

Ph.D. thesis submitted by Eva Bednářová is focused on the synthesis of new chiral 2,2'-bipyridines and 2,2'-bipyridine *N,N'*-dioxides and their application as ligands in transition metal catalysis or as organocatalytic reagents in stereoselective transformations. The thesis follows up on the topic focused on bipyridine-based catalysts studied in the group of professor Kotora at the Department of Organic Chemistry, Charles University. The project was carried out jointly in Prague and at the University of Montpellier under supervision of doctor Frédéric Lamaty.

Introductory part (“State of art”) describes in detail (on 74 pages) a synthesis of bipyridine ligands and their applications in various metal-based catalytic systems. A special interest is devoted to Bolm’s ligand and its analogues including bis(oxazoliny)bipyridines. This part deals also with 2,2'-bipyridine *N,N'*-dioxides which are intensively studied in the laboratory of applicant. Introduction is supplemented by short review on catalytic [2+2+2] cyclootrimerization of alkynes and nitriles which is versatile tool for synthesis of substituted pyridines. It should be stated that content of the introduction part corresponds to the topic of the work and it brings necessary background for a reader of the thesis.

Results and discussion is divided into six parts describing three individual projects. In the first part, new method for [2+2+2] cyclootrimerization has been developed. Advantageously, it tolerates halogen substituents which can be consequently utilized for late-stage derivatization of thus prepared pyridines. The second project is focused on the synthesis of chiral 2,2'-bipyridines and their application as ligands in transition-metal catalysed asymmetric reactions. Importantly, for the preparation of bipyridine ligands, substituted halopyridines from the first part were used. Catalytic system with ligand **296** showed robustness in application for various reactions mainly being not sensitive on the reaction conditions like the system with original Bolm’s ligand **8**. Last project was focused on the synthesis of *N,N'*-dioxides and their applications as Lewis acids in organocatalytic procedures. The newly prepared compounds did not overcome original dioxides **141** and **142** published previously by Kotora’s group but they brought interesting data to elucidate structure-efficiency relationship in this class of catalysts.

Overall, the thesis is logically constructed. Style of presentation is on good level. All conclusions are supported by relevant data and they are clearly stated. Schemes, Figures and other illustrations meet standard criteria for publishing in the area of organic chemistry. New compounds are adequately characterized by <sup>1</sup>H and <sup>13</sup>C NMR, by IR spectroscopy and by HR-MS. Enantiomeric purity is well documented by HPLC on chiral phase and/or by values of optical rotation. I appreciate Experimental part which is written at very good level.

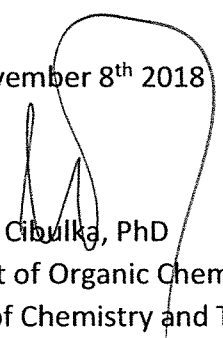
There are some comments and recommendations which should be addressed within the defence:

1. Statement on page 47 "Regarding the chiral bipyridine *N,N'*-dioxides, only compounds with central, axial and combination of both elements of chirality were used as Lewis-base catalysts" gives the impression that a lot of dioxides with the other type of chirality have been synthesized but not tested yet. Is it true? Which types of chirality could be expected within this group of compounds?
2. On page 59, general scheme for the mechanism of [2+2+2] cyclootrimerization is presented. Some steps are expected to be reversible. Could applicant comment this issue?
3. It would be helpful to describe atoms in the Figure 13. Using colours is not clear.
4. I like the experiments towards explanation of halogen exchange during cyclootrimerizations of the corresponding halopyridines in the presence of Cp\*RuCl(cod) (pages 87-90). Nevertheless, it would be nice to discuss a role of pyridine nitrogen in the process. It seems only halogen in alpha-position to pyridine nitrogen is exchanged (e.g. chlorine replaces iodine in **244aa** and not in **245aa**). Is there any experiment which could support or rebut this hypothesis?
5. Chapter "0" appears in some parts of thesis.
6. Scheme 75 does not describe the situation accurately. It seems that there is no reaction. According to description on page 143, mixture of products was formed. It should be clear from the scheme. Was the product **334** presented in the reaction mixture?
7. Is there any explanation for differences in diastereoselectivity of dimerization observed by applicant for formation of **334** and that described by Denmark in the case of formation of compound **143**?

#### Evaluation:

I would like to conclude that the research in the thesis is original with high scientific value. The results are part of at least 3 papers; two of them were published in highly impacted journal *Advanced Synthesis and Catalysis*. In all papers, applicant is the first author. At least one more paper is expected to be published soon. It should be stated that the applicant clearly demonstrated skills and the ability to work independently in the areas of synthetic organic chemistry and catalysis. Overall I consider the PhD thesis on very high level. Therefore I recommend **PhD thesis to be accepted** and doctoral degree to be awarded to author after successful defence.

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