Studies on the steric structure and stability of the gas-phase complexes of macrocyclic receptors with anions using ion mobility - mass spectrometry, collision-induced dissociation and computational methods

The negatively charged species, i.e. anions, play important role in many chemical and biological processes, e.g. chloride ion (Cl^-) is the main body electrolyte, and mutation of the ion-channel responsible for its transport across cell-membrane cause cystic fibrosis. Other important anions - phosphates - are major component of bones, nucleic acids and nucleotides (ATP, cAMP, ADP). On the other hand, excessive use of fertilizers by the agricultural industry is responsible for the contamination of water bodies by nitrogen (NO_2^-, NO_3^-) and phosphates ions. Increased levels of these nutrient anions greatly promote the growth of cyanobacteria and algae, which in some cases may result in eutrophication. In Poland, this phenomenon, in particular harmful algal blooms, is often seen in summer in water of Gulf of Gdansk. The other troublesome anion is fluoride (F^-) which excessive accumulation in the body may cause skeletal and dental fluorosis.

In contrast to positively charged species, i.e. cations, anions are challenging targets for recognition studies as they are highly solvated and possess a wide range of sizes and shapes, while most of the cations are spherical. A successful route toward development of selective and effective anion receptor systems take advantage from the rational combination of advanced organic synthesis and modern physicochemical and computational methods. The classical methods, i.e. nuclear magnetic resonance (NMR) and single-crystal X-ray diffraction (X-ray) which are routinely utilized to investigate supramolecular complexes, however, have some disadvantages such as high price of analysis, their time-consuming nature, and requirement of large sample volumes. These limitations greatly reduced the eventual application of these methods in screening studies when a large number of easily synthetically available putative anion receptors has to be examined. In this scenario, an interesting approach relay on the fast examination of small samples of anion complexes in the gas-phase. The ion mobility technique coupled with mass spectrometry (IM-MS) and collision-induced dissociation (CID) seemed particularly attractive in this context. In combination with quantum chemical calculations the recently developed IM-MS technique allow exact determination of the structure of ionic species whereas the CID method can gives information about the relative stability of the ionic complexes. So far, the IM-MS method was never exploited to study the structures of anionic complexes.

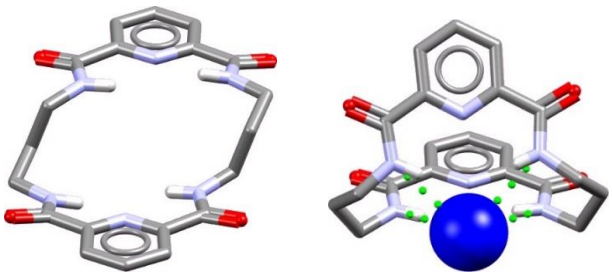

Figure 1. X-ray structures of the free receptor (left) and its chloride complex (right) show how anion-binding triggers the change of the macrocycle conformation.

The main aim of this study is verification if the IM-MS and CID methods also work for studying the more challenging anion complexes, and eventually to test if IM-MS may be utilized for screening studies of such complexes.

As synthetic models we will explore two classes of potent and easily accessible macrocyclic receptors that have been developed in our Institute, i.e. simple macrocycles with different ring sizes as well as more complex unclosed cryptands having a suitable flexible substituent connected directly to the interior of the ring.

Data previously obtained from the liquid and solid phase suggests that such class of macrocycles change their conformation (i.e. their shape) during complexation with the suitable anion (weakly bound anions have no effect). This process, exemplified in Figure 1, could be potentially tracked in gas-phase. It is particularly interesting to study how homologous macrocyclic receptors change their conformation upon anion binding, and equally important how this process is correlated with the relative stability of the complex.

The results of our project can contribute to designing new, selective receptors for anions, which can be used to develop rapid, accurate and cheap tests for the presence and concentration of selected anions in body fluids and water from lakes and rivers.