

REVIEWER REPORT

From Dr. Petko Nedyalkov Denev, assoc. prof. at the Institute of Organic Chemistry with Centre of Phytochemistry, Bulgarian Academy of Sciences

on the materials, presented in competition for acquisition of academic degree **“professor”** at the **Institute of Organic Chemistry with Centre of Phytochemistry (IOCCP), Bulgarian Academy of Sciences (BAS)**

in area of higher education: 4. **“Natural sciences, mathematics and informatics”**

professional field: 4.2. **"Chemical sciences"**

scientific specialty: **“Organic chemistry”**

for the needs of the Laboratory „Organic synthesis and stereochemistry“ (OSS) at IOCCP.

In the competition for "professor" announced in the State Gazette, issue 89 from 08.11.2022 and on the website of IOCCP, there is only one candidate – assoc. prof. Svilen Plamenov Simeonov from laboratory OSS at IOCCP-BAS.

1. General presentation of the received materials

For the participation in the announced competition, only one candidate has submitted documents. This is assoc. prof. Svilen Simeonov from laboratory OSS at IOCCP, BAS. The set of materials presented by assoc. prof. Dr. Simeonov is in accordance with the Law for the Development of the Academic Staff in Republic of Bulgaria and the corresponding rules of IOCCP. At its first meeting, the scientific jury unanimously decided that his candidacy meets the criteria of the IOCCP, BAS for occupying the academic position "professor ". The documents for the competition include: Reference (on a sample) 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; Scientific CV; Diplomas for obtaining the educational and scientific degree "doctor" and for awarding the academic position "associate professor"; Extended abstract of a dissertation for obtaining the educational and scientific degree "doctor; Habilitation reference in Bulgarian and English; Complete list of scientific publications, as well as lists and copies of scientific publications by group of indicators B and Γ for participation in the competition; List of participation in conferences accompanied by supporting materials; List of citations; Information about the candidate's participation in research projects; List and evidence of awards received; List of participations as an invited speaker; Scopus reference for H-index.

The candidate - assoc. prof. Svilen Simeonov, PhD has attached a list of a total of 38 scientific publications for his entire scientific career. In the current competition, he participates with 17 publications, distributed by categories of indicators as follows:

- 5 publications participating in the competition as an equivalent number of articles for a habilitation thesis.

- 12 publications participating in the contest under group of indicators Γ (according to Appendix 1 of the Regulations for the Development of the Academic Staff of the IOCCP).

All 17 scientific papers are on the subject of the competition, were published outside the PhD dissertation and were not used in a competition for the acquisition of the academic position "associate professor". For these reasons, they are accepted for review and count toward the final grade. The distribution of the scientific works by the relevant quartiles (Q) is as follows:

Q1	- 16
Q4	- 1

Sixteen (94%) of the seventeen publications in the competition are in Q1 journals, which is a very good testament to their quality and to the applicant's work.

2. Short biography of the applicant

Svilen Simeonov obtained a master's degree in "Organic Chemistry" from the Faculty of Chemistry and Pharmacy of Sofia University "St. Kliment Ohridski" in 2004. After that, he worked for a short time in the field of production at Unifarm AD. In the period 2006 - 2010, he worked as an "assistant" at IOCCP-BAS, and in 2014 obtained a PhD degree in "Organic Chemistry" at the Faculty of Pharmacy of the University of Lisbon, after defending a dissertation on the topic: "New synthetic methodologies from biorenewable resources". Dr. Simeonov's stay at this university largely determined his future scientific interests aimed at developing new methods for a biorefinery based on biorenewable furan derivatives. After defending his doctoral dissertation, Svilen Simeonov once again held the academic position "assistant" at IOCCP until his habilitation in 2018, after which he held also an administrative position at the Institute as head of the "Organic Synthesis and Stereochemistry" laboratory. He is the head of the Bulgarian team in three international projects financed by UNESCO and the Horizon 2020 program, as well as one finished and one ongoing project financed by the National Scientific Fund. In addition, he participated in two more national projects financed by the Ministry of Education and Science and one by the National Scientific Fund. During the implementation of all these projects, significant financial resources were attracted to IOCCP. Assoc. prof. Simeonov's educational activity consists of the supervision of one doctoral student and two graduate students. He has been an invited guest lecturer at the Sorbonne University in Paris and the University of Lisbon. He is also the winner of two prestigious scientific awards: Award for young researchers "Green Chemistry for Life" awarded by UNESCO in 2015 and award "Acad. Bogdan Kurtev" for achievements in the field of organic chemistry (2017 - 2019). The attached curriculum vitae lacks information about the candidate's expert and scientific-organizational activities.

3. General characteristics of the applicant's activities

The points declared by the applicant according to the groups of scientometric indicators, defined in the rules of IOCCP-BAS for acquiring scientific degrees and for occupying academic positions, for the academic position "Professor" are as follows:

Indicator	Minimal requirements of IOCCP, BAS	Points declared by the candidate
A	50	50
Б	0	
B	100	125
Г	250	287
Д	200	1802
E	150	469.6
Ж (H-index)	≥ 10	17

Indicators group A: Assoc. prof. Simeonov presented an extended abstract of a dissertation for the acquisition of the educational and scientific degree "Doctor" in "Organic Chemistry" on the topic: "New synthetic methodologies from biorenewable resources", prepared at the Faculty of Pharmacy of the University of Lisbon, which earned him 50 points by this metric.

Indicators group B: In the five publications presented by the candidate as an equivalent number of articles for a habilitation work, Prof. Simeonov is the first and/or corresponding author. This is a testament to his leading role in producing these articles. The articles are of a very high scientific quality and all were published in Q1 journals. They are mainly on the development of new methods for biorefinery based on biorenewable furan derivatives, and the total IF of these publications is almost 47, which is impressive. These publications bring the candidate 125 points, which exceeds the required minimum of 100 points, required by the rules of IOCCP-BAS.

Indicators group Г: All 12 publications from this group have an impact factor, with 11 of them again in issues from Q1, and one in Q4, (Total IF – over 98). In six (50%) of these publications, assoc. prof. Simeonov is again the corresponding author, which once again shows his leading role in conducting the research. According to this indicator, assoc. prof. Simeonov collects 287 points, which exceeds the required minimum of 250 points laid down in the rules of the IOCCP-BAS.

Indicators groups Д and Ж: The total number of citations (without self-citations) of assoc. prof. Svilen Simeonov's scientific works exceeds 2000 according to a reference in Scopus. This is very indicative of the relevance of his scientific research and the interest it arouses in the scientific community. In the competition, he applied with 901 citations beyond those presented for the award of the academic position "associate professor" and PhD degree. These citations are mostly from foreign authors in foreign editions of major academic publishers. The received 1802 points exceed 9 times the minimum legal requirements. In the H-index reference, self-citations from all authors should be removed, thus the candidate's H-index becomes 14. This correction is

insignificant and rather formal, and by this indicator, the minimum requirements of the IOCCP (H-index 10.) are also significantly exceeded.

Indicators group E: In this group of indicators, the candidate presents data on leading and participation in international and national scientific projects. He was the head of the Bulgarian team in three international projects, as well as one finished and one ongoing project, financed by the National Scientific Fund. It is noteworthy that, in addition to purely research projects, Dr. Simeonov has led projects from the Bulgarian side aimed at creating networks with leading research organizations in Europe (Twinning of Horizon 2020), training young scientists and promoting scientific cooperation between the Balkan countries (UNESCO). It should be noted that, in addition to the significant funds (over BGN 1248000) raised for these projects, they undoubtedly have and will have a pronounced beneficial effect on increasing the capacity and prestige of IOCCP-BAS. According to this group of indicators, the obtained nearly 470 points exceed more than three times the minimum of 150 items from the rules of IOCCP-BAS.

All publications on the competition are in the field of organic chemistry and bioorganic chemistry, and could be divided into two main directions:

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

Assoc. prof. Simeonov's publications and contributions are the most numerous in the first direction, and it would not be an exaggeration to say that he is recognizable at the national and international level, especially with his research on it. As a contribution with great applied potential, I define the research on the Achmatowicz rearrangement for obtaining pentane-1,2,5-triol (125PT) from furfuryl alcohol, for which the candidate was awarded the prestigious "Acad. Bogdan Kurtev" award for scientific achievement in the field of organic chemistry in Bulgaria. In this research, assoc. prof. Simeonov's team proposes a completely new and original synthetic strategy to achieve pentane-1,2,5-triol from furfuryl alcohol, which does not involve using the low-selective ring-cleavage reactions by catalytic hydrolysis of carbon-oxygen bonds. Initially this was done in liquid phase using the commercial 5% Ru/C catalyst (Publication 1B). Aiming at the potential industrial application of the method, a synthetic approach has been developed for a continuous mode of production, in which a high yield of 125PT was achieved. Nevertheless, in their next work, the authors further developed the process by overcoming some problems associated with using liquid-phase reduction such as the high cost of catalysts, high catalyst/substrate ratios, and the negative effect of solvent and starting compound concentration. In order to overcome these drawbacks, gas-phase hydrogenation of intermediate 1 was carried out (Publication 2B). For this purpose, 6 mono- and bi-component SBA-15 and KIT-6 mesoporous silicates containing Ni and/or Pt nanoparticles have been prepared and characterized, which show a high selectivity in the reduction of intermediate up to 125PT. These results were used to develop a highly selective process for the preparation of 125PT using 10Ni1Pt/KIT-6 as a catalyst. 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. In collaboration with the Institute of Polymers - BAS, the obtained 125PT was used as a monomer to prepare a new nanogel with application as a drug-delivery system of doxorubicin (publication 3Г). 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. By using Ru-catalyzed allylic alcohol isomerization of Achmatowicz derivatives, a new synthetic route for the preparation of biorenewable and biologically active lactones was developed, the isomerization proceeding with reduction of olefin to give 4-keto- δ -valerolactones (publication 4 Γ). The method has been successfully applied to obtain 4-ketovalerolactone, as well as in the total asymmetric synthesis of the natural, biologically active acetogenins (S,S)-muricatacin and (S,S)-L-factor. The next series of studies by assoc. prof. Simeonov were aimed at overcoming the problems related to the instability of the 5-hydroxymethyl furfural (HMF) molecule. The authors proposed a new methodology for the stabilization of HMF, based on the use of Na₂S₂O₄, which effectively inhibits the unwanted reactions of dimerization and polymerization (publication 5B). The authors concluded that the stabilizing effect is probably due to the balanced antioxidant activity and weak basicity of the sodium salt used. In parallel with this, another practical problem related to the difficult purification of HMF has been overcome. The use of 2% Na₂S₂O₄ in the vacuum distillation process resulted in a significant increase in the yield (>85%) and purity (>99.9%) of the distilled product, which is of great importance to the industry. A tandem synthetic strategy based on biocatalytic desymmetrization of diethyl ester of furan-2,5-dicarboxylic acid (FDCA), which is an industrial product obtained from HMF, was also developed. As a result, all possible positions in the FDCA molecule were successfully modified (publication 6B). A new method for the synthesis of HMF from glucose in a tetraethyl ammonium bromide/water system has also been developed, with high purity and 70% yield (publication 7 Γ). In another study, the authors proposed an interesting approach to overcome the instability of HMF in obtaining the dimeric product OBMF obtained by the esterification of two molecules of HMF by conducting the reaction for the first time in the absence of a solvent and using a vacuum to remove the water obtained during the reaction. Thus, by facilitating the etherification reaction, OBMF was obtained in good yields (Publication 8 Γ). Using acidic heterogeneous catalysts and flow reactors, a process was developed for the preparation of 5-tert-butoxymethyl furfural by esterification of HMF with tertiary butanol (publication 9 Γ), and by oxidation of 5-chloromethylfurfural with pyridine-N-oxide as an oxidant and CuSO₄ as a catalyst 2,5-diformyl furan, another valuable product with a number of applications in industry, was obtained.

Another series of studies by assoc. prof. Simeonov is aimed at synthetic modifications of natural compounds. For example, the presence of an amide function in the structure of the alkaloid lupanine has been used to obtain new C2 modified analogues of another alkaloid with physiological effects – sparteine. These showed a strong ability to irreversibly block voltage-gated sodium channels, reaching up to 100%, making them a potential new class of therapeutic agents with long-term analgesic effect (publication 11 Γ). Using acid catalysis and precise control of reaction conditions, both selective methanolysis of the glucoside only and simultaneous methanolysis of the glucoside and hydroxytyrazole fragments with subsequent cascade synthetic transformation of the monoterpene leading to biologically active compounds from oleuropein have been achieved (publication 12 Γ). Other studies of the candidate are devoted to an topical ecological problem - CO₂ capture by new nanoporous materials obtained by modification of mesoporous silicates with organic amines (publication 14 Γ). A new low-cost method for the preparation of amides from amines and esters using KOBu-t/DMSO or n-BuLi/THF basic systems, which are non-toxic and readily available, has also been developed. For the first time, a one-step autocondensation of methylanthranilate was achieved, leading to the preparation in just one step of an intermediate key to the total synthesis of some quinazolinone

alkaloids (publication 15Γ). Two review papers have also been prepared on methods for the preparation of shikimic acid and its epimers by synthetic, extractive and microbial processes (Publication 16Γ) and methods using non-covalent interactions to direct the regioselectivity of transition metal-catalyzed carbon-hydrogen functionalization bonds in aromatic cores (Publication 17Γ).

4. Evaluation of the candidate's personal contribution

All scientific publications presented in the competition are co-authored, but the fact that in 12 of the 17 presented publications assoc. prof. Simeonov is the first and/or corresponding author leaves no doubt about his personal contribution and leading role in their elaboration and publishing.

5. Critical comments and recommendations

I have no critical remarks regarding both the submitted documents and the candidate's scientific activities. The documents on the presented competition are arranged and presented very well, which greatly facilitates their review and analysis. A very good impression is also made by the fact that the habilitation reference is prepared in a short and concise manner, but at the same time it is very informative.

6. Personal impressions

I know assoc. prof. Svilen Simeonov as a colleague from IOCCP-BAS, from our participation in the meetings of the Scientific council of the Institute, as well as from some presentations of his developments within the framework of various initiatives and scientific forums. However, until now I did not have a comprehensive view of his scientific work. My impression is that he is a serious and thorough scholar and a responsive colleague.

CONCLUSION

Documents and materials presented by the only candidate in the competition assoc. prof Svilen Simeonov, PhD meet all the requirements of the Law for the development of the academic staff in the Republic of Bulgaria, the Rules for its implementation and the corresponding rules of BAS and IOCCP-BAS. He has submitted a sufficient number of scientific papers, beyond the ones used in the defense of educational and scientific degree “doctor” and the academic position “associate professor”. They are of a very high scientific quality and contain original scientific and applied contributions mainly in the following directions:

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

They have received international recognition as the majority of them have been published in specialized, prestigious journals in the field of organic chemistry. A large part of his theoretical developments have practical applicability, and the results achieved in the scientific and research activity meet the specific requirements of IOCCP-BAS rules for the application of the Law for development of the academic staff in Republic of Bulgaria.

After a thorough acquaintance with the materials and scientific works presented in the competition, the analysis of their significance and the contributions contained in them, I can say that the scientific output of assoc. prof. Simeonov is impressive. Therefore, with full conviction I give my positive assessment and recommend the Scientific Jury to prepare a report-proposal to the Scientific Council of IOCCP-BAS for the selection of assoc. prof. Svilen Plamenov Simeonov to the academic position of "Professor" at IOCCP-BAS, in professional field 4.2. "Chemical Sciences", specialty "Organic chemistry" for the needs of laboratory "Organic Synthesis and Stereochemistry" at IOCCP - BAS.

17.03.2023

Reviewer:

Prof. Petko Denev, PhD