

Supervisor reference letter to commence the examination of the dissertation thesis of MSc. Sara Eunice Agosthino Monteiro

MSc. Sara Eunice Agosthino Monteiro start her study in accredited study program Organic Technology at the Chart of Technology, Institute of Organic Chemistry and Technology, Faculty of Chemical Technology, University of Pardubice Czech Republic in October 2015. The main theme of her work was the research of synthesis of key intermediates of bioactive non-halogenated synthetic prostaglandin analogue of $\text{PGF}_{2\alpha}$ - Alfaprostol. Sara's work continued the previous experience of the supervisor and his group and followed up on the results of the technological project which was focused on the development of producing technology of Alfaprostol.

As already mentioned Alfaprostol is bioactive non-halogenated synthetic prostaglandin analogue of $\text{PGF}_{2\alpha}$, clinically is used as a luteolytic agent. For this reason, Sara focused on a literature search to verify the current state of the art regarding the synthesis of this atypical prostaglandin molecule. Subsequently, the structure of Alfaprostol was subjected to a retrosynthetic analysis. It was decided, propargyl alcohol moiety, which differentiates the Alfaprostol from other natural and synthesized prostaglandins, will be the part of molecule suitable for research from the perspective of organic synthesis and organic technology respectively. The research was focused on the synthesis of propargyl moiety with existing industrial intermediates, but at the same time using modern synthetic methods with the aim of obtaining a key intermediate for synthesis and potential production of AP.

Sara dove into this project with a high intention with proper exemplary ignition. However, chemistry has shown her to have certain patterns, while Sara has found that not what is described in the literature as a common reaction works and can be applied to advanced chiral molecules as the Corey alcohol derivatives. Sara soon realized that a failed experiment was an integral part of the research and, in my opinion, it was more than necessary. However, she has worked very diligently, conscientiously and she shown that the key intermediate of Alfapropstol synthesis can be synthesized using modern synthetic approaches.

Sara was able to successfully present her work at scientific conferences and publish the results of her experimental work in scientific journals (*Tetrahedron Letters*, **2017**, 58, 2228 and *Org.*

Prep. Proced. Int., **2019**, Accepted for publication on 28th September 2019.), at the same time Sara has also shown that she is able to work with literature sources, appropriately sort the information and then summarize it as a review paper (*ChemistrySelect*, **2019**, 4, 11247-1125).

Sara passed all planned examinations during her studies, as well as the state doctoral exam she passed on 22nd May 2018.

In conclusion, MSc. Sara Eunice Agosthino Monteiro has demonstrated knowledge, stubbornness and systematic approach in her experimental work, as well as extensive knowledge in carrying out during examinations of chosen subjects.

As her supervisor, **I recommend submitting her dissertation thesis to the defense process.**

Pardubice, Dec. 3, 2019

assoc. prof. Aleš Imramovský, Ph.D.
Ph.D. supervisor