

REPORT

by

Assoc. Prof. Dr. Georgy Grancharov

Member of the Academic Jury set to render a decision

on the competition for filling the academic position of an **Associate Professor** in the Professional Field **4.2. Chemical Sciences** according to the Classifier of the Areas of Higher Education and the Professional Fields (Scientific Specialty **“Organic Chemistry”**)

This Report is prepared in response to Order № RD-09-139 of 23/07/2026 issued by the Director of the Institute of Organic Chemistry with Centre of Phytochemistry, Bulgarian Academy of Sciences, following the decision made by the Academic Jury that was held on 25/08/2026.

The Report is in compliance with *Development of Academic Staff in the Republic of Bulgaria Act (DASRB)*, the *Rules for the Application of the Development of Academic Staff in the Republic of Bulgaria Act*, the *Rules of BAS* and with the *Rules set at the Institute of Organic Chemistry with Centre of Phytochemistry, Bulgarian Academy of Sciences, for applying the Act aforementioned*.

The report consists of two chapters and a conclusion. There is only one candidate in the procedure Dr. Ivaylo Momcilov Slavchev, Assistant Professor in the Department of Organic Synthesis and Stereochemistry, the Institute of Organic Chemistry with Centre of Phytochemistry, Bulgarian Academy of Sciences.

1). Assessment of the scientific and research accomplishments of the candidate

1.1. Analysis of the application materials and documents presented by candidate

Dr. Ivaylo Slavchev participates in the current competition with 16 scientific publications, the majority of which were produced and presented within the last five years. Six of the submitted publications are categorized under Indicator B.4 (Habilitation Work), while the remaining 10 fall under Indicator G.7 (Additional Publications outside the Habilitation Work). In three of the articles under Indicator B.4, Senior Assistant Professor Dr. Ivaylo Slavchev is listed as the first author; his position within the research team demonstrates his active participation and commitment to the work. Three of the publications in this category belong to the highest quartile (Q1), which undoubtedly reflects the quality of the research. This indicator yields 130 points, exceeding the required 100 points. Regarding Indicator G.7, eight publications fall within the Q1 quartile, and two within the Q2 quartile. In many of these instances, he is listed among the lead authors, depending on the composition of the research team. This indicator yields 240 points, exceeding the required 220 points. All the submitted works address relevant topics and maintain a high scientific standard, as evidenced by their citation counts. Dr. Ivaylo Slavchev showed 40 citations, earning him 80 points (at a rate of 2 points per citation). The minimum requirement for the position of Associate Professor (35 citations, 70 points) has been fully met. The presented science materials submitted in this manner fully comply with the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria and its Implementing Regulations, as well as the regulations of the Bulgarian Academy of Sciences (BAS) and the Institute of Organic Chemistry with Centre of Phytochemistry (IOCCP-BAS) regarding the Law, and they qualify the candidate to participate in the competition.

1.2. Main scientific contributions - habilitation work (indicator „B.4“)

A) Methodological studies of new approaches to the formation of amide bond (publication B1)

Two new methods for forming amide bonds have been investigated and developed, offering advantages over existing standard methods. These methods focus on the direct amidation of esters of lower alcohols with a wide range of simple amines in the presence of a strong base. One of the methods is primarily suited for aromatic amines, while the other has proven effective for both aliphatic and aromatic amines. Tested with a total of over 50 different amines and esters, the proposed methods demonstrate high efficiency, versatility, and practical feasibility. Furthermore,

the methodology has been shown to be tolerant of various functional groups presenting in the reaction mixture (carbonyl, hydroxyl, nitro, and carboxyl).

B) Synthesis and antiviral activity of new diaryl ethers and their analogues (publications B2 and B3)

New antiviral agents have been synthesized, characterized, and biologically evaluated. These compounds possess a diaryl ether structure and show promise as anti-enteroviral agents. Publication B2 describes the design and synthesis of 12 new diaryl ether derivatives. Most of these were synthesized in anhydrous DMSO by heating the corresponding phenols with 2-chloro-5-nitrobenzonitrile in the presence of NaOH; they were obtained in high yields via a one-step synthesis. The *in vitro* activity against Cocksackievirus B1 (CBV1), Cocksackievirus B3 (CBV3), and Poliovirus 1 (PV1) was investigated. Their *in vitro* cytotoxicity was determined, and some of the most active diaryl ethers were evaluated for *in vivo* effects.

In publication B3, this work was extended to include the design and synthesis of 60 new diaryl ether derivatives. Their *in vitro* activity was evaluated, and three of the most active derivatives were subjected to *in vivo* activity testing.

C) Synthesis and comprehensive biological evaluation of new compounds bearing camphene skeleton (publication B4)

The biological activity of novel camphor derivatives was investigated, involving the design and synthesis of 20 new arylidene-camphors and 15 pyrimidines possessing a camphane skeleton. The newly synthesized substances were tested against reference and resistant strains of *Mycobacterium tuberculosis*, as well as various pathogenic bacteria and fungi; furthermore, their cytotoxicity was evaluated both *in vitro* and *in vivo*.

The synthesis of the compounds was carried out in two stages, yielding good yields. In the first stage, the synthetic strategy involved transforming readily available, enantiomerically pure (+)-camphor into a series of conjugated ketones. These reactions were performed under reflux in dry toluene under an inert atmosphere, using LDA as a base and aldehydes as starting reagents. In the second stage, most of the ketones were converted in a single step into the corresponding aryl-substituted 2-aminopyrimidines via condensation with an excess of guanidine hydrochloride and the base potassium tert-butoxide, conducted in refluxing dry tert-butanol under ambient air.

Most of the compounds demonstrated promising antimicrobial and antifungal activity. The arylidene-camphors exhibited significant levels of cytotoxicity, whereas the 2-aminopyrimidines with camphane skeletons can be considered less toxic.

D) Semi-synthetic amides bearing fenchane skeleton and their anti- and pro-oxidant activity (publication B5)

The pro- and antioxidant activity of natural and semi-synthetic compounds with anti-tuberculosis activity for which the inhibition of oxidation is an important factor was investigated. For this purpose, natural compounds such as piperine and curcumin were selected, alongside synthetic compounds consisting of a fenchane skeleton and cinnamoyl-like moieties linked via an amide bond. The latter had been synthesized previously in the laboratory, and their anti-tuberculosis activity had been evaluated.

Curcumin exhibited the highest antioxidant activity, whereas piperine and the synthetic amides containing a fenchane skeleton displayed pro-oxidant activity relative to the control sample.

E) Design and synthesis of new sensors for heavy metals (publication B6)

The relationship between the structure and properties of a series of four naphthalimide-based ligands, designed for the selective and differential detection of Hg(II) and Cu(II) ions, is presented. The naphthalimide ligands are functionalized with a dansyl group that induces intramolecular electron transfer — a feature crucial to the system's dual sensitivity.

The ligands exhibit a rare CHEF (chelation-enhanced fluorescence) mechanism for the detection of Hg(II), wherein fluorescence is amplified upon metal chelation — contrary to the quenching effect typically associated with heavy metal ions like mercury. This enables the highly selective and sensitive detection of Hg(II) ions in solution, making the system suitable for environmental and biological monitoring. In contrast, the Cu(II) complexes undergo reduction to Cu(I) via ligand-to-metal electron transfer.

2. Opinions, notes and recommendations

The author has tried to comprehensively present his primary scientific contributions within the habilitation thesis. In addition to the listed publications, his participation in numerous research projects is also noteworthy. I have no significant criticisms, but rather a recommendation and a question for the candidate:

- My recommendation is that it would be beneficial to also highlight scientific contributions outside the scope of the habilitation thesis — specifically those falling under category “G.7”. Doing so would further highlight his achievements, the indisputable relevance of the research conducted, and its scientific significance.

- My question concerns the candidate’s future scientific development: which area of his work can be considered as the primary focus, and which of the numerous presented results hold the greatest potential for practical application in the future?

3. Conclusion

The active research activity outlines Dr. Ivaylo Slavchev as an ambitious scientist working in the development of new methodologies for forming amide bonds; the synthesis and biological evaluation of novel antiviral agents based on diaryl ethers; the synthesis and comprehensive biological assessment of new arylidene-camphors, pyrimidines with a camphane skeleton, and amides with a fenchane skeleton; as well as the design and synthesis of novel naphthalimides functionalized with a dansyl group, intended for use as sensors for heavy metals. The candidate fully meets the minimum requirements of the law according to the Act, the Rules for the Application of the Act, the Rules of BAS and with the Rules set at the Institute of Organic Chemistry with Centre of Phytochemistry, BAS for applying the Act aforementioned. On the grounds of the documentations presented by the candidate, and the above assessment, I confidently recommend the Honorable Academic Jury to render a positive decision on **Assistant Professor Dr. Ivaylo Slavchev** filling the position of an **Associate Professor** at the Institute of Organic Chemistry with Centre of Phytochemistry, Bulgarian Academy of Sciences in the professional field **4.2 Chemical Sciences** (Scientific Specialty “**Organic Chemistry**”).

Date: 15/10/2026

Report prepared by:

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Member of the Academic Jury