J Incl Phenom Macrocycl Chem (2007) 59:1–9
DOI 10.1007/s10847-007-9315-2

REVIEW ARTICLE

Nanoscale substrate recognition by porphyrin dendrimers with patched structures

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Received: 9 January 2007 / Accepted: 20 March 2007 / Published online: 9 May 2007

Abstract Dendrimer technology has enabled us to build macromolecules with nanosized defined structures. By introducing unsymmetrical patched structures in dendrimers, sophisticated artificial receptors exhibiting nanoscale substrate recognition can be obtained. In this review article, our recent studies on molecular recognition by porphyrin dendrimers with patched structures are summarized. Three topics are presented: (1) oligopeptide-patched dendrimers as a nanoscale receptor of cytochrome *c* protein; (2) pocket dendrimers as a nanoscale receptor for bimolecular guest accommodation; and (3) energy transfer in unsymmetrical dendrimers. These dendrimers nicely mimic proteins and enzymes, and also act as photofunctional artificial receptors, in which porphyrin's strong photoabsorption and intense fluorescence signals can respond sensitively to the substrate binding.

Keywords Bimolecular recognition · Cytochrome *c* · Dendrimer · Energy transfer · Fluorescence Light-harvesting · Nanosize · Oligopeptide Porphyrin · Protein recognition

Introduction

Dendrimer technology has become well established in recent years, and has enabled us to build macromolecules with nano-sized defined structures [1, 2]. Macromolecules comprising branched repeat units have globular shaped three-dimensional structures with sole molecular weights. As described in many review articles, many types of dendritic molecules are known, while various synthetic approaches to efficient construction of dendrimers continue to be explored [3].

The functionalization and application of dendrimers have been investigated in a wide range of research areas based on the uniqueness of their size, shape, and space. In particular, the inner space of a dendrimer surrounded by a shell made of highly dense terminal groups is suitable for the incorporation of guest molecules. Such an isolated space can be used for molecular recognition, catalytic reaction, drug delivery, etc [4–8].

Recently, much effort has been expended to introduce heterogeneity into dendrimer or dendron structures to obtain more elaborate functions using different types of functional groups in one dendrimer structure [9–11]. For example, dendrimers containing both hydrophilic and hydrophobic parts dynamically change their structure corresponding to the polarity of the solvent.

In this review, our recent studies on the design and functions of ''patched dendrimers'' are described, in which different types of dendrons are unsymmetrically introduced on the zinc(II) porphyrin core. The ''patch'' gives the porphyrin dendrimer an additional interface to bind with another molecule or macromolecule. Patched dendrimers with porphyrin cores show molecular recognition phenomena at the nanoscale, which provides good insight into the biological molecular recognition performed by proteins and enzymes (Fig. 1).

Porphyrins and metalloporphyrins have been employed as functional host molecules, photo- and redox-active devices, and enzyme mimics. Porphyrins have many advantages as the functional core of a dendrimer: (1) rigid and definite structure with a periphery available for connecting

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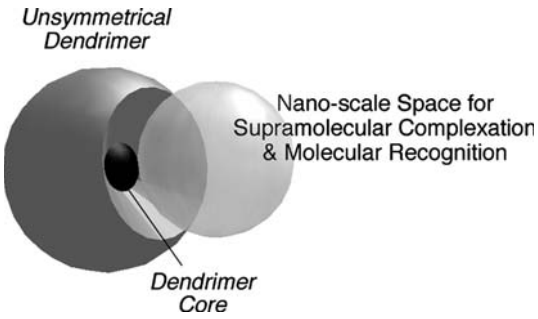


Fig. 1 Concept of ''patched'' dendrimer for nanoscale molecular recognition

several dendritic branches; (2) rich photochemistry such as strong photoabsorption, energy and electron transfer, and intense fluorescence; (3) substrate binding at the axial positions of the central metal ion; and (4) catalytic activity by the metal center. As many biological proteins utilize metalloporphyrins or related molecules in their enzymatic active sites, porphyrin dendrimers are employed as novel artificial mimics of metalloenzymes [12]. We investigated the nanoscale molecular recognition and photochemical properties of patched dendrimers with a zinc porphyrin core.

Oligopeptide-patched dendrimer as a nanoscale receptor of cytochrome *c* protein

Synthetic receptor molecules that can bind complementarily to protein surfaces are important for the detection and sensing of proteins [13]. Selective binding of molecules to the receptor sites of proteins can also inhibit their enzymatic and signaling functions. The protein surfaces have electrostatically positive or negative domains, hydrophobic domains, or hydrogen bonding domains to communicate or dock with other molecules. For effective protein–protein interactions, multi-point recognition or complementarity over a wide surface area is generally required. Hamilton et al. introduced various anionic substituents on the four aromatic rings of calix[4]arene or four *meso*-phenyl rings of 5,10,15,20-tetraphenylporphine (TPP), and studied their binding affinity to protein surfaces [14, 15]. Since the multi-anionic site of these synthetic receptors are fixed on rigid macrocyclic scaffolds, the binding affinities depend on the number and location of the cationic sites on the protein surfaces. Hayashi et al. prepared reconstituted myoglobin as a cytochrome *c* receptor, in which artificial heme derivatives with dendritic polyanionic end groups were replaced with the original heme unit of myoglobin [16]. The eight carboxylate anions located around the heme crevice interact with the cationic surface of cytochrome *c* to yield a supramolecular complex. They analyzed the electron transfer process from the triplet excited state of reconstituted zinc myoglobin to the bound cytochrome *c*.

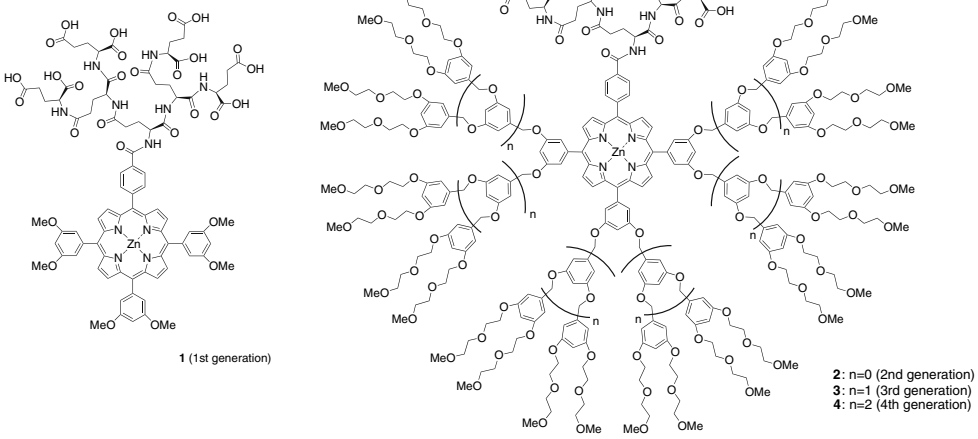
Dendrimers are an appropriate platform to prepare an interface to proteins, because a large number of terminal functional groups can be displayed on its surface. An oligo(glutamic acid) dendron has been used to construct water-soluble dendrimers, where the terminal carboxylate groups enhance the solubility of the dendrimer in water [17]. Hirsh et al. used this peptide or another poly(carboxylate) as an anionic dendron with fullerene C_{60} as the functional core of the dendrimer [18]. They prepared a zinc analog of cytochrome *c* for photochemical investigations as the supramolecular complex between zinc cytochrome *c* and fullerene dendrimer exhibits fluorescence quenching of the zinc cytochrome *c* by photoinduced electron transfer to C_{60}.

''Proteo-dendrimers'' **2–4** (Fig. 2) were designed to give an oligo(glutamic acid) dendron containing eight carboxylic acid terminal groups on one part of the dendrimer [19]. The remaining three phenyl rings were connected to aryl-ether (Fréchet-type) dendrons with polyether terminal groups to increase the solubility of the dendrimer in water. The oligopeptide dendron worked as a polyanionic patch that can strongly interact with the polycationic surface of cytochrome *c* protein. The aryl-ether dendrons are not thought to have any specific interactions with proteins, but they can have a sterical influence on protein-dendrimer interaction. Figure 3 shows the molecular modeling of cytochrome *c* and the 4th generation proteo-dendrimer **4**. As the polyanionic patch is located at one side of the dendrimer, it is expected to interact with the polycationic site around the heme crevice of cytochrome *c*. By restricting the area for interaction with outer proteins, more selective binding with targeted proteins and formation of structurally predictable supramolecular complexes become possible.

The zinc porphyrin core of a proteo-dendrimer shows a fluorescence signal suitable for observing the interaction with cytochrome *c*, while cytochrome *c* has a covalently bound nonfluorescent heme (iron(III) porphyrin) as the redox active center. When the zinc porphyrin dendrimer bound to cytochrome *c*, the fluorescence signal of the zinc porphyrin was strongly quenched. Fluorescence titration was performed to determine the binding constants with cytochrome *c* for 2nd–4th generation proteo-dendrimers **2–4**. These dendrimers formed supramolecular complexes with cytochrome *c* at a concentration level of 10^{-7} M in a phosphate buffer solution containing 10% dimethylformamide (DMF).

Although, dendrimers **2–4** have the same peptide patch and zinc porphyrin core, the generation of dendrimer strongly influenced the stoichiometry, binding constant, and fluorescence quenching efficiency. The titration curve and Job plots for fluorescence quenching indicated the

Fig. 2 Proteo-dendrimers as cytochrome *c* receptors



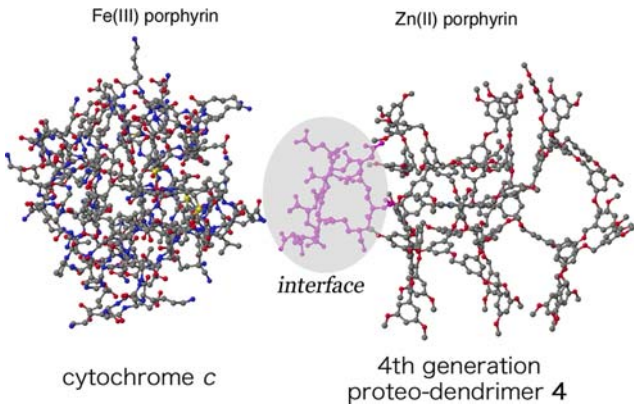


Fig. 3 Molecular modeling of cytochrome *c* and 4th generation proteo-dendrimer **4**

formation of both 2:1 and 1:1 (dendrimer:cytochrome *c*) complexes (Fig. 4). The 1:1 complexes showed significant fluorescence quenching of the zinc porphyrin core, while the secondary bound zinc porphyrin dendrimer in the 2:1 complexes did not show strong quenching by cytochrome *c*. When seven equivalents of cytochrome *c* were added to the zinc porphyrin dendrimer, the relative fluorescence intensity of zinc porphyrin depended on the dendrimer generation: I/I_0 was 0.33 for **2**, 0.53 for **3**, and 0.72 for **4** (I_0 is the fluorescence intensity of zinc porphyrin in the absence of cytochrome *c*). The differences in these values mainly reflect the fluorescence quenching efficiencies of the 1:1 complexes formed. The 2nd and 3rd generation dendrimers, **2** and **3**, had similar binding constants (log K_1: 7.6 and 7.7), while the 4th generation dendrimer **4** showed a smaller binding constant (log K_1: 6.5). The sterically hindered dendrons of **4** may disturb the electrostatic interactions between polyanionic peptide dendron and cytochrome *c*.

Cytochrome b_5 is known to be a redox partner of cytochrome *c* and to form a stable 1:1 complex with it through complementary electrostatic interactions [20]. The binding constants of dendrimers with cytochrome *c* were larger than the reported value with cytochrome b_5 (log $K = 4.8$). Competitive binding with cytochrome b_5 revealed that the fluorescence of zinc porphyrin was only partially recovered (ca. 20% recovery) by the addition of 14 equivalents of cytochrome b_5, suggesting that the proteo-dendrimer bound to cytochrome *c* more strongly than cytochrome b_5 by occupying similar binding sites. This means that the proteo-dendrimers are effective nanoscale protein receptors.

Electrostatic interactions between the polyanionic patch domain of dendrimer and the positive charges of cytochrome *c* play a dominant role in the complexation as shown in other receptor molecules. When partially lysine-acetylated cytochrome *c* and microperoxidase-8, a degradation product of cytochrome *c* with fewer positive charges, were employed instead of cytochrome *c*, the binding strength was greatly weakened, indicating that the positively charged sites on cytochrome *c* were essentially involved in the complexation with the proteo-dendrimers (Fig. 4a).

Proteo-dendrimers are completely synthetic nano-sized receptor molecules for cytochrome *c*. By limiting the interaction space on the dendrimer surface, nonstoichiometric aggregation between cationic cytochrome *c* and the anionic dendrimers could be prevented, and the supramolecular complexes formed had high stabilities in aqueous solutions. As the zinc porphyrin core has rich photochemistry, the present proteo-dendrimers can be used to read out photochemical properties, modulate biological functions, and help in the understanding of the molecular recognition properties of the targeted proteins.

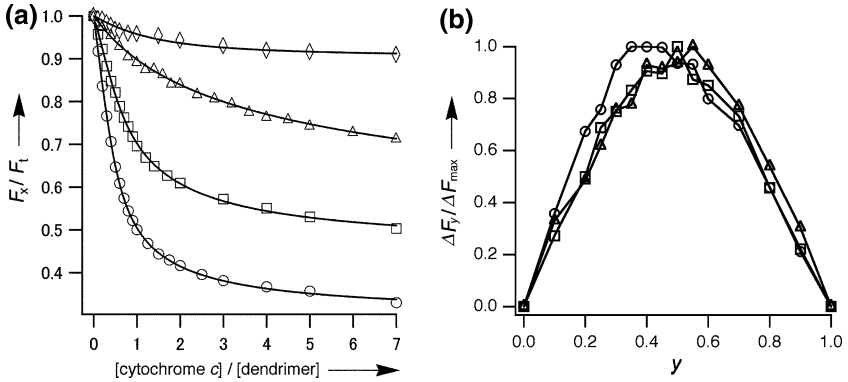


Fig. 4 (**a**) Fluorescence quenching of proteo-dendrimers by horse heart cytochrome *c* and its acetylated derivative and (**b**) Job plots of proteo-dendrimers with horse heart cytochrome *c*. ○: **2** + cytochrome *c*; □: **3** + cytochrome *c*; Δ: **4** + cytochrome c; ◇: **3** + acetylated cytochrome *c*. Conditions: (**a**) cytochrome *c*, 0–1.75 × 10^{-6} M; dendrimer, 2.5 × 10^{-7} M; λ_{ex} = 558 nm; λ_{em} = 610 nm; Solid lines were drawn based on nonlinear curve fitting: (**b**) *y* = [cytochrome *c*]/([cytochrome *c*] + [dendrimer]); total concentration of two species was held at 5.0 × 10^{-7} M for **2** and **3** or 2.5 × 10^{-7} M for **4**. Buffer solution: 5.0 × 10^{-3} M sodium phosphate buffer, pH 7.0 (containing 10% DMF v/v)

Pocket dendrimer as a nanoscale receptor for bimolecular guest accommodation

One of the most significant characteristics of a dendrimer is the availability of its inner sphere for guest accommodation. Dendrimers have been used as enzyme models, [21] capsules for drug delivery systems, and a variety of receptors [22]. In general, as the generation of dendrimer increases, the molecular density at the periphery increases and the transfer rate of going in and out through the dendrimer shell is slower. Even small molecules such as oxygen cannot smoothly enter into the high generation dendrimer through its highly dense shell [23]. On the contrary, relatively open space is thought to remain around the dendrimer core. The physical properties of the dendrimer inner spheres have been of interest, [24] and the hydrophobic interiors of dendrimers have been widely noted as unique reaction media in aqueous solutions [25, 26].

Dendrimers with metalloporphyrins as functional cores work well as artificial heme-protein models. Substrate binding by giant molecules is an important phenomenon from the viewpoint of understanding the molecular recognition of enzymes. Pioneering work on molecular recognition using the inner sphere of a porphyrin dendrimer has been done by Aida et al. and Suslick et al [27–29]. The guest molecules were accommodated in the dendrimer sphere by axial coordination to the metalloporphyrins. Dendrimer branches can sterically affect the guest binding properties and provide unique shape and size selectivity.

Bimolecular guest accommodation, in which two different kinds of molecules are bound at the active center of a protein, is one of the most important phenomena in enzymatic reactions and other biological recognition processes. Elaborate synthetic receptors with nano-sized cavities available for guest accommodation have been prepared and their successful promotion of bimolecular reactions within the cavities demonstrated [30–32]. Although, dendrimers act as supports for transition metal catalysts and provide unique sites for bimolecular reactions, the number of dendrimers that can accommodate two or more molecules is still limited.

To realize bimolecular guest accommodation by artificial host molecules, we prepared unsymmetrical metalloporphyrin dendrimers **5**–**8** called ''pocket dendrimers'' and compared their guest binding properties with the corresponding fully covered dendrimers **9**–**12** (Fig. 5) [33]. Additional effective guest binding space becomes available and another recognition site can be introduced near the dendrimer core by preparing pockets in dendrimer structures.

The receptor functions of zinc porphyrin dendrimers for 3- and 4-substituted pyridine derivatives **13**–**17** were investigated by titration experiments measuring the visible absorption changes of the porphyrin. Pyridine derivatives coordinate to the zinc center at the axial position to form penta-coordinated complexes, inducing red shifts in the porphyrin absorption bands. The formation constants of the 1:1 complex determined by titration experiments with UV/Vis absorption spectra were compared among 1st–4th generation dendrimers and between the pocket and fully covered dendrimers.

The guest binding site above the plane of the porphyrin core is relatively open even in the 4th generation dendrimers **8** and **12**. However, the dendrimer branches adopt various conformations in solution and have an inhibitory effect on guest binding. Even when relatively small benzyl nicotinate **13** was used as the guest, the branches of higher

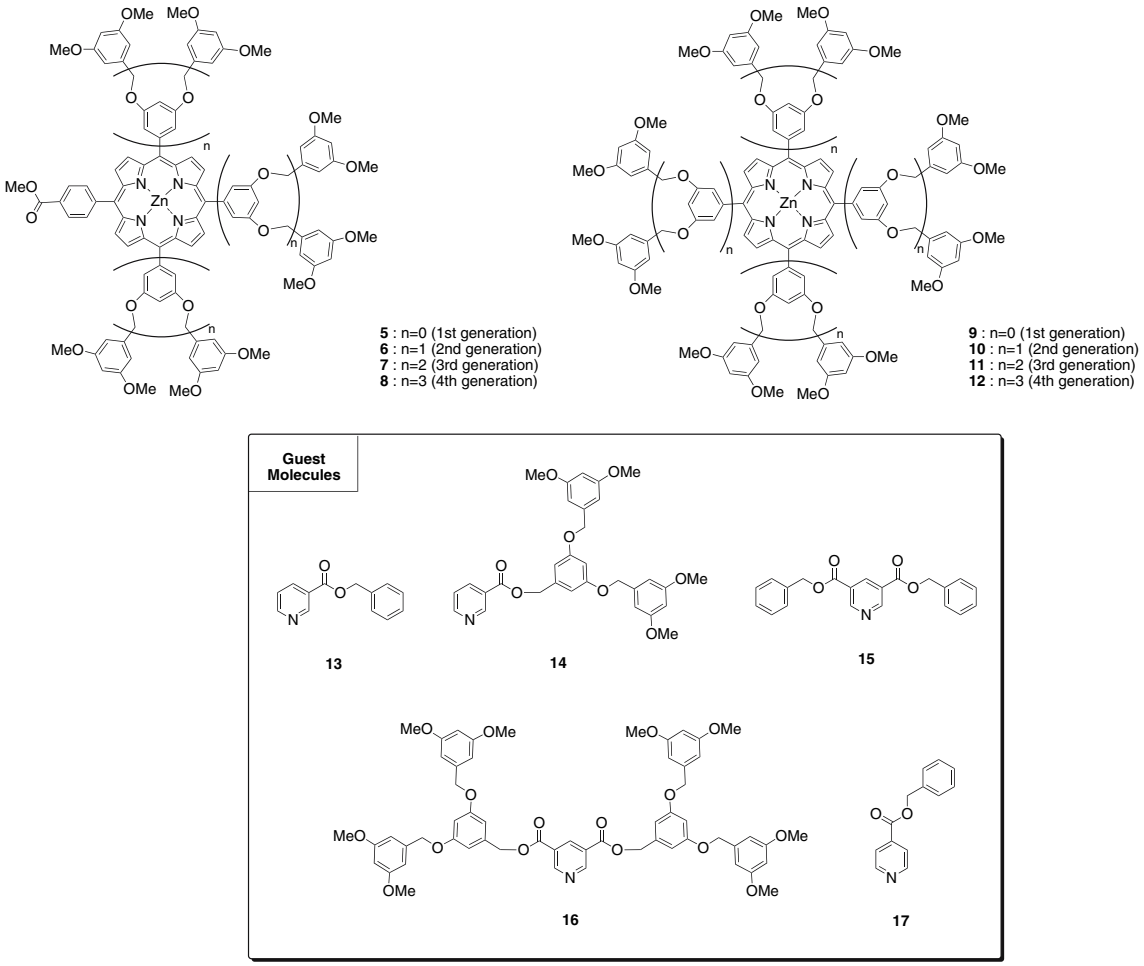


Fig. 5 Pocket (**5**–**8**) and fully covered (**9**–**12**) dendrimers and their pyridine guests

generation dendrimers decreased the binding constant (Fig. 6). Decreases in binding constants were seen for all the employed pyridine guests **13**–**17** upon increase in the dendrimer generation. The effect of introducing a binding pocket for guest molecules was most clearly seen in the 3rd generation dendrimers **7** and **11**. While pocket dendrimer **7** bound pyridine guest **13** with similar binding constants as the 1st generation dendrimer **5**, the binding constant with fully covered dendrimer **11** was ca. 50% smaller than **5**. In the 4th generation dendrimer, such a difference between pocket dendrimer **8** and fully covered dendrimer **12** was not obvious, since the pocket dendrimer **8** also showed a much smaller binding constant than that of **7**. Molecular modeling experiments suggest that the pocket space in the 4th generation dendrimer is not sufficiently formed, being occupied by the neighboring branches. As a consequence, the 3rd generation pocket dendrimer has been found to provide enough space for binding guest pyridines above the porphyrin core.

To achieve the second guest accommodation in the dendrimer, a 2,6-diamidopyridine unit was further incorporated in the pocket of the 3rd generation pocket dendrimer to produce bimolecular receptor **18** (Fig. 7). The 2,6-diamidopyridine unit interacts with a thymine group via three-point hydrogen bonding. When thymine derivative **19** was added to dendrimer **18**, the NMR signals of the amide protons of **18** were largely shifted to the downfield suggesting formation of hydrogen bonding. A titration experiment gave a saturation curve for the chemical shift values of amide protons based on 1:1 complexation, and the binding constant was determined as 170 M^{-1} in $CDCl_3$ which was comparable to that with the corresponding branchless porphyrin **20** (210 M^{-1}). Although, the self-association of porphyrin **20** by hydrogen bonding between two diaminopyridine units was observed at high concentration, such behavior was not observed with 3rd generation dendrimer **18**. The dendrimer branches have a role to prevent self-association of functional

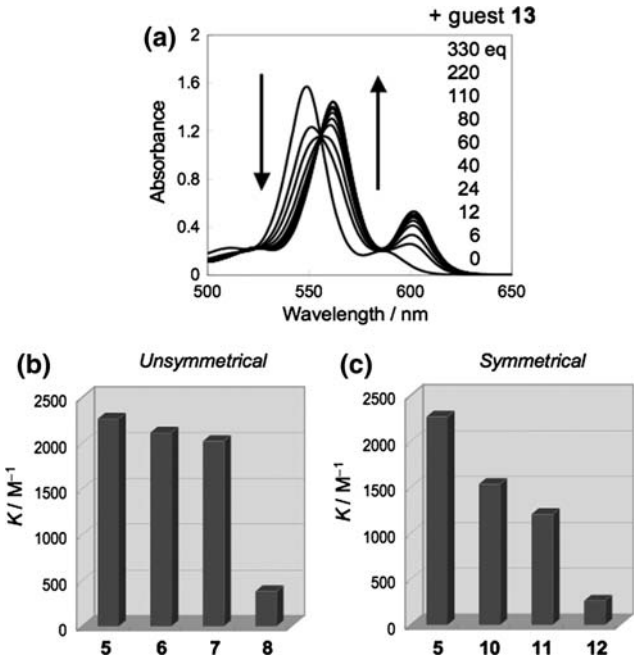


Fig. 6 Complexation between pyridine guest **13** and dendrimers. (**a**) Absorption spectral changes of 3rd generation dendrimer **7** upon addition of pyridine guest **13.7**, 6.00×10^{-5} M in chloroform; 1 cm optical path length; 25 °C. (**b** and **c**) Complex stability constants with pyridine guest **13** for unsymmetrical and symmetrical dendrimers

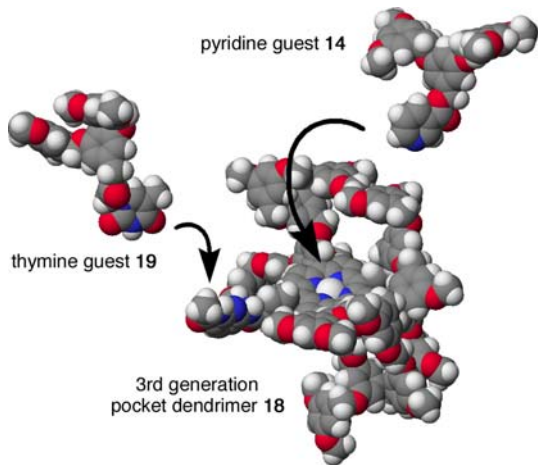


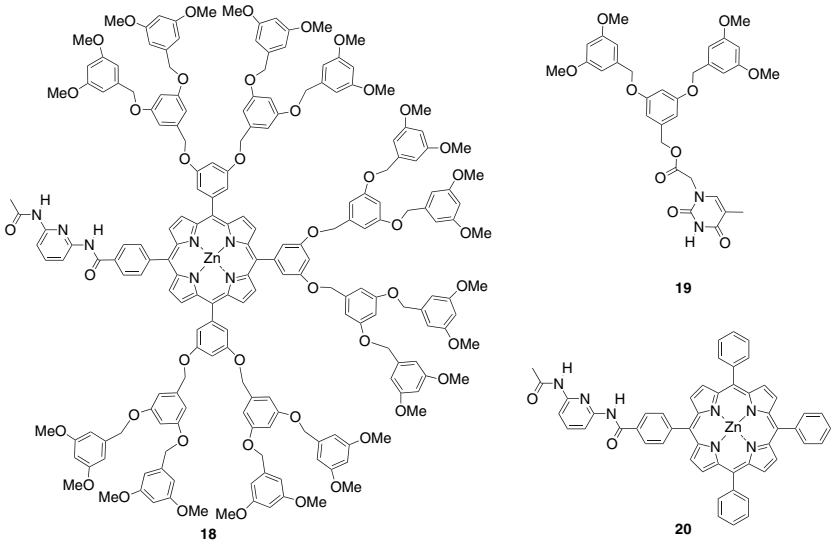
Fig. 8 Bimolecular binding by 3rd generation pocket dendrimer **18**

cores by separating them well in solution. In the presence of two different guest molecules, pyridine and thymine derivatives, the pocket dendrimer clearly showed simultaneous binding of these two guests as schematically shown in Fig. 8. The chemical shift values of amide protons and the absorption spectrum of porphyrin Q-bands indicated that more than 90% of pyridine derivative coordinated to the zinc center and 56% of thymine derivative still remained bound at the diamidopyridine moiety. Since these binding events took place near the dendrimer core, the pocket dendrimer was able to provide a unique space for bimolecular recognition. Bimolecular accommodation observed in the unsymmetrical dendrimer will lead to nice mimicking of molecular recognition and enzymatic reaction of proteins.

Energy transfer in unsymmetrical dendrimer

Photochemical events taking place in dendrimers have been attracting interest for their mechanisms, functions, and applications [34–38]. Because of the highly branched structures, many chromophores can be arranged around one photofunctional core at fixed distances [39–41]. A resemblance to photoantennae in biological photosynthesis systems makes it attractive to use dendrimers as models for

Fig. 7 Host compounds for bimolecular binding and the thymine guest



light-harvesting systems to realize efficient photoenergy conversion [42–44]. Although, the selection of chromophores and their linkage essentially determine the overall energy transfer efficiency, the shape and morphology are also important factors influencing the photodynamic processes.

Aida et al. investigated the morphological effects of fifth generation aryl ether dendrimers with a different number of dendron substituents around the tetraphenylporphyrin core [45]. They reported that a fully substituted (spherical morphology) dendrimer exhibited a higher quantum yield of energy transfer from the peripheral aryl ether moiety to the porphyrin core than partially substituted ones. It was explained that such a high quantum yield was a consequence of enhanced probability of energy transfer due to the fast energy migration among the continuous array of the same chromophores in the fully substituted dendrimer.

We have investigated the generation and morphological dependence of energy transfer in a single dendrimer molecule using 1st–4th generation zinc porphyrin dendrimers **5**–**12** together with the corresponding unsymmetrical dendrimers with a different number of aryl ether dendrons (their structures are not shown) [46]. Energy transfer efficiencies from the peripheral dendron to the zinc porphyrin core showed only small decreases along with the expansion of the dendron size, but they all have high quantum efficiency of energy transfer (β_{ET} = 85% for **6**, 89% for **7**, and 79% for **8**). The excitation energy seems to rapidly migrate to the porphyrin core compared to the rate of radiative and nonradiative decay from the aromatic ring in the dendrons. The 4th generation dendrimers were used to examine the morphological dependence, and the energy transfer efficiencies of dendrimers with 1, 3, and 4 branches were compared. The morphological effect was not obvious in these dendrimers, perhaps due to low molecular density even in the fully covered dendrimer at the 4th generation. Here, the quantum yield of energy transfer slightly decreased with increase in the number of dendritic substituents. Temperature dependence of excitonic energy transfer in these dendrimers revealed that the molecular vibrations of peripheral dendrons are coupled to singlet energy transfer from the periphery to the porphyrin core [47]. By freezing the molecular vibration at low temperature, the energy transfer efficiency was decreased.

The fluorescence properties of zinc porphyrin such as photon energy and fluorescence lifetime were not at all affected by the attachment of dendrons in the employed dendrimers up to the 4th generation. Since excitation of the peripheral aromatic rings also caused porphyrin fluorescence by efficient intramolecular energy transfer, the dendrons worked as photoantennae for sensitizing the central zinc porphyrin. Our results confirmed that a dendritic structure is useful for light harvesting to excite the photofunctional core even if it is not completely substituted by the dendrons. As the unsymmetrical dendrimers have the ability to supramolecularly conjugate with another macromolecule, this provides a technique to obtain novel photofunctional materials.

Conclusion

Dendritic molecules with unsymmetrical structures are useful to introduce additional functions in dendrimers. As compared with the corresponding symmetrical fully covered dendrimers, they can bind and communicate with other molecules more selectively, and recognize substrates more dynamically. Although the removal of one part of dendrons creates an open space, the characteristics of dendrimers such as isolated functional core and light-harvesting ability have not been lost. More sophisticated artificial receptors that realize molecular recognition at the nanoscale can be developed by the ‘‘patched dendrimer’’ architecture.

Acknowledgments The author thanks the Organizing Committee of Host-Guest and Supramolecular Chemistry Society, Japan for giving him the HGCS Japan Award of Excellence 2006 and the opportunity to write this review article. He acknowledges all collaborators for their efforts. He especially thanks Prof. Hiroshi Tsukube for his suggestions and discussion about all the research on dendrimers, Dr. Dharam Paul for his contribution to dendrimer synthesis, and Dr. Ichiro Akai for being a co-worker and for discussion about the energy transfer processes in dendrimers. Figures 4 and 7 were reproduced with permission from the Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim.

This is a paper selected for ‘‘HGCS Japan Award of Excellence 2006’’.

References

1. Fréchet, J.M.J., Tomalia, D.A.: Dendrimers and Other Dendritic Polymers, p. 647. Wiley, Chichester (2001)
2. Newkome, G.R., Moorefield, C.N., Vögtle, F.: Dendrimers and Dendrons: Concepts, Syntheses, Applications, p. 623. Wiley-VCH, Weinheim (2001)
3. Grayson, S.M., Fréchet, J.M.J.: Convergent dendrons and dendrimers: From synthesis to applications. Chem. Rev. **101**, 3819–3867 (2001)
4. Hecht, S., Fréchet, J.M.J.: Dendritic encapsulation of function: Applying nature's site isolation principle from biomimetics to materials science. Angew. Chem. Int. Ed. **40**, 74–91 (2001)
5. Smith, D.K., Diederich, F.: Functional dendrimers: Unique biological mimics. Chem. Eur. J. **4**, 1353–1361 (1998)
6. Diederich, F., Felber, B.: Supramolecular chemistry and self-assembly special feature: Supramolecular chemistry of dendrimers with functional cores. Proc. Natl. Acad. Sci. USA **99**, 4778–4781 (2002)
7. Boas, U., Heegaard, P.M.H.: Dendrimers in drug research. Chem. Soc. Rev. **33**, 43–63 (2004)

8. van Heerbeek, R., Kamer, P.C.J., van Leeuwen, P.W.N.M., Reek, J.N.H.: Dendrimers as support for recoverable catalysts and reagents. Chem. Rev. **102**, 3717–3756 (2002)
9. Newkome, G.R., Kotta, K.K., Moorefield, C.N.: Design, synthesis, and characterization of conifer-shaped dendritic architectures. Chem. Eur. J. **12**, 3726–3734 (2006)
10. Wu, P., Malkoch, M., Hunt, J.N., Vestberg, R., Kaltgrad, E., Finn, M.G., Fokin, V.V., Sharpless, K.B., Hawker, C.J.: Multivalent, bifunctional dendrimers prepared by click chemistry. Chem. Commun. 5775–5777 (2005)
11. Ong, W., Gómez-Kaifer, M., Kaifer, A.E.: Dendrimers as guests in molecular recognition phenomena. Chem. Commun. 1677–1683 (2004)
12. Weyermann, P., Gisselbrecht, J.-P., Boudon, C., Diederich, F., Gross, M.: Dendritic iron porphyrins with tethered axial ligands: New model compounds for cytochromes. Angew. Chem. Int. Ed. **38**, 3215–3219 (1999)
13. Peczuh, M.W., Hamilton, A.D.: Peptide and protein recognition by designed molecules. Chem. Rev. **100**, 2479–2494 (2000)
14. Park, H.S., Lin, Q., Hamilton, A.D.: Protein surface recognition by synthetic receptors: A route to novel submicromolar inhibitors for α-chymotrypsin. J. Am. Chem. Soc. **121**, 8–13 (1999)
15. Zhou, H., Baldini, L., Hong, J., Wilson, A.J., Hamilton, A.D.: Pattern recognition of proteins based on an array of functionalized porphyrins. J. Am. Chem. Soc. **128**, 2421–2425 (2006)
16. Hayashi, T., Hisaeda, Y.: New functionalization of myoglobin by chemical modification of heme-propionates. Acc. Chem. Res. **35**, 35–43 (2002)
17. Sadler, K., Tam, J.P.: Peptide dendrimers: Applications and synthesis. Rev. Mol. Biotechnol. **90**, 195–229 (2002)
18. Braun, M., Atalick, S., Guldi, D.M., Lanig, H., Brettreich, M., Burghardt, S., Hatzimarinaki, M., Ravanelli, E., Prato, M., van Eldik, R., Hirsch, A.: Electrostatic complexation and photoinduced electron transfer between Zn-cytochrome *c* and polyanionic fullerene dendrimers. Chem. Eur. J. **9**, 3867–3875 (2003)
19. Paul, D., Miyake, H., Shinoda, S., Tsukube, H.: Proteo-dendrimers designed for complementary recognition of cytochrome *c*: Dendrimer architecture toward nanoscale protein complexation. Chem. Eur. J. **12**, 1328–1338 (2006)
20. Ng, S., Smith, M.B., Smith, H.T., Millett, F.: Effect of modification of individual cytochrome *c* lysines on the reaction with cytochrome b_5. Biochemistry **16**, 4975–4978 (1977)
21. Habicher, T., Diederich, F., Gramlich, V.: Catalytic dendrophanes as enzyme mimics: Synthesis, binding properties, micropolarity effect, and catalytic activity of dendritic thiazoliocyclophanes. Helv. Chim. Acta **82**, 1066–1095 (1999)
22. Mattei, S., Wallimann, P., Kenda, B., Amrein, W., Diederich, F.: Dendrophanes: Water-soluble dendritic receptors as models for buried recognition sites in globular proteins. Helv. Chim. Acta **80**, 2391–2417 (1997)
23. Jiang, D.-L., Aida, T.: A dendritic iron porphyrin as a novel haemoprotein mimic: Effects of the dendrimer cage on dioxygen-binding activity. Chem. Commun. 1523–1524 (1996)
24. Ballauff, M., Likos, C.N.: Dendrimers in solution: Insight from theory and simulation. Angew. Chem. Int. Ed. **43**, 2998–3020 (2004)
25. Kaanumalle, L.S., Ramesh, R., Maddipatla, V.S.N.M., Nithyanandhan, J., Jayaraman, N., Ramamurthy, V.: Dendrimers as photochemical reaction media. Photochemical behavior of unimolecular and bimolecular reactions in water-soluble dendrimers. J. Org. Chem. **70**, 5062–5069 (2005)
26. Garcia-Martinez, J.C., Lezutekong, R., Crooks, R.M.: Dendrimer-encapsulated Pd nanoparticles as aqueous, room-temperature catalysts for the stille reaction. J. Am. Chem. Soc. **127**, 5097–5103 (2005)
27. Tomoyose, Y., Jiang, D.-L., Jin, R.-H., Aida, T., Yamashita, T., Horie, K., Yashima, E., Okamoto, Y.: Aryl ether dendrimers with an interior metalloporphyrin functionality as a spectroscopic probe: Interpenetrating interaction with dendritic imidazoles. Macromolecules **29**, 5236–5238 (1996)
28. Bhyrappa, P., Young, J.K., Moore, J.S., Suslick, K.S.: Dendrimer-metalloporphyrins: Synthesis and catalysis. J. Am. Chem. Soc. **118**, 5708–5711 (1996)
29. Sen, A., Suslick, K.S.: Shape-selective discrimination of small organic molecules. J. Am. Chem. Soc. **122**, 11565–11566 (2000)
30. Hof, F., Craig, S.L., Nuckolls, C., Rebek, J. Jr.: Molecular encapsulation. Angew. Chem. Int. Ed. **41**, 1488–1508 (2002)
31. Fiedler, D., Leung, D.H., Bergman, R.G., Raymond, K.N.: Selective molecular recognition, C-H bond activation, and catalysis in nanoscale reaction vessels. Acc. Chem. Res. **38**, 349–358 (2005)
32. Yoshizawa, M., Fujita, M.: A self-assembled coordination cage as a molecular flask. Pure Appl. Chem. **77**, 1107–1112 (2005)
33. Shinoda, S., Ohashi, M., Tsukube, H.: Pocket dendrimers as nanoscale receptors for bimolecular guest accommodation. Chem. Eur. J. **13**, 81–89 (2007)
34. De Schryver, F.C., Vosch, T., Cotlet, M., van der Auweraer, M., Müllen, K., Hofkens, J.: Energy dissipation in multichromophoric single dendrimers. Acc. Chem. Res. **38**, 514–522 (2005)
35. Chen, J., Li, S., Zhang, L., Li, Y.-Y., Chen, J., Yang, G., Li, Y.: Direct observation of the intramolecular triplet-triplet energy transfer in poly(aryl ether) dendrimers. J. Phys. Chem. B **110**, 4047–4053 (2006)
36. Mo, Y.-J., Jiang, D.-L., Uyemura, M., Aida, T., Kitagawa, T.: Energy funneling of IR photons captured by dendritic antennae and acceptor mode specificity: Anti-Stokes resonance Raman studies on iron(III) porphyrin complexes with a poly(aryl ether) dendrimer framework. J. Am. Chem. Soc. **127**, 10020–10027 (2005)
37. Thomas, K.R.J., Thompson, A.L., Sivakumar, A.V., Bardeen, C.J., Thayumanavan, S.: Energy and electron transfer in bifunctional non-conjugated dendrimers. J. Am. Chem. Soc. **127**, 373–383 (2005)
38. Cotlet, M., Gronheid, R., Habuchi, S., Stefan, A., Barbafina, A., Müllen, K., Hofkens, J., De Schryver, F.C.: Intramolecular directional Förster resonance energy transfer at the single-molecule level in a dendritic system. J. Am. Chem. Soc. **125**, 13609–13617 (2003)
39. Takahashi, M., Morimoto, H., Miyake, K., Yamashita, M., Kawai, H., Sei, Y., Yamaguchi, K.: Evaluation of energy transfer in perylene-cored anthracene dendrimers. Chem. Commun. 3084–3086 (2006)
40. Gong, L.-Z., Hu, Q.-S., Pu, L.: Optically active dendrimers with a binaphthyl core and phenylene dendrons: Light harvesting and enantioselective fluorescent sensing. J. Org. Chem. **66**, 2358–2367 (2001)
41. Choi, M.-S., Aida, T., Yamazaki, T., Yamazaki, I.: Dendritic multiporphyrin arrays as light-harvesting antennae: Effects of generation number and morphology on intramolecular energy transfer. Chem. Eur. J. **8**, 2667–2678 (2002)
42. Adronov, A., Fréchet, J.M.J.: Light-harvesting dendrimers. Chem. Commun. (*feature article*) 1701–1710 (2000)
43. Ahn, T.S., Thompson, A.L., Bharathi, P., Müller, A., Bardeen, C.J.: Light-harvesting in carbonyl-terminated phenylacetylene dendrimers: The role of delocalized excited states and the scaling of light-harvesting efficiency with dendrimer size. J. Phys. Chem. B **110**, 19810–19819 (2006)
44. Loiseau, F., Campagna, S., Hameurlaine, A., Dehaen, W.: Dendrimers made of porphyrin cores and carbazole chromophores as peripheral units. Absorption spectra, luminescence properties,

and oxidation behavior. J. Am. Chem. Soc. **127**, 11352–11363 (2005)
45. Jiang, D.-L., Aida, T.: Morphology-dependent photochemical events in aryl ether dendrimer porphyrins: Cooperation of dendron subunits for singlet energy transduction. J. Am. Chem. Soc. **120**, 10895–10901 (1998)
46. Akai, I., Kato, T., Kanemoto, K., Karasawa, T., Ohashi, M., Shinoda, S., Tsukube, H.: Morphology dependence of excitonic energy transfer in light- harvesting dendrimers having benzyl ether-type peripheries. Phys. Stat. Sol. (C) **3**, 3420–2425 (2006)
47. Akai, I., Kato, T., Okada A., Kanemoto, K., Karasawa, T., Kimura, M., Ohashi, M., Shinoda, S., Tsukube, H.: Depression of excitonic energy transfer by freezing molecular vibrations in meta-linked branching dendrimers. Phys. Stat. Sol. (C) **3**, 3414–3419 (2006)