

REVIEW

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of the documents submitted for participation in the competition for the academic position of Associate Professor at the Institute of Organic Chemistry with Centre of Phytochemistry, Bulgarian Academy of Sciences (IOCCP–BAS), in professional field 4.2. Chemical Sciences, scientific specialty Organic Chemistry, for the needs of the Laboratory of Organic Synthesis and Stereochemistry
Candidate: Chief Assistant Professor Dr. Ivaylo Momchilov Slavchev

1. General overview of the submitted materials

Chief Assistant Professor Dr. Ivaylo Momchilov Slavchev is participating in the announced competition for the academic position of Associate Professor in professional field 4.2. Chemical Sciences, scientific specialty Organic Chemistry, for the needs of the Laboratory of Organic Synthesis and Stereochemistry at the Institute of Organic Chemistry with Centre of Phytochemistry, Bulgarian Academy of Sciences (IOCCP–BAS).

The submitted materials include a curriculum vitae, a habilitation report on scientific contributions, lists of publications under indicators B and G, a report on fulfilment of the criteria for appointment to the academic position of Associate Professor, and other documents relating to the candidate's research activity.

The scientific results submitted for the competition cover several interconnected areas of contemporary organic and medicinal chemistry. They include the development of synthetic methods for amide-bond formation; the synthesis and investigation of the biological activity of new organic compounds; the preparation of derivatives with camphane and fenchane skeletons; and the development of fluorescent systems for the recognition of metal ions.

The research is characterised by an interdisciplinary approach in which synthetic organic chemistry is combined with biological, spectroscopic, structural and theoretical studies. This approach enables not only the preparation of new organic compounds, but also the assessment of their properties and potential practical applications.

According to the submitted report on the criteria, the candidate declares 130 points under indicator B, 240 points under indicator G and 80 points under indicator D, against stated minimum requirements of 100, 220 and 70 points, respectively. A total of 50 points is declared under indicator A. Thus, the reported quantitative indicators exceed the stated minimum requirements.

2. Biographical information and professional development

Chief Assistant Professor Dr. Ivaylo Momchilov Slavchev obtained his Bachelor's degree in Chemistry from Sofia University "St. Kliment Ohridski" in 2007 and his Master's degree in Medicinal Chemistry from the same university in 2013.

Between 2014 and 2018, he undertook doctoral studies at the Institute of Organic Chemistry with Centre of Phytochemistry of the Bulgarian Academy of Sciences and at Université Paris Descartes, France. He was awarded the degree of Doctor in 2019.

His professional career includes work as a process technologist in industrial production, as well as research activity at IOCCP–BAS. After periods working as a chemist at the institute, he has held the academic position of Chief Assistant Professor since April 2020.

The candidate's professional development demonstrates a consistent orientation towards synthetic organic chemistry and the study of biologically active compounds. His education in medicinal chemistry and the international component of his doctoral training provide a sound basis for interdisciplinary research connecting organic synthesis with the evaluation of biological and physicochemical properties.

3. General overview of research activity and publication record

The research activity of Chief Assistant Professor Dr. Slavchev is documented in publications in international scientific journals indexed in Web of Science and Scopus. The six publications submitted under indicator B have appeared in journals ranked in quartiles Q1, Q2 and Q3. Ten publications are included under indicator G, mainly in Q1 and Q2 journals.

Among the publications under indicator B, two papers in Bioorganic & Medicinal Chemistry Letters and Bioorganic Chemistry stand out; they address the synthesis and antiviral activity of new derivatives. Other notable contributions include the paper in RSC Advances on the direct amidation of esters, the study of camphane derivatives published in ChemistrySelect, research on the antioxidant and pro-oxidant activity of semisynthetic amides, and a paper in Dyes and Pigments on a fluorescent system based on dansyl and naphthalimide fragments. The publications under indicator G broaden the candidate's research profile and include studies of antitumour and antimycobacterial activity, molecular mechanisms of drug resistance, structural and conformational characteristics of organic molecules, and new fluorescent sensors.

According to the submitted report, the candidate declares 40 citations in scientific publications indexed in Web of Science and Scopus, corresponding to 80 points. This indicator demonstrates that some of his published results have gained recognition in the scientific literature. The publication record also shows that the candidate works in research teams with diverse expertise. This is particularly important for studies requiring the combination of organic synthesis, biological assays, spectroscopic methods and theoretical analysis. In several publications, the candidate also holds a leading position in the author list, indicating his active involvement in the development and execution of the research tasks.

4. Analysis of scientific contributions

4.1. Methodological studies on direct amide-bond formation

The paper "Base-promoted direct amidation of esters: beyond the current scope and practical applications", published in RSC Advances in 2022, addresses an important problem in synthetic organic chemistry: the development of more direct and practically applicable methods for amide-bond formation. The amide group is one of the most widespread structural motifs in organic molecules, including pharmaceuticals, natural products and functional materials. Traditional methods for amide synthesis often require prior activation of the carboxyl group and the use of additional reagents, which may increase the number of synthetic steps and the amount of waste generated.

The study developed two approaches for the direct amidation of esters with amines in the presence of a strong base. A broad range of substrates was investigated, including weakly nucleophilic aromatic amines and unactivated esters of lower alcohols. Of particular note is the identification of differences in the reactivity of the systems employed, which enable selective acylation of an aromatic amino group in the presence of an aliphatic amino group. The practical value of the methods was demonstrated by the preparation of various amides and phosphoramidates, as well as by the direct synthesis of compounds with established applications.

The study shows that direct amidation can be applied to a variety of substrates, including those bearing additional functional groups. The contribution is primarily methodological: extending the scope of direct amidation and demonstrating selective transformations represent significant results for synthetic chemistry. Another important feature is the effort to use reagents more economically and reduce the need for additional synthetic steps.

4.2. Synthesis and investigation of the antiviral activity of new diaryl ether derivatives

Two publications included in the habilitation portfolio concern the synthesis and biological evaluation of new diaryl ether derivatives and their analogues with potential antiviral activity.

The 2017 paper in *Bioorganic & Medicinal Chemistry Letters* reports the synthesis of new MDL-860 analogues and the evaluation of their activity against enteroviruses. This work was followed by a 2019 paper in *Bioorganic Chemistry*, which examined broader compound series and included in vitro and in vivo studies, as well as an analysis of quantitative structure–activity relationships.

The synthetic strategy is based on nucleophilic aromatic substitution reactions, allowing the introduction of a variety of substituents into the aromatic core. This approach afforded series of diaryl ether derivatives, as well as analogues containing sulfur- or nitrogen-based functional groups. The structures of the new compounds were confirmed by spectroscopic and mass-spectrometric methods.

An important aspect of the research is the systematic assessment of antiviral activity against poliovirus type 1 and coxsackieviruses B1 and B3, combined with cytotoxicity measurements. This approach makes it possible to distinguish compounds with genuine potential for further investigation from those whose biological effects are limited.

The results show that certain members of the diaryl ether series exhibit significant activity against some of the viruses tested. Selected compounds were also evaluated experimentally in vivo. At the same time, the activity could not be explained solely by membership in a particular structural class, and the relationships between structure and biological effect proved complex.

The scientific contribution of these studies lies in the preparation of new compounds, their systematic biological evaluation, and the expansion of knowledge concerning structural features that determine antiviral activity. It should be emphasised that the activity observed for individual compounds provides a basis for further research, but does not in itself demonstrate therapeutic efficacy.

4.3. Synthesis of camphane derivatives and investigation of their antimicrobial activity

The 2022 paper in *ChemistrySelect* addresses the synthesis, characterisation and comprehensive assessment of the antibacterial activity and cytotoxicity of new arylmethylened ketones and pyrimidines containing a camphane skeleton.

The study involved the preparation of new arylidenecamphors and heterocyclic derivatives, followed by assessment of their activity against *Mycobacterium tuberculosis*, various pathogenic bacteria and fungi. Additional cytotoxicity and metabolic-stability studies were conducted for some compounds.

The results concerning antimycobacterial activity are particularly noteworthy. Some of the synthesised arylidenecamphors showed activity against the reference strain *M. tuberculosis* H37Rv, with certain compounds exhibiting values of the same order of magnitude as those of the reference drug used. Their activity against clinical isolates was, however, more limited, highlighting the need for a careful assessment of the prospects for further development of these structures.

Other compounds with promising results were identified in the antibacterial and antifungal assays, including examples with a broader spectrum of activity. The parallel assessment of cytotoxicity is an important element of the work, as it provides an initial indication of whether the observed biological activity is accompanied by undesirable effects on host cells.

The contribution of this study lies in the development of synthetic approaches to new derivatives with a camphane skeleton and in the comprehensive evaluation of their biological properties. The work demonstrates the need to combine synthetic chemistry with microbiological and toxicological studies in the search for new biologically active compounds.

4.4. Investigation of the antioxidant and pro-oxidant properties of semisynthetic amides with a fenchane skeleton

The 2024 paper in *Comptes Rendus de l'Académie Bulgare des Sciences* investigates the antioxidant and pro-oxidant activity of curcumin, piperine and semisynthetic amides with a fenchane skeleton. The study aims to establish how molecular structure influences lipid oxidation. To this end, natural compounds were compared with synthetic derivatives containing a fenchane fragment, an amide group and substituted aromatic groups.

The results show that the effects of the investigated compounds depend on concentration and structural features. Curcumin displays clear antioxidant activity, whereas piperine and some of the synthetic derivatives exhibit a pro-oxidant effect under the experimental conditions used. Differences associated with substitution of the aromatic core were also observed.

The scientific value of this work lies in its attempt to relate the structural characteristics of semisynthetic derivatives to their behaviour in a model lipid-oxidation system. The results contribute to a better understanding of the fact that the presence of structural fragments commonly associated with antioxidant properties does not necessarily guarantee such an effect in a particular molecule.

Given the limited number of synthetic derivatives investigated, conclusions regarding structure–property relationships should be regarded as preliminary. This does not diminish the value of the work as a basis for subsequently expanding the series and clarifying in greater depth the mechanisms underlying the observed behaviour.

4.5. Development of fluorescent systems for metal-ion recognition

The 2025 paper in *Dyes and Pigments* focuses on the synthesis and investigation of dansyl–naphthalimide systems with potential for metal-ion recognition.

The study developed ligands in which a dansyl fragment is combined with a naphthalimide structure. Their photophysical properties and behaviour in the presence of Hg(II) and Cu(II) ions were investigated. Combining different chromophoric and coordinating fragments makes it possible to obtain systems with differentiated optical responses to individual metal ions.

Of particular interest is the observed fluorescence enhancement upon binding Hg(II), described by the CHEF (chelation-enhanced fluorescence) mechanism. For Cu(II), evidence of reduction to Cu(I) was obtained and supported by EPR and XPS analyses. Thus, the study goes beyond simply recording changes in the fluorescence signal and includes an attempt to provide a mechanistic explanation for the observed interactions.

The synthetic work involved the preparation of the target ligands and intermediates, whose structures were confirmed by NMR spectroscopy, HRMS and other appropriate methods. The photophysical and sensing studies demonstrate the possibility of distinguishing metal ions through different optical and redox responses.

The contribution of this publication lies in the development of new molecular systems in which metal-ion recognition is combined with control over electron transfer and fluorescence properties. The results may be relevant to the development of sensor systems for analytical and environmental applications.

4.6. Overall assessment of the scientific contributions

The publications discussed above show that Chief Assistant Professor Dr. Slavchev's research is not limited to the preparation of new organic compounds, but also encompasses the investigation of their reactivity,

biological activity and physicochemical properties. The main scientific contributions can be summarised as follows:

1. Methodological contributions to organic synthesis: development and extension of the applicability of base-promoted direct amidation of esters, including reactions with weakly nucleophilic amines and selective transformations.
2. Contributions to medicinal chemistry: synthesis of new diaryl ether derivatives and analogues, systematic investigation of their antiviral activity, and identification of compounds with promising biological properties.
3. Contributions to the synthesis of biologically active derivatives of natural compounds: preparation of new camphane and fenchane derivatives and evaluation of their antimicrobial, antimycobacterial, antioxidant and pro-oxidant activity.
4. Contributions to the molecular design of functional systems: development of dansyl–naphthalimide ligands with differentiated fluorescent and redox responses to metal ions, and investigation of the mechanisms of interaction.

A common feature of these research areas is the use of organic synthesis as the principal tool for creating molecular diversity, followed by targeted investigation of structure and properties. This approach enables the advancement of fundamental knowledge while identifying opportunities for future applications.

5. Project activity and scientific collaborations

The submitted curriculum vitae indicates that the candidate has experience in implementing and leading research projects. He is reported to have led three national projects funded by the Bulgarian National Science Fund, concerning the discovery of drug candidates through the modification of natural compounds, the development of styryl and polymethine fluorophores, and the preparation of new derivatives of camphor and (R)-2-aminobutanol with potential antitubercular activity.

The candidate has also participated in other national and international research projects in medicinal chemistry, antiviral research, functional materials and the valorisation of renewable feedstocks.

Leading research projects is an important element of a scientist's professional development, as it requires the formulation of research questions, planning of experimental work, coordination of collaboration and responsibility for achieving the objectives. In this case, the project activity is thematically consistent with the candidate's publication record and demonstrates an ability to work on long-term research tasks.

Scientific collaborations with teams possessing expertise in biological assays, spectroscopic investigations and theoretical analysis also play a significant role in the research presented. This model of cooperation is particularly appropriate for contemporary medicinal and functional organic chemistry, where complex scientific problems require the combination of different methods and areas of expertise.

6. Critical comments and recommendations

The scientific works submitted by Chief Assistant Professor Dr. Ivaylo Momchilov Slavchev are characterised by thematic diversity, an interdisciplinary approach and an effort to obtain new organic compounds with interesting synthetic, biological and physicochemical properties. The combination of methodological developments in organic synthesis with studies of biological activity and the design of functional molecular systems is particularly commendable.

Promising directions for future development include further broadening the applicability of the synthetic methods developed, deepening the investigation of molecular structure–biological activity relationships, and improving the fluorescent systems with a view to their potential analytical applications. Continuing this research would build on the results achieved and expand the possibilities for their practical use.

I consider the candidate's research activity to provide a sound basis for further development in these areas and for establishing an independent research profile in organic and medicinal chemistry. The submitted materials do not give rise to any substantial critical comments that would alter my positive assessment of the candidate's scientific achievements and professional development.

7. Conclusion

The documents submitted by Chief Assistant Professor Dr. Ivaylo Momchilov Slavchev for participation in the competition meet the requirements of the Development of the Academic Staff in the Republic of Bulgaria Act, the Regulations for its Implementation, and the Regulations governing the conditions and procedure for appointment to the academic position of Associate Professor at IOCCP-BAS. Dr. Slavchev is applying with a sufficient number of high-quality scientific publications published after the award of his doctoral degree. The scientific results presented demonstrate his active research work and his contributions to organic synthesis and the development of organic compounds with potential applications in medicinal and analytical chemistry.

Having examined the materials submitted for the competition, I give my positive assessment and recommend that the Scientific Jury submit a proposal to the Scientific Council of IOCCP-BAS to elect Chief Assistant Professor Dr. Ivaylo Momchilov Slavchev to the academic position of Associate Professor in professional field 4.2. Chemical Sciences, scientific specialty Organic Chemistry.

Date: 9 October 2026

Reviewer:

(Prof. Dr. Yulian Zaganyarski)