Formation and Host Ability of Aromatic Micelles with Oligo(Amino Acid) Cavities in Water

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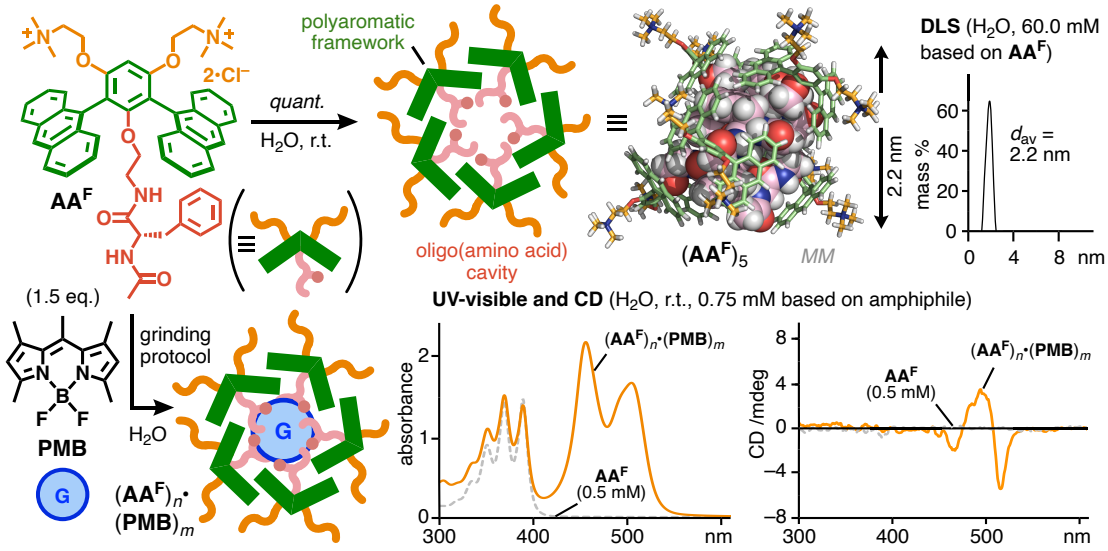
Mimicking natural protein cavities in water with molecular assemblies represents a challenge due to the weak interactions of amino acids. Most mimics rely on long amphiphilic peptides resulting in large/infinite assemblies with limited host functions and stabilities.[1] Aromatic micelles formed from bent amphiphiles possess strong host abilities and high stability, yet purely abiotic cavities.[2] We anticipated that the internal functionalization of aromatic micelles with amino acids or short peptides would provide discrete oligo(amino acid) cavities with unusual host functions in water.

We here report the synthesis of bent amphiphile **AA^F** featuring a phenylalanine-based group at the concave side, including Negishi and peptide couplings as the key steps (Figure, top left). The amphiphile quantitatively assembles in water into aromatic micelle (**AA^F**)$_n$, as indicated by NMR, fluorescence, and DLS analyses, providing a highly condensed oligo(amino acid) cavity with ~2 nm in diameter (Figure, top right). The resulting cavity efficiently encapsulates hydrophobic aromatic dyes (e.g., BODIPYs and coumarins) as well as aliphatic drugs. Notably, the CD spectrum shows a dye-derived Cotton effect, due to moderate chirality transfer from the chiral amino acid residues to the encapsulated achiral dyes. Furthermore, substituting the amino acids with tripeptides enables fine-tuning of the host properties of the aromatic micelle.



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