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REVIEW

of PhD thesis „*Synthesis, characterization and application of polymer-metal complexes*",

presented by Victoria Trifonova Trifonova – PhD student on a self-study basis at the Biotechnology Department of "Prof. Dr. Asen Zlatarov" University – Burgas for obtaining of Educational and Scientific Degree "Doctor" in the Area of Higher Education 5. Technical Sciences, Professional Field 5.10. Chemical Technologies, Doctoral Program: Chemistry of High molecular weight compounds

by **Prof. Dr. Ivaylo Vladimirov Dimitrov**,

Institute of Polymers – Bulgarian Academy of Sciences,

member of the Scientific Jury appointed by the Rector of "Prof. Dr. Asen Zlatarov" University – Burgas through order № УД-304/28.11.2019

Victoria Trifonova graduated from "D-r K. Vezenkov" Medical College – Burgas. She obtained her master's degree in Chemistry and Chemistry Teaching from "Prof. Dr. Asen Zlatarov" University – Burgas in 2001. Victoria Trifonova started a job in 2003 at the same University initially as a chemical-laboratory assistant and since 2007 till present – as an assistant professor at the Department of Inorganic and Analytical Chemistry. At the end of 2018 she was enrolled as a PhD student on a self-study basis in the Doctoral Program: Chemistry of High molecular weight compounds at the "Prof. Dr. Asen Zlatarov" University – Burgas.

Victoria Trifonova's dissertation is focused on the formation and evaluation (experimentally and theoretically) of catalytically active metal complexes of dendrimers, α-amino acids, di- and tripeptides. The field of research is up-to-date and is of great interest because of the opportunities for applying the results obtained in a number of technological processes, as well as for better understanding the complex processes occurring in living organisms.

The PhD Thesis is prepared in compliance with the requirements of the "*Rules on the Terms and Conditions for Granting Scientific Degrees and Academic Positions at the University "Prof. Dr. Asen Zlatarov" – Burgas*. It is written on 136 pages, including 39 figures, 23 tables and 7 schemes. Additionally, 3 figures and 6 tables are presented as appendices. Totally 163 references from the scientific literature were cited, 29 (about 18%) of which are from papers published in the last 5 years. The dissertation contains the following sections: Introduction – 2 pages, Literature Survey – 33 pages, Conclusions from the

Literature Overview – 1 page, Objective and Tasks – 1 page, Experimental Part – 7 pages, Results and Discussion – 56 pages, followed by Conclusions, Scientific Contributions, List of cited literature and Appendices.

The results of Victoria Trifonova's dissertation have been published in four scientific publications and in one sent for publication during the dissertation submission and in the meantime accepted and also published paper. Three of the publications are in journals that have been referenced and indexed in world-renowned databases of scientific information - Web of Science and Scopus (two of them with impact factors - according to JCR® and Google Scholar metrics). The remaining two scientific publications are published in non-refereed scientific peer-reviewed journals. In three of the publications, Victoria Trifonova is listed as the first author. This fact together with the Declaration of Originality presented by the PhD student, demonstrates her significant contribution to the elaboration and writing of the dissertation-related publications. In addition to the published work, the results of the research related to this dissertation have been presented at four conferences with international participation.

The submitted thesis synopsis is 46 pages long and its content corresponds to the results described in the dissertation.

The *Literature Survey* begins with an overview of polymer-metal complexes - their advantages over low-molecular-weight complexes and the interest they provoke in various scientific fields. The most commonly used approaches for the preparation of polymer-metal complexes are discussed, as well as the main types of functional groups (ligands) that the corresponding polymer must be functionalized with in order to be capable of complexing metal ions. Other specific requirements for polymeric carriers are also indicated. An overview of the interactions (donor-acceptor, covalent, ionic or π-bonds) occurring between the macroligand and transition metal ions depending on the type of functional groups in the polymer is presented. An attention is also paid to the various methods used for quantitative and qualitative characterization of polymer-metal complexes. Furthermore, the described in the literature mechanisms of catalytic oxidation of alkenes with organic hydroperoxides catalyzed by transition metal complexes are discussed paying a particular attention to the use of polymer-metal complexes as catalysts. Dendrimers have been described as a relatively new class of polymers, known for their unique and well-defined architecture, their highly functionalized surface, offering the opportunities to be used as ligands for metal ion complexation. The constituent elements of the dendrimer structure, the differences between dendrimers and other synthetic polymers, and the two approaches for the preparation of dendrimers (divergent and convergent), are correctly and concisely described. Various generations of dendrimers functionalized with suitable for complexation with transition metal ions peripheral groups have been reviewed. Finally, the formation of complexes of amino acids and peptides (as building blocks of protein molecules) with transition metal ions is

reviewed based on the presence of suitable for complexation functional groups and their important functions in living organisms.

The conclusions drawn from the literature survey were helpful in defining the main objective of the dissertation, namely: *to investigate complexes of high-molecular-weight compounds with transition metal ions via experimental and theoretical (quantum chemical) methods and to evaluate their potential application as oxidation catalysts of alkenes with organic hydroperoxides.* Consequently, four well-defined tasks for the objective's successful implementation were defined.

The *Experimental Part* contains a description of the solvents and reagents used, the procedures for their purification, as well as the commercially available polymer products, amino acids, di- and tripeptides used. Information for the methods applied to characterize metal complexes and to evaluate their catalytic activity is also provided in this section. The procedures for the complexes preparation and the synthetic procedures concerning dendrimers modifications are described. The quantum chemical methods used in theoretical studies are also explained in detail.

The *Results and Discussion* section presents both experimental studies of the structure and catalytic activity of metal complexes with various (macro)ligands, and also sought results correlation and validation by applying theoretical (quantum chemical) methods. For example, previous experimental results obtained for Mo(VI) complexes with poly(propylene imine) dendrimers of the second (D8, with 8 surface amino groups) and of fourth generation (D32, with 32 surface amino groups), suggest a geometry with five-coordinate metal centers, which is a rare case for nitrogen-donor ligands. For this reason, the PhD student sought further confirmation of the experimental data by applying quantum chemical calculations. Modeling and optimization of the possible structures for the coordination of the MoO_2^{2+} ion with the smallest tridentate fragment of the dendrimer were performed. The most appropriate theoretical model was selected by which the realization of five-coordinate metal complex with the tridentate ligand was confirmed. The same approach was applied to optimize the structure of the Mo(VI) complex with the aforementioned second generation dendrimer, confirming the structure of the five-coordinate complex proposed based on the experimental results. In the next step of the investigation polyoxyethylene modified dendrimers D8 and D32 were prepared. For this purpose, methoxypolyoxyethylene (Mn = 2000 and 5000 g/mol) pre-modified with carboxyl end group was used to react with the primary amine groups of the dendrimers applying the carbodiimide method. Molybdenum complexes with both types of modified dendrimers have been formed and studied. Based on the experimental and literature data, the most plausible ways of coordinating metal ions with polyamide ligands have been proposed. The complexes were also evaluated as catalysts in the reaction of cyclohexene oxidation with hydroperoxide. The selectivity of the modified dendrimer-metal complexes was found to decrease by increasing the molecular weight of the polymer carrier as a whole

and by increasing the length of the polyether chains in the same generation of modified dendrimers. This was explained by the more difficult access of the oxidizer molecules to the catalytic centers.

The PhD student expands her experimental and theoretical studies to the structural and catalytic activity of metal complexes of amino acids, di- and tripeptides. For example, the molecular structure and coordinating ability of the dipeptide glycylglycine as a ligand was investigated using quantum chemical methods. As a next step the molecular structure and electronic properties of its dioxomolybdenum(VI) complex were predicted. A quantum chemical calculation of the spectral properties in the IR-region of the ligand and the complex was also performed. The results are in good correlation with the experimentally obtained Fourier-transform infrared spectroscopic data. Based on the obtained information, the structure of the bidentate complex is proposed. The catalytic activity of glycylglycine complexes with MoO_2^{2+} and VO^{2+}, Cu^{2+}, Fe^{2+} и Co^{2+} ions was further investigated, with the highest selectivity for oxidation being found for the molybdenyl and vanadyl complexes of glycylglycine.

Applying a semi-empirical quantum chemical method, a theoretical study of the structure of the complexes of amino acids (DL-lysine, L-methionine and phenylalanine) and the tripeptide glutathione with metal ions was performed. The obtained and characterized metal complexes were also investigated as catalysts in the oxidation of cyclohexene in the presence of *tert*-butyl hydroperoxide, once again revealing the highest oxidation selectivity for the molybdenum complexes.

The *conclusions* drawn from the theoretical and experimental studies of (macro)ligands and their complexes with metal ions accurately reflect the results obtained and are in accordance with the *objective* and *tasks* set in the dissertation.

I would like to distinguish the following two scientific contributions of the dissertation:

- *the synthesis and spectral characterization of novel, molybdenyl and vanadyl complexes of second and fourth generation of poly(propylene imine) dendrimers modified with polyether chains;*
- *the use of quantum chemical methods for the detailed description of the complexes' electronic and spatial structure and the proposed discussion about the correlation between experimental data on the structure of the novel complexes and their catalytic activity.*

I have the following questions, notes and recommendations regarding the dissertation:

1. Are there any attempts to quantify the degree of dendrimers modification with polyoxyethylene chains?

2. The Experimental Part lacks data (e.g. from ^{1}H NMR spectroscopy or analytical method such as end-groups titration) proving the complete conversion of the methoxypolyoxyethylene hydroxyl end groups into carboxyl ones.
3. It would be better to use the accepted Bulgarian term for "main chain" (p. 16); "chloromethane" instead of "dichloromethane" is written in the text (p. 44); three different names are used for same compound (succinic anhydride) throughout the text.

Conclusion

The dissertation fully meets the requirements of the *Development of Academic Staff in the Republic of Bulgaria Act, the Rules for its implementation and the Rules for the Terms and Conditions for Granting Scientific Degrees and Academic Positions at the University "Prof. Dr. Asen Zlatarov" – Burgas.* The volume of the research carried out, the competent discussion of the results obtained and the originality of the contributions justify my positive assessment of the dissertation and allow me to recommend to the members of the Honorable Scientific Jury to award Victoria Trifonova the educational and scientific degree "doctor".

Подпис заличен
Чл.2 от ЗЗЛД

06.02.2020 Reviewer: _____

Sofia /Prof. Dr. Ivaylo Dimitrov/