Synthesis of dynamic peptide-resorcinarene capsules and examination of their properties

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Peptides, as chiral and biocompatible compounds, are attractive building blocks for formation of complex supramolecular systems. However, due to their conformational lability, structures formed during their self-assembly are difficult to predict.

The dissertation presents application of a rigid macrocyclic building block, tetraformylresorcin[4]arene, as a scaffold for formation of highly ordered porous structures based on short peptides. I have synthesized a series of dimeric supramolecular capsules using peptides' methyl amides (up to 4 amino acid residues) connected to the macrocyclic scaffold by imine bonds. Subsequent non-covalent dimerization (by complementary binding motifs of hydrogen bonds resembling β-barrels) leads to formation of capsules that have internal cavities with volumes up to 883 $Å^3$. I have found that homochiral or heterochiral capsules are selectively formed, depending on the length of peptides. These preferences are explained by complementarity of the binding motifs. I have also demonstrated that these capsules can be efficiently obtained from mixtures of racemic peptides by chiral self-sorting processes. I have demonstrated that self-assembly is an efficient thermodynamic force that drives this self-sorting and is able to induce considerable structural changes (here a change of a tautomeric form).

Comparison of experimental and calculated ECD spectra of peptide cavitands leads to the conclusion that they have different inherent chirality in the monomeric form than in the self-assembled dimeric form. Thus self-assembly leads to the change of the inherent chirality. I have confirmed this process and characterized it by ^{1}H NMR and ECD titration as well as theoretical calculations (TD DFT).

In order to increase capsules' stability and change their geometry, I have designed and synthesized a series of azapeptides, which form dimeric supramolecular capsules featuring semicarbazone linkers. Indeed, they prove to be more stable and possess more voluminous cavities than the imine capsules. The proper sequence of amino acids enables synthesis of capsules that have side chains positioned inside the cavity, which is a promising strategy towards functionalization of the capsules for catalytic applications. I have also demonstrated that semicarbazone capsules can be obtained by chiral self-sorting. However, chiral self-sorting is efficient only for the longest azapeptides. Through a dynamic combinatorial approach, I have obtained a unique heterodimeric capsule, that cannot be formed through a classic approach. All capsules and self-assembly processes were characterized in the solution (NMR, circular dichroism) and in the solid state (X-ray).

The peptide-based capsules that have been synthesized are the first known examples of discrete porous structures obtained with using biocompatible peptide elements.