

## **ASYMMETRIC DIELS-ALDER REACTION OF GLYOXALATES: THE SEARCH FOR NEW CATALYSTS AND USE IN THE SYNTHESIS OF DERIVATIVES OF NATURAL PRODUCTS**

The main goal of the project is to use the enantioselective cycloaddition reaction of glyoxylate to dienes (hetero-Diels-Alder reaction (hetero-DA)) in stereocontrolled synthesis of ulosonic acids (3-deoxy-aldonic, KDO, KDG, KDN, DAH). This project involves extending the previous knowledge in the area of enantioselective DA reaction of glyoxylate and proposes new catalysts in this reaction. This research focuses primarily on innovative usage of chiral complexes of zinc and iron, which have not been effectively employed in this reaction. During the studies, we will concentrate on the application of organocatalysis in the aforementioned reaction. Organocatalysts may activate a glyoxylate molecule using H-Bond strategy. Both routes: the reaction being catalyzed by the metal complexes and organocatalysts, are an important extension of contemporary knowledge in the area of DA reaction. Adducts, obtained in this stage will be precursors in the synthesis of ulosonic acids - an important group of natural compounds.

The model reaction is an example of the hetero-Diels-Alder reaction of 1,3-diene and dieneophile, which in this case is glyoxylate. The use of glyoxylate as the starting material is essential for this project. In this way the reaction can be used in the stereoselective construction of the pyranose ring – backbone of ulosonic acids (and other sugars). The hetero-Diels-Alder reaction is one of the best methods for constructing six-membered heterocyclic systems. However using this type of reaction in the synthesis of the title compounds is uncommon and requires new solutions. The proposed outline highlights the key problem of reaction stereoselectivity and then its adopt in the target a *de novo* synthesis of bioactive compounds.

The concept of this work includes: preparing substrates for the model hetero-Diels-Alder reaction, optimizing the reaction conditions, selection of new catalysts and the interim analysis. The developed innovative method will be further used in the synthesis of ulosonic acids. This will be the final stage of the project. The key concept of research is the use of low-cost catalysts based on abundant and environmentally friendly metals such as zinc and iron. This will reduce the cost of synthesis and open up the possibility of applying these methods in the industry. In addition, the project plan comprises use of organocatalysis and the hydrogen bond activation strategy. The application of this inventive idea will allow to eradicate the use of metals in the synthesis. This is very important in planning the synthesis of modern drugs (*Zaninamivir*), and the synthetic strategy is conceptually consistent with this project.

*Experience of Stereoselective Synthesis Group in this field, as well as the available equipment at Jagiellonian University will allow for a full, prompt and correct characterization and analysis of results.*

This project brings out considerable organic chemistry issues. One of them is the stereoselective formation of carbon-carbon bonds. The new methodology of the hetero-Diels-Alder reaction contributes to a considerable extent to a solution of this problem. The search for catalysts will expand our knowledge on the use of organocatalysts, zinc and iron compounds in an asymmetric cycloaddition reaction. The experience of *Stereoselective Synthesis Group* in the area of application of chiral Lewis acids containing zinc and iron as well as organocatalysis will allow the implementation of the proposed research and publication of the results in leading scientific journals. Thanks to this initial results we specify new direction in our research. Finally, the methodology will be an alternative to the synthesis of six-membered heterocyclic systems which will be employed in the synthesis of complex natural products, particularly ulosonic acids.