The [3,3]-sigmatropic rearrangement of allyl cyanates and hydroacylation as a tool for the preparation of α- and γ-amino ketones and their derivatives

The aim of this project is the development of a new method for the synthesis of α- or γ-amino ketones and their derivatives (e.g. amino alcohols, aza-heterocycles, etc.) via a combination of [3,3]-sigmatropic rearrangement and hydroacylation reaction.

α-Amino ketones are useful scaffolds in both synthetic and medicinal chemistry due to the fact that they play a crucial role in many biologically active natural products and pharmaceuticals. They are also useful for the construction of structurally diverse molecules. α-Amino ketones can also be used as versatile building blocks for the synthesis of nitrogen- and oxygen-containing molecules, including 1,2-amino alcohols and 1,2-diamines, which are used extensively in organic synthesis as chiral auxiliaries, ligands, and chiral resolving reagents. γ-Amino ketones are also endowed with diverse biological activity, and are useful building blocks in organic synthesis, similarly to the α-amino ketones discussed above. In particular, they are highly valuable precursors of 1,4-amino alcohols, 1,4-diamines, and pyrrolidine derivatives.

The novel synthetic pathway for the preparation of the target amino ketones proposed in this project includes two key steps: [3,3]-sigmatropic rearrangement of activated allyl alcohols (mainly allyl cyanates) to allylamines and hydroacylation of the double bond of the resulting allylamines. Such an approach will enable the preparation of structurally diverse α- or γ-amino ketones and their derivatives. The second step, hydroacylation, will be conducted in either inter- or intramolecular manner, which in our opinion will extend the scope of the studied methodology significantly. A major part of the studies will be dedicated to the synthesis of optically enriched α- and γ-amino ketones. In addition, in a further step of the proposed project, the hydroacylation reaction will be replaced by other hydrocarbonylation processes. In particular, we will focus on hydroesterification, hydroformylation, and the most difficult to perform – hydrocarbamoylation of the double bond. We expect this approach to additionally extend the scope of the investigated synthetic method, and open an access to complex, highly functionalized amino carbnonyl derivatives, e.g. amino esters, amino aldehydes or amino amides. All of them are versatile and attractive building blocks for organic synthesis, and can serve as precursors of biologically and pharmaceutically active molecules. In addition to the main part of the project, we are going to demonstrate the utility of the developed methodology by the synthesis of naturally occurring biologically active compounds and medications.

We expect that our long-term experience and outstanding laboratory equipment guarantee the successful realization of all research tasks presented in the current research proposal. We are of the opinion that the proposed project will contribute to the methodology of synthetic organic chemistry, and will serve as a useful tool for the preparation of highly desirable complex organic molecules, including biologically and pharmacologically active compounds.