

Dendrimer Porphyrins and Phthalocyanines

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1. Introduction

The development of dendrimer porphyrins has been inspired and prompted by many interesting functions of porphyrin derivatives in biological systems. Natural porphyrin derivatives, including hemes, chlorophylls, and bacteriochlorophylls, are integrated into protein scaffolds that are essential for their biological activities.¹ For example, the protein matrices of hemoproteins provide active centers with a special hydrophobic pocket having a specific steric hindrance. In the case of hemoglobin and myoglobin, the embedded active iron centers are protected sterically and hydrophobically against irreversible oxidation, thereby enabling reversible O₂-binding to take place.² In the light-harvesting complexes of purple bacteria, wheel-like supramolecular assemblies of many bacteriochlorophyll units are also realized with the assistance of proteins; they play an important role in the efficient capturing of energy from sunlight and transferring it to the photosynthetic reaction center.^{3–6} Because of their morphological similarities to proteins, three-dimensional dendrimer architectures can act as attractive scaffolds for the site-specific positioning of porphyrin functionalities in nanoscale size regimes.

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Dendrimers are characterized as regularly branched, three-dimensional architectures with various properties that can be tailored and controlled, such as the size and shape of the molecule and the position of functional groups either in the core of the molecule, in the branching units, and/or on the exterior surface.^{7,8} Dendrimer porphyrins were first reported in 1993 by one of the present authors: a porphyrin unit was integrated into the center of a poly(benzyl ether) dendrimer (**1_n·2H**) to form a synthetic model of a hemoprotein (Chart 1).⁹ Half of a year later, Diederich et al. reported the synthesis and redox properties of poly(ether-amide) dendrimer porphyrins **2_n·Zn** (Chart 2).¹⁰ In 1996, Suslick et al. studied the action of manganese porphyrin-cored poly(aryl ester) dendrimers for oxidation.¹¹ After the publication of such pioneering works, dendrimer porphyrins began to attract considerable attention. The main purpose of this review Article is to highlight some of the unique structural and functional aspects of dendrimer porphyrins in relation to the biological activities of hemoproteins and photosynthetic systems, as well as in the context of host–guest chemistry, self-assembly, materials sciences, and biomedical applications. Although this Article may feature some studies that have already been highlighted in other reviews and books,^{12–18} they are included again to discuss the structure–property–function relationships of dendrimer porphyrins, which could provide a guiding principle for the rational molecular design of functional molecules and materials on the nanometer scale. Because phthalocyanines have molecular structures and properties similar to those of porphyrins, dendrimer phthalocyanines are also included in this review.^{19–21}

2. Synthetic Strategies and Structural Variations

Unique features of the step-by-step iterative synthesis of dendrimers allow porphyrin or phthalocyanine functionalities to be precisely positioned in their nanoscopic three-dimensional architectures, as illustrated in Figure 1.

Most porphyrin-cored dendrimers thus far reported have been synthesized by the introduction of dendritic substituents at the *meso*-positions of a porphyrin macrocycle (Figure 2A). The synthetic strategies that are used (Scheme 1) follow either a divergent (route 1) or a convergent approach (routes 2 and 3). The divergent route was first used by Diederich and co-workers to grow a poly(ether-amide) dendrimer from a porphyrin core (**2_n·Zn**)¹⁰ and was later applied to the synthesis of dendrimer porphyrins bearing dendritic wedges of glutamate (**56** and **59**),^{22,23} 2,2-bis(methylol) propanoate,^{24–26} and β-D-glucopyranose.²⁷ The divergent synthetic approach may often suffer from the disadvantage that the final products contain structural defects. This problem may be avoided by



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using convergent approaches (routes 2 and 3). In route 2, dendrons that have been prepared convergently are attached to a porphyrin core. The dendrimer porphyrins (**1_n·2H**), first reported in 1993, made use of this convergent strategy; their synthesis was accomplished by the Williamson condensation of a tetrakis(3,5-dihydroxyphenyl)porphyrin with a poly-(benzyl ether) dendron bromide.⁹ Likewise, poly(aryl ester) dendrimer metalloporphyrins (**10·MnCl**) have been prepared convergently by the dicyclohexyl carbodiimide (DCC)-

mediated condensation of the corresponding polyester dendrons bearing a carboxylic acid group at the focal core, with the phenolic OH groups of tetrakis(3,5-dihydroxyphenyl)porphyrin.¹¹ Further examples synthesized using this approach include dendrimer porphyrins that bear dendritic wedges comprised of phenylene (**16_n–18**),^{28,29} platinum-acetylide,³⁰ phenylazomethine (**26**),³¹ pyrimidine,³² aryl amide,³³ and glycerol units.³⁴ Meanwhile, an alternative convergent approach (route 3) was developed by Fréchet et al. and reported in 1998, where poly(benzyl ether) dendrons with an aldehyde group at the focal core were subjected to Lindsey condensation with pyrrole.³⁵ This method was successfully applied to the synthesis of dendrimer porphyrins with dendritic side groups of stilbene,³⁶ carbazole,^{37,38} and truxene units.³⁹ When compared to route 2, this synthetic strategy is better for the rapid synthesis of lower-generation dendrimer porphyrins, while the synthesis of higher-generation (e.g., ≥G4) homologues may suffer from low yields. The synthesis of noncovalent dendrimer porphyrins has also been reported. Examples include an electrostatic assembly of a porphyrin bearing four phenylsulfonate groups with a poly(benzyl ether) dendron carrying a quaternary ammonium ion at the focal core.⁴⁰

Another type of dendrimer porphyrins includes those in which the dendritic units are attached to the pyrrole-β or axial positions of the porphyrin macrocycle (Figure 2B–D). For example, Vinogradov and co-workers have synthesized a porphyrin-cored dendrimer (**58**) with 12 poly(ester-amide) dendritic side groups that are attached to both the *meso*- and the pyrrole-β positions (Figure 2C).⁴¹ To the best of our knowledge, dendrimer porphyrins in which the dendritic wedges are attached only to the pyrrole-β positions (Figure 2B) have not yet been reported. However, the structure shown in Figure 2D has been reported, as exemplified by a rhodium(III) porphyrin with dendron units σ-bonded to the macrocycle in the axial direction.⁴² Exposure of this dendrimer porphyrin to visible light results in homolytic cleavage of the carbon–rhodium bond, generating a carbon-centered dendritic free radical. When this photochemical reaction is performed in a CO atmosphere, this organometallic dendrimer porphyrin can be converted into the corresponding acylrhodium species, although at a rate that strongly depends on the size of the dendron. In addition to this example, dendritic phosphorus(V) porphyrins with axial carbazole-based dendritic substituents (**41**) have also been synthesized.⁴³ As expected, the cofacial porphyrin–porphyrin interaction is suppressed in compound **41**.³⁸

The encapsulation of phthalocyanines is an interesting subject because they tend to aggregate to a much greater extent than porphyrins. The first phthalocyanine-cored dendrimer, reported by Kimura et al. in 1997, was divergently synthesized by allowing a poly(ether-amide) dendritic structure to grow from a zinc phthalocyanine core.^{44,45} Majoral and co-workers then employed a divergent strategy for the synthesis of a phthalocyanine with eight phosphorus dendritic substituents; these substituents were grown to generation numbers of up to 8 (**9**).^{46–48} The convergent approach was first adopted by McKeown and co-workers, who cyclized a poly-(benzyl ether) dendritic phthalonitrile to produce a phthalocyanine-cored dendrimer.^{49–53} The same strategy was employed by the groups of Ng,⁵⁴ Kasuga,⁵⁵ and McGrath.⁵⁶ A silicone phthalocyanine with dendritic units at its axial positions has also been prepared by reacting a dichlorosilicone precursor with a poly(benzyl ether) dendritic alcohol.^{50–53,57}

Chart 1

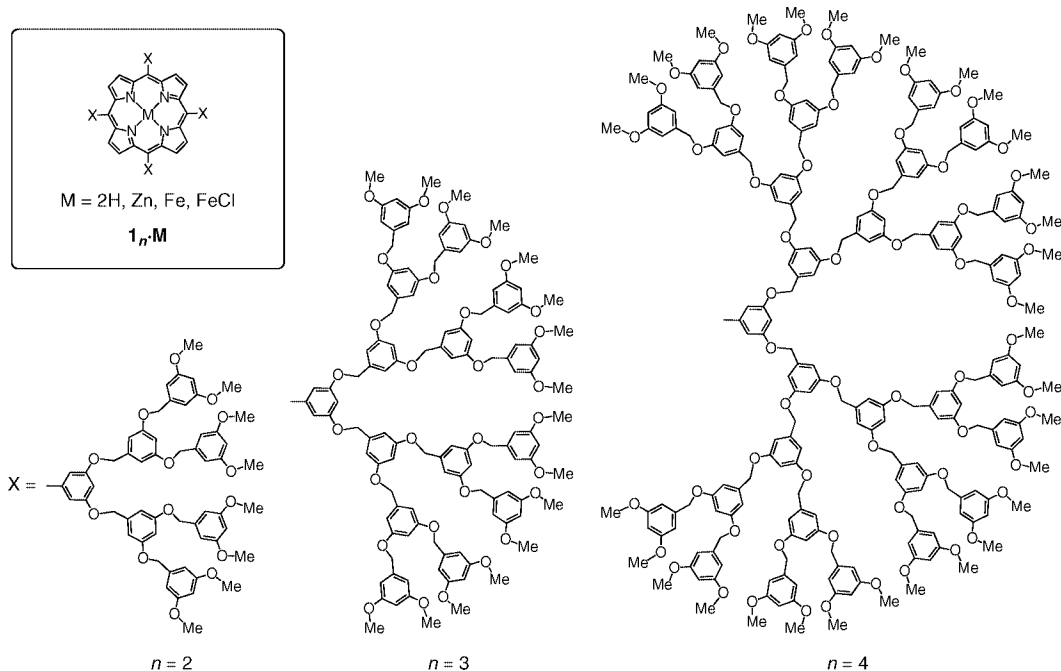
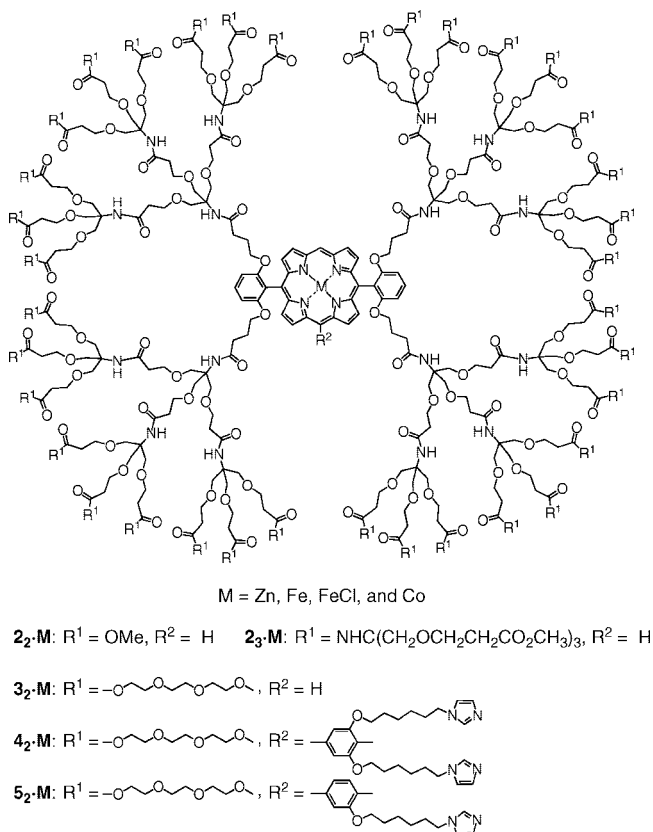


Chart 2



As compared to dendrimers that encapsulate only a single porphyrin or phthalocyanine unit, those with multiple chromophores are much more difficult to synthesize; carefully designed construction diagrams consisting of a specific sequence of finely optimized iterative steps are required to obtain the desired products in good yields. Once the target dendrimers are contaminated with side products, purification becomes a very serious issue. One may also struggle with problems involving solubility and identification of intermedi-

ates and final products. Particular skills for mass spectrometry are required, because NMR spectroscopy does not always work properly. From this viewpoint, convergent synthetic approaches may be preferable.

3. Behaviors of Encapsulated Porphyrins and Phthalocyanines

The spectral profiles of porphyrin and phthalocyanine derivatives are rather sensitive to their environments and can be used as probes for exploring the interior of dendritic molecules.^{58,59} Large dendrimers tend to adopt a spherical morphology, like those of globular proteins. Computer-generated molecular models of **1_n·2H**, for example, suggest that the morphology of the dendrimer framework changes in stepwise fashion from “open” (**1₂·2H**) to “semiclosed” (**1₃·2H**) to “closed” (**1₄·2H**) as the generation number increases.⁶⁰ The highest-generation dendrimer **1₄·2H** adopts a near-globular shape, with a diameter of approximately 5 nm. The dendritic shell appears to provide a special microenvironment for the focal porphyrin unit and thus affects its fundamental properties.

Aida et al. have reported that the Soret absorption band of the zinc porphyrin unit of **1_n·Zn** shows a progressive red shift with increasing generation number.⁶⁰ For example, a fourth-generation molecule **1₄·Zn** in CH_2Cl_2 displays a Soret absorption band at 427.0 nm, very close to that in 1,3-dimethoxybenzene ($\lambda_{\text{Soret}} = 427.7$ nm), a monomeric model of the dendrimer shell. In contrast, a nondendritic zinc porphyrin reference in CH_2Cl_2 displays its Soret absorption band at 421.3 nm, which is blue-shifted by 6.3 nm from that in 1,3-dimethoxybenzene. In relation to these observations, Fréchet and co-workers concluded somewhat controversially, on the basis of measurements of analogous zinc porphyrin dendrimers, that the difference in the absorption maxima of the core measured in DMF and THF has very little dependence on the generation number of the dendrimer shell.⁶¹ Although the solvatochromism in relation to the issue of dendritic encapsulation has been studied for porphyrins with dendritic side groups consisting of glutamate,²³ 2,2-

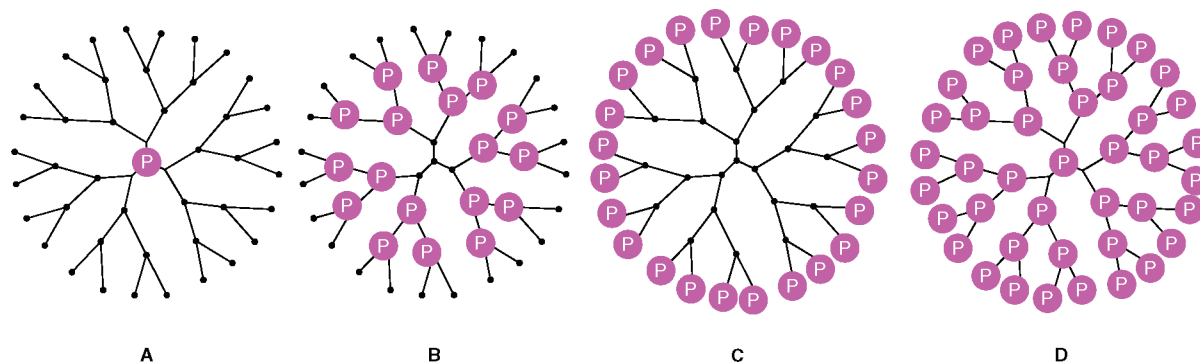


Figure 1. Structural classification of dendrimer porphyrins so far reported. Symbol “P” denotes a porphyrin unit.

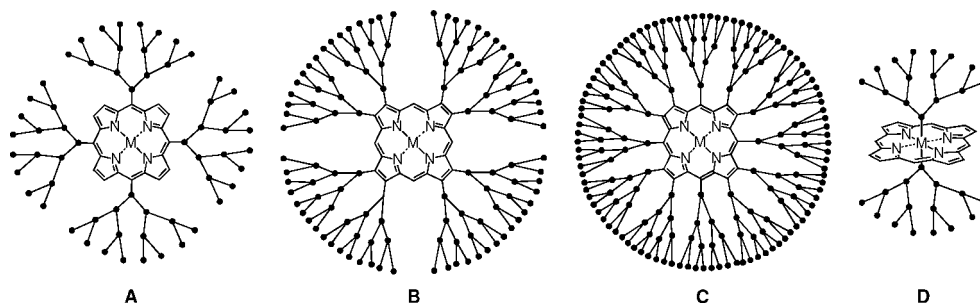
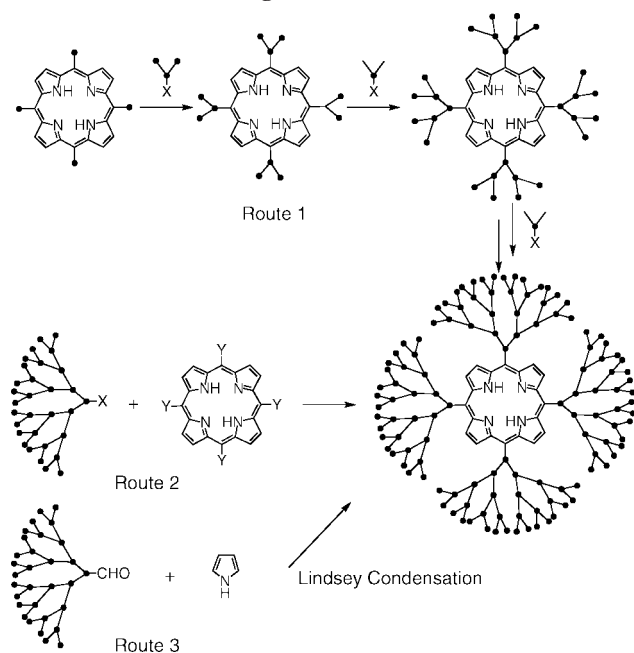


Figure 2. Structural classification of porphyrin-cored dendrimers.

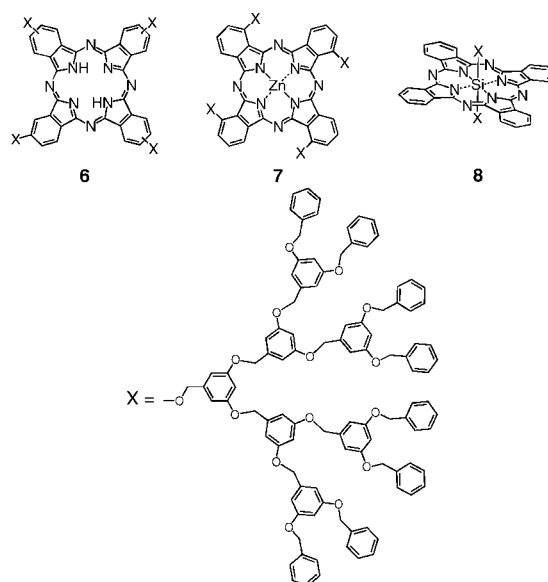
Scheme 1. Synthetic Routes to Type-A Porphyrin-Cored Dendrimers Shown in Figure 2



bis(methylol) propionate,^{24–26} phenylene,²⁹ platinum-acetyl-
ide,³⁰ phenylazomethine,³¹ pyrimidine,³² carbazole,³⁷ and
stilbene,⁶² the results differ from dendrimer to dendrimer,
and no general conclusion has yet been made.

Phthalocyanines have a much stronger tendency than porphyrins to aggregate via a π -electronic interaction. Hence, it is interesting to investigate if the dendritic encapsulation can suppress the aggregation of phthalocyanines efficiently. Kimura and co-workers grew a Newkome's polyether-amide dendritic structure divergently from the four peripheral positions of a zinc phthalocyanine.^{44,45} McKeown and co-workers modified the periphery of a phthalocyanine with four poly(benzyl ether) dendrons.^{19,20,49–53} However, even with

Chart 3



four third-generation dendrons, dendrimer **6** (Chart 3) still shows some spectroscopic signatures typical of self-associated phthalocyanines even under highly dilute conditions. For example, the ^1H NMR signals due to the 12 protons attached to the phthalocyanine core are considerably broadened even at a low concentration such as 1×10^{-4} M in CDCl_3 . Electronic absorption spectroscopy in CHCl_3 at 1×10^{-5} M displays a broad phthalocyanine Q-band centered at 630 nm, which is blue-shifted from that of an unassociated phthalocyanine. These observations indicate a strong cofacial interaction of the phthalocyanine cores. The aggregation of **6** becomes more serious in its film state, prepared by spin-coating, where the phthalocyanine Q-band is further blue-shifted to 620 nm. Ng and co-workers have reported water-soluble phthalocyanine-cored dendrimers having sodium carboxylate surface groups and claimed that the third-generation dendritic substituents can effectively suppress the

phthalocyanine aggregation.^{21,54} In addition to **6**, dendrimer **7** bearing four poly(benzyl ether) dendrons at the α -positions of the phthalocyanine core has been reported.⁵⁵ Unlike **6**·Zn that shows Soret and Q-bands of the phthalocyanine unit at 337 and 683 nm in CH₂Cl₂, respectively, compound **7** displays the corresponding absorption bands at 322 and 705 nm, suggesting that its phthalocyanine core associates much less than that of **6**·Zn. Of interest, this compound also shows absorption bands (723 and 759 nm) in the longer wavelength region from the ordinary Q-band absorption of phthalocyanine. When compound **7** is allowed to stand in solution at room temperature, these characteristic absorption bands are gradually intensified at the expense of the Q-band absorption. The authors have proposed tentatively that these unique bands originate from a possible distortion of the phthalocyanine macrocycle. The more efficient way to suppress the aggregation of phthalocyanines is to attach dendritic substituents to the axial position of their metal center.⁵⁷ For example, dendrimer **8** displays a phthalocyanines Q-band at 680 nm in toluene and 688 nm in the film state with a width of half peak of only 2 nm. The small bathochromic shift and narrow bandwidth of the Q-band in the film state illustrate that dendrimer **8** substantially exists as a monomeric species. Later, a perfectly dispersed phthalocyanine, even in the solid state, has been synthesized by incorporation of a dendritic wedge into all available positions in a phthalocyanine macrocycle.^{47,48,56}

Porphyrin and phthalocyanine derivatives are luminescent. By encapsulation of such emitting pigments using dendritic macromolecules, one may anticipate an enhancement of their luminescent properties by suppressing collisional quenching of their excited states. Indeed, the fluorescence quantum yield of a porphyrin unit, encapsulated within a carbazole-phenylazomethane double layered dendritic structure, for example, becomes larger upon increment of the generation number of the dendrimer units.⁶⁹ However, this is a rare case. In many other examples where the dendrimer frameworks are constructed with, for example, benzyl ether,^{61,76} 2,2-bis(methylol) propionate,²⁶ β -D-glucopyranose,²⁷ and phenylene²⁸ units, the size of the dendrimer framework has little influence on the fluorescence properties of the core porphyrins including their bandwidths, quantum yields, and lifetimes. In contrast, the fluorescence of phthalocyanines is, in most cases, enhanced when it is properly encapsulated by a larger dendritic framework.^{44,47} Despite the presence of such inconsistent effects, the dendrimer framework, in general, can reduce the access of small quenchers, thereby retarding the quenching processes.^{21,54,63} This observation has motivated the utilization of dendritic porphyrins and phthalocyanines for organic light-emitting diodes with an expectation that the surrounding matrices may be tailored for efficient transport of charge carriers. So far, several trials have been reported,^{64–71} some of which show interesting dendrimer effects. However, the overall performances are not sufficient for practical applications.

To conduct further investigation on the issue of encapsulation, the electrochemical properties of dendrimer porphyrins have been studied. Diederich et al. prepared synthetic models of cytochrome *c*;⁷² water-soluble poly(ether-amide) dendrimers with an iron(III) porphyrin core (**3_n**·FeCl)⁷³ were developed from their zinc porphyrin analogues (**2_n**·Zn).¹⁰ In CH₂Cl₂, both lower-generation **3₁**·FeCl and higher-generation **3₂**·FeCl show reversible waves for the reduction potential of Fe^{III}/Fe^{II} couple at nearly identical voltages,

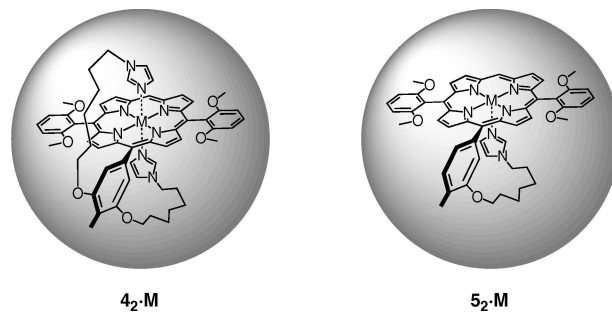


Figure 3. Axial ligation in **4₂**·M and **5₂**·M. Adapted with permission from ref 74 and ref 75. Copyrights 1999 and 2002 Wiley-VCH Verlag GmbH & Co. KGaA.

−0.01 and +0.07 V, versus the standard calomel electrode (SCE), respectively. Of interest, in aqueous media, their reduction potentials are considerably different from one another; higher-generation **3₂**·FeCl (+0.19 V) shows a 420 mV more positive reduction potential than does lower-generation **3₁**·FeCl (−0.23 V). These results suggest that the environmental polarity strongly affects the shape of the dendritic pocket of **3₂**·FeCl (i.e., solvation of the iron porphyrin core). In CH₂Cl₂, the dendritic pocket of **3₂**·FeCl is conformationally rather open, so that the microenvironment for the iron porphyrin core is similar to that of lower-generation **3₁**·FeCl. In contrast, in aqueous media, the hydrophobic iron porphyrin core in **3₂**·FeCl may be tightly surrounded and protected by the large dendritic cage from the access of water molecules. Consequently, the oxidized (more charged) state of the iron porphyrin core in **3₂**·FeCl is destabilized. In contrast, because of the small dendritic substituents, the dendritic pocket of lower-generation **3₁**·FeCl does not impede aqueous solvation of the iron porphyrin core. The remarkable difference in reduction potential between **3₂**·FeCl and **3₁**·FeCl is similar to that observed between cytochrome *c* and cytochrome *c* heme octapeptide with a more solvent-exposed redox center.⁷²

Later, the same group prepared **4_n**·FeCl as a more advanced model of cytochrome *c*, where the iron(III) porphyrin macrocycle was designed to accommodate at its axial position an imidazole unit that is covalently attached to the *meso*-position (Figure 3).^{74,75} The redox potential of the iron center of **4_n**·FeCl becomes more positive when the generation number (*n*) of the dendrimer shell is increased from 1 to 2. Noteworthy, the redox potentials of **4₂**·FeCl measured in CH₂Cl₂, CH₃CN, and water, which have very different polarities, are essentially identical. Thus, one may conclude that the densely packed dendritic superstructure of **4₂**·FeCl creates a unique local microenvironment around the heme center, in a fashion similar to the role played by protein shells in cytochromes. It should also be noted that the dendritic shell influences the reversibility of the redox nature of the core. For example, while the redox process occurs fully reversibly in **2₂**·Zn, higher-generation molecule **2₃**·Zn displays an irreversible redox behavior.¹⁰ This irreversible nature becomes more pronounced when the zinc porphyrin core is surrounded by a poly(benzyl ether) dendrimer shell.⁷⁶

To investigate the interpenetrating interactions between different dendrimer substituents, the axial coordination chemistry of zinc porphyrins with imidazole has been studied.⁶⁰ As described above, the molecular model of fourth-generation **1₄**·Zn suggests that the environment around the zinc porphyrin core is extremely congested. However, titration experiments involving imidazole-appended poly-

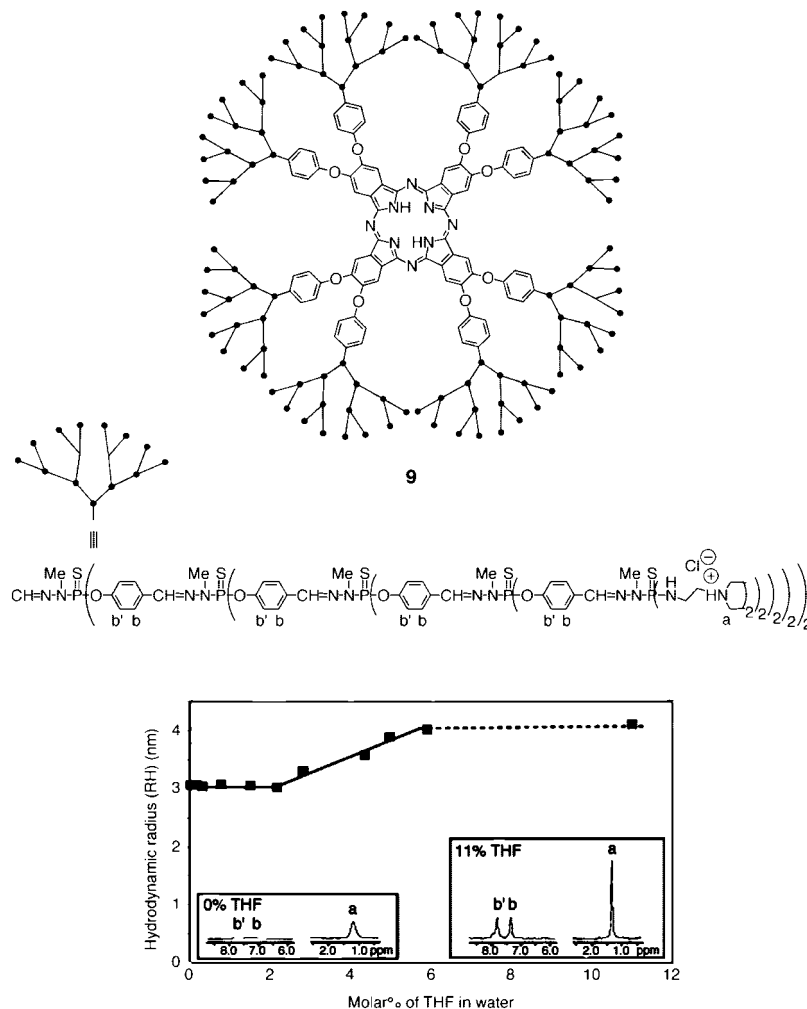


Figure 4. Variation of the hydrodynamic radius (R_H) of **9** in water as a function of the THF content. Inset: A part of the $^1\text{H NMR}$ spectrum of **9** in D_2O (left) and that in $\text{D}_2\text{O/THF-}d_8$ (89/11 in mol %, right). Adapted with permission from ref 46. Copyright 2004 American Chemical Society.

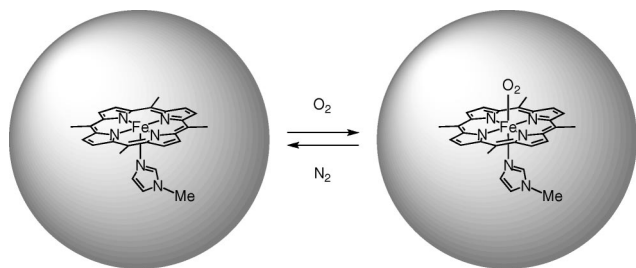
(benzyl ether) dendrons with different generation numbers indicated that $\mathbf{1}_4\cdot\text{Zn}$ can accommodate even the third-generation dendritic imidazole at the axial position of the zinc porphyrin core, albeit with a small binding constant. Because this axial ligation requires the dendritic imidazole to interpenetrate deeply into the dendrimer shell of $\mathbf{1}_4\cdot\text{Zn}$, poly(benzyl ether) dendrimers likely possess a conformational flexibility.

Majoral et al. introduced the concept of “dendritic molecular sponge” based on results of a NMR study of the phthalocyanine-cored phosphorus dendritic amphiphile (**9** in Figure 4).⁴⁶ Because of the presence of ammonium ion groups on its surface, dendrimer **9** is soluble in water. Upon stepwise addition of THF to this aqueous solution, a progressive increase in the hydrodynamic radius (R_H) of **9** takes place, from ~ 3 nm in pure water to ~ 4.1 nm at a THF content of 5–6% (Figure 4). This observation led to the claim that the interior of **9**, which is initially frozen because of its hydrophobic nature, accommodates THF and becomes swollen, “blooming” like a dry sponge. Accordingly, in $\text{D}_2\text{O/THF-}d_8$, both the $^1\text{H NMR}$ signals corresponding to the internal phenylene groups (Figure 4, inset) and an electronic absorption band of the phthalocyanine core become progressively sharper as the THF content increases.

4. Mimicking Hemoproteins

As was already described, the design of dendrimer porphyrins was inspired by the unique structures of hemoproteins, whose active centers are embedded in protein matrices. Such shielded microenvironments are essential for the heme centers to work properly. A variety of sterically hindered iron porphyrins have been designed and investigated to act as synthetic models of hemoproteins.² As compared to these rather small model systems, dendritic analogues are considered to possess significant advantages due to their tunable three-dimensional architectures.^{58,59}

The first dendrimer porphyrins ($\mathbf{1}_n\cdot\mathbf{2H}$) were designed to mimic hemoproteins.⁹ The success of this design was demonstrated by the fourth-generation homologue ($\mathbf{1}_4\cdot\text{Fe}$), in which the iron(II) complex was proven to function in a fashion similar to O_2 -carrying hemoproteins. In the presence of 1-methylimidazole, $\mathbf{1}_4\cdot\text{Fe}$ binds to and holds O_2 in both dry and wet toluene (Scheme 2).⁷⁷ This is in sharp contrast to the action of a nondendritic iron(II) porphyrin reference, which upon exposure to O_2 is instantly and irreversibly converted into the corresponding μ -oxo dimer. The O_2 -adduct of $\mathbf{1}_4\cdot\text{Fe}$ is long-lived even at room temperature, with a half-life ($t_{1/2}$) of more than 2 months. Furthermore, bubbling with N_2 results in regeneration of the deoxygenated form of $\mathbf{1}_4\cdot\text{Fe}$. This oxygenation–deoxygenation cycle can be repeated

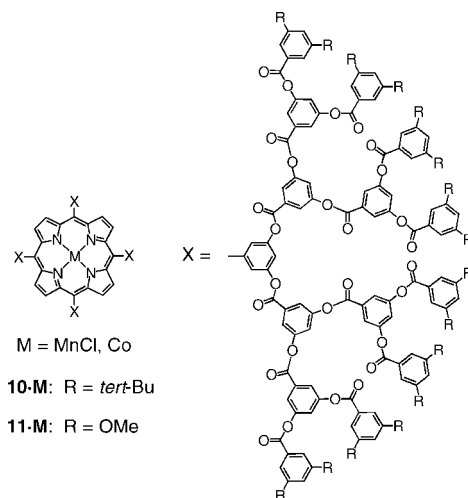
Scheme 2. Reversible O₂-Binding in Dendritic Iron Porphyrins **1_n·Fe in the Presence of 1-Methylimidazole⁷⁷**


many times. Although lower-generation **1₂**·Fe and **1₃**·Fe display reversible O₂-binding activity, their O₂ adducts are substantially less stable than that of **1₄**·Fe, with *t*_{1/2} values of only 1.5 h for **1₂**·Fe·O₂ and 6 h for **1₃**·Fe·O₂. Thus, the large, spherical dendrimer shell efficiently protects the active site at the core from irreversible oxidation. It is also worthwhile to note that the large dendrimer shell exhibits low gas permeability, resulting in a high resistance of the O₂ adduct of **1₄**·Fe to carbonylation in a CO atmosphere.

Similar to **1_n**·Fe, poly(ether amide) dendrimers with an iron(II) porphyrin core such as **3₂**·Fe and **5₂**·Fe exhibit reversible binding capabilities toward O₂ and CO in dry toluene including 1,2-dimethylimidazole.^{78–80} The affinity of **3₂**·Fe toward O₂ is approximately 1500 times greater than that of T-state hemoproteins, while the affinities of **3₂**·Fe and hemoproteins toward CO are similar. The authors of this study suggested that the high O₂ affinity of **3₂**·Fe may originate from a possible hydrogen-bonding interaction between the terminal oxygen atom of bound O₂ and nearby amide N–H groups in the dendritic shell. The next step was to design poly(benzyl ether) dendrimer iron(II) porphyrins with a variety of distal ligands that can function as potential hydrogen-bonding donors.^{81,82} However, upon exposure to O₂, these dendritic iron complexes decomposed rapidly. In addition to iron porphyrins, dendritic cobalt(II) porphyrins have also been investigated to bind O₂.⁸³ In related studies, a dendritic nonheme metalloprotein mimic has been synthesized by the O₂-driven assembly of a copper-ligating dendrimer bearing a 1,4,7-triazacyclononane core,⁸⁴ followed by the formation of a di-iron(III) analogue.⁸⁵ Again, the stabilities of these μ-oxo-bridged bimetallic complexes are highly dependent on the size of the dendrimer cage.

To mimic the substrate-selective transformations that are mediated by cytochrome P450, manganese porphyrins shielded by oxidatively robust poly(aryl ester) dendrimers have been developed by Suslick and co-workers.^{11,86} Dendrimer **10**·MnCl (Chart 4) catalyzes the epoxidation of alkenes in regio-selective and shape-selective fashions, using iodosylbenzene as the oxidant. In the epoxidation of nonconjugated dienes and 1:1 mixtures of linear and cyclic alkenes under competitive conditions, compound **10**·MnCl selects less hindered double bonds to a much greater extent than does nondendritic analogue Mn(TPP)Cl (Figure 5). This preference becomes more pronounced as the size of the dendrimer increases. Similar to this finding, zinc complexes of these dendrimer porphyrins display shape-selective ligation of nitrogenous bases.⁸⁷ Likewise, the epoxidation reactions of olefins with polyphenylene, poly(ether-amide), and poly(benzyl ether) dendrimers encapsulating iron(III)^{29,88} and ruthenium(II)^{89,90} porphyrins, respectively, have been reported to proceed regioselectively.

To mimic the biological functions of vitamin B₁₂, the azobisisobutyronitrile (AIBN)-mediated alkenylation of a

Chart 4


cobalt(II) porphyrin with propargyl alcohol has been studied.^{91,92} This reaction is initiated by the transient formation of a cobalt(III) hydride species from the cobalt(II) porphyrin and AIBN, with the elimination of acrylonitrile (Scheme 3). Propargyl alcohol is then inserted into the

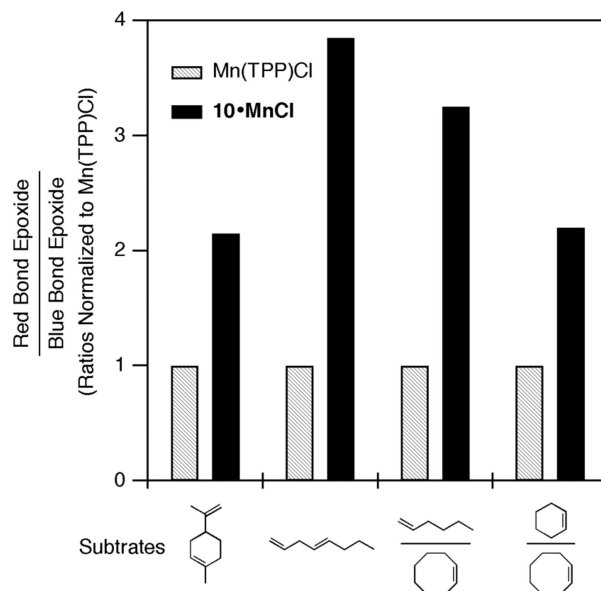
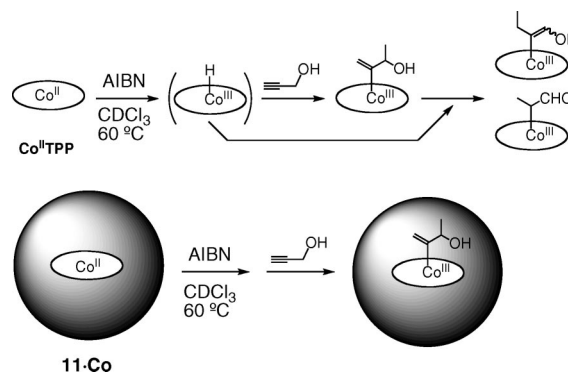


Figure 5. Epoxidation of nonconjugated dienes and 1:1 mixtures of linear and cyclic alkenes catalyzed by Mn(TPP)Cl and dendritic **10**·MnCl. Adapted with permission from ref 11. Copyright 1996 American Chemical Society.

Scheme 3. Alkenylation of Co^{II}TPP and Co(II) Porphyrin-Cored Dendrimer **11·Co with Propargyl Alcohol^{91,92}**


$\text{Co}^{\text{III}}\text{--H}$ bond to produce an alkenylcobalt(III) species, $\text{Co}^{\text{III}}\text{--C(=CH}_2\text{)CH}_2\text{OH}$. The most interesting feature of this reaction is that it proceeds highly selectively with a large poly(aromatic ester) dendrimer (**11**·Co) to produce only $\text{Co}^{\text{III}}\text{--C(=CH}_2\text{)CH}_2\text{OH}$ in 91% yield. In sharp contrast, when a nondendritic analogue or lower-generation homologues of **11**·Co are subjected to this reaction, other products such as $\text{Co}^{\text{III}}\text{--C(CH}_3\text{)=CHOH}$ and $\text{Co}^{\text{III}}\text{--CH(CH}_3\text{)CHO}$ form concomitantly. These organocobalt(III) species are the isomerization products of $\text{Co}^{\text{III}}\text{--C(=CH}_2\text{)CH}_2\text{OH}$, formed by secondary reactions with the intermediate cobalt(III) hydride species. Thus, the high selectivity observed for the reaction of **11**·Co is due to steric suppression of the secondary reactions between the product $\text{Co}^{\text{III}}\text{--C(=CH}_2\text{)CH}_2\text{OH}$ and cobalt hydride species by the large dendritic shell.

5. Mimicking Light-Harvesting Complexes

Artificial light-harvesting antenna systems are fascinating synthetic targets for chemists. In the photosynthetic complexes of purple bacteria, numerous bacteriochlorophyll units are spatially organized into wheel-like assemblies, referred to as the light-harvesting antenna complexes LH1 and LH2. These assemblies play a vital role in absorbing dilute photons in the visible region and funneling the acquired energy to the reaction center with an efficiency of 100%.^{3–6} In the design of artificial light-harvesting systems, a great number of chromophores need to be incorporated to acquire a large absorption cross-section.^{93–95} Furthermore, such chromophores must be spatially organized in such a way that they facilitate directional energy transfer in a cooperative manner. These requirements may be met by dendritic architectures,^{12,96} wherein a large number of chromophoric pigments can be placed at the periphery of dendritic macromolecules and/or in their branch units. In fact, a variety of multichromophoric dendrimers have so far been developed for realizing the so-called “antenna effect” essential for biological systems. Among these, dendrimer porphyrins have attracted particular attention, because natural systems make use of porphyrin derivatives as light-harvesting pigments.

5.1. Energy Migration and Transfer in Dendrimers with a Single Porphyrin Unit

Porphyrin derivatives have pronounced absorption bands in the visible region and exhibit red fluorescence, which make them potential energy traps for many organic dyes. In one of the initial studies of light-harvesting dendrimers, Aida et al. found that highly efficient singlet energy transfer occurs in **14**·**2H**, from the poly(benzyl ether) dendritic wedges to the free-base porphyrin core.⁹⁷ The energy transfer efficiency (Φ_{ENT}) is significantly affected by the morphology and generation number of the dendritic framework (Table 1). Dendrimer **14**·**2H**, which is comprised of four fourth-generation poly(benzyl ether) dendritic wedges, exhibits a Φ_{ENT} value of 80.3% in CH_2Cl_2 at 20 °C upon excitation of the benzyl ether units at 280 nm. In contrast, **124**·**2H** (Table 1), which is an analogue of **14**·**2H** with three dendritic substituents, exhibits a Φ_{ENT} value of only 31.6%. A further decrease in the number of dendritic wedges lowers the energy transfer efficiency to 19.7% (**134**·**2H** in Table 1) and 10.1% (**144**·**2H** and **154**·**2H** in Table 1). Compound **13**·**2H**, a lower-generation homologue of tetra-substituted **14**·**2H**, exhibits a Φ_{ENT} value (79.2%) at 20 °C comparable to that of **14**·**2H**. However, in contrast to **14**·**2H**, the Φ_{ENT} value of **13**·**2H**

Table 1. Quantum Yields of Energy Transfer from Poly(benzyl ether) Dendrons to the Focal Porphyrin Core in Dendrimer Porphyrins **14**·**2H**, **124**·**2H**, **134**·**2H**, **144**·**2H**, and **154**·**2H**⁹⁷


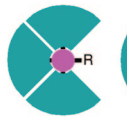
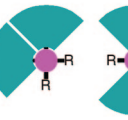
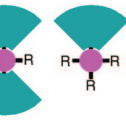


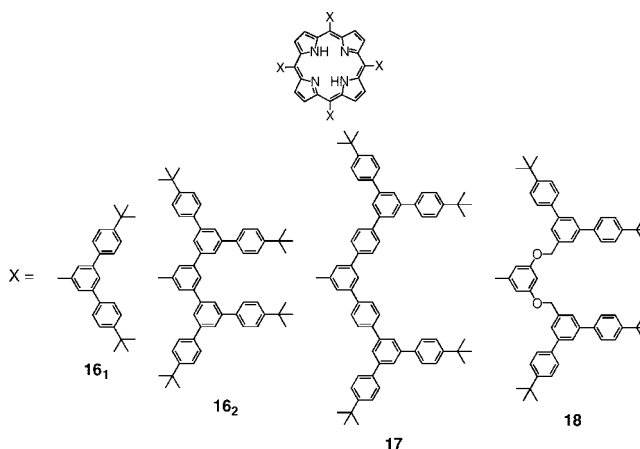
Compd.					
Φ_{ENT} (%)	80.3	31.6	19.7	10.1	10.1
					

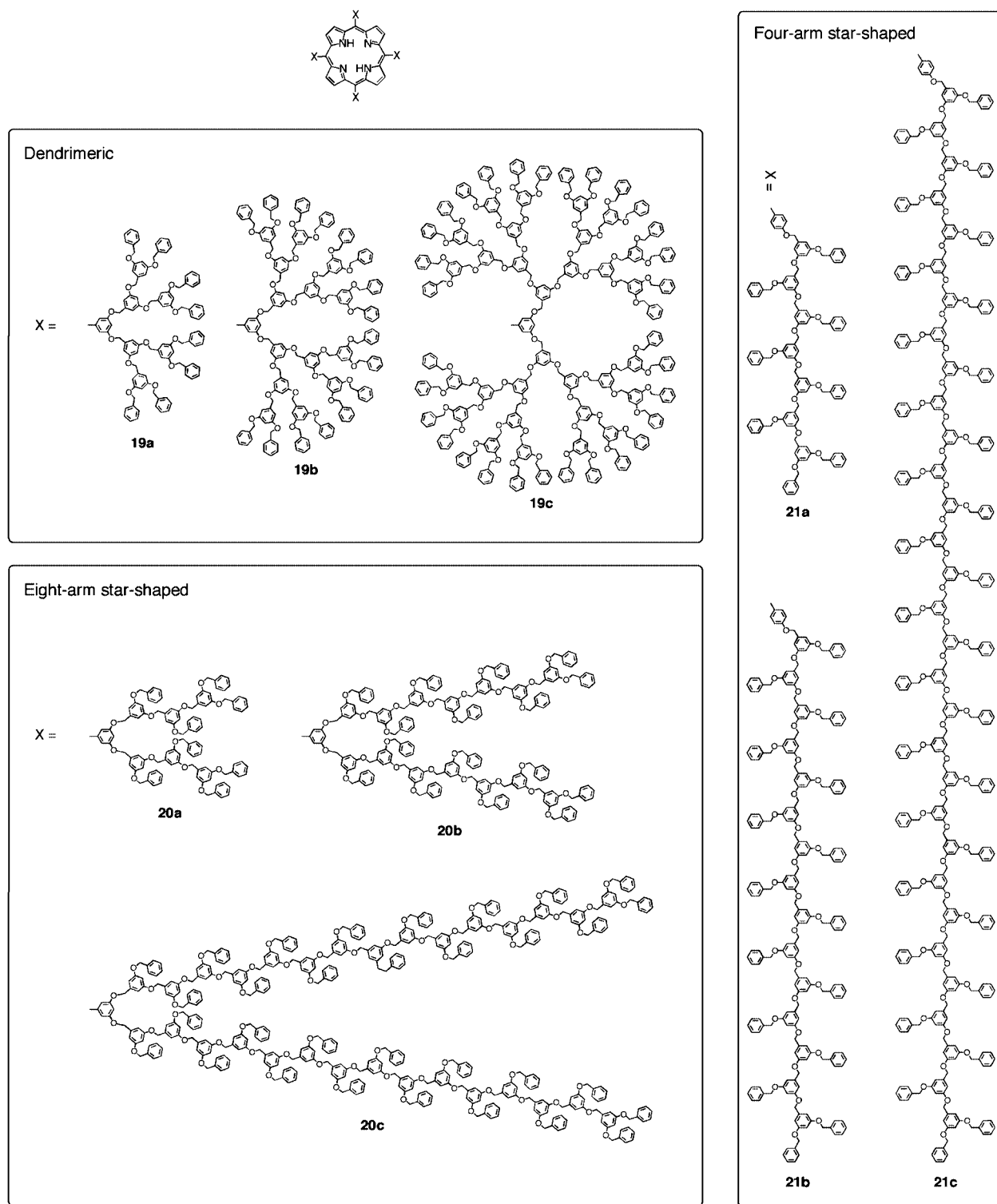
Chart 5



upon heating to 80 °C is dramatically decreased to 35.6%. Introduction of a nonbranched benzyl ether unit between the dendritic wedges and the porphyrin core also results in a significant drop of Φ_{ENT} from 79.2 to 53.7% at 20 °C. All of these observations suggest that the enhanced energy transfer in dendrimer **14**·**2H** is due to the dense packing of the dendron subunits, as shown by ¹H NMR relaxation time measurements. Such a densely packed configuration promotes an efficient energy-migration process over the dendritic framework, as evidenced by fluorescence anisotropy measurements. It is important to note that the energy transfer in **14**·**2H** takes place via a through-space Förster mechanism, where the excitation energy hops from one benzyl ether unit to the next, the units being suspended in a dendritic architecture. In this sense, the energy transfer in **14**·**2H** is analogous to the processes occurring in biological light harvesting.

A similar study has been carried out with polyphenylene-based rigid dendrimer porphyrins.²⁹ Upon excitation of the dendritic wedges in CH_2Cl_2 , compound **162** (Chart 5) emits light mostly from the porphyrin core, indicating the occurrence of an efficient energy transfer from the polyphenylene dendritic side groups to the focal porphyrin unit. The Φ_{ENT} value of **162** is as high as 98%, but the first-generation analogue **161** exhibits a smaller Φ_{ENT} value (66%). Although the addition of a 1,4-phenylene unit to **162** between the dendritic wedges and porphyrin core (**17**) results in an enhancement of the donor–acceptor spectral overlap, the value of Φ_{ENT} falls to 74%. Furthermore, when the polyphenylene dendrons are attached to the porphyrin core through an ether bond (**18**), the value of Φ_{ENT} is only 42%, which is

Chart 6



significantly lower than those of **16₂** and **17**. This observation indicates that the efficient dendron-to-porphyrin energy transfer benefits from the presence of a through-bond pathway.

Hawker, Fréchet, and co-workers compared the intramolecular energy transfer properties of three different macromolecular architectures: the fourth-generation dendrimer (**19a–19c**) (Chart 6) and its eight- and four-arm star-shaped isomers **20a–20c** and **21a–21c**.⁹⁸ Interestingly, they found that dendrimer **19c** exhibits a much larger Φ_{ENT} value (83.9%) than do **20c** (57.0%) and **21c** (34.2%) (Figure 6).

Furthermore, the dendrimer series show only a slight decline in Φ_{ENT} from 89.7% to 83.9% when the generation number increases from 3 (**19a**) to 5 (**19c**). In sharp contrast, the eight-arm series exhibit a significant decrease in energy transfer efficiency from 87.8% (**20a**) to 57.0% (**20c**), while four-arm series show even the steepest decrease from 84.8% (**21a**) to 34.2% (**21c**) when the number of repeating units becomes larger. These observations demonstrate the great advantage of using dendritic architectures for periphery-to-core energy transfer. Intramolecular energy transfer has also been investigated for other dendrimer porphyrins, such as those having

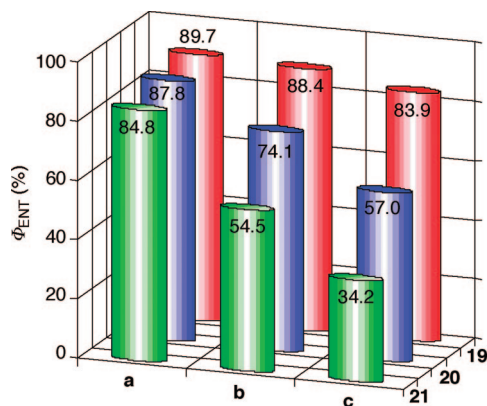


Figure 6. Quantum yields of energy transfer from benzyl ether units to the focal porphyrin core in dendrimer porphyrins **19a–19c**, **20a–20c**, and **21a–21c**. Adapted with permission from ref 98. Copyright 2002 American Chemical Society.

dendritic wedges of platinum-acetylide³⁰ and carbazole^{37,38} derivatives at the *meso*-positions of the porphyrin macrocycle.

With the aim of realizing cascade-type energy transfer, dendrimers that contain multiple chromophoric units of different types at particular sites have been synthesized. Through elaborate molecular design, they can be tailored to absorb light over a wide spectral range and transfer the energy to the acceptor core, where light is emitted at a single wavelength. Examples include porphyrin-cored dendrimer **22** (Chart 7), which bears 16 coumarin units in the outer layer and 8 naphthopyranone units in the inner layer.⁹⁹ Excitation of either the coumarin or the naphthopyranone units results in emission only from the focal porphyrin core, indicating the presence of an energy-transfer cascade from the outer layer, where the coumarin units are located, to the inner layer containing naphthopyranone, and then to the focal porphyrin unit.

Dendritic light-harvesting antennae for the collection of low-energy photons have attracted attention not only from a fundamental viewpoint, but also for their potential use in bioimaging and photodynamic therapy (see final section). Fréchet and co-workers synthesized dendrimer **23·2H**, which consists of a porphyrin core integrated with 8 energy-donating chromophore units of AF-343 (**24** as a reference, Chart 8), a two-photon absorbing (TPA) dye (8100 GM, where 1 GM = 10⁻⁵⁰ cm⁴ s).¹⁰⁰ Under single photon excitation conditions with 385 nm light, the emission from the AF-343 chromophore in **24** appears at 492 nm (Figure 7). In contrast, when **23·2H** is excited at the same conditions, this emission is hardly observable. Instead, an emission predominantly from the porphyrin core appears, indicating an efficient energy transfer from the peripheral AF-343 units to the porphyrin core (Φ_{ENT} = 97%). Of interest, when **23·2H** is illuminated with a 780 nm laser in which AF-343 units have a strong two-photon absorption, the emission again originates mainly from the porphyrin core. Furthermore, its intensity is 17 times greater than that of **25**, a reference compound for the porphyrin core of **23·2H**. This result clearly indicates the occurrence of a resonance energy transfer from the two-photon-excited AF-343 unit to the porphyrin core. For the purpose of biomedical applications, a water-soluble version of **23·2H** has been synthesized, which bears at its periphery triethylene glycol monomethyl ether units.¹⁰¹

Hot-band excitation (HBE) is a process that may also allow for the harvesting of low-energy photons. An illustration of

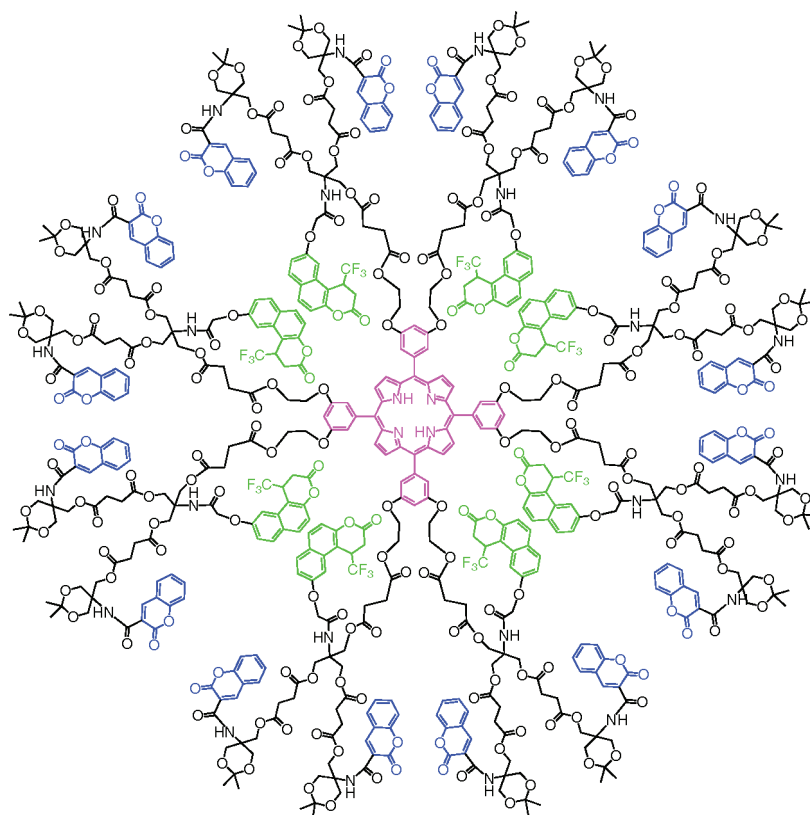
this possibility is provided by the conjugated poly(phenylazomethine) dendrimer **26** (Chart 9), which has a porphyrin unit at its center.¹⁰² Poly(phenylazomethine) dendrimers, which allow stepwise assembly of metal ions in their frameworks,^{31,103–109} have been used for dye-sensitized solar cells,^{110,111} catalysts,¹¹² and templates for the synthesis of metal nanoparticles.¹¹³ These dendrimers, in conjunction with porphyrins, can also be used as light-harvesting antenna.¹⁰² Upon exposure to a 730 nm laser, which is ~1600 cm⁻¹ lower than the absorption maximum of the porphyrin Q-band, dendrimer **26** emits fluorescence from the porphyrin core at approximately 660 nm. The energy difference between the excitation wavelength and emission maximum is 1450 cm⁻¹, which is roughly 7 times as large as the thermal energy (207 cm⁻¹) at room temperature. The observed emission was attributed to a frequency up-converted process via the HBE mechanism. The HBE intensity is dependent on the generation number of the dendrimer; a higher-generation dendrimer enables a larger HBE intensity and therefore a larger hot-band absorption cross-section. Later, this dendrimer has been found to possess a large entangled two-photon absorption cross-section.¹¹⁴

In relation to the harvesting of low-energy photons, an azobenzene unit encapsulated in a fourth-generation poly-(benzyl ether) dendrimer has been reported to undergo *cis*-to-*trans* isomerization when exposed to noncoherent infrared (IR) light of 1600 cm⁻¹ absorbed by the dendrimer framework.¹¹⁵ This observation is intriguing because vibrational excitation energy is known to be thermalized instantaneously and dissipate but is not localized. Together with the fact that lower-generation homologues as well as nondendritic azobenzenes are not at all responsive to IR light, one may assume that an unusual process takes place involving the retardation of vibronic energy dissipation in large poly(benzyl ether) dendrimers. Kitagawa et al. investigated this possibility by applying continuous wave (CW) anti-Stokes Raman spectroscopy to a fourth-generation poly(benzyl ether) dendrimer with a chloroiron(III) porphyrin unit at its center (**14·FeCl**).¹¹⁶ When **14·FeCl** is exposed to noncoherent IR light of 1600 cm⁻¹ for vibronic excitation of the dendron units, a rise in the Boltzmann temperature for an axial Fe–Cl stretching mode at 355 cm⁻¹ results, which is much larger than the corresponding increase observed for a porphyrin in-plane mode at 390 cm⁻¹. Although the dendrimer shell captured most of the IR energy, no anti-Stokes Raman band was found for the phenyl ν_8 mode at 1597 cm⁻¹. From these observations, the energy of the IR photons, captured by the dendrimer shell, appears to be directionally transferred to the axial Fe–Cl bond of the iron porphyrin core very rapidly and then relaxed to the porphyrin macrocycle. This observation is again intriguing and certainly needs further studies to clarify the mechanism.

5.2. Energy Migration and Transfer in Dendrimers with Multiple Porphyrin Units

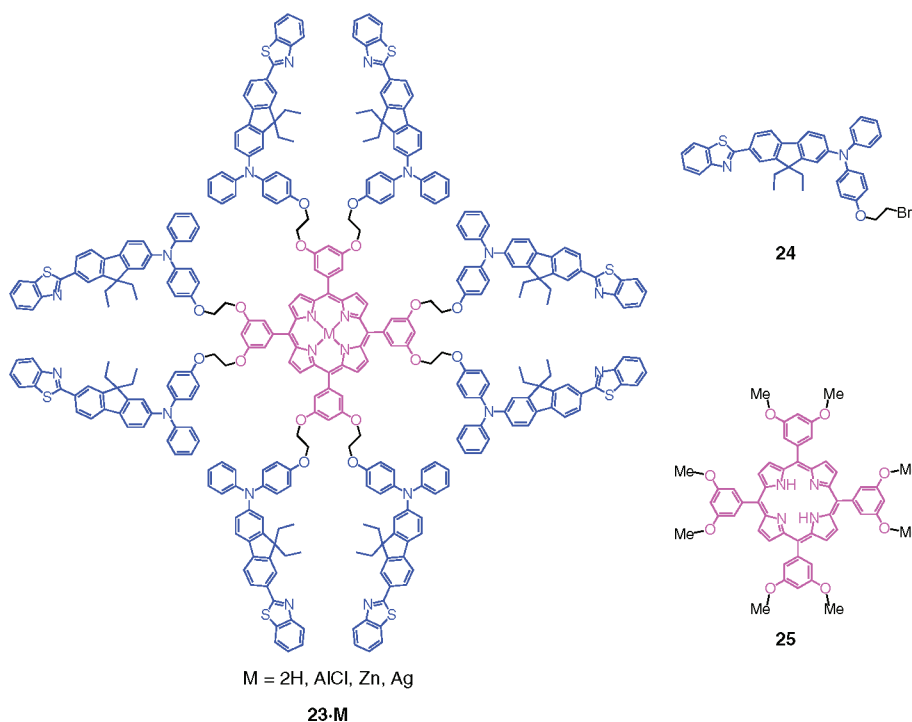
Light-harvesting purple bacteria make use of a large number of specifically arranged bacteriochlorophyll units for harvesting photons in the visible range. To mimic such fascinating light-harvesting processes, a variety of synthetic models have been reported.^{117,118} Dendrimers provide an attractive scaffold for this purpose, because they can accommodate a large number of porphyrin units that may be arranged specifically on the nanoscopic scale.

Chart 7



22

Chart 8



With the aim of mimicking light-harvesting complexes LH1 and LH2, which possess wheel-like arrays of bacteriochlorophyll units, dendrimers **27** and **28** have been synthesized (Chart 10). These compounds anchor 24 and 36 zinc porphyrin (P_{Zn}) units, respectively, on the periphery of hexaarylbenzene-cored poly(aryl ester) dendrimers.¹¹⁹ The excitation energy is efficiently transferred along the arrayed

zinc porphyrin units, as confirmed by time-resolved fluorescence and absorption anisotropy measurements. For example, when dendrimer **27**, which contains two-branched porphyrin segments, was excited with a polarized laser pulse, a transient absorption spectrum with an anisotropic character was observed. This anisotropy decayed rapidly, with two components having lifetimes of 18.9 and 130.7 ps. Although

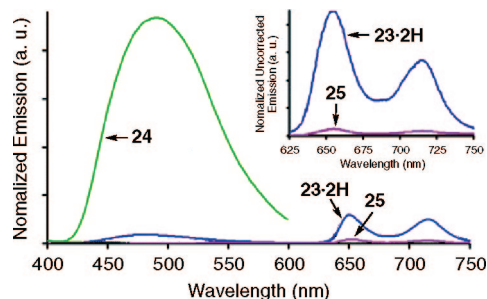
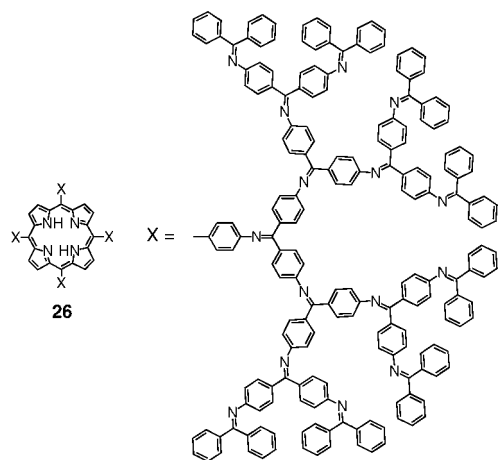


Figure 7. Fluorescence spectra of compounds **23·2H**, **24**, and **25** in CHCl_3 at room temperature upon excitation at 385 nm. The spectra are normalized to the absorbance at 385 nm. Inset: Fluorescence spectra of compounds **23·2H** and **25** in benzene- d_6 at room temperature upon excitation with 780 nm laser. Adapted with permission from ref 100. Copyright 2004 American Chemical Society.

Chart 9



a two-component decay of the anisotropy also occurred for dendrimer **28**, which consists of three-branched porphyrin segments, the components had longer lifetimes (33.1 and 205.0 ps) than those of **27**. Together with other photophysical observations, this provides evidence that the porphyrin units in **27** may form a continuous array, which is beneficial for long-distance energy migration, while the porphyrin units in **28** likely form clusters, where energy migration may be localized. It was later found that the addition of a bipyridyl guest molecule, which is capable of being intercalated in the peripheral porphyrin units of **27**, results in suppression of the $\text{P}_{\text{Zn}}-\text{P}_{\text{Zn}}$ interaction and an enhancement of the fluorescence quantum yield.¹²⁰ Intramolecular energy migration has also been investigated in a large and flexible poly(propylene imine) dendrimer with 64 peripheral zinc porphyrin units.^{121–126} In addition, more complex system **29a** has been reported (Chart 11), which possesses 16 zinc porphyrin (P_{Zn}) units on one hemisphere and 16 free-base porphyrin (P_{FB}) units on the other hemisphere of a fifth-generation poly(L-lysine) dendrimer.^{127,128} Photoexcitation of the P_{Zn} units results in energy transfer to the P_{FB} units with an efficiency of 43%. As a reference compound, dendrimer **29b**, which contains randomly mixed P_{Zn} and P_{FB} units on the dendrimer surface, shows a much higher energy transfer efficiency (85%).¹²⁹ Thus, the photoexcitation of a P_{Zn} unit in **29a** might be followed by energy migration, although with a certain loss of energy, to neighboring P_{Zn} units in the same hemisphere before transfer to a P_{FB} unit in the other hemisphere takes place.

Aida et al. have investigated multiporphyrin dendrimer **30** (Chart 12),^{130,131} which consists of four wedges of a dendronized P_{Zn} heptamer acting as energy-donating units and a focal P_{FB} unit acting as an energy trap. When the P_{Zn} unit is excited, the focal P_{FB} core emits fluorescence that is much more intense than that of the fluorescence emitted upon direct excitation of the P_{FB} core. Therefore, the dendritic zinc porphyrin units serve as antennae; the value of Φ_{ENT} for the P_{Zn} -to- P_{FB} energy transfer process has been estimated as 71%. In contrast, dendron **31**, a conical modification of **30** consisting of a heptameric zinc porphyrin dendritic array, shows a much lower efficiency (19%) for the P_{Zn} -to- P_{FB} energy transfer. Thus, the morphology of the chromophore array plays an important role in determining the efficiency of the intramolecular energy transfer. As suggested by a fluorescence depolarization study, the energy transfer in **30** likely takes place cooperatively among the dendronized P_{Zn} units, a situation analogous to the photochemical events in bacterial light-harvesting complexes. More recently, a light-harvesting array containing a rigid backbone, functionalized with peripheral zinc porphyrin termini and a free-based porphyrin core, has been reported,¹³² where the energy transfer from the zinc porphyrin units to the free-based porphyrin core is 55%.

An inert and stable erbium(III)-cored complex (**32**, Chart 13) accommodating dendritic metalloporphyrin ligands has been reported.¹³³ Each metalloporphyrin ligand in **32** bears three poly(benzyl ether) dendritic substituents and one 4-carboxylphenyl group eligible for the complexation with an Er^{3+} ion. Thus, when this dendritic porphyrin ligand is mixed with an $\text{Er}(\text{III})$ ion, a stable 9-coordinate complex (**32**) is formed. Of interest, when a dendritic $\text{Pt}(\text{II})$ porphyrin ligand is used for the formation of **32**, a near-infrared (NIR) emission from the $\text{Er}(\text{III})$ core results upon excitation of the ligating metalloporphyrin units. This interesting energy-transfer event is highly dependent on the central metal ion of the dendritic porphyrin units. For example, no NIR emission takes place when the dendritic porphyrin units accommodate a Zn ion. A detailed mechanistic study has revealed that the energy transfer from the dendritic $\text{Pt}(\text{II})$ porphyrin ligand to the $\text{Er}(\text{III})$ core takes place through the triplet state. Of further interest, the dendritic substituents, attached to the porphyrin macrocycles in **32**, can significantly enhance the NIR emission from the $\text{Er}(\text{III})$ core.

5.3. Electron Transfer in Dendrimer Porphyrins and Phthalocyanines

Photoinduced electron transfer (PET) is of great interest in relation to the conversion of solar energy into chemical energy in natural photosynthesis. To generate long-lived charge-separated species, essential for photosynthesis, the electron donor and acceptor units must be properly arranged.

Early examples of molecules in which PET takes place through dendritic frameworks include a negatively charged dendrimer with a zinc porphyrin core (**33·Zn**, Chart 14).¹³⁴ This dendrimer electrostatically traps a number of methyl viologen (MV^{2+}) molecules on its surface, spontaneously forming a spatially separated donor–acceptor system. When the zinc porphyrin core is photoexcited, a long-range electron transfer occurs from the singlet-excited zinc porphyrin core, through the dendrimer framework, to the trapped MV^{2+} molecules.

The covalent attachment of electron-accepting units onto the periphery of porphyrin-cored dendrimers has been

Chart 10

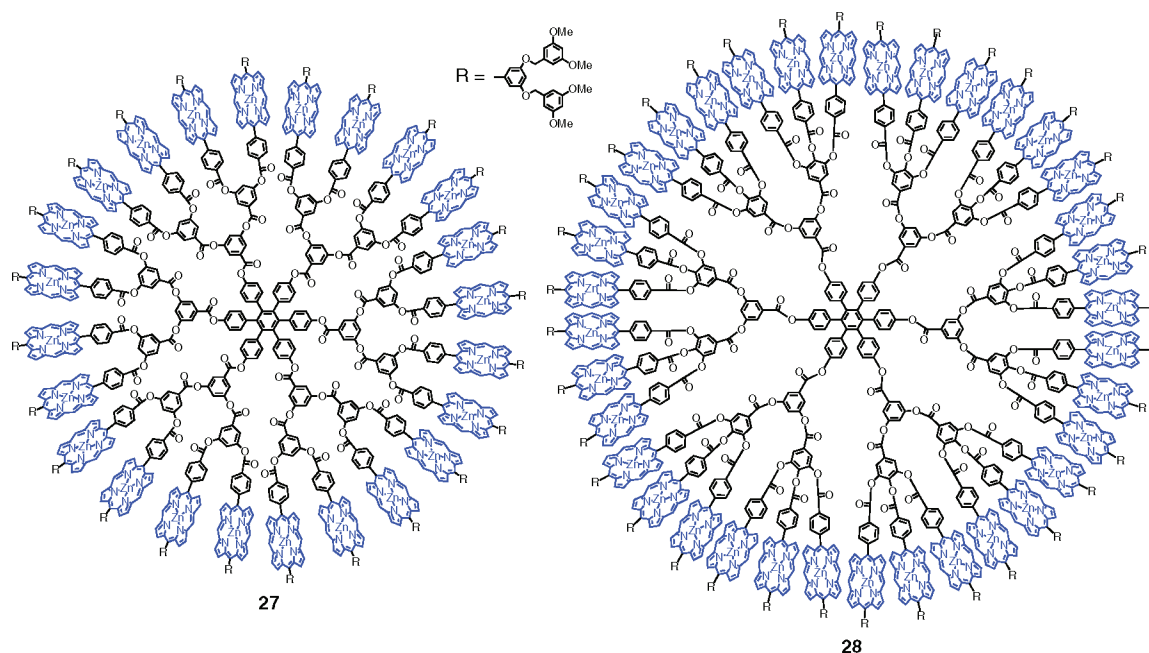
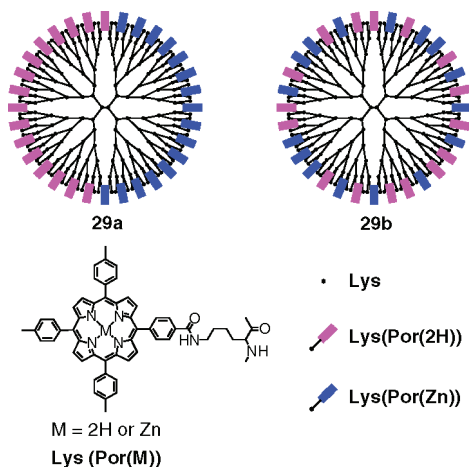


Chart 11



reported.^{135–137} For example, poly(ether-amide) dendrimer **35** (Chart 15) possesses 108 electron-accepting anthraquinone units on its surface.^{135,136} Photoexcitation of the porphyrin core results in fluorescence emission with a quenching efficiency of only 58%, indicating that **35** is not an efficient PET system. Because the fluorescence quenching efficiency of the first-generation homologue is 75%, the thick dendrimer shell in **35** between the porphyrin core and the anthraquinone units may suppress the electron transfer. More recently, porphyrin-cored dendrons bearing multiple quinone units attached to their “internal” positions have been reported.¹³⁸ Upon irradiation with visible light in the presence of 4-*tert*-butylthiophenol, the quinone units are converted into quinols. Such a behavior mimics the function of quinone pools in photosynthesis.

Fullerenes can act as attractive electron acceptors due to their small reorganization energies.¹³⁹ Thus, a variety of porphyrin-fullerene dyads, triads, and higher oligomers have been investigated as components for photoinduced electron transfer.^{140,141} Röder and co-workers have reported a porphyrin-fullerene dyad encapsulated within a globular dendritic framework,¹⁴² where the dendritic wedges are attached to the fullerene unit by a 5-fold cyclopropanation reaction.

The spectroscopic, electrochemical, and photophysical properties of the porphyrin-fullerene dyad depend on the generation number of the surrounding dendritic framework. Later, Prato et al. have synthesized a liquid crystalline version of this porphyrin-fullerene dyad and investigated photoinduced electron transfer properties.¹⁴³ Okada and co-workers have reported a snowflake-shaped dendritic donor–acceptor dyad with a porphyrin core and a fullerene (or anthraquinone) terminus.^{144,145} π -Conjugated linkages between the porphyrin and fullerene units allow a highly efficient porphyrin-to-fullerene energy transfer. Aida et al. have studied dendritic multiporphyrin arrays with a covalently attached C₆₀ focal core (**36_n**, $n = 1–3$, Chart 16), with the aim of combining energy migration/transfer and electron transfer.¹⁴⁶ Upon excitation with visible light in PhCN at 22 °C, the dendritic zinc porphyrin array of **36_n** captures the light energy and then channels it to the focal zinc porphyrin unit, resulting in an electron transfer to the focal C₆₀ unit. It is noteworthy that molecules **36₃** and **36₂** are comparable in terms of both their quantum efficiency (Φ_{CS}) and their charge separation rate constant (k_{CS}) (51% and $0.43 \times 10^9 \text{ s}^{-1}$ for **36₃** and 49% and $0.40 \times 10^9 \text{ s}^{-1}$ for **36₂**, respectively), despite the fact that **36₃** possesses a greater number of zinc porphyrin units located away from the C₆₀ terminus. Furthermore, **36₃** exhibits a smaller charge-recombination rate constant ($k_{CR} = (1.5 \pm 0.2) \times 10^6 \text{ s}^{-1}$) than do **36₂** ($(2.4 \pm 0.3) \times 10^6 \text{ s}^{-1}$) and **36₁** ($(2.9 \pm 0.3) \times 10^6 \text{ s}^{-1}$), and thus has the longest lifetime (0.66 μs) in this series. The activation energy for charge recombination in **36₃** (12.4 kJ mol⁻¹) is much greater than the activation energies of **36₂** (7.8 kJ mol⁻¹) and **36₁** (7.5 kJ mol⁻¹). These observations indicate that the zinc porphyrin radical cation, which is generated initially at the focal point of **36₃** by electron transfer, may be able to migrate away from the C₆₀ terminus toward the dendrimer periphery via an intramolecular hole-hopping process. Thus, the large dendritic wedge in **36₃** not only serves as an excellent antenna for the harvesting of visible light but may also slow the recombination process.

Dendrimers **37_n** ($n = 1–3$, Chart 17) possess a silicon phthalocyanine core with axial fullerodendritic units.¹⁴⁷

Chart 12

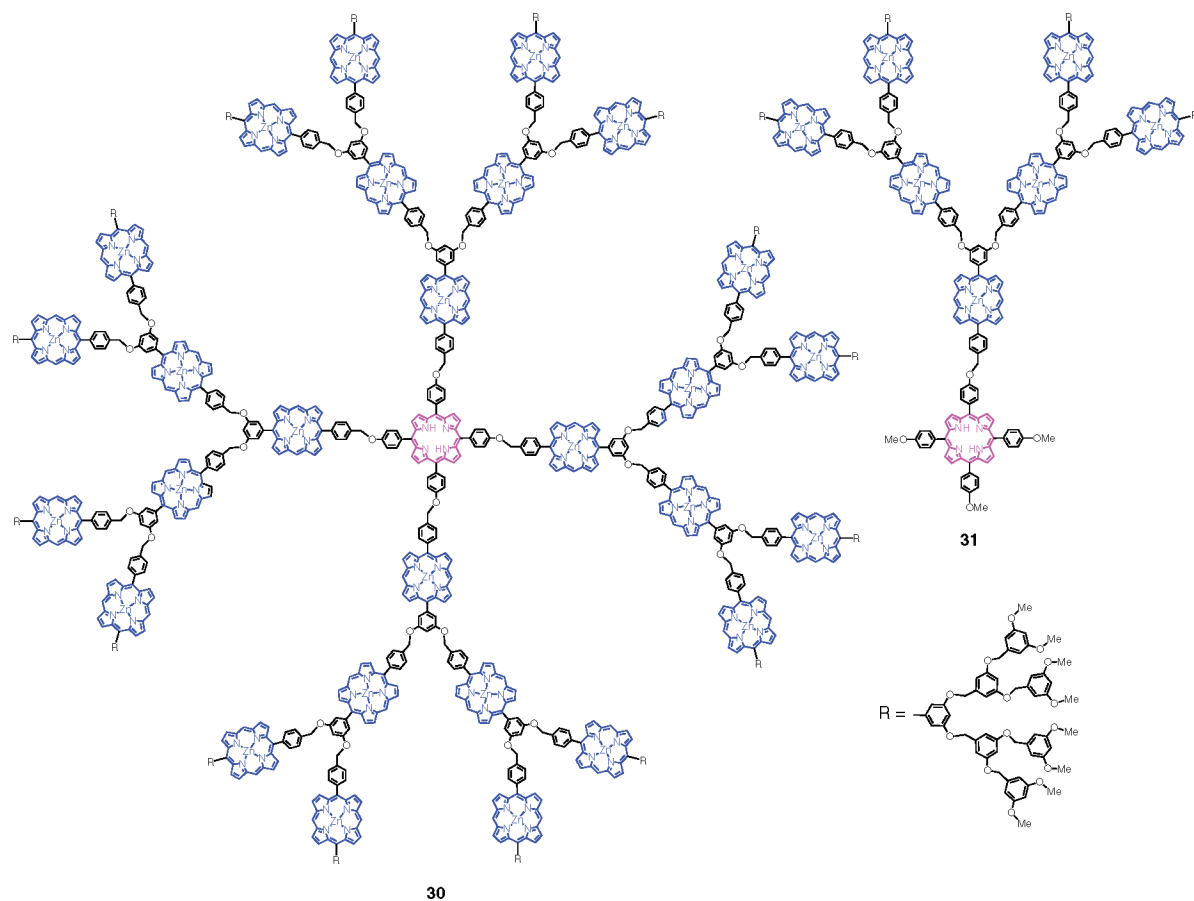
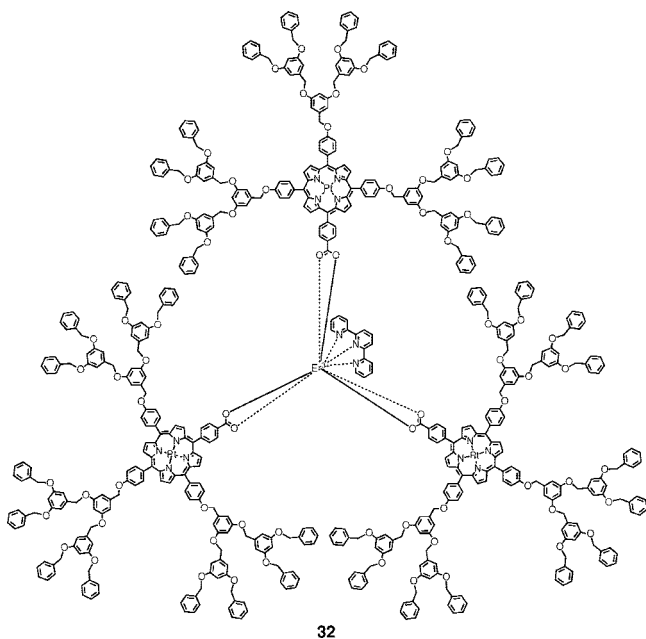
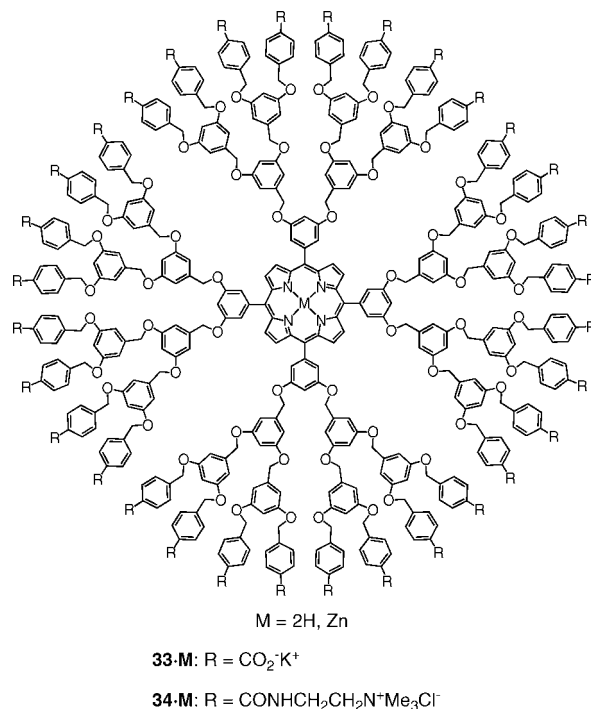


Chart 13



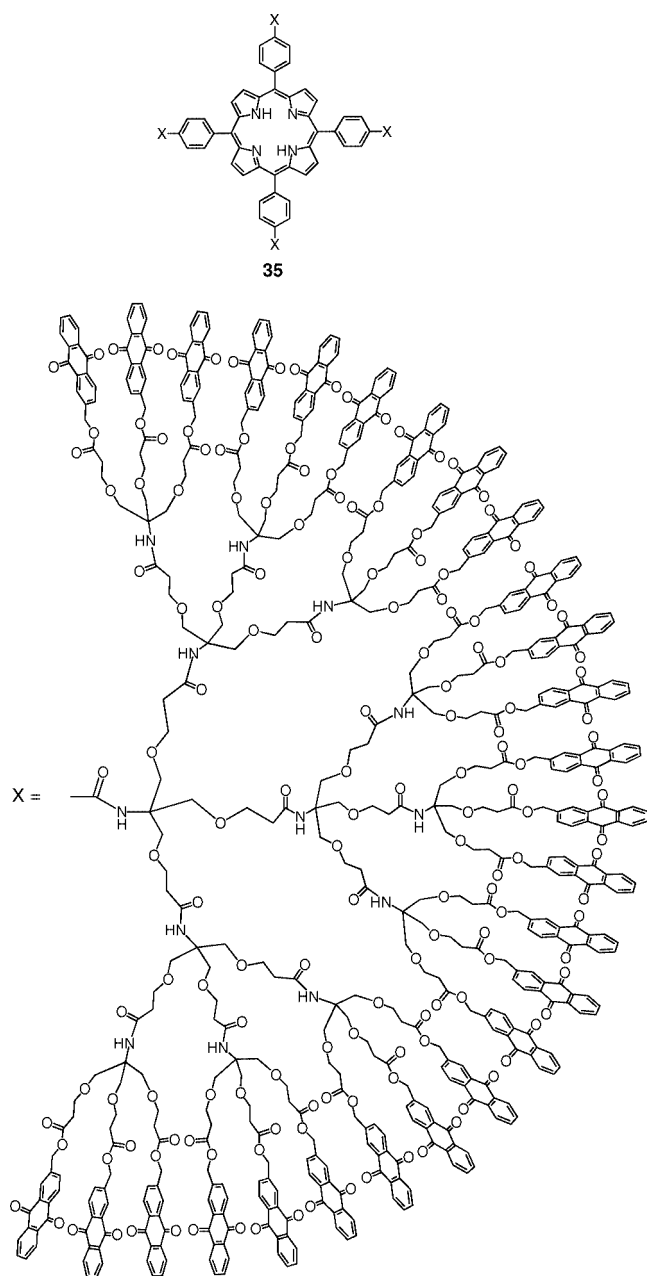
Photoexcitation of the phthalocyanine core triggers the transfer of electrons to the fullerene units, resulting in the formation of a charge-separated state. In a polar solvent such as PhCN, the lifetime of the charge-separated state increased with the number of fullerene units: 33 ns for **37₁**, 149 ns for **37₂**, and 200 ns for **37₃**. The fact that **37₃** displayed the longest charge separation lifetime implies that electron migration takes place between the C₆₀ units.

Chart 14



In addition to the covalent approach to the construction of porphyrin–fullerene dendrimers, Aida et al. have developed a noncovalent approach involving the complexation of a series of rigid poly(aryl ester) dendrimers carrying 6, 12 (**43**), and 24 (**27**) peripheral zinc porphyrin units with bipyridine guests possessing 1–3 (**38** in Scheme 4) fullerene

Chart 15



units.¹⁴⁸ For example, fullerene trimer **38** strongly binds to dendrimer **27** to form complex **27**⊃**38**, which is supposed to possess a photoactive layer consisting of spatially segregated donor and acceptor arrays on its surface (Scheme 4). These complexes are rather stable and can be isolated by size-exclusion chromatography. Furthermore, some of them can be visualized by ultrahigh-vacuum scanning-tunneling microscopy (UHV-STM). When the zinc porphyrin units are photoexcited, electron transfer takes place from the porphyrin unit to the fullerene guest, resulting in the formation of a charge-separated state. The numbers of donor and acceptor units have a strong influence on the charge separation process. The charge separation rate constant (k_{CS}) in CH_2Cl_2 at 20 °C increases with the number of zinc porphyrin or fullerene units present. It is noteworthy that complex **27**⊃**38**, the largest member of the series, exhibits a k_{CS} value of $2.3 \times 10^{10} \text{ s}^{-1}$, which is almost an order of magnitude greater than that of the complex formed by the smallest dendrimer in this study containing 6 zinc porphyrin units and a

bipyridine guest with one fullerene unit ($0.26 \times 10^{10} \text{ s}^{-1}$). These observations imply an interesting possibility that dense packing of both the zinc porphyrin and the fullerene units on the dendrimer surface promotes the charge-separation process. Meanwhile, the charge recombination rate constant (k_{CR}) remains in the range of 4.5×10^6 to $6.7 \times 10^6 \text{ s}^{-1}$ for all of these complexes. Consequently, the largest system, **27**⊃**38**, which contains 24 zinc porphyrin units and approximately 30 fullerene units (after chromatography) on the dendrimer surface, displays the best photochemical performance in this family. Importantly, the k_{CS}/k_{CR} ratio of **27**⊃**38** (3400), which is regarded as a figure of merit for the PET process, is more than an order of magnitude greater than the ratios reported for porphyrin–fullerene supramolecular dyads and triads.^{149–152} It is obvious that a large number of fullerene units enhance the probability of electron transfer occurring from the zinc porphyrin unit. Furthermore, efficient energy migration along the densely packed zinc porphyrin array¹¹⁹ may facilitate the electron transfer.

Carbon nanotubes (CNTs) are known to act as electron acceptors and can potentially be used in the construction of PET systems because of their unique one-dimensional electron-conducting nature.¹⁵³ Prato and co-workers synthesized molecule **39** (Chart 18), a single-wall CNT (SWNT) appended with a large number of porphyrin-functionalized poly(amidoamine) dendrimers.¹⁵⁴ Compound **39** was prepared by allowing the dendritic branches to grow directly from the SWNT surface using a divergent approach, followed by anchoring the porphyrin units onto the periphery of the dendritic substituents. Transmission electron microscopy (TEM) confirmed the presence of long high-aspect-ratio objects that are several micrometers in length and a few to several tens of nanometers in diameter (Figure 8). These micrographs indicate that a large number of dendritic wedges prevent the heavy aggregation of pristine HiPCO SWNTs and provide dispersed SWNTs or very thin bundles. This methodology allows one to envelop SWNTs with an electron-donating layer to form a one-dimensional coaxial heterojunction, desirable for a variety of electronic or optoelectronic applications. Excitation of the porphyrin units results in a transfer of electrons to the SWNT core, as evidenced by quenching of the porphyrin fluorescence with an efficiency of ~85%. Transient absorption spectroscopy demonstrated the occurrence of a rapid charge separation ($k_{CS} = (1.5 \pm 0.5) \times 10^{10} \text{ s}^{-1}$) and a slow charge recombination ($k_{CR} = (2.9 \pm 0.5) \times 10^6 \text{ s}^{-1}$). More recently, supramolecular structures consisting of dendritic porphyrins and SWNTs have been reported,¹⁵⁵ where the noncovalent interactions enable the hybridized systems to cause a suitable electron transfer through a process occurring from the dendritic porphyrin core to the graphenic wall of carbon nanotubes.

The examples of PET systems discussed above mostly combine electron-accepting functionalities with dendronized porphyrins or phthalocyanines as electron donors. In contrast, compound **40** (Chart 19) utilizes a phthalocyanine derivative as the electron-accepting component by combining it with a dendronized tetrathiafulvalene (TTF) as the electron donor.¹⁵⁶ When the phthalocyanine core is photoexcited, electron transfer from a TTF unit to the photoexcited phthalocyanine core takes place, resulting in quenching of the phthalocyanine fluorescence. However, when the TTF unit is electrochemically oxidized, the phthalocyanine fluorescence is also quenched as the consequence of electron transfer from the phthalocyanine center back to the TTF^+ unit. Similarly,

Chart 16

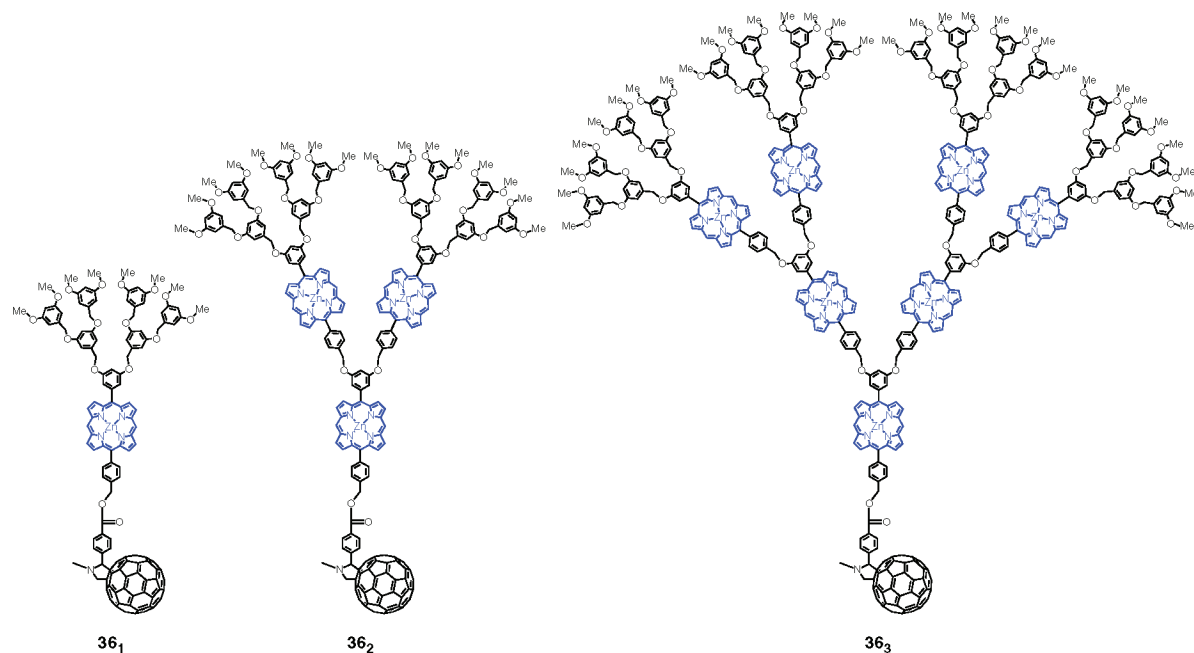
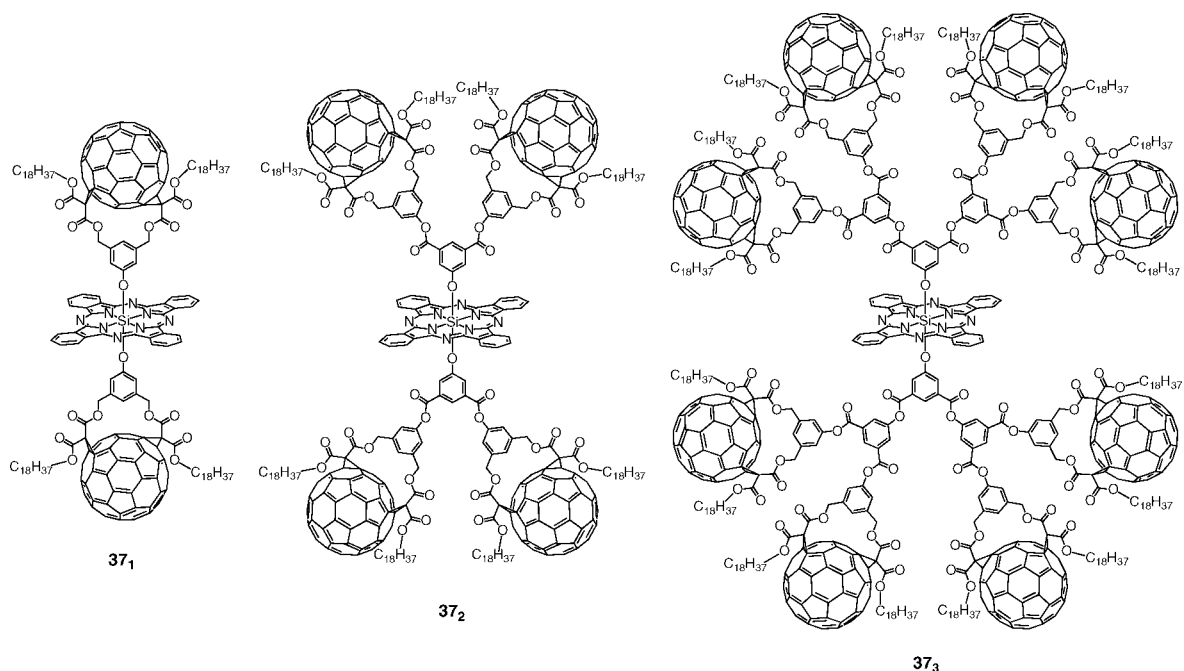


Chart 17



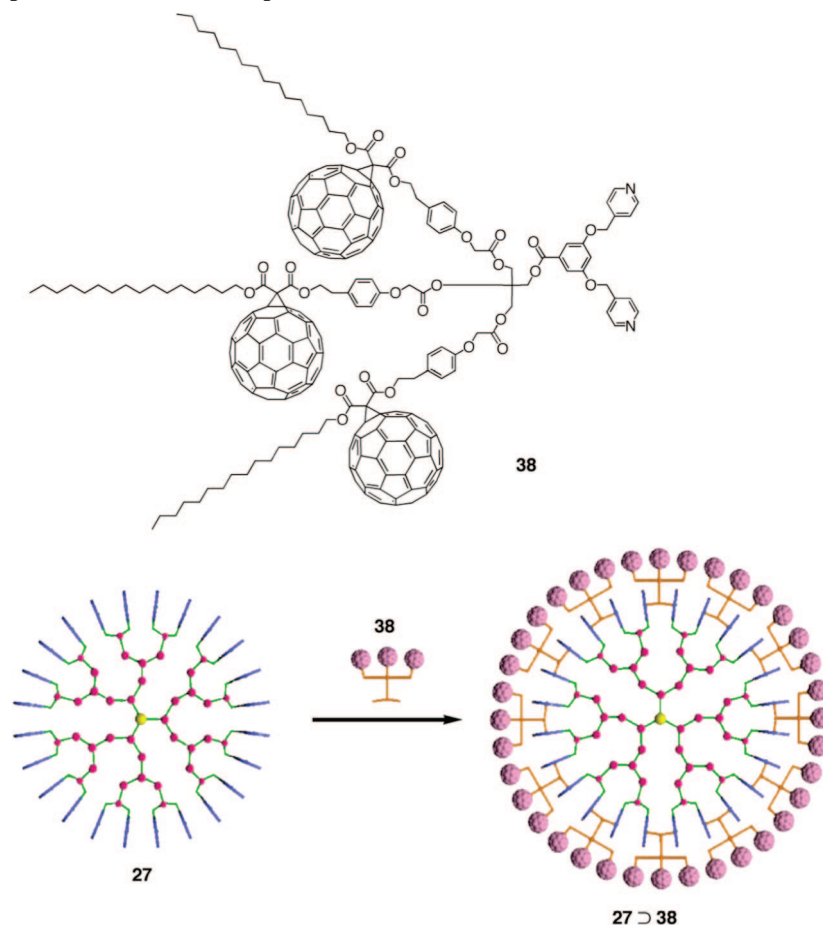
electron transfer takes place from the multiple peripheral ferrocene units to a fluorinated porphyrin at the focal core of a dendron, resulting in quenching of the porphyrin fluorescence.¹⁵⁷ Dendrimer **41** has been reported to provide an excellent PET system, in which electron transfer from the axial carbazole dendrons to the photoexcited phosphorus(V) porphyrin core takes place with an efficiency of nearly 100%.⁴³

6. Host–Guest Chemistry and Supramolecular Assembly

Metal porphyrin and phthalocyanine complexes, along with their free-base forms, are attractive motifs for use in supramolecular chemistry because they are capable of accommodating Lewis bases and assembling via strong π – π

interactions. When these features can be combined with certain properties intrinsic to the dendritic architecture, one may realize novel and unique functions that can hardly be achieved by nondendritic small molecules. For the host–guest chemistry with dendritic macromolecules, steric and encapsulation effects, along with multivalency, may often play a very important role. Steric effects are particularly important when the hosting units are embedded deeply in the dendrimer frameworks. Dendrimers can accommodate a large number of hosting units, which may function cooperatively in supramolecular assembling events.

In a recent study, gold nanoparticles with pyridyl groups attached to their surfaces were deposited on a Langmuir–Blodgett (LB) film of a π -conjugated zinc porphyrin oligomer wrapped with poly(benzyl ether) dendritic wedges, to

Scheme 4. Schematic Representation of the Complexation of 27 with 38^a

^a Adapted with permission from ref 148. Copyright 2006 American Chemical Society.

Chart 18

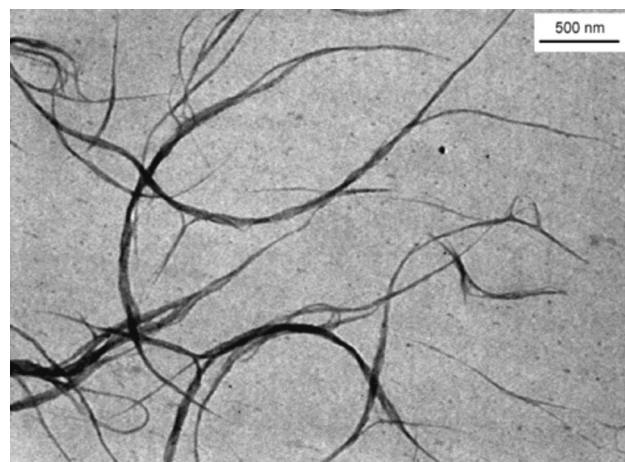
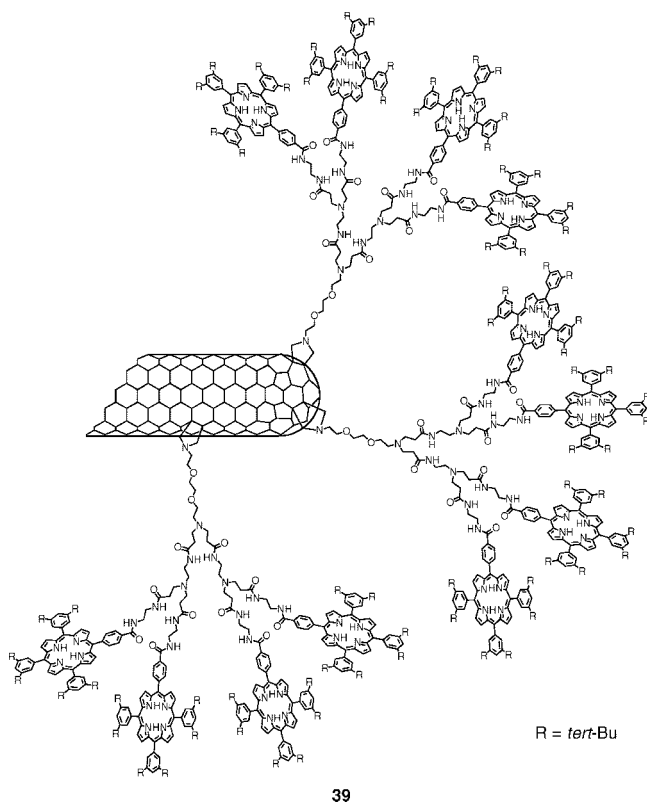
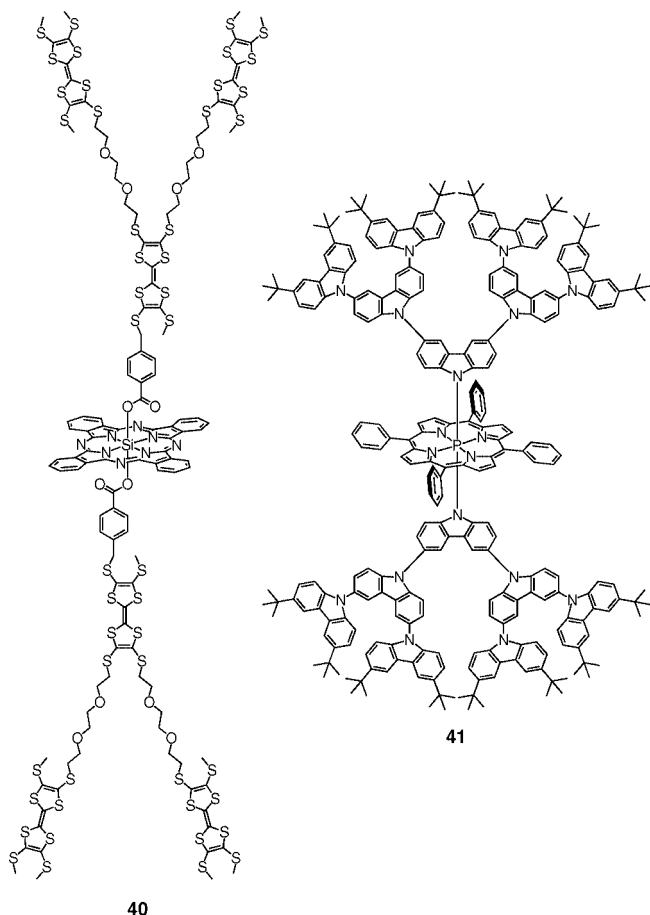


Figure 8. Transmission electron micrograph of compound **39** assembled in DMF. Reprinted with permission from ref 154. Copyright 2006 American Chemical Society.

fabricate a photofunctional composite film.¹⁵⁸ Circular dichroism spectroscopic study on the interaction of a chiral bispyridine (**44** in Figure 9) with dendritic multiporphyrin arrays having 12 (**43**, Chart 20), 24 (**27**), and 36 peripheral zinc porphyrin units (**28**) showed that these dendrimers can chiroptically sense **44**.¹⁵⁹ For example, when titrated with **44**, compound **27** exhibits an intense induced circular dichroism (ICD) signal at the Soret absorption band of the zinc porphyrin units, whose sense is determined by the absolute structure of **44** (Figure 9, red and blue curves).

Chart 19



The maximum amplitudes of the ICD measured for two-branched **27** and **43** were larger than that for three-branched **28**. Furthermore, in terms of the contribution of a single zinc porphyrin unit to the ICD, dendrimer **43** with 12 zinc porphyrin units was the best among the three dendrimers studied. It should also be noted that compound **42**, a nondendritic reference compound for the two-branched zinc porphyrin units in dendrimers **27** and **43**, cannot chiroptically sense **44** (Figure 9, black curve), indicating that a cooperative action of the dendronized zinc porphyrin units is responsible for the chiroptical sensing. The porphyrin-cored dendrimers with Hamilton receptors have been reported as efficient chirality sensors for depsipeptide dendrons.¹⁶⁰

Recently, Tsukube and co-workers have reported a series of dendrimer porphyrins with an unsymmetrically substituted zinc porphyrin core **45_n** ($n = 0-3$, in Figure 10a) named

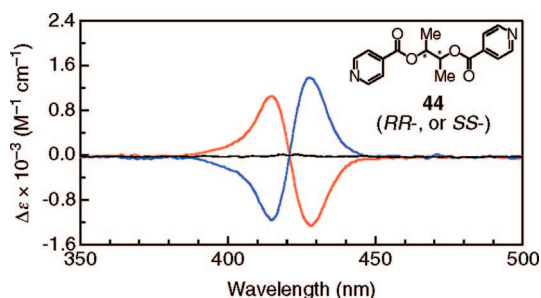


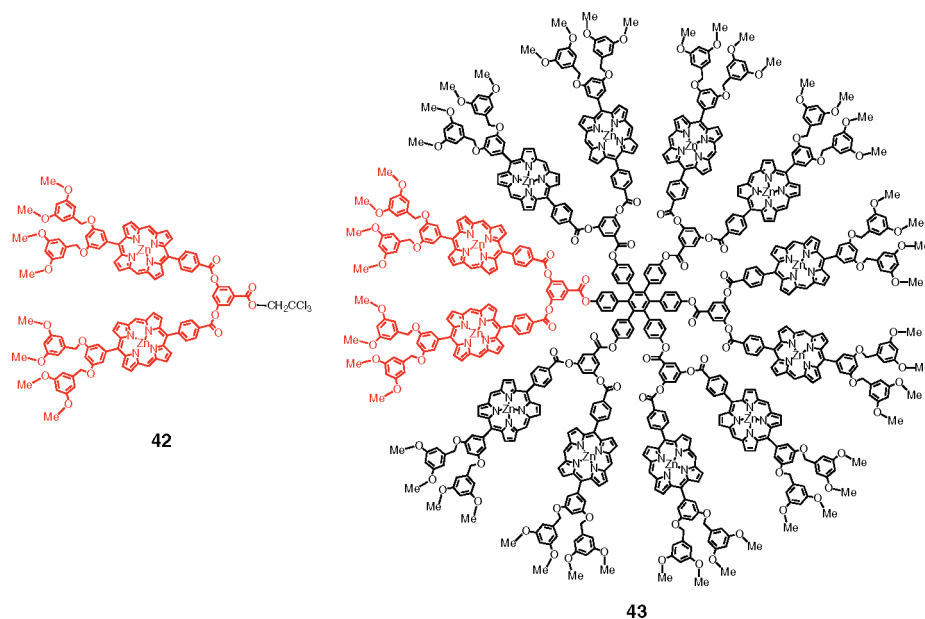
Figure 9. Circular dichroism (CD) spectra of **27** in the presence of *RR*-**44** (red curve) and *SS*-**44** (blue curve) ($[guest]/[27] = 1000$), and that of **42** in the presence of *RR*-**44** (black curve) ($[guest]/[42] = 3113$) in $CHCl_3$ at 25 °C. Adapted with permission from ref 159. Copyright 2005 American Chemical Society.

“pocket dendrimers”, which possess dendritic wedges on the three sides of the metalloporphyrin unit (Figure 10a).^{161,162} The remaining one side is open for the entrance of guest molecules. Even large dendrimer **45₂** binds pyridine guest **46** (Figure 10a) with a binding constant comparable to that observed for dendrimer **45₀** (Figure 10b). This is in sharp contrast with the reported binding behavior of fully covered dendrimer **1₂·Zn**, whose binding constant is only one-half of that of **45₀**. Of interest, such a difference between the pocket and fully covered dendrimers cannot be observed for higher-generation **45₃** and **1₃·Zn**, suggesting that the zinc porphyrin core of **45₃** may substantially be covered entirely with the three dendron substituents. Introduction of a receptor moiety such as diamidopyridine into the dendrimer pocket of **45₂** produces dendrimer **47** (Figure 11). Compound **47** is capable of simultaneously accommodating two different substrates, for example, thymine and pyridine guests, through complementary hydrogen-bonding and metal–ligand interactions, respectively (Figure 11).

More recently, Kimura and co-workers have reported an interesting intramolecular axial ligation phenomenon with zinc porphyrin-cored dendrimers (**48** as an example, Chart 21), synthesized by attaching poly(benzyl ether) dendrons to the zinc porphyrin core through click chemistry.¹⁶³ Detailed studies show that the triazole units, formed by click chemistry, behave not only as the linkers but also as ligands capable of providing a stable axial ligation to the zinc porphyrin core. The axial ligation stability is highly influenced by the position of the triazole linkers within the dendrimers. Furthermore, the triazole units in **48** constitute a direct pathway within the dendrimer architecture for electron transfer from the zinc porphyrin core to the peripheral electron acceptors, resulting in a significant rate enhancement of the photoinduced electron transfer as compared to dendrimer **33·Zn**, a similar dendritic zinc porphyrin without triazole linkers.

Because of a multiple $\pi-\pi$ interaction, molecularly engineered porphyrin oligomers are known to interact with fullerenes not only in the solid state but also in solution.¹⁶⁴ By taking advantage of this fact, a dendritic host containing a zinc porphyrin cyclic dimer at its focal core (**49**, Chart 22) has been shown to trap fullerenes inside.¹⁶⁵ Because the poly(benzyl ether) dendritic wedges of **49** are soluble in a variety of solvents and compatible with other polymers, dendrimer **49** enables the molecular-level dispersion of fullerenes in both organic solvents and polymer matrices. Kimura and co-workers reported that a derivative of dendritic **16₂** carrying long alkyl chains on its periphery forms a liquid crystalline (LC) assembly with a columnar mesophase at 39–110 °C.¹⁶⁶ Upon mixing with C_{60} , the temperature range over which the LC mesophase is formed increases to 99–250 °C, where the texture observed by polarized optical microscopy changes from mosaic to needle-like. In addition, spin-selective triplet energy transfer takes place from entrapped C_{60} to polyphenylene-based dendritic porphyrins.¹⁶⁷ Meanwhile, Shinkai et al. reported a positive allosteric effect in the complexation of C_{60} with the hexameric zinc porphyrin dendrimer **52** (Scheme 5), which has a rigid phenyleneethynylene backbone.¹⁶⁸ Because of a restricted conformational motion resulting from this rigid molecular design, the zinc porphyrin units in **52** behave like “tweezers” during the complexation process. Binding of the first C_{60} molecule between two neighboring zinc porphyrin units results in directing the neighboring porphyrin units to adopt a face-

Chart 20



to-face orientation, appropriate for trapping further C_{60} molecules (Scheme 5). Consequently, dendritic **52** can accommodate three molecules of C_{60} in an allosteric manner. Fukuzumi and co-workers reported that a flexible aromatic dendrimer bearing multiple porphyrin units on its periphery can trap a number of fullerene units.^{169–171} The resultant supramolecular complex, upon clustering on SnO_2 electrodes, shows a photovoltaic response.

By using dendrimer porphyrin **50**, synthesis of a supramolecular “peapod”, composed of one-dimensionally aligned fullerene molecules inside a dendrimer-coated supramolecular porphyrin nanotube, has been reported.¹⁷² Dendrimer **50** bears an acyclic zinc porphyrin dimer at its focal core with six carboxylic acid side groups, which is capable of forming inclusion complexes with fullerenes such as C_{60} and C_{70} (Scheme 6). These complexes are thermodynamically unstable due to a conformational freedom, but can be stabilized by subsequent dimerization through the hydrogen-bonding interaction of the CO_2H groups, located on the other side of the dendron unit. Bilateral supramolecular polymerization of these cyclodimeric inclusion complexes then follows, again taking place via the hydrogen-bonding interaction of the oriented CO_2H groups, to give peapod-like fullerene-containing zinc porphyrin nanotubes. Transmission electron microscopy revealed the presence of very long ($>1 \mu m$)

nanofibers with a uniform diameter of 15 nm (Figure 12a). At $-40^\circ C$ in 1,1,2,2-tetrachloroethane- d_2 , included C_{60} , for example, showed a broad ^{13}C NMR signal at δ 139.6 ppm, indicating that the motion of C_{60} within the nanotube is constrained. In the absence of fullerenes, dendrimer **50** only forms a hydrogen-bonded, ill-defined aggregate (Figure 12b).

Porphyrins in dendritic architectures can serve as a spectroscopic probe and provide information on the assembly processes of dendritic macromolecules. Poly(benzyl ether) dendrimer **51**, which has a zinc porphyrin bis-carboxylic acid at its core, has been reported to undergo supramolecular polymerization, affording very long nanofibers composed of a zinc porphyrin *J*-aggregate.¹⁷³ Because of the presence of a dendritic coat, these nanofibers can disperse in solution. Spin-coating of the nanofiber dispersion on a glass plate gave a chiroptically active thin film, whose sense is determined by the direction of spinning. Considering that dendrimer **51** is achiral, this observation suggests an interesting possibility that the spin-coating process gives rise to *J*-aggregated porphyrin arrays with a helical geometry, at either the molecular or the macroscopic level. More recently, a similar chiroptical response has been observed by stirring a solution of the nanofibers of **51** in a cuvette using a mechanical or magnetic stirrer (Figure 13).¹⁷⁴ Detailed investigations revealed that this chiroptical response originates from a

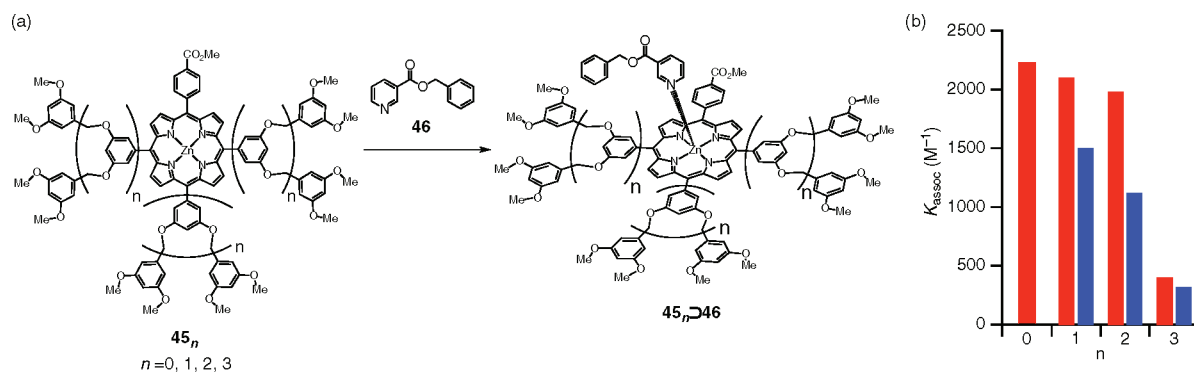
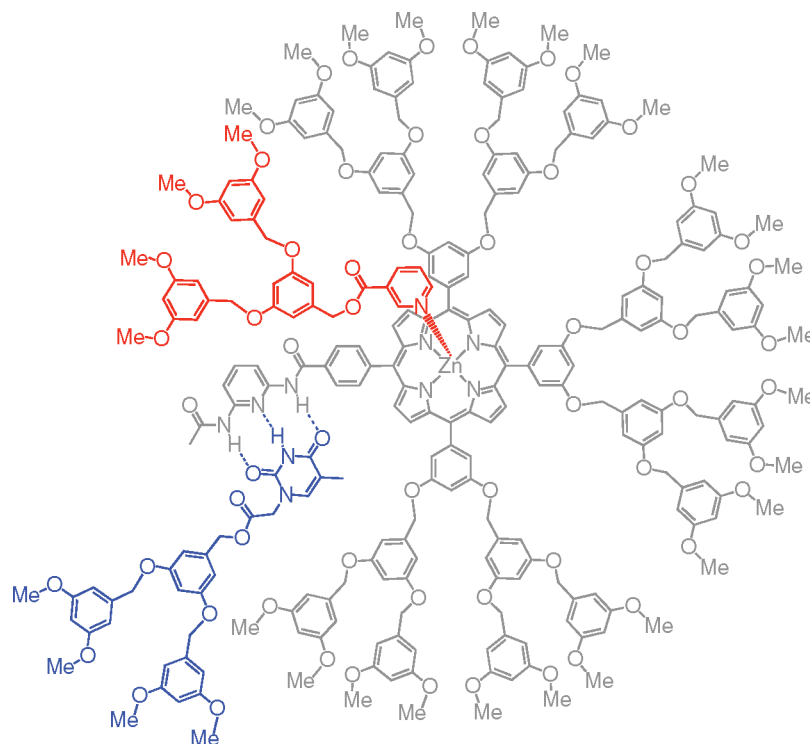


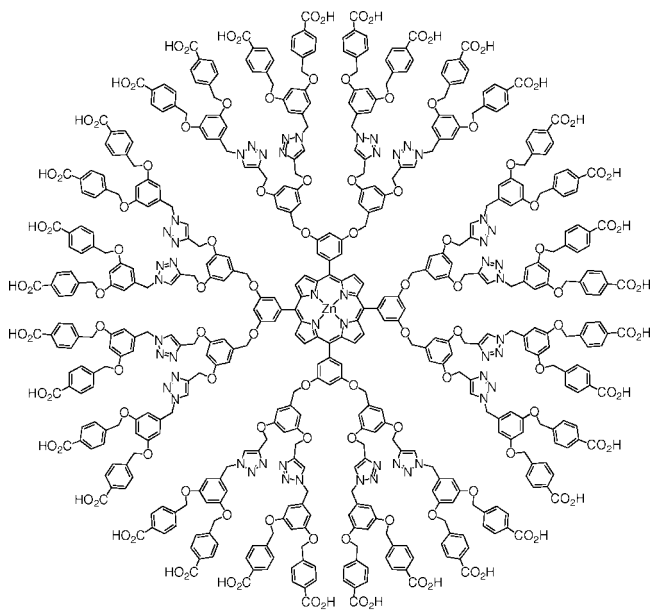
Figure 10. (a) Complexation between dendrimer zinc porphyrins 45_n and pyridine derivative **46**. (b) Association constants of **46** with 45_n (red) and reference compounds $1_n \cdot Zn$ (blue) in $CHCl_3$ at $25^\circ C$. Adapted with permission from ref 161. Copyright 2007 Wiley–VCH Verlag GmbH & Co. KGaA.



47

Figure 11. Bimolecular guest accommodation with pocket dendrimer **47** by axial ligation and complementary hydrogen bonding. Adapted with permission from ref 161. Copyright 2007 Wiley-VCH Verlag GmbH & Co. KGaA.

Chart 21

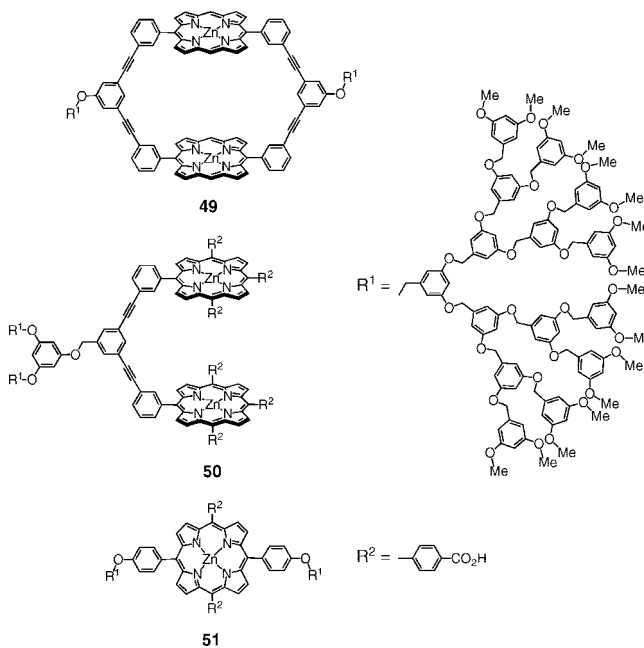


48

macroscopic helical orientation of the nanofibers, analogous to that of mesogenic molecules in cholesteric liquid crystals. The nanofibers in the cuvette align mainly in the vertical direction due to a centripetal force generated by the motion of the stirrer, and then sense the rotary flow of the fluid. The successful spectral visualization of vortex flows by the nanofibers of **51** is rather surprising considering that the sample dispersion is a nonviscous fluid.^{175–177}

Electrostatic supramolecular interactions are important for polyelectrolytes and may be useful for the layer-by-layer casting of dendritic macromolecules with different functions. An electrostatic interaction between negatively and positively

Chart 22

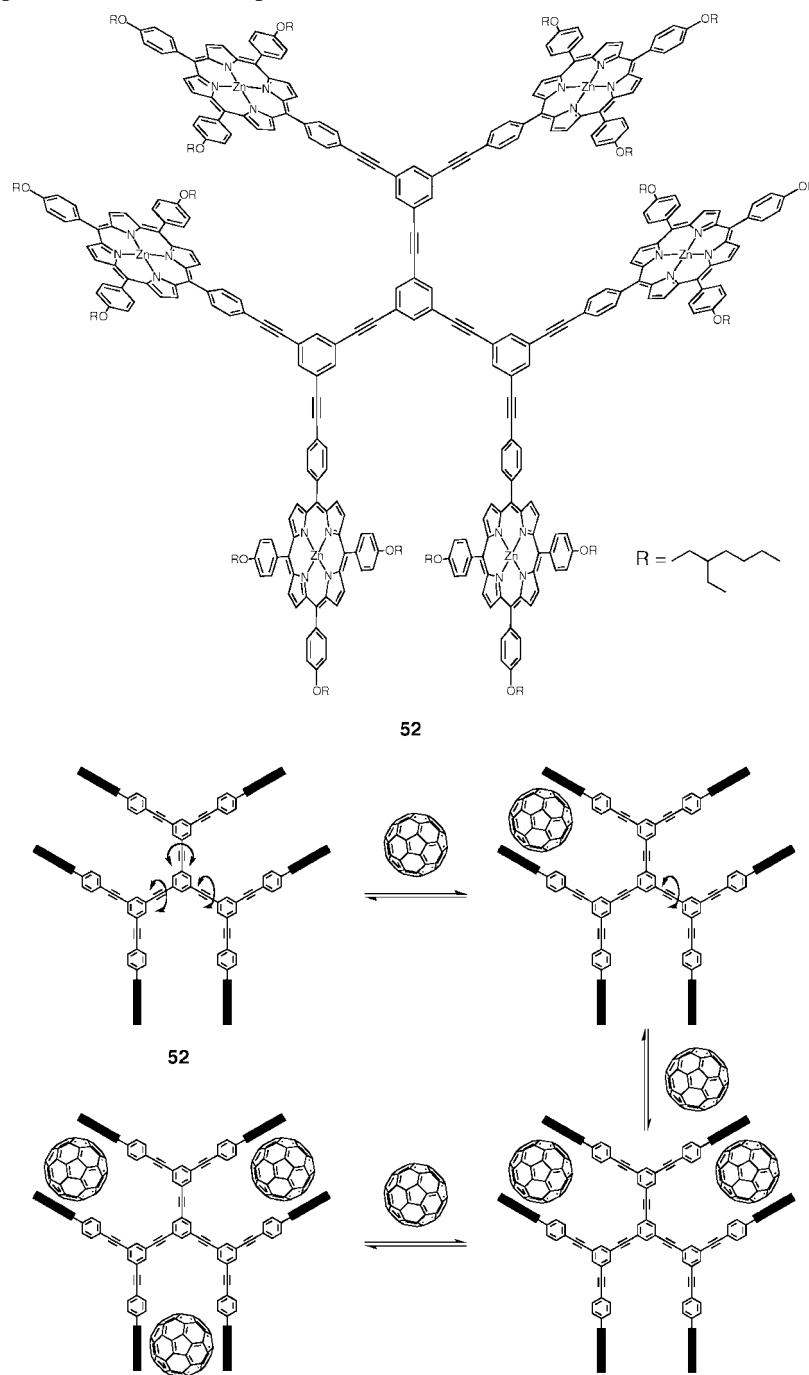


49

50

51

charged dendrimers has been investigated for **33·2H** and **34·Zn**, which bear free-base and zinc porphyrin cores, respectively.¹⁷⁸ The assembly of this system can be studied by utilizing the fluorescence resonance energy transfer (FRET), known to occur between zinc and free-base porphyrins. When a buffered solution of **33·2H** is mixed with an equimolar amount of **34·Zn**, an insoluble aggregate is formed (Scheme 7). In contrast, when either of these dendrimers is in excess with respect to the other, no precipitation takes place because the dendrimer in excess can wrap entirely around its counterpart to form a core–shell assembly with a surface that contains only negative or

Scheme 5. Schematic Representation of the Complexation of Dendrimer **52** with C_{60} ^a

^a Adapted with permission from ref 168. Copyright 2002 Wiley–VCH Verlag GmbH & Co. KGaA.

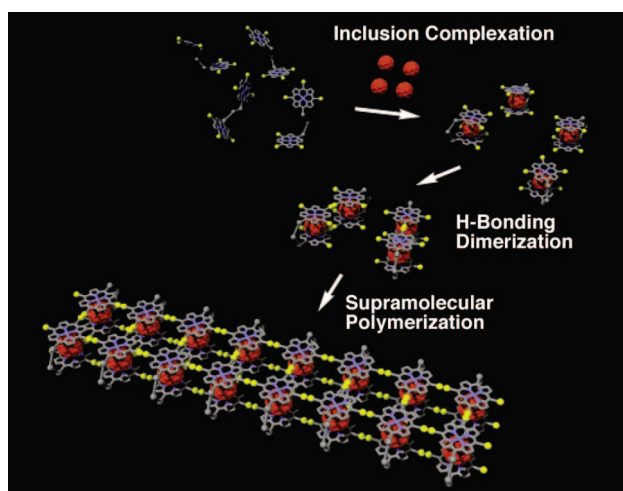
positive charges. Such a composition-dependent change in solubility does not occur for linear polyelectrolytes because they become tightly entangled with one another. Fluorescence anisotropy suggested that the core dendrimer is surrounded by four molecules of the oppositely charged dendrimer. In a similar study, Ng et al. reported that a surfactant can help the solubilization of a carboxylate-appended phthalocyanine-cored dendrimer in water via an electrostatic interaction.^{179,180}

Amphiphilic molecular design is useful for the controlled assembly of dendrimers in water. Kobayashi and co-workers reported the synthesis of silicon phthalocyanine-cored amphiphilic dendron **53** (Chart 23), which bears a single hydrophobic alkyl chain on one side of the core and a bulky hydrophilic poly(benzyl ether) dendritic wedge with periph-

eral carboxylate groups on the other side.¹⁸¹ In water, this mushroom-shaped amphiphilic dendron self-assembles into spherical micelles where the critical micelle concentration is very low (10^{-7} – 10^{-6} M). Upon addition of excess acetic acid to protonate the carboxylate groups of **53**, the micelles are broken, and **53** is extracted into an organic phase (Figure 14a). When aqueous KOH solution is added to the resulting biphasic system to ionize the resultant CO_2H groups, dendrimer **53** reverts back to the aqueous phase and forms micelles. This pH-dependent, reversible micellar assembly (Figure 14b) can be used for trapping and releasing hydrophobic guest species.

Zimmerman and co-workers reported an interesting phenomenon referred to as “molecular imprinting”.^{182,183} Here,

Scheme 6. Schematic Representation of the Coassembly of CO₂H (Yellow)-Appended Dendritic Acyclic Zinc Porphyrin Dimer **50 with Fullerenes To Form a Supramolecular "Peapod"^a**



^a Adapted with permission from ref 172. Copyright 2003 American Chemical Society.

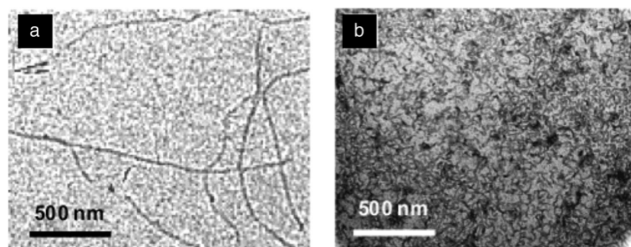


Figure 12. TEM micrographs of (a) a mixture of **50** and C₆₀ and (b) **50** alone. Samples were cast from 1,1,2,2-tetrachloroethane after being once heated at 120 °C, followed by incubation at 40 °C for 4 days, and staining with RuO₄. Reprinted with permission from ref 172. Copyright 2003 American Chemical Society.

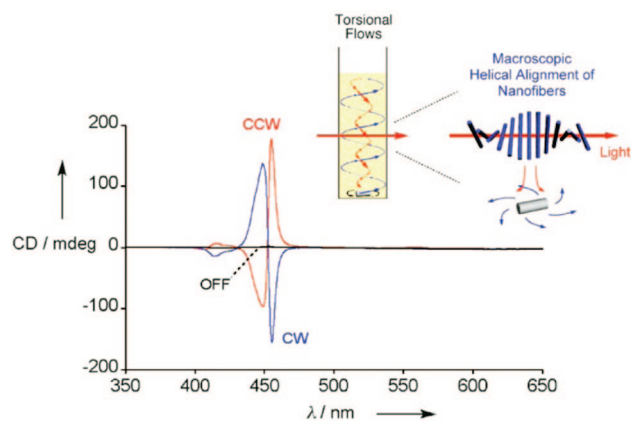
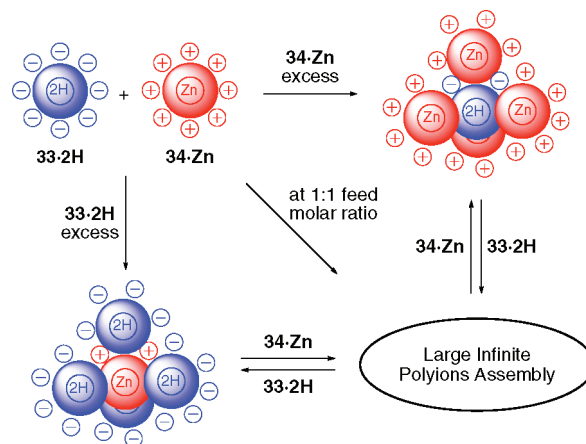


Figure 13. Circular dichroism (CD) spectra of a benzene solution of **51** (6.0×10^{-6} M) upon bottom rotary stirring at 1350 rpm in clockwise (CW, blue curve) and counterclockwise (CCW, red curve) directions, and without stirring (OFF, black curve). The inset shows a schematic representation of the torsional flows generated upon bottom counterclockwise (CCW) rotary stirring and the accompanying macroscopic helical alignment of the nanofibers. Adapted with permission from ref 174. Copyright 2007 Wiley–VCH Verlag GmbH & Co. KGaA.

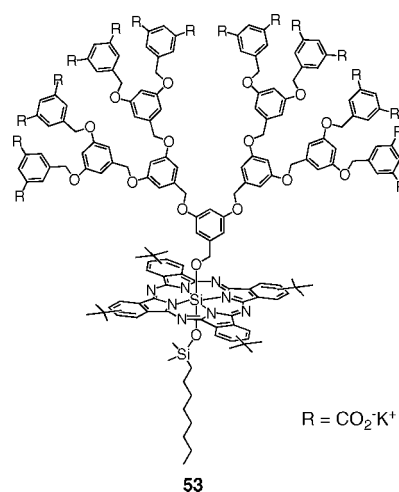
a porphyrin-cored dendrimer **54** (Scheme 8) was designed to possess a total of 64 allylic end groups and a porphyrin core that is removable by hydrolysis of the connecting ester linkages. By the action of a Grubb's catalyst, dendrimer **54**

Scheme 7. Schematic Representation of the Electrostatic Aggregation of Negatively Charged Dendrimer Porphyrin **33·2H and Positively Charged Dendrimer Porphyrin **34·Zn^a****



^a Adapted with permission from ref 178. Copyright 1998 Wiley–VCH Verlag GmbH & Co. KGaA.

Chart 23



was cross-linked at the periphery. Subsequent ester hydrolysis resulted in the removal of the porphyrin core from the cross-linked dendrimer shell, producing a spherical nanocapsule with an imprinted memory of the guest species (Scheme 8). This nanocapsule is able to host a variety of porphyrin derivatives with a certain degree of selectivity. The same authors have reported that a tubular polymer can be obtained via a similar cross-linking/hydrolysis strategy applied to a coordination polymer of a dendritic tin porphyrin.¹⁸⁴

7. Biomedical Applications

7.1. Photodynamic Therapy

Dendrimer porphyrins and phthalocyanines have attracted attention as sensitizers for photodynamic therapy (PDT).^{185,186} PDT is a promising method of treating cancer with several advantages as compared to other methods such as chemotherapy, including smaller side effects and a lower likelihood of sequelae. PDT uses a photosensitizer to absorb light and transfer the acquired excitation energy or an electron to O₂ to generate reactive species such as singlet oxygen (¹O₂) and peroxide radicals. These species are highly toxic and can kill tumor tissues. Conventional photosensitizers based on small chromophoric compounds tend to aggregate in aqueous

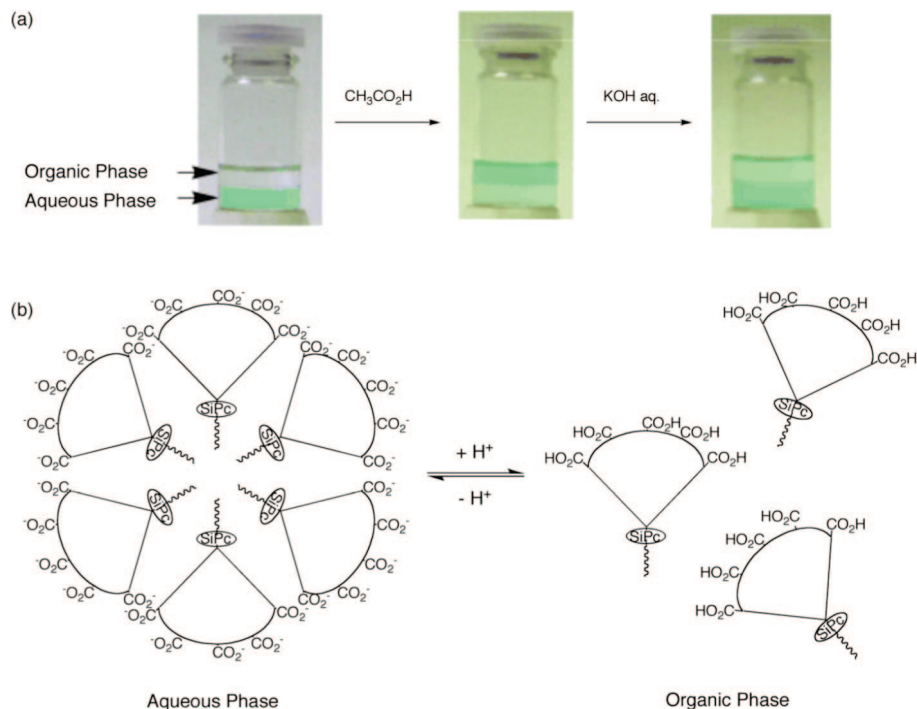


Figure 14. (a) Photographs of the transfer of **53** from an aqueous phase to an ethyl acetate phase by the addition of excess $\text{CH}_3\text{CO}_2\text{H}$, then back to the aqueous phase by the addition of KOH with vigorous stirring. (b) Schematic representation of the proposed conformations of **53** in the aqueous and organic phases. Adapted with permission from ref 181. Copyright 2003 Wiley–VCH Verlag GmbH & Co. KGaA.

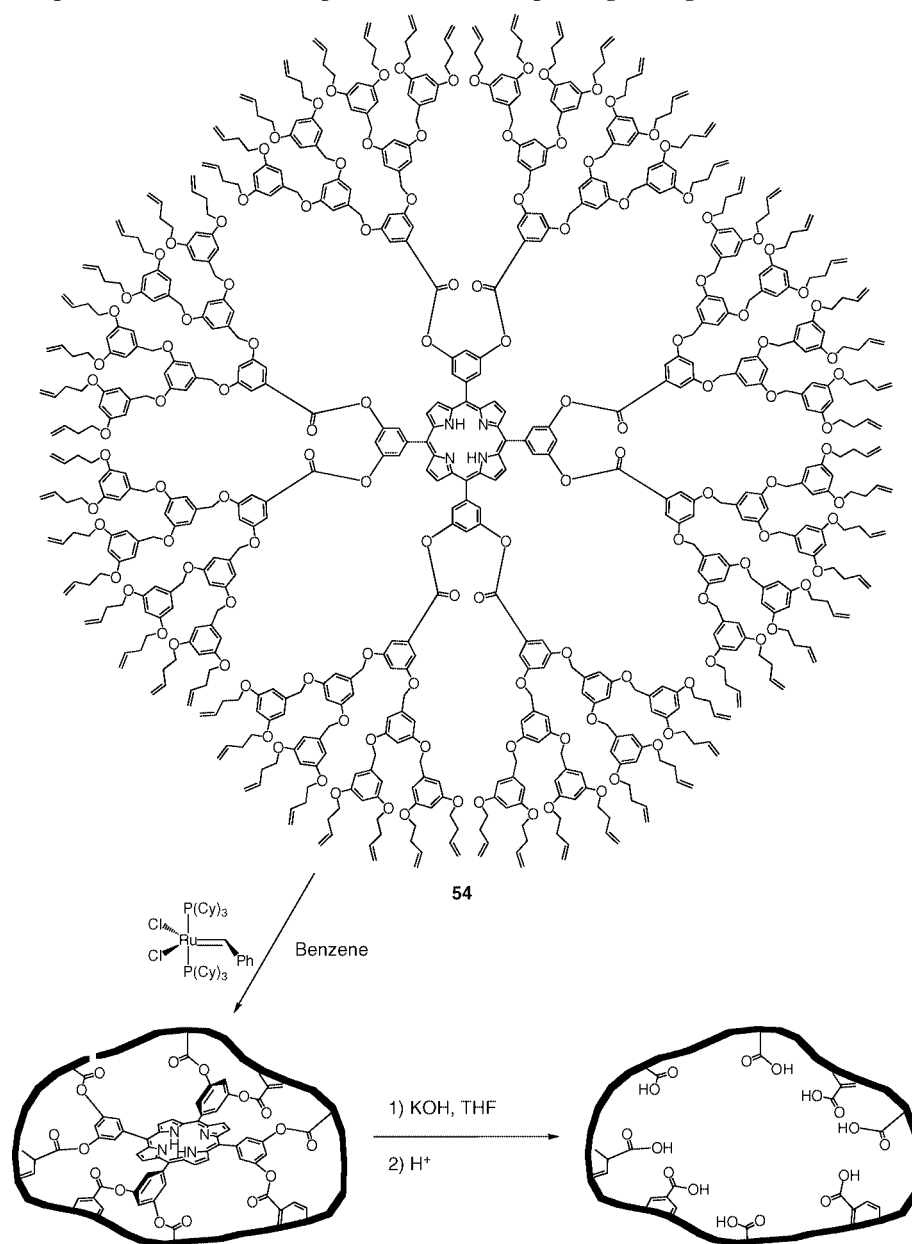
media due to π -stacking and hydrophobic interactions, resulting in self-quenching of their photoexcited states. Thus, the photodynamic (PD) effect becomes significantly weaker. Dendrimer-encapsulated chromophores are attractive for PDT because the inner chromophores are isolated from aggregation and photoactive. For PDT with small photosensitizers, another issue to consider is that such photosensitizers tend to accumulate in the skin during PDT treatments, leading to serious side effects. This issue may also be solved when dendrimer-encapsulated chromophores are used. Last, but most importantly, the large dimensions of dendrimers may allow prolonged circulation in the blood and higher accumulation of dendronized photosensitizers in the tumor tissues via the so-called EPR (enhanced permeation retention) effect.

Kataoka and co-workers have reported that zinc porphyrin-cored dendrimers with ionic surfaces can be used as a new class of photosensitizers for PDT.¹⁸⁷ Experiments using Lewis lung carcinoma (LLC) cells have demonstrated that the dendrimer porphyrins **33**·**Zn** and **34**·**Zn** can be taken up by LLC cells and eventually localized in the membrane-limited organelles. When photoirradiated, positively charged **34**·**Zn** exhibits a PD efficacy several orders of magnitude greater than that of protoporphyrin IX, a conventional photosensitizer for PDT. The PD effect of negatively charged **33**·**Zn** is smaller than that of **34**·**Zn**, most likely due to electrostatic repulsion between **33**·**Zn** and the negatively charged cellular membranes. Dendrimer **33**·**Zn** exhibits a lower cell association tendency than does **34**·**Zn**. It is also worth noting that these dendrimer porphyrins display a much lower dark toxicity to cells than does protoporphyrin IX (113-fold for **33**·**Zn** and 157-fold for **34**·**Zn**).

Kataoka et al. also found that the incorporation of **33**·**Zn** into a polyion complex (PIC) micelle, achieved by mixing **33**·**Zn** with a positively charged block copolymer such as poly(ethylene glycol)-*block*-poly(L-lysine)

(PEG-*b*-PLL) in a stoichiometric charge ratio, enhances the cellular uptake of **33**·**Zn** by 6–8 times.^{188–190} The PIC micelles are highly stable even at high salt concentrations, but are sensitive to pH changes; they can be disrupted, resulting in the release of **33**·**Zn**, once they are taken up in the slightly acidic interior of tumor tissues. Although approximately 38 molecules of **33**·**Zn** are clustered inside the PIC micelles, they do not show any fluorescence quenching even after the uptake of the PIC micelles into cells. Again, this unique photochemical property is provided by the site-isolation effect of the large dendrimeric shell. In a phosphate-buffered saline solution containing 10% fetal bovine serum as a singlet oxygen acceptor, the PIC micelles show a photoinduced oxygen consumption signature with a rate comparable to that of free **33**·**Zn**. The PD effect of PIC micelles containing **33**·**Zn** toward LLC cells is 280 times greater than that of free **33**·**Zn**. In contrast, the lower-generation homologues of **33**·**Zn** exhibit remarkably shorter fluorescence lifetimes and lower oxygen-consumption abilities, thereby leading to a small PD effect.¹⁹¹ Recently, PIC micelle-encapsulated **33**·**Zn** has been used in the PDT treatment of age-related macular degeneration (AMD), a condition caused by choroidal neovascularization (CNV), which is the leading cause of visual loss in developed countries.¹⁹² Promisingly, the PIC micelles exhibit a long-term impact with low photodamage and cause few side effects. Positively charged **34**·**Zn** can also form PIC micelles when mixed with negatively charged poly(ethylene glycol)-*block*-polyaspartate (PEG-*b*-PAA).^{188,193} When incorporated into the PIC micelles, **34**·**Zn** shows an enhanced PD effect and a reduced dark toxicity. More recently, a glycodendrion having a porphyrin unit at its focal point has been investigated as a photosensitizer for PDT.¹⁹⁴

Ordinary porphyrin derivatives absorb light of wavelengths ranging from 400 to 600 nm. Therefore, the excitation of porphyrin derivatives in vivo is hindered by

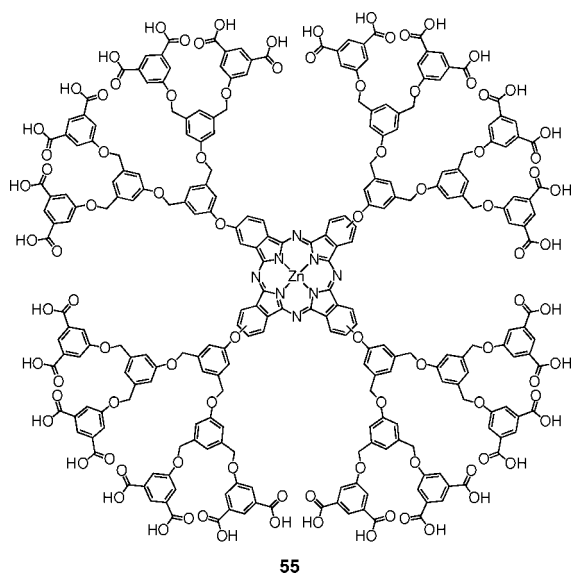
Scheme 8. Schematic Representation of the Concept of “Molecular Imprinting” Using Dendrimer **54**^{182,183}

skin tissue. For this reason, the zinc phthalocyanine-cored dendrimer **55** (Chart 24), which absorbs light of a longer wavelength than its porphyrin analogues, has been developed as a potential photosensitizer for PDT.^{195,196} This dendrimer also serves as an efficient sensitizer for photochemical internalization (PCI), a technology that utilizes light to facilitate the delivery of DNA, drugs, and other biological factors directly inside cells.^{197–199} In this application, shown in Scheme 9a, plasmid DNA (pDNA) is packaged with cationic peptides **CP**₄, formed by dimerization of the cationic peptide **CP**₂ containing a nuclear localization sequence (NLS), and the resulting hybrid is wrapped by the anionic dendrimer phthalocyanine **55**. This ternary complex is taken up by cells via an endocytic pathway, such that it becomes preferentially localized in endosomes and lysosomes. In such an acidic environment, the peripheral carboxylate groups of **55** are protonated, causing the release of **55** from the ternary complex. Dendrimer **55** subsequently interacts with the endosomal/lysosomal membranes (Scheme 9b). Upon photoirradiation, **55** generates ¹O₂, which disrupts the

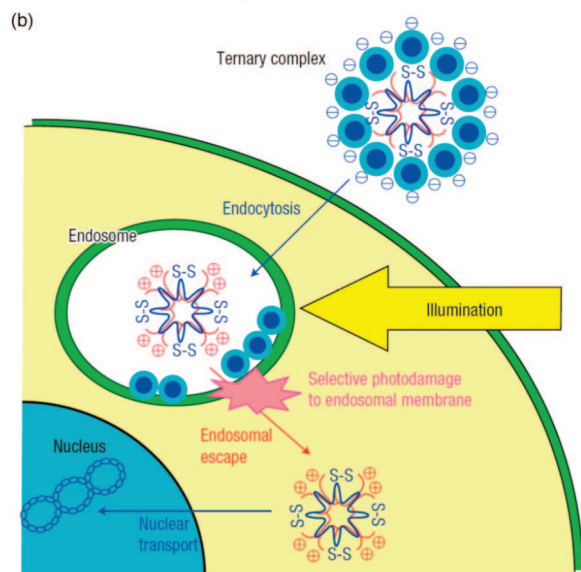
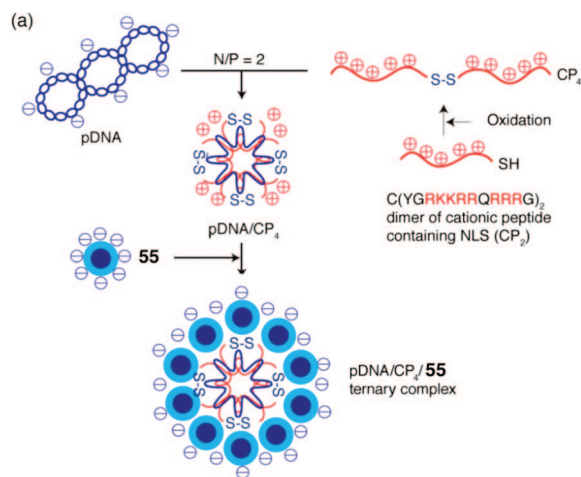
endosomal/lysosomal membranes such that the pDNA–**CP**₄ complex is released and becomes eligible for nuclear transport guided by the NLS sequence. Under illumination, the ternary complex pDNA/**CP**₄/**55** shows a greater than 100-fold enhancement of the *in vitro* transgene expression as compared to the pDNA/**CP**₄ binary complex without **55**. The photocytotoxicity of **55** is significantly lower than that of AlPcS_{2a}, an aluminum phthalocyanine derivative known as a representative photosensitizer for PCI. *In vivo* experiments with rats demonstrate that transgene expression occurs selectively at the irradiated sites. More recently, surface modification of polyamidoamine (PAM-AM) dendrimers with 5,10,15-tri(4-acetamidophenyl)-20-mono(4-carboxyl-phenyl)porphyrin (TAMCPP) has been investigated as sensitizers for PCI.²⁰⁰

As was already discussed, two-photon excitation technologies have attracted increasing attention for their potential use in PDT, because one can use near-infrared light that can penetrate deeply into the body. It is known that ¹O₂ can be generated by the transfer of energy from triplet-excited porphyrins. If two-photon excitation allows

Chart 24



Scheme 9. Schematic Representations of (a) the Preparation of a pDNA/CP₄/55 Ternary Complex, and (b) Its Role in Transgene Expression^a



^a Adapted with permission from ref 197. Copyright 2005 Nature Publishing Group.

Chart 25

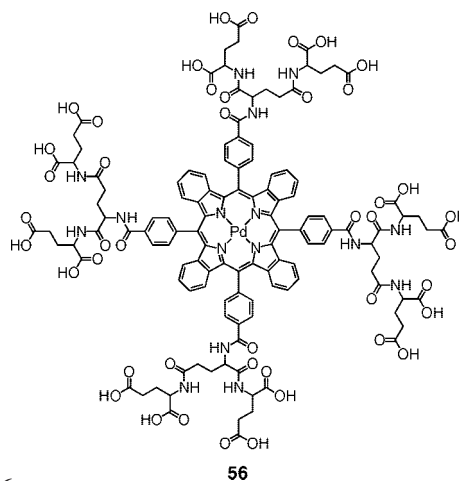
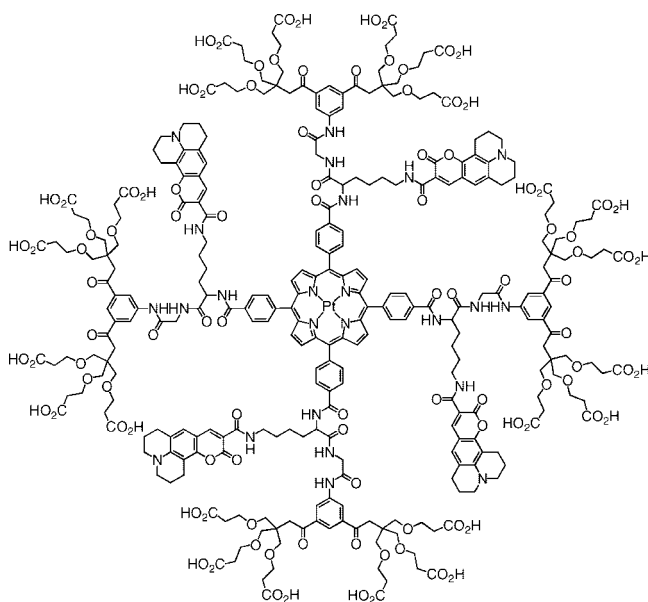


Chart 26



the formation of triplet-excited porphyrins, PDT may become of even greater practical use. Fréchet and co-workers investigated whether the two-photon excitation-induced energy transfer, observed in dendrimer **23·2H**, can be used for the generation of ¹O₂.¹⁰⁰ A core consisting of a phosphorescent metalloporphyrin such as chloroaluminum porphyrin was chosen, and it was demonstrated that **23·AlCl** can generate ¹O₂ by two-photon excitation of the dendronized AF-343 units at 780 nm.

7.2. Biosensing

Sensing of O₂ and mapping of its distribution in tissue are important subjects in the field of bioimaging. Vinogradov and co-workers developed Pd porphyrin-cored polyglutamate dendrimers, exemplified by **56** (Chart 25), as O₂-indicators for living tissues.^{201–205} Porphyrin complexes of palladium(II) and platinum(II) are known to be phosphorescent under anaerobic conditions. The O₂ sensing method is based on the fact that the lifetime of this phosphorescence is highly dependent on the concentration of O₂. The polyglutamate dendritic shell of **56** is expected to allow good biological compatibility and water solubility. To avoid self-quenching of the phosphorescence, the dendrimeric shell should be large enough to suppress

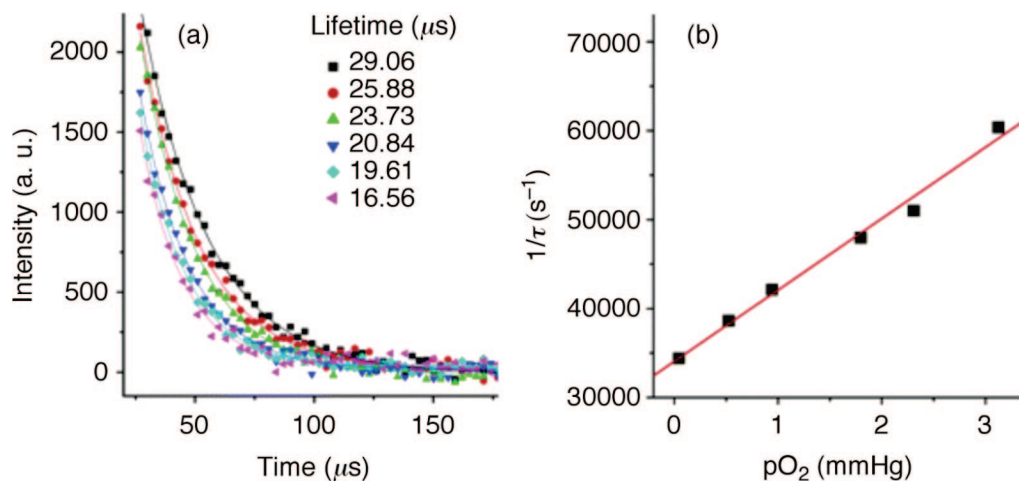
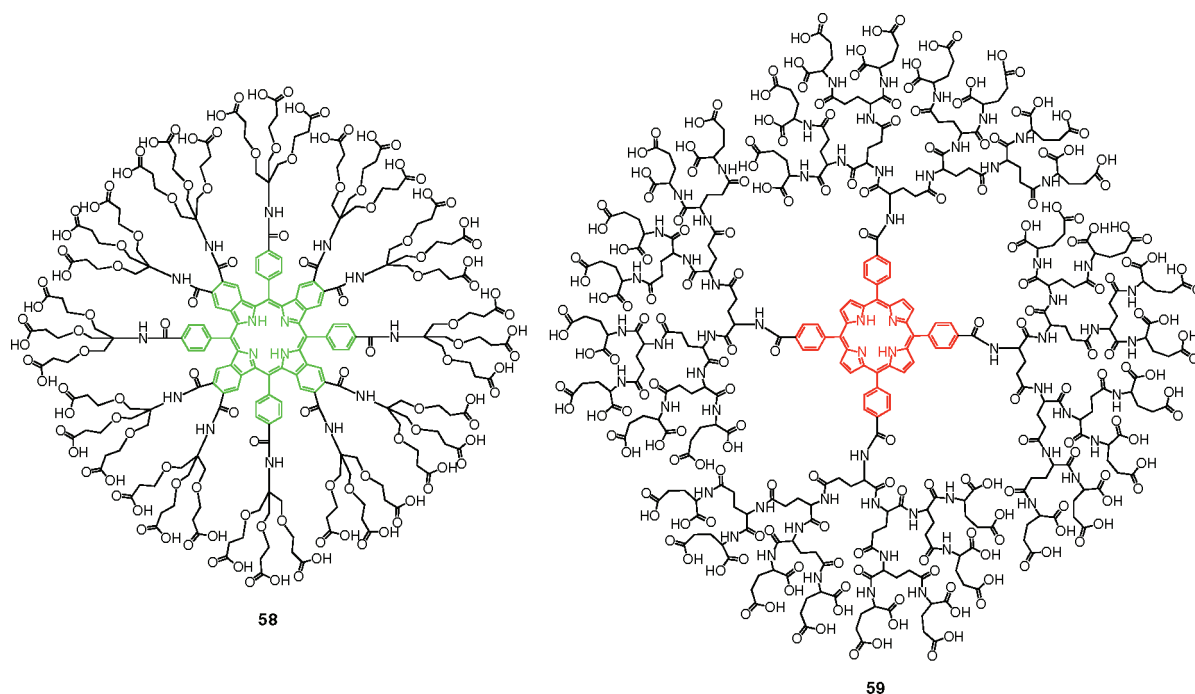


Figure 15. (a) Phosphorescence decay of **57** in DMF upon two-photon excitation at different O₂ concentrations and (b) the corresponding Stern–Volmer plots. Reprinted with permission from ref 207. Copyright 2005 American Chemical Society.

Chart 27



aggregation of the photoexcited core in water. One great advantage of the polyglutamate dendrimer, in comparison with other dendrimers, is its high O₂ permeability. Thus, even with a large polyglutamate dendrimer shell, the metalloporphyrin core can still sense O₂.^{22,206} In vivo experiments have demonstrated that dendrimer **56** can noninvasively determine the O₂ distribution in subcutaneous and retinal tumor growths in rats, and topographically image O₂ in living tissues. With the aim of developing this technique to allow near-infrared light to be used, the same group has developed dendrimer **57** (Chart 26), which bears multiple two-photon absorbing Coumarin 343 units and a phosphorescent core.²⁰⁷ Under two-photon excitation conditions with a 780 nm laser source, the Pt porphyrin core phosphoresces via an efficient energy transfer from the two-photon excited AF-343 units. The phosphorescent lifetime is again O₂-dependent (Figure 15).

Vinogradov et al. have also demonstrated the potential of carboxylate-terminated dendrimer porphyrins for biological pH sensing.^{23,41} The fluorescence profiles of free-base por-

phyrins are known to be sensitive to protonation and deprotonation of the nitrogen core. Poly(ester-amide) and polyglutamate dendrimers **58** and **59** (Chart 27), respectively, were synthesized. Because the former contains a free-base tetraaryltrabenzoporphyrin unit and the latter a tetraarylporphyrin unit, the two complexes show intrinsically different fluorescence and absorption spectral profiles. When **58** and **59** are selectively positioned outside and inside the phospholipid vesicles, respectively, only the spectra of **58** respond to a pH change induced by the addition of an acid or base to the solution (Figure 16). In contrast, in the presence of the channel-forming peptide gramicidin, both **58** and **59** respond to a pH change spectroscopically. This achievement not only takes advantage of the site-isolation effect of dendrimers to allow the emission of light in aqueous media, but also makes use of the poor membrane permeability of dendrimers.

Dendrimer **60** (Chart 28) has been reported as a new synthetic receptor for protein recognition.^{162,208,209} The molecular structure of **60** has been designed to possess several

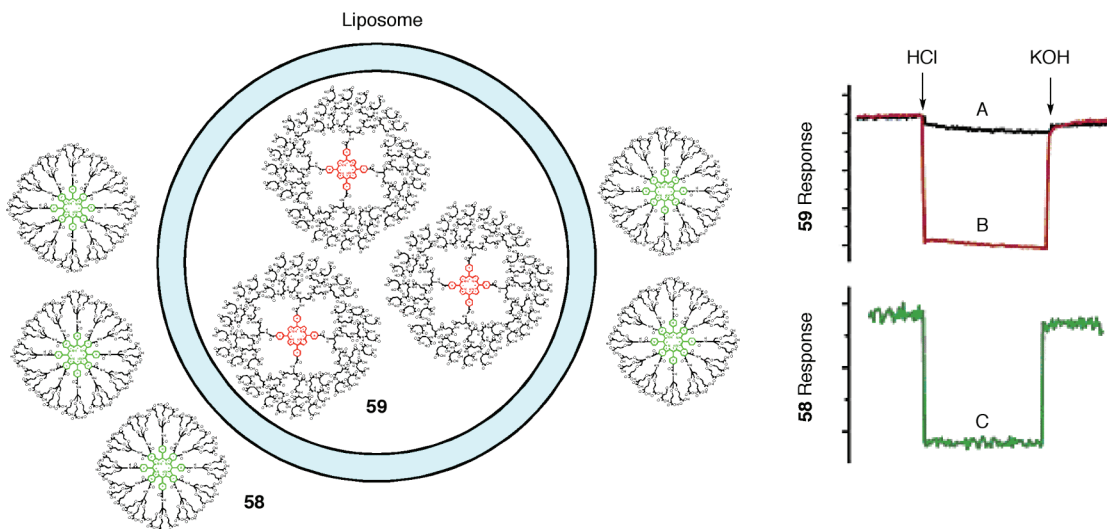
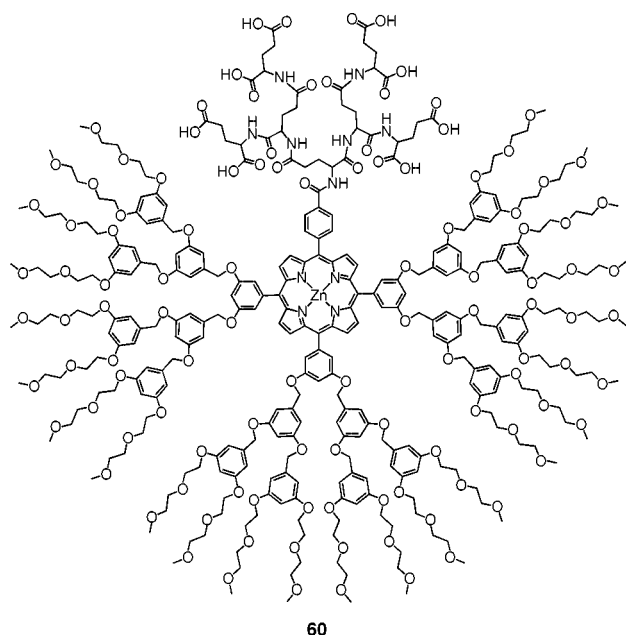


Figure 16. Phospholipid liposome with **59** captured inside and **58** staying outside its vesicular structure (10 mM phosphate buffer). Responses of **59** to applied pH changes in the absence (curve A, black) and presence (curve B, red) of 0.5 mg/mL of gramicidin. The responses of **58** (curve C, green), located outside the liposome, are not affected by gramicidin. Adapted with permission from ref 41. Copyright 2003 American Chemical Society.

Chart 28



key features: (1) asymmetrically distributed polyanionic hepta(glutamic acids) responsible for the interactions with the polycationic patch on the cytochrome *c* surface, (2) a zinc porphyrin core working as a fluorescence signaling device, (3) a hydrophilic polyether surface for enhancing the water solubility, and (4) nonpeptide dendritic components providing a peripheral, hydrophobic structure. Thus, dendrimer **60** is capable of binding with cytochrome *c* proteins in aqueous media. The binding process can be traced by fluorescence quenching of the zinc porphyrin core. The affinity thus measured is greater than biological cytochrome *b5*.

8. Conclusions

Since the first report was published in 1993,⁹ the development of dendrimer porphyrins including their phthalocyanine analogues has prompted two large research communities to merge, one involved with tetrapyrrole macrocycles and the

other focused on molecularly engineered macromolecules. It has also encouraged a great number of highly creative works in interdisciplinary research areas, where researchers are occasionally inspired by the biological functions of porphyrin derivatives, where they can take advantage of iterative precision synthesis techniques for shape-specific macromolecules, and where new ideas can be applied to the design of functional molecules with nanometer-scale dimensions. The knowledge gained from such specialized macromolecules may promote the development of next-generation smart materials that address essential issues related to both energy and health. For feature perspectives, there are still many things that seem to be very interesting. For example, dendrimer porphyrins for light harvesting are still very preliminary as compared to natural light-harvesting complexes in the sense that studies with dendritic scaffolds have been just made in a single molecular level but not yet at the assembling state. Thus, light-harvesting dendrimers with a controlled self-assembling nature to form regularly aligned cylinders may be one of the interesting targets for realizing a highly efficient, long-range energy transfer. As for biomedical applications, dendrimer porphyrins with switchable surface properties might be interesting, because such compounds can be elaborated into drug delivery systems operative via an active mechanism.

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