

Searching for novel drugs and pesticides, among others, relies on rational design of inhibitors of enzymes indispensable for pathogen (cancer cells, bacteria, fungi) development and growth. Such a design bases on three-dimensional structure of these enzymes. Structure of the enzymes is available either from crystallographic studies or by using NMR in solution. Unfortunately, enzyme in solution occurs in several labile forms (conformers) and only one of them binds the inhibitor (the form visible by NMR is an average picture of all the conformers). Moreover, upon binding the inhibitor usually changes the three-dimensional structure of the protein. NMR could follow these changes if the inhibitor contains heteroatom visible.

This project considers construction of inhibitors containing both phosphorus and fluorine atoms in their structure, atoms which enable to detect and follow by NMR small changes around the inhibitor and thus to deduce the exact structure of the enzyme upon its binding. Basing on the experience of authors of the project such inhibitors will be constructed and synthesized and their utility will be evaluated. The results of the project should not only help in better understanding of the enzyme architecture, form a basis for the design of novel drugs but also to obtain of inhibitors able to act towards aminopeptidases, which are considered as targets for anticancer agents.