

Dissertation evaluation report

Title of thesis: Adamantane based multitopic guests and their binding properties

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Review:

The submitted doctoral Thesis represents an interesting contribution from the group of Dr. Robert Vícha (Tomáš Baťa University, Zlín) based on the incorporation of adamantane moieties into the multitopic guest molecules and studying their supramolecular binding behaviour with appropriate macrocycles using several techniques.

The thesis has a common form with a logical division into several chapters. The first part (Introduction) deals with two big families of macrocyclic compounds (cyclodextrins CD and cucurbituriles CB) and their applications in supramolecular chemistry. This chapter also briefly mentions the role of adamantane moieties in the host-guest interactions. The second part (Experimental) mostly shows the preparation and characterization of 24 compounds, some of them being guest molecules used for the complexation studies. These studies are described in the next part (Results and Discussion) showing the host-guest interactions thoroughly studied by the combination of NMR titrations experiments and ESI-MS studies. Interestingly, these experiments were suitably completed by the measurement of thermodynamic parameters of the binding using isothermal titration calorimetry (ITC).

Theses itself is clearly and perceivably written, with a minimum number of errors and misprints. In my opinion, the thesis contains interesting findings from the area of supramolecular chemistry of CDs and CBs, the results are scientifically sound and the thesis contributes to the field of the host-guest chemistry of macrocyclic compounds.

Nevertheless, there are some weak spots and conceptual imperfections that should be mentioned here:

Remarks and notes:

I cannot find any explicitly stated aims of the theses. Moreover, even the motivation for the whole work is only very briefly mentioned, the same is true about the reasons for the design of the guest molecules. All these items would deserve discussion in more details.

There are several unsuccessful attempts at the guest synthesis discussed in the Results and Discussion part. Despite the fact that the whole synthetic sequences remain unfinished there are many intermediates that were isolated and probably characterized. I do not understand why these intermediates and characterizations are completely missing in the Experimental? In my opinion, unlike paper the Theses seems to be an ideal platform even for unsuccessful results as these results could be interesting for potential successors.



p. 61-62: Ulmann type coupling (synthesis of **34** or **35**) is rather old-fashion reaction usually leading to low yields. On the other hand there is a lot of homocoupling procedures based on Pd or Ni catalysts in the literature. Why didn't you try any such reaction?

p. 62-63: Synthesis of compound **34** is described in the literature (ref. 256 in the Thesis, *J. Org. Chem.* **2006**, *71*, 7854) and the same is true about compound **59**. In fact, compound **34** was prepared starting from **33** via **59** as an intermediate. While you have achieved 0% yield in both cases, the reported overall yield (from **33** to **34**) is 82%! Could you explain why you did not use the original procedure described? (You used TEA/MeCN while the original literature employed KOAc/DMF??)

p. 71, Table 3 and others: The calorimetric titration experiments would deserve some more detailed explanation, e.g.: description of the role of competitive guests in the measurements of thermodynamic data in Table 3.

p. 77: Could you explain a dramatic difference between your result (1% yield) and the literature data (90% yield) for the same reaction (preparation of 4-(bromomethyl)-benzaldehyde - compound **46**)?

p.77: Mc Murry reaction has many various reaction conditions. Have you ever tried any other reaction conditions than you showed e.g. in scheme 16 (0.8% yield of compound **10**)?

Some values given in the Experimental part are rather strange, e.g.: 6.0000 g for starting compound! Are you really able to measure with this accuracy (tenths of milligrams)?

Numerical values in temperature assignment should be separated from Celsius by space. From this point of view, many reaction schemes (description of reaction conditions) are wrong.

Recommendation: I have to stress that the most of the above-written remarks are more or less marginal. Despite some weaknesses mentioned above the Thesis contains many interesting findings mostly dealing with a supramolecular behaviour of selected guests. The quality of this work is also reflected by the fact that part of this Thesis has been already published in an internationally recognized journal, and two other manuscripts are currently submitted. Finally, I can recommend this Thesis for the defence and subsequent awarding of the academic degree PhD. to Mr. Shantanu Ganesh Kulkarni.

Pavel Lhoták
in Prague, 12th September 2016