



Evaluation Report on the Doctoral Thesis

Design, Synthesis, and Application of Novel Bifunctional (Thio)urea Organocatalysts Derived from Saccharides & Catalytic Asymmetric C–H Arylation of (η^6 -Arene)Chromium Complexes

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The presented dissertation thesis is focused on the development of new synthetic procedures in the field of organocatalysis and consists of two rather independent parts.

In the first part, three new types of saccharide-derived urea and thiourea organocatalysts were proposed, synthesized and evaluated. The first type was based on the symmetrically substituted urea/thiourea with two 2-amino-2-deoxysaccharide units, the second type contained urea or thiourea substituted with saccharide at one side and with *trans*-cyclohexane-1,2-diamine on the other side and the third type contained saccharide and α -amino acid derived tertiary phosphine. Retrosynthetic analysis was applied to propose the synthetic pathways to appropriate building blocks that together would form the target catalyst. Obviously, the synthesis of first type of organocatalyst was the most complicated and therefore several options were tried. Although most of the reactions performed quite well, none of the reactions gave the crucial isothiocyanate and the final product has not been obtained yet. On the other hand, both catalysts of type II and III were prepared and evaluated for their catalytic function and this is a great success. The second part was done during the students' internship in Larrosas' group at the University of Manchester and is dedicated to the synthesis of planar chiral chromium complexes *via* the direct catalytic asymmetric C-H arylation. The largest portion of the work was in the synthesis of enantiomerically pure axially chiral phosphine ligands, ligands with chiral center on the phosphorus atom, and Buchwald-type catalysts. All of them were prepared and tested for their catalytic ability. This part therefore may also be considered as a great success.

The thesis has a traditional structure with a very informative introduction part that describes the field of organocatalysis with the main focus on the topics close to the aims of the thesis. It contains the majority of the most relevant references of the related work. The introduction is followed by results and discussion part (separated for both parts) that starts with specific aims and rationale of the thesis, followed by the design of new organocatalysts and proposed experiments, comments to the discoveries, conclusion, experimental part, list of publications and references.

General comments to the text and content:

- The theoretical part including the literature research and references is highly informative, still conceive, it was pleasure to read.
- The discussion is focused on the mechanisms of the reactions and explanation of all important aspects including stereoselectivity, reactivity, etc.
- In my opinion, the discussion part should contain a brief comments on the determining of the structure(s) of (a) selected product(s). Although this is usually not the part of the articles in scientific



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journals, it is my opinion that in the PhD thesis, this shows the reviewers that the student is capable of the interpretation of the spectral data.

- Page 61, 3rd paragraph, I believe that there should be “.....catalysts of type I have not been prepared yet...” Not “... type III...”
- $\text{C}_2\text{H}_5\text{COOH}$ should probably be dicyclohexylacetic acid rather than dicyclohexylcarboxylic acid

Questions and topics for the discussion:

1. In the first part of the project, it seems that all three types of the catalysts should have had both urea and thiourea core. Is there any reason, why type I and II were only proposed and synthesized as thiourea-based?
2. Since both catalysts of the type II and III were successfully prepared, I am curious why the catalytic ability of the type II was only determined in one reaction while the type III was evaluated much more thoroughly. It seems to me, that the type III was considered the most important, is that correct? Why?
3. In the Scheme 76, there is several times significant difference between the yield of (*S*) isomer and (*R*) isomer, e.g. 98 % : 73 %; 95 % : 69 %. Is there any explanation for that?
4. Scheme 81 - How did the proposed reactions in the scheme work after you had left the Larrosa's group? Did anybody try them?

Despite of all the comments and questions mentioned above, I must state that all aims of this thesis were completely fulfilled. All of the conclusions are fully supported by the experiments. The amount of work is enormous, all new compounds were fully characterized by the standard set of physical and spectral data. This thesis resulted in two first-author publications in respected journals (especially *ACS Catalysis* is one of the best journals in this research field) and in addition, the applicant is a co-author of four publications that are not related to the topic of this thesis but this still confirms the high ability of the author to collaborate with other researchers on a vast variety of topics. The thesis is a very nice piece of work and the author had to master a variety of techniques to achieve all of the proposed goals.

In conclusion, the presented results are original and of a high scientific value and therefore I recommend the Thesis for the defense and further proceedings for obtaining the PhD degree.

In Olomouc 19.5.2021

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