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Examiner's report on the doctoral thesis of Shantanu Ganesh Kulkarni

The thesis reports synthesis of organic compounds containing two, three, and four imidazolium or benzimidazolium substituents and differing with central core and side substitution. These compounds were investigated as supramolecular guests for their non-covalent interactions with cyclodextrin and cucurbituril macrocycles. The supramolecular studies were performed using ^1H NMR spectroscopy, isothermal titration calorimetry (ITC), and mass spectrometry. The thesis is based on one published article and two being in the preparation. It is divided into three main parts: Introduction, Experimental, Results and Discussion. Somehow surprisingly these parts are not labeled as chapters and they are absent in Table of Content which complicates orientation in the text. Author based his research on 271 references which are placed in the end of the text in proper format. The thesis is written in good English.

Introduction part takes more than 30 pages. It summarizes supramolecular chemistry of cyclodextrins (CD) and cucurbiturils (CB). Several chapters discussing similar topics can be found in the Introduction (e.g. "Toxicity studies and regulatory affairs" and "Biomedical applications of CD-drug complexes"). Combining these similar topics within the text would increase readability of this part. The readability is the main issue of the Introduction. There are too many different topics discussed, with small attempts to stress the most important points through several cited papers. The main role of introduction is to introduce own research which is latter discussed. This attempt, if any, was unsuccessful as I learned about motivation for the presented research for the first time in Conclusion (apart of one sentence in Abstract).

Experimental part is clearly presented. Final compounds, those prepared for the first time, were fully characterized. The preparation of previously described compounds is accompanied by citation of original work. The synthesis of imidazolium derivatives (51- 58) is not described in Experimental part despite the fact that majority of them were successfully prepared as apparent from discussion.

Results and discussion part is divided into three main chapters. Synthesis and supramolecular properties of tetratopic, tritopic, and ditopic guest molecules are discussed in each chapter.

The chapter about tetracationic guests is limited on synthesis of these compounds. Any of tested reactions did not offered targeted compounds.

The chapter about tritopic compounds describes successful preparation of guests 4 and 6. Formation of supramolecular complexes with CB7 and these guests were subsequently studied. I enjoyed reading this part as results are clearly presented and conclusions are made by careful evaluation of data obtained from NMR, ITC, and MS. Results reported in this chapter were recently published as a paper in Journal of Inclusion Phenomena and Macroscopic. Publication of data prior thesis submission seems to have positive impact on the quality of scientific presentation. But I regret to see that a good quality artwork published in the paper appeared in the thesis with rather low quality.

The chapter about ditopic guest brought interesting results. Synthetic part was conducted with care. Host-guest study is based mostly on NMR titrations backed up with ITC. As results from these experiments are interesting more experiments are required in majority of cases to come to final conclusions. ESI MS as well as additional ITC experiments are needed to support proposed conclusion which are based mainly on NMR. I also miss better and deeper interpretation of obtained results. Paragraph titled “(E)/(Z) interconversion of guests 20 and 21 under UV irradiation and thermal treatment” is only introduction to an interesting problem and I was disappointed that not further experiments were reported on this topic.

In summary I recommend the thesis for the award of the Ph.D. degree after a successful defence.

Questions

Can author specify in detail his contribution on synthetic and supramolecular parts?

Page 25: Is binding between β -CD and biotin as stable as the value given in thesis?

Page 71: Did you attempt to determine the association constant between 4@CB[7]₂ and β -CD? Could you predict if the binding of β -CD to one binding site of 4 would be higher compared to that one for 4@ β -CD complex?

Page 83: There are clear conclusion missing about binding between compound 20 and γ -CD. What is a binding mode and stoichiometry of the complex?

Page 85-86: The formation of 20@CB[8]₂ and 20@CB[7]₂ was proposed from NMR experiments but ITC (Figure 33) showed the complex of 1:1 stoichiometry. Author should rationalize, which of these two scenarios take place in reality.

Page 97. Last two sentences on the page: “It should be pointed out that only one set of signals was observed during titration. This indicate fast exchange mode which is usually related to the relatively weaker binding.” Can author think about different reason for the presence of only one set of signals during NMR titration?

Other comments

Mixture of E and Z isomers of resulting ditopic imidazolium compounds is labeled as 17 but Z isomer of the same compound is labeled as 10. This is rather confusing and complicates orientation in the text. The same applies for ditopic benzimidazolium compounds (53 and 58).

Page 73 – Table 2 should be changed to Table 3.

According Scheme 1 compound 58 was prepared in yield of 55%, but it is only 3 % according text (page 80)?

Brno, September 12, 2016

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