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Porphyrin–Peptoid Conjugates: Face-to-Face Display of Porphyrins on Peptoid Helices

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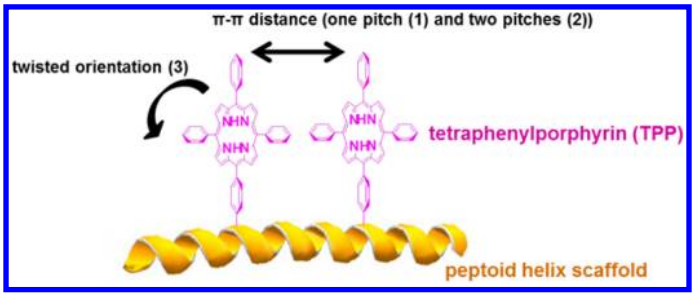
ABSTRACT



Distance, orientation, and number controlled porphyrin–peptoid conjugates (PPCs) were efficiently synthesized. Cofacial (1, 2, and 4), slipped-cofacial (3), and unstructured (5) arrangements of porphyrins provided distinct optical and electronic properties characterized by UV–vis and circular dichroism spectroscopy. In addition, ECCD spectra confirmed the handedness of peptoid helices.

Porphyrins, a class of naturally occurring pigments, have been actively investigated due to their interesting photophysical and chemical properties. As the judicious arrangement of porphyrins has resulted in a number of interesting molecules for applications ranging from sensors to new optoelectronic materials,[1] much effort has been made to construct defined oligomeric porphyrin arrays,[1] particularly, to mimic the natural photosynthetic antenna systems.[2] As nature utilizes optimally organized pigments in the light-harvesting complexes (LHCs),[3] a high level of control over the arrangement of porphyrinic dyes is required to provide the desired optoelectronic properties in the artificial LHCs. Some of the artificial LHCs showed distinct optical properties which reflect the degree of exitonic interaction between porphyrin monomers in the array.[4]

To date, most of the studies regarding interactions between porphyrins are focused on two π planes arranged in a side-by-side manner (i.e., porphyrins are on the same plane).[2a,5] In contrast, fewer face-to-face arrangements of porphyrins are investigated possibly due to the lack of an efficient scaffolding material and synthetic accessibility. Peptides,[6] nucleic acids,[7] viruses,[8] organogels,[9] synthetic polymers,[4b] and dendrimers[2b] have been used as scaffolds

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to display porphyrinic dyes; however, studies using a scaffolding material that can both precisely control the position and relative orientation of porphyrins and provide a face-to-face array of porphyrins have not yet been introduced.

Peptoids are a class of peptidomimetic polymers based on oligo-*N*-substituted glycine backbones.[10] The chemical structure of peptoids differs from that of peptides only in that side chains are attached to the backbone amide nitrogen instead of the α-carbon. As a bioinspired material, peptoids are monodisperse and sequence specific; therefore, precise control of chain length, side chain functionality, and monomer sequence is possible. On the other hand, the non-natural tertiary amide bonds render them highly stable against proteolysis compared to their natural counterparts.[11] Peptoid oligomers can be readily synthesized up to ~50 monomers using a conventional solid-phase peptide synthesis technique.[12] These peptoid oligomers, if α-chiral side chains are incorporated, can form well-defined helical structures that are induced by local steric and electronic interactions.[13] The conformations of peptoid helices have been characterized as stable polyproline type-I-like structures which exhibit a periodicity of three residues per turn (i.e., helical turns are repeated for every three residues) with a pitch length of approximately 6.0 Å.[13a−c,14] These unique structural features of peptoids are proven to be useful for creating novel functional molecules by facilitating a position-specific display of functional groups such as cationic charges,[15] metal binders,[16] a catalytic active site,[17] and steroid hormones.[18]

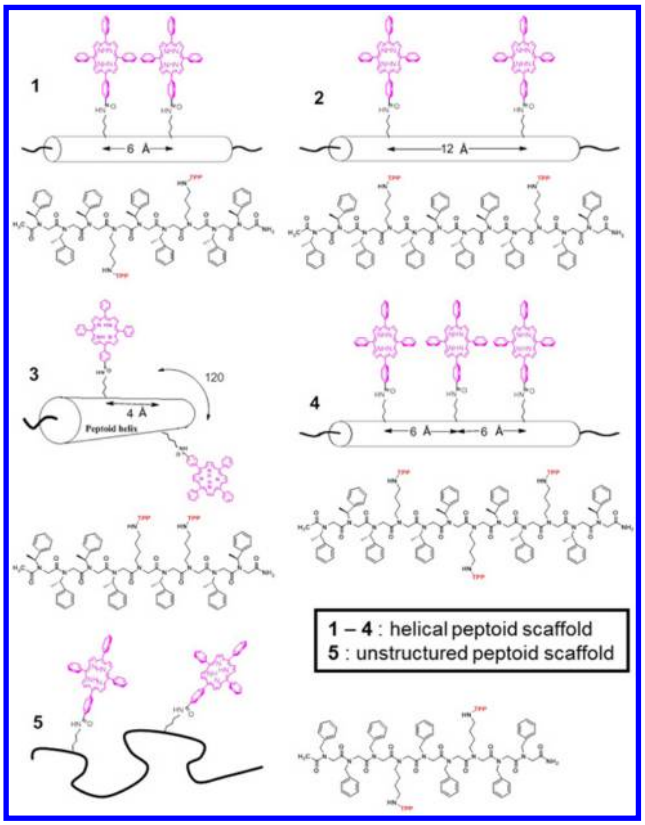

Figure 1. Distance, orientation, and number controlled porphyrin−peptoid conjugates (PPCs).

By employing a biomimetic molecular design approach, our goal is to construct an array of photosensitizers displayed on the peptoid helix and to study energy transfer events upon various arrangements of the photosensitizers. In due course, we present herein an efficient synthetic strategy for a face-to-face arrangement of porphyrins on peptoid helices. Unlike other natural or synthetic polymers, peptoid helices exhibit unique stability and well-defined structural features in various conditions such as solvents and temperature,[13e] providing an excellent scaffolding material. As shown in Figure 1, we designed four porphyrin−peptoid conjugates (PPCs) with precisely defined distance, orientation, and number of porphyrins (**1**−**4**). Distance dependency can be examined by comparing PPCs having two porphyrins positioned 1 pitch (**1**) and 2 pitches (**2**) apart. Additionally, two porphyrins in a distorted orientation (**3**), three porphyrins on one face (**4**), and an unstructured analogue of **1** (**5**) were prepared. Preliminary spectroscopic studies such as UV−vis and

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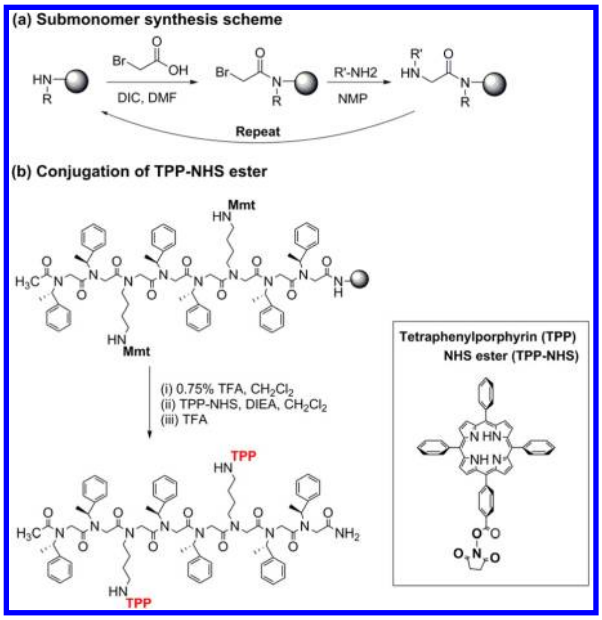
circular dichroism (CD) spectroscopy revealed interesting characteristics of the PPCs. The structurally well-defined PPCs will provide a useful platform to understand the optoelectronic behavior of porphyrins and to develop an artificial LHC.

The sequences and structures of five PPCs (**1**–**5**) and corresponding control peptoids for a CD spectroscopy study (**6**–**9**) are provided in Figure S1 and Table S1 (Supporting Information). The peptoid nonamers and dodecamers were synthesized by microwave-assisted solid-phase synthesis according to the submonomer protocol.[12b] For conjugates **1**–**4**, α-chiral side chain *N*spe (or (*S*)-(−)-1-phenylethylamine) was used to induce a helical fold, and *N*lys (or 1,4-diaminobutane) was incorporated at the position of porphyrin conjugation. To obtain **5**, *N*pm (or benzylamine) was used instead of *N*spe. Once the desired sequence was reached, *N*-terminal amine was acetylated, and then the methyoxytrityl (Mmt) group was deprotected by repeated treatments of 0.75% TFA in dichloromethane (Scheme 1).

Scheme 1. Synthesis of Porphyrin–Peptoid Conjugates (PPCs)



Tetraphenylporphyrin (TPP) carboxylic acid (or 5-(4-carboxyphenyl)-10,15,20-triphenylporphyrin) was prepared according to Lindsey's protocol (see Supporting Information).[19] Initially, coupling of TPP carboxylic acid to resin bound *N*lys primary amine was attempted using an HATU/DIEA system; however, only a poor yield was observed. Successful porphyrin conjugation was accomplished when we employed a *N*-hydroxysuccinimide (NHS) ester/DIEA conjugation method. The structure of TPP-NHS (or 5-(4-carboxyphenyl succinimidyl ester)-10,15,20-triphenylporphyrin)[20] is shown in Scheme 1. All crude peptoids were purified to >97% purity by preparative reversed-phase HPLC, and the molar mass was identified by ESI-MS.

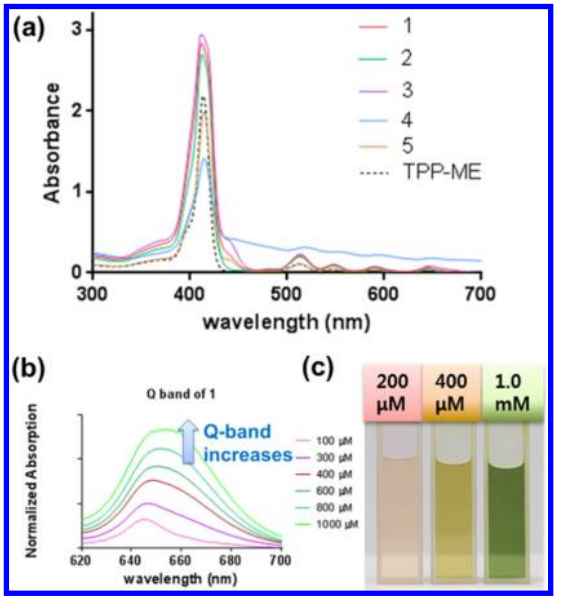


Figure 2. UV–vis absorption spectra of **1**–**5**. TPP-ME (5-(4-methoxycarbonylphenyl)-10,15,20-triphenylporphyrin or tetraphenylporphyrin methyl ester) is used as a porphyrin monomer control. (a) 100 μM in acetonitrile. (b) Q-band increase as increasing concentration of **1** in acetonitrile. (c) Concentration dependent color change of **1**.

Similar to porphyrin monomers such as TPP-ME, UV–vis absorption spectra of all the PPCs showed a strong Soret band at λ_{max} 410–415 nm and Q-bands at λ_{max} 645–650 nm (Figure 2a). The Soret bands of **1**–**4** are noticeably broadened; particularly, a nonzero absorption coefficient between 400 and 700 nm is observed for **4**, which can be advantageous for light-harvesting over a broad spectral range.[21] All conjugates except **2** showed a bathochromic shift (red shift) around 438 nm, and the shift became stronger as the concentration of the conjugate solution increased (see Supporting Information Figure S4). In the Q-band region, a stronger absorption around 640–660 nm was observed for PPC **1** as the concentration increased (Figure 2b). The concentration dependent bathochromic shift provides typical evidence of porphyrin J-aggregation in solution and suggests the existence of self-assembled species via edge-to-edge interaction as well as the excitonic coupling of the transition dipole moments of the chromophores.[22] Interestingly, even at high concentrations (up to 1.0 mM) PPC **2** showed no red-shifted absorption as TPP-ME did not (Supporting Information Figures S4–S5).

Upon dilution of the solutions containing **1** and **3**, we noticed a striking color change from green to bright purple

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(Figure 2c), which provides visual evidence for the concentration dependent red-shifted absorption and J-aggregate formation. In contrast, the solution containing **2** stays bright purple in all the concentrations we used (up to 1.0 mM). PPCs with a disrupted structure (**4**) and an unstructured peptoid scaffold (**5**) (Figure 3a) showed poor solubility in acetonitrile, and the bright purple solution of **4** and **5** at lower concentrations formed precipitates as the concentration increased higher than 0.2 mM.

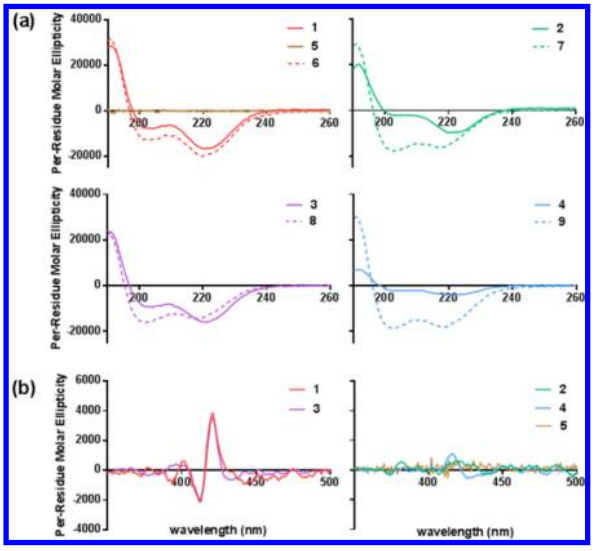

Figure 3. Circular dichroism (CD) spectra of **1**–**9** in acetonitrile (50 μM) were recorded as per-residue molar ellipticity (deg cm^2/dmol) at (a) 190–260 nm and (b) 350–500 nm. Data were aquired at room temperature.

CD spectra were measured at 190–260 nm to monitor the peptoid backbone carbonyl n$\rightarrow\pi^*$ (~220 nm) and $\pi\rightarrow\pi^*$ (~192 and 202 nm) transitions (Figure 3a). As expected, peptoids without porphyrins (**6**–**9**) exhibited typical polyproline type-I (PPI) like CD signatures with two negative Cotton effects at 202 and 220 nm,[13a] and PPC **5**, which used 100% achiral side chains, showed no net CD signal. The maintenance of helical folds was observed for **1** and **3** after porphyrin conjugation; particularly, the CD spectrum of **3** indicated a decreased contribution from *trans*-amide-containing conformers (202 nm) and increased contribution from *cis*-amide-containing conformers (220 nm), which suggests that the slipped-cofacial porphyrin arrangement provided an increased population of PPI type helical conformers.[23] Unlike nonamers, dodecameric PPCs (**2** and **4**) showed disrupted helical integrity upon porphyrin conjugation, where the degree of structural disruption became severe as the number of porphyrins increased from two to three. It is interesting to note that the molecular weight of porphyrins takes up roughly 50% of the whole PPC's molecular weight in **1**, **3**, and **4**; however, only **4** showed severe structural disruption.

The through-space coupling of porphyrins in a chiral environment gives rise to exciton-coupled circular dichroism (ECCD), which is identified by a bisignate CD signature at the Soret region of porphyrin.[24] As shown in Figure 3b, the ECCD spectra were observed for PPCs **1** and **3** with an intense sign of the split Cotton effect. These couplets reflect the chirality between the transition dipole moments of interacting porphyrins. Three PPCs showed little or no ECCD: (1) dodecameric PPC **2** with two porphyrins positioned farther apart (~12 Å); (2) dodecameric PPC **4** with severely disrupted peptoid secondary structure; and (3) nonameric PPC **5** with an unstructured peptoid scaffold.

Handedness of the peptoid helix can be determined by the ECCD of PPCs. As Takei et al. reported with their porphyrin displayed helical polyisocyanides, the positive CD couplet (a positive-to-negative pattern going from longer to shorter wavelength) indicates a right-handed helix.[25] Their conclusion perfectly agrees with an earlier study on peptoids that found peptoid helices composed of *N*spe submonomers form a right-handed helix,[26] which is confirmed by our ECCD spectra.

In summary, we employed the peptoid helix as a scaffolding material to construct a precisely defined cofacial, slipped-cofacial, and unstructured array of porphyrins. The degree of J-aggregation, color change, and excitonic coupling between porphyrins could be modulated by distance, orientation, and number controlled porphyrin–peptoid conjugates. Further spectroscopic and mechanism studies are currently underway, and eventually we anticipate this study can offer new insight into the design of artificial photosynthetic complexes.

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Supporting Information Available. Detailed procedures for the synthesis, characterization, and purification of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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The authors declare no competing financial interest.