Anion-Binding Cyclopeptides and Cyclopseudopeptides

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Macrocyclic molecules such as calixarenes, cyclophanes, or cyclodextrins are widely used in Supramolecular Chemistry as artificial receptors. Cyclopeptides have received less attention in this context although they exhibit a number of attractive features, one being the close structural relationship to many of the systems used by Nature for substrate recognition. Systematic work carried out in my group has established a group of cyclopeptides comprising alternating natural and non-natural aromatic amino acid subunits as a versatile receptor class. In this context, the ability of a cyclic hexapeptide containing proline and 6-aminopicolinic acid subunits turned out to be particularly interesting as this peptide has the, for a neutral compound, unusual ability to interact with inorganic anions such as sulfate and halides in competitive aqueous solvent mixtures. Although anion affinities approaching the nanomolar range could be achieved under certain conditions, solubility of most cyclopeptide derivatives prepared in the course of our investigations required a more or less pronounced proportion of an organic solvent in the medium in which the binding studies were performed. It therefore remained unclear for some time whether anion binding could be achieved also in 100% water. Recently, we succeeded in preparing a water-soluble cyclopeptide-based receptor that allowed us to perform binding studies in a variety of solvents and solvent mixtures, including in water. Not only could we demonstrate by using this compound that anion complexation occurred even in the absence of an organic solvent in the aqueous medium used for the binding studies, we could also correlate anion affinity with several solvent parameters and thus obtained detailed insight into possible principles underlying anion binding.

We also wondered whether the unusual properties of our anion-binding peptides are limited to this receptors class alone or whether they can be transferred to analogous systems. In this context, we prepared a number of cyclic pseudopeptides containing 1,2,3-triazole units as surrogates for the amide bonds along the cyclopeptide backbone. Some of these pseudopeptides indeed exhibited related receptor properties as the parent peptide. Others behaved totally differently in that they possessed affinity for anions that were typically not bound by the cyclopeptides. An octapeptide analog of the original hexapeptide, for example, preferred binding to aggregates of dihydrogenphosphate anions, albeit only in organic solvents.

In this lecture, our recent work on these cyclopeptides and cyclopseudopeptides will be summarized and our current attempts to use these receptors for practical applications shortly outlined.