

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

Project title:

Asymmetric addition reactions catalyzed by metal complexes with chiral ligands obtained from natural monoterpenes

1.1. Project goals

The aim of the project is the synthesis of the new ligands using natural bicyclic monoterpenes and their use in selected addition reactions of aryl, alkynyl, propargyl, and allyl groups to aldehydes, ketones, imines, and enones.

- Modifications of selected monoterpenes towards the synthesis of appropriate ligands: diamines and amino alcohols and their derivatives, and then their use in the addition of acetylene and propargyl derivatives to aldehydes and imines catalyzed with zinc and copper compounds.
- Synthesis of optically active diarylmethanols, also with heteroaryl substituents, by the addition of arylboronic acids to the corresponding aldehydes in the presence of chiral metal complexes.
- Asymmetric conjugated addition of arylboronic acids to α,β -unsaturated ketones and vinyl epoxides.

1.2. Outline

Over the past two decades, catalytic asymmetric reactions have become one of the most important research fields allowing the synthesis of many useful organic compounds. Despite diverse catalysts, which were developed and used under different reaction conditions, there is still place to search for the effective chiral ligands that, in combination with appropriate transition metals, will catalyze the addition reactions. Optically active diarylmethanols, propargylic alcohols or homoallylic alcohols are precursors to many biologically active compounds, which could be analyzed in specialized laboratories. Amino alcohols synthesized from turpentine monoterpenes, α - and β -pinene, developed in my laboratory have been successfully used in highly enantioselective reduction of ketones with borane and under transfer hydrogenation conditions.

1.3. Work plan

Considering the above, in this PhD project, methods for the synthesis of the new chiral amino alcohols, diamines, and their derivatives starting from the basic turpentine components, α - and β -pinene and 3-carene, will be developed.

The rigid bicyclic structure of prepared chiral ligands should have a good effect on the enantioselectivity of the addition of organometallic compounds. In the initial stage of

research, we will check the effectiveness of the obtained amino alcohols using model compounds and known reaction conditions in which alkynylation or arylation of aldehydes is mediated by dialkylzinc compounds. The possibility of using other zinc compounds as substitutes for pyrophoric diethyl zinc will also be tested. The scope of applicability of the developed additions will be checked in reactions with variously substituted aldehydes, acetylenes and arylboronic acids, especially modified with fluorine substituents. Particular emphasis will be placed on studying the enantioselectivity of the addition of different acetylenes and the catalytic activity of the used ligands to decrease the catalyst loading. It seems that alkynylation and arylation of ketones is the least developed field with only a few reports describing enantiomeric excess over 90%.

Although allylation reactions, especially stoichiometric, are well studied, we will also check catalytic version to verify the effect of chiral ligands, allylation reagents and metallic precursors for this group of compounds. Different types of activation were developed for catalytic allylation. Most catalysts are Lewis acids, activating the electrophilic substrate - e.g. aldehyde. Lewis base catalysts and bifunctional catalysts have been developed to a much lesser extent.

The last reaction type that we would like to study is the asymmetric conjugated addition of arylboronic acids to α,β -unsaturated ketones mediated by zinc or copper compounds. In parallel with unsaturated ketones, we will examine whether conjugated addition of aryl groups is possible with vinyl epoxides that have not previously been studied in this reaction.

1.4. Literature

1. T. Bauer, *Coord. Chem. Rev.* **2015**, *299*, 83–150.
2. C.-H. Ding, X.-L. Hou, *Chem. Rev.* **2011**, *111*, 1914–1937.
3. M. Ćwiklińska, M. P. Krzemiński, A. Tafelska-Kaczmarek, *Tetrahedron: Asymmetry* **2015**, *26*, 1453-1458.
4. A. Kmieciak, M. P. Krzemiński, *Tetrahedron: Asymmetry* **2017**, *28*, 467-472.
5. Z. Rafiński, M. P. Krzemiński, *Catalysts* **2019**, *9*, 117; doi:10.3390/catal9020117.

1.5. Required initial knowledge and skills of the PhD candidate

Good knowledge of organic chemistry.

Strong motivation and predispositions for scientific work (regularity and timeliness).

Diligence and willingness to work hard despite the failures encountered.

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

Mastering advanced experimental techniques and improving the ability to determine the structures of compounds using spectroscopic methods.

Independence in achieving the set research goals, at the same time the ability to work in a group.