Department of Biophysics

Faculty
of Science

Přírodovědecká fakulta UK

Studijní oddělení

Albertov 6

128 00 Praha 2

Olomouc, 3rd December 2020

Opponent review of PhD Thesis of MSc. Roberto Fernandez Alvarez

The present PhD Thesis written by MSc. Roberto Fernandez Alvarez under the supervision of Assoc. Prof. Pavel Matějíček and with advises of Dr. Mariusz Uchman deals with a new class of nanomaterials which are based on boron cluster chemistry. The Thesis is logically arranged in classical chapters including abstract, list of abbreviations, preface, theoretical background with references, experimental section, research aims, results, summary and general conclusions.

Four scientific papers published in very good impacted international journals form the resulting part of the Thesis. The major part of the research is devoted to cobalt bisdicarbollide (COSAN) behaviour in solution - two papers published in Langmuir in 2018 (Publication I and II in this Thesis). Furthermore, COSAN interaction with polymers was examined and the results published in J. Colloid Interface Sci. 2019 (Publication IV in this Thesis). Moreover, a direct incorporation of ortho-carborane into the polymer chain of a triblock terpolymer and its properties were investigated in Publication III of this Thesis (Polym. Chem. 2019). Intentionally, I mention Publication III as the last one, i.e. after Publication IV, because I would prefer this order.

In Publication I, one can learn that anionic boron hydride cluster compounds (e.g. COSAN and dodecaborate) are intrinsically amphiphilic or aquaneutral, they lack the traditional head-and-tail structure, although they self-assemble into micelles. Their micellization is an enthalpy-driven process, on the contrary to classical surfactants (where entropic contribution prevails). Three main theories (non-classical hydrophobic effect, chaotropic effect, and size-dependent hydration) as an explanation of the small entropic contribution in COSAN micellization process were justified.

In Publication II, a new analysis of ITC (isothermal titration calorimetry) curves was developed leading to a deeper understanding of the thermodynamic causes of COSAN micellization. Several aspects of COSAN self-assembly in micelles, such as the effect of counterions and cosolvent presence (acetonitrile) were thoroughly investigated by MSc. Fernandez Alvarez in Publication II. The experimental results and theoretical simulations proved that the C-H bonds of COSAN molecules are oriented towards the inside of their micelles.

The precipitation of a model polyelectrolyte micelles, namely PS-P2VP (polystyrene-block-poly(2-vinyl pyridine)) with fixed aggregation number, induced by the addition of COSAN (a model hydrophobic anion) was the main research aim in Publication IV of the Thesis. Interestingly, the same level of COSAN caused the precipitation regardless the degree of charge in the P2VP chains (representing the charged corona of the micelles formed by polyelectrolyte). Experimental, as well as, theoretical (coarse grained simulations) approaches were adopted for this research and the hydrophobicity of COSAN was revealed to be responsible for such effect. The general implication lies obviously in possible loading of negatively charged pharmaceuticals into polymeric vectors.

Publication III reports on a specific derivate of closo-dodecaborane which was used as a pendant group in a triblock terpolymer prepared by reversible addition fragmentation chain transfer (RAFT) polymerization. It should be pointed out that this was the first synthesis of a triblock terpolymer with carboranes. Depending on the process of preparation either worms, or spheres are prepared as for morphologies. The obtained micelles were exploited as a dual-stimuli responsive system: reversible fluorescent pH-probe and irreversible fluorine ions (F^-) detection.

There is no doubt that these papers were thoroughly reviewed by experts in the field, therefore, it is not necessary to check them into details. On the other hand, I would like to mention a few mistakes which occur in theoretical background. It should be immediately noted that these mistakes do not lower the quality of this Thesis. They are as follows (the mistake is underlined):

- Page 1, fourth line of the text under figure 1.1.: 3c-2e bonds (three centers-<u>three</u> electrons).
- Page 7, penultimate line of the text: (1,2-, <u>1.7</u>-, and 1,12-$C_2B_{10}H_{12}$).
- Page 8, part 1.1.2-: referencing is missing – e.g. Teixidor´s group
- Page 11, part 1.1.3c-: referencing is missing – "in 2006 by Matejicek et al."

- Figure 1.9. on page 16: the caption in figure, namely, B(2-6)-H Middle Belt does not correlate with the main text.
- Page 18, 3rd paragraph, 7th line: referencing is missing behind: "Plesek and coworkers."
- Page 19, part 1.2.2.-, 3rd line – the sentence does not continue and in brackets a comma is missing: "Their applications are vast thus only selected examples from the most traditional areas (medicine, radionuclei_ radio extraction and catalysis)."
- Page 23, part 1.3.1.-, the last sentence does not end: "A great example of this is the"
- Page 27, citation 46 – year of publication is missing
- Page 30, after equation (2.9): the diffusion coefficient and refractive index are not specified

Misspelling:

- Page 2, 2nd paragraph, 9th line: Electrons that are use in exo-cluster…
- Page 11, 2nd paragraph, 2nd line: molecular dynarkimics (MD)
- Page 15, penultimate line of the text in part 1.2.1b-: polarity confers it water solubility.
- Page 16, 5th line: This is achieved by treating $B_{11}H_{14}^-$ with and arylhalocarbene…
- Page 18, 3rd paragraph, 2nd line: B(8) contains the most electron density and its easily…
- Page 21, part 1.2.2c-, 5th line from the bottom: the solubility variating with
- Page 24, part 1.3.2.-, 2nd paragraph, 4th line: to yield a insoluble
- Page 29, part Static Light Scattering, right after equation (2.2): "the scattering angle of,"
- Page 33, part 2.1.3.-, 3rd line: "and its frequently.."
- Page 34, "it" is missing in the last sentence of part 2.1.3.-: "With equations 2.16 and 2.17, is possible…"

Referencing to Publication IV and publication III are swapped in chapter Summary and general conclusions in the first paragraph, 3rd sentence.

My compliments to MSc. Roberto Fernandez Alvarez for his expertise in so many different fields, e.g. self-assembly of molecules and polymers, organic chemistry, separation and isolation of bio-metabolites, protein purification and application of nanocapsules. Already now, he is an experienced experimentalist being able to use various techniques including nanotechnological, enzymological, spectroscopic,

calorimetric, microscopic, and X-ray diffraction. Moreover, he is well trained in several synthetic procedures such as Ring Opening polymerization, RAFT polymerization, Schlenk techniques, click chemistry and boron cluster chemistry. He possesses a very sound CV with 7 highly impacted publications (in four of them he is the first author) and 6 conference contributions (1 oral, 5 posters). He was awarded by STARS scholarship (2016-2020) and by GAUK (2017-2020). He also participated in two GACR projects in years 2016-2019. Last, but not least, I admire his language skills which include not only Spanish and English, but also Czech and French.
Finally, I have a few questions:

1) Please, can you remind me the size of COSAN and other carborane structures alone? What is the average size of micelles formed by COSAN and can it be adjusted somehow?
2) Based on your experience, could you predict the behaviour of COSAN in the interaction with uncharged polymers in organic solvents? Can it be expected that the precipitation is hindered, however, a characteristic structure containing COSAN and uncharged polymer created? Hypothetically, could be then the COSAN-uncharged polymer structure transferred to aqueous environment?
3) Do you think that COSAN can have interesting magnetic properties?
4) Please, would it be possible to prepare bisdicarbollide compound with iron ions instead of Co(III)?
5) For a better readability, I would appreciate a schematic depiction of all intermolecular interactions of boron clusters as they are discussed in section 1.1.3a.

I fully recommend this PhD Thesis to be defended and subsequently MSc. Fernandez Alvarez to become a doctor (Ph.D. title awarded).

Assoc. Prof. RNDr. Karolína M. Šišková, Ph.D.