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Review to Tomáš Svoboda`s Bachelor thesis

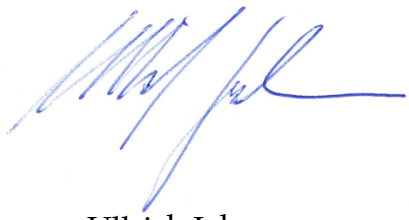
Ladies and Gentlemen,
Phenolic natural products are important compounds in many areas of organic and medicinal chemistry as well as in biology. Therefore, it is an important challenge to find efficient approaches to them. Podophyllotoxin is an iconic lignan natural product that has inspired generations of chemists and biologists because of its diverse biological actions and remains an important synthetic target.
Tomáš Svoboda took the challenge in his experimental work toward his bachelor degree to develop a new approach to podophyllotoxin. He aimed for an approach that is based on a tandem approach consisting of conjugate addition of an appropriately functionalized aryllithium to a cinnamate followed by a Mannich reaction step. A ring closing metathesis (RCM) was supposed to form the C-ring of the natural product. Finally, another conjugate addition was envisaged to lead to the D-ring. He started his investigation with applying an asymmetric copper-catalyzed vinylation reaction of 2-bromopiperonal. After initial difficulties he was able to reproduce the conditions and provides a good result for this challenging reaction. In parallel he also prepared the racemic version, which he used in the following initial exploration of the success potential of the chosen strategy. Over the course of his experimental studies, he reduced the tandem conjugate addition/Mannich reaction and subsequent amine elimination successfully to practice. The following RCM reaction required expectedly optimization, but conditions for a successful dihydronaphthalene formations were found. Finally, Tomas undertook model studies to perform the final conjugate addition, which were not successful so far, but provided valuable insight for further investigation.

The thesis is typically organized. In the introduction the state of the art is comprehensively summarized, including the occurrence of podophyllotoxin, its biological activities and biosynthesis and derived analogs. The to be applied synthetic key methodology is briefly summarized. The aims of the work are logically derived and clearly formulated. The experimental section is detailed, and the analytical data are complete. The results are concisely summarized in tabular form and properly discussed. Conclusions and the reference section conclude the thesis.

Overall, Tomas Svoboda provided a valuable thesis. His results show that the strategy is feasible to approach podophyllotoxin and analogs. Therefore, I recommend acceptance of the bachelor thesis and further proceeding to the defense.

For further information, please, do not hesitate to contact me.

Best regards



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