REFEREE REPORT

by Atanas Atanasov Kurutos, PhD
Associate Professor at the Institute of Organic Chemistry with Centre of Phytochemistry - Bulgarian Academy of Sciences (IOCCP-BAS)

reviewer according to IOCCP-BAS Director's Order № РД-09-200/15.12.2022

of the materials submitted for participation
in the competition to occupy the academic position **"professor"**

at the Institute of Organic Chemistry with Centre of Phytochemistry - Bulgarian Academy of Sciences (IOCCP-BAS)
in the field of higher education **4. "Natural sciences, mathematics and informatics"**,
professional field **"Chemical Sciences - 4.2, scientific specialty "Organic Chemistry"**

In the competition for the academic position "Professor", announced in the State Journal, issue no. 89 of 08.11.2022 and on the website of **the Institute of Organic Chemistry with Centre of Phytochemistry - Bulgarian Academy of Sciences (IOCCP-BAS)**, the only participated candidate Dr. Svilen Plamenov Simeonov, associate professor from the Institute of Organic Chemistry with Centre of Phytochemistry - Bulgarian Academy of Sciences (BAS-BAS) has submitted the respective documents.

1. General presentation of the received materials

The documents submitted by the applicant Dr. Svilen Simeonov are in accordance with the requirements of the Law for the development of the academic staff in Republic of Bulgaria, the Rules for its implementation, the Rules for the Development of the Academic Staff of IOCCP-BAS and meet the criteria of IOCCP-BAS for occupation of an academic position "Professor".

The applicant has submitted a set of documents containing:

1) Request letter from the candidate to the Director of IOCCP-BAS for participation in the competition; 2) *Curriculum vitae* according to the European model; 3) Reference for the fulfillment of the minimum requirements according to the regulations for the terms and conditions for acquiring scientific degrees and for occupying academic positions at IOCCP-BAS dated 06.01.2023; 4) Diploma for acquisition of educational and scientific degree "PhD" issued on 30.09.2015; 5) Certificate for the awarding of an academic position "associate professor" at the IOCCP-BAS issued on 29.05.2017; 6) Abstract in English from 2014 for obtaining educational and scientific degree "PhD"; 7) Habilitation thesis in Bulgarian and English; 8) A complete list of 38 publications, all published after 2009; 9) List of publications (after 2018) as per indicator B; 10) List of publications (after 2017) per indicator Г; 11) List of participations (5 posters presentations) in conferences (2 in Bulgaria and 3 abroad); 12) List of 901 observed citations on a total of 30 cited publications that are referenced and indexed in WoS and Scopus; 13) List of information on participation in 8 research projects financed by national and international sources (Total funds raised for projects led by the candidate: BGN 1,248,060); 14) List of awards; 15) List of 2 participations as an invited speaker in 2022; 16) H-index reference without self-citations (H-index = 17 according to Scopus);

The candidate Dr. Svilen Simeonov has submitted a list of 38 scientific papers projecting the entire period of his scientific work, of which 17 (5 papers according to indicator Б and 12 items according to indicator Г) are not included in his PhD dissertation and are considered in the final evaluation, as well as 8 research projects, which are also taken into account when forming the final evaluation, are accepted for review. The 17 scientific publications presented for current competition were published after 2017, which demonstrate a relatively high publication activity. The publications consist of three or more co-authors, which is a consequence of the interdisciplinary nature of the scientific developments. Documents (in the form of official notes) for participation in scientific research projects, and data on the obtained economic effect are also presented.

2. Brief CV of the applicant

Assoc. Prof. Svilen Simeonov graduated from SU “St. Kl. Ohridski”, Faculty of Chemistry and Pharmacy in 2002, majoring in “Chemistry”. In 2004, he obtained a master's degree with a specialty in “Organic Chemistry” from the same unversity. In March 2004, he worked as an analytical chemist at Unipharm AD until December 2005. During the period 01.2006-02.2010, he held the position of "Assistant" at IOCCP-BAS. From 02.2010 to 07.2010 he worked as a researcher at the Superior Technical Institute, Lisbon - Portugal. In 2010, Dr. Simeonov was enrolled as a doctoral student at the University of Lisbon - Faculty of Pharmacy, where he obtained a scientific degree “PhD” in 2014 in the field of “Organic Chemistry”. From April 2014 to July 2014, he participated in a doctoral exchange in the group of Prof. Nuno Maulide - Faculty of Chemistry - the University of Vienna - Austria. During the period from June 2016 to August 2016, he participated in a program in the frames of a collaborative research with Prof. Marko Mihovilović - Institute of Applied Synthetic Chemistry, Technical University of Vienna, Austria. In 2017, Dr. Simeonov held the academic position of “associate professor” in the Laboratory of Organic Synthesis and Stereochemistry, of which he has been the head since 2018.

3. Assessment of the applicant's contributions and scientific and practical activity

Dr. Svilen Simeonov has submitted a list and copies of 17 publications, as well as an extended habilitation reference for scientific contributions, for participation in current competition. All articles were published in journals indexed by Web of Science and/or SCOPUS and have an impact factor or impact rank, respectively. The articles can be grouped as follows: Q1 – 16 publications and Q4 – 1 publication, as well as by number of co-authors (with 3 co-authors – 3 papers, with 4 co-authors – 4 papers, with 5 co-authors – 2 papers, with 6 co-authors – 2 papers, with 7 co-authors – 1 paper, with 8 co-authors – 1 paper, with 8 co-authors – 2 papers, with 10 co-authors – 1 paper, with 11 co-authors – 1 paper).

The scientific work of Dr. Simeonov has found a wide response in the international literature. 2082 citations (without self-citations according to Scopus reference) in refereed and indexed journals and in monographs abroad have been identified so far. Of these, 1265 citations (61% of total citation number) came from a review article (*Green Chem.*, 2011,13, 754-793), indicating the candidate's expertise and in-depth knowledge in this area of organic chemistry. The presented citations considered in the current competition are 901, i.e. received during the period 2017-2022. At the time of writing the present review, a search in Scopus shows, that Dr. Simeonov has an H-index of 14 for the entire period of his scientific contribution. In addition to the 901 citations presented in the competition, an extended search in Scopus shows, that the observed citations (excluding self-citations by all authors) on the present 17 publications per indicators В and Г for the competition are 155.

Part of Dr. Simeonov's research has been popularized among the scientific community with a total of 5 participations in national and international scientific forums during the period 2019-2022.

The candidate also demonstrates extensive experience in conducting research and managing scientific research projects, funded by national and international funding organizations. From the presented reference, Dr. Simeonov is a leader of 3 international (UNESCO and H2020) and 2 national (financed by FNI) projects. He is also a participant in 3 more projects financed by Bulgarian sources. From the material presented in this way, it is obvious, that Dr. Svilen Simeonov is a productive scientist, capable of finding means for conducting scientific research, working and leading research teams, as well as generating scientific output in accordance with the generally accepted high international standards.

During the period of his professional realization, Dr. Simeonov has been a supervisor of:

i) 1 completed postdoctoral fellowship of Dr. Adolfo Fernández-Figueiras during the period 2020-2022;

ii) two graduates:

- Nikolay Stanev - master's degree thesis on the topic “Synthesis of furan derivatives from biorenewable sources”, defended in 2017 at SU “St. Kliment Ohridski”, Faculty of Chemistry and Pharmacy, Department of Organic Chemistry and Pharmacognosy. Master’s degree program “Contemporary methods of the synthesis and analysis of organic compounds”;

- Georgi Gerginov – bachelor degree thesis on the topic “Green approaches for effective shikimic acid from *Illicium verum*”, defended in 2019 at the University of Chemical Technology and Metallurgy-Sofia;

In addition, Dr. Simeonov has been a co-supervisor of Andre Martins - Master's thesis entitled “Extractção Selectiva do Ácido Labdanólico de Extracto Natural Utilizando Polímeros Molecularmente Impressos” - 2011 Faculty of Pharmacy, University of Lisbon.

Last but not least, he has been a consultant to Anton Simeonov - Master thesis topic: “Enantioresolution of a Series of Chiral Benzyl Alcohols by HPLC on a Dinitrobenzoylphenylglycine Stationary Phase after Achiral Pre-column Derivatization” - 2009 at the Institute of Organic Chemistry with Centre of Phytochemistry, BAS.

He is currently the supervisor of 1 master degree thesis of Ekaterina Vakarelska, and 1 ongoing PhD degree of Hristo Petkov.

Dr. Svilen Simeonov's significant project activity gives me a reason to believe, that he has the necessary competencies for successful implementation of scientific leadership.

Analysis of the main scientific contributions

Dr. Svilen Simeonov makes a self-assessment of his scientific contributions in a form of an extended habilitation thesis, which thoroughly and precisely reflects the main conclusions in the attached publications. The candidate's research activity fully corresponds to the direction of the announced competition. The research carried out entirely falls into the field of organic synthesis and green chemistry, and the contributions are of a fundamental and scientifically applied nature. I would like to emphasize that in his research, the candidate utilizes some of the most contemporary methods for the synthesis and analysis of organic compounds. In the attached extended reference, Dr. Simeonov has summarized the main scientific contributions, grouped mainly in 3 areas of fundamental and applied nature:

1. Development of new methods for biorefinery, based on biorenewable furan derivatives;
2. Synthetic modifications of natural products;
3. Other topics.

The detailed review of the results, summarized by the candidate, reflected in the extended habilitation report, outline the main focus of his research activity on the development of new methods for biorefinery, based on biorenewable furan derivatives. I highly value the results of these studies. A significant contribution is the proposal of a completely new concept, namely a synthetic approach to obtain pentane-1,2,5-triol (125PT) in a liquid phase, using commercial catalyst 5% Ru/C (employing 0.05M concentration of the starting furfuryl alcohol - FA). Subsequently, a more attractive model for industrial application based on a synthetic approach for continuous production using a reactor is presented. A key component of the latter method is the use of a third flow reactor containing a Lindlar catalyst. This allows the hydrogenation to proceed more efficiently, thereby increasing the productivity (*ChemSusChem*, 2019, 12, 2748-2754 / IF 7.962, Q1 (2019) / 7 citations noted as per Scopus). Another, particularly important aspect from an environmental point of view, related to further in-depth research on the preparation of pentane-1,2,5-triol (125PT) is by using mono- and dualcomponent mesoporous silicates containing Ni and/or Pt nanoparticles. These results led to the development of an extremely highly selective process for the preparation of 125PT using 10Ni1Pt/KIT-6 as a catalyst. From the conducted large-scale research, it was concluded that the method is characterized by a number of advantages of green chemistry, such as the absence of organic solvents, mild reaction conditions and atmospheric pressure (*Green Chem.*, 2019, 21, 5657-5664 / IF 9.480, Q1 (2019) / 4 citations noted as per Scopus). I find these studies extremely interesting, with applied and economic potential. The obtained 125PT was used in collaborative research with colleagues from the Institute of Polymers - BAS, where it has been utilized as a monomer to obtain a new nanogel with application as an antitumor drug delivery system of doxorubicin. (*Polymers*, 2022, 14, 3694 / IF 4.967, Q1 (2021)). Based on the obtained results, the authors conclude, that the nanogel is characterized by biodegradability, high encapsulation capacity and effective protection against photodegradation of doxorubicin, which is a major obstacle to its application in practice. Special attention should be paid to the new synthetic route developed for the production of bioresonable monomers and

biologically active lactones. The method was applied to the preparation of the important monomer 4-ketovalerolactone (KVL), as well as in the total asymmetric synthesis of natural, biologically active acetogenins. The obtained results have practical application and are accepted as a contribution of confirmatory and applied nature (*ACS Catal.* 2023, 13, 3, 1916–1925 / IF 13.700, Q1(2021)). A significant research contribution with a pronounced applied character is also the fact, that for the first time a methodology was developed for the stabilization of 5-hydroxymethyl furfural (HMF), based on the use of the widely available and cheap sodium salt - sodium dithionite, which effectively inhibits unwanted dimerization and polymerization reactions. The wide biorefinery applicability of HMF, as well as the availability and negligible toxicity of $Na_2S_2O_4$, outline the importance of this scientific contribution to practice (*ChemSusChem*, 2018, 11, 1612-1616 / IF 7.804, Q1 (2018) / 36 citations noted as per Scopus). A significant part of the research in this direction is also aimed at studies of the biocatalytic desymmetrization of the diethyl ester of furan dicarboxylic acid (FDC), using the enzyme CAL-B as a catalyst and the subsequent introduction of aromatic substituents by amide-directed Ru-catalyzed activation of carbon -hydrogen bond. A tandem synthetic strategy was demonstrated where all possible positions in the FDC molecule were successfully modified. In addition to the diversification of the HMF platform by using its more stable derivative FDC, the scientific contributions of this development include the creation of new and more efficient synthetic routes for the preparation of substituted furans - a class of compounds with broad biological activity (*ChemSusChem*, 2019, 12, 4629-4635). IF 7.962, Q1 (2019) / 18 citations noted as per Scopus). Another worth noting contribution can be found in a series of experiments, where a new method for the synthesis of HMF from glucose in a tetraethyl ammonium bromide/water system as a reaction medium and commercial acid resins modified with Cr^{3+} as catalysts was developed (*RSC Adv*., 2017, 7, 7555-7559 / IF 2.936, Q1 (2017) / 25 citations noted as per Scopus). The preparation of a series of acid-modified silica gels, which were employed as catalysts for the dimerization of HMF, also occupies a central place in the research activity of Dr. Simeonov. For the first time, the reaction was carried out in the absence of solvent and vacuum (*ChemCatChem*, 2018, 10, 5406-5409 / IF 4.495, Q1 (2018) / 5 citations noted as per Scopus). Another HMF ether of industrial interest is the 5-*tert*-butoxymethyl furfural (*tert*-BMF), which finds application as a fuel additive. A new process for the preparation of *tert*-BMF by esterification of HMF with tertiary butanol has been developed applying acidic heterogeneous catalysts and flow reactors, (*Energy Technology* 2019, 7, 1900780 / IF 3.404, Q1 (2019) / 6 citations noted as per Scopus). By oxidation of 5-chloromethylfurfural with pyridine-*N*-oxide as oxidant and $CuSO_4$ as a catalyst, 2,5-diformyl furan (DFF) was obtained in good yields (*Molecules* 2017, 22, 329 / IF 3.098, Q1 (2017) / 10 citations noted as per Scopus). The original scientific contribution in the research of Dr. Simeonov in the second scientific direction is devoted to synthetic modifications of natural products. An indisputable achievement is the preparation of new C2 modified analogues of sparteine (*ChemMedChem*, 2017, 12, 1819-1822 / IF 3.009, Q1 (2017) / 4 citations noted as per Scopus). By activating the amide function in the lupanine structure with trifluoromethanesulfonic anhydride and subsequent addition of organomagnesium compounds, the preparation of a set of compounds was demonstrated, which were made available for biological research at the Department of Neurophysiology and Neuropharmacology, Medical University of Vienna. All newly obtained compounds revealed a high level of irreversible blockade of VGSC (voltage-gated sodium channels) reaching up to 100%, classifying them as a potential new class of therapeutic agents with long-lasting analgesic action. By using natural (-)-(1*R*,5*S*)-cytisine as a starting material, (+)-(1*R*,5*S*,11a*S*)-9 tetrahydrodeoxycytisine was obtained as a free base, mono- and dihydrochloride. For the first time, an unambiguous assignment of the signals in the proton and carbon NMR spectra was carried out and a comparative analysis of the data from single crystal X-ray diffraction and NMR spectroscopy was made (*Bul. Chem.Comm*. 2017, 49, 103-109 / IF 0.242, Q4 (2017)). As an additional significant contribution, the use of acid catalysis and precise control on the reaction conditions in order to achieve both selective methanolysis of the glucosidic and simultaneous methanolysis of the glucosidic and hydroxytyrazole fragments of oleuropein with subsequent cascade synthetic transformation of the monoterpene leading to obtain biologically active compounds (*ChemSusChem*, 2018, 11, 2300-2305 / IF 7.804, Q1 (2018) / 7 citations noted as per Scopus). Related to the scientific research activity of Dr. Simeonov on other subjects, nanoporous materials were obtained by modification of mesoporous silicates with organic amines. The CO_2 absorption capacity of the materials was determined in static and dynamic mode, and the 1-methylpiperazine modified mesoporous silicate MCM-48-P showed an extremely high absorption capacity of 4.2 mmol/g. (*Nanomaterials*, 2021, 11, 2831 / IF 5.719, Q1 (2021) / 2 citations noted as

per Scopus). Another key achievement of the candidate is the development of a new method for the convenient and inexpensive preparation of amides starting from amines and esters, while using KOBu-t/DMSO or *n*-BuLi/THF base systems, both of which are readily available and considered as non-toxic. The method tolerates a variety of substituents and functional groups in the starting esters and amines (*RSC Adv*., 2022, 12, 20555-20562 / IF 4.036 Q1 (2021). For the first time, a one-step self-condensation of methyl anthranilate has been achieved, leading to a key step for the total synthesis of some quinazolinone alkaloids. Due to the significant volume of accumulated results, a highlight of the candidate's research contributions is the preparation of a review article in 2018, covering methods for the preparation of Shikimic acid and its epimers by synthetic, extractive and microbial processes, as well as its synthetic modifications and application in the total synthesis, preparation of the drug Tamiflu, etc. (*Chem. Rev*., 2018, 118, 10458-10550 / IF 54.301, Q1 (2018)). The significance of these studies is distinguished based on the 28 observed citations as per Scopus. A second review publication is devoted to methods using noncovalent interactions to direct the regioselectivity of transition metal-catalyzed carbon-hydrogen bond functionalization in aromatic cores (*ACS Omega* 2022, 7, 6439-6448 / IF 4.132, Q1 (2021) / 3 citations noted as per Scopus).

Prospect for future research work

In addition to the above summarized contributions, it is important to note that at the end of the habilitation thesis, the guidelines for future research leave an excellent impression and identify Dr. Simeonov as a researcher with a clear vision for the development of the scientific directions outlined by his work.

According to the documentation submitted by the candidate, his plans for future research work fall into the field of organic synthesis and green chemistry. After a decade of intensive research devoted to the chemistry of furan derivatives in addition to their deepening, the candidate's future research plans are aimed at entering more seriously into new thematic directions, which include: 1) Studies of transition metal-catalyzed activation of non-reactive carbon-hydrogen chem. connections; 2) Using biorefinery to obtain compounds finding potential application in biochemistry and pharmacy; and 3) Development of new photochemical methods for CO_2 activation.

To a large extent, the above work plans are determined by the implementation of the two main research projects-Biomass4Synthons under the Horizon 2020 program and ReCat4VALUE under the NNP VIHREN, which Dr. Simeonov leads. It is expected that these scientific studies will further be developed together with colleagues from IOCCP-BAS and other research institutions in the country, and within the framework of already established broad international collaborations. Furthermore, attracting young researchers to join these research areas is a top priority in his future scientific career. Currently, Dr. Svilen Simeonov is a supervisor of a full-time PhD student, and within the framework of the NNP VIHREN project, the enrollment of a second PhD candidate is planned. Through the collaborations established within the Biomass4Synthons project, it is expected that foreign researchers who wish to apply as.

4. Assessment of the candidate's personal contribution

Of the 17 submitted for the competition publications according to indicators B and Г, Dr. Simeonov is the corresponding author of 11 of publications (65%) and first author of 3 of them (18%), which reflects his noticeable personal contribution to the conducted research. Due to the interdisciplinary nature of the research, several co-authors, both from Bulgaria and abroad, participate in the scientific works presented by Dr. Simeonov. In all 5 publications as per indicator B, the candidate is listed as a corresponding author (on 2 papers or 40% of them he is also first author - *ChemSusChem*, 2019, 12, 2748-2754 and *Green Chem*., 2019, 21, 5657-5664). According to the list of a total of 12 publications as per indicator Г, the candidate is listed as a corresponding author to 6 publications (or 50% of them). He is also the first author of 1 publication (*Bul. Chem. Comm.*, 2017, 49, 103-109). The average impact factor of the publications is evaluated to be above 5, namely ranging from 0.242 (*Bulg. Chem. Comm*. – 1 publ.) to 54.301 (*Chem. Rev.*). The conducted research and the published results have marked scientific and scientific-applied contributions in the relevant scientific areas.

From the presented materials it is clear, that to a large extent the obtained results and the formulated contributions reflect personal contribution of Dr. Svilen Simeonov. In many of them, he is listed as corresponding and/or first author. His qualities as a leading researcher in the field of the current competition can also be judged by his election as Head of the Laboratory of Organic Synthesis and Stereochemistry at IOCCP-BAS.

According to the presented autobiography and the list of awards accompanied by supporting material, the candidate has been honored for his research contribution with the following awards: 1) 2015, UNESCO, FOSAGRO, UPAC, “Green Chemistry for Life”, award for young researchers; and 2) award “Acad. Bogdan Kurtev” 2017-2019 for achievements in the field of organic chemistry.

5. Critical remarks and recommendations

I have no critical remarks to the submittes documents and scientific research.

6. Personal impressions

I personally know Dr. Svilen Simeonov as a colleague from IOCCP-BAS, and have excellent impressions of him as a colleague and a scientist. He is motivated, hardworking, humble, responsive, and dedicated to his work, with ideas and perspective for development, with a wide range of interests and high competence in the field of organic chemistry. Dr. Simeonov is a highly qualified, inventive, in-depth and self-critical researcher with a sense of current issues in the field of organic chemistry, and works well in a team, which undoubtedly led to his significant scientific achievements. I believe, that with his professional experience and competence, the candidate contributes to increasing the authority not only of the lab of Organic Synthesis and Stereochemistry, but also of IOCCP-BAS in the field of organic chemistry and natural sciences.

CONCLUSION

From the presented publications it is clear, that Dr. Svilen Simeonov has established remarkable collaborations with research groups both in Bulgaria and abroad, as well as with world-renowned scientists in the field of chemistry. Once again, I would like to emphasize the interdisciplinary nature of the scientific activity of the candidate, which is confirmed by the above and the content of the published scientific works. This is confirmed by the candidate's good publication activity and high citation rate. The response in the world literature of the candidate's scientific research is impressive. Obviously, he is visible, recognizable, which is undeniable proof that he works in an up-to-date scientific field.

The documents and materials presented by Dr. Svilen Simeonov **meet all the requirements** of the Law for the development of the academic staff in Republic of Bulgaria, the Rules for its implementation, the Rules for the Development of the Academic Staff of IOCCP-BAS, and meet the criteria of IOCCP-BAS for occupation of an academic position “Professor”

The candidate has submitted a significant number of scientific works, published after the defense of his “PhD”. The candidate's works contain original scientific and applied contributions, reflected in scientific journals published by international academic publishing journals. Undoubtedly, the candidate has the necessary scientific qualifications. The results achieved by Dr. Svilen Simeonov fully correspond to the specific requirements of the Regulations of IOCCP-BAS.

After getting acquainted with the materials and the scientific works presented for the competition, and uppon analyzing their significance and the scientific, and applied contributions, I find it reasonable to give my **positive assessment** and to recommend the Scientific Jury to prepare a report-proposal to The Scientific Council of IOCCP-BAS for the election of **Associate Professor Dr. Svilen Plamenov Simeonov to the academic position of "Professor"** in IOCCP-BAS in the professional direction 4.2. Chemical sciences, scientific specialty “Organic Chemistry”.

Sofia, 15 March 2023

Reviewer: Atanas Kurutos

Digitally signed by Atanas Kurutos
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Assoc. professor Atanas Kurutos, PhD