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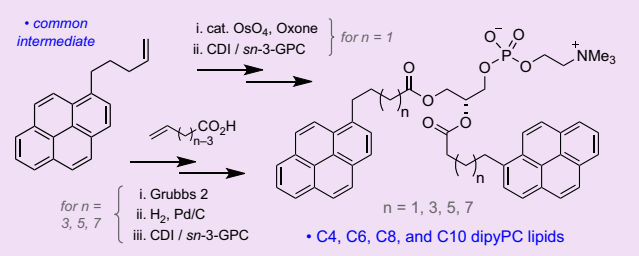
Paper

Streamlined Synthesis of Di-ω-(pyren-1-yl) alkanoylphosphatidylcholine Lipids from 5-(Pyren-1-yl)-1-pentene: Fluorescent Probes for Sensing Amphiphilic Membrane Lateral Pressure

Saikiran Aita[1], Damian B. Maxwell[1], Colin P. Johnson[2], Juan M. Vanegas[2], Paul R. Blakemore[1]

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GRAPHICAL ABSTRACT



ABSTRACT

1,2-Di-ω-(pyren-1-yl)alkanoyl-*sn*-glycero-3-phosphocholines with C4, C6, C8, and C10 alkanoyl chain lengths, which are useful fluorescent probes for sensing changes in the physical properties of amphiphilic membranes such as fluidity or lateral pressure, were prepared in —two to three steps from 5-(pyren-1-yl)-1-pentene as a common precursor. This pyrenylpentene was generated from 1-bromopyrene by halogen–metal exchange (*n*-BuLi, TMEDA, THF, 0 °C) followed by alkylation of the aryllithium with 5-bromo-1-pentene (66% yield). The C4 lipid target was uniquely prepared by oxidative cleavage of the pyrenylpentene intermediate (cat. OsO_4, Oxone, DMF, rt; 53% yield) followed by diacylation of *sn*-glycero-3-phosphocholine with the resulting 4-(pyren-1-yl)butanoic acid (CDI, CH_2Cl_2, rt; DBU, DMSO, 40 °C; 50% yield). The C6, C8, and C10 lipid targets were accessed by conversion of 5-(pyren-1-yl)-1-pentene to the appropriate chain-length ω-(pyren-1-yl)alkanoic acid (C6: 72% yield; C8: 72% yield; C10: 77% yield), by olefin cross-metathesis (with Grubbs 2 catalyst, CH_2Cl_2, 40 °C) with acrylic acid, 4-pentenoic acid, or 6-heptenoic acid, respectively, followed by hydrogenation (H_2, Pd/C, EtOAc-EtOH); and then, diacylation of *sn*-glycero-3-phosphocholine with the pyrenyl alkanoic acid using the above CDI-based method (C6: 43% yield; C8: 39% yield; C10: 59% yield). In all cases, potentially useful 1-ω-(pyren-1-yl)alkanoyl-*sn*-glycero-3-phosphocholines were obtained as minor products from the esterification process (21–36% yield).

Keywords cross olefin metathesis, excimer, fluorescent lipid probes, membrane lateral pressure, phosphatidylcholines, pyrene

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Introduction

Membranes serve many critical roles in biological systems including compartmentalization of cellular processes, providing a barrier for the selective permeation of molecules in an out of the cell, and an active matrix for signaling transduction processes. Cellular membranes have a complex and dynamic distribution of lipid species, with different chain lengths, number of unsaturations, and headgroup chemistries, that not only varies spatially but is also asymmetric between leaflets.[1–5] Cell membranes can modulate the activity of transmembrane and peripherally

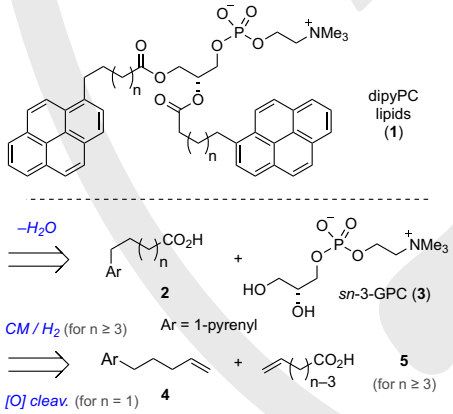
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associated proteins through a diverse set of mechanisms, including: (i) direct binding to allosteric sites as in G-protein-coupled receptor modulation by cholesterol and anionic lipids[6–12] and (ii) changes in the activation threshold of mechanosensitive channels due to physical properties such as bilayer thickness and lipid spontaneous curvature,[13–16] and sorting due to local changes in curvature.[17,18] The physical properties of lipid bilayers and their role in regulating biological functions have been studied through numerous experimental techniques including fluorescence microscopy. Fluorescent lipid probes are highly sensitive to their local environment and have therefore been used to quantify membrane properties such as viscosity, headgroup polarity, phase transitions, order and packing, and lateral tension.[19–25]

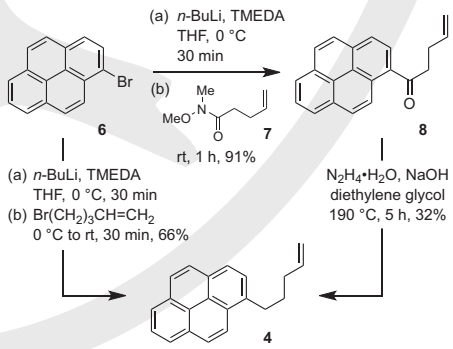
Sunamoto et al. first introduced dipyrene-labeled lipids to study the phase transition in dipalmitoylphosphatidylcholine bilayers with and without cholesterol.[26,27] The presence of the two pyrene groups in close proximity enables the formation of an excited state dimer, or excimer, whose fluorescence spectrum is red-shifted with respect to that of the monomer. As such, quantification of the monomer and excimer fluorescence can be used to characterize changes in the local membrane environment due to differences in lipid chemistry or external factors such as temperature or pressure.[28,29] Later studies showed that dipyrene lipids could be further used to quantify the lateral stress in membranes[30] and, more specifically, to estimate changes in the lateral pressure profile.[31,32] Pyrene-labeled lipids have also been used to study the activity of enzymes such as phospholipases A and C.[33,34] In spite of their utility, the commercial availability of such dipyrenylalkanoylphosphatidylcholine lipids (dipyPCs, **1**, **Scheme 1**) is now limited to only a few derivatives from specialist suppliers, while existing synthetic routes for their preparation are arduous and inefficient (vide infra). To facilitate an ongoing investigation into the effects of acyl chain unsaturation on the lateral pressure profiles of model lipid membranes, we sought to develop a more streamlined approach to dipyPCs (carbon chain lengths of 4, 6, 8, and 10) that would conveniently provide these important molecular probes in short order and in the pure form necessary for membrane studies.

DipyPC lipids (**1**) are still typically prepared along similar lines to the inaugural approach of Sunamoto[26]; namely, peracylation of *sn*-glycero-3-phosphocholine (**3**) with a *ω*-(pyren-1-yl)alkanoic acid (**2**) obtained from an alkanedioic acid by its conversion to the half-ester/half-acyl chloride, Friedel–Crafts acylation of pyrene, followed by Wolff–Kishner reduction with concomitant saponification of the intermediate ketoester.[35] Notwithstanding the comparatively long sequence required to access pyrenyl acids **2** in this manner, problems with both chemical yield and purification have been noted,[32] and one must start over from the beginning for each different chain length dipyPC required. To address these shortcomings, a different synthesis of pyrenyl acids **2** was envisioned in which 5-(pyren-1-yl)-1-pentene (**4**) would serve as a precursor to all congeners with chain lengths of four or more (i.e., **2** with $n \geq 1$). Six and higher chain length pyrenyl alkanoic acids **2** ($n \geq 3$) are targeted in a brace of steps from **4** by olefin cross-metathesis (CM)[36–38] with broadly available *ω*-alkenoic acids **5**, followed by hydrogenation, while 4-(pyren-1-yl)butanoic acid **2** ($n = 1$) is targeted from the same intermediate by its oxidative cleavage.[39] Although not of interest for our purposes, should the pentanoic acid **2** ($n = 2$) be wanted it could be targeted from alkene **4** by hydroboration followed by oxidation.[40]

Reduction of the above plan to practice began with experiments directed at finding an optimal route to 5-(pyren-1-yl)-1-pentene (**4**). This material has previously been prepared but only in step intensive fashion[41] and so a more direct means to access it was sought (**Scheme 2**). A foray to realize alkene **4** via Wolff–Kishner reduction of ketone **8** was initially thwarted with the finding that attempted Friedel–Crafts acylation of pyrene with 4-pentenoyl chloride[42] led only to decomposition of the electrophile without affording any **8**.[43] Subsequently, ketone **8** was instead secured by halogen–metal exchange from 1-bromopyrene (**6**), followed by addition of the resulting pyrenyllithium to known Weinreb amide derivative **7**.[44] Owing to the fact that Wolff–Kishner reduction of **8** gave the pivotal intermediate **4** in a disappointingly low (32%) yield, a direct conversion of bromopyrene **6** to pyrenylpentene **4** was explored with welcome results. Thus, ultimately it was found that a simple protocol of Br/Li interchange with *n*-butyllithium (TMEDA, THF, 0 °C) from aryl bromide **6**



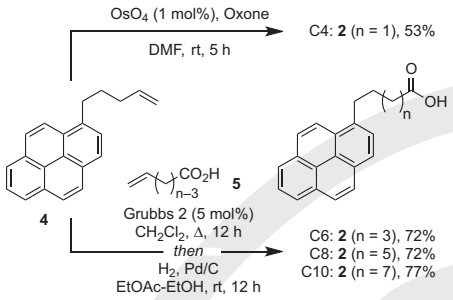
Scheme 1 Structure of di-*ω*-(pyren-1-yl)alkanoylphosphatidylcholine lipids (dipyPCs, **1**) and a retrosynthetic analysis for their streamlined elaboration from 5-(pyren-1-yl)-1-pentene (**4**) as a common intermediate.



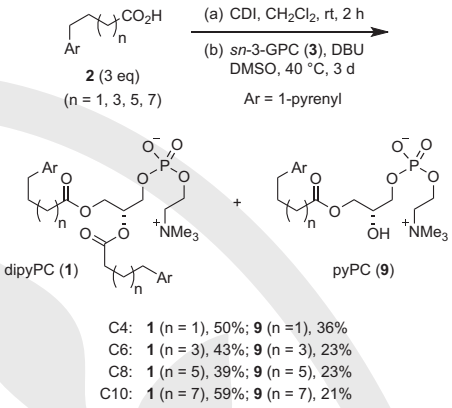
Scheme 2 Two synthetic approaches to 5-(pyren-1-yl-1-pentene (**4**).

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Scheme 3 Conversion of 5-(pyren-1-yl)-1-pentene (**4**) to C4, C6, C8, and C10 ω-(pyren-1-yl)alkanoic acids (**2**, *n* = 1, 3, 5, 7) using either oxidative cleavage or olefin CM/hydrogenation with corresponding ω-alkenoic acids (**5**) as indicated.



Scheme 4 Synthesis of 1,2-di-ω-(pyren-1-yl)alkanoyl-*sn*-glycero-3-phospho-cholines (**1**) (and associated monoesters **9**) by esterification of *sn*-glycero-3-phosphocholine (**3**) with C4, C6, C8, and C10 ω-(pyren-1-yl)alkanoic acids (**2**, *n* = 1, 3, 5, 7).

followed by addition of 5-bromo-1-pentene gave the pivotal intermediate **4** with ease via a scalable single-pot process and with an acceptable yield.[45]

With a robust and straightforward preparation of the common precursor (**4**) secured, its further conversion to the desired range of ω-(pyren-1-yl)alkanoic acids (**2**, *n* = 1, 3, 5, 7) was explored (**Scheme 3**). Oxidative cleavage of pyrenylpentene **4** using the osmylation-based protocol of Borhan[39] proceeded as intended, albeit only a modest yield of the C4 acid **2** (*n* = 1) was obtained. Pyrenylpentene **4** has been successfully used for olefin CM before,[38] and the expectation that it would engage as required with ω-alkenoic acids **5** in the presence of the second-generation Grubbs ruthenium alkylidene catalyst (Grubbs 2)[46] was borne out by experiment. Thus, each of the targeted C6, C8, and C10 acids **2** (*n* = 3, 5, 7) was obtained in good overall yield after CM between **4** and the appropriate **5**, followed by immediate hydrogenation of the initial alkene cross products before subsequent purification by column chromatography (SiO_2).

Finally, diesterification of *sn*-glycero-3-phosphocholine (**3**) using carbonyldiimidazole (CDI) to activate the ω-(pyren-1-yl)alkanoic acids (**2**, *n* = 1, 3, 5, 7) was achieved using a slight modification of the known method (**Scheme 4**).[32,35] In all cases, pure samples of the desired C4, C6, C8, and C10 dipyPCs (**1**) were obtained in good enough yields for ongoing membrane experiments and each was accompanied by minor quantities of 1-monoacylated *sn*-glycero-3-phosphocholines (**9**), which are useful should a pyrenylated phospholipid with a distinct side chain at O2 be needed.

In summary, an operationally straightforward and step-efficient synthesis of dipyPC lipids (**1**) was developed that deploys readily accessed 5-(pyren-1-yl)-1-pentene (**4**) as a common precursor. The strategy makes preparation of series of dipyPCs particularly convenient and herein the synthesis of C4, C6, C8, and C10 dipyPC lipids (**1**, *n* = 1, 3, 5, 7) was demonstrated. This approach could be adapted to prepare phosphatidylcholines with distinct alkanoyl moieties at C1-OH and C2-OH by subjecting the 1-monoacylated side-products (**9**) obtained to a second round of esterification with a different carboxylic acid. The dipyPCs prepared here will be used to estimate depth-dependent lateral pressure profiles within phosphatiylcholine membranes with varying degrees of unsaturation. The experimental data will be used to validate lateral pressure calculations obtained from molecular dynamics simulations showing that *cis* double bonds in lipids such as 1-palmitoyl-2-oleoyl-glycero-3-phosphocholine and 1,2-dioleoyl-glycero-3-phosphocholine produce large repulsive pressures that alter membrane fluidity and local mechanical properties of the membrane.[47,48]

Preparative chromatographic separations were performed on silica gel 60 (35–75 μm) and reactions were followed by TLC analysis using silica gel 60 plates (2–25 μm) with fluorescent indicator (254 nm) and visualized by UV or phosphomolybdic acid. All commercially available reagents were used as received. Anhydrous solvents were obtained from a Pure Process Technologies solvent purification system and dispensed under Ar. Melting points were recorded on a Mel-Temp melting point apparatus and are uncorrected. Infrared spectra were recorded on a PerkinElmer Spectrum II FT-IR using an ATR probe for solids or a thin film between NaCl plates for oils (neat). NMR spectra were recorded on Bruker Avance spectrometers at the field strength specified from 5-mm diameter tubes and carbon spectra were collected in proton-decoupled mode. Chemical shift in ppm is quoted relative to tetramethylsilane (δH = δC = 0 ppm) for **1** (*n* = 1, 3, 5, 7), or to solvent signals for all other compounds calibrated as follows, *d*-chloroform: δH ($CHCl_3$) = 7.26 ppm, δC ($CDCl_3$) = 77.2 ppm; d_6-DMSO: δH ($D_3CSOCHD_2$) = 2.50 ppm, δC (D_3CSOCD_3) = 39.5 ppm; d_4-methanol: δH (CHD_2OD) = 3.31 ppm, and δC (CD_3OD) = 49.0 ppm. Numbers in parentheses following carbon atom chemical shifts refer to the number of attached hydrogen atoms as revealed by the DEPT spectral editing technique. Low (MS) and high-resolution mass spectra (HRMS) were obtained using electrospray ionization (ESI) in positive ion mode. Ion mass/charge (*m*/*z*) ratios are reported as values in atomic mass units and high-resolution measurements were obtained using a TOF mass analyzer.

1-(Pyren-1-yl)pent-4-en-1-one (8)

An oven-dried 25-mL RB flask equipped with a magnetic stir bar was charged with 1-bromopyrene (**6**, 200 mg, 0.711 mmol, 1.02 eq.) under Ar. Anhydrous THF (5 mL) was added and the solution was cooled to 0 °C with stirring. Distilled TMEDA (0.14 mL, *d* = 0.775, 109 mg, 0.938 mmol, 1.34 eq.) was then added followed by dropwise addition of *n*-BuLi (1.60 M in hexanes, 0.56 mL, 0.896 mmol, 1.25 eq.) during 5 min. The resulting dark red solution was stirred at 0 °C for 30 min. A precooled (0 °C) solution of Weinreb amide **7** (100 mg, 0.698 mmol, 1.00 eq.)[44] in anhydrous THF (2 mL + 2 mL washings) was then added dropwise during 5 min. The reaction mixture was stirred at 0 °C for 30 min and then allowed to warm to room temperature and stirred for a final 2 h. The reaction mixture was quenched by careful addition of sat. aq. NH_4Cl (10 mL) followed by H_2O (5 mL). The reaction mixture was transferred to a separatory funnel, and the organic phase was separated. The aqueous layer was extracted with Et_2O (2 × 10 mL) and the combined organic phases were dried (Na_2SO_4) and concentrated in vacuo. The crude residue was purified by column chromatography (SiO_2, eluting with 5% EtOAc in hexanes) to afford aryl ketone **8** as an orange oil; yield 180 mg (0.633 mmol, 91%).

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IR (neat): 3039, 2918, 1671, 1639, 1594, 1506, 909, 843 cm^{-1}.

^1H NMR ($CDCl_3$, 700 MHz): δ = 8.89 (d, *J* = 9.3 Hz, 1 H), 8.32 (d, *J* = 8.0 Hz, 1 H), 8.25 (d, *J* = 6.9 Hz, 1 H), 8.24 (d, *J* = 6.5 Hz, 1 H), 8.20 (d, *J* = 9.3 Hz, 1 H), 8.17 (d, *J* = 7.6 Hz, 1 H), 8.16 (d, *J* = 8.1 Hz, 1 H), 8.07 (d, *J* = 8.4 Hz, 1 H), 8.05 (t, *J* = 7.8 Hz, 1 H), 5.99 (ddt, *J* = 16.9, 10.2, 6.5 Hz, 1 H), 5.14 (dm, *J* = 17.1 Hz, 1 H), 5.06 (dm, *J* = 10.2 Hz, 1 H), 3.33 (t, *J* = 7.4 Hz, 2 H), 2.65 (q, *J* = 7.0 Hz, 2 H).

^{13}C NMR ($CDCl_3$, 175 MHz): δ = 204.3 (0), 137.4 (1), 133.9 (0), 132.8 (0), 131.3 (0), 130.7 (0), 129.69 (1), 129.63 (1), 129.5 (0), 127.2 (1), 126.6 (1), 126.4 (1), 126.17 (1), 126.16 (1), 125.2 (0), 125.0 (1), 124.5 (0), 124.2 (1), 115.7 (2), 41.8 (2), 29.0 (2).

MS (ESI^+): *m/z* 285 (100) $[M+H]^+$.

HRMS (ESI^+): *m/z* calcd for $C_{21}H_{17}O^+$: 285.1274; found: 285.1278.

5-(Pyren-1-yl)-1-pentene (4)

By direct alkylation of 1-lithiopyrene: An oven-dried 250-mL RB flask equipped with a magnetic stir bar was charged with 1-bromopyrene (**6**, 5.00 g, 17.8 mmol, 1.0 eq.) under Ar. Anhydrous THF (50 mL) was added and the solution was cooled to 0°C with stirring. Distilled TMEDA (3.20 mL, *d* = 0.775, 2.48 g, 21.3 mmol, 1.2 eq.) was added, followed by dropwise addition of *n*-BuLi (13.4 mL, 1.60 M in hexanes, 21.4 mmol, 1.20 eq.) during 5 min. The resulting dark red solution was stirred at 0°C for 30 min. A solution of 5-bromopent-1-ene (2.32 mL, *d* = 1.258, 2.92 g, 19.6 mmol, 1.1 eq.) in anhydrous THF (10 mL + 5 mL washings) was then added dropwise during 5 min. The reaction mixture was stirred at 0°C for 30 min and then allowed to warm to room temperature and stirred for a further 2 h. The reaction mixture was quenched by slow addition of sat. aq. NH_4Cl (25 mL), followed by H_2O (15 mL). The mixture was transferred to a separatory funnel, and the organic phase was separated. The aqueous layer was extracted with EtOAc (2 × 30 mL) and the combined organic phases were dried (Na_2SO_4) and concentrated in vacuo. The crude residue was purified by column chromatography (SiO_2, eluting with 2% EtOAc in hexanes) to afford pyrenylpentene **4** as a bright yellow oil; yield 3.17 g (11.7 mmol, 66%).

*By Wolff–Kishner reduction of ketone **8**:* A solution of aryl ketone **8** (850 mg, 2.99 mmol, 1.0 eq.) in ethylene glycol (85 mL) was treated with NaOH (5.97 g, 149 mmol, 50 eq.) and hydrazine monohydrate (7.25 mL, *d* = 1.03, 7.47 g, 149 mmol, 50 eq.). The reaction mixture was heated with stirring at 190°C (solid NaCl bath temp.) for 8 h and then allowed to cool to room temperature. The mixture was poured slowly into H_2O (150 mL) and extracted with EtOAc (3 × 100 mL). The combined organic extracts were then dried (Na_2SO_4) and concentrated in vacuo. The crude residue was purified by column chromatography (SiO_2, 2% EtOAc in hexanes) to afford pyrenylpentene **4** as a bright yellow oil; yield 260 mg (0.96 mmol, 32%).

IR (neat): 3039, 2928, 1639, 1434, 1182, 909, 840 cm^{-1}.

^1H NMR ($CDCl_3$, 700 MHz): δ = 8.29 (d, *J* = 9.2 Hz, 1H), 8.18 (d, *J* = 6.6 Hz, 1 H), 8.16 (d, *J* = 6.4 Hz, 1 H), 8.13 (d, *J* = 5.1 Hz, 1 H), 8.11 (d, *J* = 6.6 Hz, 1 H), 8.05 (d, *J* = 8.8 Hz, 1 H), 8.02 (d, *J* = 8.9 Hz, 1 H), 8.00 (t, *J* = 7.6 Hz, 1H), 7.89 (d, *J* = 7.7 Hz, 1 H), 5.94 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1 H), 5.12 (dq, *J* = 17.1, 1.6 Hz, 1 H), 5.06 (dm, *J* = 10.2, 1 H), 3.37 (t, *J* = 7.9 Hz, 2 H), 2.26 (q, *J* = 7.1 Hz, 2 H), 1.98 (quintet, *J* = 7.7 Hz, 2 H).

^{13}C NMR ($CDCl_3$, 175 MHz): δ = 138.7 (1) , 137.0 (0), 131.6 (0), 131.1 (0), 129.9 (0), 128.8 (0), 127.7 (1), 127.4 (1), 127.3 (1), 126.7 (1), 125.9 (1), 125.3 (0), 125.2 (0), 125.0 (1), 124.9 (1), 124.8 (1), 123.6 (1), 115.2 (2), 33.9 (2), 33.1 (2), 31.1 (2).

MS (ESI^+): *m/z* 271 (100) $[M+H]^+$.

HRMS (ESI^+): *m/z* calcd for $C_{21}H_{19}^+$: 271.1481; found: 271.1480.

^1H and ^{13}C NMR spectral data are in agreement with those previously reported.[41]

4-(Pyren-1-yl)butanoic Acid (2, *n* = 1)

A solution of pyrenylpentene **4** (1.00 g, 3.70 mmol, 1.0 eq.) in DMF (10 mL) was treated with OsO_4 (0.38 mL, 2.5 wt% in *t*-BuOH, 9.5 mg, 0.037 mmol, 1 mol%) and stirred at room temperature for 5 min. Oxone (potassium peroxymono-sulfate, 4.55 g, 14.8 mmol, 4.0 eq.) was then added in one portion and the resulting mixture was stirred at room temperature for 5 h. After this time, Na_2SO_3 (2.80 g, 22.2 mmol) was added to reduce any remaining oxidants and the mixture was stirred for a further 1 h. Ice water (30 mL) was added, and the mixture was extracted with EtOAc (3 × 40 mL). The combined organic phases were washed with 1 M aq. HCl (3 × 25 mL), dried (Na_2SO_4), and concentrated in vacuo. The crude residue was purified by column chromatography (SiO_2, 30% EtOAc in hexans) to afford pyrenylbutanoic acid **2** (*n* = 1) as an off-white solid; yield: 562 mg (1.95 mmol, 53%); mp 183–185°C.

IR (ATR): 3036, 2927, 1693, 1603, 1462, 1241, 1181, 846 cm^{-1}.

^1H NMR (d_6-DMSO, 700 MHz): δ = 12.12 (bs, 1 H), 8.40 (d, *J* = 9.2 Hz, 1 H), 8.28–8.26 (m, 2 H), 8.23–8.20 (m, 2 H), 8.13 (AB quartet, 2 H), 8.05 (t, *J* = 7.5 Hz, 1 H), 7.94 (d, *J* = 7.7 Hz, 1H), 3.36–3.32 (m, 2 H, partially obscured by residual H_2O signal), 2.39 (t, *J* = 7.2 Hz, 2 H), 2.01 (quintet, *J* = 7.7 Hz, 2 H).

^{13}C NMR (d_6-DMSO, 175 MHz): δ = 174.4 (0), 136.3 (0), 130.9 (0), 130.4 (0), 129.3 (0), 128.2 (0), 127.50 (1), 127.45 (1), 127.3 (1), 126.5 (1), 126.1 (1), 125.0 (1, 2 C), 124.8 (1), 124.2 (0), 124.1 (0), 123.4 (1), 33.3 (2), 32.0 (2), 26.8 (2).

MS (ESI^+): *m/z* 289 (100) $[M+H]^+$.

HRMS (ESI^+): *m/z* calcd for $C_{20}H_{17}O_2^+$: 289.1223; found: 289.1233.

^1H and ^{13}C NMR spectral data are in agreement with those previously reported.[49]

6-(Pyren-1-yl)hexanoic acid (2, *n* = 3)

Representative procedure for olefin CM/hydrogenation. A stirred solution of pyrenylpentene **4** (500 mg, 1.85 mmol, 1.0 eq.) and acrylic acid (**5**, *n* = 3, 0.95 mL, *d* = 1.05, 998 mg, 13.8 mmol, 7.5 eq.) in CH_2Cl_2 (10 mL) under Ar was treated with Grubbs second-generation catalyst (57 mg, 0.067 mmol, 4 mol%)[46] and heated at reflux for 12 h. The reaction mixture was allowed to cool to room temperature and concentrated in vacuo. The residue was then dissolved in EtOAc (50 mL) and extracted with sat. aq. $NaHCO_3$ (3 × 30 mL). The combined aqueous extracts were acidified to pH 1 with 2 M aq. HCl and extracted with EtOAc (2 × 15 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated in vacuo to afford crude 6-(pyren-1-yl)hex-2-enoic acid as an off-white solid (517 mg, ca. 1.64 mmol). The crude material was dissolved in EtOAc/EtOH (1:3, 12 mL), the reaction vessel was purged with argon (x3), then 10 wt% Pd/C (17 mg) was added and the atmosphere was exchanged for H_2 gas using a balloon. The reaction mixture was stirred vigorously at room temperature under H_2 for 12 h, then diluted with CH_2Cl_2 (15 mL) and filtered through a pad of Celite. The filter cake was washed well with CH_2Cl_2 (2 × 10 mL) and the combined filtrate and washings were concentrated in vacuo. Purification of the resulting residue by column chromatography (SiO_2, 30% EtOAc in hexanes) afforded pyrenylhexanoic acid **2** (*n* = 3) as an off-white solid; yield: 421 mg (1.33 mmol, 72% over 2 steps); mp 195–202°C.

IR (ATR): 3300 (br), 2922, 2852, 1725, 1631, 1458, 1266, 1033, 847 cm^{-1}.

^1H NMR (d_6-DMSO, 700 MHz): δ = 8.34 (d, *J* = 9.1 Hz, 1H), 8.28–8.24 (m, 2 H), 8.23–8.20 (m, 2 H), 8.12 (AB quartet, 2 H), 8.05 (t, *J* = 7.5 Hz, 1 H), 7.95 (d, *J* = 7.7 Hz, 1 H), 3.35–3.30 (m, 2 H, partially obscured by residual H_2O signal), 2.21 (t, *J* = 7.1 Hz, 2 H), 1.80–1.76 (m, 2H), 1.61–1.56 (m, 2 H), 1.47–1.42 (m, 2 H).

^{13}C NMR (d_6-DMSO, 175 MHz): δ = 174.5 (0), 137.0 (0), 130.9 (0), 130.4 (0), 129.5 (1), 129.2 (0), 128.1 (0), 127.5 (1), 127.2 (1), 126.5 (1), 126.1 (1), 124.94 (1), 124.92 (1), 124.8 (1), 124.3 (0), 124.2 (0), 123.5 (1), 33.7 (2), 32.5 (2), 31.3 (2), 28.7 (2), 24.5 (2).

MS (ESI^+): *m/z* 317 (100) [M+H]+.

HRMS (ESI^+): *m/z* calcd for $C_{22}H_{21}O_2^+$: 317.1536; found: 317.1534.

^1H NMR spectral data are in agreement with those previously reported.[35]

8-(Pyren-1-yl)octanoic acid (2, *n* = 5)

Pyrenylpentene **4** (600 mg, 2.22 mmol, 1.0 eq.) and pent-4-enoic acid (**5**, *n* = 5, 1.70 mL, *d* = 0.98, 1.67 g, 16.6 mmol, 7.5 eq.) were transformed by analogy to the procedure given above for the synthesis of congener **2** (*n* = 3) to afford pyrenyloctanoic acid **2** (*n* = 5) as an off-white solid; yield: 548 mg (1.59 mmol, 72% over 2 steps); mp 140–143°C.

IR (ATR): 3045, 2926, 2857, 1698, 1467, 1287, 1264, 840 cm^{-1}.

^1H NMR (d_6-DMSO, 700 MHz): δ = 11.95 (br s, 1 H), 8.34 (d, *J* = 9.1 Hz, 1 H), 8.28–8.25 (m, 2 H), 8.22–8.20 (m, 2H), 8.12 (AB quartet, 2 H), 8.05 (t, *J* = 7.4 Hz, 1 H), 7.95 (d, *J* = 7.6 Hz, 1 H), 3.35–3.30 (m, 2 H, partially obscured by residual H_2O signal), 2.18 (t, *J* = 7.1 Hz, 2 H), 1.76 (quintet, *J* = 7.0 Hz, 2 H), 1.48 (quintet, *J* = 7.2 Hz, 2 H), 1.42 (quintet, *J* = 6.8 Hz, 2 H), 1.35 (quintet, *J* = 6.8 Hz, 2 H), 1.27 (quintet, *J* = 6.7 Hz, 2 H).

^{13}C NMR (d_6-DMSO, 175 MHz): δ = 174.5 (0), 137.1 (0), 130.9 (0), 130.4 (0), 129.2 (0), 128.0 (0), 127.46 (1), 127.45 (1), 127.2 (1), 126.4 (1), 126.1 (1), 124.91 (1), 124.89 (1), 124.7 (1), 124.23 (0), 124.18 (0), 123.5 (1), 33.7 (2), 32.6 (2), 31.5 (2), 29.0 (2), 28.64 (2), 28.55 (2), 24.5 (2).

MS (ESI^+): *m/z* 345 (100) $[M+H]^+$.

HRMS (ESI^+): *m/z* calcd for $C_{24}H_{25}O_2^+$: 345.1849; found: 345.1848.

^1H NMR spectral data are in agreement with those previously reported.[35]

10-(Pyren-1-yl)decanoic acid (2, *n* = 7)

Pyrenylpentene **4** (600 mg, 2.22 mmol, 1.0 eq.) and hept-6-enoic acid (**5**, *n* = 7, 2.25 mL, *d* = 0.946, 2.13 g, 16.6 mmol, 7.5 eq.) were transformed by analogy to the procedure given above for the synthesis of congener **2** (*n* = 3) to afford pyrenyldecanoic acid **2** (*n* = 7) as an off-white solid; yield: 637 mg (1.71 mmol, 77% over 2 steps); mp 74–76°C.

IR (neat): 3038, 2926, 2856, 1706, 1602, 1468, 1282, 1220, 840 cm^{-1}.

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^{1}H NMR (d_6-DMSO, 700 MHz): δ = 11.94 (br s, 1 H), 8.30 (d, *J* = 9.1 Hz, 1 H), 8.25 8.23 (m, 2 H), 8.20–8.16 (m, 2 H), 8.10 (AB quartet, 2 H), 8.03 (t, *J* = 7.5 Hz, 1 H), 7.90 (d, *J* = 7.7 Hz, 1 H), 3.26 (t, *J* = 7.6 Hz, 2 H), 2.15 (t, *J* = 7.3 Hz, 2 H), 1.71 (quintet, *J* = 7.0 Hz, 2 H), 1.47–1.42 (m, 2H), 1.381.33 (m, 2 H), 1.27–1.18 (m, 8H).

^{13}C NMR (d_6-DMSO, 175 MHz): δ = 174.5 (0), 137.1 (0), 130.9 (0), 130.4 (0), 129.2 (0), 128.0 (0), 127.45 (1), 127.42 (1), 127.1 (1), 126.4 (1), 126.1 (1), 124.89 (1), 124.88 (1), 124.7 (1), 124.3 (0), 124.2 (0), 123.4 (1), 33.7 (2), 32.6 (2), 31.5 (2), 29.0 (2), 28.9 (2, 2C), 28.7 (2), 28.5 (2), 24.5 (2).

MS (ESI$^+$): *m/z* 373 (100) [M+H]$^+$.

HRMS (ESI$^+$): *m/z* calcd for $C_{26}H_{29}O_2^+$: 373.2162; found: 373.2159.

^{1}H NMR spectral data for **2** (*n* = 7) are in broad agreement with those previously reported.[26]

(*R*)-2,3-Bis[(4-pyren-1-yl)butanoyl)oxy]propyl [2-(trimethylammo-nio) ethyl] phosphate (1, *n* = 1)

Representative procedure for esterification. A solution of 4-(pyren-1-yl)butanoic acid (**2**, n= 1**,** 250 mg, 0.867 mmol, 3.0 eq.) in dry CH_2Cl_2 (15 mL) was treated with 1,1′-CDI (165 mg, 1.02 mmol, 3.5 eq.) and stirred at room temperature for 2 h. The mixture was concentrated in vacuo and the residual crude acyl imidazole was dissolved in dry DMSO (5 mL) under Ar. *sn*-Glycero-3-phosphocholine (**3**, 75 mg, 0.292 mmol, 1.0 eq.) and DBU (0.26 mL, *d* = 1.02, 265 mg, 1.74 mmol, 6.0 eq.) were added to the DMSO solution and the reaction mixture was heated at 40 °C with stirring for 3 d. After this time, the mixture was allowed to cool to rt, poured into Et_2O (75 mL), and then stirred for 10 min to induce precipitation. The deposited solid was collected by filtration, washed with Et_2O (10 mL), and then dissolved off the filter paper using $CHCl_3$ (10 mL) and the resulting solution concentrated in vacuo. Purification of the crude residue by column chromatography (SiO_2, eluting with CH_2Cl_2-MeOH-H_2O, 70:25:5) gave, in order of elution: C4-dipyPC **1** (*n* = 1, 116 mg) as a waxy orange solid and C4-pyPC **9** (*n* = 1, 55 mg) as a waxy yellow solid.

Data for C4-dipyPC (**1**, *n* = 1): yield 116 mg (0.145 mmol, 50%).

IR (neat): 3040, 2946, 1733, 1603, 1488, 1243, 1183, 1089, 843 cm^{-1}.

^{1}H NMR (CDCl3, 700 MHz): δ 8.04 (t, J = 9.2 Hz, 2 H), 8.02–8.00 (m, 2 H), 7.99–7.97 (m, 2 H), 7.88–7.81 (m, 10 H), 7.60 (t, *J* = 8.5 Hz, 2 H), 5.26–5.24 (m, 1 H), 4.41 (dm, *J* = 9.7 Hz, 1 H), 4.16 (dd, *J* = 11.9, 7.0 Hz, 1 H), 4.05 (br s, 2 H), 3.96–3.94 (m, 2 H), 3.32 (s, 2 H), 3.14–3.10 (m, 4 H), 2.91 (s, 9 H), 2.38–2.27 (m, 4 H), 2.02–1.96 (m, 4 H).

^{13}C NMR (CDCl3, 175 MHz): δ 173.3 (0), 173.0 (0), 135.6 (0), 135.5 (0), 131.34 (0), 131.33 (0), 130.8 (0, 2 C), 129.9 (0, 2 C), 128.6 (0, 2 C), 127.46 (0, 2 C), 127.44 (1, 2 C), 127.41 (1), 127.37 (1), 127.3 (1), 127.2 (1), 126.68 (1), 126.65 (1), 125.9 (1), 125.8 (1), 124.95 (1), 124.93 (0), 124.91 (1), 124.87 (0), 124.85 (1), 124.82 (1), 124.79 (1, 2 C), 123.19 (1), 123.15 (1), 70.9 (1, d, J_{CP} = 7.4 Hz), 66.2 (2, d, J_{CP} = 6.1 Hz), 63.7 (2, d, J_{CP} = 4.2 Hz), 63.2 (2), 59.3 (2, d, J_{CP} = 4.4 Hz), 54.2 (3, 3 C), 34.0 (2), 33.7 (2), 32.53 (2), 32.49 (2), 26.8 (2), 26.6 (2).

MS (ESI$^+$): *m/z* 798 (100) [M+H]$^+$.

HRMS (ESI$^+$): *m/z* calcd for $C_{48}H_{49}NO_8P^+$: 798.3190; found: 798.3212.

Data for C4-pyPC (**9**, *n* = 1): yield 55 mg (0.104 mmol, 36%).

IR (neat): 3369, 3040, 2934, 1728, 1603, 1480, 1232, 1184, 1086, 843 cm^{-1}.

^{1}H NMR (CD_3OD, 500 MHz): δ 8.36 (d, *J* = 9.4 Hz, 1 H), 8.20–8.15 (m, 2 H), 8.14–8.11 (m, 2 H), 8.05–8.01 (m, 2 H), 7.99 (t, *J* = 7.7 Hz, 1 H), 7.89 (d, *J* = 7.9 Hz, 1 H), 4.26–4.21 (m, 1 H), 4.21 (dd, *J* = 11.4, 4.4 Hz, 1 H), 4.15 (dd, *J* = 11.4, 6.1 Hz, 1 H), 4.00–3.96 (m, 1 H), 3.94–3.86 (m, 2 H), 3.55–3.53 (m, 2 H), 3.40–3.37 (m, 2 H), 3.12 (s, 9 H), 3.07 (s, 1 H), 2.52 (t, *J* = 7.4 Hz, 2 H), 2.15 (quintet, *J* = 8.0 Hz, 2 H).

^{13}C NMR (CD_3OD, 125 MHz): δ 175.1 (0), 137.3 (0), 132.8 (0), 132.3 (0), 131.4 (0), 130.0 (0), 128.63 (1), 128.56 (1), 128.4 (1), 127.7 (1), 127.0 (1), 126.2 (0), 126.1 (0), 126.0 (1, 2 C), 125.9 (1), 124.5 (1), 69.9 (1, d, J_{CP} = 7.7 Hz), 67.8 (2, d, J_{CP} = 5.7 Hz), 67.5–67.4 (2, m), 66.3 (2), 60.4 (2, d, J_{CP}= 5.0 Hz), 54.61–54.55 (3, 3C, m), 34.5 (2), 33.6 (2), 28.1 (2).

MS (ESI$^+$): *m/z* 528 (100) [M+H]$^+$.

HRMS (ESI$^+$): *m/z* calcd for $C_{28}H_{35}NO_7P^+$: 528.2146; found: 528.2157.

^{1}H and ^{13}C NMR spectral data for **1/9** (*n* = 1) are in broad agreement with those previously reported.[35]

(*R*)-2,3-Bis[(6-pyren-1-yl)hexanoyl)oxy]propyl [2-(trimethylammo-nio) ethyl] phosphate (1, *n* = 3)

sn-Glycero-3-phosphocholine (**3**, 75 mg, 0.292 mmol) was esterified with 6-(pyren-1-yl)hexanoic acid (**2**, n= 3, 276 mg, 0.873 mmol) by analogy to the procedure given above for the synthesis of C4-dipyPC (**1**, *n* = 1) to give (after chromatography, as before) C6-dipyPC **1** (*n* = 3, 107 mg) as a waxy orange solid and C6-pyPC **9** (*n* = 3, 37 mg) as a waxy yellow solid.

Data for C6-dipyPC (**1**, *n* = 3): yield 107 mg (0.125 mmol, 43%).

IR (neat): 3040, 2932, 2858, 1734, 1603, 1488, 1244, 1182, 1089, 843 cm^{-1}.

^{1}H NMR ($CDCl_3$, 700 MHz): δ = 8.14 (d, *J* = 9.1 Hz, 2 H), 8.08–8.05 (m, 4 H), 7.99 (d, *J* = 8.3 Hz, 4 H), 7.92–7.90 (m, 6 H), 7.73 (d, *J* = 7.7 Hz, 2 H), 5.21–5.18 (m, 1 H), 4.38 (dd, *J* = 12.0, 2.7 Hz, 1 H), 4.15 (br s, 2 H), 4.11 (dd, *J* = 12.0, 7.1 Hz, 1 H), 3.96–3.89 (m, 2 H), 3.52 (br s, 2 H), 3.22–3.18 (m, 4 H), 3.08 (s, 9 H), 2.27 (t, *J* = 7.4 Hz, 2 H), 2.23 (t, *J* = 7.4 Hz, 2 H), 1.78 – 1.72 (m, 4 H), 1.65–1.58 (m, 4 H), 1.44–1.36 (m, 4 H).

^{13}C NMR ($CDCl_3$, 175 MHz): δ 173.5 (0), 173.2 (0), 136.8 (0, 2 C), 131.5 (0, 2 C), 130.9 (0, 2 C), 129.8 (0, 2 C), 128.6 (0, 2 C), 127.6 (1, 2 C), 127.26 (1), 127.25 (1), 127.2 (1, 2 C), 126.61 (1), 126.60 (1), 125.88 (1), 125.87 (1), 125.08 (0, 2 C), 125.05 (0, 2 C), 124.91 (1), 124.90 (1), 124.86 (1), 124.85 (1), 124.76 (1), 124.74 (1), 123.4 (1, 2 C), 70.7 (1, d, J_{CP} = 7.5 Hz), 66.4 (2, d, J_{CP} = 5.9 Hz), 63.5 (2, d, J_{CP} = 5.0 Hz), 63.1 (2), 59.3 (2, d, J_{CP} = 4.6 Hz), 54.32 (3, 3 C), 34.3 (2), 34.1 (2), 33.3 (2, 2 C), 31.50 (2), 31.49 (2), 29.3 (2), 29.2 (2), 24.93 (2), 24.85 (2).

MS (ESI$^+$): *m/z* 854 (100) [M+H]$^+$.

HRMS (ESI$^+$): *m/z* calcd for $C_{52}H_{57}NO_8P^+$: 854.3816; found: 854.3816.

Data for C6-pyPC (**9**, *n* = 3): yield 37 mg (0.066 mmol, 23%).

IR (neat): 3369, 3044, 2929, 1724, 1601, 1467, 1229, 1182, 1086, 839 cm^{-1}.

^{1}H NMR (CD_3OD, 500 MHz): δ 8.29 (d, *J* = 9.3 Hz, 1 H), 8.17–8.15 (m, 2 H), 8.11 (d, *J* = 8.7 Hz, 2 H), 8.01 (AB quartet, 2 H), 7.97 (t, *J* = 7.6 Hz, 1 H), 7.87 (d, *J* = 7.8 Hz, 1 H), 4.28–4.22 (m, 2 H), 4.16 (dd, *J* = 11.4, 4.5 Hz, 1 H), 4.10 (dd, *J* = 11.4, 6.1 Hz, 1 H), 3.97–3.94 (m, 1 H), 3.91–3.85 (m, 2 H), 3.58–3.55 (m, 2 H), 3.35–3.30 (m, 2 H), 3.15 (s, 9 H), 2.36 (t, *J* = 7.4 Hz, 2 H), 1.84 (quintet, *J* = 7.7 Hz, 2 H), 1.70 (quintet, *J* = 7.5 Hz, 2 H), 1.50 (quintet, *J* = 7.6 Hz, 2 H).

^{13}C NMR (CD_3OD, 125 MHz): δ 175.3 (0), 138.2 (0), 132.8 (0), 132.3 (0), 131.2 (0), 129.8 (0), 128.6 (1), 128.4 (1), 128.2 (1), 127.5 (1), 126.9 (1), 126.2 (0), 126.1 (0), 125.89 (1), 125.87 (1), 125.7 (1), 124.5 (1), 69.8 (1, d, J_{CP} = 7.6 Hz), 67.8 (2, d, J_{CP} = 5.7 Hz), 67.46–67.35 (2, m), 66.2 (2), 60.4 (2, d, J_{CP} = 5.0 Hz), 54.62–54.56 (3, 3C, m), 34.8 (2), 34.2 (2), 32.7 (2), 30.2 (2), 25.9 (2).

MS (ESI$^+$): *m/z* 556 (100) [M+H]$^+$.

HRMS (ESI$^+$): *m/z* calcd for $C_{30}H_{39}NO_7P^+$: 556.2459; found: 556.2475.

^{1}H and ^{13}C NMR spectral data for **1/9** (*n* = 3) are in broad agreement with those previously reported.[35]

(*R*)-2,3-Bis[(8-pyren-1-yl)octanoyl)oxy]propyl [2-(trimethylammo-nio) ethyl] phosphate (1, *n* = 5)

sn-Glycero-3-phosphocholine (**3**, 45 mg, 0.175 mmol) was esterified with 8-(pyren-1-yl)octanoic acid (**2**, n= 5, 180 mg, 0.522 mmol) by analogy to the procedure given above for the synthesis of C4-dipyPC (**1**, *n* = 1) to give (after chromatography, as before) C8-dipyPC **1** (*n* = 5, 62 mg) as a waxy yellow solid and C6-pyPC **9** (*n* = 5, 23 mg) as a waxy pale yellow solid.

Data for C8-dipyPC (**1**, *n* = 5): yield 62 mg (0.068 mmol, 39%).

IR (neat): 3040, 2927, 2857, 1732, 1602, 1468, 1242, 1183, 1082, 840 cm^{-1}.

^{1}H NMR ($CDCl_3$, 700 MHz): δ = 8.19 (d, *J* = 9.1 Hz, 2 H), 8.09 (d, *J* = 7.4 Hz, 4 H), 8.03–8.00 (m, 4 H), 7.97–7.90 (m, 6 H), 7.77 (d, *J* = 7.7 Hz, 2 H), 5.21–5.17 (m, 1 H), 4.38 (dd, *J* = 12.0, 2.7 Hz, 1 H), 4.23 (br s, 2H), 4.11 (dd, *J* = 12.0, 7.1 Hz, 1 H), 3.98–3.92 (m, 2 H), 3.73–3.64 (m, 2 H), 3.25–3.21 (m, 4 H), 3.20 (s, 9 H), 2.26 (t, *J* = 7.5 Hz, 2 H), 2.23 (t, *J* = 7.5 Hz, 2 H), 1.79–1.72 (m, 4 H), 1.58–1.51 (m, 4 H), 1.42–1.37 (m, 4 H), 1.35–1.22 (m, 8 H).

^{13}C NMR ($CDCl_3$, 175 MHz): δ 173.6 (0), 173.2 (0), 137.16 (0), 137.15 (0), 131.5 (0, 2 C), 131.0 (0, 2 C), 129.7 (0, 2 C), 128.6 (0, 2 C), 127.6 (1, 2 C), 127.23 (1, 2 C), 127.17 (1, 2 C), 126.5 (1, 2 C), 125.8 (1, 2 C), 125.09 (0, 2 C), 125.08 (0, 2 C), 124.85 (1, 2 C), 124.83 (1, 2 C), 124.7 (1, 2 C), 123.5 (1, 2 C), 70.6 (1, d, J_{CP} = 7.2 Hz), 66.3 (2, d, J_{CP}= 5.3 Hz), 63.7 (2, d, J_{CP}= 4.3 Hz), 63.0 (2), 59.5 (2, d, J_{CP} = 4.0 Hz), 54.5 (3, 3 C), 34.4 (2), 34.2 (2), 33.6 (2, 2 C), 31.9 (2, 2 C), 29.69 (2), 29.68 (2), 29.32 (2), 29.29 (2), 29.17 (2), 29.15 (2), 25.00 (2), 24.92 (2).

MS (ESI$^+$): *m/z* 910 (100) [M+H]$^+$.

HRMS (ESI$^+$): *m/z* calcd for $C_{56}H_{65}NO_8P^+$: 910.4442; found: 910.4442.

Data for C8-pyPC (**9**, *n* = 5): yield 23 mg (0.039 mmol, 23%).

IR (neat): 3370, 2926, 2856, 1730, 1468, 1234, 1086, 840 cm^{-1}.

1H NMR (CD_3OD, 700 MHz): δ 8.31 (d, *J* = 9.3 Hz, 1 H), 8.20–8.15 (m, 2 H), 8.13–8.12 (m, 2 H), 8.03 (AB quartet, 2 H), 7.99 (t, J = 7.6 Hz, 1 H), 7.88 (d, *J* = 7.9 Hz, 1 H), 4.28–4.23 (m, 2 H), 4.16 (dd, *J* = 11.4, 4.5 Hz, 1 H), 4.10 (dd, *J* = 11.4, 6.4 Hz, 1 H), 3.98–3.94 (m, 1 H), 3.92–3.86 (m, 2 H), 3.60–3.59 (m, 2 H), 3.37–3.33 (m, 2 H), 3.18 (s, 9 H), 2.34 (t, *J* = 7.6 Hz, 2 H), 1.88–1.83 (m, 2 H), 1.65–1.59 (m, 2 H), 1.50 (quintet, *J* = 7.9 Hz, 2 H), 1.45–1.30 (m, 4 H).

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^{13}C NMR (CD_3OD, 175 MHz): δ 175.4 (0), 138.5 (0), 132.9 (0), 132.4 (0), 131.2 (0), 129.8 (0), 128.6 (1), 128.5 (1), 128.2 (1), 127.5 (1), 127.0 (1), 126.24 (0), 126.19 (0), 125.90 (1), 125.86 (1), 125.7 (1), 124.5 (1), 69.8 (1, d, J_{CP} = 7.6 Hz), 67.8 (2, d, J_{CP} = 5.7 Hz), 67.50–67.43 (2, m), 66.2 (2), 60.4 (2, d, J_{CP} = 5.0 Hz), 54.67–54.63 (3, 3 C, m), 34.9 (2), 34.4 (2), 33.1 (2), 30.6 (2), 30.3 (2), 30.1 (2), 25.9 (2).

MS (ESI$^+$): *m*/*z* 584 (100) [M+H]$^+$.

HRMS (ESI$^+$): *m*/*z* calcd for $C_{32}H_{43}NO_7P^+$: 584.2772; found: 584.2776.

^{1}H and ^{13}C NMR spectral data for **1**/**9** (*n* = 5) are in broad agreement with those previously reported.[35]

(*R*)-2,3-Bis[(10-pyren-1-yl)decanoyl)oxy]propyl [2-(trimethyl-ammonio) ethyl] phosphate (1, *n* = 7)

sn-Glycero-3-phosphocholine (**3**, 50 mg, 0.194 mmol) was esterified with 8-(pyren-1-yl)octanoic acid (**2**, n= 7, 220 mg, 0.591 mmol) by analogy to the procedure given above for the synthesis of C4-dipyPC (**1**, *n* = 1) to give (after chromatography, as before) C10-dipyPC **1** (*n* = 7, 111 mg) as a waxy light yellow solid and C10-pyPC **9** (*n* = 7, 25 mg) as a waxy yellow solid.

Data for C10-dipyPC (**1**, *n* = 7): yield 111 mg (0.115 mmol, 59%).

IR (neat): 3039, 2926, 2856, 1734, 1602, 1468, 1239, 1183, 1090, 840 cm^{-1}.

^{1}H NMR ($CDCl_3$, 700 MHz): δ 8.21 (d, *J* = 9.2 Hz, 2 H), 8.10 (d, *J* = 7.5 Hz, 4 H), 8.04–8.00 (m, 4 H), 7.98–7.91 (m, 6 H), 7.79 (d, *J* = 7.7 Hz, 2 H), 5.22–5.18 (m, 1 H), 4.39 (dm, *J* = 9.9 Hz, 1 H), 4.25 (br s, 2 H), 4.12 (dd, *J* = 11.9, 7.3 Hz, 1 H), 3.97–3.90 (m, 2 H), 3.70 (br s, 2 H), 3.26–3.24 (m, 13 H), 2.27 (t, *J* = 7.4 Hz, 2 H), 2.24 (t, *J* = 7.7 Hz, 2 H), 1.81–1.75 (m, 4 H), 1.58–1.50 (m, 4 H), 1.44–1.37 (m, 4 H), 1.32–1.28 (m, 6 H), 1.27–1.20 (m, 10 H).

^{13}C NMR ($CDCl_3$, 175 MHz): δ 173.7 (0), 173.3 (0), 137.34 (0), 137.33 (0), 131.5 (0, 2 C), 131.0 (0, 2 C), 129.8 (0, 2 C), 128.7 (0, 2 C), 127.6 (1, 2 C), 127.3 (1, 2 C), 127.2 (1, 2 C), 126.6 (1, 2 C), 125.9 (1, 2 C), 125.14 (0, 2 C), 125.13 (0, 2 C), 124.9 (1, 4 C), 124.7 (1, 2 C), 123.57 (1), 123.55 (1), 70.7 (1, d, J_{CP} = 7.4 Hz), 66.5 (2, d, J_{CP} = 5.6 Hz), 63.5 (2, d, J_{CP} = 4.7 Hz), 63.1 (2), 59.4 (2, d, J_{CP} = 4.5 Hz), 54.5 (3, 3C), 34.4 (2), 34.2 (2), 33.7 (2, 2 C), 32.0 (2, 2 C), 29.91 (2), 29.90 (2), 29.66 (2), 29.64 (2), 29.58 (2), 29.57 (2), 29.43 (2), 29.40 (2), 29.24 (2), 29.21 (2), 25.1 (2), 25.0 (2).

MS (ESI$^+$): *m*/*z* 966 (100) [M+H]$^+$.

HRMS (ESI$^+$): *m*/*z* calcd for $C_{60}H_{73}NO_8P$: 966.5068; found: 966.5060.

Data for C10-pyPC (**9**, *n* = 7): yield 25 mg (0.041 mmol, 21%).

IR (neat): 3367, 2925, 2856, 1727, 1601, 1468, 1233, 1183, 1086, 839 cm^{-1}.

^{1}H NMR (CD_3OD, 700 MHz): δ 8.31 (d, *J* = 9.4 Hz, 1 H), 8.19–8.16 (m, 2 H), 8.14–8.11 (m, 2H), 8.04 (AB quartet, 2 H), 7.99 (t, *J* = 7.6 Hz, 1 H), 7.88 (d, *J* = 7.9 Hz, 1 H), 4.30–4.24 (m, 2 H), 4.17 (dd, *J* = 11.4, 4.5 Hz, 1 H), 4.10 (dd, *J* = 11.3, 6.4, Hz, 1 H), 3.98–3.95 (m, 1 H), 3.92–3.86 (m, 2 H), 3.62–3.59 (m, 2 H), 3.36–3.30 (m, 2 H), 3.19 (s, 9 H), 2.32 (t, *J* = 7.1 Hz, 2 H), 1.85 (quintet, *J* = 7.8 Hz, 2 H), 1.62–1.56 (m, 2 H), 1.52–1.47 (m, 2 H), 1.42–1.37 (m, 2 H), 1.35–1.27 (m, 6 H).

^{13}C NMR (CD_3OD, 175 MHz): δ 175.4 (0), 138.5 (0), 132.9 (0), 132.3 (0), 131.1 (0), 129.8 (0), 128.6 (1), 128.4 (1), 128.2 (1), 127.5 (1), 126.9 (1), 126.22 (0), 126.18 (0), 125.88 (1), 125.85 (1), 125.7 (1), 124.5 (1), 69.9 (1, d, J_{CP} = 7.6 Hz), 67.8 (2, d, J_{CP} = 5.6 Hz), 67.49–67.42 (2, m), 66.2 (2), 60.4 (2, d, *J* = 4.9 Hz), 54.67–54.63 (3, 3 C, m), 34.9 (2), 34.4 (2), 33.1 (2), 30.7 (2), 30.54 (2), 30.48 (2), 30.3 (2), 30.1 (2), 25.9 (2).

MS (ESI$^+$): *m*/*z* 612 (100) [M+H]$^+$.

HRMS (ESI$^+$): *m*/*z* calcd for $C_{34}H_{47}NO_7P^+$: 612.3085; found: 612.3087.

^{1}H NMR spectral data for **1** (*n* = 7) are in broad agreement with those previously reported.[26]

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Statements and Additional Information

Declaration of GenAI Use No AI tools were used during the writing of this manuscript.

Contributors' Statement S.A.: Investigation, Writing—review & editing. D.B.M.: Investigation. C.P.J.: Conceptualization. J.M.V.: Conceptualization, Project administration, Writing—original draft, Writing—review & editing. P.R.B.: Conceptualization, Project administration, Writing—original draft, Writing—review & editing.

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