An Efficient Stereocontrolled Route to Both Enantiomers of Platelet Activating Factor and Analogues with Long-Chain Esters at C_2: Saturated and Unsaturated Ether Glycerolipids by Opening of Glycidyl Arenesulfonates

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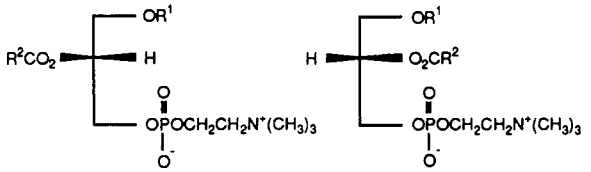
Both enantiomers of various ether/ester glycerophosphocholines (*R*)- and (*S*)-**1**, including platelet activating factor (PAF, **2**), have been synthesized from arenesulfonate derivatives of glycidol ((*R*)- and (*S*)-**3**) that are readily available in high enantiomeric purity. Regio- and stereospecific opening of (*R*)- or (*S*)-**3** with 1.0–1.4 equiv of long-chain saturated or unsaturated alcohol using boron trifluoride etherate as catalyst in CH_2Cl_2 or $CHCl_3$ solvent afforded 1(3)-*O*-alkyl-3(1)-*O*-arenesulfonyl-*sn*-glycerol (**4**) in good yields (73–83%) and with the same very high optical purity of the parent glycidyl arenesulfonate (94–99% ee). For saturated alkyl/acyl **1** and **2**, *O*-benzylation of **4** was achieved with retention of the arenesulfonate group by using benzyl trifluoromethanesulfonate in the presence of excess 2,6-di-*tert*-butyl-4-methylpyridine; the C_2 hydroxyl of unsaturated *O*-alkyl **4** was protected as the methoxymethyl ether under mild conditions in which the arenesulfonate group is retained. Displacement of the arenesulfonate group and introduction of the phosphocholine group to produce PAF analogues complete this synthetically useful route to chiral ether–ester phospholipids with various alkyl and acyl functionalities.

Ether-linked phosphoglycerides bearing a long-chain ester at C_2 ((*R*)-**1**) are important structural constituents of cellular membranes of various tissues.[1] Since they contain the *O*-alkyl linkage, alkylacyl phosphoglycerides **1** may also play important roles in cellular functions by serving as precursors of bioactive ether-linked lipids. The potent ether-linked mediator of many biochemical and physiological activities, platelet activating factor (PAF, (*R*)-**2**), can be synthesized when cells are appropriately stimulated by the sequential action of a phospholipase A_2 and an acetyl-CoA transferase on alkylacylglycerophosphocholine.[2]



$R^1 = C_{16}H_{33}$, $C_{18}H_{35}$-Δ^9-*cis*, $C_{18}H_{35}$-Δ^6-*cis*

Alkylacyl-PC (*R*)-**1**: $R^2 = C_{15}H_{31}$ (*S*)-**1**: $R^2 = C_{15}H_{31}$

PAF (*R*)-**2**: $R^2 = CH_3$ (*S*)-**2**: $R^2 = CH_3$

Many glycerol derivatives have been used as starting materials in chemical syntheses of alkylacyl glycerophospholipids (**1**). For example, *rac*-1-*O*-alkylglycerol, which is available by alkylation of the isopropylidene derivative of glycerol, can be converted into **1** by acylation and phosphorylation procedures.[3] 1-*O*-Alkyl-*sn*-glycerol was prepared from D-mannitol in eight steps, and the same route without Walden inversion gave 3-*O*-alkyl-*sn*-glycerol;[4a–d] 1,2-*O*-isopropylidene-*sn*-glycerol is a key intermediate in this synthetic scheme, and 2,3-*O*-isopropylidene-*sn*-glycerol[4e–g] and its tosylate[4f,h] also serve as a useful chiral C_3-synthon. *rac*-1-*O*-Alkyl-2-*O*-benzylglycerophosphocholine, which is available from 1,3-benzylideneglycerol,[5a] and *rac*-1-deoxy-1-iodo-3-*O*-alkylglycerol[5b] have also served as precursors of **1**. Naturally occurring *O*-alkylglycerols are also starting materials for the preparation of alkyl phospholipids with a limited range of alkyl chains at the 1(3) position.[4c] A mixture of 1-*O*-alkyl-2-acyl-*sn*-glycerols was obtained from the liver oil of the ratfish (*Hydrolagus colliei*), which can be converted to alkylacylglycerophosphocholine.[6] A semisynthetic synthesis of the *sn*-1 and *sn*-3 enantiomers of alkylacylglycerophosphocholine was accomplished by treatment of *rac*-alkylacylglycerophosphocholine with phospholipase A_2, followed by isolation and reacylation of 1-*O*-alkylglycerophosphocholine.[7]

Platelet activating factor ((*R*)-**2**) has been the object of many synthetic efforts that have employed natural sources as the starting material, such as D-mannitol,[8a] D-tartaric acid,[8b,c] (*S*)-malic acid,[8d] and L-glyceric acid.[8e] Since the chirality of the naturally occurring starting material determines the configuration of the product in this synthetic approach, we sought to develop a stereocontrolled route to the enantiomers of **2** that does not rely on a naturally occurring precursor.

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(3) For reviews, see: (a) Baumann, W. J. *Ether Lipids: Chemistry and Biology*; Snyder, F., Ed.; Academic: New York, 1972; pp 51–79. (b) Paltauf, F. *Ether Lipids: Biochemical and Biomedical Aspects*; Mangold, H. K., Paltauf, F., Eds.; Academic: New York, 1983; pp 211–227. (c) Eibl, H. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 257–271.

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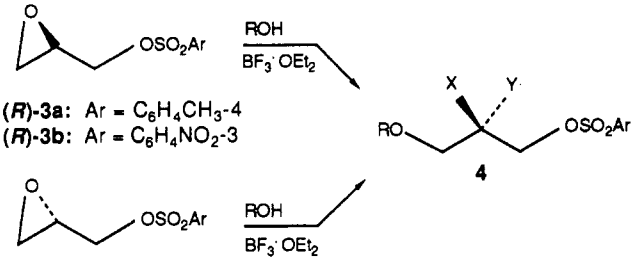
Table I. Preparation of Saturated and Unsaturated Ether-Linked Glycerol Arenesulfonates by Stereospecific Opening of 3 Catalyzed by $BF_3 \cdot OEt_2$[a]

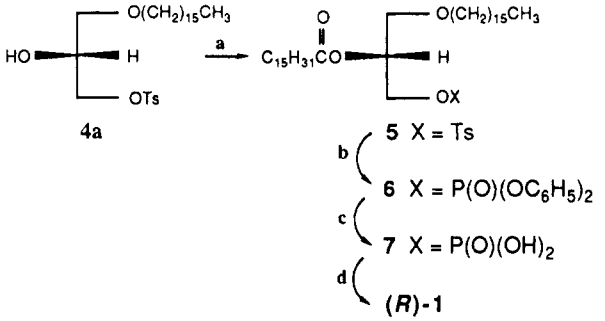


	ring-opened product				yield,[b] %	$[\alpha]^{25}_D$, deg	% ee[c]
	X	Y	R	Ar			
4a	OH	H	hexadecyl	$C_6H_4CH_3$-4	80	−6.24[d]	94.0 (97.7)[e]
4'a	H	OH	hexadecyl	$C_6H_4CH_3$-4	79	+6.37[d]	95.7
4b	OH	H	oleyl	$C_6H_4NO_2$-3	73	−7.04[f]	>99
4'b	H	OH	oleyl	$C_6H_4NO_2$-3	76	+6.88[f]	97.1
4c	OH	H	petroselinyl	$C_6H_4NO_2$-3	82	−6.98[f]	>99
4'c	H	OH	petroselinyl	$C_6H_4NO_2$-3	75	+6.86[f]	98.1
4d[g]	OH	H	hexadecyl	$C_6H_4NO_2$-3	83	−6.45[f] (−6.93)[h]	93.3[g]
4'd[i]	H	OH	hexadecyl	$C_6H_4NO_2$-3	80	+6.12[f] (+6.76)[h]	88.4[i]

[a] Substrate **3** and long-chain alcohol (1.0–1.4 equiv) were reacted in CH_2Cl_2 or ethanol-free $CHCl_3$ at room temperature for 18–24 h in the presence of ~5 mol % $BF_3 \cdot OEt_2$. The regioselectivity (exclusive attack at C_3) was determined by reversed-phase HPLC (4.6 × 250 mm C_{18} Carbosphere). Recrystallized **3b** (99% ee) was used to prepare **4b**, **4'b**, **4c**, and **4'c**. [b] Isolated yield. [c] Determined by HPLC on a chiral stationary-phase (4.6 × 250 mm) column (Pirkle type IA, J. T. Baker). [d] *c* 5.0, C_6H_6. [e] **4a** was recrystallized three times from ether–hexanes prior to conversion to the (*R*)-(+)-MTPA ester. [f] *c* 2.33, $CHCl_3$. [g] The percent ee of the commercially available starting material [(*R*)-**3b**], $[\alpha]^{25}_D$ −21.42° (*c* 2.14, $CHCl_3$), was 92.2. [h] $[\alpha]^{25}_D$ (*c* 2.33, $CHCl_3$) normalized to 99% ee of **3**, which is attained by two recrystallizations.[14] [i] The percent ee of the commercially available starting material [(*S*)-**3b**], $[\alpha]^{25}_D$ +20.82° (*c* 2.14, $CHCl_3$), was 89.6.

Previous syntheses of lipids from epoxide starting materials have been limited to the preparation of *ester*-linked glycerolipids. For example, the conversions of (*S*)-glycidol to optically active acylglycerols,[9] *rac*-glycidol to *rac*-mono- and 1,2-diacylglycerols[10] and phospholipids,[10c] *rac*-glycidyl esters to *rac*-1,3-diacylglycerols,[11] and glycidyl derivatives **3a** and **3b** to diacyl glycerophospholipids[12] have been reported. As part of a program to prepare ether-linked lipid precursors by the nucleophilic opening of derivatized epoxy alcohols with alcohols,[13] we undertook a synthesis of both enantiomers of PAF (**2**) and of related phospholipids **1** bearing a long-chain ester at the 2 position via the ring opening of stable, crystalline arenesulfonate derivatives of glycidol **3**. Epoxide opening is catalyzed by $BF_3 \cdot OEt_2$, and the attack of long-chain saturated or unsaturated alcohol occurs exclusively at C_3 of **3**. The approach to the preparation of **1** outlined in Scheme I was disappointing, however, because reaction of the arenesulfonate of alkylacylglycerol **5a** with silver diphenyl phosphate led to (*R*)-**1** in low optical purity. Moreover, this approach could not be applied successfully to the synthesis of **2** because direct acetylation of alcohol **4a** gave a low yield of the desired 3-arenesulfonate of 1-*O*-alkyl-2-acetyl-*sn*-glycerol. Therefore, the synthesis of **1** and **2** outlined in Scheme II was developed.

Scheme I. Synthesis of (*R*)-1 from Glycidyl Tosylate [(*R*)-3a] without the Use of Protecting Groups[a]



[a] Reagents: (a) $C_{15}H_{31}COCl$, hexane/py (81%); (b) $AgOP(O)(OC_6H_5)_2$, xylene (75%); (c) H_2, PtO_2, HOAc (79); (d) choline tosylate, Cl_3CCN, py (35%).

Results and Discussion

Opening of 3 with Long-Chain Alcohols. Epoxide opening with *n*-hexadecyl, oleyl, and petroselinyl alcohols occurred exclusively at C_3, as shown by reversed-phase HPLC (C_{18} Carbosphere column),[13a] giving **4** as the only regioisomer in good yields (73–83%). Table I shows that the $BF_3 \cdot OEt_2$-catalyzed opening of **3a** takes place stereospecifically, affording the opening product **4** in very high enantiomeric excess (ee, 94–99%) as determined by HPLC on a chiral stationary phase.[13a] Glycidyl 3-nitrobenzenesulfonate (**3b**), when recrystallized twice from ethanol,[14] gave **4** in higher ee than did glycidyl tosylate (**3a**). However, the ee of the hydroxy tosylates **4a** produced from **3a** can be enhanced to ≥97% by multiple recrystallization of **3a**[14] or of **4a** (Table I). Thus, both arenesulfonate de-

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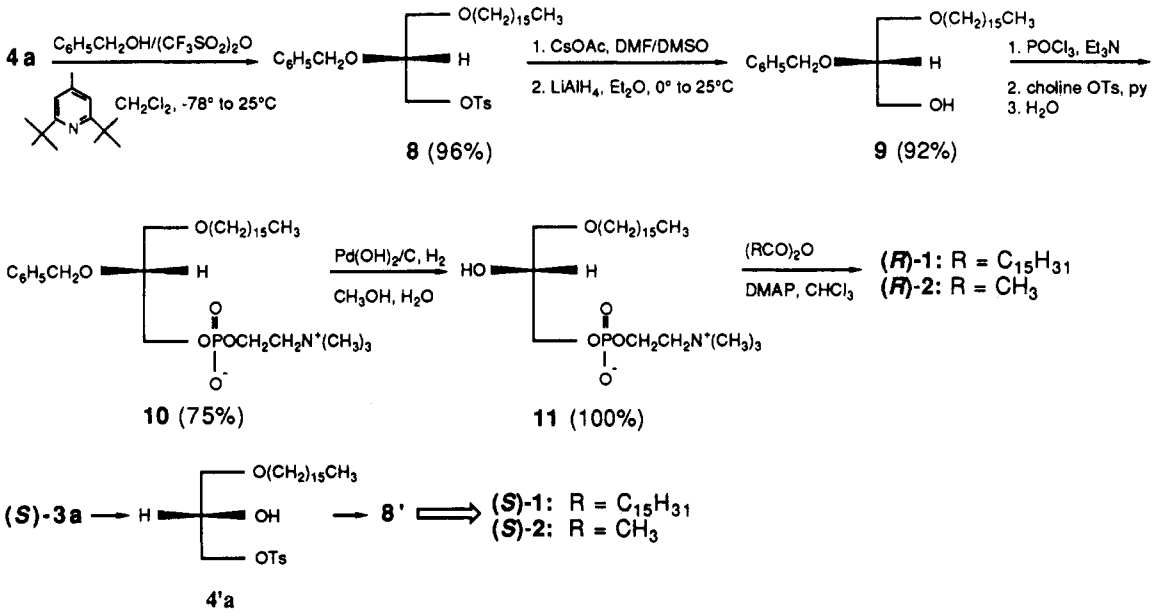
Scheme II. Stereocontrolled Synthesis of (*R*)- and (*S*)-1 via 2-*O*-Protected Glycerol 8



rivatives are effective chiral C_3 synthons for the preparation of ether-linked lipids.

Preparation of 1 from 4. Partial racemization took place in Scheme I, apparently during the conversion of tosylate **5a** to diphenyl phosphate ester **6** in refluxing xylenes. (Low yields were obtained when refluxing benzene and toluene were used.) We have recently suggested that a resonance-stabilized dioxolane-type oxocarbonium ion is the intermediate responsible for partial racemization during the conversion of 1,2-distearoyl-*sn*-glycero-3-*p*-toluenesulfonate into its diphenyl phosphate ester in refluxing xylenes.[12] Detosylation of **4a** into 1-*O*-hexadecyl-2-palmitoyl-*sn*-glycerol was not attempted because acyl migration from the secondary to primary position is recognized as a serious problem.[12,15]

To obtain isomerically and enantiomerically pure products **1** and **2**, we developed an alternative route, which is outlined in Scheme II. The key features of Scheme II are (a) O-benzylation of ring-opened arenesulfonate **4a** under basic conditions that proved to be so mild that epoxide formation via arenesulfonate displacement did not occur and (b) conversion of *O*-benzyl tosylate **8** into *O*-benzylglycerol **9** by displacement using cesium acetate followed by lithium aluminum hydride reduction. It should be noted that acetate displacement proceeded much more rapidly with 3-nitrobenzenesulfonates **12** and **13** than with tosylate **8**; thus, use of **3b** as starting material offers an advantage over **3a** when displacement–reduction reactions are involved. Alcohol **9** and its enantiomer (**9'**) were converted to optically pure ether–ester phosphocholines (*R*)- and (*S*)-**1**, **2** by using standard procedures. Attempts to prepare (*R*)-**2** via direct acetylation of **4a** were unsuccessful, although acylation with long-chain acid anhydrides and acyl chlorides gave **5** in satisfactory yields. The *O*-acetyl analogue of **5** may undergo acetyl migration with tosylate displacement through a dioxolane-type intermediate to give a mixture of the 2- and 3-acetyl derivatives of 1-*O*-alkylglycerol. To avoid this side reaction, we used a route to **2** involving protection of the C_2 hydroxyl as the benzyl ether **8** (Scheme II) and subsequent conversion to lysophosphocholine **11** after removal of the benzyl group.

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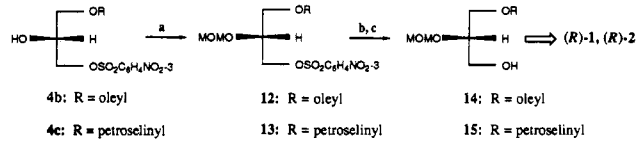
Scheme III. Stereocontrolled Synthesis of Unsaturated Ether-Linked Analogues of 1 and 2[a]



[a] Reagents: (a) $CH_2(OMe)_2$, P_2O_5, $CHCl_3$; (b) CsOAc, DMF/DMSO 4:1; (c) $LiAlH_4$, Et_2O, 0–25 °C.

To obtain unsaturated ether intermediates of **4**, the C_2 hydroxyl was protected as its methoxymethyl ether, again by using mild conditions in which the arenesulfonate group is retained (see Scheme III). The methoxymethyl ether, which has not been used previously to our knowledge in lipid synthesis,[16] is shown here to be a useful protecting group of the C_2-hydroxyl group of substituted glycerol derivatives bearing unsaturated alkyl chains.

The new approach to 1-*O*-alkyl-2-acyl-*sn*-glycero-3-phosphocholine using chiral epoxides such as **3a** and **3b** as starting materials will make it possible to conveniently prepare phospholipids with systematic modifications of the alkyl and acyl functionalities at the *sn*-1 and *sn*-2 positions, respectively, and is compatible with the preparation of alkylacyl phosphoglycerides with labeled chains. Products **1** and **2** and related analogues will be of value in studies of the influence of chirality on the interaction of phospholipids with other membrane components and of the action of lipolytic enzymes on alkylacyl phosphoglycerides.[17]

(16) After this work was completed, we became aware of the use of the methoxyethoxymethyl group for protection of lipid intermediates: Surles, J. R.; Wykle, R. L.; O'Flaherty, J. T.; Salzer, W. L.; Thomas, M. J.; Snyder, F.; Piantadosi, C. *J. Med. Chem.* **1985**, *28*, 73–78.

(17) Although the interactions of the *sn*-1 and *sn*-3 enantiomers of **1** with serum proteins and cholesterol appeared to be of comparable strength as judged by bilayer destabilization[7] and NMR studies (Hermetter, A.; Paltauf, F. *Chem. Phys. Lipids* **1982**, *31*, 283–289), respectively, diastereomeric interactions are expected to occur between phospholipids and other membrane components when the phospholipid chiral center is accessible to other chiral centers involved in the interaction (Bouloussa, O.; Dupeyrat, M. *Biochim. Biophys. Acta* **1988**, *938*, 395–402). Indeed, the configuration at C_2 seems to affect lipid packing organization in the subgel phase formed by pure diester phosphatidylcholines (Boyanov, A. I.; Koynova, R. D.; Tenchov, B. G. *Chem. Phys. Lipids* **1986**, *39*, 155–163) and may this influence the structural arrangements of gel phases formed by alkylacyl phospholipids.

Summary

In the present paper we have shown that (*R*)- and (*S*)-**3** are useful chiral building blocks for the synthesis of both enantiomers of phosphocholines **1** and **2**. The chiral purity of each stereoisomer of **4** was established by examination of the diastereomeric mixture of the (*R*)-(+)-MTPA ester by chiral HPLC. Comparison of the optical rotations of the stereoisomers of **4**, **9**, **10**, and **11** with the literature values also indicates that the ring-opening reaction with 1-hexadecanol and subsequent reactions occur with high stereospecificity. In fact, the optical rotations of these compounds are higher than those reported by Hirth and Barner,[18] who used 1,2-*O*-isopropylidene-*sn*-glycerol as the starting material. Our route is thus a facile and valuable alternative to the use of 1,2-isopropylidene-*sn*-glycerol and 2,3-isopropylidene-*sn*-glycerol. Since partial racemization can occur during storage of isopropylidene-*sn*-glycerol[3c] and complete racemization can occur in the presence of a trace of acidic impurity,[19] the use of chiral glycidyl derivatives as starting materials offers significant advantages. Furthermore, the use of unsaturated long-chain (such as oleyl and petroselinyl)[20] alcohols as nucleophiles in the ring-opening reaction gives precursors of unsaturated analogues of PAF (**2**) and **1** in excellent chemical and optical yields.

Experimental Section

General Procedures. The solvents used were dried as follows: dichloromethane and ethanol-free chloroform were distilled from calcium hydride and stored over type 3A molecular sieves. Hexane was distilled from the stored over sodium. Xylene was distilled from calcium hydride and stored over type 4A molecular sieves. Alcohol-free chloroform was obtained from J.T. Baker (Phillipsburg, NJ). Triethylamine was dried and stored over calcium hydride. Commercially available BF_3·OEt_2 from Aldrich (8.1 M) was distilled and then diluted with 9 volumes of dichloromethane. The stock solutions of BF_3·OEt_2 (0.81 M) in dichloromethane were used as the catalyst in the ring-opening reactions described here within about 2 months. Other chemicals were obtained from the following sources: (*R*)-(−)- and (*S*)-(+)-glycidyl tosylate (oxiranemethanol 4-methylbenzenesulfonate), (*R*)-(−)- and (*S*)-(+)-glycidyl 3-nitrobenzenesulfonate, oleyl alcohol, petroselinyl alcohol, palmitoyl chloride, palmitic anhydride, 4-(dimethylamino)-pyridine, 2,6-di-*tert*-butyl-4-methylpyridine, phosphorus oxychloride, phosphorus pentoxide, trichloroacetonitrile, and trifluoromethanesulfonic anhydride were from Aldrich. Choline tosylate[21] and silver diphenyl phosphate[22] were prepared as described previously. (*R*)-(+)-α-Methoxy-α-(trifluoromethyl)-phenylacetic acid (MTPA) was obtained from Aldrich and Fluka Chemical Corp.

Reactions were monitored on 0.25-mm thick silica gel GF TLC plates purchased from Analtech, Newark, DE. Detection of the compounds on TLC plates was by short-wavelength ultraviolet light or by spraying with 10% sulfuric acid in ethanol or with molybdate spray as described previously.[21] Flash chromatography was carried out with silica gel 60 (230-400 ASTM mesh) of E. Merck, purchased from Aldrich.

All ^1H NMR spectra were recorded at 200 MHz unless indicated otherwise. Melting points are uncorrected.

1-*O*-Hexadecyl-*sn*-glycerol 3-*O*-*p*-Toluenesulfonate ((−)-4a). This compound was prepared as described in the preceding article; 94.0% ee, 97.7% ee after three recrystallizations from ether–hexanes.[23]

3-*O*-Hexadecyl-*sn*-glycerol 1-*O*-*p*-Toluenesulfonate ((+)-4′a). This compound was prepared by the procedure described in the preceding article; 95.7% ee.[23]

1-*O*-Oleyl-*sn*-glycerol 3-*O*-*m*-Nitrobenzenesulfonate ((−)-4b). To a mixture of 104 mg (0.40 mmol) of (*R*)-(−)-**3b** [$[\alpha]^{25}_D$ −23.3° (*c* 2.14, $CHCl_3$)] and 107 mg (0.40 mmol) of oleyl alcohol in 3 mL of dichloromethane was added 4 drops (~5 mol %) of a 10% stock solution of boron trifluoride etherate in dichloromethane. After the mixture had stirred at room temperature under nitrogen for 18 h, the solvent was removed under reduced pressure, leaving a residue that was purified by flash chromatography (elution with 20% ethyl acetate–hexanes) to give 156 mg (73%) of **4b** as a pale yellow oil: TLC (20% ethyl acetate–hexanes) R_f 0.26; $[\alpha]^{25}_D$ −7.04° (*c* 2.33, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 8.78 (t, 1 H, *J* = 1.7 Hz, C_6H_4), 8.54 (m, 1 H, C_6H_4), 8.29 (m, 1 H, C_6H_4), 7.81 (t, 1 H, *J* = 7.9 Hz, C_6H_4), 5.34 (m, 2 H, vinyl), 4.23 (dd, 1 H, J_{AC} = 4.7 Hz, J_{AB} = 10.2 Hz, $CH_CCH_AH_BOSO_2Ar$), 4.19 (dd, 1 H, J_{BC} = 5.7 Hz, J_{AB} = 10.4 Hz, $CH_CCH_AH_BOSO_2Ar$), 4.01 (m, 1 H, C*H*OH), 3.37–3.48 (7, 4 H, $CHCH_2OC_{18}H_{35}$, $OCH_2C_{17}H_{33}$), 2.44 (s, 1 H, OH), 2.01 (m, 4 H, $CH_2CH{=}CHCH_2$), 1.27 (br s, 24 H, $(CH_2)_{12}$), 0.88 (br t, 3 H, ω-CH_3). Determination of the enantiomeric excess of the (*R*)-(+)-MTPA ester of (−)-**4b** by chiral stationary phase HPLC gave 99% ee.[24] Anal. Calcd for $C_{27}H_{45}O_7SN$: C, 61.45; H, 8.59; N, 2.65. Found: C, 60.82; H, 8.81; N, 2.75.

3-*O*-Oleyl-*sn*-glycerol 1-*O*-*m*-Nitrobenzenesulfonate ((+)-4′b). This compound was prepared in 76% yield from (*S*)-**3b** as described above: $[\alpha]^{25}_D$ +6.88° (*c* 2.33, $CHCl_3$); 97.1% ee.[24]

1-*O*-Petroselinyl-*sn*-glycerol 3-*O*-*m*-Nitrobenzenesulfonate ((−)-4c). A mixture of 130 mg (0.5 mmol) of (*R*)-(−)-**3b** [$[\alpha]^{25}_D$ −23.3° (*c* 2.14, $CHCl_3$)], 160 mg (0.60 mmol) of petroselinyl alcohol, and 3 drops of 10% boron trifluoride etherate in 3 mL of dichloromethane was stirred under nitrogen for 24 h. The solvent was removed under reduced pressure, and the residue was purified by flash chromatography (elution with 20% ethyl acetate in hexanes) to give 217 mg (82%) of (−)-**4c** as a colorless oil; TLC (20% ethyl acetate–hexanes) R_f 0.26; $[\alpha]^{25}_D$ −6.98° (*c* 2.33, $CHCl_3$); IR (neat) 3566–3319, 3120, 3013, 2919, 2849, 1602, 1537, 1461, 1445, 1431, 1373, 1349, 1190, 1119, 973, 932, 879, 761, 732, 668 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.78 (t, 1 H, *J* = 1.7 Hz, C_6H_4), 8.54 (m, 1 H, C_6H_4), 8.29 (m, 1 H, C_6H_4), 7.80 (t, 1 H, *J* = 8.0 Hz, C_6H_4), 5.34 (m, 2 H, vinyl), 4.24 (dd, 1 H, J_{AC} = 4.7 Hz, J_{AB} = 10.2 Hz, $CH_CCH_AH_BOSO_2Ar$), 4.21 (dd, 1 H, J_{BC} = 5.8 Hz, J_{AB} = 10.2 Hz, $CH_CCH_AH_BOSO_2Ar$), 4.01 (m, 1 H, C*H*OH), 3.38–3.47 (m, 4 H, $CHCH_2OC_{18}H_{35}$, $OCH_2C_{17}H_{33}$), 2.44 (s, 1 H, OH), 2.01 (m, 4 H, $CH_2CH{=}CHCH_2$), 1.27 (br s, 24 H, $(CH_2)_{12}$), 0.88 (br t, 3 H, ω-CH_3). Determination of the enantiomeric excess of the (*R*)-(+)-MTPA ester of (−)-**4c** by chiral stationary phase HPLC gave >99% ee.[24] Anal. Calcd for $C_{27}H_{45}O_7SN$: C, 61.45; H, 8.59; S, 6.08; N, 2.65. Found: C, 61.38; H, 8.80; S, 6.18; N, 2.67.

3-*O*-Petroselinyl-*sn*-glycerol 1-*O*-*m*-Nitrobenzenesulfonate ((+)-4′c). This compound was prepared from (*S*)-**3b** in 75% yield as described above; $[\alpha]^{25}_D$ +6.86° (*c* 2.33, $CHCl_3$); 98.1% ee.[24]

1-*O*-Petroselinyl-2-*O*-(methoxymethyl)-3-*O*-((*m*-nitrophenyl)sulfonyl)-*sn*-glycerol ((−)-13). To a mixture of 159 mg (0.30 mmol) of ring-opened intermediate (−)-**4c** and an excess (3 mL, 33.9 mmol) of dimethoxymethane in 3 mL of dry chloroform was added 750 mg (5.3 mmol) of phosphorus pentoxide. The mixture was stirred at room temperature under nitrogen for 24 h, then cooled to 0 °C, and treated with 10% aqueous sodium carbonate solution (about 2 mL, added dropwise) to consume the excess phosphorus pentoxide. The product was extracted into chloroform (2 × 50 mL), and the organic layer was dried (K_2CO_3) and evaporated to give 168 mg (98%) of (−)-**13**: TLC (25% ethyl acetate–hexanes) R_f 0.36; $[\alpha]^{25}_D$ −4.97° (*c* 1.88, $CHCl_3$); IR (neat) 3084, 2919, 2849, 1608, 1537, 1461, 1373, 1349, 1307, 1273, 1119, 1114, 1038, 973, 879, 808, 732, 673, 662, 585 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.78 (t, 1 H, *J* = 1.7 Hz, C_6H_4), 8.54 (m, 1 H, C_6H_4), 8.29 (m, 1 H, C_6H_4), 7.80 (t, 1 H, *J* = 7.9 Hz, C_6H_4), 5.35 (m, 2 H, vinyl), 4.63 (s, 2 H, CH_3OCH_2O), 4.33 (dd, 1 H, J_{AC} = 3.8 Hz, J_{AB} = 10.4 Hz, $CH_CCH_AH_BOSO_2Ar$), 4.22 (dd, 1 H, J_{BC} = 5.7 Hz, J_{AB} = 10.4 Hz, $CH_CCH_AH_BOSO_2Ar$), 3.94 (m, 1 H, C*H*OMOM), 3.35–3.49 (m, 4 H, $CHCH_2OC_{18}H_{35}$, $OCH_2C_{17}H_{33}$), 3.33 (s, 3 H, CH_3OCH_2),

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(24) HPLC was carried out on a chiral stationary phase (Pirkle type IA) column (4.6 × 250 mm, J. T. Baker); base-line separation of the diastereomeric (*R*)-MPTA esters was achieved by using a flow rate of 0.5 mL/min and elution with hexanes–*i*-PrOH 87.5:12.5.

2.01 (m, 4 H, $CH_2CH{=}CHCH_2$), 1.27 (br s, 24 H, $(CH_2)_{12}$), 0.88 (br t, 3 H, ω-CH_3).

1-*O*-Petroselinyl-2-*O*-(methoxymethyl)-*sn*-glycerol ((+)-15). A mixture of arenesulfonate (−)-13 (114 mg, 0.2 mmol) in 4 mL of dimethylformamide–dimethyl sulfoxide 4:1 and cesium acetate (154 mg, 0.8 mmol) was stirred under nitrogen for 4 h at room temperature. The mixture was extracted with diethyl ether (2 × 75 mL), washed with water (2 × 50 mL), dried over sodium sulfate, filtered, and concentrated in vacuo to a volume of ~5 mL. The crude acetate was cooled to 0 °C, and lithium aluminum hydride (16 mg, 0.4 mmol) was added in one portion. The mixture was stirred at 0 °C for 30 min and at room temperature for 1 h and then quenched by slow addition of water. The mixture was filtered to remove aluminum salts and extracted with chloroform (40 mL). The organic layer was dried over $MgSO_4$ and concentrated in vacuo to give a residue that was purified by flash chromatography (elution with hexanes–ethyl acetate 4:1). There was isolated 69 mg (89%) of (+)-15 as a clear, colorless oil: TLC (25% ethyl acetate–hexanes) R_f 0.34; $[\alpha]^{25}_D$ +19.92° (*c* 4.20, $CHCl_3$); IR (neat) 3448, 3013, 2919, 2849, 1461, 1155, 1114, 1032, 917 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.33 (m, 2 H, vinyl), 4.75 (s, 2 H, CH_3OCH_2O), 3.44–3.78 (m, 7 H, *CH*OMOM, $CHCH_2OC_{18}H_{35}$, $OCH_2C_{17}H_{33}$, CH_2OH), 3.42 (s, 3 H, CH_3OCH_2), 2.76 (br s, 1 H, OH) 2.01 (m, 4 H, $CH_2CH{=}CHCH_2$), 1.28 (br s, 24 H, $(CH_2)_{12}$), 0.87 (br t, 3 H, ω-CH_3).

1-*O*-Hexadecyl-2-*O*-palmitoyl-*sn*-glycerol 3-*p*-Toluenesulfonate ((−)-5). To a solution of 376 mg (0.80 mmol) of (−)-4a in 8 mL of hexane containing 97 μL (1.20 mmol) of pyridine was added dropwise 264 mg (0.96 mmol) of palmitoyl chloride in 10 mL of hexane. After the mixture was heated under reflux for 4 h, water (2 mL) was added to destroy the excess palmitoyl chloride, and refluxing was continued for 10 min. The mixture was cooled and diluted with hexane. The organic layer was washed with dilute sulfuric acid, water, saturated aqueous sodium bicarbonate solution, and water, then dried ($MgSO_4$), filtered, and concentrated by rotary evaporation. The free fatty acid was removed by dissolving the crude product in 100 mL of methanol–dichloromethane–hexane, 40:33:27, followed by extraction with 40 mL of 1 N potassium hydroxide. The upper layer containing the fatty acid salt was separated from the lower layer, which was diluted with 100 mL of hexane and washed with water three times to neutrality. The organic extracts were dried with $MgSO_4$ and concentrated by rotary evaporation to give a residue that afforded 452 mg (81%) of (−)-5 after two recrystallizations from cold (−20 °C) acetonitrile; mp 55–56 °C; TLC (20% ethyl acetate–hexanes) R_f 0.70; $[\alpha]^{25}_D$ −7.62° (*c* 0.32, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.75 (d, 2 H, J = 8.5 Hz, C_6H_4), 7.32 (d, 2 H, J = 8.5 Hz, C_6H_4), 5.04 (m, 1 H, CH_2CHCH_2), 4.35 (dd, 2 H, J = 4.5 and 11.5 Hz, CH_2OTs), 3.48 (dd, 2 H, J = 4.5 and 11.5 Hz, $CH_2OC_{16}H_{33}$), 3.35 (t, 2 H, J = 7.0 Hz, $OCH_2C_{15}H_{31}$), 2.43 (s, 3 H, $OSO_2C_6H_4CH_3$-*p*), 2.22 (t, 2 H, J = 8.0 Hz, $O_2CCH_2C_{14}H_{29}$), 1.29 (br s, 54 H, $OCH_2(CH_2)_{14}$ and $O_2CCH_2(CH_2)_{13}CH_3$), 0.86 (br t, 6 H, ω-CH_3). Anal. Calcd for $C_{42}H_{76}O_6S$: C, 70.64; H, 10.86; S, 4.79. Found: C, 70.58; H, 10.86; S, 4.79.

3-*O*-Hexadecyl-2-*O*-palmitoyl-*sn*-glycerol 1-*p*-Toluenesulfonate ((+)-5′). This compound was prepared as described above for (−)-5; yield, 83%; TLC (20% ethyl acetate–hexanes) R_f 0.70; $[\alpha]^{25}_D$ +7.48° (*c* 0.32, $CHCl_3$).

Diphenyl 1-*O*-Hexadecyl-2-*O*-palmitoyl-*sn*-glycero-3-phosphate ((+)-6). A mixture of 100 mg (0.14 mmol) of (−)-5 and 126 mg (0.35 mmol) of silver diphenyl phosphate in 7.5 mL of dry xylene was refluxed in the dark under nitrogen atmosphere for 6 h. The mixture was cooled to room temperature, filtered through a Celite pad, and washed with chloroform (3 × 30 mL). Evaporation of the solvent gave a yellow oil that was purified by flash chromatography (elution with hexanes–ethyl acetate 8:1). There was isolated 82 mg (75%) of diphenyl phosphate ester (+)-6, mp 44–45 °C; TLC (hexanes–ethyl acetate 8:1) R_f 0.28; $[\alpha]^{25}_D$ +2.14° (*c* 0.5, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.41 (br s, 10 H, C_6H_5), 5.04 (m, 1 H, CH_2CHCH_2), 4.41 (t, 2 H, J = 7.6 Hz, $CH_2OP(O)(OC_6H_5)_2$), 3.48 (d, 2 H, J = 8.2 Hz, $CH_2OC_{16}H_{33}$), 3.35 (t, 2 H, J = 7.0 Hz, $OCH_2C_{15}H_{31}$), 2.22 (t, 3 H, J = 8.0 Hz, $O_2CCH_2C_{14}H_{29}$), 1.29 (br s, 54 H, $OCH_2(CH_2)_{14}$ and $O_2CCH_2(CH_2)_{13}CH_3$), 0.86 (br t, 6 H, ω-CH_3).

1-*O*-Hexadecyl-2-*O*-palmitoyl-*sn*-glycero-3-phosphatidic Acid (7). A mixture of 100 mg (0.44 mmol) of platinum oxide in 10 mL of glacial acetic acid was stirred in a 50-mL two-necked flask under hydrogen atmosphere for 1 h at room temperature. A solution of 107 mg (0.14 mmol) of (+)-6 in 20 mL of acetic acid–cyclohexane 1:1 was added rapidly via syringe, and the mixture was stirred at room temperature for 6 h. The mixture was filtered through a Celite pad, which was washed with chloroform. Evaporation of the filtrate under vacuum gave a white solid, which was dissolved in a small volume of chloroform. Precipitation twice from cold (−20 °C) acetonitrile afforded 70 mg (79%) of 7, which was used in the next step without further purification.

1-*O*-Hexadecyl-2-*O*-palmitoyl-*sn*-glycero-3-phosphocholine ((*R*)-(−)-1; See Scheme I). To a solution of 70 mg (0.11 mmol) of phosphatidic acid 7 in 5 mL of dry pyridine were added 305 mg (1.1 mmol) of choline tosylate and 3 mL of trichloroacetonitrile. The mixture was heated under nitrogen at 50 ± 5 °C for 2 days, during which time the mixture became brown. After 10 mL of chloroform–methanol 1:1 was added, the solvents were removed under reduced pressure, leaving a brown residue. The residue was dissolved in 20 mL of tetrahydrofuran–water 9:1, and the solution was applied to a column of Amberlite MB-3 (25 g) that had been previously equilibrated with the same solvent system. Elution with 500 mL of tetrahydrofuran–water 9:1, evaporation of the solvents under reduced pressure, and azeotropic evaporation of water in a rotary evaporator with 2-propanol (3 × 50 mL) gave a brown residue that was purified by flash chromatography (elution with chloroform–methanol–water 65:25:4). There was isolated 27 mg (35%) of the desired phosphocholine (*R*)-(−)-1: TLC (chloroform–methanol–water 65:25:4) R_f 0.33; $[\alpha]^{25}_D$ −1.09° (*c* 0.52, $CHCl_3$–CH_3OH, 1:1) (32% optical purity, see below). Treatment of (*R*)-1 prepared by this procedure with phospholipase A_2 (*Naja naja*, Sigma Chemical Co.) in pH 7.4 buffer at 38 °C resulted in incomplete hydrolysis to 1-*O*-hexadecyl-2-lyso-*sn*-glycero-3-phosphocholine and palmitic acid (R_f 0.13 and 0.86, respectively, in chloroform–methanol–water, 65:25:4). Comparison of the $[\alpha]^{25}_D$ values of (*R*)-1 prepared by the routes outlined in Schemes I and II also indicates that partial racemization at C_2 occurred in Scheme I, probably at the refluxing xylene temperature used in the conversion of tosylate (−)-5 to diphenyl phosphate ester (+)-6; partial racemization via a dioxolane-type intermediate has been proposed previously.[12]

1-*O*-Hexadecyl-2-*O*-benzyl-*sn*-glycerol 3-*O*-*p*-Toluenesulfonate ((−)-8). Trifluoromethanesulfonic anhydride (168 μL, 1.0 mmol) was added to 5 mL of dry dichloromethane at −78 °C in an oven-dried 50-mL round-bottom flask equipped with a Claisen head and a nitrogen-filled balloon. A solution of 104 μL (1.0 mmol) of benzyl alcohol and 205 mg (1.0 mmol) of 2,6-di-*tert*-butyl-4-methylpyridine in 2 mL of dry dichloromethane was added dropwise over a 5-min period. After the reaction was stirred at −78 °C for 15 min, a solution of 235 mg (0.5 mmol) of (−)-4a and 268 mg (1.3 mmol) of 2,6-di-*tert*-butyl-4-methylpyridine in 2 mL of dry dichloromethane was added dropwise over a 5-min period. The mixture was stirred for 30 min at −78 °C and then allowed to warm to room temperature with stirring until all of (−)-4a had disappeared (about 4 h) as monitored by TLC (25% ethyl acetate–hexanes). The excess of benzyl trifluoromethanesulfonate was then destroyed by slowly adding 167 μL (2.07 mmol) of pyridine. The reaction mixture was diluted with 30 mL of dichloromethane and washed with water (3 × 10 mL). The organic phase was dried (Na_2SO_4), the solvents were evaporated under reduced pressure, and the residue was purified by flash chromatography (elution with hexanes–ethyl acetate 8:1) to furnish 268 mg (96%) of *O*-benzyl product (−)-8 as a colorless oil: TLC (hexanes–ethyl acetate 8:1) R_f 0.33; $[\alpha]^{25}_D$ −7.32° (*c* 5.0, $CHCl_3$); IR ($CHCl_3$) 1602, 1499, 1360, 1182, 1102, 820, 766, 756, 707 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.77 (d, 2 H, J = 8.3 Hz, Ar), 7.29 (m, 7 H, Ar), 4.58 (s, 2 H, $OCH_2C_6H_5$), 4.17 (dd, 1 H, J_{AC} = 4.1 Hz, J_{AB} = 10.4 Hz, $CH_CH_AH_BOTs$), 4.08 (dd, 1 H, J_{BC} = 5.8 Hz, J_{AB} = 10.4 Hz, $CH_CH_AH_BOTs$), 3.75 (m, 1 H, CH_2CHCH_2), 3.45 (collapsed AB quartet, 2 H, J = 7.86 Hz, $\Delta\nu$ = 4.66, $CH_2OC_{16}H_{33}$), 3.34 (t, 2 H, J = 6.6 Hz, $OCH_2C_{15}H_{31}$), 2.43 (s, 3 H, $OSO_2C_6H_4CH_3$), 1.26 (br s, 28 H, $OCH_2(CH_2)_{14}$), 0.89 (br t, 3 H, ω-CH_3).

3-*O*-Hexadecyl-2-*O*-benzyl-*sn*-glycerol 1-*O*-*p*-Toluenesulfonate ((+)-8′). This compound was prepared in 92% yield as described above for (−)-8; $[\alpha]^{25}_D$ +7.48° (*c* 5.0, $CHCl_3$).

1-*O*-Hexadecyl-2-*O*-benzyl-*sn*-glycerol ((−)-9). To a solution of 192 mg (1.0 mmol) of cesium acetate in 5 mL of dry dimethyl sulfoxide–dimethylformamide 4:1 was added 280 mg (0.5 mmol) of (−)-8. After the mixture was stirred at room temperature for 36 h under a drying tube, water (30 mL) was added and the product was extracted with ether (3 × 50 mL). The organic phase was dried with Na_2SO_4, and the solvents were concentrated under reduced pressure to a volume of about 10 mL. The solution was cooled to 0 °C, and 40 mg (1.0 mmol) of lithium aluminum hydride was added. After the mixture was stirred for 30 min at 0 °C and for 2 h at room temperature, water was added. The aluminum salts were removed by filtration and the product was extracted with chloroform (60 mL). Evaporation of the solvents under reduced pressure gave 187 mg (92% overall yield) of (−)-9 as a low-melting solid, mp 27–28 °C (lit.[18] mp 28–30 °C); $[\alpha]^{25}_D$ −9.27° (*c* 5.0, C_6H_6) [lit.[18] $[\alpha]^{25}_D$ −8.76° (*c* 5.0, C_6H_6)]; IR (Nujol) 3450, 1520, 1126, 1072, 742, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.37 (s, 5 H, C_6H_5), 4.81 (d, 1 H, J = 12.0 Hz, $OCH_AH_BC_6H_5$), 4.69 (d, 1 H, J_{AB} = 12.0 Hz, $OCH_AH_BC_6H_5$), 3.25–3.98 (m, 7 H, CH_2OCH_2, CH_2OH, CH_2CHCH_2), 2.15 (s, 1 H, OH), 1.26 (br s, 28 H, $OCH_2(CH_2)_{14}$), 0.88 (br t, 3 H, ω-CH_3).

3-*O*-Hexadecyl-2-*O*-benzyl-*sn*-glycerol ((+)-9′). This compound was prepared in 93% overall yield by the procedure described above for (−)-9; mp 29–31 °C (lit.[18] mp 28–30 °C); $[\alpha]^{25}_D$ +9.19° (*c* 5.0, C_6H_6) [lit.[18] $[\alpha]^{25}_D$ +8.70° (*c* 5.0, C_6H_6)].

1-*O*-Hexadecyl-2-*O*-benzyl-*sn*-glycero-3-phosphocholine ((+)-10). To a solution of 134 mg (0.90 mmol) of phosphorus oxychloride and 163 μL (0.90 mmol) of triethylamine in 4 mL of alcohol-free chloroform at −10 °C under nitrogen was added a solution of 243 mg (0.72 mmol) of (−)-9 in 4 mL of alcohol-free chloroform over a 30-min period. The mixture was allowed to warm to room temperature and was stirred for an additional 30 min. Choline tosylate (300 mg, 1.08 mmol) and pyridine (0.5 mL) were added, and the mixture was stirred under nitrogen for 16 h. Water (0.2 mL) was introduced, and stirring was continued for 30 min. After the solvents were removed under reduced pressure, 30 mL of dichloromethane–toluene 1:1 was added to the residue, and the mixture was filtered. Evaporation of the filtrate left a residue that was dissolved in tetrahydrofuran–water 9:1 and passed through an Amberlite MB-3 column two times (elution with tetrahydrofuran–water 9:1). The solvents were removed under vacuum, and the residue was purified by flash chromatography (elution with chloroform–methanol–water 65:35:4) to give 318 mg (75%) of (+)-10 as a white solid: mp 200 °C; $[\alpha]^{25}_D$ +3.92° (*c* 5.0, $CHCl_3$–CH_3OH 1:1) [lit.[18] $[\alpha]^{25}_D$ +3.54° (*c* 5.0, $CHCl_3$–CH_3OH 1:1)]; IR (Nujol) 3413 (H_2O), 3048, 1493, 1256, 1106, 1089, 1069, 1067, 705, 645 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.41 (s, 5 H, C_6H_5), 4.74 (s, 2 H, $OCH_2C_6H_5$), 3.32–4.62 (m, 11 H, CH_2OCH_2, $CHCH_2OP$, $P(O)(O^-)OCH_2$, $CH_2N^+(CH_3)_3$, CH_2CHCH_2), 3.25 (s, 9 H, $N^+(CH_3)_3$), 1.26 (br s, 28 H, $OCH_2(CH_2)_{14}$), 0.88 (br t, 3 H, ω-CH_3).

3-*O*-Hexadecyl-2-*O*-benzyl-*sn*-glycero-1-phosphocholine ((−)-10′). This compound was prepared in 73% yield by the procedure described above for (+)-10; $[\alpha]^{25}_D$ −3.95° (*c* 5.0, $CHCl_3$–CH_3OH 1:1) [lit.[18] $[\alpha]^{25}_D$ −3.53° (*c* 5.0, $CHCl_3$–CH_3OH 1:1)].

1-*O*-Hexadecyl-2-lyso-*sn*-glycero-3-phosphocholine ((−)-11). A mixture of 150 mg (0.24 mmol) of (+)-10 and 100 mg of 20% palladium hydroxide on carbon in 9 mL of methanol and 1 mL of water was stirred under hydrogen atmosphere for 24 h. The mixture was filtered through Celite, the Celite was washed with methanol, and the filtrate was evaporated under reduced pressure. The residue was dried by azeotropic removal of water using 2-propanol, giving 128 mg (100%) of (−)-11, mp 250 °C (dec); $[\alpha]^{25}_D$ −6.09° (*c* 1.04, $CHCl_3$–CH_3OH 1:1) [lit.[18] $[\alpha]^{25}_D$ −6.03° (*c* 1.04, $CHCl_3$–CH_3OH 1:1)]; IR (Nujol) 3280, 1252, 1095, 1062 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.48–3.51 (m, 11 H, CH_2OCH_2, $CHCH_2OP$, $P(O)(O^-)OCH_2$, $CH_2N^+(CH_3)_3$, CH_2CHCH_2), 3.28 (s, 9 H, $N^+(CH_3)_3$), 1.26 (br s, 28 H, $OCH_2(CH_2)_{14}$), 0.88 (br t, 3 H, ω-CH_3). Anal. Calcd for $C_{24}H_{52}O_6PN·1.5H_2O$: C, 56.67; H, 10.89; N, 2.71. Found: C, 56.66; H, 10.80; N, 2.24.

3-*O*-Hexadecyl-2-lyso-*sn*-glycero-1-phosphocholine ((+)-11′). The same procedure described above for the preparation of (−)-11 was used to prepare 11′ in 100% yield; mp 250 °C (dec); $[\alpha]^{25}_D$ +6.11° (*c* 1.05, $CHCl_3$–CH_3OH 1:1).

1-*O*-Hexadecyl-2-*O*-palmitoyl-*sn*-glycero-3-phosphocholine ((*R*)-(−)-1; See Scheme II). A mixture of 53 mg (0.12 mmol) of (−)-11, 291 mg (0.60 mmol) of palmitic anhydride, and 15 mg (0.12 mmol) of 4-(dimethylamino)pyridine in 2 mL of alcohol-free chloroform was stirred under nitrogen for 24 h. The solvents were removed under reduced pressure, leaving a residue that was purified by flash chromatography (elution with 200 mL of chloroform, followed by 200 mL of chloroform–methanol 9:1, and 500 mL of chloroform–methanol 3:2). There was isolated 85 mg (98%) of (*R*)-(−)-1, which was lyophilized from 3 mL of benzene; $[\alpha]^{25}_D$ −3.38° (*c* 0.53, $CHCl_3$–CH_3OH 1:1); ^1H NMR ($CDCl_3$) δ 5.16 (m, 1 H, CH_2CHCH_2), 3.25–3.59 (m, 10 H, CH_2OCH_2, $CHCH_2OP$, $P(O)(O^-)OCH_2$, $CH_2N^+(CH_3)_3$), 3.22 (s, 9 H, $N^+(CH_3)_3$, 2.33 (t, 3 H, J = 8.0 Hz, O_2CCH_2), 1.26 (br s, 54 H, $OCH_2(CH_2)_{14}$ and $O_2CCH_2(CH_2)_{13}$), 0.88 (br t, 3 H, ω-CH_3). Anal. Calcd for $C_{40}H_{82}O_7PN·3H_2O$: C, 61.06; H, 11.05; N, 1.81; P, 4.00. Found: C, 59.80; H, 11.06; N, 1.73; P, 4.00.

3-*O*-Hexadecyl-2-*O*-palmitoyl-*sn*-glycero-1-phosphocholine ((*S*)-(+)-1). This compound was prepared in 97% yield by the procedure described above for (*R*)-(−)-1; $[\alpha]^{25}_D$ +3.42° (*c* 0.50, $CHCl_3$–CH_3OH 1:1). Anal. Calcd for $C_{40}H_{82}O_7PN·4H_2O$: C, 60.06; H, 11.45; N, 1.77; P, 3.91. Found: C, 60.09; H, 11.06; N, 1.72; P, 4.61.

1-*O*-Hexadecyl-2-*O*-acetyl-*sn*-glycero-3-phosphocholine ((*R*)-2). A mixture of 30 mg (0.060 mmol) of lyso-PAF (11), 7 mg (0.066 mmol) of 4-(dimethylamino)pyridine, and 110 μL (1.2 mmol) of acetic anhydride in 2 mL of chloroform was stirred at room temperature for 24 h. The solvents were removed under reduced pressure to leave a residue that was purified by flash chromatography (elution with $CHCl_3$–CH_3OH–H_2O, 65:25:4), yielding 30 mg (93%) of (*R*)-2 as a white solid, mp 248 °C (dec); $[\alpha]^{25}_D$ −3.39° (*c* 0.53, $CHCl_3$–CH_3OH, 1:1); lit.[8c] $[\alpha]^{25}_D$ −3.30° (*c* 0.53, $CHCl_3$–CH_3OH, 1:1); ^1H NMR ($CDCl_3$) δ 5.11 (m, 1 H, CH_2CHCH_2), 4.20 (m, 4 H, CH_2CHCH_2), 3.40–3.52 (m, 10 H, CH_2OCH_2, CH_2OP, $P(O)(O^-)OCH_2$, $CH_2N^+(CH_3)_3$), 3.30 (s, 9 H, $N^+(CH_3)_3$), 2.08 (s, 3 H, O_2CCH_3), 1.29 (br s, 28 H, $(CH_2)_{14}$), 0.89 (t, J = 8.0 Hz, 3 H, ω-CH_3); IR (KBr) 3428, 2926, 2856, 1732, 1627, 1460, 1372 cm^{-1}. Anal. Calcd for $C_{26}H_{54}O_7PN·1.5H_2O$: C, 56.71; H, 10.43; N, 2.54. Found: C, 56.66; H, 10.80; N, 2.24.

3-*O*-Hexadecyl-2-*O*-acetyl-*sn*-glycero-1-phosphocholine ((*S*)-2). The above procedure was repeated with 11′, giving (*S*)-2 in 92% yield; $[\alpha]^{25}_D$ +3.20° (*c* 0.53, $CHCl_3$–CH_3OH, 1:1); lit.[8c] $[\alpha]^{25}_D$ +3.18° (*c* 0.53, $CHCl_3$–CH_3OH, 1:1).

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