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**DICUS**  
DIPARTIMENTO DI CHIMICA  
"UGO SCHIFF"

Sesto Fiorentino, June 12, 2023

To the Scientific Discipline Council of Chemical Sciences at the Wrocław University of Science and Technology

Object: Review of the doctoral dissertation of Mr. Franz Steppeler, M.Sc. entitled:  
*Synthesis of chiral 2-azabicycloalkane derivatives and their application in asymmetric synthesis*

Sir,

The [4+2] Diels-Alder cycloaddition reaction (D-A) is among the more powerful tool in synthetic organic chemists' hand for the construction of six membered ring systems in particular and complex organic skeleton in general. Along with its historical relevance, day after day new D-A based on new reaction conditions, new catalysts, and new reagents renew and increase its value. In this scientific scenario the PhD thesis of Mr. Franz Steppeler represents a nice and valuable contribution. Before to go in details I confirm that, generally speaking, this doctoral dissertation demonstrates that the candidate Franz Steppeler possess general theoretical knowledge in organic chemistry as well as the ability to conduct research independently. Additionally, the subject matter of the doctoral dissertation offers several original solutions to different scientific problems related with D-A and enantioselective organocatalysts. At the same time the original solutions reported to the different problems faced can be applied in the social and economic sphere.

In more details, the introduction section of this doctoral dissertation demonstrates the general theoretical knowledge of the candidate on the research topic faced. In particular, the problems related with the several degrees of selectivity (chemo-, regio-, stero-, and enantioselectivity) during organic synthesis is well described. At the same time the importance and impact of heterocyclic systems either in organic chemistry and biology is well explained. Based on the knowledge and skills of the research group where the



candidate carried out his PhD the stereoselective synthesis of 2-azanorborane derivatives *via* asymmetric *aza*-Diels-Alder cycloaddition was studied in detail. The DA-products obtained were structurally elaborated for the preparation of a series of triazole and thiourea derivatives. These derivatives were, in turn, studied for their ability as calix[4]arene based thiourea organocatalysts.

As a clear demonstration of Mr. Franz Steppeler ability of independently conduct scientific work, a number of thiourea derivatives were designed as bifunctional organocatalysts using chiral moieties based on proline or *Cinchona* alkaloids and used in model Michael-addition reactions that afford up to 96% enantiomeric excesses. Eventually, all triazoles and a selection of the derived thioureas prepared during the PhD were tested for their biological activity. Triazoles were tested as antiproliferative agents against various malicious cancer cell lines and chosen triazoles and thioureas exhibited a promising behaviour as antiviral and antifungal agents. As a further demonstration that results achieved in this PhD represent an original solution to selected scientific problems, the candidate presents 3 patents among the scientific products of his research.

Among other relevant scientific products, the candidate presents 6 poster and 1 oral communications to national and international meetings, 1 book chapter and 4 publications on peer reviewed international journals. Eventually, during his PhD the candidate spend two short periods visiting abroad universities (University of Montpellier, Institut des Biomolécules Max Mousseron (IBMM), and University of Bristol, School of Chemistry) in both cases under the supervision of world leading experts in stereoselective synthesis, namely Prof. Alberto Marra and Prof. Varinder Aggarwal.

I wish to communicate to the Scientific Discipline Council of Chemical Sciences at the Wrocław University of Science and Technology that the doctoral dissertation of Mr. Franz STEPPELER, M.Sc. entitled: "Synthesis of chiral 2-azabicycloalkane derivatives and their application in asymmetric synthesis" meets the conditions set out in art. 187 of the Act of July 20, 2018, Law on Higher Education and Science (i.e. Journal of Laws of 2018, item 1688, as amended). In fact, the doctoral dissertation demonstrates Mr. Franz Steppeler general



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theoretical knowledge in chemistry and in particular stereoselective synthesis as well as the ability to conduct independent research. Moreover, the subject matter of the doctoral dissertation is an original solution to a scientific problem and offers application of the scientific results achieved.

Sincerely

Stefano Menichetti

Professor of Organic Chemistry