

REVIEW

on the competition for the occupation of the academic position "Associate Professor" at the Faculty of Chemistry and Pharmacy, Sofia University "St. Kliment Ohridski" in the field of chemical sciences, code 4.2.

(Organic chemistry – Organic synthesis)

declared in the State Gazette, issue 105 from 11.12.2020

Candidate (sole): Assist. Prof. Dr. Nikola Tomov Burdzhiev

Review: Prof. Dr. Vanya Bogdanova Kurteva, IOCCP-BAS; Member of the Scientific Jury, appointed by Order RD-38-9 from 07.01.2021

Assist. Prof. Dr. Nikola Burdzhiev presented all required documents in hard copy and electronic form, which are in accordance with the Act for the Development of the Academic Staff in the Republic of Bulgaria (ADASRB), the Regulations for the application of the ADASRB, the Regulations for the terms and conditions for acquiring academic degrees and occupying academic positions of the Sofia University "St. Kliment Ohridski" and the Recommendations on the criteria for acquiring scientific degrees and occupying academic positions at the Sofia University for the professional field "Chemical Sciences", related to the procedure for occupying the academic position "Associate Professor". The documentation submitted has been prepared correctly, transparently and in accordance with all requirements and recommendations.

I. Personal and professional data of the applicant

Assist. Prof. Burdzhiev has nearly 15 years of work experience in the specialty at the Faculty of Chemistry and Pharmacy of Sofia University "St. Kl. Ohridski". In 2007 the Higher Attestation Commission awarded him the educational and scientific degree "Doctor" in the scientific specialty 01.05.03. "Organic chemistry". Since 2007 he has held the positions of chemist, senior assistant and assistant professor. During the period 2015-2019 he completed 3 short-term specializations at the University of Oxford, UK, Max Planck Institute of Technology in Mainz, Germany, and at the University of Barcelona, Spain.

Since 2011 Dr. Burdzhiev is a member of the National Commission for the annual National Olympiad in Chemistry and Environmental Protection and the annual National Competition in Chemistry and Environmental Protection. In 2018 he was awarded the Badge of Honor of Sofia University "St. Kliment Ohridski" Second degree.

II. General characteristics of scientific, applied and pedagogical activity and their reflection in the scientific literature

Dr. Burdzhiev presented for participation in the competition a list of scientific papers for his entire creative period, a list and copies of scientific papers with which he participated in this competition, and a habilitation thesis. A reference for fulfillment of the national requirements is presented. The distribution by indicators is as follows: indicator A - 50 points; indicator C - 109 points; indicator D - 224 points; indicator E - 108 points; and indicator G - 115 points. As can be clearly seen, the applicant's contributions fully cover the national requirements. His scientific output includes 27 scientific papers, of which 24 in peer-reviewed international journals and 3 textbooks. In this competition Dr. Burdzhiev participates with 19 scientific reports in refereed scientific journals. The distribution of scientific reports according to the rank of the journal in which they are published is as follows: 4 in journals with rank Q1 (21.05%), 7 with rank Q2 (36.8%), 1 with rank Q3 (5.3%), 4 with rank Q possessing IF (21.05%), and 3 with rank Q4 without IF (15.8%). The data clearly show that a significant part of the scientific reports (57.85%) are published in the two highest categories, Q1 and Q2. These data clearly show that the scientific output of Dr. Burdzhiev fully covers the additional recommended criteria set out in the Recommendations for the criteria for obtaining scientific degrees and holding academic positions at Sofia University for the professional field "Chemical Sciences" related to the procedure for employment of the academic position "Associate Professor".

According to indicator "C" Dr. Burdzhiev participates with 6 articles in journals with IF, which are as follows: 1 article in a journal with rank Q1, 3 articles in journals with rank Q2 and 2 articles in journals with rank Q4. There is also a habilitation paper on "Polyfunctional heterocyclic compounds - synthetic and spectral studies", written on 35 pages as a review article summarizing the results on the topic published in 86 references and supported by 19 schemes, 6 figures and 1 table. The literature sources include all 6 scientific communications with which Dr. Burdzhiev participates in the current competition on indicator C. The latter are clearly distinguished from the cited articles of other authors. The preparation of this material is of undeniable benefit to the candidate, who in recent years has shown a strong interest in interdisciplinary topics.

According to indicator "D" Dr. Burdzhiev participates with 13 articles in refereed and indexed journals, which are as follows: 3 articles in journals with rank Q1, 4 articles in journals with rank Q2, 1 article in a journal with rank Q3, and 5 articles in journals of rank Q4, 2 of which in journals with IF and 3 in journals without IF. It is important to emphasize that the candidate's

scientific articles on this indicator include 2 review papers (articles 11 and 16), one of which in the renowned international edition *European Journal of Medicinal Chemistry* (IF₂₀₁₉ 5.572; Q1). Dr. Burdzhiev's articles have found a wide response in international literature. Lists of noticed citations in refereed and indexed in ISI Web of Knowledge and / or SCOPUS journals are presented, which show that his scientific articles have been cited 97 times in the scientific literature, as 54 citations are from the articles included in this competition. A detailed analysis shows that the observed 54 citations are on 11 of the 19 articles presented in the competition, i.e. the average citation rate of the articles in the competition is 2.84 (54/19) and of the cited articles is 4.91 (54/11). The Hirsch index is 7.

The report on the scientific contributions is written concisely and clearly outlines the personal contributions of Dr. Burdzhiev. The achieved results, published entirely in a scientific paper, with which the candidate participates in the competition, are divided into three directions: 1. Synthesis of heterocyclic compounds by reactions of cyclic anhydrides and subsequent modifications in order to obtain compounds with potential biological activity (Articles 2-7, 9-11 of those submitted for the competition); 2. Synthesis and spectral characterization of heterocyclic compounds with potential application in practice (articles 1, 8, 12-15 of the submitted for the competition); and 3. Spectral properties of heterocycles used in practice (Articles 16-19 of the competition submission). A small inaccuracy should be noted here. It is indicated that the reference in direction 2 includes articles "[4, 5, 11, 14-15]" from the list of all scientific communications of the applicant, where the article 13 is omitted, i.e. the articles included are [4, 5, 11, 13-15].

Dr. Burdzhiev has successfully managed 1 research project funded by the Research Fund of Sofia University "St. Kliment Ohridski" entitled "Reactions of monocyclic anhydrides with cyclic imines - a method for the synthesis of diastereomeric heteropolycyclic compounds". He has participated in the implementation of tasks on over 15 projects funded by the NSF at the Ministry of Education and Science, NSF at Sofia University "St. Cl. Ohridski" and Operational Programs. According to a group of indicators G participates in the current competition with the above-mentioned project, of which he is the leader, and with 7 projects financed by the NSF at Sofia University "St. Cl. Ohridski", in which he is a participant.

The pedagogical activity of Dr. Burdzhiev includes 5 lecture courses at the Faculty of Chemistry and Pharmacy of Sofia University "St. Cl. Ohridski", which are as follows: "Organic Chemistry II" for the specialty Chemistry in part-time form of education (compulsory); "Structure and biological activity of organic compounds" for the specialty Chemistry in full-time education (compulsory); "Structure and biological activity of organic compounds" for the specialty Chemistry in part-time education (compulsory); "Structure and biological activity of organic

compounds" for all chemical specialties in full-time education (optional); and "Chemistry of heterocyclic compounds" for all chemical specialties in full-time education (optional). Conducts practical classes for students at the Faculty of Chemistry and Pharmacy of Sofia University "St. Kl. Ohridski", which include seminars and exercises in "Chemistry of heterocyclic compounds" for all chemical specialties in regular form of education; seminars on "Structure and biological activity of organic compounds" for all chemical specialties in full-time and part-time form of education; exercises in "Modern techniques in NMR spectroscopy" for all specialties in full-time education; and practical exercises in the course "Instrumental Methods for Analysis II" for all specialties in full-time education. Conducts seminars and exercises on "Organic Chemistry I and II" of students of all specialties at the Faculty of Chemistry and Pharmacy and the Faculty of Biology of Sofia University "St. Kl. Ohridski" in full-time and part-time form of education. In recent years, there is a total employment in the range of 459-642.8 hours and classroom employment of 399-575 hours per school year.

In the period 2010-2020, Dr. Burdzhiev is the research supervisor of 9 successfully defended graduates, 4 in bachelor's and 5 in master's form of education.

III. Basic scientific contributions

Assist. Prof. Dr. Nikola Burdzhiev is a distinct experimenter with scientific developments that fall into three main directions:

- ✓ Synthesis of heterocyclic compounds;
- ✓ Spectral characterization of heterocyclic compounds;
- ✓ Heterocyclic compounds with potential application in practice.

The main research achievements of Dr. Burdzhiev are in the area of the synthesis of heterocyclic compounds and their transformations. Among them,

A significant part concerns the preparation of *carboxylic acids of heterocyclic compounds* by reaction of cyclic anhydrides with azomethine compounds. Oxopyrrolidine, oxopiperidine and oxomorpholine carboxylic acids were obtained, with high diastereoselectivity observed. The conditions were optimized and the factors influencing the reaction out-put were ascertained. The products were subjected to a series of reactions for transformation into carboxamides and amines, some of which were performed under ultrasound. Special attention is paid to the conversion of the carboxyl group into a peptide. Some of the obtained piperazine derivatives and aminomethyl pseudo-peptides have shown antihistaminic activity, where concentration dependence was found for piperazine-containing compounds.

Based on the reaction between cyclic imines with monocyclic anhydrides, a one-step method for the synthesis of benzo[a]quinolizidines, an important pharmacophore fragment in many natural

and synthetic biologically active compounds, as well as their bioisosteric oxygen and sulfur analogues, has been developed. The obtained experimental data are important for elucidating the mechanism of the reaction, which is why studies with quantum chemical approaches are currently being conducted. A series of dibenzo[a, g]quinolizidine derivatives with potential biological activity were synthesized, from which the five-ring heterocyclic structure of dibenzo[a, g]pyrrolo[3,4-i]quinolizidinedione was obtained for the first time.

Tetrahydroisoquinolines having an indole, phthalimide or imidazole moiety in the molecule have been obtained, some of which have been subjected to preliminary studies for antiaromatase activity.

Modern *spectral methods* have been used to assign the structure of the products. The relative configurations of the newly obtained compounds were established by application of a suitable combination of one-dimensional and two-dimensional NMR techniques. The structures of a number of compounds were confirmed by single crystal X-ray diffraction.

In search of new effective *optical sensors and ligands for the extraction and separation of metal ions*, a series of derivatives of 2-acetyl-1,3-indandione have been obtained. It has been found that its reaction with the aza-corona ether leads to deacetylation occurring in parallel with the condensation with aldehyde, for which no data have been found in the world scientific literature. The obtained ligands were subjected to complexation with metal ions, in which a change in their optical characteristics was observed. A fast and efficient approach has been developed for the preparation of square acid dye from square acid, which is a key intermediate in the synthesis of cyanine dyes, materials with valuable photoelectric properties.

Complexes of a new derivative of hydantoin with palladium (II) and palladium (IV) were obtained, which were found to have concentration-dependent cytotoxicity on human tumor cell lines.

A *highly soluble formulation of the drug Itraconazole* was prepared using surfactants and phospholipids. It has been found that double-chain surfactants such as phosphoglycerols reduce solubility, while single-chain surfactants increase it significantly, which is directly dependent on the length of the aliphatic tail. A detailed study with proton NMR spectroscopy revealed the reasons for the drastic increase in the solubility of the drug.

An approach based on the combined application of NMR spectroscopy and gas chromatography with mass spectral detector for qualitative and quantitative analysis of mixtures distributed on the black market containing *synthetic cannabinoids* has been developed.

Based on a thorough review of the scientific literature, formed as a review article, future macroheterocyclic synthetic objects with potential application as chelating agents in the analysis of pharmaceutical products containing *radioactive copper isotopes* have been designed.

3. Critical remarks and suggestions

I also have some small critical remarks. The author's reference for the contributions of the scientific works of Dr. Burdzhiev includes only scientific reports presented in this competition, but the numbering of the articles corresponds to the numbering from the list of all articles. It would be much easier to follow if the numbering followed the list of scientific articles submitted for the competition. There is a slight discrepancy in the data given in different documents. The CV states that Dr. Burdzhiev is a member of the National Commission for the annual National Olympiad in Chemistry and Environmental Protection and the annual National Competition in Chemistry and Environmental Protection since 2012, but from the attached orders for the appointment of the relevant committees, it is clear that these activities start in 2011. In some places, the use of foreigners is noticed, such as crown ether instead of corona ether and solubilization instead of dissolution, which should be avoided, especially when teaching students. These small notes, however, do not in any way affect the overall excellent impression of the scientific output presented.

CONCLUSION

It is undisputed for me that Assist. Prof. Dr. Nikola Burdzhiev is a productive researcher with established qualities and a promising career. Analysing the candidate's scientific achievements, the relevance and perspective of the topics, active participation in research projects, active teaching and his personal qualities and skills, I think that the applicant meets all the requirements of the Act for the Development of the Academic Staff in the Republic of Bulgaria, the Regulations for the application of the ADASRB, the Regulations for the terms and conditions for acquiring academic degrees and occupying academic positions of the Sofia University "St. Kliment Ohridski" and the Recommendations on the criteria for acquiring scientific degrees and occupying academic positions at the Sofia University for the professional field "Chemical Sciences", related to the procedure for occupying the academic position "Associate Professor", and I strongly recommend that the Faculty Council of the Faculty of Chemistry and Pharmacy at Sofia University award to

Assistant Professor Dr. Nikola Tomov Burdzhiev

the academic position of "Associate Professor" in the field of higher education 4. Natural sciences, mathematics and informatics, professional field 4.2. Chemical Sciences (Organic chemistry – Organic synthesis).

Sofia, April 12, 2021

Prepared the review

(Prof. Dr Vanya Kurteva)