REVIEW

of the materials submitted for the competition for the academic position "Associate Professor" in the professional field 4.2 Chemical Sciences (Theoretical Chemistry), announced in State Gazette, issue. 79 of October 08, 2019

The only candidate is **Senior Assistant Dr. Nadezhda Vasileva Markova**

Reviewer: Professor Dr. Nikolay Georgiev Vassilev, Institute of Organic Chemistry with Centre of Phytochemistry, BAS

1. Biographical information and eligibility

Senior Assistant Dr. Nadezhda Markova is currently working in the Laboratory „Structural Organic Analysis“ of the Institute of Organic Chemistry with Centre of Phytochemistry (IOCCP) at the Bulgarian Academy of Sciences (BAS), where her entire career has been ongoing. She graduated as a Master in Organic Chemistry from the Shumen University “St. Konstantin Preslavski” in 2000. Since 2002 she is a full-time PhD student in Theoretical Chemistry at IOCCCF - BAS and in 2006 defended his PhD thesis on "Theoretical studies of tautomeric equilibria in organic molecules taking into account the specific influence of the solvent" at IOCCP-BAS under the supervision of Prof. Venelin Enchev.

The documents for participation in the competition of the applicant fulfill the requirements of the IOCCP-BAS Regulations for the implementation of the Law on the Development of the Academic Staff in the Republic of Bulgaria, and the scientific and educational profile of the applicant is in accordance with the requirements for associate professor in the professional field 4.2. Chemical Sciences (Theoretical Chemistry).

2. General characteristics of the applicant's activities

Senior Assistant Dr. Nadezhda Markova fulfills and exceeds the minimum required points of the IOCCF-BAS by groups of indicators for the academic position "Associate Professor", as can be seen from the attached information. The candidate participates in the competition with a list of 18 scientific papers. In this list, 5 scientific publications are equated to rehabilitation work (group of indicators "B", indicator "4") and the other scientific publications

are in group of indicators "D", indicator "7". All publications are related to the competition, all of them are published in specialized international journals referenced in the ISI Web of Knowledge and/or SCOPUS and with Impact Factor (IF). The distribution of the 5 scientific publications equated to habilitation thesis according to the rank of scientific journals is as follows: four are in scientific publications with Q1 and one is in scientific publications with Q2. The distribution of the other scientific publications with which the applicant participates in the competition for the academic position of Associate Professor according to the rank of scientific journals is as follows: one is in scientific publications with Q1, five are in scientific publications with Q2, four are in scientific publications with Q3 and three are in scientific publications with Q4. According to the attached information, the total number of citations is 54. According to the Scopus database, the applicant's h-index is 7. This value is indicative of high scientific productivity combined with a wide response in the literature and exceeds the required minimum (≥5) of the regulations of IOCCP-BAS.

Senior Assistant Dr. Nadezhda Markova has included in his documents an habilitation thesis, summarizing on 25 pages his own scientific research in the following three directions:

- Tautomeric equilibria at nucleobases derivatives.
- Tautomeric equilibrium in nucleosides.
- Keto-enol tautomerism in salicylideneanilines.

In habilitation thesis, tautomeric processes are considered in which the influence of water is regarded through two different types of solvent-solute interactions: long-range polarization (nonspecific) interactions and specific short-range hydrogen bond interactions. Both types of interactions are considered in the structural components of DNA and RNA and their derivatives, whereas in the keto-enol tautomerism of salicylidenanilines, only the electrostatic influence of water on direct proton transfer is considered.

The habilitation thesis includes also plans for the future, where scientific plans are in the fields of computational chemistry: reaction mechanisms in organic systems; clarification of molecular structure using quantum-chemical methods; tautomerism in organic compounds; modeling of processes of formation of prebiotic compounds and a new scientific field - quantum-chemical and docking methods in phytochemistry.

The habilitation thesis cites 79 literature sources, with 5 of them being scientific publications equated to habilitation thesis, and 13 of them being part of the scientific publications with which the candidate participates in the competition for the academic position of “Associate Professor”.

3. Publications submitted for participation in this competition

The scientific works of Senior Assistant Dr. Nadezhda Markova are at a very high scientific level, are relevant to the topic of the competition and are in the field of theoretical chemistry. In most of the scientific publications, combined experimental and theoretical characterizations of the systems studied have been used. The studies carried out can be categorized as novelty for science as well as enrichment of scientific knowledge by elucidating the structure and properties of various molecular systems.

The scientific contributions of Senior Assistant Dr. Nadezhda Markova can be grouped in the following areas:

A. The study of the mechanism of organic reactions (Publications 3 and 4 in the list under item D):

An ab initio study of a model system with intramolecular hydrogen bonds, a small difference in the energies of the tautomeric forms, and a relatively low activation energy barrier was carried out. In the presence of a constant external electric field, depending on its direction and amplitude, different tautomeric forms are stabilized, indicating that the proposed system can be the basis for the design of molecular electronic devices with heterogeneous applications. (Publication 3 of the list under indicator D).

Based on DFT calculations of all the conformations of the newly synthesized compound 3,6-bis(4,5-dihydroxyoxaz-2-yl)benzene-1,2-diol, a mechanism for intramolecular proton transfer in the first singlet excited state is proposed. Two successive tautomerization reactions were performed. This mechanism is consistent with the experimentally observed absorption and fluorescence properties of the compound. (Publication 4 of the list under indicator D).

B. Combined theoretical and experimental study of the structure and properties of organic and coordination compounds (other publications in the list under indicator D).

The structure of the newly synthesized brominated amide derivatives of cinnamoyl amino acids, spirohydantoins, 1,8-naphthalimides and hydrazine with various biological activities (antitumor, antimicrobial, anticonvulsant, etc.) has been elucidated by theoretical calculations, theoretical prediction of IR and NMR spectra and comparison with experimental data from IR and NMR spectroscopy. (Publications 7-10 and 13 of the list under item D).

The photophysical properties of the two tautomeric forms of 2-urea-1,3-indadione (CAID) have been theoretically and experimentally studied. Due to these properties, the compound could be used as a potential biomarker and sunscreen. The UV and fluorescence spectra of CAID have been theoretically predicted and experimentally recorded and both enol forms have been shown to exist in solution. (Publication 5 of the list under Indicator D).

Structural and spectral characteristics of two newly synthesized compounds 2-(methylthio)-1,3-diazaspiro[4.4]non-2-en-4-one and 2-(methylthio)-1,3-diazaspiro[4.4]non-2-ene-4-thione has been studied by X-ray diffraction, IR and NMR spectroscopy in solid and quantum-chemical methods. The tautomeric form presented in solution has been shown to be different from that in the solid state. The significant deviation in the position of the IR characteristic frequency of C=N group in the non-polar solvent and the crystalline phase for both compounds implies that in the solid state there is a "conjugated tautomeric form" while in solution a "non-conjugated tautomeric form". Both tautomeric forms are presented in polar solvent. This phenomenon has been proposed to be called "desmokatatropy". (Publication 6 of the list under Indicator D).

Ab initio and DFT methods as well as NMR spectroscopy were used to study the structure of N-(4-benzalaniline)-15-crown-5 and its alkali and alkaline earth metal complexes. (Publication 6 of the list under Indicator D).

The structure and tautomeric preference in solution of 2-amino-thiazolidin-4-one, its isomer 4-amino-thiazolidin-2-one, and of the pseudothiohydantoin-2-amino-4-oxo-thiazoline have been clarified by quantum chemical calculations. The results obtained are consistent with the IR spectral studies. (Publication 11 of the list under Indicator D).

An *in silico* study of polybutylcyanoacrylate was carried out as a carrier of the active drug substance: 5-fluorouracil and daunorubicin. (Publications 1 and 2 of the list under indicator D).

4. Project activity and dissemination of results

Senior Assistant Dr. Nadezhda Markova is the team leader of one completed and two ongoing projects with the NSF and has worked on the implementation of 4 national and 4 international projects. This shows that she is a sought-after partner because of her skills and competencies for *in silico* organic chemistry research.

The results of her research work are presented as 18 oral and 40 poster reports at various national and international conferences. The submitted papers are highly appreciated and the candidate has received three awards for best article.

Senior Assistant Dr. Nadezhda Markova has participated in the training of PhD students, graduates and students. As part of the Student Practices project, she was a mentor of 9 students. Under her supervision, the bachelor's and master's degrees of graduate student Nina Stoyanova-

Nankova were successfully defended. She also participated in the preparation and advanced training of two doctoral students.

The candidate's scientific and organizational skills have been demonstrated through participation in program committees at two international conferences.

5. Assessment of the applicant's personal contribution

I personally know the candidate since her appointment to the IOCCP-BAS. We have discussed various aspects of molecular modeling and I have witnessed its scientific development. Therefore, her personal contribution to the research presented to me is indisputable.

CONCLUSION: Senior Assistant Dr. Nadezhda Markova fulfills all the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria and the Rules for the Conditions and Procedures for Acquiring the Academic Position "Associate Professor" at the Institute of Organic Chemistry with the Center of Phytochemistry, BAS. The valuable scientific production presented for participation in the competition is sufficient in volume, has been published in renowned scientific journals with high IF and has found wide echo in the literature.

Based on the above, I am convinced of my positive assessment and suggest Senior Assistant Dr. Nadezhda Markova to be elected to the academic position of “Associate Professor” in the professional field 4.2. Chemical Sciences (Theoretical Chemistry) at the Institute of Organic Chemistry with the Center of Phytochemistry, BAS.

14.02.2020 Reviewer:

(Prof. Dr. Nikolay Vassilev)