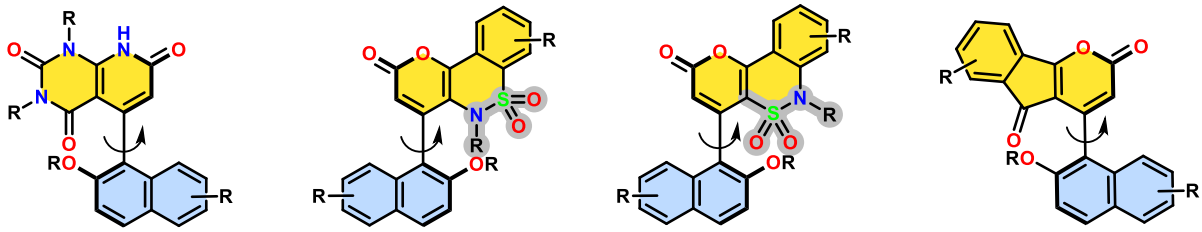
1. PHD PROJECT DESCRIPTION (4000 characters max., including the aims and work plan)

Project title: *De novo heteroarenes formation through atroposelective annulations toward axially chiral systems*

1.1. Project goals: The essence of the Project is an extensive exploration of important and challenging NHC-catalyzed cascade reactions based on new strategies involving enantioselective organocatalytic atroposelective annulations of enolizable heterocycles and enamines. Special attention will be focused on the formation of polyheterocyclic motifs bearing C-C axis, and more importantly synthetic strategies giving the access to the whole spectrum of structurally and stereochemically complex target products. The investigations will include the following NHC-catalyzed reactions representing different modes of activation of the carbonyl group, as well as a dual activation strategy integrating N-heterocyclic carbene (NHC), Brønsted acids (BAs), and Lewis acids as additives for better control of transfer chirality. An additional aspect of the work will be the use of quantum-mechanical calculations to analyze the mechanism and determine the share of individual intermolecular interactions in the stabilization of transition states of selected chemical transformations, and also for determining rotation barriers. The main scientific objectives are: • NHC-catalyzed atroposelective synthesis of axially chiral uracyl-fused arylpyridinones • NHC-catalyzed atropoenantioselective cycloaddition of sterically hindered ynals and benzo[e][1,2]thiazin-4-ones 1,1-dioxide • Atroposelective construction of benzo[c]pyrano[2,3-e][1,2]thiazinone-fused arenes • Enantioselective [3+3] annulation of indan-1,3-diones catalyzed by N-heterocyclic carbenes.



The research project will be carried out as part of the newly awarded Preludium BiS 4 research grant. The National Science Centre will fully cover the research funding and scholarship (5000 PLN brutto) after the mid-year evaluation, PLN 6000. As part of the grant, the doctoral student will undertake a 3-6 month scientific internship abroad.

1.2. Outline: Obtaining optically pure organic compounds in the stereocontrolled manner is still the subject of intensive research due to the need to obtain numerous substances in enantio- and diastereomerically pure forms. In particular, the growing demand for chiral

compounds with a defined absolute configuration applies to the pharmaceutical and agrochemical industries. The identification of new reaction profiles is one of the fundamental challenges of modern organic chemistry [1]. This research project is aimed at opening a new research area located in the field of asymmetric catalysis with the use of chiral organic catalysts and introducing into the literature innovative, stereocontrolled atroposelective transformations that enabling access to non-classical patterns of reactivity and interesting bioactive structural motifs characterized by a broad spectrum of activity. It is worth emphasizing that the development of catalytic and stereoselective synthetic approaches allowing access to new reactions meets the requirements of "green chemistry" [2]. Therefore, the essence of the Project is an extensive exploration of important and challenging NHC-catalyzed cascade reactions based on new strategies involving enantioselective organocatalytic atroposelective annulations of enolizable heterocycles and enamines. Special attention will be focused on the formation of polyheterocyclic motifs bearing C-C axis, and more importantly synthetic strategies giving the access to the whole spectrum of structurally and stereochemically complex target products.

1.3. Work plan: The scope of the research will primarily involve acquiring knowledge and skills to conduct multistage syntheses of structurally complex substrates. A key aspect will be optimizing reaction conditions towards atroposelective synthesis of heteroaromatic products. The research scope includes four structural variants. As part of the project, the doctoral student will undertake a research internship in one of the foreign centers for 3-6 months, funded by NAWA.

1.4. Literature *(max. 10 listed, as a suggestion for a PhD candidate)*

[1] a) Asymmetric Organocatalysis, Eds. List B., Maruoka K., Thieme Verlag, 2012. b) "Comprehensive Enantioselective Organocatalysis: Catalysts, Reactions, and Applications" Dalko P., Ed., Wiley-VCH, Weinheim, 2013. c) Asymmetric Organocatalysis - from Biomimetic Concepts to Applications in Asymmetric Synthesis, Eds. Berkessel A., Gröger H., Wiley-VCH, 2005. d) Asymmteric Organocatalysis in Natural Drug Synthesis, Eds Wasser M., Springer-Verlag Wien 2012.

[2] N-Heterocyclic Carbene in Organocatalysis, Eds Biju A., Wiley-VCH, 2018.

a) Kozlowski M.C., Morgan B. J., Linton E.C.,*Chem.Soc.Rev.***2009**,38,3193. b) J. Wang et.all., *ACS Med. Chem.Lett.* **2017**, *8*,299. c) J. Wencel-Delord et. all. *Chem.Soc.Rev.* **2015**, *44*, 3418. d) G. Yang, D. Guo, D. Meng, J. Wang, *Nat.Commun.* **2019**, *10*, 3062. e) S. Zhuo et. all *Angew. Chem. Int. Ed.* **2019**, *58*, 1784. f) A. T. Biju et. all. *Angew. Chem. Int. Ed.* **2021**, *60*, 12264. g) J. Wang et. all *Nat.Commun.* **2018**, *9*, 611. h) B. Tan et. all *Chem. Rev.* **2021**, *121*, 4805

1.5. Required initial knowledge and skills of the PhD candidate

Good knowledge of organic chemistry
Predispositions and strong motivation for scientific work (regularity and timeliness)
Independence in achieving the set research goals, at the same time the ability to work in a group

1.6. Expected development of the PhD candidate's knowledge and skills

PhD candidate will gain knowledge and skills in field of advanced synthestic chemistry. Candidate will get specialized knowledge in asymmetric synthesis, organocatalysis, atropoisomers and their physicochemical characterization by separation and other instrumental techniques. During the study student will be able to present obtained data in form of high-impact factor publication. As part of the PhD project, it is planned to develop new technological solutions with a high level of creativity, legally protected by a patent.