Innovative organocatalytic strategies in functionalization of drugs, natural products and biological compounds.

Catalytic reactions are pivotal for many processes used in chemical industry, chiefly because they offer a possibility of synthesis of compounds of specific structures. The search for new catalysts capable of ensuring even more selective course of chemical reactions has been undertaken by many research groups all over the world. It has been established that development of science and technology entails growing contamination of the natural environment, contributing significantly to climate change. In view of the above, all of us and in particular scientists should strive to restrict the use of resources of materials and energy. Realization of the ideas of 'green chemistry' in designing new methods of synthesis that would limit the use of hazardous and toxic reagents as well as minimize the amounts of energy and time of reactions, while ensuring high selectivity of the process and easy isolation of final products, makes a challenge worth meeting. The proposed project is meant to answer the challenge posed by development of civilization and in the light of the 2021 Noble Prize in chemistry for "asymmetric organocatalysis based on small organic molecules" fits perfectly in the current trends in science. The tasks planned in the project concern the design of new catalysts that would ensure selective course of many organic transformations. In the project we will concentrate on the organic molecules characterized by large steric hindrance around the active center , whose catalytic potential will be tested. It is postulated that the introduction of sterically crowded substituents into the catalyst structure should considerably improve the process selectivity. One of the objectives of the planned studies is to design procedures that would not need the addition of salts, bases, co-catalysts as well as mixtures of toxic and volatile solvents.

The overriding aim of the project is synthesis of supersteric *N*-heterocyclic carbenes (NHC) that would be used as organocatalysts of the reactions between the α,β-unsaturated carbonyl compounds and a range of nucleophiles. The appropriate design of NHC catalysts is expected to ensure greater control of chemo- and stereoselectivity of a given reaction that would lead to high isolated yields of the final products. The C-X (X = N, P, S, Se, O) bonds are common in natural products, so the design of effective catalytic methods for their generation will significantly contribute to fast development of organic chemistry, bio-organic chemistry and material science. In the project we plan to use the newly designed catalytic systems in the processes of functionalization of hybrid nanomaterials (silsesquioxanes) leading to syntheses of new organosilicon derivatives of high application potential. It is expected that the introduction of heteroatoms to the silicon cubes will improve the thermal properties of silsesquioxanes, which will be carefully tested. What is also interesting, many drugs, natural products and biocompounds contain nucleophilic or unsaturated carbonyl moieties. Thus, the obtained methodology will be used for their functionalization that would hopefully bring greater therapeutic effects. Moreover, the obtained products will be subjected to further chemical transformations in order to characterize their application potential. All newly synthesized compounds, not described in literature, will be isolated, purified and characterized by the available analytical methods. As knowledge of the reaction pathway is of great importance, the experimental and theoretical mechanistic studies will make a significant part of the project. They are expected to expand the knowledge of mechanisms of selected reactions and identification of factors responsible for selectivities of processes. Comprehensive mechanistic studies will contribute to easier and more effective designing of further efficient catalytic methods fully consistent with the principles of 'green chemistry'.

Successful realization of the project will substantially extend the knowledge of organic chemistry and catalysis. Minimization of side products, more economic and ecological procedures of syntheses of biologically important compounds are just a few of the advantages following from the use of catalytic protocols proposed on the basis of optimization of the reactions run in the presence of nonmetallic catalysts. Results of the mechanistic studies will bring new perspectives on the synthesis of more innovative catalysts ensuring higher yields of products in the mildest possible conditions.