Ph.D. Thesis Review

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Ph.D. thesis title: Exploring the Unconventional Reactivity of Electron-Deficient Dendralenes Towards Nucleophiles

Reviewer: doc. RNDr. Miroslav Soural, Ph.D.

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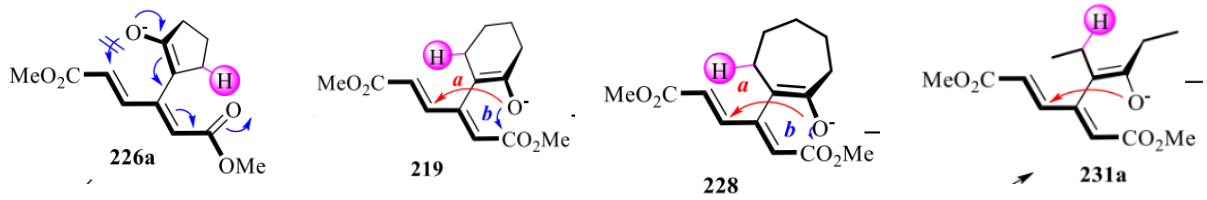
The Ph.D. thesis of Stefanie Magela Perdomo is devoted to the study of electron-poor [3]dendralenes. Using previously developed procedures, a series of compounds bearing ester functional groups as EWGs were synthesized and subjected to reactions with H, C, O, N and S nucleophiles. Different reaction outcomes were obtained based on the type of Michael acceptor and donor. In the case of C/S donors, the corresponding products were identified by NMR analysis and hypothetical reaction mechanisms were proposed and studied. Attempts to form C-O and C-N bonds were unsuccessful. In some cases, the different reactivity was explained by theoretical studies using DFT calculations.

The scope of the submitted work is 154 pages and is divided into individual chapters in the standard way. The theoretical part deals with the classification, preparation and properties of dendralenes and also the principle of Michael addition. The scope and focus of this part is optimal and the text is at a good graphic level. Some formal shortcomings consist in the inconsistency of the schemes, in which the structures do not always have the same graphical parameters, and some of the adopted graphics are a bit blurred. I think that the work would deserve a bit more care in this regard, but this fact does not reduce the scientific level of the thesis in any way. The goals of the work are clearly and unambiguously defined in a separate chapter. However the most important part of the work lies in the discussion section, which contains a detailed description of the achieved results and their racionalization. The structure of individual products is carefully discussed and elucidated with the help of NMR spectroscopy and the suggested transformations are justified by the proposals of reaction mechanisms, which are supported by studies using deuterated reagents. In this regard, I greatly appreciate the effort to provide a detailed insight into the course of the reactions, especially in cases where similar substrates gave different products. The experimental part contains a complete summary of the procedures and analytical data, in which I did not find any obvious shortcomings. The final summary and outlook for the future are given clearly and concisely, although I would appreciate more details in the section dedicated to future research directions.

Overall, I am pleased to state that the submitted dissertation contains a quantity of original and interesting results that can be used for further research. This is evidenced by the fact that the achieved results were published in highly respected journal in the field of organic chemistry. My feeling from the thesis is highly positive. The author has clearly demonstrated the ability to solve a difficult scientific projects involving the formation of unexpected products, determination of their structure and study of reaction mechanisms. In my opinion, the dissertation meets all the standard requirements and therefore **I recommend it for defense**.

Questions and topics for discussion:

1) Compounds A and C in Scheme 47 are classified in the text as zwitterionic, which is not visible in the displayed structures. Please explain.
2) If a nucleophile attacks the pull-pull dendralene scaffold containing two EWGs, it always adds in the sense of a Michael addition towards one EWG, while an anti Michael addition towards the other one. Taking this fact in account, what exactly determines the formal classification of a given reaction?
3) Can you explain a different expectation at intermediates displayed below? Why there is a possible „anti Michael“ course of reaction indicated at **226a** in contrast to **219**, **228** and **231a**?



4) Page 73 and 74: Can you somehow explain different reactivity of **40e** and **40g** towards KCN?
5) How do you explain non-reactivity towards aza donors (page 97), even in the case of reactive nucleophiles such as pyrrolidine? Have you considered other solvents such as DMSO, DMF or NMP which would enable to use a higher temperature?

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Reviewer´s signature

In Olomouc 9. 3. 2026

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