

REVIEW

by Prof. Dr. Milen Georgiev Bogdanov,
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on the materials submitted for the competition to occupy the academic position of **“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
4.2. Chemical Sciences, specialty "Organic Chemistry"

In the competition for the academic position “Professor”, announced in the State Journal, issue. 43/31.05.202019 and on the website of IOCCP-BAS, the only candidate Assoc. Prof. Dr. Svilen Plamenov Simeonov from the Institute of Organic Chemistry with Centre of Phytochemistry has submitted the respective documents.

1. General presentation of the received materials

The documents submitted by the applicant 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 meets the criteria of IOCCP-BAS for occupation of an academic position "Professor".

The candidate, Assoc. Prof. Simeonov, has submitted a total of 38 scientific works, of which 17 are for participation in the current competition: 5 in category C and 12 in category D. All of them fall within the scope of the competition and for this reason are subject to review. A habilitation work has also been submitted, as well as a list of citations of scientific works, participation in scientific conferences, participation in and management of research projects, and received awards, all of which have also been taken into account in the final evaluation.

2. Brief CV of the applicant

Svilen Simeonov graduated in 2004 with a Master's degree in Chemistry from the Faculty of Chemistry at Sofia University "St. Kliment Ohridski", and in 2014 he defended his doctoral thesis on the topic of "New Synthetic Methods from Bio-Renewable Sources" (supervisor Prof. Carlos Afonso) at the Faculty of Pharmacy at the University of Lisbon, Lisbon, Portugal. Dr. Simeonov's career began in 2004 at Unifarm AD as a chemical analyst. In 2006, he began his scientific career at the Institute of Organic Chemistry with Centre of Phytochemistry - Bulgarian Academy of Sciences, where he held the positions of assistant (2006-2010, 2014-2017) and associate professor (2017-present). Since 2018, he has been the Head of the Laboratory of Organic Synthesis and Stereochemistry. In addition to his doctoral studies abroad (2010-2014), Assoc. Prof. Simeonov also has two short specializations at the University of Vienna (04-07.2014, with Nuno Maulide) and the Vienna University of Technology (06-08.2016, with Marco Michalovich). Assoc. Prof. Simeonov is a member of the editorial board of Catalyst, Frontiers in Chemistry. In 2015, he was awarded the UNESCO Award for Leading Young Researchers in "Green Chemistry for Life", and for achievements in the field of Organic Chemistry, he received the "Acad. Bogdan Kurtov" Award for 2017-2019. During his academic appointment as an associate professor, he documented four participations in scientific conferences, as well as two invited

lectures as a guest lecturer (University of Sorbonne, Paris, France and University of Lisbon, Lisbon, Portugal). There is no information provided about active membership in scientific organizations, other review and editorial boards, review preparation, or conducted lecture courses. In the last 5 years, Assoc. Prof. Dr. Svilen Simeonov has been the coordinator for Bulgaria on two projects funded by UNESCO programs and one project funded by FNI, and he is a coordinator for a project under the Horizon 2020 program.

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

Assoc. Prof. Simeonov has submitted a list and copies of 17 scientific publications (12 according to Indicator D and 5 according to Indicator C) for participation in the competition, as well as an extended habilitation work for his scientific contributions. All articles have been published in journals indexed by Web of Science and/or SCOPUS and have an impact factor and/or impact rank, respectively. The articles can be grouped as follows: 16 articles in specialized journals falling in the first quartile (Q1) and 1 in the fourth (Q4).

Assoc. Prof. Simeonov's scientific works have received wide recognition in the international literature. So far, over 2500 citations have been noticed, of which 2236 are in refereed and indexed journals in ISI Web of Knowledge and/or SCOPUS and in foreign monographs. The citations on the publications considered in this competition are 132, i.e. obtained in the period 2018-2013, after taking up the academic position "Associate Professor". At the time of preparing this review, the SCOPUS reference shows that Assoc. Prof. Simeonov has an H-index of 17 for the entire creative work period, with 2 of the articles contributing to this index being the subject of the current competition.

According to the submitted documents, some of Assoc. Prof. Simeonov's research has been disseminated among the scientific community with four participations in international and national scientific forums and two invited lectures at foreign universities.

Assoc. Prof. Simeonov demonstrates extensive experience in conducting research and leading scientific research projects funded by international and national organizations (funds attracted by projects > 1.2 million BGN).

From the presented material, it is clear that Assoc. Prof. Simeonov is a productive scientist, capable of finding funding for scientific research, working in and leading research teams, and generating scientific output in accordance with internationally accepted high standards. During his professional career, Assoc. Prof. Simeonov has been a supervisor of two successfully defending graduates and currently supervises one PhD student. Given the available financial resources and projects in current topics, it is undoubtedly that the number of co-workers and scientific contributions by Assoc. Prof. Simeonov will continue to increase in the future.

The scientific research activity of the candidate fully corresponds to the direction of the announced competition. The main scientific contributions of Assoc. Prof. Simeonov are in the field of organic synthesis and green chemistry, and the main scientific contributions can be summarized in two main directions:

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

Assoc. Prof. Simeonov evaluates his scientific contributions in the form of an extended habilitation work, which reflects in detail and accurately the main conclusions in the applied publications. The most important of them can be summarized as follows:

- A new concept has been proposed for obtaining pentane-1,2,5-triol (125PT) from furfuryl alcohol (FA), which does not involve the use of low-selective ring-opening reactions through catalytic hydrolysis of carbon-oxygen bonds. The concept is based on the Achmatowicz rearrangement, followed by hydrogenation of the reactive intermediate. To overcome the difficulties associated with the high cost of catalysts, high catalyst/substrate ratios, solvent effects, and concentration of starting compounds, a highly selective process for obtaining 125PT using monocomponent Pt-modified catalysts has been developed. 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. The resulting 125PT has been used as a monomer to obtain a new nanogel with application as an antitumor drug delivery system for doxorubicin. The nanogel is characterized by biodegradability, high encapsulating capacity, and effective protection against the photodegradation of doxorubicin, which is a major obstacle to its practical application.
- By using Ru-catalyzed isomerization of allylic alcohol in the structure of Achmatowicz products, a new synthetic route has been developed for obtaining biorenewable monomers and biologically active lactones. Unlike the catalytic isomerizations of Achmatowicz products reported in the literature, which use ketone reduction, the isomerization reported by the candidate proceeds by alkene reduction, leading to the formation of 4-keto-d-valerolactones. The method has been applied for obtaining the important monomer 4-ketovalerolactone, as well as in the total asymmetric synthesis of natural, biologically active acetogenin, (S,S)-muricatocin and (S,S)-L-factor. The mechanism of the reaction has been studied in detail using isotope labeling and DFT calculations. A contradiction with the currently accepted reaction mechanisms has been established.
- A methodology for stabilizing 5-hydroxymethylfurfural (HMF) has been developed based on the use of the widely available and inexpensive sodium dithionite ($\text{Na}_2\text{S}_2\text{O}_4$), which effectively inhibits unwanted reactions of dimerization and polymerization. The broad applicability of HMF in the biorefinery, as well as the accessibility and low toxicity of $\text{Na}_2\text{S}_2\text{O}_4$, highlight the significance of this scientific contribution for practical use.
- A tandem synthetic strategy has been developed based on biocatalytic desymmetrization of diethyl ester of furan-2,5-dicarboxylic acid (FDCA, a major source for the production of HMF) using the enzyme CAL-B as a catalyst, followed by the introduction of aromatic substituents through amide-directed Ru-catalyzed activation of carbon-hydrogen bond. By varying the reaction conditions, all possible positions in the FDCA molecule have been successfully modified. In addition to diversifying HMF through the use of its more stable derivative, FDCA, the scientific contributions of this development also include the creation of new and more efficient synthetic pathways for obtaining substituted furans – a class of compounds with broad biological activity.
- A method for the synthesis of HMF from glucose in a tetraethylammonium bromide/water system, using modified Cr^{3+} commercial acidic resins as catalysts, has been developed. The target product is isolated with high purity and yield. The obtained bifunctional catalysts show good stability and preservation of catalytic activity for up to 4 cycles. It has been established

that the loss of catalytic activity is due to the decrease of active acidic sites of the catalyst, which can be restored by regeneration with HCl.

- A new method for the convenient and inexpensive preparation of amides from amines and esters using basic systems KO^tBu-t/DMSO or n-BuLi/THF, which are non-toxic and easily accessible, has been developed. The method tolerates various substituents and functional groups in the starting esters and amines. It is also applicable for the synthesis of phosphoramidates from triethyl phosphate, whose reported preparation in the literature requires expensive and toxic starting phosphorus compounds, as well as high temperatures, long reaction times, and the presence of metal catalysts. The selective acylation of unprotected diamines possessing aliphatic and aromatic amino groups has been demonstrated. For the first time, a one-step autocondensation of methylanthranilate leading to the synthesis of key intermediates for the total synthesis of some quinazolinone alkaloids has been achieved.

In addition to the selected contributions mentioned in a general sense, it is important to note that the guidelines for future research presented at the end of the habilitation work leave an excellent impression on me as a reviewer and demonstrate Assoc. Prof. Simeonov's clear vision as a researcher for the development of the scientific direction outlined in his work. There are plans for continuation and more serious involvement in new thematic directions, including:

- Research on the catalyzed activation of non-reactive carbon-hydrogen chemical bonds by transition metal catalysis;
- Use of biorefinery to obtain compounds with applications in biochemistry and pharmacy;
- Development of new photochemical methods for CO₂ activation.

To a large extent, these plans are determined by the implementation of two main research projects - Biomass4Synthons under the "Horizon" 2020 program and ReCat4VALUE under the VHIRREN program, both of which are led by Assoc. Prof. Simeonov.

4. Assessment of the candidate's personal contribution

I have no doubts about Assoc. Prof. Simeonov's personal contribution to the obtained results and the corresponding publications. In a large part of them, he is the leading author. His qualities as a leading researcher in the field of the current competition can also be judged from his selection as Head of the Laboratory of Organic Synthesis and Stereochemistry at the IOCCP-BAS.

CONCLUSION

The documents and materials presented by Assoc. Prof. Dr. Svilen Plamenov Simeonov meet all the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria, the Regulation for its Implementation, the Regulation for its Implementation at the Bulgarian Academy of Sciences (BAS) and the Regulation of the Institute of Organic Chemistry with Centre of Phytochemistry (IOCCP)-BAS.

The candidate has presented a sufficient number of scientific papers published after the materials used in the defence of the doctoral dissertation and the acquisition of the academic position of "Associate Professor". Assoc. Prof. Simeonov's scientific qualification is indisputable. His works have

original scientific and practical contributions and have been published in renowned international journals. They have received broad international recognition.

After reviewing the materials and scientific papers submitted in the competition and analysing their significance and scientific and practical contributions, I find it reasonable to give my positive assessment and recommend to the Scientific Jury to prepare a report-proposal to the Scientific Council of IOCCP-BAS for the appointment of Assoc. Prof. Dr. Svilen Plamenov Simeonov to the academic position of "Professor" in IOCCP-BAS in the professional field 4.2. Chemical Sciences, scientific specialty "Organic Chemistry".

16 March 2023 r.

Reviewer:
/Prof. Dr. Milen Georgiev Bogdanov/