

REVIEWS

Regarding: competition for the academic position "Associate Professor" in professional field 4.2. Chemical sciences (Structural analysis and physicochemical characterization of small organic molecules), for the needs of the department "Structural crystallography and materials science" at IMC-BAS.

Reviewer: Prof. Dr. Ognyan Ivanov Petrov, SU St. Kliment Ohridski, Faculty of Chemistry and Pharmacy, member of the scientific jury appointed by Order No. 26 RD-09/10.01.2024 of the Director of IMK-BAS.

1. Contest participants and applicant eligibility

In the competition for the occupation of the academic position "Associate Professor" in professional direction 4.2. Chemical sciences, announced in the State Gazette no. 95/14.11.2023, one candidate participated - Assist. Prof. Rusi Ivanov Rusev, PhD from the Institute of Mineralogy and Crystallography "Acad. Iv. Kostov" (IMK) - BAS.

Pursuant to Art. 56 of the Regulations for the Implementation of the Law on the Development of the Academic Staff in the Republic of Bulgaria (Law), a Commission was appointed to examine the documents and draw up a protocol for the admission or non-admission of the candidates to the competition. Within the statutory period, the Commission on documents has decided to admit to the competition the only candidate, Assist. Prof. PhD. Rusi Rusev. The first meeting of the Scientific Jury was held on 25.01.2024. The Chairman of the Scientific Jury was elected and two reviewers were confirmed. The scientific jury unanimously accepted that the candidate's Assist. Prof. PhD Rusi Ivanov Rusev scientific production for participation in the competition corresponds to the minimum national requirements and the requirements of the Institute of Mineralogy and Crystallography "Acad. Iv. Kostov" (IMK) - BAS.

Assist. Prof. PhD Rusi Rusev has provided all the required documents for the occupation of the academic position "Associate Professor" in accordance with the Law and the Rules for its Application, as well as with the Rules (PPZRAS) of IMK-BAS. The candidate has a recognized educational and scientific degree PhD on the basis of Diploma No. 001392 dated 15.09.2021, issued by IMC-BAN. The publications for the competition presented by the candidate are not duplicated with those for the acquisition of the PhD and there is no evidence of established plagiarism.

2. Brief biographical data and career profile of the candidate

Assist. Prof. Rusi Ivanov Rusev, PhD, was born in 1993 in the city of Ruse. He acquired a bachelor's degree in 2016, and then a master's degree in "Fine Organic Synthesis" with excellent results (Diploma No. 002746/23.10.2017, issued by HTMU Sofia). From 2014 to 2020 Rusi Rusev worked

as a chemist at the Institute of Mineralogy and Crystallography - "Acad. Ivan Kostov" – BAS. Later, in the period January 2018 - July 2021, he was a full-time doctoral student at the same institute. In 2021, he defended his dissertation on the topic "Synthesis, structural characterization and antimicrobial activity of quaternary ammonium compounds" with supervisor Prof. B. Shivachev. From 2021 until now, he successively holds the academic positions of "Assistant" and " Chief Assistant " at IMC-BAS and has a work experience of 3 years in the specialty.

3. Evaluation of the candidate's scientific contributions

The evaluation of the candidate was carried out in accordance with the requirements of the Law, the Regulations for the implementation of the Law and the Regulations of the IMC-BAS

The candidate has attached a report on the fulfillment of the minimum national requirements from the Law, as well as the Regulations (PPZRAS, effective from 21.10.2021) of the Institute of Mineralogy and Crystallography, BAS.

Summary report on achieved and minimum required points by groups of indicators

A group of metrics	Indicators	PhD		Associate Professor	
		Required	Achieved	Required	Achieved
A	Indicator 1	50	50	50	50
Б	Indicator 2	–	–	–	–
B	Indicator 3 or 4	–	–	100	100
Г	Sum of Indicator 5 - 10	30	34.66	220	273
Д	Indicator 11	–	–	60	132
Total		80	84.66	400	555

The analysis of the data from the reference shows that the Assist. Prof. R. Rusev meets the national requirements and criteria of the Institute of Mineralogy and Crystallography - BAS for the appointment of academic position "Associate Professor" in professional direction 4.2. Chemical Sciences. Even according to indicators Г and Д, these criteria are exceeded.

For participation in the competition, Assist. Prof. Rusev submitted 21 publications, distributed as follows: 4 publications with Q1 (100 points) covering indicator B and 17 publications under indicator Г. Of these 17 publications, 3 are with Q1, 5 are with Q2, 4 are with Q4 and 5 are in

editions with SJR in Scopus but without IF. Allocated in this way, the total number of points for indicator Γ is 273 points, which exceeds the minimum required. 15 of the articles presented by the candidate are published in international journals, making 71%, and the remaining 6 are in national journals. In one of the publications, R. Rusev is the first author, in 9 he is the second author.

A report prepared by Assist. Prof. Rusev shows 66 citations of 7 of the publications. This means that according to indicator Δ the candidate has 132 points, not 112 points as written in his reference. Dr. Rusev's Hirsch index (h), according to Scopus, is 4.

The scientific results of Rusev's research have been popularized through participation in 2 international and 4 national scientific forums with 1 report and 5 posters. He also actively participates in 6 national projects financed by the National Research Institute, one of which he is the head of.

Competition publications can be considered interdisciplinary. Rusev's main contribution is the determination of the structure of organic compounds using X-ray structural analysis, and he has no involvement in the biological studies and syntheses described in the publications, except as specifically mentioned.

All publications are related to the competition topic "Structural Analysis and Physicochemical Characterization of Small Organic Molecules" and can be divided into two thematic areas as follows.

- *Structural analysis and physicochemical characterization of organic molecules with a view to application in medicinal chemistry (publications No. B4.1, B4.4, Γ 7.5, Γ 7.6, Γ 7.7, Γ 7.10 and Γ 7.16)*

A series of synthetic analogues of the natural *cis*-stilbene Combretastatin A-4 have been structurally investigated as potential anticancer agents. It was established by X-ray structure that the studied substances crystallize mainly in orthorhombic, monoclinic and triclinic crystal systems. In addition, detailed crystallographic analysis found that their crystal structures are stabilized by a combination of weak intermolecular hydrogen interactions and close contacts of C-Aromatic...O=C, C(π - π -stacking) between neighboring conjugated systems. Molecular docking was carried out on the basis of which, through structural data and mathematical calculations, the type of ligand-protein interactions can be determined. The tubulin-statmin complex was chosen as the protein target, and the colchicine-active pocket was chosen as the binding site in the protein. From the studies carried out, it was found that the most active compounds interacted with Cys241 or with Cys241 and Lys352 in the protein complex, compared to the interactions of colchicine with Cys241 and Val181 (No. B4.1, B4.4).

The development of new Thioflavin T derivatives is related to the search for more specific markers for the early diagnosis of Alzheimer's disease. The crystal structure of the tetradecamer oligonucleotide sequence of short-chain DNA - d(CCGGGGTACCCCGG)₂, in pure form, as well as

in the presence of a synthetic homologue of the known fluorescent substance Thioflavin T (Г7.5), was clarified.

Publications Г7.6 and Г7.7 cover the synthesis and structural analysis of amantadine and rimantidine amides as potential biologically active substances. Their antiparkinsonian and antiviral effects have been studied. As a result of the X-ray structural analysis, the structure of the new compounds was confirmed and molecular docking was carried out.

Publication Г7.10 reported a new polymorphic modification of bisacodyl, a drug widely used as a laxative, and publication D7.16. is related to the preparation of casein-like nanoparticles to be used as potential carriers of the model molecule - tolfenamic acid. The main contributions of Assist. Prof. Rusev are expressed in the study of the thermal behavior of unloaded and loaded with tolfenamic acid casein-like nanoparticles by means of differential scanning calorimetry.

- *Fundamental scientific research containing detailed structural analysis and physicochemical characterization (publications with numbers B4.2, B4.3, Г7.1 to Г7.4, Г7.8, Г7.9, Г7.11 to Г7.15 and Г7.17*

Publications B4.2 and B4.3 relate to the synthesis and structural characterization of azomethine derivatives of 3-aminohydantoin. X-ray structural analysis shows that all the obtained compounds crystallize in the stable *trans* (E) form. In addition, the presence of carbonyl (-C=O) and azomethine (-CH=N-) groups in the investigated compounds determines the presence of a network of intramolecular hydrogen interactions. Although the mentioned two papers have been published in reputed international journals and have passed independent evaluation, I consider it incorrect to call the compounds Schiff Bases. The compounds in question are azomethine derivatives not of amines, but of hydrazides with aldehydes, therefore it is more correct to call them hydrazones.

Publication Г7.1 reviews the synthesis of a series of novel 4-acylpyrazolones containing cyclic amines in the acyl moiety. Through X-ray structural analysis, it was found that in the solid state, the products exist in the form of intra- and intermolecular zwitterions.

Titanosilicates and zeolites included in publications Г7.2 and Г7.3 were characterized by a combination of electron microscopy, powder X-ray phase analysis, infrared spectroscopy, and their chemical composition was determined by X-ray fluorescence analysis. The preparation and physicochemical characteristics of titanosilicates and their modification are discussed. The possibility of using them for the purification of polluted waters has been studied.

Publications Г7.4, Г7.8 and Г7.17 are purely synthetic in nature and concern the design of polydentate N,O-ligands. Their coordination ability and the possibility of their application as catalysts in a model reaction for the enantioselective addition of diethylzinc to aldehydes were studied. Based on the X-ray structural analysis, conclusions were made regarding the role of the various substituents and functional groups in the studied molecules.

Compounds from the class of coumarins (Г7.13), pyrimidines (Г7.14) and acylpyrazolones (Г7.15) were synthesized and their physicochemical characteristics were determined in detail. The combination of NMR and X-ray structural analysis found that the pyrimidine derivative forms a 1:1 solvate with a methanol molecule that is stable in both solution and solid state. Two conformational polymorphs of (3-acetamidophenyl)boronic acid have been reported. After solving their crystal structures, the two polymorphs were found to have a different pattern of hydrogen interactions. The crystal structures of five magnesium complexes were investigated. I noticed a lot of wrong structures in the introduction of post Г13. Such are the structures of flavopiridol (alvocidib), warfarin and cefazolin. It happens that sometimes there are mistakes, but mistakes on half of the molecules, suggests some carelessness on the part of the authors.

Publication Г7.12 describes single crystals of natural habazite that have been completely replaced by ammonium cations. Subsequent ion exchange of ammonium habazite ($\text{NH}_4\text{-CHA}$) with 1M solutions of ZnCl_2 and NiCl_2 leads to the formation of zinc and nickel forms. Replacement of NH_4^+ with Zn^{2+} and Ni^{2+} is not complete as determined by FTIR.

In summary, the original scientific contributions of Assist. Prof. Rusi Rusev are related to the physicochemical characterization of substances through the use of powder and single crystal structural analysis, thermal studies and spectroscopic methods. More than 50 new crystal structures have been solved, specified and described in detail, which makes it possible to draw reliable conclusions about the relationship between crystal structure and properties of the studied materials. All structures are deposited in the international database for organic crystalline substances - Cambridge structural database (CSD).

4. Critical comments and recommendations

I have no critical comments on the materials of the competition and on the conducted research, which has been published in refereed specialized journals.

However, I have some recommendations. It is good to pay a little more attention to terminology and nomenclature. In addition to my previous comments, I would like to note the use of terms such as "catechol-omethyltransferase" instead of "catechol-O-methyltransferase" or "diethyl zinc" instead of "diethylzinc". I would recommend Assist. Prof. Rusi Rusev to focus on a specific topic in the future. Getting acquainted in detail with the submitted publications on the competition, I am left with the unpleasant impression that his participation is to some extent related to performing auxiliary or technical work, which I am convinced is not the case.

5. Conclusion

The scientific works presented for the competition by Assist. Prof. Rusi Rusev show that his performance indicators exceed the requirements for occupying the academic position "Associate Professor", according to the Law, the Regulations for its implementation and the Regulations for the conditions and procedures for acquiring scientific degrees and for occupying academic positions in Institute of Mineralogy and Crystallography Acad. Ivan Kostov' – BAS. The analysis of the materials submitted for participation in the competition gives me full reason to express my positive assessment of the work of Assist. Prof. Rusi Ivanov Rusev, Ph.D., and to recommend to the scientific jury to support his election for the academic position "Associate Professor" in professional field 4.2. Chemical sciences (Structural analysis and physicochemical characterization of small organic molecules) for the needs of the department "Structural crystallography and materials science" at IMC-BAS.

20.03.2024

Reviewer:

Sofia

(Prof. O. Petrov)