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Prague, December 5, 2020

Evaluation of a Ph.D. thesis:

Design of boron cluster-containing nanostructures in solution
Submitted by MSc. Roberto Fernandez Alvarez

Boron clusters are a fascinating group of compounds, especially because of their structural diversity and plethora of unique and unprecedented physico-chemical properties. Although some of the boron clusters found successful applications and showed convincing biological activities, their wider use is still limited. Besides their demanding preparation, one of the fundamental reasons is in the lack of understanding their behavior in solutions, especially in water. Experienced researchers working in this field often point out that chemistry and behavior of boron clusters are fundamentally different from any other types of molecules, especially organic ones. This is more than true for the topics investigated in this thesis.

The proposed thesis looks on solution chemistry of [3,3'-cobalt(III) bis(1,2-dicarbollide)](-1) anion (COSAN) and a polymer containing 1-methyl-1,2-dicarba-*closo*-dodecaborane from various points of views. All are connected by interest in detailed understanding of their association in solutions and the related thermodynamic and structural description of the assemblies. Moreover, polystyrene-*block*-poly(2-vinyl pyridine) copolymers are investigated as model vectors for a potential delivery of COSAN as a representant of metallacarborane-based pharmacophores. Based on this, the dissertation comes with original ideas and provides interesting interpretation of the observed phenomena from colloidal and polymer chemistry.

The thesis is well organized and presents a wealth of original material on a topical subject of literally vital interest of many. On the formal side, the manuscript is divided as follows: In the introductory part (chapter 1) are presented the structural and behavioral complexity of boron clusters, in the experimental part (chapter 2) are explained the used instrumental methods, research aims are summarized in chapter 3. The core of the thesis is in four author's selected published works (chapter 4). The Publication I attempts to clarify the role of COSAN as an amphiphile and to describe the thermodynamics of its micellization. Publication II continues in this focus and brings a complex interpretation of the COSAN micellization using the mass action model. Publications III and IV deal with interactions of boron clusters with polymers. In Publication III, 1-methyl-1,2-dicarba-*closo*-dodecaborane is covalently grafted to the triblock polymer and directs its conformational changes and fluorescence. Publication IV describes formation of micelles upon interaction of COSAN with polystyrene-*block*-poly(2-vinyl pyridine) copolymers. Besides the selected four representative first-author works, the contribution of the candidate is reflected in another 3 co-authored papers and number of conference presentations.

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The thesis contains a not negligible number of minor mistakes and typos, which, however, do not significantly decrease the overall quality of the thesis and do not require to be explicitly listed. Language quality would deserve more careful spelling and editing by a native speaker. Technically, I mention a few details which may be avoided in the next outputs of the candidate. The multiple substitutions of the borane clusters in Figure 1.5. are depicted using a single covalent bond to one boron vertex of the cluster. Although this is intuitively clear, it is chemically incorrect. In Figure 1.6., the lone pairs of electrons in water molecules resemble rather atoms attached *via* covalent bonds, which is confusing. In Scheme 1.1., there is used a different formalism for depicting the cluster vertexes than in the previous schemes. The structures are understandable, but an additional legend may explain why the hollow spheres are used in parallel with boron atoms denoted as B. Throughout the thesis, the Greek prefix *ortho* is used as grammatically incorrect "*orto*". COSAN anion should be named [3,3'-cobalt(III) bis(1,2-dicarbollide)](-1), but not [3,30-cobalt(III) bis(1,2-dicarbollide)](-1). I also note that the workload of the candidate in Publication IV is not specified (page vii).

I would use the opportunity to pose the following questions to the author:

i) The unusual amphiphilic character of COSAN leads to enthalpy-driven association which is different from the "classical" surfactants. In the Publication I, COSAN is compared with these surfactants. Have you considered or even investigated how the COSAN will act in a mixture with surfactants showing "classical" amphiphilic topology?
ii) The fitted curves in enthalpograms of H COSAN (Fig. 4.2.1.) and Na COSAN (Fig. 4.2.7., water) show a flat maximum at about 7 mM and slight decrease towards the zero concentration. Does this course have a physical meaning or is it an artefact of the used model (equation xviii in SI)? I would expect rather a plateau at low concentrations followed by a drop towards the higher concentrations.
iii) Can you foresee some interesting applications where the enthalpy-driven micellization of COSAN would play a distinct role which cannot be substituted by "classical" amphiphiles?

I am pleased by the volume and variety of good-quality work in this dissertation, and by the number of the first-author publications that it has yielded. This is a convincing contribution and the author deserves to be congratulated. There is no doubt in my mind that the dissertation meets the requirements and I recommend that the Committee accepts it as a basis for conferring a Ph.D. degree.

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