$]; IR (film): 1750 cm^{-1}; EIMS (m/e): 638 (M^++1−C_4H_9), 265 ($C_{17}H_{33}CO^+$), 131 (t-BuSiMe$_2$), 57 (100%), 43; ^{1}H NMR ($CDCl_3$): δ 5.40–5.30 (m, 2H, CH=CH), 5.10–4.90 (m, 1H, CHOCO), 3.80–3.70 (m, 2H, CH_2O), 3.60–3.50 (dd, 2H, J=1.4 Hz, J=5.0 Hz, CH_2O), 3.50–3.30 (m, 2H, CH_2O), 2.40–2.20 (t, 2H, CH_2CO), 2.10–1.90 (m, 4H, $2CH_2C$=), 1.70–1.50 (m, 4H), 1.50–1.20 (s, 46H), 1.00–0.90 (m, 15H, $5CH_3$), 0.10–0.00 [s, 6H, $(CH_3)_2Si$]; Anal. calcd for $C_{43}H_{86}O_4Si$: 73.82 (C%), 12.24 (H%). Found: 74.19 (C%), 11.86 (H%).

1-Octadecyl-2-[(z)-9-octadecenoyl]-3-t-butyldimethylsilylglycerol ***5d***

Yield: 80.0%; $[\alpha]^{20}_D$=+6.7 [c=1.2 $CHCl_3$]; IR (film): 1750 cm^{-1}; EIMS (m/e): 265 ($C_{17}H_{33}CO^+$), 131 (t-BuSiMe$_2$), 57 (100%), 43; ^{1}H NMR ($CDCl_3$) δ 5.40–5.30 (m, 2H, CH=CH), 5.10–4.90 (m, 1H, CHOCO), 3.80–3.70 (m, 2H, CH_2O), 3.60–3.50 (dd, 2H, J=1.40 Hz, J=5.0 Hz, CH_2O), 3.50–3.30 (m, 2H, CH_2O), 2.40–2.20 (t, 2H, CH_2CO), 1.70–1.50 (dt, 4H), 2.10–1.90 (m, 4H, $2CH_2C$=), 1.40–1.20 (s, 52H), 0.90–0.80 (m, 15H, $5CH_3$), 0.10–0.00 [s, 6H, $(CH_3)_2Si$]; ^{13}C NMR ($CDCl_3$) δ 178.7 (C=O), 135.4, 135.2, 78.5, 77.0, 74.4, 67.2, 42.7, 39.9, 37.3, 35.1, 34.9, 34.7, 34.5, 32.6, 32.0, 31.5, 30.4, 28.1, 23.7, 19.4.

1-Hexadecyl-2-ethenoyl-3-t-butyldimethylsilylglycerol ***5e***

Yield: 60.0%; $[\alpha]^{20}_D$=+13.08 [c=0.32 $CHCl_3$]; IR (film): 1750–1735 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 6.50–6.30 (dd, 1H, J=1.7 Hz, J=17.1 Hz, CH=), 6.25–6.10 (dd, 1H, J=10.30 Hz, J=17.3 Hz), 6.00–5.80 (dd, 1H, J=1.6 Hz, J=10.3 Hz, CH=), 5.00–4.90 (m, 1H, CHOCO), 3.90–3.70 (m, 2H, CH_2O), 3.50–3.40 (m, 2H, CH_2O), 1.60–1.50 (m, 2H), 1.40–1.20 (s, 26H), 0.90–0.80 (m, 12H, $4CH_3$), 0.10–0.00 [s, 6H, $(CH_3)_2Si$]; HREIMS (m/e): 427.3474 ($M^+-C_4H_9$). Calcd: 427.3469.

1-Octadecyl-2-ethenoyl-3-t-butyldimethylsilylglycerol ***5f***

Yield: 32.0%; $[\alpha]^{20}_D$=+3.08 [c=1.55 $CHCl_3$]; IR (film): 1750–1735 cm^{-1}; EIMS (m/e): 457 ($M^+-C_2H_3CO$), 131 (t-BuSiMe$_2$), 129 (100%), 57, 43; ^{1}H NMR ($CDCl_3$) δ 6.40–6.20 (dd, 1H, CH=), 6.20–6.10 (dd, 1H, CH=), 5.90–5.80 (dd, J=1.6 Hz, J=10.3 Hz, CH=), 5.00–4.90 (m, 1H, CHOCO), 3.90–3.70 (dd, 2H, J=3.6 Hz, J=5.1 Hz, CH_2O), 3.50–3.40 (m, 2H, CH_2O), 1.60–1.50 (t, 2H), 1.30–1.20 (s, 30H), 0.90–0.80 (m, 12H, $4CH_3$), 0.10–0.00 [s, 6H, $(CH_3)_2Si$]; Anal. calcd for $C_{30}H_{60}O_4Si$: 69.82 (C%), 12.64 (H%). Found: 70.12 (C%), 12.64 (H%).

General procedure for esterification of protected glycerol with fatty acid anhydride

To a solution of 1-alkyl-3-t-butyldimethylsilylglycerol (0.16–0.18 mmol) in dry dichloromethane (15 ml), α-linolenic acid anhydride (0.83–0.90 mmol) and 4-(N,N-dimethylamino) pyridine (0.18 mmol) were added and stirred for four days at room temperature under protection of nitrogen. The reaction was completed as shown by TLC and the organic solvent removed under reduced pressure to give a crude oil which was then purified by silica gel chromatography eluting with petroleum ether–ethylacetate (100:1) resulting in an oil.

1-Hexadecyl-2-[(z,z,z)-9,12,15-octadecatrienoyl]-3-t-butyldimethylsilylglycerol ***5g***

Yield: 60.9%; $[\alpha]^{20}_D$=+6.6 [c=0.80 $CHCl_3$]; IR (film): 1750 cm^{-1}; EIMS (m/e): 634 (M^++1−C_4H_9), 261 ($C_{17}H_{29}CO^+$), 131 (t-BuSiMe$_2$), 57 (100%); ^{1}H NMR ($CDCl_3$) δ 5.50–5.30 (m, 6H, 3CH=CH), 5.10–4.90 (m, 1H, CHOCO), 3.90–3.70 (m, 2H, CH_2O), 3.50–3.30 (m, 4H, CH_2OCH_2), 2.90–2.80 (t, 4H, J=5.9 Hz, J=5.5 Hz, 2=CCH_2C=), 2.40–2.20 (t, 2H, CH_2CO), 2.10–1.90 (m, 4H, $2CH_2C$=), 1.70–1.50 (dt, 4H), 1.30–1.20 (s, 34H), 1.00–0.90 (m, 3H, CH_3), 0.80–0.70 (s, 12H, $4CH_3$), 0.10–0.00 [s, 6H, $(CH_3)_2Si$]; Anal. calcd for $C_{43}H_{82}O_4Si$: 74.72 (C%), 11.96 (H%). Found: 75.00 (C%), 12.10 (H%).

1-Octadecyl-2-[(z,z,z)-9,12,15-octadecatrienoyl]-3-t-butyldimethylsilylglycerol ***5h***

Yield 80.0%; $[\alpha]^{20}_D$=+2.80 [c=0.85 $CHCl_3$]; IR (film): 1760 cm^{-1}; EIMS (m/e): 261 ($C_{17}H_{29}CO^+$), 131 (t-BuSiMe_2), 79 (100%), 57; ^1H NMR ($CDCl_3$) δ 5.40–5.20 (m, 6H, 3CH=CH), 5.10–4.90 (m, 1H, CHOCO), 3.80–3.60 (m, 2H, CH_2O), 3.50–3.30 (m, 4H, CH_2OCH_2), 2.90–2.60 (t, 4H, J=5.9 Hz, J=5.5 Hz, 2=CCH_2C=), 2.40–2.20 (t, 2H, CH_2CO), 2.10–1.90 (m, 4H, $2CH_2C$=), 1.70–1.40 (dt, 4H), 1.30–1.20 (s, 38H), 1.00–0.90 (m, 3H, CH_3), 0.80–0.70 (s, 12H, $4CH_3$), 0.10–0.00 [s, 6H, $(CH_3)_2Si$]; Anal. calcd for $C_{45}H_{86}O_4Si$: 75.14 (C%), 12.05 (H%). Found: 75.20 (C%), 12.20 (H%).

General procedure for deprotection of silyl group from glycerol derivatives with PPTS

To a solution of compound **5a–h** (0.17 mmol) in a mixed solvent of dichloromethane and methanol (6 ml, CH_2Cl_2–methanol 2:1), PPTS (0.17 mmol) was added. The reaction was kept at 0–5°C for 4 to 14 days and monitored by TLC until the reaction was complete. The solvent was removed under reduced pressure at room temperature to give crude oil and purified by silica gel chromatography eluting with petroleum ether–ethyl acetate (8:1 and 4:1) resulting in an oil.

*1-Hexadecyl-2-palmitoyl-*D*-glycerol* ***6a***

Yield: 86.1%; $[\alpha]^{20}_D$=+3.4 [c=1.00 $CHCl_3$]; IR (film): 1750 cm^{-1}; EIMS (m/e): 536 (M^+-H_2O), 239 ($C_{15}H_{31}CO^+$), 131 (t-BuSiMe_2), 57 (100%), 43; ^1H NMR ($CDCl_3$) δ 5.10–4.90 (m, 1H, CHOCO), 3.90–3.75 (d, 2H, CH_2O, J=3.9 Hz), 3.70–3.60 (m, 2H, J=5.0 Hz, J=5.2 Hz, CH_2O), 3.50–3.40 (m, 2H), 2.40–2.20 (t, 2H, J=7.4 Hz, J=7.6 Hz, CH_2CO), 1.70–1.50 (dt, 4H), 1.50–1.20 (s, 46H), 1.10–1.00 (t, 3H, CH_3),0.90–0.80 (t, 3H, J=6.3 Hz, J=6.6 Hz, CH_3); Anal. calcd for $C_{35}H_{70}O_4$: 75.07 (C%), 13.50 (H%). Found: 75.59 (C%), 13.28 (H%).

*1-Octadecyl-2-palmitoyl-*D*-glycerol* ***6b***

Yield: 75.0%; $[\alpha]^{20}_D$=+3.3 [c=1.14 $CHCl_3$]; IR (film): 3500–3300 cm^{-1}, 1750–1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.10–4.90 (m, 1H, CHOCO), 3.80–3.60 (d, 2H, J=3.8 Hz, CH_2OH), 3.70–3.60 (t, 2H, J=5.5 Hz, J=5.9 Hz, CH_2O), 3.50–3.40 (m, 2H, CH_2O), 2.40–2.20 (t, 2H, J=7.5 Hz, J=6.9 Hz, CH_2CO), 1.70–1.50 (dt, 4H), 1.30–1.20 (s, 54H), 1.10–1.00 (t, 3H, J=6.8 Hz, J=6.9z, CH_3), 0.90–0.80 (t, 3H, CH_3); Anal. calcd for $C_{37}H_{74}O_4$: 75.56 (C%), 13.51 (H%). Found: 75.80 (C%), 14.00 (H%).

*1-Hexadecyl-2-[(z)-9-octadecenoyl]-*D*-glycerol* ***6c***

Yield 66.7%; $[\alpha]^{20}_D$=+5.5 [c=0.32 $CHCl_3$]; IR (film): 3500–3200, 1740 cm^{-1}; EIMS (m/e): 557 (M^+-OH), 556 (M^+-H_2O), 265 ($C_{17}H_{33}CO^+$), 131 (t-BuSiMe_2), 57 (100%); ^1H NMR ($CDCl_3$) δ 5.40–5.30 (m, 2H, CH=CH), 5.10–4.90 (m, 1H, CHOCO), 3.90–3.80 (d, 2H, J=4.3 Hz, CH_2OH), 3.70–3.60 (t, 2H, J=5.2 Hz, J=5.0 Hz, CH_2O), 3.50–3.30 (m, 2H, CH_2O), 2.40–2.20 (t, 2H, J=7.4 Hz, J=7.6 Hz, CH_2CO), 2.10–1.90 (m, 4H, $2CH_2C$=), 1.70–1.50 (dt, 4H), 1.40–1.20 (s, 46H), 1.10–1.00 (m, 3H, CH_3), 0.90–0.80 (t, 3H, CH_3); Anal. calcd for $C_{37}H_{72}O_4$: 75.53 (C%), 13.59 (H%). Found: 76.18 (C%), 13.32 (H%).

*1-Octadecyl-2-[(z)-9-octadecenoyl]-*D*-glycerol* ***6d***

Yield: 80.0%; $[\alpha]^{20}_D$=+6.6 [c=1.25 $CHCl_3$]; IR (film): 1750 cm^{-1}; EIMS (m/e): 265 ($C_{17}H_{33}CO^+$), 131 (t-BuSiMe_2), 57 (100%); ^1H NMR ($CDCl_3$) δ 5.40–5.30 (m, 2H, CH=CH), 5.10–4.90 (m, 1H, CHOCO), 3.80–3.70 (m, 2H, CH_2O), 3.65–3.40 (dd, 2H, J=1.5 Hz, J=5.1 Hz, CH_2O), 3.50–3.30 (m, 2H, CH_2O), 2.40–2.20 (t, 2H, CH_2CO), 2.10–1.90 (m, 4H, $2CH_2C$=), 1.70–1.50 (m, 4H), 1.40–1.20 (s, 52H), 0.90–0.80 (m, 6H, $2CH_3$); Anal. calcd for $C_{39}H_{76}O_4$: 76.80 (C%), 12.90 (H%). Found: 76.55 (C%), 12.71 (H%).

*1-Hexadecyl-2-ethenoyl-*D*-glycerol* ***6e***

Yield: 75.0%; $[\alpha]^{20}_D$=+5.7 [c=1.50 $CHCl_3$]; IR (film): 1750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.50–6.30 (dd, 1H, J=1.7 Hz, J=17.1 Hz, CH=), 6.25–6.10 (dd, 1H, J=10.30 Hz, J=17.3 Hz), 6.00–5.80 (dd, 1H, J=1.7 Hz, J=10.3 Hz, CH=), 5.00–4.90 (m, 1H, CHOCO), 3.80–3.70 (m, 2H, CH_2O), 3.70–3.50 (m,

2H, CH_2O), 3.50–3.40 (m, 2H, CH_2O), 1.90–1.80 (m, 2H), 1.70–1.60 (m, 1H), 1.40–1.20 (s, 26H), 0.90–0.80 (m, 3H, CH_3); ^{13}C NMR ($CDCl_3$) 166 (C=O), 132 (C=), 128 (C=), 73.3, 72.6, 63.0, 31.9, 29.6, 29.3, 22.6, 14.1.

*1-Octadecyl-2-ethenoyl-*D*-glycerol* ***6f***

Yield: 70.0%; $[\alpha]^{20}_D$=+4.00 [c=1.00 $CHCl_3$]; IR (film): 3650–3400, 1750–1735 cm^{-1}; EIMS (m/e): 381 (M^+-OH), 343 ($M^+-C_2H_3CO$), 57 (100%), 43; ^1H NMR ($CDCl_3$) δ 6.40–6.30 (dd, 1H, CH=), 6.10–6.00 (dd, 1H, CH=), 5.90–5.80 (dd, J=1.6 Hz, J=10.3 Hz, CH=), 5.00–4.90 (m, 1H, CHOCO), 3.90–3.70 (dd, 2H, J=3.6 Hz, J=5.1 Hz, CH_2O), 3.60–3.50 (m, 1H, CH_2O), 3.50–3.40 (m, 2H, CH_2O), 1.60–1.50 (t, 2H), 1.30–1.20 (s, 30H), 0.90–0.80 (m, 3H, CH_3); HREIMS (m/e): 381.3368 (M^+-OH). Calcd: 381.3359.

*1-Hexadecyl-2-[(z,z,z)-9,12,15-octadecatrienoyl]-*D*-glycerol* ***6g***

Yield 85.3%; $[\alpha]^{20}_D$=+2.8 [c=0.80 $CHCl_3$]; IR (film): 3500–3400, 1750 cm^{-1}; EIMS (m/e): 559 (M^+-OH), 261 ($C_{17}H_{29}CO^+$), 57 (100%). ^1H NMR ($CDCl_3$): δ 5.50–5.30 (m, 6H, 3CH=CH), 5.10–4.90 (m, 1H, CHOCO), 3.80–3.70 (m, 2H, J=4.5 Hz, CH_2OH), 3.70–3.50 (t, 2H, J=4.9 Hz, J=5.1 Hz, CH_2OCH_2), 3.50–3.40 (m, 2H, CH_2O), 2.90–2.80 (t, 4H, J=6.0 Hz, J=5.4 Hz, 2=CCH_2C=), 2.40–2.20 (t, 2H, J=7.7 Hz, J=7.4 Hz, CH_2CO), 2.10–1.90 (m, 4H, $2CH_2C$=), 1.70–1.50 (m, 4H), 1.30–1.20 (s, 34H), 1.05–0.95 (t, 3H, J=7.5 Hz, J=7.4 Hz, CH_3), 0.80–0.70 (s, 3H, J=7.0 Hz, J=6.4 Hz, CH_3); Anal. calcd for $C_{37}H_{68}O_4$: 77.06 (C%), 11.89 (H%). Found: 77.56 (C%), 12.40 (H%).

*1-Octadecyl-2-[(z,z,z)-9,12,15-octadecatrienoyl]-*D*-glycerol* ***6h***

Yield 81.0%; $[\alpha]^{20}_D$=+3.0 [c=0.88 $CHCl_3$]; IR (film): 3500–3400, 1760 cm^{-1}; EIMS (m/e): 605 (M^++1), 261 ($C_{17}H_{29}CO^+$), 57 (100%). ^1H NMR ($CDCl_3$) δ 5.40–5.30 (m, 6H, 3CH=CH), 5.10–4.90 (m, 1H, CHOCO), 3.90–3.80 (m, 2H, J=4.5 Hz, CH_2OH), 3.70–3.60 (t, 2H, J=4.9 Hz, J=5.1 Hz, CH_2O), 3.50–3.40 (m, 4H, CH_2OCH_2), 2.90–2.80 (t, 4H, J=5.9 Hz, J=5.5 Hz, 2=CCH_2C=), 2.40–2.20 (t, 2H, J=7.4 Hz, J=8.4 Hz, CH_2CO), 2.20–2.00 (m, 4H, $2CH_2C$=), 1.70–1.50 (m, 4H), 1.30–1.20 (s, 38H), 1.05–0.95 (m, 3H, CH_3), 0.80–0.70 (t, 3H, CH_3); Anal. calcd for $C_{39}H_{72}O_4$: 77.42 (C%), 11.99 (H%). Found: 77.96 (C%), 12.20(H%).

*General procedure for phosphorylation and amination of 1-alkyl-2-acyl-*D*-glycerol dermatives*

To a solution of compound **6a–h** (0.07–0.11 mmol), triethylamine (2 ml) in dry dichloromethane (10 ml) was added. β-Chloroethylphosphoryl dichloride [$ClCH_2CH_2OP(O)Cl_2$] (0.5 ml) was then added and stirred at room temperature under protection of nitrogen for overnight. The reaction was complete as shown by TLC and purified by silica gel chromatography eluting with chloroform–methanol–water (65:30:4) resulting in a yellow oil intermediate for the next step of the reaction without being identified. Thus, to a solution of trimethylamine in ethanol (2 ml) in dry chloroform (2 ml), a yellow oil was added and sealed at 70–80°C for 72 hours until the reaction was complete. The solvent was then removed under reduced pressure to obtain a yellow product, and the yellow product was purified by silica gel chromatography eluting with choroform–methanol–water (65:30:4) resulting in a yellow oil.

1-Hexadecyl-2-palmitoyl-sn-glycero-3-phosphocholine ***7a***

Yield: 60.0%; R_f=0.28 ($CHCl_3$:CH_3OH:H_2O, 60:35:4); $[\alpha]^{20}_D$=+6.5 [c=0.70 $CHCl_3$:CH_3OH, 2:1]; EIMS (m/e): 535, 239 ($C_{15}H_{31}CO^+$), 57 (100%), 43; ^1H NMR ($CDCl_3$) δ 5.00–4.90 (m, 1H, CHOCO), 4.50–3.80 (m, 4H, CH_2O, $2POCH_2$), 3.70–3.20 (m, 15H, CH_2OCH_2, CH_2NMe_3), 2.40–2.30 (t, 2H, J=7.4 Hz, J=7.6 Hz, CH_2CO), 1.70–1.50 (m, 4H), 1.30–1.20 (s, 50H), 1.10–1.00 (t, 3H, CH_3, J=6.8 Hz, J=6.9 Hz), 0.90–0.80 (t, 3H, J=6.3 Hz, J=7.0 Hz, CH_3); ^{31}P ($CDCl_3$) 12.23 ppm; Anal. calcd for $C_{40}H_{82}O_7NP$: 66.73 (C%), 11.48 (H%). Found: 66.25 (C%), 11.46 (H%).

1-Octadecyl-2-palmitoyl-sn-glycero-3-phosphocholine ***7b***

Yield: 68.0%; R_f=0.28 ($CHCl_3$:CH_3OH:H_2O, 60:35:4); $[\alpha]^{20}_D$=+6.5 [c=0.75 $CHCl_3$:CH_3OH, 2:1]; EIMS (m/e): 563, 239 ($C_{15}H_{31}CO^+$), 57 (100%), 43. ^1H NMR ($CDCl_3$) δ 5.00–4.90 (m, 1H, CHOCO),

4.50–3.80 (m, 4H, CH_2O, $2POCH_2$), 3.70–3.20 (m, 15H, CH_2OCH_2, CH_2NMe_3), 2.40–2.30 (t, 2H, J=7.6 Hz, J=7.4 Hz, CH_2CO), 1.70–1.50 (m, 4H), 1.30–1.20 (s, 54H), 1.10–1.00 (t, 3H, CH_3, J=6.8 Hz, J=6.9 Hz), 0.90–0.80 (t, 3H, J=6.3 Hz, J=7.0 Hz, CH_3); ^{31}P ($CDCl_3$) 5.00 ppm; Anal. calcd for $C_{42}H_{86}O_7NP$: 66.73 (C%), 11.78 (H%). Found: 66.25 (C%), 11.46 (H%).

1-Hexadecyl-2-[(z)-9-octadecenoyl]-sn-glycero-3-phosphocholine ***7c***

Yield: 63.0%; R_f=0.28 ($CHCl_3$:CH_3OH:H_2O, 60:35:4); $[\alpha]^{20}_D$=+8.00 [c=0.75 $CHCl_3$:CH_3OH, 2:1]; EIMS (m/e): 556, 265 ($C_{17}H_{33}CO^+$), 57 (100%), 43; ^1H NMR ($CDCl_3$) δ 5.40–5.30 (m, 2H, CH=CH), 5.10–4.90 (m, 1H, CHOCO), 4.80–3.90 (m, 4H, $2POCH_2O$), 3.80–3.30 (m, 15H, CH_2OCH_2, CH_2NMe_3), 2.40–2.20 (t, 2H, J=7.4 Hz, J=7.6 Hz, CH_2CO), 2.10–2.00 (m, 4H, $2CH_2C$=), 1.70–1.50 (dt, 4H), 1.50–1.20 (s, 46H), 1.10–1.00 (m, 3H, CH_3), 0.90–0.80 (t, 3H, J=6.3 Hz, J=6.6 Hz, CH_3); ^{31}P ($CDCl_3$) 1.43 ppm; Anal. calcd for $C_{40}H_{82}O_7NP$: 66.87 (C%), 12.31 (H%). Found: 67.02 (C%), 12.50 (H%).

1-Octadecyl-2-[(z)-9-octadecenoyl]-sn-glycero-3-phosphocholine ***7d***

Yield: 75.0%; R_f=0.27 ($CHCl_3$:CH_3OH:H_2O, 60:35:4); $[\alpha]^{20}_D$=+7.8 [c=0.75 $CHCl_3$:CH_3OH, 2:1]; EIMS (m/e): 584, 265 ($C_{17}H_{33}CO^+$), 57 (100%), 43; ^1H NMR ($CDCl_3$) δ 5.50–5.40 (m, 2H, CH=CH), 5.10–5.00 (m, 1H, CHOCO), 4.80–3.90 (m, 4H, $2POCH_2O$), 3.80–3.30 (m, 15H, CH_2OCH_2, CH_2NMe_3), 2.40–2.30 (t, 2H, J=7.4 Hz, J=7.6 Hz, CH_2CO), 2.20–2.00 (m, 4H, $2CH_2C$=), 1.70–1.50 (dt, 4H), 1.50–1.20 (s, 50H), 1.10–1.00 (m, 3H, CH_3), 0.90–0.80 (t, 3H, J=6.3 Hz, J=6.6 Hz, CH_3); ^{31}P ($CDCl_3$) 4.00 ppm; Anal. calcd for $C_{44}H_{88}O_7NP$: 68.27 (C%), 11.46 (H%). Found: 68.31 (C%), 11.68 (H%).

1-Hexadecyl-2-ethenoyl-sn-glycero-3-phosphocholine ***7e***

Yield: 74.0%; $[\alpha]^{20}_D$=+3.0 [c=0.70 $CHCl_3$:CH_3OH, 2:1]; EIMS (m/e): 535 (M^+), 55 ($C_2H_3CO^+$) (100%), 43; ^1H NMR ($CDCl_3$) δ 6.50–6.40 (dd, 1H, J=1.7 Hz, J=17.1 Hz, CH=), 6.25–6.10 (dd, 1H, J=10.60 Hz, J=17.3 Hz), 6.00–5.80 (dd, 1H, J=1.7 Hz, J=10.3 Hz, CH=), 5.00–4.90 (m, 1H, CHOCO), 4.60–3.80 (m, 4H, $2POCH_2$), 3.70–3.20 (m, 15H, CH_2OCH_2, CH_2NMe_3), 1.90–1.80 (m, 1H), 1.70–1.60 (m, 1H), 1.40–1.20 (s, 26H), 0.90–0.80 (m, 3H, CH_3); ^{31}P ($CDCl_3$) 0.70 ppm; ^{13}C NMR ($CDCl_3$) 168.4 (C=O), 129.6 (C=), 129.3 (C=), 71.4, 68.8, 58.9, 53.8, 53.4, 33.9, 31.5, 30.2, 28.9, 28.7, 26.7, 25.6, 24.6, 22.2, 14.5.

1-Octadecyl-2-ethenoyl-sn-glycero-3-phosphocholine ***7f***

Yield: 66.0%; $[\alpha]^{20}_D$=+3.8 [c=0.80 $CHCl_3$; CH_3OH: 2:1]; EIMS (m/e): 563 (M^+), 55 ($C_2H_3CO^+$) (100%), 43; ^1H NMR ($CDCl_3$) δ 6.50–6.40 (dd, 1H, J=1.7 Hz, J=17.1 Hz, CH=), 6.25–6.10 (dd, 1H, J=10.60 Hz, J=17.3 Hz), 6.00–5.90 (dd, 1H, J=1.7 Hz, J=10.3 Hz, CH=), 5.00–4.90 (m, 1H, CHOCO), 4.60–3.80 (m, 4H, $2POCH_2$), 3.70–3.20 (m, 15H, CH_2OCH_2, CH_2NMe_3), 1.90–1.80 (m, 1H), 1.70–1.60 (m, 1H), 1.40–1.20 (s, 30H), 0.90–0.80 (m, 3H, CH_3); ^{31}P ($CDCl_3$) 0.90 ppm; ^{13}C NMR ($CDCl_3$) 168.4 (C=O), 129.6 (C=), 129.3 (C=), 71.4, 68.8, 58.9, 54.8, 53.4, 33.9, 31.5, 30.6, 28.9, 28.7, 26.8, 25.6, 23.6, 22.2, 14.5.

1-Hexadecyl-2-[(z,z,z)-9,12,15-octadecatrienoyl-sn-glycero-3-phosphocholine ***7g***

Yield 65.0%; R_f=0.25 ($CHCl_3$:CH_3OH:H_2O, 60:35:4); $[\alpha]^{20}_D$=+6.2 [c=0.90 $CHCl_3$:CH_3OH, 2:1]; EIMS (m/e): 589, 559, 522, 543, 409, 353, 289, 261 ($C_{17}H_{29}CO^+$), 57 (100%), 43; ^1H NMR ($CDCl_3$) δ 5.40–5.30 (m, 6H, 3CH=CH), 5.10–4.90 (m, 1H, CHOCO), 4.50–4.40 (s, 2H, CH_2O), 4.20–3.80 (s, 4H, CH_2OCH_2), 3.70–3.30 (m, 13H, $CH_2CH_2NMe_3$), 2.90–2.80 (t, 4H, J=5.5 Hz, J=5.7 Hz, 2=CCH_2C=), 2.40–2.30 (t, 2H, J=7.6 Hz, J=7.4 Hz, CH_2CO), 2.10–1.90 (m, 4H, $2CH_2C$=), 1.50–1.10 (m, 42H), 1.10–1.00 (m, 3H, CH_3, J=7.5 Hz, J=6.9 Hz), 0.80–0.70 (s, 3H, J=6.9 Hz, J=5.9 Hz, CH_3); ^{31}P ($CDCl_3$) 2.54 ppm; Anal. calcd for $C_{40}H_{82}O_7NP$: 67.98 (C%), 10.87 (H%). Found: 67.70 (C%), 10.39 (H%).

1-Octadecyl-2-[(z,z,z)-9,12,15-octadecatrienoyl-sn-glycero-3-phosphocholine 7h

Yield 64.0%; R_f=0.26 ($CHCl_3$:CH_3OH:H_2O, 60:35:4); $[\alpha]^{20}_D$=+10.9 [c=0.40 $CHCl_3$:CH_3OH, 2:1]; EIMS (m/e): 601, 340, 261 ($C_{17}H_{29}CO^+$), 57 (100%), 43; ^1H NMR ($CDCl_3$): δ 5.40–5.30 (m, 6H, 3CH=CH), 5.10–4.90 (m, 1H, CHOCO), 4.50–4.40 (s, 2H, CH_2O), 4.20–3.80 (s, 4H, CH_2OCH_2), 3.70–3.30 (m, 13H, $CH_2CH_2NMe_3$), 2.90–2.80 (t, 4H, J=5.5 Hz, J=5.7 Hz, 2=CCH_2C=), 2.40–2.30 (t, 2H, J=7.6 Hz, J=7.4 Hz, CH_2CO), 2.10–1.90 (m, 4H, $2CH_2C$=), 1.50–1.10 (m, 42H), 1.10–1.00 (m, 3H, CH_3, J=7.5 Hz, J=6.9 Hz), 0.80–0.70 (s, 3H, J=6.9 Hz, J=5.9 Hz, CH_3); ^{31}P ($CDCl_3$) 11.38 ppm; Anal. calcd for $C_{42}H_{80}O_7NP$: 69.48 (C%), 11.12 (H%). **Found: 70.00 (C%), 11.80 (H%).

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