TO THE ACADEMIC COUNCIL OF THE FACULTY OF CHEMISTRY
UNIVERSITY OF BELGRADE

At the regular meeting of the Academic Council of the Faculty of Chemistry, University of Belgrade, held on October 13, 2016, we have been chosen as the Committee members for evaluation of the scientific basis of the proposed PhD thesis and the eligibility of the candidate Stepan M. Stepanović, MSc. in Chemistry. The candidate proposed the following title:

"Density functional approximations for spin state energetics in transition-metal complexes"

After reviewing the submitted documentation of the candidate Stepan M. Stepanović, MSc. in Chemistry, we submit to the Academic Council of the Faculty of Chemistry, University of Belgrade the following

REPORT

A. Basic information about the candidate

Stepan M. Stepanović was born on October 01, 1985 in Belgrade, Serbia, where he finished elementary and high school. He started his Bachelor studies at the Faculty of Chemistry, University of Belgrade in 2004. He graduated in September 2011 with GPA of 8.37/10.00 and a grade of 10/10 for his diploma work. He started graduate academic studies (MSc) at the Faculty of Chemistry, University of Belgrade in October 2011. He finished studies in September 2012 with GPA 9.50/10, and a grade 10/10 for his Master’s thesis. He started his PhD studies at the Chair of General and Inorganic Chemistry, Faculty of Chemistry, University Belgrade in October 2012. From October 01, 2012 he is employed at the Institute of Chemistry, Technology and Metallurgy(IChTM), University of Belgrade, as member of the project „Rational Design and Synthesis of Bioactive and Coordination Compounds and Functional Materials Relevant for (bio)Nanotechnology“. The candidate participated in teaching at the following course, at the Faculty of Chemistry:

- Theory of Chemical Bonding
The candidate is a member of COST Action CM1305 (ECOSTBio: Explicit Control Over Spin-states in Technology and Biochemistry) and has visited the University of Girona, Spain, for 2 months (November - December 2014), during the Short-Term Scientific Mission, COST-STSM-CM1305-21136. The candidate was awarded by EYCN (European Young Chemists Network) the best poster presentation during the 3rd Conference of Young Chemists of Serbia, 2015.

B. Scientific papers published in the international journals and conference proceedings:

Papers published in the leading international journals (M20)

Papers published in the leading international journals (M21a)


Papers published in the leading international journals (M21)


**Papers published in the outstanding international journals (M22)**


**M23 - Paper published in the international journal**


**Papers published in the international conference proceedings as abstracts (M34)**


2. Filip Vlahovic, **Stepan Stepanovic**, Aleksandar Nikolic, Matija Zlatar, Milorad Kuraica, The choice of active center through reaction mechanism of azo dyes oxidative degradation, 24th Congress of Chemists and Technologists of Macedonia with international participation, September 2016, Ohrid, Macedonia, Book of abstracts page 160, EN010.


M64 - Papers published in the national conference proceedings as abstracts

1. Stepan Stepanović, Maja Gruden, Marcel Swart, The role of spin states in catalytic mechanism of the intra- and extradiol cleavage of catechols by O₂, Third conference of young chemists of Serbia, October 2016, Belgrade, Serbia, Book of abstracts page TH P02.

C. Description of PhD theme

1. Scientific Field

Scientific Field: Chemistry

Field of academic expertise: General and Inorganic Chemistry (Theoretical Chemistry)

2. The subject of dissertation

The subject of the proposed PhD dissertation will be the Density Functional Theory (DFT) study of the ground and close lying spin states and their influence on the properties and reactivity of the biomimetic model complexes and potential spin-crossover (SCO) systems. The identity of the ground spin state and the analysis and description of close lying states of different multiplicity is of crucial importance for the understanding of the microscopic origin of the reactivity, electrochemistry and photochemistry in biomolecules, industrial catalysis and in spin crossover compounds.

Many fascinating features of coordination chemistry originate from the fact that transition-metal (TM) complexes possess partially filled d-shells and can manifest different spin multiplicities that are the source of dramatic changes in the properties due to small modifications in a metal ion environment. The description of this phenomena and the rational analysis on the basis of DFT is not a trivial task, and one of the aims of this PhD work is the thorough validation studies of different Density Functional Approximations (DFAs),
specifically designed for spin states, as well as other modern functionals on the properties of biomimetic model complexes and potential SCO systems.

In the second part of the thesis, the candidate will study the effect of different close lying spin states on a catalytic mechanism of well-described model compound that mimics the catalytic cycles of the important O$_2$ activating enzyme class. To do so, the level of theory that has proven to be the most accurate in the validation studies performed in the first part of his thesis will be used.

Whenever there is a possibility of degenerate spin state, the analysis of the Jahn-Teller effect on the spin state ordering and the overall molecular properties will also be examined.

1. Scientific objectives

The aim of the proposed doctoral dissertation will be to test the existing methodology for the treatment of the spin states in complicated transition metal systems, and propose suitable computational recipes for accurate determination of geometries, spin states and all related properties.

The main scientific objectives of this dissertation will be to perform a computational studies from which we could understand the connection between the spin state and the structure, properties and reactivity of a diverse class of transition-metal complexes that are biomimetic model systems and SCO candidates. One of the ultimate goals would be to achieve explicit control of spin states of TM compounds through rational design of ligand coordination that will direct the synthesis of interesting and applicable SCO molecules and more selective and catalytically active biomimetic systems.

2. Methodology

Quantum mechanical modeling has become a widely accepted approach to obtain the knowledge that is either not easily available through experiments or to reduce the cost associated with the synthesis, characterization and testing of the potential candidates for the desired application. But, most of all, it has become the means to understand the origin of the molecular properties, and to derive the connection between the electronic structure and macroscopic observables. As a consequence, it has grown into a tool to anticipate how fine-tuning in the molecular structure can affect the phenomenon we are interested in.
Accurate wave function based methods can be applied to transition-metal complexes, but need to be handled by experts in the field and come at great computational expense. Thus, they are limited to relatively small systems, if drastic simplifications in basis set or the method itself are not introduced. As a consequence, DFT has become the preferred methodology for electronic structure theory of coordination compounds, mainly because it provides good compromise between the computational cost and accuracy. The challenge in application of DFT for spin states was first noted in 2001, and it was concluded that early Generalized Gradient Approximation (GGA) DFAs favored low-spin states, while hybrid functionals including HF exchange favored high-spin states. In the following years, many DFAs showed partial success, but mainly failures in the attempts to tackle the problem of close lying spin states in TM complexes. In 2004, the combination of a relatively new exchange functional, OPTX, with the PBE correlation part gave excellent results for the spin states of iron complexes, and hence a new DFA was born (OPBE).

Since OPBE showed very good performance of for spin states, and later as well S_N2 reaction barriers, it was mixed with PBE that gives good results for weak interactions. After incorporation of Grimme’s D_2 dispersion energy, the SSB-D functional was created. Future refinement to make it numerically more stable and inclusion of Grimme’s D_3 dispersion energy, led to its successor functional S12g.

One of the aims of this PhD work is a thorough validation of different DFAs, specifically designed for spin states (e.g. OPBE, SSB-D and S12g), as well as other modern functionals for the prediction of spin state energetics of biomimetic model complexes and SCO candidates. The thorough examination of available theoretical methods will direct us towards the best theoretical methodology for the study of the effect of different close lying spin states on a catalytic mechanism of catechol dioxygenase mimic complexes.

The treatment of the degenerate states is one of the impediments in the applications of DFT to TM chemistry. In this thesis, whenever there is a possibility of degenerate spin state, the candidate will apply multi-determinant DFT, to estimate the spin state energetics and to deduce the Jahn-Teller parameters, in order to evaluate the influence of Jahn-Teller stabilization on the spin state ordering.

3. Importance of the topic

It has long been recognized that metal spin states play a central role in the reactivity of important biomolecules, in industrial catalysis and in spin crossover compounds. The latter
offer many exciting possibilities for novel, switchable materials with applications in computer storage and display devices. Elucidating the role and effect of different spin states on the properties of a system is presently one of the most challenging endeavors both from an experimental and theoretical point-of-view.

Spin states play an important role in enzymatic reactions, in metal-oxo complexes, in spin crossover compounds and there exists even spin-state catalysis. Heme-containing proteins perform a wide range of functions including electron transfer, oxygen transfer and storage, gas sensing, gene regulation and catalysis. In the case of catalysis, the active complex often involves a metal-oxo (M=O) species, as is e.g. the case in horse radish peroxidase, catalase and cytochrome P450. Thus, the P450s have received considerable attention from pharmacologists, toxicologists, biochemists, and chemists since their discovery. The prototypical and most studied example of this family is P450cam which shows an intriguing catalytic cycle that includes a number of spin flips. The catalytic mechanism of these enzymes is often poorly understood, in particular regarding the spin-state and the effect this may have on the functioning of the enzymes.

Also non-heme proteins use high-valent oxoiron species to couple the activation of dioxygen to the oxidation of their substrates. In most cases, an oxygen atom is inserted into an unactivated C–H bond of the substrate. The generation of well-described model compounds can provide vital insights into the mechanism of such biological and chemical oxidation reactions. Consequently, considerable effort has been made by synthetic chemists to prepare viable models for the putative reaction intermediates in the catalytic cycles of O$_2$ activating. Surprisingly, whereas the enzymatic species are usually high-spin (quintet), most of the biomimetic complexes have intermediate spin, which affects their reactivity patterns. Computational chemistry has contributed essential insight into properties of these reactive intermediates and their mechanisms, thus leading to fruitful experimental-theoretical interplay.

Under favorable circumstances, the spin states of TM complex are close enough in energy such that an external perturbation like heat or pressure can induce a spin-state change or SCO. SCO compounds can act as single-molecule switches/sensors. The in silico design of new SCO and Light-Induced Excited Spin State Trapped (LIESST) materials is a new area, with great interest for molecular electronics, data storage, etc.

4. Expected Results
To provide a systematic analysis of the effect of the spin state and the ligand charge on coordination preferences for a Mn\(^{II}\), Fe\(^{II}/Fe^{III}\), Co\(^{II}\), Ni\(^{II}\), Cu\(^{II}\) and Zn\(^{II}\) for the 2,6-diacetylpyridinebis(semioxamazide) ligand and its mono- and di-anionic analogues. Complexes of polydentate acylhydrazone ligands with d-metals are particularly interesting since they have remarkable structural features that lead to a diversity of potential applications.

To analyze and explain spin state energetics in polypyrrozolylborato complexes of first-row transition metals. To explore the effects of substitution at the position 3 and 5 of pyrazolyl rings, as well as the influence of Jahn-Teller distortion on spin state switching, and altogether, to gain deeper insight in the chemistry of these important enzymatic mimics and SCO molecules.

To provide systematic validation study for the new S12g DFA, for the spin state energetics of nine iron complexes that show a diversity of experimentally observed spin ground states and represent biomimetic molecules for P450cam and similar active sites. The study of these challenging systems should result in further insight in the performance of the promising S12g functional, in comparison with already proven OPBE level of theory.

To clarify, by using DFA that showed best performance in the previous studies, the mechanism of the catalytic cycle for catechol dioxygenase mimics. These model systems are selected not only because of their significance, but also due to their intriguing properties: similar biomimetic molecules can give different products, and there are many intermediates with complicated electronic structure and close lying spin states in the catalytic cycle.

The expected results will be published in relevant international journals.

D. CONCLUSION

Based on the facts presented in this report, the PhD Committee concludes that candidate Stepan M. Stepanović, MSc. in chemistry, meets all the requirements for working on the doctoral thesis in order to obtain the academic title of PhD in chemistry. The Committee believes the planned research fits into the modern trends of chemistry and will
provide a significant contribution to the field of inorganic and computational chemistry. Therefore, the Committee proposes to the Academic Council of the Faculty of Chemistry, University of Belgrade to accept the proposed Ph.D. topic of the candidate Stepan M. Stepanović, MSc. in chemistry, as scientifically relevant and approve working on PhD thesis titled:

"Density functional approximations for spin state energetics in transition-metal complexes"

We suggest Dr. Maja Gruden-Pavlović, Associate Professor at the Faculty of Chemistry, University of Belgrade and Dr. Marcel Swart, ICREA Research professor at Institut de Química Computacional i Catàlisi (IQCC), University of Girona, Spain, as supervisors of this thesis.

Members of the PhD Committee:

Prof. Dr. Maja Gruden-Pavlović,
Associate Professor, Faculty of Chemistry, University of Belgrade

Prof. Dr. Marcel Swart
ICREA Research professor at
Institut de Química Computacional i Catàlisi (IQCC), University of Girona

Prof. Dr. Miloš Milčić,
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Dr. Matija Zlatar,
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