An application of new catalytic reactions of chiral 4-vinyl- and 4-ethynyl-azetidin-2-ones in the stereodivergent synthesis of nonracemic heterocyclic compounds.

Due to their well-known antibiotic activity, β-lactams (azetidin-2-ones) have been a matter of interest of numerous research groups specializing in chemistry, biology and medicine since the discovery of Penicillin G by Alexander Fleming in 1928. Since that time a great number of methods of asymmetric synthesis of these compounds have been developed. Thus a variety of them are readily available in both enantiomeric forms in excellent optical purity. Besides the above-mentioned biological activity, β-lactams are characterized by a range of other unique features such as high reactivity resulting from the strained 4-membered ring, the chirality content that can be easily transferred into a variety of products and the rigidity of the structure, which often makes the reactions involving them very stereoselective. These attributes make azetidin-2-ones an interesting chiral building blocks potentially useful in the synthesis of a variety of derivatives not containing a β-lactam fragment. An example of such a process is the introduction of the β-amino acid moiety to baccatin isolated from yew tree needles *via* β-lactam ring opening by hydroxyl group present in the structure of this natural product. Taxol resulting from this transformation is one of the most powerful antitumor agents used in modern cancer therapy. However, the publications on the use of azetidin-2-ones as synthons in organic synthesis constitute only a small part of the literature on biological properties and methods of synthesis of these fascinating compounds. This makes studies in this field interesting and justified.

The aim of this research proposal is to develop a method of the asymmetric synthesis of difficult to prepare, highly substituted allenes, homoallylic alcohols and amines *via* the reactions of readily available chiral β-lactams with a range of electrophilic partners including aldehydes, ketones, imines and their synthetic equivalents. In the next stage of the planned research, these products will be applied for the asymmetric synthesis of various nonracemic N- and O-heterocycles, which are common subunits of natural and synthetic compounds of medicinal interest. It is noteworthy that this type of synthetic strategy, characterized by high chemo- and stereodiversity of products obtained in a short and efficient pathway e.i. stereodivergent is extremely desirable, especially in the field of medicinal chemistry where the ability to prepare a large number of similar compounds (hundreds and even thousands) differing slightly in the structure or only in the relative and absolute configuration is of great importance.

Is it worth noticing that the method that will be developed is an interesting example of one of the most efficient transformations in organic synthesis - the allylation reaction. Although many indium-mediated allylations have been successful with diverse electrophilic species, the known methodologies have mainly focused on simple allylindium reagents (generated *in situ* from allyl bromide or allyl acetate). The use of β-lactams in combination with the Pd(0)/InI methodology provides a unique nucleophilic species – a cyclic ε-amido-allylindiums and ε-amido-propargylindiums, which appear to react with aldehydes in a completely different, as compared to simple allylmetals, and not fully understood manner. This makes the planned study interesting also from the viewpoint of modern organometallic chemistry.

Despite great progress in asymmetric catalysis, methodologies based on diastereoselective transformations of cheap, readily available chiral compounds, which β-lactams are, remain an interesting alternative. Especially in industrial processes, where the time devoted to the optimization (catalytical methods are usually characterized by low substrate tolerance) and simplicity of product isolation (diastereoisomers, in contrast to enantiomers, can usually be purified by crystallization or using chromatographic techniques), methods of synthesis based on enantiomerically pure starting materials or cheap chiral auxiliaries (natural or semisynthetic) are very desirable.