

REVIEW

for a competition for the academic position of "Associate Professor" at the Institute of Organic Chemistry with Centre of Phytochemistry of the Bulgarian Academy of Sciences in the professional field 4.2 Chemical Sciences, scientific specialty "Organic Chemistry", published in the State Gazette, issue No. 55 of 16.06.2026.

Candidate (sole applicant): Dr. Ivaylo Momchilov Slavchev

Reviewer: Assoc. Prof. Dr. Irena Philipova, Institute of Organic Chemistry with Centre of Phytochemistry – Bulgarian Academy of Sciences (IOCCP, BAS); member of the scientific jury appointed by Order No. RD-09-139/23.07.2026 of the Director of IOCCP-BAS.

Dr. Ivaylo Slavchev has submitted all required documents in accordance with the Law for the Development of the Academic Staff in the Republic of Bulgaria (LDASRB), the Regulations for its Implementation, the Regulations on the Terms and Conditions for Acquiring Academic Degrees and Holding Academic Positions at the Bulgarian Academy of Sciences, and the Regulations on the Terms and Conditions for Acquiring Academic Degrees and Holding Academic Positions at the Institute of Organic Chemistry with Centre of Phytochemistry at the Bulgarian Academy of Sciences, related to her participation in the competition for the academic position of "Associate Professor".

I. Personal and professional data of the candidate

Dr. Ivaylo Slavchev graduated from the Faculty of Chemistry of Sofia University "St. Kl. Ohridski" in 2013 with a Master's degree in Medicinal Chemistry. The same year he started working at the Institute of Organic Chemistry with the Centre for Phytochemistry - Bulgarian Academy of Sciences. During the period 2014-2018 he was a PhD student in the lab. "Organic Synthesis and Stereochemistry", jointly with Descartes University, Paris. In 2019 he defended his dissertation for the educational and scientific degree "doctor" on the topic "Synthetic Transformations of Natural Products", after which he continued his academic development in the same laboratory as a chemist and subsequently as a chief assistant (from 2020 - until now).

II. General characteristics of the scientific and applied scientific activity

To participate in this competition, the candidate has submitted a report on compliance with the minimum requirements for holding the academic position of "associate professor" at IOCCP-BAS, as follows:

In group A - 50 points (required 50 points): Dissertation on the topic "Synthetic Transformations of Natural Products" for obtaining the ONS "Doctor" in the professional field: 4.2. Chemical Sciences, scientific specialty "Organic Chemistry".

By indicator 4 in group B - 130 points (100 points required): A total of 6 publications are presented, distributed according to the relevant Q factors, as follows:- Q1 - 3 pcs., Q2 - 2 pcs., Q3 - 1 pc. He is the first author in 3 articles under this indicator.

By indicator 7 in group D – 240 points (220 points required): 10 publications are presented, distributed according to the relevant Q factors, as follows: Q1 – 8 pcs., Q2 - 2 pcs.

By indicator 11 in group D – 80 points (70 points required).

The data show that the candidate's contributions meet the national requirements and the requirements of the Law for the Development of the Academic Staff in the Republic of Bulgaria (LDASRB), the Regulations for its Implementation, the Regulations on the Terms and Conditions for Acquiring Academic Degrees and Holding Academic Positions at the Bulgarian Academy of Sciences, and the Regulations on the Terms and Conditions for Acquiring Academic Degrees and Holding Academic Positions at the Institute of Organic Chemistry with Centre of Phytochemistry at the Bulgarian Academy of Sciences for holding the academic position of “Associate Professor”.

III. Main scientific contributions

The habilitation report is written clearly and well-structured. The materials presented by Dr. Ivaylo Slavchev testify to active scientific research activity of high quality. The research carried out falls into the field of organic synthesis and medicinal chemistry, and the contributions are of a fundamental and applied scientific character. They are the result of interdisciplinary research and are summarized in 5 thematic directions, namely: (1) methodological studies of new approaches for the formation of an amide bond, (2) synthesis and antiviral activity of new diaryl ethers and their analogues, (3) synthesis and complex biological evaluation of new compounds with a camphan skeleton, (4) semi-synthetic amides with a fenhan skeleton and their anti- and pro-oxidant activity and (5) design and synthesis of new sensors for heavy metals.

Research in the first direction is focused on base-catalyzed amidation of weakly reactive esters with simple nucleophilic amines [B1]. Two new synthetic methods have been developed that allow the direct conversion of unactivated esters of lower alcohols into amides promoted by strong base. The research focuses on substrates that are traditionally difficult to work with and little reported in the literature. The method using DMSO/*t*-BuOK is applicable mainly to aromatic amines. To overcome the limitations of the system, an alternative protocol, THF/*n*-BuLi, has been developed, suitable for aromatic, aliphatic and sterically hindered amines, as well as lactones, and esters containing a carboxyl or nitro group. The studies cover a wide range of esters and amines, and reveal the scope and limitations of the reaction. Of essential importance is the tolerance of the reaction to different functional groups (carbonyl, hydroxyl, nitro, carboxyl). Several practical applications of the developed reaction are also proposed. The direct synthesis of the insect repellent DEET (*N,N*-diethyl-*meta*-toluamide) was achieved, obtained directly from the methyl ester of the corresponding acid and diethylamine. Also, a protocol for the direct acylation of diphenylguanidine was published for the first time.

The original scientific contribution of the research within the second scientific area lies in the synthesis and biological evaluation of novel antiviral agents. Enteroviruses cause mild infections but can be associated with more serious conditions such as encephalitis, myocarditis, poliomyelitis, acute heart failure, and insulin-dependent diabetes that may ultimately become life-threatening. In this context, the research topic is both timely and of significant public importance.

The work is based on the synthesis of a series of 12 new compounds featuring a 2-cyano-4-nitrophenyl group linked to various aromatic or alkyl groups via oxygen, nitrogen, or sulfur [B2].

All compounds were obtained in high yields *via* one-step reactions of the corresponding phenols, thiophenols, or amines with 2-chloro-5-nitrobenzonitrile, using procedures described in the literature. The compounds were evaluated for their *in vitro* antiviral activity in cell culture experiments against three enteroviruses: Coxsackievirus B1 (CVB1), Coxsackievirus B3 (CVB3), and Poliovirus 1 (PV1). MDL-860 was used as a reference. Three of the tested compounds, derivatives of di- and trifluorophenols, exhibited strong antiviral effects against CVB1 and PV1. *In vivo* studies conducted with these compounds in CVB1-infected mice demonstrated significant protective effects, achieving a 50% efficacy rate. It is important to note that the new compounds exhibit very low toxicity.

Research in this area was extended to the synthesis of 60 analogues of the antiviral agent MDL-860, all sharing a common 2-cyano-5-nitro-substituted benzene ring, to determine the limits of structural variation within the ether moiety of MDL-860 [B3]. All target compounds were synthesized *via* one-step nucleophilic aromatic substitution reactions involving the reaction of various phenols, thiols, amines, and *N*-heterocycles with 2-chloro-5-nitrobenzonitrile in the presence of a base. *In vitro* assays evaluating activity against CVB1, CVB3, and PV1 revealed that six diaryl ethers exhibited high activity against at least one of the tested viruses, alongside very low cytotoxicity toward human cells. The compound 2-(2,5-difluorophenoxy)-5-nitrobenzonitrile is particularly noteworthy, as it demonstrates a broad spectrum of activity against all tested viruses, similar to the reference compound MDL-860. The derivatives showing the highest activity against Coxsackievirus B1 were further evaluated *in vivo* using neonatal mice infected with the virus; the results indicated moderate protective effects. Adequate QSAR models were constructed to describe the antiviral activity of the compounds against PV1 and CVB1.

The third area of the research summarizes the results regarding the biological activity of novel camphor derivatives. The study involved the design and synthesis of 20 new arylidene-camphors and 15 pyrimidines containing a camphane skeleton [B4]. A modified two-step method was developed for the preparation of sterically hindered 2-aminopyrimidines. A series of conjugated ketones was obtained through the reaction of enantiomerically pure (+)-camphor with various aldehydes. These ketones were subsequently transformed into the corresponding aryl-substituted 2-aminopyrimidines *via* condensation with guanidine hydrochloride in the presence of a base. All compounds were isolated with good to excellent yields. The newly synthesized compounds underwent comprehensive evaluation for antibacterial activity and cytotoxicity. Four of the tested compounds demonstrated *in vitro* activity against *M. tuberculosis* H37Rv. Overall, the 2-aminopyrimidines exhibited good *in vitro* antimicrobial activity against various bacterial and fungal strains when compared to the reference antibiotics gentamicin and amphotericin B. Compound **198**, which contains a 1,2,3-trimethoxybenzyl moiety, emerged as a potential broad-spectrum antibiotic active against all tested bacteria and fungi, with MIC values comparable to those of gentamicin.

Research into the design and synthesis of novel heavy-metal sensors represents a significant contribution. Four new ligands featuring a naphthalimide scaffold, designed for the selective and differential detection of Hg(II) and Cu(II) ions, have been synthesized and characterized [B6]. The naphthalimide ligands are functionalized with a dansyl group, defined as a fluorophore moiety known for its high fluorescence quantum yield. Initially, a series of

naphthalimide intermediates were synthesized and subsequently transformed into the target compounds. It was found that the dyads distinguish between Hg(II) and Cu(II) ions, enabling dual-sensing capabilities. Mechanistic studies indicate that the electron-transfer pathways are finely tuned to prevent charge delocalization, thereby ensuring distinct photophysical responses for each metal ion.

Group **G** comprises publications of an interdisciplinary nature, focusing on the synthesis and biological activity of compounds with diverse structures and properties. Novel ferrocene-containing camphor sulfonamides have been synthesized as promising agents against lung cancer cells [G1]. Research has also focused on nitrofuoyl amides as potential anti-tuberculosis candidates, demonstrating strong antibacterial activity [G2, G4, G5]. Investigations into the synthesis of new MDL-860 analogues as potential antiviral agents are ongoing. Furthermore, research on the design and synthesis of novel dansyl ligands has been expanded to investigate their photophysical properties [G6, G10].

The submitted habilitation report also outlines the candidate's plans for future scientific development. Plans include continuing methodological studies on various chemical reactions to improve existing synthetic protocols and optimize key industrial processes. Future work will involve expanding antiviral research in collaboration with key partners from China, investigating new compounds with antimicrobial activity in partnership with the Institute of Microbiology, and conducting photophysical studies on new ligands with potential applications as chemosensors, fluorescent markers, functionalized nanomaterials, and more. A promising avenue for future research is the synthetic functionalization of silicate nanomaterials for use in CO₂ capture from waste gases.

IV. Assessment of the candidate's personal contribution

The scientific contributions presented in the competition are the result of interdisciplinary research, and all the scientific publications involved are co-authored. Undoubtedly, Dr. Ivaylo Slavchev's contribution are in the design, synthesis, and characterization of the new compounds.

V. Critical remarks

I have no critical remarks regarding the materials and research studies submitted for the competition. It should be noted that the competition documents are well-organized and arranged, which facilitates their analysis and evaluation. The habilitation report is substantive and effectively presents Dr. Slavchev's scientific contributions.

VI. Personal contribution

I have known Dr. Slavchev personally since he joined the Institute of Organic Chemistry with Centre of Phytochemistry (BAS), and I have followed his scientific development. My impression is that he is a highly active and thorough researcher.

CONCLUSION

The research activities and research metric indicators of Dr. Ivaylo Slavchev, reflected in the documents and materials submitted for the competition, meet all requirements for the academic position of "Associate Professor" in accordance with the Law for the Development of the Academic Staff in the Republic of Bulgaria (LDASRB), its regulations for the implementation, the Regulations of the Bulgarian Academy of Sciences, and the Regulations of the Institute of Organic Chemistry with Centre of Phytochemistry at the Bulgarian Academy of Sciences (IOCCP–BAS).

Based on the materials submitted for the competition and the scientific and applied-scientific contributions reflected therein, I offer a positive assessment and recommend that the other members of the Scientific Jury prepare a report proposing to the Scientific Council of the IOCCP for the election of Dr. Ivaylo Momchilov Slavchev to the academic position of "Associate Professor" at IOCCP–BAS in professional field 4.2. Chemical Sciences, scientific specialty "Organic Chemistry", for the needs of the "Organic Synthesis and Stereochemistry" Laboratory.

30.09.2026

Review prepared by:

(Assoc. Prof. Irena Philipova, PhD)