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Synthesis of Benzophenone-Containing Analogues of Phosphatidylcholine

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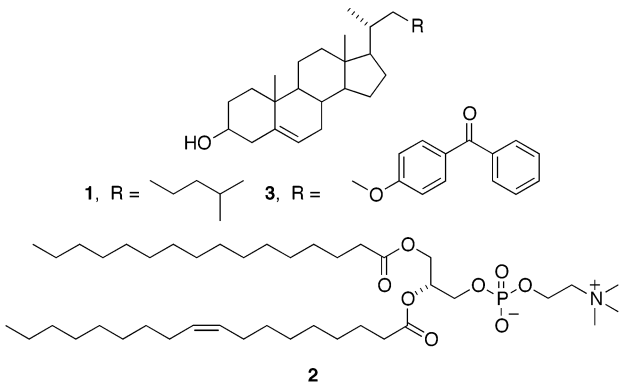
As part of a collaborative study of cellular efflux of cholesterol and phospholipids, photoactivable analogues **4**−**8** of phosphatidylcholine (PC) having benzophenone groups in the choline moiety and at the end of the C2 and C1 alkyl chains have been synthesized. The efficient preparation via Suzuki coupling of the appropriate long-chain benzophenone-containing carboxylic acid and alcohol and their incorporation by adaptation of known approaches into the acyl- and ether-linked PC analogues **6**−**8** are described. Development of a method for radiolabeling these PC analogues, via hydrogenation of a double bond in modified side chains, is also described.

Introduction

Phospholipids are a major structural component of cellular bilayer membranes and play important roles in many cellular processes.[1] One of these roles is maintaining cholesterol homeostasis in peripheral cells through participation in cellular cholesterol efflux and HDL formation.[2] As part of a collaborative study of the sequence of events involved in this transport of cholesterol and phospholipids out of cells,[3] we required photoactivable analogues of both cholesterol (**1**) and phosphatidylcholine (PC, **2**[4]), the major phospholipid involved in cholesterol efflux, for use in photoaffinity labeling experiments. This paper describes the synthesis of several analogues of phosphatidylcholine-containing benzophenone photophores.

Preparation of photoactivable analogues of phospholipids was pioneered by Khorana,[5,6] and a number of additional examples have subsequently been synthesized, usually containing azide or diazirine groups,[7−12] most notably the 3-trifluoromethyl-3-aryldiazirine developed by Brunner.[13] PC analogues containing the benzophenone photophore have also been utilized,[14−16] including the intriguing transmembrane probe, investigated by Nakatani and Ourisson,[17] having a benzophenone fixed between two phospholipids. The benzophenone group was selected for our studies as well because it has several distinct advantages[17−20] over the other commonly used photophores: it is stable and easily introduced; it is photoactivable at relatively long wavelengths (ca. 350 nm), which minimizes damage to proteins; it has a relatively high efficiency and selectivity for α-carbon atoms of amino acids in its photochemical reactions, and, it is hydrophobic, like the lipids into which it is to be incorporated. We have already demonstrated the suitability of the benzophenone photophore by successful covalent labeling of proteins involved in cholesterol efflux with the benzophenone-containing cholesterol analogue **3** (FCBP).[3]



For studies with photoactivable analogues of PC (**2**), we wished to use compounds that closely resembled **2**

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(1) Dowhan, W.; Bogdanov, M. *New Compr. Biochem.* **2002**, *36*, 1−35.
(2) Fielding, C. J.; Fielding, P. E. *Biochim. Biophys. Acta* **2001**, *1553*, 175−189.
(3) Fielding, P. E.; Russel, J. S.; Spencer, T. A.; Hakamata, H.; Nagao, K.; Fielding, C. J. *Biochemistry* **2002**, *41*, 4929−4937.
(4) Phosphatidylcholines occur naturally with differing fatty acid chains on C1 and C2, and commercial PCs are mixtures of compounds. Structure **2** shows the C1 palmitoyl, C2 oleoyl version, which is a major component of natural PCs.
(5) Chakrabarti, P.; Khorana, H. G. *Biochemistry* **1975**, *14*, 5021−5033.
(6) Gupta, C. M.; Radhakrishnan, R.; Gerber, G. E.; Olsen, W. L.; Quay, S. C.; Khorana, H. G. *Proc. Natl. Acad. Sci. U.S.A.* **1979**, *76*, 3139−3143.
(7) Schroit, A. J.; Madsen, J.; Ruoha, A. E. *Biochemistry* **1987**, *26*, 1812−1819.
(8) Perides, G.; Harter, C.; Traub, P. *J. Biol. Chem.* **1987**, *262*, 13742−13749.
(9) Zachowski, A.; Fellmann, P.; Herve, P.; Devaux, P. F. *FEBS Lett.* **1987**, *223*, 315−320.
(10) Goldmann, W. H.; Niles, J. L.; Arnaout, M. A. *Eur. J. Biochem.* **1999**, *261*, 155−162.
(11) Janssen, M. J. F. W.; van Voorst, F.; Ploeger, G. E. J.; Mose, P.; Larsen, M. R.; de Kroon, A. I. P. M.; de Kruijff, B. *Biochemistry* **2002**, *41*, 5702−5711.
(12) Li, G. Ph.D. Dissertation, City University of New York, New York, 2002; *Diss. Abstr. Int. B.* **2002**, *62*, 5734; UMI no. 3037416.

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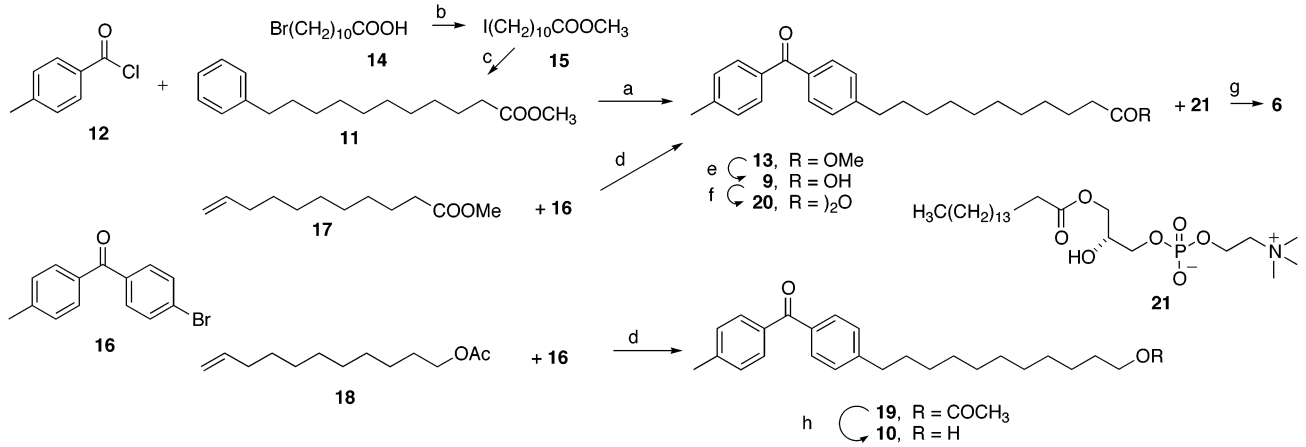
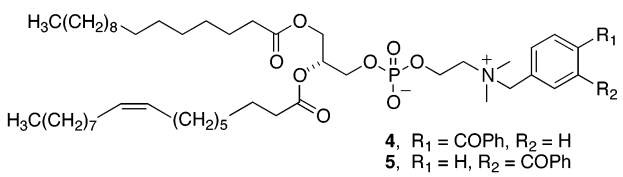
SCHEME 1[a]

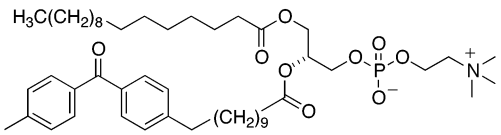


[a] Reagents: (a) $AlCl_3$, CH_2Cl_2. (b) CH_3I, K_2CO_3, acetone. (c) Ph_2CuLi, THF. (d) **17** + 9-BBN, THF; **16**, Cs_2CO_3, Ph_3As, $Pd(dppf)Cl_2$, DMF, THF, H_2O. (e) 95% EtOH, KOH. (f) DCC, CCl_4. (g) DMAP, $CHCl_3$. (h) 90% EtOH, KOH.

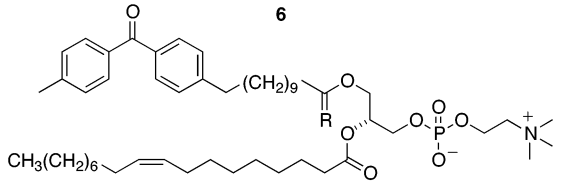
structurally, but we also wished to incorporate the photolabile functionality at widely separated positions within **2** in order to probe differing areas of proteins or other lipids to which the surrogates for **2** were bound. Accordingly, it was decided to prepare PC analogues containing benzophenones at three distinct sites: in the choline moiety, as in **4** and **5**; in the C2 chain, as in **6**; and in the C1 chain, attached by either the natural acyl linkage, as in **7**, or by a nonlabile ether linkage, as in **8**.



4, R_1 = COPh, R_2 = H
5, R_1 = H, R_2 = COPh



6



7, R = O
8, R = H_2

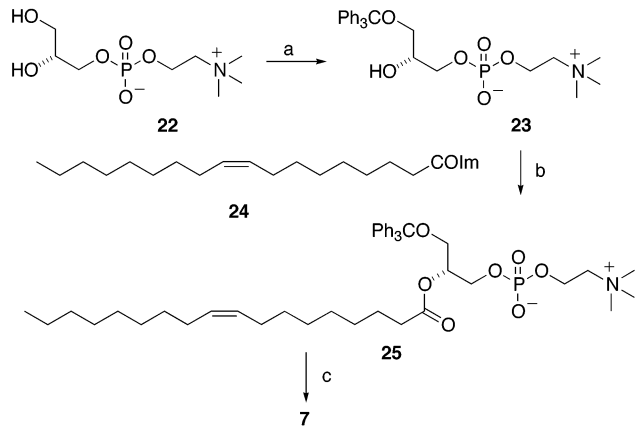
Results and Discussion

Analogues **4** and **5** were prepared via demethylation of commercially available **2**[4] with DABCO[21] followed by alkylation of the resulting tertiary amine, according to Stoffel's procedure,[22] with either 4-bromomethylbenzophenone or 3-bromomethylbenzophenone. If subsequently required, radiolabeled **4** and **5** could readily be prepared by use of the known[23,24] tritiated alkylating agents.

For the synthesis of PC analogues **6**−**8**, preparation of the benzophenone-containing fatty acid surrogates carboxylic acid **9** and alcohol **10** was first required. Synthesis of **9** via Friedel−Crafts reaction of methyl 11-phenylundecanoate (**11**) with 4-methylbenzoyl chloride (**12**) to afford **13** has been reported[25] (Scheme 1), but in our hands this produced a mixture of isomers, resulting from the fact that the commercially available phenylundecanoic acid used as starting material was a mixture of isomers, as clearly indicated by ^{1}H NMR. Pure **11** was prepared, as shown in Scheme 1, from 11-bromoundecanoic acid (**14**) via treatment with iodomethane and K_2CO_3 to afford 94% yield of **15**, followed by coupling with diphenylcuprate in 80% yield. However, since Friedel−Crafts acylation of **11** with **12** afforded only 23% yield of ester **13** in our initial attempts, the following much more efficient synthesis was developed. Bromomethylbenzophenone **16**, prepared from bromobenzene, oxalyl chloride, and toluene by the method of Taber and Sethuranam,[26] or in better yield from 4-bromobenzoyl chloride and toluene by the method of Nakatani et al.,[27] was converted to **13** in 93% yield via Suzuki coupling[28,29] with methyl

(13) Brunner, J.; Senn, H.; Richards, F. M. *J. Biol. Chem.* **1980**, *255*, 3313−3318.
(14) Page, G. P.; Rosenbusch, J. P. *Biochem. J.* **1986**, *235*, 651−661.
(15) Montecucco, C.; Schiavo, G. *Biochem. J.* **1986**, *237*, 309−312.
(16) Lala, A. K.; Kumar, E. R. *J. Am. Chem. Soc.* **1993**, *115*, 3982−3988.
(17) Nakatani, Y.; Yamamoto, M.; Diyizou, Y.; Warnock, W.; Dollé, V.; Hahn, W.; Milon, A.; Ourisson, G. *Chem. Eur. J.* **1996**, *2*, 129−138.
(18) Dormán, G.; Prestwich, G. D. *Biochemistry* **1994**, *33*, 5661−5673.
(19) Prestwich, G. D.; Dormán, G.; Elliott, J. T.; Marecak, D. M.; Chaudhardy, A. *Photochem. Photobiol.* **1997**, *65*, 222−234.
(20) Weber, P. J. A.; Beck-Sickinger, A. G. *J. Pept. Res.* **1997**, *49*, 375−383.
(21) Dac, L. K.; Guenter, H.; Hans, B. *Ger. Offen.* **1979**, DE 2728893, p. 11.
(22) Stoffel, W. *Methods Enzymol.* **1975**, *35*, 533−541.
(23) Ceruso, M.; Prestwich, G. D. *Bioorg. Med. Chem. Lett.* **1994**, *4*, 2179−2184.
(24) Lee, H.-K.; Denner-Ancona, P.; Sakakibara, J.; Ono, T.; Prestwich, G. D. *Arch. Biochem. Biophys.* **2000**, *381*, 43−52.
(25) Markovic, D. Z.; Durand, T.; Patterson, L. K. *Photochem. Photobiol.* **1990**, *51*, 389−394.
(26) Taber, D. F.; Sethuranam, M. R. *J. Org. Chem.* **2000**, *65*, 254−255.
(27) Nakatani, K.; Dohno, C.; Nakamura, T.; Saito, I. *Tetrahedron Lett.* **1998**, *39*, 2779−2782.
(28) Johnson, C. R.; Braun, M. P. *J. Am. Chem. Soc.* **1993**, *115*, 11014−11015.

SCHEME 2[a]



[a] Reagents: (a) Ph_3CCl, $ZnCl_2$, DMF. (b) DMSO, Na; **24**, THF. (c) **20**, BF_3-OEt_2, CH_2Cl_2.

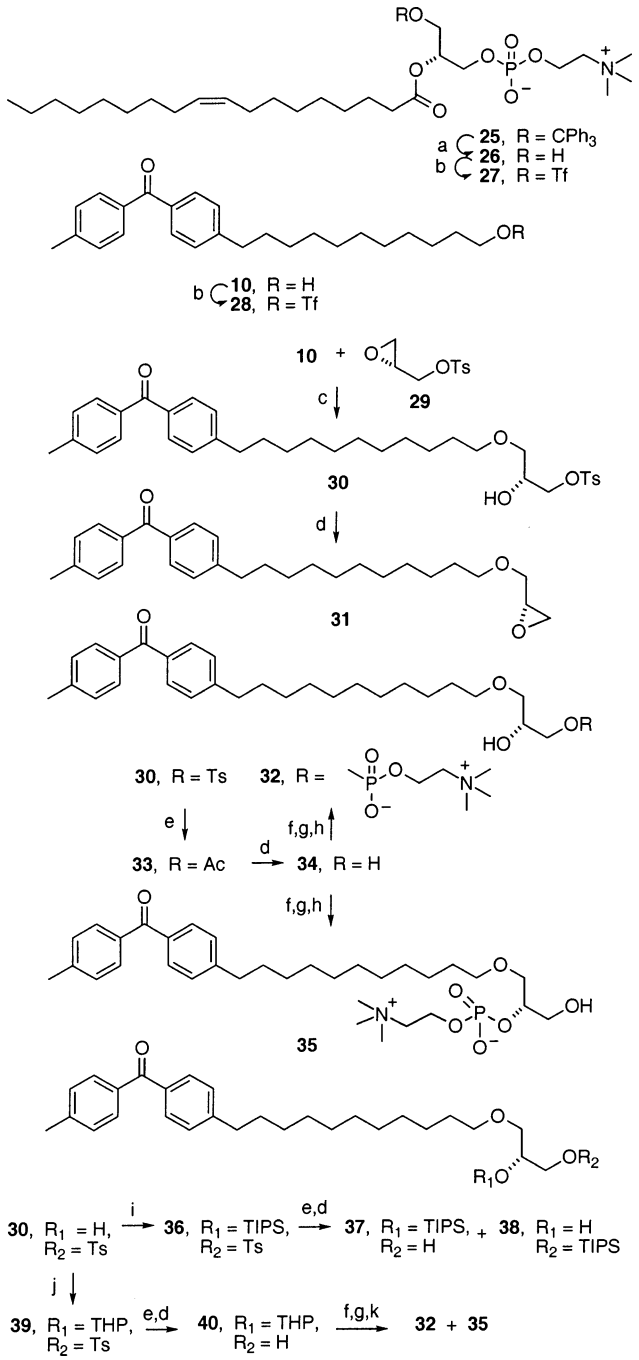
10-undecenoate (**17**), which had been subjected to hydroboration with 9-BBN. Saponification of **13** afforded 99% yield of crystalline **9**. Preparation of alcohol **10** was efficiently accomplished by analogous Suzuki coupling of **16** with 10-undecenyl acetate (**18**)[30] to afford **19**, followed by hydrolysis to **10**.

For preparation of PC analogue **6** having photoactivable fatty acid surrogate **9** attached at C2, **9** was first converted to anhydride **20** by use of DCC. Acylation of commercially available 1-palmitoyl-*sn*-glycero-3-phosphocholine (**21**) with **20** was then conducted according to the procedure of Ali and Bittman[31] (Scheme 1), which they report to result in less than 1% migration of the C1 acyl group to C2 during the reaction, as carefully determined by a series of experiments. We employed ^{31}P NMR, as previously described,[32] to determine whether such migration had occurred in the acylation with **20**. Only one ^{31}P peak was observed in **6**, indicating that in our case migration of the palmitoyl group from C1 to C2 was likewise insignificant.

Among the several approaches that have been developed for the synthesis of C1 acyl-linked phospholipids such as **7**,[33] the most direct appeared to be that of Hermetter,[34] which proved to be readily adaptable to incorporation of the benzophenone-containing **9** (Scheme 2). Glycerophosphocholine (**22**) was freed from its commercially available cadmium chloride complex and, as had been done by Hermetter,[34] was protected as its C1 trityl ether **23**, which was converted to the C2 acylated **25** by reaction with oleoylimidazole (**24**). In the key step, **25** was treated with anhydride **20** in the presence of $BF_3 \cdot OEt_2$ to afford 79% of the desired **7**.

Previous syntheses of phospholipids with C1 ether linkages, as in PC analogue **8**, have usually involved use of a protecting group at C2 other than the natural acyl

SCHEME 3[a]



[a] Reagents: (a) 14% BF_3-H_3COH, CH_2Cl_2. (b) Tf_2O, CH_2Cl_2, 2,6-di-*t*-butyl-4-methyl-py. (c) BF_3-OEt_2, $CHCl_3$. (d) K_2CO_3, H_3COH. (e) CsOAc, DMF, DMSO. (f) $POCl_3$, Et_3N, THF. (g) choline-OTs, py, CH_2Cl_2. (h) H_2O. (i) TIPSOTf, 2,6-lutidine, CH_2Cl_2. (j) dihydropyran, PPTS, CH_2Cl_2. (k) H_2O, THF, Δ.

substituent. We initially, and unrewardingly, tried simpler, more direct approaches to **8**. First, intermediate **25** was deprotected with BF_3 in methanol to afford the known[35] **26** (Scheme 3), which was treated with triflic anhydride, to form **27**, and then with the anion of alcohol **10**, but the desired substitution reaction to form **8** was not realized. Reaction of triflate **28** derived from **10** with

(29) Chemler, S. R.; Danishefsky, S. J. *Org. Lett.* **2000**, *2*, 2695–2698.
(30) Bosch, M. P.; Petschen, I.; Guerrero, A. *Synthesis* **2000**, 300–304.
(31) Ali, S.; Bittman, R. *Chem. Phys. Lipids* **1989**, *50*, 11–21.
(32) Chupin, V. V.; Ostapenko, O. V.; Klykov, V. N.; Anikin, M. V.; Serebrenikova, G. A. *Chem. Phys. Lipids* **1996**, *81*, 35–43.
(33) Bittman, R. In *Phospholipids Handbook*; Cevc, G., Ed.; Dekker: New York, 1993; Chapter 6, pp 141–232.
(34) Hermetter, A.; Stütz, H.; Franzmair, R.; Paltauf, F. *Chem. Phys. Lipids* **1989**, *50*, 57–62.
(35) Borsotti, G.; Guglielmetti, G.; Spera, S.; Battistel, E. *Tetrahedron* **2001**, *57*, 10219–10227.

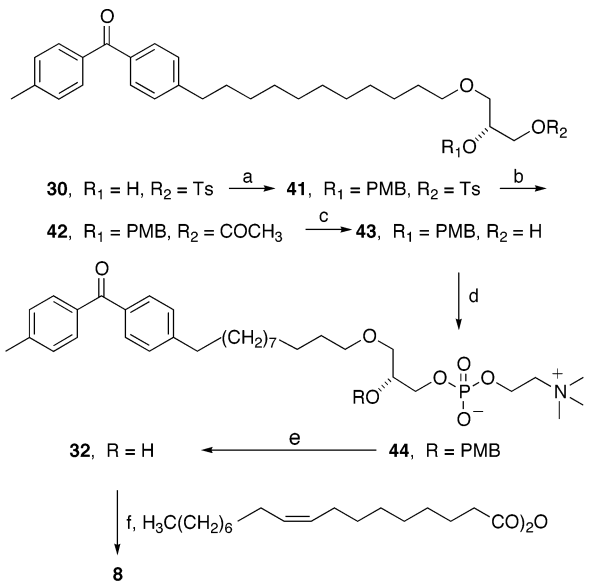
the anion of **26** likewise failed, as did attempts to effect C1 ether formation directly from deprotonated **22**.

It was next decided to adopt the elegant and efficient approach developed by Guivisdalsky and Bittman,[36,37] utilizing (2*R*)-(−)glycidyl tosylate (**29**) as starting material, and this eventually led to successful preparation of **8**. In the key first reaction,[36] the C1 ether linkage was forged by reaction of **29** with benzophenone-containing alcohol **10** in the presence of BF_3·OEt_2 to give 81% yield of **30**, which was used as the basis for all further experiments leading to **8**. Guivisdalsky and Bittman[36] carefully determined by two methods that this type of reaction proceeds with almost complete retention of configuration at C2, and we obtained confirmation that **30** also was obtained with ≥95% ee by examination of the ^{1}H NMR spectrum of its Mosher ester,[38] which showed exclusively for the C3 methylene protons a pattern essentially identical with that previously observed for the corresponding enantiomer of a closely analogous structure.[36]

In previous syntheses of C1 ether-linked phospholipids using this approach, it was at this stage that a C2 protecting group had been introduced. In an attempt to eliminate use of such a protecting group, **30** was converted to epoxide **31** by treatment with K_2CO_3 in methanol, as shown in Scheme 3, since an example of opening of a similar epoxide with phosphorylcholine has been reported.[39] However, the analogous reaction of **31** with phosphorylcholine, in an attempt to form **32**, was unsuccessful. Next, following established procedures,[37] **30** was converted with cesium acetate to acetate **33**, accompanied by some **31**, and thence to diol **34** with K_2CO_3 in aqueous methanol; however, attempted introduction of the phosphocholine moiety selectively at C3 of **34** by standard procedures[37] produced a 3:1 mixture of the desired **32** with C2 derivative **35**, as indicated by the appearance of two peaks in the ^{31}P NMR spectrum of the product. Use of a C2 protecting group seemed unavoidable, but the benzyl group used by Bittman[37] was judged to be unsuitable because we had observed in our work with cholesterol analogue **3**[3,40] that hydrogenation conditions sufficient to remove the benzyl group would also cause reduction of the carbonyl group of the benzophenone moiety.

Two different types of protecting groups were tried before success in preparing **8** was achieved with a third. First, **30** was converted to the C2 TIPS derivative **36**, but subsequent conversion of the C3 tosylate to the free C3 hydroxyl group by the usual two-step procedure[37] led to a 1:4 mixture of the desired **37** with **38**, resulting from migration of the TIPS group, analogous to that previously observed.[41] When **30** was instead converted to THP ether **39**, the two-step conversion to **40** was successful, but introduction of the phosphocholine group via successive

SCHEME 4[a]



[a] Reagents: (a) 4-methoxybenzyltrichloroacetimidate, F_3CSO_3H, Et_2O. (b) CsOAc, DMSO, DMF. (c) K_2CO_3, H_3COH. (d) $POCl_3$, Et_3N, $CHCl_3$; choline tosylate, Py. (e) DDQ, CH_2Cl_2, H_2O. (f) BF_3−OEt_2, CH_2Cl_2.

treatment with $POCl_3$ and choline tosylate,[42] followed by deprotection, led, as revealed by ^{31}P NMR, to a 2:1 mixture of **32** with **35**, in which the phosphocholine group had migrated from C3 to C2.

Success was finally attained by use of the *p*-methoxybenzyl protecting group at C2 (Scheme 4). The usual conditions for introducing this group, *p*-methoxybenzyl chloride in the presence of base, converted **30** to epoxide **31**, but use of 4-methoxybenzyl trichloroacetimidate in the presence of trifluorosulfuric acid[43] afforded 87% yield of the desired **41**. Through now familiar transformations,[37] **41** was converted via **42** to **43** with a C3 hydroxyl group, upon which the phosphocholine moiety was installed[37] to produce **44**. Removal of the *p*-methoxybenzyl group of **44** was effected with DDQ[44] to afford 58% yield of **32**, and reaction of **32** with oleic anhydride in the presence of DMAP afforded 76% yield of the desired ether-linked analogue **8**. However, ^{31}P NMR of this product revealed that it contained a small amount of an impurity, presumably the isomer resulting from C3 to C2 migration of the choline moiety before acylation, as previously observed.[32] Such migration could be prevented by use of $HClO_4$ as an acylation catalyst, as also previously reported,[32] but ^{1}H NMR indicated that this procedure apparently effected some isomerization of the oleoyl double bond. Pure **8** was finally obtained, also in 76% yield (21% overall from **29**), by conducting the acylation with BF_3·OEt_2 as the catalyst. Detailed examination of the ^{13}C NMR spectra of **8**, in comparison with those of

(36) Guivisdalsky, P. N.; Bittman, R. *J. Org. Chem.* **1989**, *54*, 4637−4642.
(37) Guivisdalsky, P. N.; Bittman, R. *J. Org. Chem.* **1989**, *54*, 4643−4648.
(38) Dale, D. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543−2549.
(39) Cimetiere, B.; Jacob, L.; Julia, M. *Tetrahedron Lett.* **1986**, *27*, 6329−6332.
(40) Russel, J. S. Ph.D. Dissertation, Dartmouth College, Hanover, NH, 1999.
(41) Seela, F.; Fröhlich, T. *Helv. Chim. Acta* **1994**, *77*, 399−408.
(42) Prashad, M.; Tomesch, J. C.; Wareing, J. R. *Chem. Phys. Lipids* **1990**, *53*, 121−126. No THP group migration during a similar reaction is reported by these authors, but no evaluation of the product by ^{31}P NMR or other means is reported.
(43) Nakajima, N.; Horita, K.; Abe, R.; Yonemitsu, O. *Tetrahedron Lett.* **1988**, *29*, 4139−4142.
(44) Oikawa, Y.; Yoshioka, T.; Yonemitsu, O. *Tetrahedron* **1982**, *23*, 885−888.

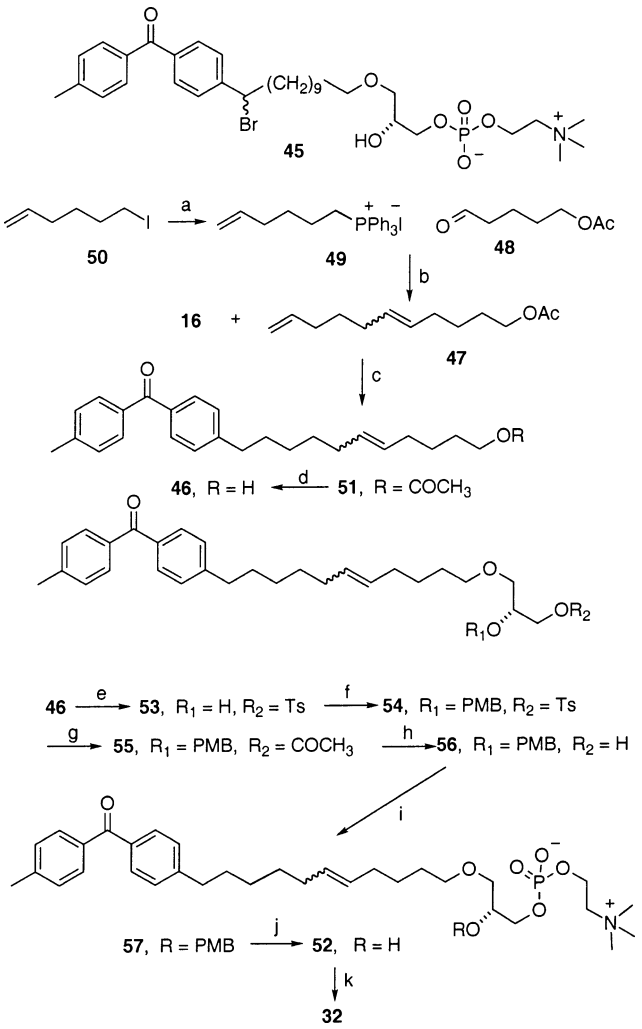
oleic acid (cis) and elaidic acid (trans), established, on the basis of the absence of the relatively deshielded allylic carbon atoms characteristic of trans isomers,[45,46] that use of BF_3·OEt_2 had not effected any isomerization of the double bond in the C2 oleoyl side chain.

In order for PC analogues **4**−**8** to be used effectively in the planned biochemical photolabeling experiments, it was necessary that they also be prepared in radiolabeled form. Methodology for effecting tritiation at a late stage in the syntheses was first investigated in the series of intermediates leading to the less reactive ether-linked **8**. The first approach we explored involved benzylic bromination of **32**, to be followed by reconversion to labeled **32** with tritiated sodium cyanoborohydride.[47] Treatment of **32** with NBS and benzoyl peroxide led to a product that ^{1}H NMR indicated to be principally a mixture of **32** and monobromo compound **45**, with its diagnostic triplet at δ 5.0 ppm (Scheme 5). Treatment of this mixture with sodium cyanoborohydride in HMPA[48] did indeed reform **32**, but in only ca. 90% purity. Since chromatographic purification of phospholipids such as **32** is extremely difficult, a cleaner method was sought.

To this end, it was decided to repeat essentially the entire synthesis of **8** with a Cl chain containing a double bond that could be cleanly catalytically tritiated before the final installation of the C2 oleoyl moiety. The specific unsaturated benzophenone-containing C1 chain alcohol selected as our target was **46** (Scheme 5), which was attractive because precursor **47**, suitable for Suzuki coupling with **16**, seemed readily accessible by a route analogous to that used previously to prepare the corresponding alcohol as a mixture of cis and trans isomers.[49] Accordingly, acetate **48**, instead of the corresponding alcohol, and phosphonium salt **49** were coupled in a Wittig reaction to produce **47**. Phosphonium salt **49** was cleanly prepared by reaction of iodide **50** with triphenylphosphine in nitromethane,[50] but only after earlier attempts to repeat the reported[51] preparation of the corresponding phosphonium bromide in chlorobenzene surprisingly failed. Suzuki coupling of **47** with **16** afforded 63% of **51**, which was methanolyzed to furnish **46**. Conversion of **46** to the unsaturated analogue **52** of **32** was accomplished by exactly the same sequence used to prepare **32**, involving the successive reactions **46** → **53** → **54** → **55** → **56** → **57** → **52** (Scheme 5). Hydrogenation of **52** to **32** was conducted with Wilkinson's catalyst and 10% Pd/C, but the most selective catalyst found was 5% Pd/C in ethanol, which in 2 h effected reduction of the double bond of **52** without any concomitant reduction of the carbonyl group.

An analogous approach was then used to develop a method for tritiation of C1 and C2 ester-linked analogues

SCHEME 5[a]



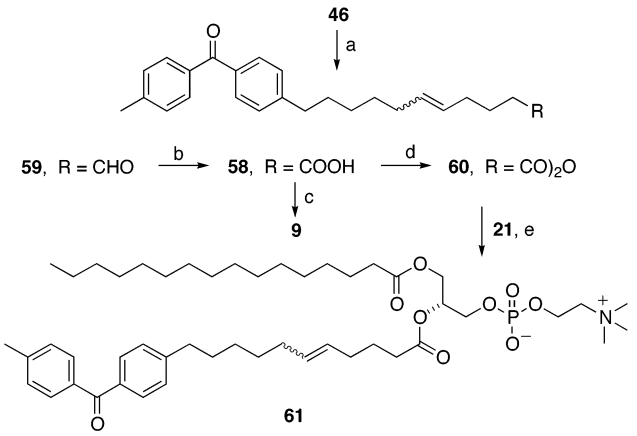
[a] Reagents: (a) Ph_3P, CH_3NO_2. (b) **49**, ^{n}BuLi, Et_2O; **48**, Et_2O. (c) **47**, 9-BBN, THF; **16**, Cs_2CO_3,Ph_3As, Pd(dppf)Cl_2, DMF, THF, H_2O. (d) K_2CO_3, CH_3OH, H_2O. (e) **29**, BF_3−OEt_2, $CHCl_3$. (f) 4-methoxybenzyltrichloroacetimidate, CF_3SO_3H, Et_2O. (g) CsOAc, DMSO−DMF. (h) K_2CO_3. CH_3OH. (i) $POCl_3$, Et_3N, $CHCl_3$; choline tosylate, Py. (j) DDQ, CH_2Cl_2, H_2O. (k) 5% Pd/C, EtOH, H_2.

7 and **6** (Scheme 6). The requisite unsaturated analogue **58** of acid **9** was prepared from unsaturated alcohol **46** by oxidation with PCC to afford aldehyde **59** and then with $NaClO_2$/NaH_2PO_4[52] to give **58**. Selective hydrogenation of **58** to **9** could be accomplished by use of 5% Pd/C in EtOAc for 40 min. Radiolabeled **7** could be prepared, when needed, by the reaction of **9**, thus tritiated, with **25**. To complete a route for the synthesis of **6** that would permit tritium incorporation, **21** was acylated with anhydride **60** derived from **58** to give **61**, the requisite precursor of radiolabeled **6**.

In summary, a series of phosphatidylcholine analogues containing benzophenone photophores in the choline moiety (**4** and **5**), in the C2 side chain (**6**), and in the C1 side chain (**7** and **8**), have been synthesized, and efficient methods for radiolabeling **7** or **8** have been developed. Preliminary biochemical evaluation of these compounds as surrogates for PC is in progress.

(45) Batchelor, J. G.; Cushley, R. J.; Prestegard, J. H. *J. Org. Chem.* **1974**, *39*, 1698−1705.
(46) Batchelor, J. G.; Prestegard, J. H.; Cushley, R. J.; Lipsky, S. R. *J. Am. Chem. Soc.* **1973**, *95*, 6358−6364.
(47) Tritiated $NaBH_3CN$ is available from American Radiolabeled Chemicals, St. Louis, MO.
(48) Hutchins, R. O.; Kandasamy, D.; Maryanoff, C. A.; Masiliamani, D.; Maryanoff, B. E. *J. Org. Chem.* **1977**, *42*, 82−91.
(49) Bailey, W. F.; Khanolkav, A. D.; Gavaskar, K. V. *J. Am. Chem. Soc.* **1992**, *114*, 8053−8060.
(50) Molander, G. A.; Shakya, S. R. *J. Org. Chem.* **1996**, *61*, 5885−5894.
(51) Hauser, C. F.; Brooks, T. W.; Miles, M. L.; Raymonds, M. A.; Butler, G. B. *J. Org. Chem.* **1963**, *28*, 372−379.
(52) Dalcanale, E. *J. Org. Chem.* **1986**, *51*, 567−569.

SCHEME 6[a]



[a] Reagents: (a) PCC, CH_2Cl_2. (b) NaH_2PO_4, $NaClO_2$, CH_3CN, H_2O. (c) 5% Pd/C, EtOH, H_2. (d) DCC, CCl_4. (e) DMAP, $CHCl_3$.

Experimental Section

L-α-Phosphatidyl-*N,N*-(4-benzoylphenyl)dimethylethanolamine (4). According to the procedure of Stoffel,[22] to a solution 133.8 mg (0.167 mmol) of L-α-phosphatidyl-*N,N*-dimethylethanolamine[21] in 3 mL of dry methanol were added 38 μL (0.33 mmol) of cyclohexylamine and 184 mg (0.668 mmol) 4-bromomethylbenzophenone, prepared according to the procedure of Zhao et al.[53] The mixture was kept in the dark for 18 h, and the solvent was removed under reduced pressure to give 360 mg of residue, which was chromatographed on silica gel with 65:25:2 $CHCl_3$/MeOH/H_2O to give 160 (95%) mg of **4** as a wax: ^{1}H NMR (500 MHz) δ 7.80 (m, 6H), 7.60 (m, 1H), 7.48 (m, 2H), 5.34 (m, 3.5H), 5.24 (m, 1H), 5.03 (s, 2H), 4.48−4.40 (m, 3H), 4.12 (m, 1H), 4.0 (m, 4H), 3.34 (s, 6H), 2.74 (m, 1H), 2.21 (m, 4H), 2.00 (m, 4H), 1.52 (m, 4H), 1.24 (m, 42H), 0.86 (m, 6H); ^{13}C NMR δ 196.3, 174.2, 173.9, 140.2, 137.4, 134.2, 133.7, 132.2, 131.1, 130.9, 130.8, 130.7, 130.6, 130.4, 129.2, 128.8, 128.6, 71.3 (d), 68.7, 65.6 (br), 64.1 (br), 63.7, 59.9 (br), 51.3, 35.0, 34.8, 32.6, 32.6, 32.2, 30.5, 30.4, 30.4, 30.4, 30.4, 30.3, 30.2, 30.1, 30.0, 29.9, 29.9, 29.9, 29.8, 27.9, 27.9, 26.3, 25.7, 25.6, 23.4, 23.4, 23.3, 14.8, 14.8; ^{31}P NMR δ −0.7 (s).

L-α-Phosphatidyl-*N,N*-(3-benzoylphenyl)dimethylethanolamine (5). As in the preparation of **4**, 160 mg (0.200 mmol) of L-α-phosphatidyl-*N,N*-dimethylethanolamine and 220 mg (0.800 mmol) of 3-bromomethylbenzophenone, prepared by the same procedure,[53] gave 321 mg of residue that was chromatographed on silica gel with 65:25:1 $CHCl_3$/CH_3OH/H_2O to give 190 mg (95%) of **5** as a wax: ^{1}H NMR (500 MHz) δ 8.00 (m, 2H), 7.74 (m, 3H), 7.56 (m, 2H), 7.46 (m, 2H), 5.33 (m, 3.5H), 5.24 (m, 1H), 5.00 (s, 2H), 4.43−4.34 (m, 3H), 4.08 (m, 1H), 4.0 (m, 4H), 3.31 (s, 6H), 2.73 (m, 1H), 2.20 (m, 4H), 1.97 (m, 4H), 1.50 (m, 4H), 1.24 (m, 42H), 0.86 (m, 6H); ^{13}C NMR δ 196.1, 174.2, 173.8, 139.1, 138.3, 137.5, 134.6, 133.6, 132.8, 130.9, 130.7, 130.7, 130.4, 130.0, 129.2, 129.0, 128.7, 71.3 (br), 69.1, 65.4 (br), 64.1 (br), 63.7, 59.8 (br), 51.1, 34.9, 34.8, 32.6, 32.6, 32.2, 30.4, 30.4, 30.4, 30.4, 30.4, 30.2, 30.1, 30.0, 29.9, 29.9, 29.9, 29.8, 27.9, 27.9, 26.3, 25.6, 25.6, 23.4, 23.4, 23.3, 14.8, 14.8; ^{31}P NMR δ −0.6 (s).

Methyl 11-Iodoundecanoate (15). To a solution of 10.0 g (37.7 mmol) of 11-bromoundecanoic acid (**14**) and 23.4 g (170 mmol) of anhydrous potassium carbonate in 250 mL of acetone was added 23.5 mL (377 mmol) of iodomethane dropwise over 15 min. The mixture was stirred at room temperature for 40 h; the precipitate that formed was filtered, and the solvent was evaporated. Saturated NH_4Cl solution (30 mL) was added to the residue, and the mixture was extracted with ether. The ether layer was washed with brine, dried ($MgSO_4$), filtered, and evaporated, and the residue was chromatographed on silica gel with 20:1 petroleum ether/ether to give 11.6 g (94%) of **15** as a colorless oil: ^{1}H NMR δ 3.69 (s, 3H), 3.22 (t, J = 7.1 Hz, 2H), 2.33 (t, J = 7.5 Hz, 2H), 1.84 (m, 2 H), 1.65 (m, 2H), 1.40 (m, 2H), 1.36 (s, 10H); ^{13}C NMR δ 174.5, 51.6, 34.2, 33.6, 30.6, 29.4, 29.4, 29.3, 29.2, 28.6, 25.0, 7.41. Anal. Calcd for $C_{12}H_{23}IO_2$: C, 44.18; H, 7.11. Found: C, 44.55; H, 7.18.

Methyl 11-Phenylundecanoate (11). According to the procedure of Posner,[54] lithium diphenylcuprate was prepared at 0 °C by slowly adding 136 mL of a 1.80 M (244.6 mmol) solution of PhLi to a suspension of 23.36 g (122.3 mmol) of CuI in 100 mL of dry THF over 50 min under N_2. A solution of **15** (10.0 mg, 30.58 mmol) in 20 mL of dry THF was added, and the resulting mixture was stirred for 4 days, poured into aqueous saturated NH_4Cl solution that had been adjusted to pH = 9 by addition of ammonium hydroxide, stirred for 1.5 h, and extracted with ether. The organic layer was washed with saturated NH_4Cl solution and brine, dried ($MgSO_4$), filtered, and evaporated, and the residue was chromatographed on silica gel with 20:1 petroleum ether/ether to give 6.71 g (80%) of **11** as a colorless oil: ^{1}H NMR δ 7.28 (m, 5H), 3.71 (s, 3H), 2.64 (t, J = 7.8 Hz, 2H), 2.35 (t, J = 7.5 Hz, 2H), 1.66 (m, 4H), 1.32 (s, 12H); ^{13}C NMR δ 174.6, 143.1, 128.6, 128.4, 125.7, 51.6, 36.2, 34.3, 31.7, 29.7, 29.7, 29.6, 29.5, 29.4, 29.3, 25.1. Anal. Calcd for $C_{18}H_{28}O_2$: C, 78.21; H, 10.21. Found: C, 78.38; H, 10.26.

Methyl 11-[4-(4-Methylbenzoyl)-phenyl]-undecanoate (13). According to modifications of procedures of Johnson[28] and Danishefsky,[29] 1-(9-borabicyclo[3.3.1]nonyl)-10-undecylenic acid methyl ester was prepared by the addition of 26.0 mL of a 0.5 M solution of 9-BBN in THF to a stirred solution of 2.14 g (10.8 mmol) of **17** in 50 mL of THF under N_2 at room temperature. Stirring was continued for 3 h. Hydroboration was judged to be complete by the disappearance of the multiplets at 5.87−5.78 and 5.03−4.93 ppm in the ^{1}H NMR spectrum of the reaction mixture. This mixture was added via cannula to a solution of 2.97 g (10.8 mmol) of **16**[27] in a mixture of 18 mL of DMF, 30 mL of THF, and 6 mL of water, to which had previously been added 10.6 g (32.4 mmol) of Cs_2CO_3, 2.16 g (2.16 mmol) of triphenylarsine, and 1.76 g (2.16 mmol) of dichloro[1,1′-bis(diphenylphosphinoferrocene]palladium(II) (Pd-(dppf)Cl_2) dichloromethane adduct. The resulting mixture was stirred at room temperature for 22 h, and then poured into a mixture of 150 mL of water and 150 mL of EtOAc. The separated organic phase was washed with water, saturated sodium bicarbonate, and brine, filtered through Celite, dried (Na_2SO_4), and concentrated to give 8.3 g of dark oil. The oil was chromatographed on silica gel with 20:1 hexane/EtOAc to give 4.3 g of yellow oil, which crystallized upon trituration with hexanes to give 3.9 g (93%) of **13**: mp 39.3−40.0 °C; ^{1}H NMR δ 7.76 (m, 4H), 7.29 (m, 4H), 3.70 (s, 3H), 2.71 (t, J = 7.6 Hz, 2H), 2.47 (s, 3H), 2.34 (t, J = 7.6 Hz, 2H), 1.65 (m, 4H), 1.32 (s, 12H); ^{13}C NMR δ 196.5, 174.5, 148.1, 143.1, 135.6, 135.4, 130.4, 129.1, 128.5, 51.6, 36.2, 34.3, 31.4, 29.7, 29.6, 29.6, 29.5, 29.4, 29.3, 25.1, 21.8. Anal. Calcd for $C_{26}H_{34}O_3$: C, 79.15; H:8.69. Found: C, 79.39; H, 8.76.

1-(4-(4′-Methylbenzophenone))-10-methyldecanoic Acid (9). To a solution of 3.0 g (7.6 mmol) of **13** in 50 mL of 95% ethanol was added 1.3 g (23 mmol) of KOH, and the resulting mixture was stirred for 12 h at room temperature, diluted with 10% HCl solution, extracted with EtOAc, washed with brine, dried ($MgSO_4$), filtered, and evaporated to give 2.9 g (99%) of **9**: mp 73.9−74.5 °C; recrystallization from ether gave 2.7 g (92%) of **9**: mp 75.7−75.9 °C; ^{1}H NMR δ 7.77−7.74 (m, 4H), 7.31 (d, J = 8.1 Hz, 4H), 2.71 (t, J = 7.7 Hz, 2H), 2.47 (s, 3H), 2.38 (t, J = 7.4 Hz, 2H), 1.74−1.60 (m, 4H), 1.40−1.30 (m, 12H); ^{13}C NMR δ 196.7, 180.3, 148.2, 143.2, 135.6, 135.5, 130.5, 129.2, 128.5, 36.3, 34.3, 31.4, 29.7, 29.7, 29.7, 29.5, 29.5, 29.3,

(53) Zhao, H.; Neamati, N.; Pommier, Y.; Burke, Jr., T. R. *Heterocycles* **1997**, *45*, 2277−2282.

(54) Posner, G. H. *Org. React.* **1975**, *22*, 253−400.

24.9, 21.9. Anal. Calcd for $C_{25}H_{32}O_3$: C, 78.91; H, 8.48. Found: C, 78.98; H, 8.44.

1-(4-Methyl-4′-benzophenonyl)-undecylenyl Acetate (19). As in the preparation of **13**, 1-(9-borabicyclo[3.3.1]-nonane)-undecylenyl acetate was prepared by hydroboration of 3.84 g (18.1 mmol) of **18**[30] in 100 mL of THF with 38.0 mL of a 0.5 M solution of 9-BBN. This mixture was added via cannula to the slurry formed by adding, to a solution of 5.00 g (18.1 mmol) of **16** in a mixture of 80 mL of DMF, 80 mL of THF and 20 mL of water, 17.7 g (54.3 mmol) of Cs_2CO_3, 1.10 g (3.60 mmol) of triphenylarsine, and 2.90 g (3.60 mmol) of $Pd(dppf)Cl_2 \cdot CH_2Cl_2$. The resulting mixture was stirred at room temperature for 24 h, heated to 40 °C for 5 h, and stirred at room temperature for 14 days. The solvent was evaporated, and the residue was taken up in 150 mL of H_2O and 150 mL of EtOAc; the resulting emulsion was filtered through a Celite pad. The organic phase was washed with water, saturated sodium bicarbonate, and brine, filtered through Celite, dried (Na_2SO_4), and concentrated to 13.6 g of dark oil, which was chromatographed on silica gel with 9:1 hexane/EtOAc to give a clear oil that crystallized on standing to give 7.10 g (97%) of **19**: mp 37.0−37.2 °C; ^{1}H NMR δ 7.74 (m, 4H), 7.30 (m, 4H), 4.09 (t, J = 7.2 Hz, 2H), 2.72 (t, J = 7.2 Hz, 2H), 2.48 (s, 3H), 2.08 (s, 3H), 1.66 (m, 4H), 1.34 (m, 14H); ^{13}C NMR δ 196.5, 171.5, 148.2, 143.2, 135.7, 135.5, 130.5, 129.2, 128.5, 64.9, 36.3, 31.5, 29.8, 29.8, 29.8, 29.7, 29.6, 29.5, 28.8, 26.2, 21.9, 21.3. Anal. Calcd for $C_{27}H_{36}O_3$: C, 79.37; H, 8.88. Found: C, 79.31; H, 8.95.

4-(4′-Methylbenzophenone)-11-undecylenol (10). To a stirred solution of 3.30 g (8.24 mmol) of **19** in 41 mL of 90% ethanol under N_2 at room temperature was added 1.40 g of KOH pellets. After 40 min, TLC indicated complete reaction of **19**. The mixture was adjusted to pH 1 by the addition of 2 N HCl, extracted with EtOAc, and the combined organic layers were washed with brine, dried (Na_2SO_4), filtered, and concentrated to give 3.40 g of white solid that was crystallized from EtOAc to give 2.44 g (81%) of **10**: mp 90.0−90.4 °C; ^{1}H NMR δ 7.77−7.73 (m, 4H), 7.32−7.29 (m, 4H), 3.69−3.67 (m, 2H), 2.74−2.69 (m, 2H), 2.47 (s, 3H), 1.69−1.31 (m, 18H); ^{13}C NMR δ 196.6, 148.2, 143.2, 135.6, 135.5, 130.5, 129.2, 128.5, 63.3, 36.3, 33.1, 31.5, 29.8, 29.8, 29.8, 29.7, 29.7, 29.5, 26.0, 21.9. Anal. Calcd for $C_{25}H_{34}O_2$: C, 81.92; H, 9.35. Found: C, 81.67; H, 9.41.

1-Palmitoyl-2-{11-[4-(4-Methylbenzoyl)-phenyl]}-undecyl-*sn*-glycero-3-phosphocholine (6). According to a modification of a prodecure by Ali and Bittman,[31] to a mixture of 51 mg (0.103 mmol) of **21** and 780 mg (1.03 mmol) of **20** in 8 mL of alcohol-free choloroform was added 15.1 mg (0.123 mmol) of 4-(dimethylamino)pyridine (DMAP). The mixture was flushed three times with N_2, stirred at room temperature under N_2 for 5.5 h, and evaporated to give 1.28 g of residue that was chromatographed on silica gel with 1:0 to 1:1 $CHCl_3$/CH_3OH to give 88 mg (100%) of waxy **6**: ^{1}H NMR (500 MHz) δ 7.70 (m, 4H), 7.26 (m, 4H), 5.20 (m, 1H), 4.40 (m, 1H), 4.31 (br, 2H), 4.11 (m, 1H), 3.94 (m, 2H), 3.82 (br, 2H), 3.37 (s, 9H), 2.67 (t, J = 7.5 Hz, 2H), 2.43 (s, 3H), 2.27 (m, 4H), 1.61 (m, 6H), 1.27 (m, 36H), 0.87 (t, J = 6.5 Hz, 3H); ^{13}C NMR δ 196.5, 173.8, 173.4, 148.1, 143.2, 135.6, 135.4, 130.4, 129.2, 128.5, 70.8 (d), 66.5 (br), 63.6 (br), 63.2, 59.6 (br), 54.6, 36.3, 34.6, 34.4, 32.2, 31.5, 30.0, 29.9, 29.9, 29.8, 29.8, 29.8, 29.8, 29.6, 29.6, 29.4, 29.4, 25.2, 25.1, 22.9, 21.9, 14.4; ^{31}P NMR δ 0.4 (s). Anal. Calcd for $C_{49}H_{80}NO_9P \cdot 2H_2O$: C, 65.86; H, 9.47; N, 1.57. Found: C, 65.82; H, 9.43; N, 1.69.

1-*O*-{11-[4-(4-Methylbenzoyl)-phenyl]}-undecanoyl-2-oleoyl-*sn*-glycero-3-phosphocholine (7). According to the procedure of Hermetter et al.,[34] to a solution of 240 mg (0.327 mmol) of **25**[34] and 125 mg (0.164 mmol) of **20** in 4 mL of dry methylene chloride was added 0.177 mL (0.40 mmol) of $BF_3 \cdot OEt_2$. The resulting mixture was stirred for 1 h at 0 °C; a solution of 500 mg of $NaHCO_3$ in 1 mL of water was added, and stirring was continued for 10 min. After the addition of 20 mL of methanol, the precipitate was removed by filtration; the organic layer was then washed with 1:1 CH_3OH/H_2O and evaporated, and the residue was chromatographed on silica gel with 9:1 to 2:1 $CHCl_3/CH_3OH$ to give 115 mg (79%) of waxy **7**: ^{1}H NMR (500 MHz) δ 7.71 (m, 4H), 7.27 (m, 4H), 5.34 (m, 2H), 5.19 (m, 1H), 4.40 (dd, J = 12, 2.2 Hz, 1H), 4.29 (m, 2H), 4.13 (dd, J = 12, 7.3 Hz, 1H), 3.92 (m, 2H), 3.76 (m, 2H), 3.34 (s, 9H), 2.69 (t, J = 7.5 Hz, 2H), 2.42 (s, 3H), 2.28 (m, 4H), 2.00 (m, 4H), 1.59 (m, 6H), 1.28 (m, 32H), 0.87 (t, J = 6.8 Hz, 3H); ^{13}C NMR δ 196.9, 174.3, 173.9, 148.6, 143.6, 136.1, 135.9, 130.9, 130.7, 130.4, 129.6, 128.9, 71.2 (d), 66.9 (br), 64.1 (br), 63.7, 60.0 (br), 55.0, 36.7, 35.0, 34.8, 32.6, 31.9, 30.5, 30.5, 30.3, 30.3, 30.3, 30.1, 30.1, 30.0, 30.0, 29.9, 29.9, 29.8, 27.9, 27.9, 25.7, 25.6, 23.4, 22.4, 14.8; ^{31}P NMR δ −0.5 (s). Anal. Calcd for $C_{51}H_{82}NO_2P \cdot 3H_2O$: C, 65.29; H, 9.45; N, 1.49. Found: C, 65.43; H, 9.44; N, 1.48.

1-*O*-{11-[4-(4-Methylbenzoyl)-phenyl]}-undecyl-3-*O*-tosyl-*sn*-glycerol (30). According to the procedure of Guivisdalsky and Bittman,[36] to a solution of 0.56 g (2.45 mmol) of **29** and 1.35 g (3.68 mmol) of **10** in 20 mL of alcohol-free $CHCl_3$ was added 3 drops of $BF_3 \cdot OEt_2$. The mixture was stirred overnight at room temperature, and the solvent was removed under reduced pressure to give 2.7 g of residue that was chromatographed on silica gel with 4:1 hexane/EtOAc to give 1.19 g (81%) of **30** as a colorless oil: ^{1}H NMR δ 7.80 (d, J = 8.0 Hz, 2H), 7.73 (m, 4H), 7.36 (d, J = 8.0 Hz, 2H), 7.28 (m, 4H), 4.10 (m, 1H), 4.04 (m, 1H), 3.98 (m, 1H), 3.46 (m, 4H), 2.69 (t, J = 7.8 Hz, 2H), 2.45 (s, 6H), 1.66 (m, 2H), 1.52 (m, 2H), 1.30 (m, 14H); ^{13}C NMR (500 MHz) δ 196.6, 148.2, 145.2, 143.2, 135.6, 135.4, 132.9, 130.5, 130.2, 129.2, 128.5, 128.2, 72.0, 70.9, 70.7, 68.5, 36.3, 31.4, 29.8, 29.8, 29.8, 29.7, 29.7, 29.7, 29.5, 26.3, 21.9, 21.9. Anal. Calcd for $C_{35}H_{46}O_6S$: C, 70.67; H, 7.80. Found: C, 70.72; H, 7.73.

Mosher Ester of 30. According to the procedure of Guivisdalsky and Bittman,[36] to 1.19 g (5.08 mmol) of (*R*)-(+)-α-methoxy-α-(trifluoromethyl)phenylacetic acid (MTPA)[38] in 1 mL of hexane were added sequentially 1.32 mL (15.2 mmol) of oxalyl chloride and 1 drop of DMF. The mixture was stirred at room temperature for 3 h. The solvent was evaporated, and the residue was distilled to give 0.866 g of colorless oily Mosher acid chloride: bp 50 °C (0.6 mmHg) (lit.[55] bp 50 °C, 0.6 mmHg). To a solution of 85 mg (0.14 mmol) of **30** in 1 mL of pyridine was added 30 μL of this (*R*)-(+)-MTPA chloride neat. The mixture was stirred for 4 h at room temperature; 50 mL of ether was added, and the organic layer was washed with water, dried over Na_2SO_4, filtered, and evaporated to give 500 mg of residue that was chromatographed on silica gel with 9:1 hexane/EtOAc to give 109 mg (94%) of colorless oily (*R*)-(+)-MTPA ester of **30**: ^{1}H NMR δ 7.78 (m, 5H), 7.56 (m, 2H), 7.45−7.30 (m, 10H), 5.42 (m, 1H), 4.32 (dd, J_{AC} = 3.0 Hz, J_{AB} = 10.9 Hz, 1H), 4.24 (dd, J_{BC} = 6.8 Hz, J_{AB} = 10.9 Hz, 1H), 3.56 (s, 3H), 3.56 (dd, J_{AC} = 5.4 Hz, J_{AB} = 10.5 Hz, 1H), 3.49 (dd, J_{BC} = 5.4 Hz, J_{AB} = 10.5 Hz, 1H), 3.32 (t, J = 6.6 Hz, 2H), 2.72 (t, J = 7.5 Hz, 2H), 2.47 (s, 6H), 1.69 (m, 2H), 1.46 (m, 2H), 1.30 (br, 14H) (lit.[36] for (−)-**2a** (400 MHz) δ 7.82 (d, J = 8.5 Hz, 2H), 7.35−7.45 (m, 5H), 7.31 (d, J = 8.5 Hz, 2H), 5.38 (m, 1H), 4.28 (dd, J_{AC} = 3.0 Hz, J_{AB} = 11.5 Hz, 1H), 4.20 (dd, J_{BC} = 7.5 Hz, J_{AB} = 11.5 Hz, 1H), 3.52 (dd, J_{AC} = 5.4 Hz, J_{AB} = 10.3 Hz, 1H), 3.51 (s, 3H), 3.46 (dd, J_{BC} = 5.4 Hz, J_{AB} = 10.3 Hz, 1H), 3.27 (t, J = 6.59 Hz, 2H), 2.45 (s, 3H), 1.26 (br s, 28H), 0.88 (brt, 3H)); ^{13}C NMR δ 196.6, 166.2, 148.2, 145.5, 143.2, 135.7, 135.5, 132.7, 132.1, 130.5, 130.2, 129.9, 129.2, 128.8, 128.5, 128.2, 127.6, 125.3, 121.5, 72.5, 72.1, 68.1, 67.9, 55.8, 36.3, 31.5, 29.8, 29.8, 29.8, 29.7, 29.7, 29.7, 29.6, 26.2, 21.9, 21.9; ^{19}F NMR δ −72.1.

1-*O*-{11-[4-(4-Methylbenzoyl)-phenyl]}-undecyl-2-*O*-(4-methoxybenzyl)-3-*O*-tosyl-*sn*-glycerol (41). According to the procedure of Nakajima et al.,[43] to a solution of 200 mg (0.336 mmol) of **30** and 114 mg (0.403 mmol) of 4-methoxy-

(55) (a) Bosshard, H. H.; Mory, R.; Schmid, M.; Zollinger, H. *Helv. Chim. Acta* **1959**, *42*, 1653−1658. (b) Egawa, Y.; Okuda, T. *Chem. Pharm. Bull.* **1963**, *11*, 589−596.

benzyl trichloroacetimidate, prepared according to the procedure of Wessel et al.,[56] in 5 mL of ether was added 1 drop of CF_3SO_3H at 0 °C. The mixture was stirred for 20 min at 0 °C, and 1 mL of saturated $NaHCO_3$ was added; the solvent was evaporated, and the residue was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried (Na_2SO_4), filtered, and evaporated to give 600 mg of residue that was chromatographed on silica gel with 9:1 to 6:1 hexane/EtOAc to give 209 mg (87%) of colorless oily **41**: ^{1}H NMR δ 7.74 (m, 6H), 7.30 (m, 6H), 7.21 (m, 2H), 6.86 (m, 2H), 4.53 (s, 2H), 4.18 (m, 1H), 4.07 (m, 1H), 3.81 (s, 3H), 3.76 (m, 1H), 3.44 (m, 2H), 3.36 (t, J = 6.8 Hz, 2H), 2.69 (t, J = 7.8 Hz, 2H), 2.45 (s, 6H), 1.67 (m, 2H), 1.50 (m, 2H), 1.29 (m, 14H); ^{13}C NMR (500 MHz) δ 196.5, 159.5, 148.2, 145.0, 143.2, 135.6, 135.5, 133.1, 130.5, 130.2, 130.0, 129.7, 129.2, 128.5, 128.2, 114.0, 75.3, 72.3, 72.0, 69.9, 69.7, 55.5, 36.3, 31.5, 29.9, 29.8, 29.8, 29.7, 29.7, 29.6, 26.3, 21.9. Anal. Calcd for $C_{43}H_{54}O_7S$: C, 72.24; H, 7.61. Found: C, 72.29; H, 7.74.

1-*O*-{11-[4-(4-Methylbenzoyl)-phenyl]}-undecyl-2-*O*-(4-methoxybenzyl)-3-*O*-acetyl-*sn*-glycerol (42). According to the procedure of Guivisdalsky and Bittman,[37] to a solution of 205 mg (0.287 mmol) of **41** in 5 mL of 4:1 DMSO/DMF was added 110 mg (0.574 mmol) of CsOAc. The mixture was stirred for 36 h, diluted with 5 mL of H_2O, and extracted with CH_2Cl_2. The extracts were washed with brine, dried (Na_2SO_4), filtered, and evaporated. The residue was chromatographed on silica gel with 6:1 hexane/EtOAc to give 113 mg (66%) of colorless oily **42**: ^{1}H NMR δ 7.76 (m, 4H), 7.30 (m, 6H), 6.90 (m, 2H), 4.64 (s, 2H), 4.30 (dd, J = 11.7, 4.2 Hz, 1H), 4.14 (dd, J = 11.7, 5.4 Hz, 1H), 3.83 (s, 3H), 3.78 (m, 1H), 3.54 (m, 2H), 3.46 (t, J = 6.6 Hz, 2H), 2.71 (t, J = 7.8 Hz, 2H), 2.47 (s, 3H), 2.09 (s, 3H), 1.69 (m, 2H), 1.60 (m, 2H), 1.33 (m, 14H); ^{13}C NMR δ 196.5, 171.2, 159.5, 148.2, 143.2, 135.6, 135.5, 130.6, 130.5, 129.7, 129.2, 128.5, 114.0, 75.6, 72.1, 72.0, 70.6, 64.3, 55.5, 36.3, 31.5, 29.9, 29.9, 29.8, 29.7, 29.6, 26.4, 21.9, 21.2. Anal. Calcd for $C_{38}H_{50}O_6$: C, 75.71; H, 8.36. Found: C, 75.93; H, 8.45.

1-*O*-{11-[4-(4-Methylbenzoyl)-phenyl]}-undecyl-2-*O*-(4-methoxybenzyl)-*sn*-glycerol (43). To a solution of 168 mg (0.278 mmol) of **42** in 1 mL of methanol was added 58 mg (0.417 mmol) of K_2CO_3. The mixture was stirred overnight, and 2 mL of saturated NH_4Cl solution was added; the solvent was removed under reduced pressure, and the residue was extracted with CH_2Cl_2. The extracts were washed with brine, dried (Na_2SO_4), filtered, and evaporated to give 400 mg of residue that was chromatographed on silica gel with 2:1 to 1:1 hexane/EtOAc to give 150 mg (96%) of **43** as a colorless oil: ^{1}H NMR δ 7.75 (m, 4H), 7.32 (m, 6H), 6.90 (m, 2H), 4.66 (d, J = 11.4 Hz, 1H), 4.58 (d, J = 11.4 Hz, 1H), 3.82 (s, 3H), 3.75−3.53 (m, 5H), 3.49 (t, J = 6.6 Hz, 2H), 2.71 (t, J = 7.5 Hz, 2H), 2.47 (s, 3H), 2.27 (br, 1H), 1.69 (m, 2H), 1.60 (m, 2H), 1.32 (m, 14H); ^{13}C NMR δ 196.5, 159.6, 148.2, 143.2, 135.6, 135.5, 130.7, 130.5, 129.7, 129.2, 128.5, 114.1, 77.8, 72.1, 72.0, 71.4, 63.3, 55.5, 36.3, 31.5, 29.9, 29.9, 29.8, 29.7, 29.6, 26.4, 21.9. Anal. Calcd for $C_{36}H_{48}O_5$: C, 77.11; H, 8.63. Found: C, 76.84; H, 8.64.

1-*O*-{11-[4-(4-Methylbenzoyl)-phenyl]}-undecyl-2-*O*-(4-methoxybenzyl)-*sn*-glycero-3-phosphocholine (44). According to the procedure of Guivisdalsky and Bittman,[37] to a solution of 0.391 g (2.55 mmol) of $POCl_3$ and 0.258 g (2.55 mmol) of Et_3N in 10 mL of chloroform was added a solution of 1.14 g (2.04 mmol) of **43** in 10 mL of $CHCl_3$ dropwise at −10 °C over 30 min. The mixture was allowed to warm to room temperature and stirred for an additional 30 min, and 0.843 g (3.06 mmol) of choline tosylate and 1.42 mL of pyridine were added. The resulting mixture was stirred for 2 days at room temperature; then, 0.57 mL of water was added, and the mixture was stirred for 30 min. The solvent was evaporated, and 50 mL of 1:1 CH_2Cl_2/toluene was added; the mixture was filtered, and the filtrate was evaporated to give 6.0 g of residue that was passed through a short column of MB-3 ion-exchange resin with 9:1 THF/H_2O. The 1.4 g of residue was chromatographed on silica gel with 65:35:5 $CHCl_3$/MeOH/H_2O to give 1.23 g (83%) of **44** as a colorless wax: ^{1}H NMR δ 7.72 (m, 4H), 7.29 (m, 6H), 6.86 (m, 2H), 4.64 (d, J = 11.4 Hz, 1H), 4.58 (d, J = 11.4 Hz, 1H), 4.23 (m, 2H), 3.92 (m, 2H), 3.79 (s, 3H), 3.78 (m, 1H), 3.60 (m, 4H), 3.42 (t, J = 6.6 Hz, 2H), 3.22 (s, 9H), 2.69 (t, J = 7.5 Hz, 2H), 2.43 (s, 3H), 1.66 (m, 2H), 1.56 (m, 2H), 1.30 (m, 14H); ^{13}C NMR δ 196.5, 159.4, 148.2, 143.2, 135.6, 135.4, 131.3, 130.4, 129.8, 129.2, 128.5, 114.0, 78.0, 72.0 (d), 71.4, 66.5 (d), 65.5 (d), 59.3 (d), 55.6, 54.4, 36.3, 31.5, 30.0, 29.9, 29.8, 29.8, 29.7, 29.6, 26.4, 21.9; ^{31}P NMR δ 0.7 (s). Anal. Calcd for $C_{41}H_{60}NO_8P\cdot1.5H_2O$: C, 65.45; H, 8.44; N, 1.86. Found: C, 65.71; H, 8.41; N, 1.87.

1-*O*-{11-[4-(4-Methylbenzoyl)-phenyl]}-undecyl-*sn*-glycero-3-phosphocholine (32). To a solution of 85 mg (0.18 mmol) of **44** in 1.8 mL of CH_2Cl_2 containing 0.1 mL of H_2O was added 40 mg (0.18 mmol) of DDQ. The mixture was stirred overnight at room temperature; the solvent was evaporated, and the 150 mg of residue was chromatographed on silica gel with 2:1:0 to 65:35:5 $CHCl_3$/CH_3OH/H_2O to give, followed by 35 mg (41%) of recovered **44**, 41 mg (58%) of white waxy **32**: ^{1}H NMR (500 MHz) δ 7.70 (m, 4H), 7.27 (m, 4H), 4.35 (m, 2H), 4.01−3.80 (m, 5H), 3.42 (m, 4H), 3.36 (s, 9H), 2.67 (t, J = 7.5 Hz, 2H), 2.44 (s, 3H), 1.64 (m, 2H), 1.52 (m, 2H), 1.30 (m, 14H); ^{13}C NMR δ 196.5, 148.2, 143.2, 135.6, 135.4, 130.4, 129.2, 128.5, 72.3, 71.9, 70.3 (d), 68.2 (br), 66.5 (br), 59.6 (br), 54.6, 36.3, 31.5, 30.0, 29.9, 29.8, 29.7, 29.6, 26.4, 21.9; ^{31}P NMR δ 0.4 (s). Anal. Calcd for $C_{33}H_{52}NO_7P\cdot0.5H_2O$: C, 64.52; H, 8.70; N, 2.28. Found: C, 64.30; H, 8.69; N, 2.36.

1-*O*-{11-[4-(4-Methylbenzoyl)-phenyl]}-undecyloxy-2-oleoyl-*sn*-glycero-3-phosphocholine (8). To a solution of 51.7 mg (0.085 mmol) of **32** and 930 mg (1.70 mmol) of oleic anhydride in 3 mL of CH_2Cl_2 was added 43 μL (0.34 mmol) of $BF_3\cdot OEt_2$ at 0 °C. The mixture was stirred for 45 min at 0 °C; a solution of 500 mg of $NaHCO_3$ in 1 mL of water was added, and the mixture was filtered and evaporated to give 1.44 g of residue that was chromatographed on silica gel with 4:1 to 1:1 $CHCl_3$/CH_3OH to give 56 mg (76%) of **8** as a colorless wax: ^{1}H NMR (500 MHz) δ 7.71 (m, 4H), 7.27 (m, 4H), 5.34 (m, 2H), 5.14 (m, 1H), 4.30 (m, 2H), 3.93 (m, 2H), 3.80 (m, 2H), 3.58 (m, 2H), 3.42 (m, 2H), 3.37 (s, 9H), 2.69 (t, J = 7.5 Hz, 2H), 2.47 (s, 3H), 2.31 (m, 2H), 2.00 (m, 4H), 1.64 (m, 4H), 1.52 (m, 2H), 1.30 (m, 34H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR δ 196.5, 173.7, 148.2, 143.2, 135.6, 135.5, 130.4, 130.2, 129.9, 129.2, 128.5, 72.3 (d), 71.9, 69.7, 66.7 (d), 64.1 (d), 59.5 (d), 54.7, 36.3, 34.7, 32.2, 31.5, 30.0, 29.9, 29.8, 29. 8, 29.8, 29.6, 29.6, 29.6, 29.5, 29.4, 29.4, 27.5, 27.5, 26.3, 25.3, 22.9, 21.9, 14.4; ^{31}P NMR δ 0.4 (s). Anal. Calcd for $C_{51}H_{84}NO_8P\cdot1.5H_2O$: C, 68.32; H, 10.08; N, 1.61. Found: C, 68.20; H, 9.77; N, 1.57.

5,10-Undecadienyl Acetate (47). According to the procedure by Bailey et al.,[49] to a solution of 23.6 g (49.93 mmol) of **49** in 150 mL of dry ether was added 22 mL (54.92 mmol) of 2.5 M *n*-BuLi at −78 °C. The mixture was stirred at room temperature for 1 h, and then a solution of 7.2 g (49.93 mmol) of **48**,[57] prepared by the procedure of Banwell et al.,[58] in 30 mL of dry ether was added dropwise at −78 °C. The mixture was stirred overnight allowing the temperature to rise to room temperature. The mixture was poured into 50 mL of ice−water and filtered, and the filtrate was diluted with 100 mL of pentane. The organic layer was washed with brine, dried (Na_2SO_4), filtered, and evaporated to give 9.9 g of residue that was chromatographed on silica gel with 25:1 pentane/ether to give 5.91 g (56%) of **47** as a 4:1 mixture of trans and cis isomers as determined by GC analysis: ^{1}H NMR (two isomers) δ 5.80 (m, 1H), 5.40 (m, 2H), 5.00 (m, 2H), 4.11 (t, J = 6.6 Hz, 2H), 2.08 (s, 3H), 2.08 (m, 6H), 1.66 (m, 2H), 1.44 (m, 4H); ^{13}C NMR

(56) Wessel, H.-P.; Iversen, T.; Bundle, D. R. *J. Chem. Soc., Perkin Trans. 1* **1985**, 2247−2250.

(57) Stowell, J. C. *J. Org. Chem.* **1970**, *35*, 244−245.

(58) Banwell, M. G.; Bui, C. T.; Simpson, G. W. *J. Chem. Soc., Perkin Trans. 1* **1978**, 791−799.

(two isomers) δ 171.5, 139.0, 130.9, 130.3, 130.2, 129.7, 114.7, 114.6, 64.7, 33.6, 33.5, 32.4, 32.2, 29.2, 29.0, 28.4, 28.3, 27.0, 26.9, 26.2, 26.1, 21.3. Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 74.03; H, 10.76.

11-[4-(4-Methylbenzoyl)phenyl]-5-undecenyl Acetate (51). In a procedure similar to those used in the preparations of **13** and **19**, to a solution of 4.4 g (21.0 mmol) of **47** in 60 mL of dry THF was added 42.0 mL of 0.5 M 9-BBN in THF dropwise at 0 °C over 30 min. The mixture was stirred at 0 °C for 1 h and at room temperature for 4 h and then added via cannula to a mixture of 7.21 g (26.2 mmol) of **16**, 25.6 g (78.6 mmol) of Cs_2CO_3, 1.60 g (5.24 mmol) of $AsPh_3$, and 4.28 g (5.24 mmol) of Pd(dppf)Cl_2·CH_2Cl_2 in 108 mL of 4:4:1 THF/DMF/H_2O. The resulting mixture was stirred at room temperature for 4 h, heated at 75 °C overnight, and flushed through a short pad of silica gel with EtOAc. The solvent was evaporated, and the residue was extracted with EtOAc, washed with brine, dried (Na_2SO_4), filtered, and evaporated to give 10.8 g of residue that was chromatographed on silica gel with 40:1 to 15:1 hexane/EtOAc to give 5.345 g (63%) of **51** as a colorless oil: ^{1}H NMR (two isomers) δ 7.75 (m, 4H), 7.34 (m, 4H), 5.41 (m, 2H), 4.09 (t, J = 6.6 Hz, 2H), 2.72 (t, J = 7.8 Hz, 2H), 2.48 (s, 3H), 2.08 (s, 3H), 2.07 (m, 4H), 1.66 (m, 4H), 1.40 (m, 6H); ^{13}C NMR (two isomers) δ 196.5, 171.4, 148.0, 143.2, 135.7, 135.5, 131.1, 130.5, 130.5, 130.5, 130.0, 129.5, 129.2, 128.5, 64.7, 64.7, 36.2, 32.7, 32.4, 32.3, 31.4, 31.3, 29.8, 29.6, 29.2, 29.0, 28.4, 28.3, 27.4, 27.0, 26.5, 26.2, 26.1, 21.9, 21.2. Anal. Calcd for $C_{27}H_{34}O_3$: C, 79.76; H, 8.43. Found: C, 79.88; H, 8.51.

11-[4-(4-Methylbenzoyl)phenyl)]-5-undecenol (46). To a solution of 5.0 g (12.30 mmol) of **51** in 50 mL of 8:1 CH_3OH/H_2O was added 2.55 g (18.45 mmol) of K_2CO_3. The mixture was stirred overnight, and then 30 mL of saturated NH_4Cl was added. The solvent was removed under reduced pressure, and the residue was extracted with EtOAc, washed with brine, dried (Na_2SO_4), filtered, and evaporated to give 4.3 g of residue that was chromatographed on silica gel with 4:1 hexane/EtOAc to give 3.79 g (94%) of colorless oily **46**: ^{1}H NMR (two isomers) δ 7.75 (m, 4H), 7.32 (m, 4H), 5.39 (m, 2H), 3.68 (t, J = 6.6 Hz, 2H), 2.72 (t, J = 7.8 Hz, 2H), 2.48 (s, 3H), 2.07 (m, 4H), 1.66 (m, 4H), 1.40 (m, 6H); ^{13}C NMR (two isomers) δ 196.6, 148.0, 143.2, 135.7, 135.4, 130.8, 130.5, 130.3, 129.8, 129.2, 128.5, 63.1, 36.2, 32.7, 32.6, 32.5, 31.3, 29.8, 29.6, 29.2, 27.4, 27.2, 26.1, 25.9, 21.9. Anal. Calcd for $C_{25}H_{32}O_2$: C, 82.37; H, 8.85. Found: C, 82.13; H, 9.02.

1-*O*-{11-[4-(4-Methylbenzoyl)-phenyl]}-5-undecenyl-3-*O*-tosyl-*sn*-glycerol (53). According to the procedure of Guivisdalsky and Bittman,[37] to a solution of 1.09 g (4.79 mmol) of **29** and 2.62 g (7.19 mmol) of **46** in 60 mL of alcohol-free chloroform was added 5 drops of BF_3·OEt_2. The mixture was stirred at room temperature for 2 days, and the solvent was removed under reduced pressure to give 5.1 g of residue that was chromatographed on silica gel with 4:1 hexane/EtOAc to give 2.28 g (81%) of **53** as a colorless oil: ^{1}H NMR δ 7.82 (d, J = 8.0 Hz, 2H), 7.75 (m, 4H), 7.36 (d, J = 8.0 Hz, 2H), 7.28 (m, 4H), 5.38 (m, 2H), 4.10 (m, 2H), 4.00 (m, 1H), 3.46 (m, 4H), 2.73 (b, 1H), 2.72 (t, J = 7.8 Hz, 2H), 2.48 (s, 6H), 2.07 (m, 4H), 1.66 (m, 2H), 1.52 (m, 2H), 1.30 (m, 6H); ^{13}C NMR δ 196.6, 148.0, 145.2, 143.3, 135.6, 135.4, 132.9, 130.8, 130.5, 130.5, 130.4, 130.2, 130.2, 129.8, 129.2 128.6, 128.2, 71.8, 71.0, 70.8, 68.5, 36.2, 32.7, 32.6, 31.4, 29.8, 29.6, 29.4, 29.2, 29.1, 29.0, 27.4, 27.2, 26.4, 26.2, 21.9. Anal. Calcd for $C_{35}H_{46}O_6S$: C, 70.92; H, 7.48. Found: C, 71.02; H, 7.38.

1-*O*-{11-[4-(4-Methylbenzoyl)-phenyl]}-5-undecenyl-2-*O*-(4-methoxy)benzyl-3-*O*-tosyl-*sn*-glycerol (54). As in the preparation of **41**, 1.42 g (2.4 mmol) of **53** and 1.02 g (3.60 mmol) of 4-methoxybenzyltrichloroacetimidate afforded 3.94 g of crude product that was chromatographed on silica gel with 9:1 to 7:1 hexane/EtOAc to give 1.71 g (100%) of colorless oily **54**: ^{1}H NMR δ 7.72 (m, 6H), 7.30 (m, 6H), 7.21 (m, 2H), 6.88 (m, 2H), 5.40 (m, 2H), 4.53 (s, 2H), 4.18 (m, 1H), 4.07 (m, 1H), 3.81 (s, 3H), 3.76 (m, 1H), 3.47 (m, 2H), 3.36 (t, J = 6.6 Hz, 2H), 2.69 (t, J = 7.8 Hz, 2H), 2.47 (s, 6H), 2.02 (m, 4H), 1.67 (m, 2H), 1.50 (m, 2H), 1.29 (m, 6H); ^{13}C NMR (500 MHz) δ 196.6, 159.6, 148.1, 145.1, 143.3, 135.6, 135.4, 133.1, 130.8, 130.5, 130.3, 130.2, 130.1, 129.8, 129.7, 129.2, 128.5, 128.2, 114.0, 75.3, 72.3, 71.8, 69.9, 69.7, 55.5, 36.2, 32.7, 32.6, 31.4, 31.3, 29.8, 29.7, 29.4, 29.3, 29.2, 29.1, 27.4, 27.2, 26.4, 26.3, 21.9. Anal. Calcd for $C_{43}H_{52}O_7S$: C, 72.44; H, 7.35. Found: C, 72.56; H, 7.31.

1-*O*-{11-[4-(4-Methylbenzoyl)-phenyl]}-5-undecenyloxy-2-*O*-(4-methoxybenzyl)-3-*O*-acetyl-*sn*-glycerol (55). According to the procedure of Guivisdalsky and Bittman,[37] to a solution of 2.23 g (3.13 mmol) of **54** in 15 mL of a 4:1 DMSO/DMF solution was added 1.20 g (6.26 mmol) of CsOAc. The mixture was stirred for 3 days, diluted with 5 mL of H_2O, and extracted with CH_2Cl_2. The extracts were washed with brine, dried, filtered, and evaporated. The residue was chromatographed on silica gel with 9:1 to 6:1 hexane/EtOAc to give 1.47 g (78%) of colorless oily **55**: ^{1}H NMR δ 7.74 (m, 4H), 7.30 (m, 6H), 6.90 (m, 2H), 5.40 (m, 2H), 4.63 (s, 2H), 4.30 (dd, J = 11.7, 4.2 Hz, 1H), 4.14 (m, 1H), 3.83 (s, 3H), 3.77 (m, 1H), 3.54 (m, 2H), 3.49 (t, J = 6.6 Hz, 2H), 2.71 (t, J = 7.8 Hz, 2H), 2.47 (s, 3H), 2.09 (s, 3H), 2.06 (m, 4H), 1.66 (m, 2H), 1.60 (m, 2H), 1.40 (m, 6H); ^{13}C NMR δ 196.4, 171.1, 159.5, 148.0, 143.2, 135.7, 135.5, 130.8, 130.6, 130.5, 130.4, 130.3, 130.2, 129.9, 129.7, 129.2, 128.5, 114.0, 75.5, 72.1, 71.8, 70.6, 64.3, 55.5, 36.3, 32.7, 32.6, 31.4, 31.3, 29.8, 29.7, 29.5, 29.4, 29.2, 29.0, 27.4, 27.3, 26.5, 26.3, 21.9, 21.2. Anal. Calcd for $C_{38}H_{50}O_6$: C, 75.97; H, 8.05. Found: C, 75.94; H, 8.07.

1-*O*-{11-[4-(4-Methylbenzoyl)-phenyl]}-5-undecenyloxy-2-*O*-(4-methoxybenzyl)-*sn*-glycerol (56). To a solution of 189 mg (0.314 mmol) of **55** in 5 mL of CH_3OH was added 65 mg (0.472 mmol) of K_2CO_3. The mixture was stirred overnight. Then, 10 mL of saturated NH_4Cl solution was added; the solvent was removed under reduced pressure, and the residue was extracted with CH_2Cl_2. The organic extracts were washed with brine, dried (Na_2SO_4), filtered, and evaporated to give 205 mg of residue that was chromatographed on silica gel with 2:1 hexane/EtOAc to give 174 mg (100%) of colorless oily **56**: ^{1}H NMR δ 7.75 (m, 4H), 7.32 (m, 6H), 6.90 (m, 2H), 5.40 (m, 2H), 4.66 (d, J = 11.4 Hz, 1H), 4.58 (d, J = 11.4 Hz, 1H), 3.82 (s, 3H), 3.77−3.46 (m, 5H), 3.48 (t, J = 6.6 Hz, 2H), 2.71 (t, J = 7.5 Hz, 2H), 2.47 (s, 3H), 2.30 (b, 1H), 2.06 (m, 4H), 1.65 (m, 4H), 1.44 (m, 6H); ^{13}C NMR δ 196.6, 159.6, 148.1, 143.2, 135.7, 135.5, 130.8, 130.7, 130.5, 130.5, 130.3, 129.9, 129.7, 129.2, 128.5, 114.1, 77.8, 72.0, 71.9, 71.4, 63.3, 55.5, 36.3, 32.7, 32.6, 31.4, 31.3, 29.8, 29.7, 29.5, 29.4, 29.2, 29.0, 27.4, 27.2, 26.5, 26.4, 21.9. Anal. Calcd for $C_{36}H_{48}O_5$: C, 77.38; H, 8.30. Found: C, 76.53; H, 8.40.

1-*O*-{11-[4-(4-Methylbenzoyl)-phenyl]}-5-undecenyl-2-(4-methoxybenzyl)-*sn*-glycero-3-phosphocholine (57). According to the procedure of Guivisdalsky and Bittman,[37] to a solution of 754 mg (4.92 mmol) of $POCl_3$ and 498 mg (4.92 mmol) of Et_3N in 20 mL of chloroform was added a solution of 2.20 g (3.94 mmol) of **56** in 20 mL of $CHCl_3$ dropwise at −10 °C over 30 min. The mixture was allowed to warm to room temperature and then stirred for an additional 30 min, and 1.63 g (5.91 mmol) of choline tosylate and 2.73 mL of pyridine were added. The mixture was stirred for 2 days at room temperature; then, 1.09 mL of H_2O was added, and the mixture was stirred for 30 min. The solvent was removed under reduced pressure, and 50 mL of 1:1 CH_2Cl_2/toluene was added. The resulting mixture was filtered and evaporated to give 7.0 g of residue that was passed through a short column of MB-3 ion-exchange resin with 9:1 THF/H_2O. The residue (5.0 g) was chromatographed on silica gel with 65:35:5 $CHCl_3$/CH_3OH/H_2O to give 2.38 g (84%) of colorless waxy **57**: ^{1}H NMR δ 7.72 (m, 4H), 7.29 (m, 6H), 6.86 (m, 2H), 5.36 (m, 2H), 4.58 (m, 2H), 4.37 (m, 2H), 4.01 (m, 2H), 3.78 (s, 3H), 3.78 (m, 3H), 3.52 (m, 2H), 3.44 (m, 2H), 3.22 (s, 9H), 2.69 (t, J = 7.5 Hz, 2H), 2.44 (s, 3H), 2.03 (m, 4H), 1.60 (m, 4H), 1.38 (m, 6H); ^{13}C NMR δ 196.5, 159.5, 148.0, 143.2, 135.6, 135.4, 131.2, 130.7, 130.3, 130.2, 129.9, 129.8, 129.2, 128.5, 114.0, 78.0, 77.9, 72.0, 71.9,

66.4 (d), 65.5 (d), 59.4 (d), 55.5, 54.3, 36.2, 32.7, 32.6, 31.3, 29.7, 29.6, 29.5, 29.1, 29.0, 27.4, 27.3, 26.5, 26.3, 21.9; ^{31}P NMR δ −1.2 (s). Anal. Calcd for $C_{41}H_{60}NO_8P\cdot1.5H_2O$: C, 67.24; H, 8.22; N, 1.91. Found: C, 67.16; H, 8.10; N, 1.94.

1-*O*-{11-[4-(4-Methylbenzoyl)-phenyl]}-5-undecenyl-*sn*-glycero-3-phosphocholine (52). To a solution of 630 mg (0.87 mmol) of **57** in 18 mL of CH_2Cl_2 and 1 mL of water was added 296 mg (1.30 mmol) of DDQ. The mixture was stirred overnight at room temperature; the solvent was evaporated, and the residue (1.5 g) was chromatographed on silica gel with 2:1:0 to 65:35:5 $CHCl_3/CH_3OH/H_2O$ to give, followed by 185 mg (29%) of **57**, 340 mg (65%) of waxy **52**: ^{1}H NMR δ 7.70 (m, 4H), 7.25 (m, 4H), 6.50 (b, 1H), 5.37 (m, 2H), 4.37 (m, 2H), 3.85 (m, 4H), 3.38 (b, 14H), 2.67 (t, J = 7.5 Hz, 2H), 2.41 (s, 3H), 2.00 (m, 4H), 1.64 (m, 2H), 1.52 (m, 2H), 1.36 (m, 6H); ^{13}C NMR δ 196.5, 148.0, 143.2, 135.6, 135.4, 130.7, 130.4, 130.3, 129.8, 129.2, 128.5, 72.1, 71.7, 69.9 (d), 68.4 (br), 66.2 (br), 59.8 (br), 54.5, 36.2, 32.7, 32.6, 31.3, 31.2, 29.8, 29.6, 29.5, 29.4, 29.2, 29.0, 27.4, 27.3, 26.4, 26.3, 21.9; ^{31}P NMR δ 0.8 (s). Anal. Calcd for $C_{33}H_{52}NO_7P\cdot0.5H_2O$: C, 64.73; H, 8.39; N, 2.29. Found: C, 64.60; H, 8.32; N, 2.32.

Conversion of 52 to 32. To a solution of 10.0 mg (0.0166 mmol) of **52** in 2 mL of ethanol was added 1.2 mg (0.331 mmol) of 5% Pd/C. The mixture was exchanged with H_2 and purged H_2 for 2 h, and then the mixture was passed through a short pad of Celite eluting with methanol. The solvent was removed under reduced pressure to give 10 mg of residue that was chromatographed on silica gel with 65:35:5 $CHCl_3/CH_3OH/H_2O$ to give 10 mg (100%) of **32** that ^{1}H NMR showed to be identical with **32** prepared from **44**.

11-[4-(4-Methylbenzoyl)-phenyl]-undec-6-enal (59). To a solution of 155 mg (0.425 mmol) of **46** in 10 mL of anhydrous CH_2Cl_2 was added 137 mg (0.638 mmol) of PCC. The mixture was stirred at room temperature for 1.25 h and then passed through a short pad of Celite with EtOAc, and the solvent was evaporated to give 220 mg of residue that was chromatographed on silica gel with 9:1 hexane/EtOAc to afford 130 mg (84%) of colorless oily **59**: ^{1}H NMR (two isomers) δ 9.80 (s, 1H), 7.76 (m, 4H), 7.30 (m, 4H), 5.40 (m, 2H), 2.72 (t, J = 7.8 Hz, 2H), 2.48 (s, 3H), 2.48 (m, 2H), 2.08 (m, 4H), 1.73 (m, 4H), 1.40 (m, 4H); ^{13}C NMR (two isomers) δ 202.8, 196.5, 148.0, 143.2, 135.7, 135.5, 131.9, 131.3, 131.2, 130.6, 130.5, 129.3, 129.2, 128.8, 128.7, 128.5, 43.5, 43.4, 36.2, 32.7, 32.1, 31.3, 31.3, 29.7, 29.6, 29.2, 29.0, 27.4, 26.7, 22.3, 22.2, 21.9. Anal. Calcd for $C_{25}H_{30}O_2$: C, 82.83; H, 8.34. Found: C, 82.88; H, 8.45.

11-[4-(4-Methylbenzoyl)-phenyl]-undec-6-enoic Acid (58). According to the procedure by Dalcanale,[52] to a solution of 2.50 g (6.90 mmol) of **59** in 6 mL of CH_3CN, 224 mg (1.86 mmol) of NaH_2PO_4 in 2.5 mL of H_2O, and 0.6 mL of 35% H_2O_2 was added a solution of 1.12 g (12.4 mmol) of $NaClO_2$ in 8.5 mL of H_2O dropwise over 20 min at 10 °C. The mixture was stirred for 3 h, and a trace amount of Na_2SO_3 and 1 mL of 10% HCl were added. The resulting mixture was extracted with EtOAc, washed with brine, dried (Na_2SO_4), filtered, and evaporated to give 3.3 g of residue that was chromatographed on silica gel with 9:1 hexane/EtOAc to afford 1.10 g (42%) of colorless oily **58**: ^{1}H NMR (two isomers) δ 7.76 (m, 4H), 7.30 (m, 4H), 5.40 (m, 2H), 2.72 (t, J = 7.5 Hz, 2H), 2.48 (s, 3H), 2.38 (m, 2H), 2.09 (m, 4H), 1.70 (m, 4H), 1.40 (m, 4H); ^{13}C NMR (two isomers) δ 196.6, 180.0, 148.0, 143.2, 135.7, 135.4, 131.8, 131.3, 131.2, 130.6, 130.5, 130.3, 129.2, 128.8, 128.7, 128.5, 125.4, 36.2, 33.6, 33.5, 32.7, 32.0, 31.3, 31.3, 29.7, 29.6, 29.2, 29.0, 27.4, 26.7, 24.9, 24.7, 21.9. Anal. Calcd for $C_{25}H_{30}O_3$: C, 79.33; H, 7.99. Found: C, 79.29; H, 8.01.

Conversion of 58 to 9. A mixture of 17.1 mg (0.045 mmol) of **58** and 4.8 mg of 5% Pd/C in 2 mL of EtOAc was flushed with H_2 three times. The mixture was stirred under H_2 for 40 min at room temperature and then filtered through a short pad of silica gel with EtOAc. The solvent was evaporated to give 15 mg (88%) of **9**: ^{1}H NMR δ 7.75 (m, 4H), 7.30 (m, 4H), 2.72 (t, J = 7.5 Hz, 2H), 2.48 (s, 3H), 2.38 (t, J = 7.5 Hz, 2H), 1.66 (m, 4H), 1.40 (m, 12H).

1-Palmitoyl-2-{11-[4-(4-Methylbenzoyl)-phenyl]}-undec-6-enoyl-*sn*-glycero-3-phosphocholine (61). According to a modification of a procedure by Ali and Bittman,[31] to a mixture of 75.0 mg (0.15 mmol) of 1-palmitoyl-*sn*-glycero-3-phosphocholine (**21**) and 1.0 g (1.51 mmol) of **60** in 12 mL of alcohol-free $CHCl_3$ was added 22.2 mg (0.18 mmol) of DMAP. The mixture was flushed with N_2 three times and stirred at room temperature under N_2 for 5.5 h, and the solvent was evaporated to give 1.89 g of residue that was chromatographed on silica gel with 1:0 to 1:1 $CHCl_3/CH_3OH$ to give 66 mg (51%) of waxy **61**: ^{1}H NMR (two isomers) δ 7.71 (m, 4H), 7.28 (m, 4H), 5.38 (m, 2H), 5.20 (m, 1H), 4.40 (m, 1H), 4.34 (br, 2H), 4.11 (m, 1H), 3.95 (m, 2H), 3.87 (br, 2H), 3.37 (s, 9H), 2.67 (t, J = 7.5 Hz, 2H), 2.46 (s, 3H), 2.29 (m, 4H), 2.05 (m, 4H), 1.61 (m, 6H), 1.40 (br, 4H), 1.27 (br, 24H), 0.87 (t, J = 6.5 Hz, 3H); ^{13}C NMR (two isomers) δ 196.5, 173.8, 173.4, 173.2, 148.0, 147.9, 143.2, 135.7, 135.4, 131.7, 131.1, 130.5, 130.4, 129.2, 129.1, 128.7, 128.5, 70.8 (d), 66.6 (br), 63.7 (br), 63.3, 59.6 (br), 54.7, 36.2, 34.4, 34.0, 33.9, 32.8, 32.2, 32.1, 31.4, 31.3, 30.0, 29.9, 29.8, 29. 8, 29.6, 29.5, 29.2, 29.1, 27.4, 26.8, 25.2, 25.1, 22.9, 21.9, 14.4; ^{31}P NMR δ −0.4 (s). Anal. Calcd for $C_{49}H_{78}NO_9P\cdot H_2O$: C, 67.37; H, 9.23; N, 1.60. Found: C, 67.65; H, 9.22; N, 1.55.

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Supporting Information Available: Procedures for additional experiments; ^{1}H and ^{13}C NMR spectra for all new compounds and key intermediates; and ^{31}P NMR spectra for most compounds containing P. This material is available free of charge via the Internet at http://pubs.acs.org.

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