Phosphorescent Pd Porphyrin−Dendrimers: Tuning Core Accessibility by Varying the Hydrophobicity of the Dendritic Matrix

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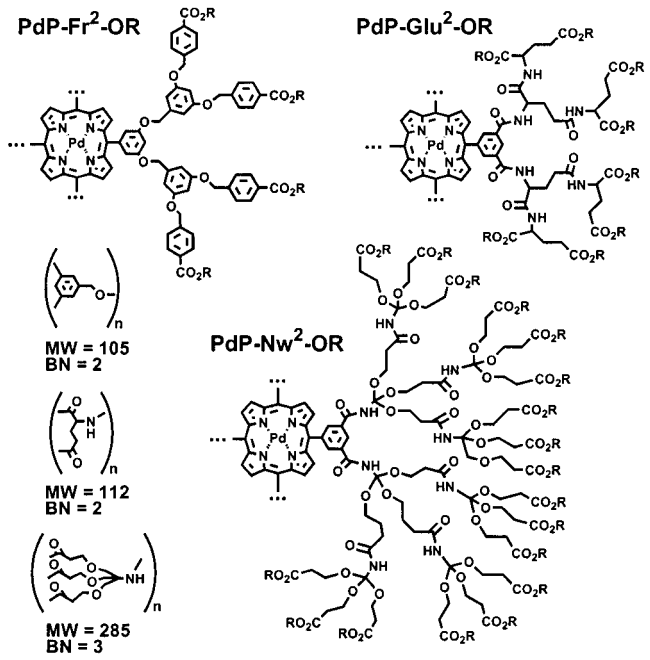
Received December 5, 2001

Dendritic encapsulation of photoactive core functionality attracted a great deal of attention in the past years.[1] It provided unique models for energy-transfer studies and made it possible to create a number of mimics of natural light harvesting systems.[2] Among all photoactive dendrimers, dendrimers with porphyrin cores[3] are of particular interest due to their close resemblance to the heme-containing proteins. Dendritic arrays not only can serve as efficient energy antennas and funnels but also can control heme microenvironment and regulate the access of small molecules to the porphyrin cores. This capability of dendrimers was successfully utilized in catalysis[4a] and shape-selective recognition[4b] and recently was used for building "protected" indicators for in vivo oxygen sensing.[5]

It is well established that quencher diffusion barriers around luminescent centers can be altered by dendrimers.[3a,i,k,6] Very little, however, is known about the relative shielding efficiency of dendrons of different chemical composition. Encapsulation by dendrimers of different rigidity has been assessed using hydrogen-bonding hosts[7] and iron−sulfur clusters;[8] however, the only direct comparison of core protection from small molecules has been made between Fréchet and Newkome-type dendrons coupled to $[Ru(bpy)_3]^{2+}$ complexes.[6a,c] This study revealed that in acetonitrile solutions bulkier poly(ether amide)s provide stronger shielding from O_2 quenching than poly(aryl ether)s of the same dendritic generation.[9] Other studies[5] suggested that dendrimer−solvent interactions play an important role in altering the accessibility of small quencher molecules to the porphyrin−dendrimer core.[10] To gain further insight into the encapsulation phenomenon, in this work we compared shielding of phosphorescent Pd porphyrins from O_2 by three different types of dendrimers in solvents of different polarities. It appeared that in more polar solvents hydrophobic dendrimers are capable of providing extremely effective isolation of the core already at very early dendritic generations.

The dendrimers chosen for this study were Fréchet-type poly(aryl ether)s, Newkome-type poly(ether amide)s, and polyglutamates (Scheme 1). All three types have been previously used for modification of porphyrins.[3a−j,l,5] Fréchet-type dendrimers are less polar and thus likely to be the most hydrophobic in the selected group. Because of the same branching number (BN = 2) and close molecular weights of the monomers, poly(aryl ether)s (MW = 105) and polyglutamates (MW = 112) are characterized by essentially the same mass increase per generation. Poly(ether amide)s (MW = 285, BN = 3), on the other hand, are similar to polyglutamates in chemical composition but have much larger per generation mass increase. All three dendrimers are relatively flexible, and therefore substantial conformational changes can be expected in solvents of different polarities.[11] The examples of the synthesized Pd porphyrin−dendrimers are shown in Scheme 1.

Scheme 1



Pd−*meta*-octahydroxyphenylporphyrin (Pd*m*OHPP)[12] for the attachment of Fréchet-type dendrons and Pd−*meta*-octacarboxyphenylporphyrin (Pd*m*OCCP)[13] for the attachment of poly(ether amide)s and polyglutamates were synthesized according to the earlier published methods. The syntheses of Fréchet-type,[3b,1,4] Newkome-type,[3d−g,15] and polyglutamic[5,16] porphyrin−dendrimers in general followed published protocols. The compounds (Scheme 1) are abbreviated in the text as PdP-Fr^N-R (Fréchet type), PdP-Nw^N-R (Newkome type), and PdP-Glu^N-R (polyglutamates), where N indicates the generation number and R is a terminal group (R = OH, OMe, OEt; TEG (triethylene glycol monomethyl ether), or PEG350 (poly(ethylene glycol) monomethyl ether, av MW 350)).

O_2-dependent quenching of phosphorescence allows for the quantification of "protection" offered by dendrimers to the core porphyrins. Over a broad range of concentrations, the Stern−Volmer oxygen quenching constant K_q is a direct measure of the diffusion barrier, which separates quencher in solution from the triplet-state Pd porphyrin.[17] Table 1 shows K_q values, which illustrate our key findings.

In both DMF and THF[18] there is a trend in decreasing quenching rates, consistent with an increase in the dendrimer size; however, these changes are rather insignificant. As expected, bulkier poly(ether amide)s exhibit a stronger effect, but still the decrease in diffusion is only about 75% at G2 when the weight of the dendrimer is more than 12 kDa. The absolute values of quenching constants of G2 Fréchet- and Newkome-

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10.1021/ma0121161 CCC: $22.00
Published on Web 02/08/2002

Table 1. Oxygen Quenching Constants of Selected Pd Porphyrin−Dendrimers (R = OH in H_2O; R = OMe, OEt in THF and DMF, Unless Otherwise Specified)

no.	dendrimer generation	K_q ($mmHg^{-1}\,s^{-1}$) H_2O[a]	DMF	THF
1	G0 (Pd*m*OCPP)	2675	9261	15979[b]
2	G0 (Pd*m*OMPP)[c]		10505	15041
	Polyglutamates (PdP-Glu^N-R)			
3	G1	2282	6739	7918
4	G2	1641	4779	7282
5	G1 (R = TEG)	1013	5959	7328
	Poly(aryl ether)s (PdP-Fr^N-R)			
6	G1	1019	7547	13032
7	G2	112	5434	9597
8	G3	90	5319	
9	G2[d]	30		
10	G2 (R = PEG350)	108	4688	7981
11	G2 (R = PEG350)[d]	109		
	Poly(ether amide)s (PdP-Nw^1-R)			
12	G1	1997	5984	7925
13	G2	1068	3572	3881

[a] Aqueous phosphate buffer, K_2HPO_4 50 mM, pH = 7.2. [b] Pd*m*OCPP-octabutyl ester. [c] Pd*m*OHPP was found not to be phosphorescent in either aqueous or organic solutions; instead, its octamethyl ether (Pd*m*OMPP) was used. [d] 2% bovine serum albumin (BSA) added to solution.

type porphyrin−dendrimers in THF are 7.2×10^8 and 2.9×10^8 $M^{-1}\,s^{-1}$, respectively (expressed in molar scale). These appear to be very close to the values reported for dendritic Ru^{2+} complexes in acetonitrile,[9] suggesting similar behavior of dendritic branches in these two solvents. The relative shielding of Ru^{2+} by both types of dendrons was, however, found slightly stronger than in the case of Pd porphyrin. The quenching constants of G2 dendritic Ru^{2+} complexes were diminished by 46% in the case of poly(aryl ether)s and by 91% in the case of poly(ether amide)s, as compared to that of unprotected $[Ru(bpy)_3]^{2+}$.

The most remarkable decline in quenching rate was observed in the series of Fréchet-type porphyrin−dendrimers in H_2O, where K_q's change roughly 30 times between G0 (Pd*m*OCPP) and G3 compounds. Surprisingly, the addition of just one layer of benzyls via ether linkages (G1) induces a 65% drop in K_q value, and by G2 the porphyrin becomes so well protected that addition of the next dendritic layer (G3) practically does not influence the quenching rate. This despite nearly doubling the molecular weight of the dendrimer.

The relative changes in quenching rates per dendrimer generation for all three dendrimers in H_2O are shown in Figure 1.

It is clearly seen that factors other than the bulk volume of the dendritic matrix play the major role in controlling O_2 diffusion. Shielding by Fréchet-type dendrons is almost twice more pronounced at G1 and more than 7 times stronger at G2 compared to polyglutamates, although these dendrimers have very similar size. Notably, even in comparison with much larger Newkome dendrimers, poly(aryl ether)s still provide significantly stronger protection. It is remarkable that G1 poly(aryl ether) dendrimer and G2 poly(ether amide) dendrimer exhibit practically the same quenching constants, while the molecular weight of the latter is almost 6 times larger.

Titration experiments performed in the presence of BSA (bovine serum albumin) revealed strong interactions between the carboxylate-terminated dendrimers

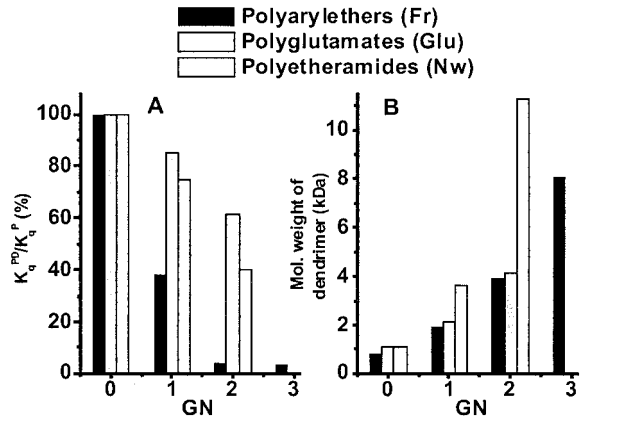

Figure 1. (A) Decrease in the values of oxygen quenching constants K_q^{PD} of Pd porphyrin−dendrimers in buffered aqueous solutions (pH = 7.2) at 23.4 °C. All values are referenced to the quenching constant K_q^{P} of unprotected Pd*m*OCPP. (B) Molecular weights of porphyrin−dendrimers.

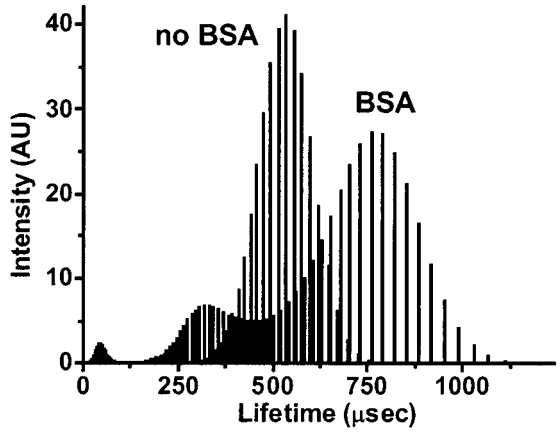

Figure 2. Phosphorescence lifetime distributions (recovered by the maximum entropy method) of PdP-Fr^2-OH in aqueous buffer with and without BSA (bovine serum albumin).

and the protein. Thus, the addition of BSA caused a 3-fold decrease in K_q of PdP-Fr^2-OH (Table 1, entries 7 and 9) and drastically changed the shape of its phosphorescence lifetime distribution (Figure 2).[19] The broadened nonuniform distribution is likely to indicate the presence of multiple binding sites for the phosphor on the protein.

To minimize these interactions, a neutral inert hydrophilic layer was formed on the dendrimer surface by esterification of the carboxylic termini with short-chain poly(ethylene glycol)s (TEG or PEG350). In the case of more "open" polyglutamic dendrimers, the modification caused a further decline in the K_q values (entries 3 and 5), while it had almost no effect on already "fully protected" G2 poly(aryl ether)s (entries 7 and 10). The most dramatic effect that the pegilation had was on the interactions of dendrimers with BSA. The K_q of PdP-Fr^2-PEG350 was found completely insensitive to the presence of the protein (Table 1, entries 10 and 11), and the same was observed for its lifetime distribution. This property makes PdP-Fr^2-PEG350 especially valuable for in vivo oxygen measurements.

In summary, a comparative study involving dendrimers with phosphorescent cores showed that the composition of dendritic matrix and solvent effects have a major influence on the encapsulation capability of dendrimers. Investigations employing small molecules other than O_2 are in progress.

Acknowledgment. This work was supported by Grants HL-60100 and CA-74062 from the National Institutes of Health (NIH) of the USA.

Supporting Information Available: Synthetic and measurement protocols, compounds characterization, and a description of the phosphorescence lifetime measurement equipment and oxygen measurement system. This material is available free of charge via the Internet at http://pubs.acs.org.

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MA0121161