Synthesis of Linear Amphipathic Porphyrin Dimers and Trimers: An Approach to Bilayer Lipid Membrane Spanning Porphyrin Arrays

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A modular building-block approach has been developed for the construction of linear amphipathic porphyrin arrays. The reaction of *meso*-(trifluoromethyl)dipyrromethane and an aldehyde under the conditions of the two-step room temperature porphyrin synthesis affords the *trans*-substituted porphyrin (13−56% yields). A similar reaction with two different aldehydes provides access to porphyrins bearing two different functional groups. An ethyne porphyrin and an iodo porphyrin (either free base or zinc) are selectively joined via Pd(0)-catalyzed coupling reactions, affording a linear array with porphyrins in defined metalation states. Coupling of a zinc−porphyrin bearing iodo and ester groups with a free base porphyrin bearing ethyne and ester groups yielded the zinc−free base porphyrin dimer. Coupling of a bis-ethyne porphyrin with a porphyrin bearing iodo and ester groups afforded the porphyrin trimer. Cleavage of the esters yielded the amphipathic porphyrin dimer and trimer arrays. The arrays with adjacent zinc and free base porphyrins undergo efficient electronic energy transfer. Both amphipathic porphyrin arrays have been incorporated into L-α-phosphatidylcholine vesicles. This versatile synthetic strategy provides access to a family of porphyrin arrays for studies of photophysical processes in supramolecular assemblies.

Introduction

The design and synthesis of artificial systems for charge separation, electron transport, and signal transduction remain central objectives in bioorganic chemistry. In biological systems each of these processes occurs in membranes. The multifaceted roles of porphyrinic molecules in charge separation and electron transport have prompted studies with synthetic porphyrins in membrane assemblies including vesicles, liposomes, and planar bilayer lipid membranes.[1] These studies have largely involved monomeric porphyrins. Much less work has been aimed at incorporating multicomponent porphyrin-based artificial photosynthetic model systems into supramolecular assemblies.[2] We have sought to devise multiporphyrin arrays that would span a bilayer lipid membrane and enable studies of transmembrane charge separation, electron transport, and signal transduction. A covalent bilayer-spanning system would allow examination of these phenomena without transmembrane diffusion of photoactive agents. With the notable exceptions of membrane-spanning steroidal porphyrins,[3] bolaamphiphiles,[4] and membrane carotenoids,[5] little work has been done toward developing bilayer-spanning synthetic molecules.

The molecular design of such a membrane-spanning system must achieve the desired photochemical and electronic interactions among porphyrins in an array and meet the structural and solubility requirements for supramolecular organization. The dramatic polarity change from the aqueous interface ($\epsilon = 78$) to the core of the membrane ($\epsilon \sim 2$) imposes a design with polar end groups and a hydrophobic core in a linear array. The thickness of lecithin-based bilayer lipid membranes (estimated 60−70 Å including the polar layers)[6] is compatible with linear arrays of two−four porphyrins depending on the lengths of the spacers between porphyrins. The desirable energy transfer, electron transfer, and/or hole-hopping features require rigid porphyrin−

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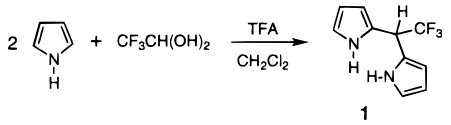
porphyrin distances and the ability to incorporate metallo and free base porphyrins at specific positions in the linear array.

The design requirements for creating an amphipathic array of porphyrins are best met with a modular building-block synthetic strategy. We recently developed a set of porphyrin building blocks that can be joined into a variety of multiporphyrin arrays.[7] Starlike pentameric arrays[8] were prepared by joining an ethyne porphyrin and a tetra-iodo porphyrin (metallo or free base) in a directed manner via homogeneous Pd-mediated coupling reactions.[9] The diphenylethyne spacer constructed in the coupling reaction is appropriate for efficient singlet state electronic energy transfer[10] and for rapid hole-hopping.[11] The diphenylethyne linker bends slightly, and free rotation of the porphyrins occurs about the ethyne unit.[12] Linear multiporphyrin arrays that function as molecular photonic devices were constructed in a similar manner using *trans*-substituted porphyrins.[13] To synthesize *trans*-substituted porphyrins, we developed a one-flask synthesis of *meso*-substituted dipyrromethanes.[14] The synthesis involves acid-catalyzed reaction at room temperature of an aldehyde in excess pyrrole in the absence of any solvent. This method has been applied to a wide variety of aldehydes affording dipyrromethane yields of 45−80%.

For the preparation of bilayer-spanning porphyrins we felt *meso*-perfluorinated substituents at two of the four *meso*-positions would be attractive for imparting hydrophobic character to the porphyrins. Numerous fluorinated porphyrins have been prepared including porphyrins with *meso*-pentafluorophenyl groups,[15] pentafluorophenyl groups appended to *meso*-phenyl groups,[16] *meso*-fluoro substituents,[17] *meso*-perfluoroalkyl groups,[18,19] or β-perfluoroalkyl groups.[20] In this paper we synthesize *trans*-substituted porphyrins bearing *meso*-perfluoroalkyl groups and then couple the bifunctional porphyrin building blocks to form amphipathic porphyrin dimers and trimers. We also characterize the static spectral properties of the porphyrins and the energy transfer processes in arrays containing free base and zinc porphyrins.

Scheme 1. One-Flask Synthesis of *meso*-(Trifluoromethyl)dipyrromethane



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Results and Discussion

I. *Trans*-Substituted Porphyrins. I.1. Synthesis. Treatment of trifluoroacetaldehyde hydrate with excess pyrrole via the solventless method[14] at room temperature failed to yield any *meso*-(trifluoromethyl)dipyrromethane. Recently Wijesekera reported the first one-flask synthesis of *meso*-(perfluoroalkyl)dipyrromethanes, including *meso*-(trifluoromethyl)dipyrromethane and *meso*-(heptafluoropropyl)dipyrromethane, by condensation of pyrrole and the corresponding perfluoroalkyl aldehyde in refluxing THF with HCl catalysis.[21] More forcing conditions are required due to the destabilizing influence of the *meso*-perfluoroalkyl group on the α-carbocation formed during the condensation leading to dipyrromethanes.[22] These *meso*-(perfluoroalkyl)dipyrromethanes were then used to prepare both electron-deficient *trans*-(perhaloalkyl)porphyrins[23] and *meso*-tetrakis(perfluoroalkyl)porphyrins,[23] the iron complexes of which were shown to be efficient catalysts for the air oxidation of alkanes.[24] In related work, DiMagno *et al.* showed that *meso*-tetrakis(heptafluoropropyl)porphyrin formed in 37% yield by reaction of 2,2,3,3,4,4,4-heptafluoro-1-(2-pyrrolyl)-1-butanol and pyrrole under dehydrating conditions at elevated temperatures, but only 8% yield was observed without removal of water.[19]

We investigated a range of reaction conditions for forming *meso*-(perfluoroalkyl)dipyrromethanes. The condensation of trifluoroacetaldehyde hydrate (0.5 M) and 2 equiv of pyrrole at room temperature in CH_2Cl_2 acidified with TFA (0.25 M) afforded a mixture composed of **1** and unreacted pyrrole as the only mobile components. Flash chromatography gave **1** in 40% yield (Scheme 1). **1** is a white solid and is stable for at least 6 months at 0 °C, but turns pale brown over 3−5 days when stored on the benchtop. These conditions resemble those used in pyrrole−aldehyde condensations leading to the porphyrinogens,[25,26] though with higher concentrations of reactants and acid catalyst. Changes in TFA concentration (0.25 −0.75 M), replacement of TFA with $BF_3{\cdot}O(Et)_2$ (0.17 M), replacement of CH_2Cl_2 with $CHCl_3$,

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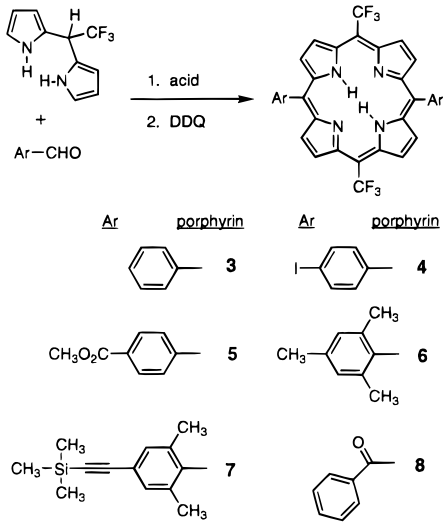
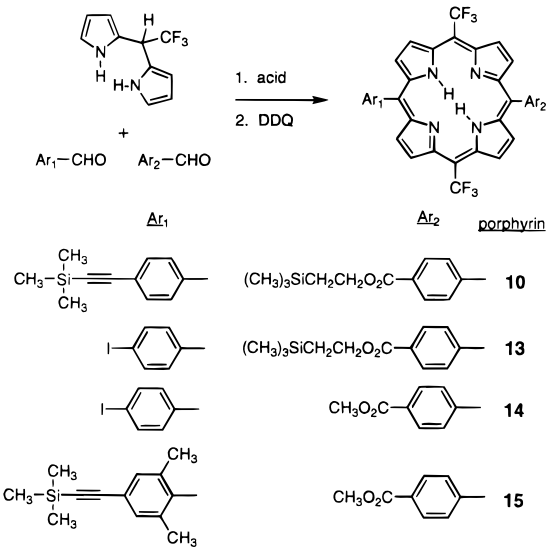
Scheme 2. One-Flask Synthesis of *Trans*-Substituted Porphyrins



Scheme 3. Mixed-Aldehyde Synthesis of *Trans*-Substituted Porphyrins Bearing Two Different Functional Groups



or using refluxing conditions (39 or 61 °C) gave a similar product distribution and the same modest yields of **1**. This same approach yielded *meso*-(heptafluoropropyl)-dipyrromethane (**2**) from pyrrole and heptafluorobutyraldehyde hydrate. The generality of these conditions increases the scope of the one-flask syntheses of β-unsubstituted *meso*-substituted dipyrromethanes.[14,21,27]

A series of *trans*-substituted porphyrins was prepared by reaction of **1** (0.01 M) with an aldehyde (0.01 M) using the conditions of the two-step one-flask room temperature synthesis of *meso*-substituted porphyrins (Scheme 2).[25,26,28] The aldehyde−dipyrromethane condensations were catalyzed with trifluoroacetic acid (TFA) or $BF_3{\cdot}O(Et)_2$ for *m*- or *p*-substituted benzaldehydes[25] or with BF_3−ethanol cocatalysis for *o*-disubstituted benzaldehydes.[26] The reactions were monitored spectroscopically, and DDQ was added when the reactions leveled off, which generally occurred around 8 h. Thus reaction of benzaldehyde and **1** (5 mM each) with 20 mM TFA gave 8% yield after 1 h, 51% after 8 h, and 54% after 24 h. With 50 mM TFA the reaction was faster (~30% after 1 h) but the final yield was about the same as with 20 mM TFA. A single chromatographic workup of the reaction mixtures usually afforded the desired porphyrin. Porphyrins **3**−**9** were prepared in 13−56% yield. In each condensation only one porphyrin was detected by TLC analysis.[29] The absence of porphyrins formed by acidolysis of the dipyrromethane is not surprising since the *meso*-CF_3 group deactivates pyrromethanes toward α-carbocation formation.[22] The lack of acidolysis of these dipyrromethanes may prove useful in the stepwise synthesis of porphyrins bearing four different *meso* substituents.[30]

Porphyrins bearing two different *trans* substituents are available by reaction of **1** with two different aldehydes (Scheme 3). Thus reaction of **1** with 4-(2-(trimethylsilyl)-ethynyl)benzaldehyde[31] and 4-((2-(trimethylsilyl)ethoxy)-carbonyl)benzaldehyde[7] afforded the porphyrin bearing one ethyne and one ester group (**10**, 15.3%), the bis-ethyne porphyrin (**11**, 8.6%), and the bis-ester porphyrin (**12**, 7.9%). The polarity imparted by the ester moiety enabled facile chromatographic separation of the three porphyrins. Similar reactions afforded porphyrins **13**−**15** in 5−17% yields.

Meso-substituted porphyrins bearing functional groups positioned in a *trans* geometry are of central importance in the synthesis of porphyrin model systems. The one-flask synthesis of **1** or **2** is simple and expedient, the resulting *trans*-substituted porphyrin bears four *meso*-substituents, and the overall pathway is compatible with sensitive functional groups.

I.2. Absorption and Fluorescence Properties. The *trans*-CF_3-substituted porphyrins exhibit distinct absorption spectra (Figure 1). The Soret band of **3** is broadened (fwhm 21−26 nm) and blue-shifted (λ_{max} 414 nm) compared with that of tetraphenylporphyrin (TPP). The visible bands have almost identical absorption maxima as TPP, but do not display the etio intensity pattern. The enhanced intensities of both band I (647 nm) and band III (546 nm) indicate increased oscillator strength for the 0−0 components of the Q_x and Q_y transitions, respectively (Table 1).[32] These spectral

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(29) In the syntheses of porphyrins **4**, **6**, **7**, and **9** a substantially slower-moving green pigment exhibiting red fluorescence was observed. The green pigment (λ_{max} in toluene 406, 422, 516, 552, 618 nm) isolated from the synthesis of **7** gave a strong parent ion at 634.1, consistent with a bilatriene ($C_{34}H_{28}F_6N_4Si$, calcd mass 634.2) formed by condensation of two molecules of **1** and one molecule of the aldehyde, followed by oxidation. On the basis of this assignment the yield of the bilatriene in the synthesis of **7** is 64%. A similar yield was estimated in the synthesis of **6**. The yields in the syntheses of **4** and **9** were about one-tenth that of the porphyrin. These green pigments were not noticed in the synthesis of the other porphyrins.

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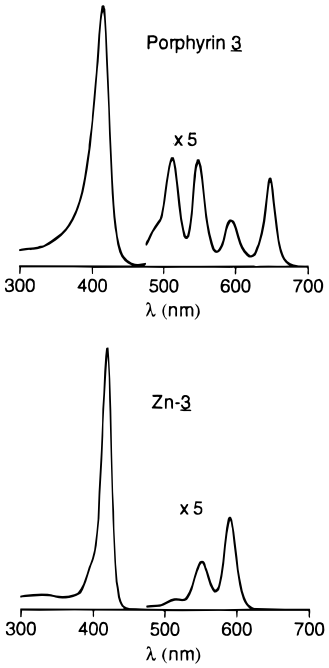


Figure 1. Absorption spectra in toluene at room temperature of **3** (top) and its zinc chelate (bottom).

features were observed for every porphyrin of this class, including **6** and **7**, which both have *o*-dimethyl groups yet do not exhibit the phyllo spectrum (band I < III < II < IV) characteristic of tetramesitylporphyrin.[26] Each zinc chelate that was prepared (from **3**, **10**, **12**, **13**) also exhibited an enhanced long wavelength transition (591 nm) compared with that of ZnTPP.

The enhanced absorption at 647 nm of the free base porphyrins is not due to chlorin contamination, as shown by three pieces of data. First, treatment of **3** with DDQ in refluxing toluene caused no change in the visible bands. Second, the fluorescence excitation spectrum (λ_{em} 720 nm) of **3** matches the absorption spectrum, which would not be expected with a chlorin impurity. Third, conversion to the zinc chelate caused disappearance of the 647 nm band and complete loss of absorbance beyond 620 nm (Figure 1), while conversion of tetraphenylchlorin to zinc−tetraphenylchlorin causes blue-shifting and intensification of the long wavelength band from 653 nm (ϵ 42 000 M^{-1} cm^{-1}) to 623 nm (ϵ 56 000 M^{-1} cm^{-1}), respectively.[37] These data show the enhanced intensity of the 647 nm band is an intrinsic property of these *meso*-CF_3-substituted porphyrins.

The fluorescence emission spectra of **3** and its zinc chelate (**Zn-3**) were unremarkable, but the quantum yields of fluorescence were 0.044 and 0.087, respectively, compared with 0.11 (TPP) and 0.03 (ZnTPP).[35] Thus *trans* substitution of perfluoroalkyl groups renders the free base porphyrin less emissive and the zinc chelate more emissive than the corresponding porphyrin with phenyl substituents.

The ^{1}H NMR spectra of the *trans*-(perfluoroalkyl)-substituted porphyrins exhibit distinctive features due to the β-pyrrole resonances. The β-pyrrole protons in a *trans*-$Ar_2(CF_3)_2$-porphyrin could be expected to give a pair of doublets, as is the case with many *trans*-substituted porphyrins, but each of these porphyrins exhibited a 6-line pattern (4 H) at ~9.6 ppm and a doublet (4 H) at ~8.8 ppm. A representative spectrum is shown for porphyrin **3** (Figure 2). Identical spectra were observed with zinc chelates; thus the low-field 6-line pattern is not a consequence of N−H tautomerization. Standard decoupling experiments confirmed the assignment of the low-field 6-line pattern to the protons flanking the *meso*-CF_3 groups and the doublet to the protons flanking the *meso*-aryl moieties. The ^{19}F NMR spectrum of **12** exhibited a triplet, indicative of coupling of the fluorines with the two flanking β-pyrrole protons and also indicating the free rotation of the *meso*-CF_3 group. Splitting of the downfield β-pyrrole resonances (4 lines) also was observed in the perfluoropropyl-substituted porphyrin **9**. Thus the splitting of the β-pyrrole resonances is a common characteristic of this family of porphyrins.

II. Linear Amphipathic Porphyrin Dimers and Trimers. II.1. Synthesis. The synthesis of porphyrin arrays is contingent on reaction conditions that maintain solubility of starting porphyrins and intermediates and are compatible with various metalation states and protecting groups.[8,9,13] The key reaction for linking the porphyrins involves the Pd-mediated coupling of an iodo porphyrin with an ethynyl porphyrin. In the present reactions we have used the Pd(0) catalyst $Pd(PPh_3)_4$ in toluene/triethylamine (5:1) at 40−50 °C, though more recently we have employed other palladium catalysts and cocatalysts.[9] The low temperatures of these coupling reactions give diminished side reactions, particularly of ethyne oligomerization products.

The synthesis and modification of a porphyrin−porphyrin dimer are shown in Scheme 4. Deprotection of **10** using Bu_4NF on silica gel in THF afforded the monodeprotected ethyne porphyrin **16** in 67% yield and the completely deprotected porphyrin in 20% yield. The coupling of **Zn-13** and **16** (3.9 mM each) was carried out in toluene/triethylamine (5:1) with a catalytic amount of the Pd(0) catalyst $Pd(PPh_3)_4$ at 40−50 °C. TLC monitoring showed four sharp spots due to the two starting materials, ethyne-linked dimer **17** (R_f 0.3), and homocoupled butadiynyl dimer (R_f 0.6). After 4 days the starting material **16** had disappeared. Chromatography on silica gel gave ready separation of zinc−free base porphyrin dimer **17** (71%) and the bis-free base butadiynyl dimer (< 2%).

The organization of porphyrin arrays in bilayer lipid membrane assemblies requires the presence of polar end groups. Treatment of **17** with excess Bu_4NF in DMF at room temperature cleanly gave the amphipathic dimer **19** in 90% yield. By CPK models the end-to-end length of dimer **19** is 39 Å. Treatment of **19** with taurine and (benzotriazol-1-yloxy)tris(dimethylamino)phosphonium hexafluorophosphate (BOP) yielded dimer **20** as the triethylamine salt upon workup and reverse phase chromatography.

A convergent synthesis of linear porphyrin trimers is outlined in Scheme 5. In the synthesis of porphyrin arrays the formation of butadiyne-linked porphyrins by homocoupling of ethyne groups can be a significant side reaction, not because the amount of material formed is so large but because the product(s) can be difficult to separate. Using a bis-iodo porphyrin as the core component sidesteps this reaction, since homocoupling of the monoethyne porphyrin forms the easily separated butadiynyl dimer. However, we elected to use a bis-ethyne porphyrin (**21**) as the core porphyrin because this route employs iodo ester porphyrin **13**, which is available

(37) Dorough, G. D.; Huennekens, F. M. *J. Am. Chem. Soc.* **1952**, *74*, 3974−3976.

Table 1. Porphyrin Spectral Parameters

compd		Soret	$Q_y(1,0)$	$Q_y(0,0)$	$Q_x(1,0)$	$Q_x(0,0)$	$\epsilon[Q(0,0)]/\epsilon[Q(1,0)]$[a]	Φ_f
TPP[b]	λ	419	514	549	591	647	0.46	0.11[c]
	ϵ	470 000	18 700	7700	5400	3400		
3[d]		414	511	546	592	647	1.16	0.044
		165 000	10 100	10 100	5270	7690		
		fwhm 27 nm						
			Q(1,0)	Q(0,0)				
ZnTPP[e]		423	548	586			0.16	0.03[c]
		544 000	22 800	3680				
Zn-3[d]		419	550	591			1.98	0.087
		214 000	8900	17 600				
		fwhm 18 nm						

[a] For the free base porphyrin the ratio of absorbances is $\epsilon[Q_x(0,0) + Q_y(0,0)]/\epsilon[Q_x(1,0) + Q_y(1,0)]$.[33] [b] In benzene.[34] [c] Literature values.[35] [d] In toluene. [e] In benzene.[36]

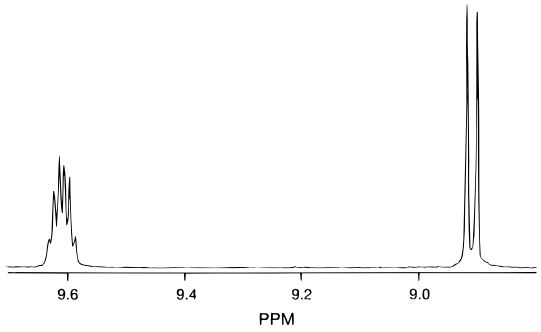


Figure 2. ^{1}H NMR resonances of the β-pyrrole protons of **3** (300 MHz, $CDCl_3$, room temperature). An identical spectrum was observed for the zinc chelate of **3**.

without requiring selective deprotection as in the synthesis of **16**.

Deprotection of **7** afforded bis-ethynyl porphyrin **21** that serves as the core porphyrin in the trimer synthesis. Porphyrins **7** and **21** resemble the *trans*-ethynyl porphyrins prepared by Anderson.[38] The Pd(0)-catalyzed coupling of **Zn-13** and **21** to form trimer **22** was performed in toluene/triethylamine (5:1) at 40−50 °C, and the reaction was monitored by analytical size exclusion chromatography (SEC) (Figure 3) and TLC. The reaction mixture remained homogeneous throughout the coupling process. In these coupling reactions two dimers can be formed, the dimer derived from reaction of **Zn-13** and **21** that is the precursor to the trimer and a butadiynyl dimer derived from two molecules of **21**. Both dimers are expected to co-chromatograph in SEC. After 7 days the dimer peak had decreased to a residual level (Figure 3C), which may be attributed to the butadiynyl dimer, and the reaction mixture was worked up. Chromatography of the crude mixture on silica gel followed by preparative gel permeation chromatography afforded purified trimer **22**. Subsequent modifications such as metalation with zinc afforded the all-zinc trimer **23**, and deprotection with Bu_4NF afforded the trimer diacid **24** in 78% yield. By CPK models the end-to-end length of trimer **24** is 59 Å.

The porphyrin monomers (**3**−**16**, **21**) and nonpolar dimers (**17**, **18**) and trimers (**22**, **23**) were characterized by absorption, fluorescence, and ^{1}H NMR spectroscopy and plasma desorption mass spectrometry. The amphipathic dimers (**19**, **20**) and trimer (**24**) were analyzed similarly, and though each analyzed correctly by plasma desorption mass spectrometry, the respective parent ions were quite weak. In each case evidence for complete deprotection was established by homogeneity and characteristic retention factors on reverse phase and silica thin layer chromatography, absence of any peaks in the ^{1}H NMR spectra characteristic of trimethylsilyl groups, and correct parent ion masses by electrospray mass spectrometry.

II.2. ^{1}H NMR Features. Upon formation of a diphenylethyne linkage, the signals arising from the two sets of phenyl protons flanking the ethyne (*meta* to the *meso* carbon) are shifted by ~0.2 ppm downfield compared with the respective monomer. This change in chemical shift is observed in all the dimers and trimers and is a diagnostic for the formation of the diphenylethyne linkage. For example, in trimer **22** the core porphyrin aryl rings bear *o*-methyl groups, and the *meta*-protons (flanking the ethyne) appear as a distinct singlet shifted 0.22 ppm downfield compared to the bis-ethyne porphyrin **7**.

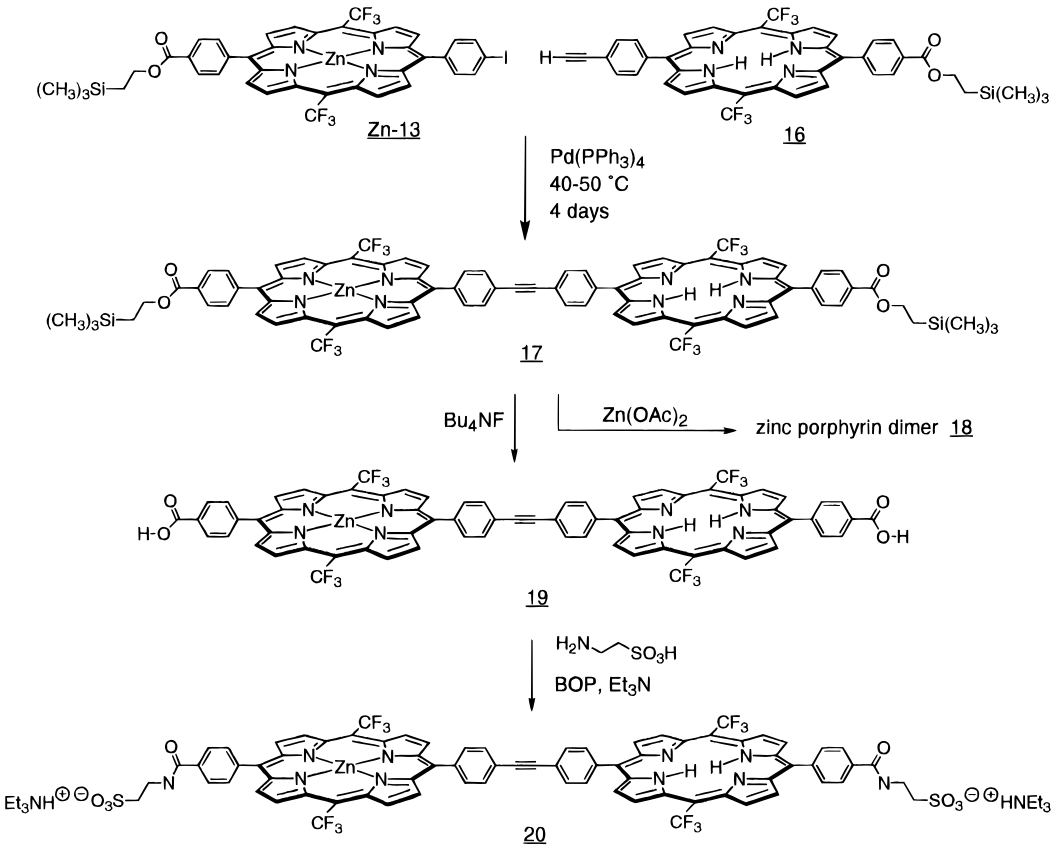
The β-pyrrole resonances also provided a convenient diagnostic for the formation of dimers and trimers. The ^{1}H NMR spectrum (THF-d_8) for the Zn-H_2 dimer **17** exhibited overlapping signals (9.80−9.60 ppm) due to the four magnetically distinct sets of β-pyrrole protons flanking the *meso*-trifluoromethyl groups and four AB doublets (9.12−8.92 ppm) due to the remaining four sets of β-pyrrole protons. In $C_2D_2Cl_4$ the downfield signals were better resolved, appearing as four multiplets (9.85−9.55 ppm) as expected due to the four magnetically distinct sets of β-pyrrole protons flanking the *meso*-trifluoromethyl groups. The trimers **22**−**24** have higher symmetry (D_{2h}) than the zinc−free base porphyrin dimer **17** (C_{2v}). In **22** three sets of multiplets due to the protons flanking the trifluoromethyl groups and three sets of doublets were observed, all of which appeared at lower field compared to the starting materials. In the all-zinc trimer **23** the β-pyrrole multiplets partially overlap due to the downfield shift of the multiplet originating from the core porphyrin.

II.3. Absorption, Fluorescence, and Energy Transfer Properties. The absorption spectrum of dimer **17** in toluene is shown in Figure 4. The Soret band in the dimer (423 nm) is red-shifted compared with porphyrins **Zn-10** (420 nm) and **10** (416 nm), which have similar peripheral substituents as the porphyrins in the dimer. The visible bands of the dimer, however, are identical in intensity and wavelength maxima of the sum of the spectra of the component parts.

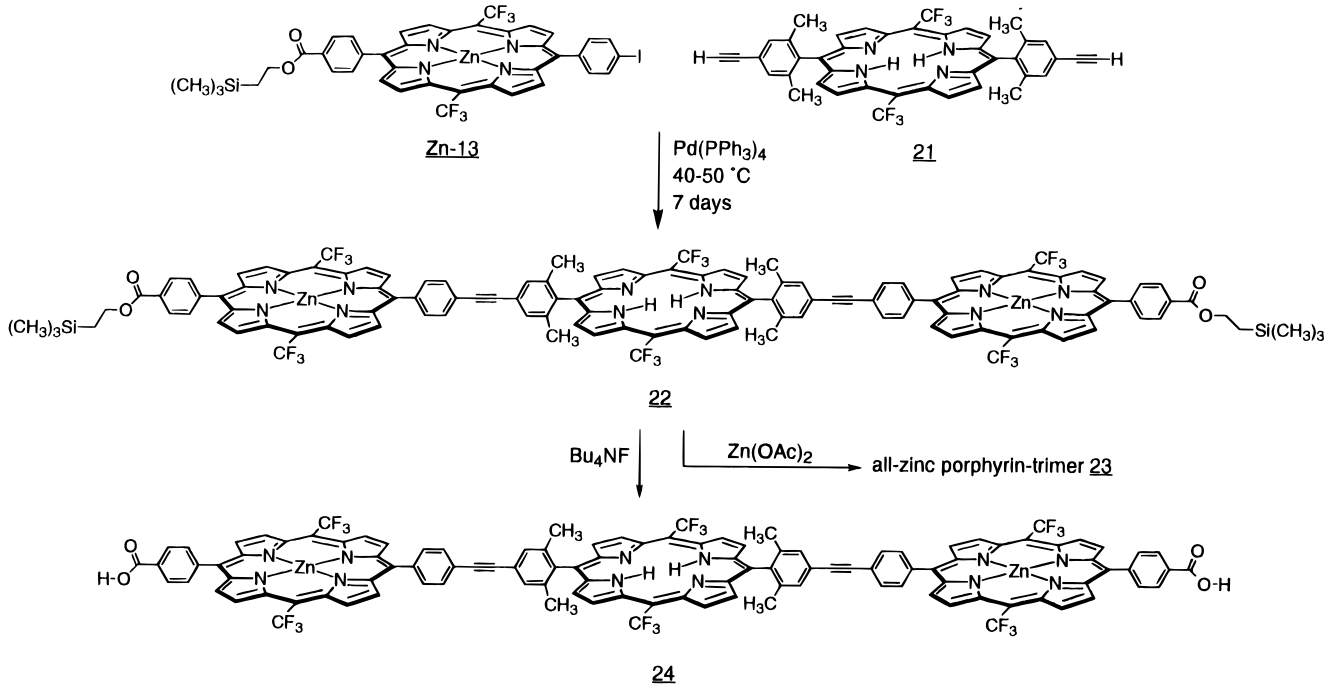
Several experiments were performed to assess the energy transfer properties of these arrays following techniques described previously.[10] The fluorescence emission spectrum of **17** obtained upon illumination at 550

(38) Anderson, H. L. *Tetrahedron Lett.* **1992**, *33*, 1101−1104.

Scheme 4. Building-Block Synthesis of Porphyrin Dimers



Scheme 5. Building-Block Synthesis of Porphyrin Trimers



nm, a wavelength where the zinc porphyrin absorbs 1.3 times that of the free base, is dominated by emission from the free base porphyrin (Figure 4). Integration of the zinc porphyrin emission, assuming the same relative (0,0) and (0,1) peak intensities as in **Zn-10**, gives $\Phi_f = 0.0056$ for the zinc porphyrin component, a decrease of 21-fold compared with **Zn-10** (Table 2). However, a precise determination of the residual zinc porphyrin fluorescence is difficult due to the overlapping spectra of zinc and free base porphyrins. Illumination at 648 nm, where only the free base porphyrin absorbs, gives the free base emission spectrum with $\Phi_f = 0.052$, a value close to that of **3**. These data indicate strong quenching of the zinc porphyrin but little if any quenching of the free base porphyrin. Illumination at the Soret λ_{max} (423 nm) gave an identical emission spectrum composed of 93.6% free base and 6.4% zinc−porphyrin emission. The excitation spectrum (λ_{em} 720 nm) of **17** is nearly identical to the absorption

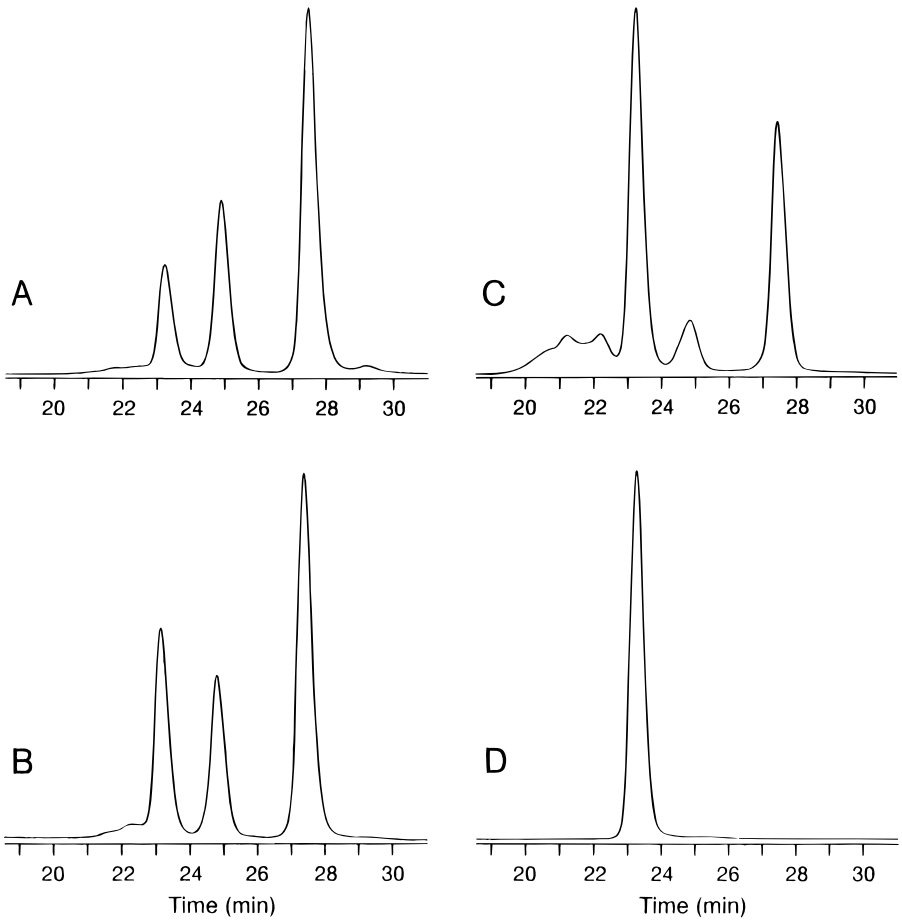


Figure 3. Trimer **22** formation monitored by analytical SEC (420 nm). No corrections have been made for differing molar absorptivities of the various porphyrin components (monomer, dimer, trimer, etc.). (A) Analysis after 1 day shows the porphyrin monomers and two distinct peaks at 23.3 and 24.9 min consistent with trimer and dimer, respectively. (B) Reaction mixture at 3 days shows the trimer peak was still increasing. (C) Reaction mixture at 7 days shows decreased dimer peak. (D) Purified trimer **22**.

spectrum (Figure 4). The close spectral matching indicates that absorption of light by the zinc porphyrin contributes to free base porphyrin emission with nearly the same efficiency as does direct absorption by the free base porphyrin.[39] These data are consistent with a very high yield of energy transfer (>90%). Trimer **22**, which has a free base porphyrin with two neighboring zinc porphyrins, also exhibited nearly identical absorption and emission features, indicating a high yield (>90%) of energy transfer. Time-resolved measurements of other diphenylethyne-linked zinc−free base porphyrin dimers indicated an energy transfer yield of 99%.[10] A more precise estimate of the energy transfer yields in these arrays also requires time-resolved spectroscopic measurements.

III. Solubilities of Porphyrins and Amphipathic Arrays. The *trans*-substituted porphyrins exhibit solubility comparable to that of TPP in organic solvents such as CH_2Cl_2 or $CHCl_3$. The hydrophobic arrays were reasonably soluble in the reaction solvent toluene/triethylamine 5:1 (dimer **17**, 4 mg/mL, 2.77 mM; trimer **22**, 2 mg/mL, 0.9 mM). The hydrophobic or amphipathic arrays (**17**, **20**, **22**, **24**) were soluble at the 2 mM level in DMF for deprotection reactions (4 mg/mL, 2.7 mM), and 10 mg of dimer diacid **19** was derivatized in 1 mL of DMF (7.3 mM). Purification was achieved readily by column chromatography in toluene/$CHCl_3$ on silica (**17**) or size exclusion chromatography in THF (**22**). The dimer **17** is moderately soluble in toluene or $CHCl_3$ (sufficient for absorption and fluorescence but insufficient for NMR studies) and poorly soluble in CH_2Cl_2 (color of solution was visible but most material remained insoluble). The trimers **22** and **23** have solubility >1−2 mg/mL in organic solvents such as toluene, CH_2Cl_2, or $CHCl_3$ and are more soluble than the dimers (**17**, **18**). The amphipathic dimers (**19**, **20**) and trimer (**24**) were soluble in THF containing a few percent methanol or $CHCl_3$ containing a few percent DMF.

The amphipathic porphyrin arrays **19**, **20**, and **24** were incorporated into L-α-phosphatidylcholine vesicles by sonication in aqueous tris(hydroxymethyl)aminomethane hydrochloride (pH 7.5) containing L-α-phosphatidylcholine following a standard procedure.[40] The turbid samples were then passed over a Sephadex G-75 column. No porphyrin was retained at the top of the Sephadex column upon elution with 20 mM aqueous tris(hydroxymethyl)aminomethane hydrochloride, indicating the porphyrin arrays were incorporated into vesicles. The absorption spectra of the vesicle solutions of **20** and **24** had the same intensity patterns as the solution spectra but the Soret bands were broadened. The fluorescence spectrum of **19** incorporated in the vesicles was identical

(39) Stryer, L.; Haugland, R. P. *Proc. Natl. Acad. Sci. U.S.A.* **1967**, *58*, 719−726.

(40) Mihara, H.; Kanmera, T.; Yoshida, M.; Lee, S.; Aoyagi, H.; Kato, T.; Izumiya, N. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 697−706.

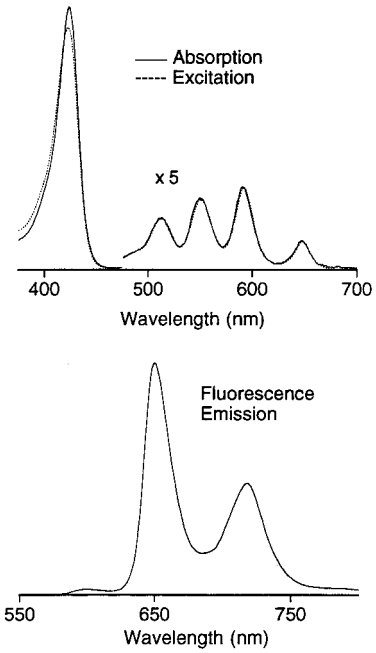


Figure 4. Spectral properties of **17** in toluene at room temperature. The absorption and excitation spectra (λ_{em} 720 nm), normalized at 648 nm, nearly match identically at all wavelengths. The fluorescence emission spectrum (λ_{ex} 548 nm) is dominated by emission from the free base porphyrin.

Table 2. Fluorescence Yields of Porphyrins[a]

compd	λ_{ex}, nm	Φ_f
TPP	548	0.11[b]
porphyrin **3**	548	0.044
porphyrin **21**	548	0.050
porphyrin **7**	548	0.044
ZnTPP	550	0.03[b]
Zn-**3**	550	0.087
Zn-**10**	550	0.093
Zn−H_2 dimer **17**	648	0.052 (free base component)
	550	0.0056 (zinc component)
Zn−H_2−Zn trimer **22**	648	0.052 (free base component)
	550	0.006 (zinc component)
Zn−Zn−Zn trimer **23**	550	0.096 (zinc component)

[a] Fluorescence yields obtained in toluene at room temperature. [b] Literature values.[35]

to the solution spectrum. The photochemical processes of these arrays in supramolecular assemblies can now be examined in a systematic manner.

Summary and Conclusions

Trans-substituted porphyrin building blocks bearing two *meso*-perfluoroalkyl substituents are readily prepared using the *meso*-(perfluoroalkyl)dipyrromethane and the prefunctionalized benzaldehyde via the room temperature synthesis of porphyrins. The mild Pd(0)-catalyzed homogeneous coupling of *trans*-substituted porphyrins bearing iodo or ethynyl groups provides a straightforward route to linear amphipathic dimers and trimers. The dimers and trimers have relatively rigid spacers, good solubility in organic solvents, and modifiable end groups. The amphipathic dimer and trimer formed stable vesicles with L-α-phosphatidylcholine. The dimer **17** and trimer **22** exhibited efficient electronic energy transfer from the zinc to free base porphyrin. This building-block synthetic strategy should also prove useful for the systematic construction of longer linear arrays of porphyrins having amphipathic properties.

Experimental Section

General. Technical grade trifluoroacetaldehyde hydrate (Lancaster, contains varying amounts of the ethyl hemiacetal) and technical grade heptafluorobutyraldehyde hydrate (PCR) were used as received. 4-Iodobenzaldehyde was purchased from Karl Industries, Inc. Other aldehydes were used as received (Aldrich, Lancaster, PCR). Tetrabutylammonium fluoride on silica gel (1.0−1.5 mmol F/g of resin), 4-(dimethylamino)pyridine, and tetrakis(triphenylphosphine)palladium-(0) were purchased from Aldrich and used as received. Pyrrole and triethylamine were distilled from CaH_2. THF and toluene were distilled from lithium aluminum hydride. CH_2Cl_2 (Fisher, reagent grade) and $CHCl_3$ (Fisher, reagent grade) were distilled from K_2CO_3. Stock solutions of $BF_3{\cdot}O(Et)_2$ were prepared by diluting $BF_3{\cdot}O(Et)_2$ (Aldrich, 8.1 M) to 2.5 M in $CHCl_3$ or CH_2Cl_2. For yield determinations of small quantities of porphyrins, a solution of the porphyrin was passed through a 0.22 μm Nylon 66 filter (Micron Separations Inc.). Porphyrins were converted to their zinc chelates following the general method described for preparation of **Zn-13**.

^{1}H NMR spectra were collected at 300 MHz (General Electric GN 300NB). Semipreparative centrifugal thin layer chromatography (CTLC) was performed with a Harrison Research Chromatotron Model 7924T. Column chromatography was performed on alumina (Fisher A540, 80−200 mesh). Flash chromatography was performed on Baker flash silica. Analytical SEC was performed on a HP 1090 HPLC using three 5 μm columns (500, 500, 100 Å in series, 30 cm each) with absorption spectral detection (420 nm) and elution with THF (0.8 mL/min).

Routine absorption spectra were collected in CH_2Cl_2/EtOH (3:1) using an HP 8451A absorption spectrometer. Quantitative studies of absorption, emission, and excitation spectra, including measurements of extinction coefficients and emission quantum yields, were determined in toluene. Absorption spectra were collected using a Varian Cary 3 with 0.5 nm band widths and 0.125 nm data intervals. Fluorescence spectra were collected using a Spex Fluoromax with 1 mm slit widths and 1 nm data intervals. Emission spectra were obtained with $A_{\lambda ex}$ ∼0.08−0.1, and excitation spectra were obtained with A_{Soret} ∼0.08−0.1 to minimize internal absorption. Each extinction coefficient is the average of three determinations. Quantum yields were determined using integrated corrected emission spectra and ratioing to TPP (0.11) or ZnTPP (0.03).[35]

Mass spectra of porphyrins and nonpolar porphyrin arrays were determined using ^{252}Cf plasma desorption mass spectrometry.[41] The amphipathic arrays were analyzed by electrospray mass spectrometry in THF/methanol solutions and are so indicated.

***meso*-(Trifluoromethyl)dipyrromethane (1).**[21] Pyrrole (6.71 g, 100 mmol), technical grade trifluoroacetaldehyde hydrate (6.45 g, 50 mmol), and 200 mL of CH_2Cl_2 were placed in a 250 mL one-neck round bottom flask. Trifluoroacetic acid (3.85 mL) was then added. The reaction mixture was stirred overnight at room temperature. The dark red mixture contained a small amount of a red oil. TLC analysis (silica, CH_2Cl_2/hexanes 2:1; iodine chamber detection) showed a small amount of unreacted pyrrole (R_f 0.53), **1** (R_f 0.27), several slower-moving components, and red material remaining at the origin. The organic solution was washed with 50 mL of water and 50 mL of 10% $NaHCO_3$, dried (Na_2SO_4), filtered, and concentrated via rotary evaporation to a red oil. Flash chromatography (two silica columns, 6 × 18 cm, CH_2Cl_2/hexanes 2:1) afforded 4.3 g (40% yield) of a white fluffy solid: mp 71−72 °C; ^{1}H NMR ($CDCl_3$) δ 8.08 (bs, 2 H, NH), 6.78−6.76 (m, 2 H), 6.26 (bs, 2 H), 6.23−6.20 (m, 2 H), 4.29 (q, 1 H). Anal. ($C_{10}H_9N_2F_3$) C, H, N.

***meso*-(Heptafluoropropyl)dipyrromethane (2).**[21] The reaction of technical grade heptafluorobutyraldehyde hydrate (12 g, 50 mmol) and pyrrole (6.21 g, 100 mmol) was performed according to the procedure for the preparation of **1**. Flash chromatography (silica, CH_2Cl_2/hexanes 1:1, 2 columns, 6 ×

(41) Lindsey, J. S.; Chaudhary, T.; Chait, B. T. *Anal. Chem.* **1992**, *64*, 2804−2814.

18 cm) yielded 5.5 g (35% yield) of a white solid: mp 74−75 °C; ^{1}H NMR ($CDCl_3$) δ 8.11 (bs, 2 H), 6.77−6.74 (m, 2 H), 6.26 (bs, 2 H), 6.23−6.22 (m, 2 H), 4.94 (t, 1 H). Anal. ($C_{12}H_9N_2F_7$) C, H, N.

5,15-Bis(trifluoromethyl)-10,20-bis(phenyl)porphyrin (3). Samples of **1** (112 mg, 0.5 mmol) and benzaldehyde (51 μL, 0.5 mmol) were dissolved in 100 mL of CH_2Cl_2 at room temperature. Then trifluoroacetic acid (385 μL, 5×10^{-2} M) was added to initiate the condensation. After the solution was stirred at room temperature for 15 h, a sample of DDQ (170 mg, 0.75 mmol) was added to convert the porphyrinogen to the porphyrin. The oxidation was allowed to proceed with stirring for 1 h at room temperature. Then 1 equiv of triethylamine was added to neutralize the acid. The mixture was rotary evaporated to dryness. TLC analysis (silica, CH_2Cl_2:hexanes 2:1) showed no benzaldehyde, the porphyrin (R_f 0.8), and black material at the origin. Flash chromatography (silica, 2.5 × 20 cm, CH_2Cl_2) gave the porphyrin as the first-eluting component (75 mg, 50%): ^{1}H NMR ($CDCl_3$) δ 9.62−9.58 (m, 4 H), 8.91 (d, 4 H, J = 5.1 Hz), 8.16−8.14 (m, 4 H), 7.87−7.78 (m, 4 H), 7.77−7.75 (m, 2 H), −2.64 (bs, 2 H); λ_{abs} 410 (fwhm = 23 nm), 508, 542, 586, 644 nm; λ_{em} 650, 720 nm. $C_{34}H_{20}F_6N_4$, calcd mass 598.1, obsd 598.2. λ_{abs} (toluene; ϵ in M^{-1} cm^{-1}) 414 (165 000; fwhm 27 nm), 511 (10 100), 546 (10 100), 592 (5270), 647 (7690); Φ_f (λ_{ex} 548 or 591 nm) = 0.044. **Zn-3**: λ_{abs} (toluene; ϵ in M^{-1} cm^{-1}) 419 (214 000; fwhm 18 nm), 550 (8900), 591 (17 600) nm; Φ_f (λ_{ex} 550 nm) = 0.087.

Porphyrins **4**−**9** were prepared following the method described for **3**.

5,15-Bis(trifluoromethyl)-10,20-bis(4-iodophenyl)porphyrin (4). Samples of **1** (112 mg, 0.5 mmol) and 4-iodobenzaldehyde (116 mg, 0.5 mmol) were condensed in 100 mL of CH_2Cl_2 at room temperature with TFA (385 μL, 5×10^{-2} M). After 15 h DDQ (170 mg, 0.75 mmol) was added. TLC analysis (silica, CH_2Cl_2:hexanes 1:1) showed the porphyrin (R_f 0.65) and a small amount of an unknown green pigment (R_f 0.3). Chromatography on alumina (CH_2Cl_2/hexanes 1:1 steadily enriched with CH_2Cl_2) afforded 119 mg of porphyrin (56%). This reaction was scaled-up linearly to the 500 mL scale, affording 396 mg of porphyrin (37%): ^{1}H NMR ($CDCl_3$) δ 9.63−9.60 (m, 4 H), 8.89 (d, 4 H, J = 5.1 Hz), 8.13 (AA′BB′, 4 H), 7.87 (AA′BB′, 4 H), −2.72 (bs, 2 H); λ_{abs} 412 (fwhm 25 nm), 510, 548, 588, 644 nm; λ_{em} 650, 720 nm. $C_{34}H_{18}F_6N_4I_2$, calcd mass 849.9, obsd 850.2.

5,15-Bis(trifluoromethyl)-10,20-bis[4-(methoxycarbonyl)phenyl]porphyrin (5). Samples of **1** (214 mg, 1 mmol) and methyl *p*-formylbenzoate (164 mg, 1 mmol) were condensed in 100 mL of CH_2Cl_2 at room temperature with BF_3·O(Et)$_2$ (132 μL of a 2.5 M solution in CH_2Cl_2, 3.3 mM). After 4 h DDQ (340 mg, 1.5 mmol) was added to the orange mixture which contained some white precipitates. Flash chromatography (silica, CH_2Cl_2) afforded 136 mg of porphyrin (38%): ^{1}H NMR ($CDCl_3$) δ 9.63−9.61 (m, 4 H), 8.84 (d, 4 H, J = 5.1 Hz), 8.47 (AA′BB′, 4 H), 8.23 (AA′BB′, 4 H), 4.14 (s, 6 H) −2.68 (bs, 2 H); λ_{abs} 412 (fwhm = 25 nm), 510, 548, 588, 644 nm; λ_{em} 650, 720 nm. $C_{38}H_{24}F_6N_4O_4$, calcd mass 714.1, obsd 714.2.

5,15-Bis(trifluoromethyl)-10,20-bis(mesityl)porphyrin (6). Samples of **1** (214 mg, 1 mmol) and mesitaldehyde (147 μL, 1 mmol) were condensed at room temperature in 100 mL of $CHCl_3$ with BF_3·O(Et)$_2$ (3.3 mM, 132 μL of 2.5 M stock solution). After 8 h DDQ (340 mg, 1.5 mmol) was added. TLC analysis (silica, hexanes/CH_2Cl_2 2:1) showed the porphyrin (R_f 0.7) and a large amount of an unknown green pigment (R_f 0.3). Flash chromatography (silica, hexanes/CH_2Cl_2 4:1) gave the porphyrin and the slower moving pigment green pigment. Final purification by CTLC (2 mm silica rotor hexanes/CH_2Cl_2 2:1) afforded 76 mg of porphyrin (22%): ^{1}H NMR ($CDCl_3$) δ 9.59−9.57 (m, 4 H), 8.83 (d, 4 H, J = 4.8 Hz), 7.33 (s, 4 H), 2.67 (s, 6 H), 1.82 (s, 12 H); λ_{abs} 410 (fwhm 21 nm), 510, 546, 590, 646 nm; λ_{em} 650, 720 nm. $C_{40}H_{32}F_6N_4$, calcd mass 682.2, obsd 682.4.

5,15-Bis(trifluoromethyl)-10,20-bis[2,6-dimethyl-4-(2-(trimethylsilyl)ethynyl)phenyl]porphyrin (7). Samples of **1** (214 mg, 1 mmol) and 2,6-dimethyl-4-(2-(trimethylsilyl)-ethynyl)benzaldehyde[7] (230 mg, 1 mmol) were condensed at room temperature in 100 mL of $CHCl_3$ with BF_3·O(Et)$_2$ (3.3 mM, 132 μL of 2.5 M stock solution). After 8 h DDQ (340 mg, 1.5 mmol) was added. TLC analysis (silica, hexanes/CH_2Cl_2 4:1) showed the porphyrin (R_f 0.8) and a large amount of an unknown green pigment (R_f 0.4). Flash chromatography (silica, hexanes/CH_2Cl_2 4:1) afforded 200 mg of the green pigment[29] and 54 mg of porphyrin (13%). This reaction was scaled-up to the 500 mL scale, affording 190 mg of porphyrin (9%): ^{1}H NMR ($CDCl_3$) δ 9.58 (m, 4 H), 8.75 (d, 4 H, J = 4.8 Hz), 7.66 (s, 4 H), 1.81 (s, 12 H), 0.39 (s, 18 H), −2.59 (bs, 2 H); λ_{abs} 414 (fwhm 23 nm), 510, 546, 592, 644 nm; λ_{em} 650, 720 nm. $C_{48}H_{44}F_6N_4Si_2$, calcd mass 846.3, obsd 846.5. λ_{abs} (toluene; ϵ in M^{-1} cm^{-1}) 416 (181 500), 512 (13 700), 545 (11 500), 591 (4590), 646 (10 800); Φ_f (λ_{ex} 548 or 591 nm) = 0.044.

5,15-Bis(trifluoromethyl)-10,20-bis(benzoyl)porphyrin (8). Samples of **1** (214 mg, 1 mmol) and phenylglyoxal monohydrate (152 mg, 1 mmol) were condensed at room temperature in 100 mL of CH_2Cl_2 with BF_3·O(Et)$_2$ (3.3 mM, 132 μL of 2.5 M stock solution). Phenylglyoxal reacts very rapidly in symmetric pyrrole−aldehyde condensations.[7] After 15 min DDQ (340 mg, 1.5 mmol) was added. Flash chromatography (silica, CH_2Cl_2) afforded 44 mg of porphyrin (14%): ^{1}H NMR ($CDCl_3$) δ 9.68−9.65 (m, 4 H), 9.18 (d, 4 H, J = 5.1 Hz), 7.91−7.89 (m, 4 H), 7.68, 7.62 (m, 2 H), 7.47−7.42 (m, 4 H), −2.61 (bs, 2 H); λ_{abs} 410 (fwhm 26 nm), 508, 542, 586, 640 nm; λ_{em} 650, 720 nm. $C_{36}H_{20}F_6N_4O_2$, calcd mass 654.1, obsd 654.2.

5,15-Bis(heptafluoropropyl)-10,20-bis(4-iodophenyl)-porphyrin (9). Samples of **2** (157 mg, 0.5 mmol) and 4-iodobenzaldehyde (116 mg, 0.5 mmol) were condensed in 100 mL of CH_2Cl_2 at room temperature with TFA (385 μL, 5×10^{-2} M). After 2 h DDQ (170 mg, 0.75 mmol) was added. TLC analysis (silica, hexanes/CH_2Cl_2 2:1) showed the porphyrin (R_f 0.7) and a small amount of an unknown green pigment (R_f 0.3). Flash chromatography (silica, CH_2Cl_2, 6 × 10 cm) afforded the porphyrin and the green pigment. Chromatography on alumina (hexanes/CH_2Cl_2 4:1, 3 × 10 cm) afforded 94 mg of porphyrin (36%): ^{1}H NMR ($CDCl_3$) δ 9.49, 9.46 (m, 4 H), 8.91 (d, 4 H, J = 5.1 Hz), 8.13 (AA′BB′, 4 H), 7.90 (AA′BB′, 4 H), −2.59 (bs, 2 H); λ_{abs} 412 (fwhm 26 nm), 510, 548, 588, 644 nm; λ_{em} 650, 720 nm. $C_{38}H_{18}F_{14}N_4I_2$, calcd avg mass 1050.4, obsd 1050.8.

5,15-Bis(trifluoromethyl)-10-[4-(2-(trimethylsilyl)ethynyl)phenyl]-20-[4-((2-(trimethylsilyl)ethoxy)carbonyl)-phenyl]porphyrin (10). Samples of **1** (428 mg, 2 mmol), 4-(2-(trimethylsilyl)ethynyl)benzaldehyde[31] (202 mg, 1 mmol), and 2-(trimethylsilyl)ethyl 4-formylbenzoate[7] (250 mg, 1 mmol) were dissolved in 400 mL of CH_2Cl_2 at room temperature. Then TFA (1.54 mL, 20 mmol, 5×10^{-2} M) was added to initiate the condensation. After the solution was stirred for 16 h at room temperature, DDQ (680 mg, 3 mmol) was added to convert the porphyrinogen to the porphyrin. The oxidation was allowed to proceed for 1 h at room temperature. Then 1 equiv of triethylamine was added to neutralize the acid. The mixture was concentrated via rotary evaporation to a dark syrup and chromatographed on silica (2.0 × 25 cm, CH_2Cl_2) to separate the three porphyrin components from the non-porphyrin species. Final separation by column chromatography (silica, 2.0 × 25 cm, hexanes/CH_2Cl_2 2:1 and hexanes/CH_2Cl_2 1:1) gave 68 mg (8.6%) of the bis-ethynyl porphyrin **11**, 70 mg (7.9%) of the bis-ester porphyrin **12**, and 128 mg (15.3%) of **10**: ^{1}H NMR ($CDCl_3$) δ 9.62−9.60 (m, 4 H, β-pyrrole), 8.87 (d, 2 H, J = 5.1 Hz), 8.84 (d, 2 H, J = 5.1 Hz), 8.46 (AA′BB′, 2 H), 8.22 (AA′BB′, 2 H), 8.09 (AA′BB′, 2 H), 7.90 (AA′BB′, 2 H), 4.64 (t, 2 H, J = 8.4 Hz), 1.32 (t, 2 H, J = 8.4 Hz), 0.40 (s, 9 H), 0.20 (s, 9 H), −2.69 (bs, 2 H); λ_{abs} (toluene, ϵ in M^{-1} cm^{-1}) 416 (186 000), 512 (13 200), 548 (10 500), 594 (5750), 646 (9330); λ_{em} 650, 719 nm. $C_{45}H_{40}F_6N_4Si_2O_2$ calcd mass 838.2; obsd 838.4. **Zn-10**: λ_{abs} (toluene, ϵ in M^{-1} cm^{-1}) 420 (234 000), 550 (11 200), 591 (18 300); λ_{em} 599, 653 nm; Φ_f = 0.093.

5,15-Bis(trifluoromethyl)-10,20-bis[4-(2-(trimethylsilyl)ethynyl)phenyl]porphyrin (11): isolated from the mixed condensation; ^{1}H NMR ($CDCl_3$) δ 9.60−9.57 (m, 4 H), 8.85 (d, 4 H, J = 5.1 Hz), 8.07 (m, 4 H), 7.89 (m, 4 H), 0.40 (s, 18 H),

−2.70 (bs, 2 H); λ_{abs} 416, 512, 548, 592, 646 nm; λ_{em} 650, 718 nm $C_{44}H_{36}F_6N_4Si_2$ calcd 790.2, obsd 790.4.

5,15-Bis(trifluoromethyl)-10,20-bis[4-((2-(trimethylsilyl)ethoxy)carbonyl)phenyl]porphyrin (12): isolated from the mixed condensation; ^{1}H NMR ($CDCl_3$) δ 9.64−9.61 (m, 4 H), 8.86 (d, 4 H, J = 5.1 Hz), 8.47 (AA′BB′, 4 H), 8.24 (AA′BB′, 4 H), 4.64 (t, 4 H, J = 8.4 Hz), 1.32 (t, 4 H, J = 8.7 Hz), 0.20 (s, 18 H), −2.68 (bs, 2 H); λ_{abs} 416, 512, 546, 592, 646 nm; λ_{em} 649, 718 nm. $C_{46}H_{44}F_6N_4Si_2O_4$ calcd mass 886.3; obsd 886.4. **Zn-12**: λ_{abs} 420, 550, 591 nm; λ_{em} 600, 655 nm. $C_{46}H_{42}F_6N_4Si_2O_4Zn$ calcd mass 948.2, obsd 948.1.

Porphyrins **13**−**15** were prepared following the method described for **10**.

5,15-Bis(trifluoromethyl)-10-(4-iodophenyl)-20-[4-((2-(trimethylsilyl)ethoxy)carbonyl)phenyl]porphyrin (13). Samples of **1** (428 mg, 2 mmol), 4-iodobenzaldehyde (232 mg, 1 mmol), and 2-(trimethylsilyl)ethyl 4-formylbenzoate[7] (250 mg, 1 mmol) were condensed in CH_2Cl_2 (400 mL) at room temperature with TFA (1.54 mL, 20 mmol, 5×10^{-2} M). After 16 h DDQ (680 mg, 3 mmol) was added. Chromatography on silica (2.0 × 25 cm, CH_2Cl_2) separated the three porphyrin components from the non-porphyrin species. A second column (silica, 2.0 × 25 cm, hexanes/CH_2Cl_2 2:1 and hexanes/CH_2Cl_2 1:1) gave 78 mg of **4** (9.2%), 150 mg of **13** (17.3%), and 72 mg of the bis-ester porphyrin **12** (8.1%). **13:** ^{1}H NMR ($CDCl_3$) δ 9.63−9.61 (m, 4 H), 8.90 (d, 2 H, J = 5.1 Hz), 8.85 (d, 2 H, J = 5.1 Hz), 8.46 (AA′BB′, 2 H), 8.23 (AA′BB′, 2 H), 8.14 (AA′BB′, 2 H), 7.89 (AA′BB′, 2 H), 4.64 (t, 2 H, J = 8.4 Hz), 1.32 (t, 4 H, J = 8.7 Hz), 0.20 (s, 9 H), −2.70 (bs, 2 H); λ_{abs} 416, 512, 548, 592, 646 nm; λ_{em} 650, 718 nm. $C_{40}H_{31}F_6N_4SiIO_2$ calcd mass 868.1; obsd 868.7.

Zn-13. A solution of the free base porphyrin **13** (104 mg, 0.12 mmol) in 25 mL of CH_2Cl_2 was treated with a solution of zinc acetate dihydrate (40 mg, 0.18 mmol) in 2 mL of methanol at room temperature. Zinc insertion was judged to be quantitative after 3 h by fluorescence excitation spectroscopy. Column chromatography (silica, hexanes/CH_2Cl_2 1:1) gave 112 mg (100%) of the zinc chelate. λ_{abs} 420, 550, 591 nm; λ_{em} 599, 652 nm. $C_{40}H_{29}F_6N_4SiIO_2Zn$ calcd mass 930.0; obsd 930.2.

5,15-Bis(trifluoromethyl)-10-(4-iodophenyl)-20-[4-(methoxycarbonyl)phenyl]porphyrin (14). Samples of **1** (214 mg, 1.0 mmol), 4-iodobenzaldehyde (116 mg, 0.5 mmol), and methyl *p*-formylbenzoate (82 mg, 0.5 mmol) were condensed in 200 mL of CH_2Cl_2 at room temperature with TFA (770 μL, 5×10^{-2} M). After 15 h DDQ (340 mg, 1.5 mmol) was added. Flash chromatography (silica, CH_2Cl_2/hexanes 2:1 steadily enriched with CH_2Cl_2) afforded the porphyrins (50 mg). Semipreparative centrifugal TLC (1 mm silica rotor, CH_2Cl_2/hexanes 1:1) gave porphyrins **4** (7.3 mg, 1.7%), **14** (20 mg, 5.1%), and **5** (8 mg, 2.2%) which were easily separated due to their polarity differences (TLC R_f 0.9, 0.4, 0.1, respectively; silica CH_2Cl_2/hexanes 2:1). **14:** ^{1}H NMR ($CDCl_3$) δ 9.63−9.61 (m, 4 H), 8.90 (d, 2 H, J = 5.1 Hz), 8.84 (d, 2 H, J = 5.1 Hz), 8.47 (AA′BB′, 2 H), 8.23 (AA′BB′, 2 H), 8.13 (AA′BB′, 2 H), 7.88 (AA′BB′, 2 H), 4.1 (s, 3 H), −2.70 (bs, 2 H); λ_{abs} 412 (fwhm 31 nm), 510, 546, 590, 644 nm. $C_{36}H_{21}F_6N_4IO_2$, calcd mass 782.1, obsd 782.1.

5,15-Bis(trifluoromethyl)-10-[2,6-dimethyl-4-(2-(trimethylsilyl)ethynyl)phenyl]-20-[4-(methoxycarbonyl)-phenyl]porphyrin (15). Samples of **1** (214 mg, 1 mmol), 2,6-dimethyl-4-(2-(trimethylsilyl)ethynyl)benzaldehyde[7] (115 mg, 0.5 mmol), and methyl *p*-formylbenzoate (82 mg, 0.5 mmol) were condensed in 100 mL of $CHCl_3$ at room temperature with $BF_3{\cdot}O(Et)_2$ (132 μL of 2.5 M solution in $CHCl_3$ 3.3×10^{-3} M). After 3 h DDQ (340 mg, 1.5 mmol) was added. Flash chromatography (silica, CH_2Cl_2/hexanes 2:1 steadily enriched with CH_2Cl_2) gave the porphyrins. Semipreparative centrifugal TLC (1 mm silica rotor, CH_2Cl_2/hexanes 1:1) gave porphyrins **7** (31 mg, 7.3%), **15** (41 mg, 10.5%), and **5** (19 mg, 5.3%) which were easily separated due to their polarity differences (TLC R_f 1, 0.5, 0.1, respectively; silica CH_2Cl_2/hexanes 2:1). **15:** ^{1}H NMR ($CDCl_3$) δ 9.61−9.57 (m, 4 H), 8.84 (d, 2 H, J = 5.1 Hz), 8.76 (d, 2 H, J = 5.1 Hz), 8.47 (AA′BB′, 2 H), 8.23 (AA′BB′, 2 H), 7.66 (s, 2 H), 4.14 (s, 3 H), 1.81 (s, 12 H), 0.39 (s, 18 H), −2.59 (bs, 2 H); λ_{abs} 412 (fwhm 25 nm), 510, 544, 590, 644 nm. $C_{43}H_{34}F_6N_4SiO_2$, calcd mass 780.2, obsd 780.5.

5,15-Bis(trifluoromethyl)-10-(4-ethynylphenyl)-20-[4-((2-(trimethylsilyl)ethoxy)carbonyl)phenyl]porphyrin (16). A sample of porphyrin **10** (101 mg, 0.12 mmol) was dissolved in 5 mL of THF at room temperature. Then tetrabutylammonium fluoride on silica gel (240 mg of 1−1.5 mmol F/g resin) was added quickly, and the mixture was stirred at room temperature for 1 h. The reaction was monitored by TLC and terminated by the addition of water. The resulting solution was washed with 30 mL of CH_2Cl_2. The organic layer was separated, washed with H_2O (3 × 30 mL), dried (Na_2SO_4), and concentrated to dryness. TLC analysis (silica, hexanes/CH_2Cl_2, 1:1) showed three porphyrin components. The product mixture was dissolved in CH_2Cl_2, and the three porphyrins were separated via column chromatography (silica, 2.0 × 25 cm, hexanes/CH_2Cl_2 2:1, $CHCl_3$/methanol/acetic acid, 90:10:2 to elute the fully deprotected porphyrin). The products isolated include a trace of starting material, 16 mg (20%) of 5,15-bis(trifluoromethyl)-10-(4-ethynylphenyl)-20-(4-carboxyphenyl)porphyrin, and 61 mg (67%) of **16**: ^{1}H NMR ($CDCl_3$) δ 9.61−9.59 (m, 4 H), 8.87 (d, 2 H, J = 5.1 Hz), 8.83 (d, 2 H, J = 5.1 Hz), 8.45 (AA′BB′, 2 H), 8.22 (AA′BB′, 2 H), 8.10 (AA′BB′, 2 H), 7.91 (AA′BB′, 2 H), 4.62 (t, 2 H, J = 8.4 Hz), 1.30 (t, 2 H, J = 8.4 Hz), 0.18 (s, 9 H), −2.71 (bs, 2 H); λ_{abs} 416, 512, 548, 592, 646 nm; λ_{em} 650, 718 nm. $C_{42}H_{32}F_6N_4SiO_2$ calcd mass 766.2; obsd 766.1.

Zn−Free Base Porphyrin Dimer 17. The porphyrin monomers **Zn-13** (65 mg, 0.07 mmol) and **16** (54 mg, 0.07 mmol) were dissolved in 18 mL of toluene/triethylamine 5:1. The solution was deaerated with Ar for 15 min. The coupling reaction was initiated at this point by the addition of a catalytic amount of $(PPh_3)_4Pd(0)$ (7 mg, 7 μmol). The reaction mixture was gently stirred at 40−50 °C. The progress of the condensation was monitored by TLC (silica, $CHCl_3$), which showed four sharp spots assigned to (low to high R_f) **Zn-13**, desired dimer **17** (R_f 0.3), homocoupled butadiynyl dimer (R_f 0.6), and **16**. After 4 days the starting material **16** had disappeared; thus the reaction mixture was worked up. The reaction mixture was diluted with 40 mL of $CHCl_3$, washed with H_2O (2 × 40 mL), dried (Na_2SO_4), and concentrated to a small volume. Column chromatography (silica, 2 × 25 cm, toluene/$CHCl_3$ 1:1) gave 78 mg (71%) of **17**: ^{1}H NMR (THF-d_8) δ 9.8−9.68 (m, 8 H), 9.12 (d, 2 H, J = 5.1 Hz), 9.08 (d, 2 H, J = 5.1 Hz), 8.96 (d, 2 H, J = 5.1 Hz), 8.92 (d, 2 H, J = 5.1 Hz), 8.52−8.45 (m, 4 H), 8.40−8.30 (m, 8 H), 8.22−8.15 (m, 4 H), 4.64 (t, 4 H, J = 8.1 Hz), 1.40−1.30 (m, 6 H), 0.20 (s, 18 H), −2.70 (bs, 2 H); λ_{abs} 424, 512, 550, 590, 646 nm; λ_{em} 600, 650, 719 nm. $C_{82}H_{60}F_{12}N_8Si_2O_4Zn$ calcd avg mass 1571.0; obsd 1572.0.

Zn−Zn Porphyrin Dimer 18. Zinc was inserted into 10 mg of **17**. Purification was achieved via column chromatography (silica, $CHCl_3$/methanol 99:1). **18:** ^{1}H NMR (THF-d_8) δ 9.80, 9.72 (m, 8 H), 9.09 (d, 4 H, J = 6 Hz), 8.95 (d, 4 H, J = 6 Hz), 8.50, 8.48 (m, 4 H), 8.35, 8.30 (m, 8 H), 8.19, 8.16 (m, 4 H), 4.64 (t, 4 H, J = 6 Hz), 1.34 (t, 4 H, J = 6 Hz), 0.2 (s, 18 H); λ_{abs} 424, 552, 590 nm; λ_{em} 601, 654 nm. $C_{82}H_{58}F_{12}N_8Si_2O_4Zn_2$ calcd avg mass 1634.3; obsd 1634.5.

Zn−Free Base Porphyrin Dimer Diacid 19. A sample of dimer **17** (15 mg, 10 μmol) was dissolved in 5 mL of DMF. Tetrabutylammonium fluoride on silica gel (1−1.5 mmol F/g resin, 100 mg, 5 equiv) was added to the solution quickly. The reaction mixture turned dark green in color. After 30 min, the DMF solution was diluted with 30 mL of brine, regenerating the porphyrin color. The aqueous layer was extracted with ethyl acetate (2 × 30 mL). The combined organic extracts were washed with brine (2 × 30 mL) and 50 mL of H_2O and dried (Na_2SO_4), and the solvent was removed by rotary evaporation to give a purple solid. The purple solid was washed with small aliquots of CH_2Cl_2, THF, and methanol. After vacuum desiccation, 12 mg (90%) was obtained. Reverse phase silica (THF/methanol 1:1, R_f = 0.4) and silica ($CHCl_3$/methanol 95:5, R_f = 0.5) showed **19** to be homogeneous: ^{1}H NMR ($CDCl_3$ + DMF-d_7 2:1) δ 9.95−9.47 (m, 8 H), 8.85 (d, 2 H, J = 5.1 Hz), 8.81 (d, 2 H, J = 4.8 Hz), 8.73 (d, 2 H, J = 5.1 Hz), 8.69 (d, 2 H, J = 5.1 Hz), 8.33−8.27 (m, 8 H), 8.09−8.07 (m, 4 H), 7.97−7.94 (m, 4 H), −3.10 (s, 2 H); λ_{abs} 424, 512, 550, 590, 646 nm; λ_{em} 600, 650, 719 nm. $C_{72}H_{36}F_{12}N_8O_4Zn$ calcd avg mass 1370.5; obsd 1371.7; electrospray negative ion m/z 1369.3.

Zn−Free Base Porphyrin Dimer Bis(taurine−triethylamine salt) 20. A sample of dimer **19** (10 mg, 7 μmol) was dissolved in 1 mL of DMF at room temperature. Then 0.5 mL of an aqueous solution containing 9 mg of taurine (0.07 mmol) and 10 μL of triethylamine (0.14 mmol) was added. The reaction mixture was cooled in an ice water bath, and (benzotriazol-1-yloxy)tris(dimethylamino)phosphonium hexafluorophosphate (BOP) (30 mg, 0.07 mmol) and triethylamine (30 μL, 0.41 mmol) were added separately. The reaction mixture was brought to room temperature and stirred overnight. The mixture was chromatographed twice (Baker C_{18}-silica, first column 1.4 × 25 cm; second column 0.6 × 20 cm, ethanol/triethylamine 99:1). The fraction containing the porphyrin was concentrated. Addition of diethyl ether precipitated the product. The solvent was decanted and the product was vacuum desiccated, giving 5 mg (45%): ^{1}H NMR ($CDCl_3$ + DMF-d_7 2:1) δ 9.40−9.30 (m, 8 H), 8.72 (d, 2 H, J = 5.1 Hz), 8.68 (d, 2 H, J = 4.8 Hz), 8.58 (d, 2 H, J = 5.1 Hz), 8.54 (d, 2 H, J = 5.1 Hz), 7.95−7.90 (m, 8 H), 8.88−8.80 (m, 4 H), 7.97−7.94 (m, 4 H), 3.75 (bs, 2 H), 2.95 (t, 4 H, J = 8.0 Hz), 2.70 (s, 18 H), 2.50 (m, 12 H), 1.05 (t, 4 H, J = 8.0 Hz), −2.95 (s, 2 H); λ_{abs} 424, 512, 550, 590, 646 nm; λ_{em} 600, 650, 719 nm. $C_{76}H_{46}F_{12}N_{10}O_8S_2Zn$ (- 2 triethylamines) calcd avg mass 1582.2; obsd electrospray negative ion m/z 1584.1; 790.8.

5,15-Bis(trifluoromethyl)-10,20-bis[2,6-dimethyl-4-ethynylphenyl]porphyrin (21). A sample of porphyrin **7** (190 mg, 0.22 mmol) was dissolved in 100 mL of THF in a 250 mL one-neck round bottom flask at room temperature. Tetrabutylammonium fluoride on silica gel (440 mg, 1−1.5 of mmol F/g resin) was added at once. After 30 min the reaction mixture was rotary evaporated to dryness. The purple solid was dissolved in 100 mL of $CHCl_3$. The solution was washed with 10% $NaHCO_3$ (2 × 50 mL), dried (Na_2SO_4), filtered, and rotary evaporated, affording 141 mg (91%): ^{1}H NMR ($CDCl_3$) δ 9.59 (m, 4 H), 8.77 (d, 4 H, J = 4.8 Hz), 7.67 (s, 4 H), 1.82 (s, 12 H), −2.52 (bs, 2 H); λ_{abs} 414 (fwhm = 23 nm), 510, 546, 592, 644 nm; λ_{em} 650, 720 nm. $C_{42}H_{28}F_6N_4$ calcd 702.2; obsd 702.4. **Zn-21**: zinc was inserted into **21** (141 mg, 0.20 mmol), affording 154 mg (100%). λ_{abs} 420, 546, 592 nm; λ_{em} 600, 660 nm. $C_{42}H_{26}F_6N_4Zn$, calcd mass 764.1, obsd 764.2.

Zn−Free Base−Zn Porphyrin Trimer 22. The Pd(0)-catalyzed ($Pd(PPh_3)_4$, 3 mg, 2.5 μmol) coupling reaction of **21** (18 mg, 0.025 mmol) and **Zn-13** (47 mg, 0.05 mmol) in 12 mL of toluene/triethylamine (5:1) was performed according to the procedure outlined for dimer **17**. The reaction was monitored by gel permeation chromatography. After 3 days of reaction an additional aliquot of catalyst (3 mg, 2.5 μmol) was added. After 7 days total the reaction mixture was worked up. Silica TLC analysis showed four sharp, mobile porphyrins bands and porphyrinic material at the base line. Column chromatography (silica, CH_2Cl_2) afforded four components, the homocoupled dimer, a trace amount of an unknown intermediate, 24 mg of trimer **22** (42%), and unreacted zinc porphyrin. Trace amounts (<2% of the total absorption) of higher-molecular-weight porphyrin materials were detected by SEC; these impurities could not be removed by silica gel chromatography. Passage over a preparative SEC column (THF, 90 × 5.5 cm) afforded the purified trimer: ^{1}H NMR (THF-d_8) δ 9.80−9.70 (m, 12 H), 9.10 (d, 4 H, J = 5.1 Hz), 9.00 (d, 4 H, J = 4.8 Hz), 8.95 (d, 4 H, J = 5.1 Hz), 8.55−8.45 (m, 4 H), 8.38−8.30 (m, 8 H), 8.38−8.30 (m, 4 H), 7.95 (s, 4 H), 4.67 (t, 4 H, J = 8.4 Hz), 2.00 (s, 12 H), 1.35−1.30 (m, 4 H), 0.20 (s, 18 H), −2.30 (bs, 2 H); λ_{abs} (log ϵ) 424 (5.82), 512 (4.34), 548 (4.56), 592 (4.67), 648 (4.13) nm; λ_{em} 599, 649, 718 nm. $C_{122}H_{84}F_{18}N_{12}Si_2O_4Zn_2$ calcd avg mass 2311.0; obsd 2312.4.

Zn−Zn−Zn Porphyrin Trimer 23. Zinc was inserted into 5 mg of **22**. Purification was achieved via column chromatography (silica, $CHCl_3$/methanol 99:1): ^{1}H NMR (THF-d_8) δ 9.80−9.70 (m, 12 H), 9.10 (d, 4 H, J = 4.8 Hz), 8.95 (d, 4 H, J = 5.1 Hz), 8.93 (d, 4 H, J = 5.1 Hz), 8.52−8.48 (m, 4 H), 8.38−8.30 (m, 4 H), 8.18−8.14 (m, 4 H), 7.91 (s, 4 H), 4.65 (t, 4 H, J = 8.4 Hz), 2.00 (s, 12 H), 0.19 (s, 18 H); λ_{abs} 425, 552, 590 nm; λ_{em} 600, 653 nm. $C_{122}H_{82}F_{18}N_{12}Si_2O_4Zn_3$ calcd avg mass 2374.4; obsd 2375.3.

Zn−Free Base−Zn Trimer Diacid 24. The trimer **22** (4.6 mg, 2 μmol) was deprotected by reaction with tetrabutylammonium fluoride (20 mg) in 1 mL of DMF according to the procedure for preparation of **19**. Vacuum desiccation afforded 3.5 mg (78%): ^{1}H NMR ($CDCl_3$ + DMF-d_7) δ 9.92−9.71 (m, 12 H), 8.87 (d, 4 H, J = 5.1 Hz), 8.63 (d, 4 H, J = 4.5 Hz), 8.57 (d, 4 H, J = 4.5 Hz), 8.20−8.06 (m, 4 H), 7.90−7.74 (m, 8 H), 7.71, 7.58 (m, 4 H), 7.44 (s, 4 H), −2.80 (s, 2 H); $C_{112}H_{60}F_{18}N_{12}O_4Zn_2$ calcd avg mass 2110.5; obsd 2113.1; electrospray negative ion m/z 1053.2.

Method for Incorporating Amphipathic Porphyrins into L-α-phosphatidylcholine vesicles.[40] The incorporation of dimer diacid **19** into L-α-phosphatidylcholine vesicles is given as a representative example. A 400 μL solution of L-α-phosphatidylcholine (Sigma, Type V-E, 100 mg of L-α-phosphatidylcholine/mL of $CHCl_3$) was mixed with 200 μL of THF and 1 drop of methanol in a pear-shaped flask. To this was added 2 mL of a $CHCl_3$ solution of **19**. Argon was then passed over the solution to evaporate the volatile solvents and deposit the nonvolatile material as a thick film on the wall of the flask. The viscous material was then diluted with 5 mL of 20 mM tris(hydroxymethyl)aminomethane hydrochloride (pH 7.5). The turbid mixture was then sonicated with a Branson Sonifier 450 at 20 °C (3 × 10 min). The vesicle solutions were passed through a column of Sephadex G-75 (1 × 20 cm, 20 mM tris(hydroxymethyl)aminomethane hydrochloride, pH 7.5). The porphyrin color moved with the vesicle fraction, and no porphyrin color remained at the top of the column after being washed with the buffer. The absorption spectrum of the **19**/vesicle fraction appeared the same as the solution spectrum except for the broadened Soret and the non-zero base line. The fluorescence emission spectrum of the **19**/vesicle fraction appeared the same as the solution spectrum.

Similar vesicle incorporation experiments were performed with **20** and **24**. No porphyrin color was visible at the top of the column during chromatography on Sephadex G-75. The absorption spectra of the vesicle solutions of **20** and **24** appeared as the solution spectra except that the Soret was broadened and a non-zero base line was observed in both cases.

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Supporting Information Available: ^{1}H NMR spectra of **3**−**24** (25 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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