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Synthesis, structural analysis, and assembly of water soluble quinoline-based oligoamide foldamers

Xiaobo Hu
CBMN, CNRS UMR5248 (Equipe I. HUC, IECB), Bordeaux, FRANCE

Foldamer chemistry is a rapidly expanding research field where chemists explore the construction of various artificial architectures that mimic the folded structures of biopolymers found in nature. Quinoline oligoamide foldamers, as an important branch of foldamers, have been shown to possess many desirable features, including stability and predictability of their folded conformations, and are promising candidates to achieve biological applications. Up to now, most investigations of quinoline oligoamide foldamers have been carried out in organic solvents. This thesis is aimed to expand their scope in aqueous medium and presents several methodologies to achieve solubility, folding, side-chain variation, aggregation and crystal growth ability in water.

First, a solid phase synthesis method was developed to enable the fast access to α-amino acid/quinoline (X/Q) hybrid oligoamide foldamers. The study of these hybrid foldamers in water showed that contrary to (XQ)n-type foldamers the (XQ2)n-type foldamers could adopt aromatic helical conformations with α-amino acid side chains aligned in space. Then, several short side chains were identified to endow aromatic foldamers with both solubility in, and crystal growth ability from water. Six quinoline oligoamides displaying these side chains were synthesized as a case study. Crystals were obtained from aqueous medium in all cases but one, exceedingly soluble in water. At last, efforts were made to construct self-assembled aromatic helix bundles in water based on hydrophobic effects and electrostatic interactions. NMR and crystallographic studies indicated that hydrophobic effects are weaker than expected and not strongly conducive of aggregation.