

REVIEW

by **Prof. Dr. Ing. Emilia Dimitrova Naydenova-UCTM, Sofia**

Member of the Academic Jury set to render a decision on the competition for filling the academic position of Associate Professor in the Professional Field 4.2. Chemical Sciences, Scientific Specialty (Organic Chemistry-Organic Synthesis) at the Faculty of Chemistry and Pharmacy, Sofia University "St. Kliment Ohridski"

This Review has been prepared in response to Order № ПД 38-113/26.02.2025 issued by the Rector of Sofia University and decision of the scientific jury meeting held on 26.03.2025.

The Review 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 Sofia University "St. Kliment Ohridski", for applying the Act aforementioned.

1. General presentation of the procedure and the candidate

The competition for filling the academic position of “Assoc. Professor” in the Professional Field 4.2. Chemical Sciences (Organic Chemistry - Organic Synthesis) was announced in State Gazette, issue № 5 of 17.01.2025, for the needs of the Department of Organic Chemistry and Pharmacognosy, Faculty of Chemistry and Pharmacy, Sofia University "St. Kliment Ohridski". Only one candidate participates in the competition – **Ch. Assist. Prof. Nevena Ivanova Petkova-Yankova, Ph.D.**

The set of documents presented by Ch. Assist. Prof. Dr. N. Petkova-Yankova, is in accordance with the Rules for the Development of the Academic Staff at Sofia University "St. Kliment Ohridski" and meets the requirements for occupying the academic position of "Associate Professor".

Chief Asst. Prof. Dr. Nevena Ivanova Petkova-Yankova graduated with a Master's degree, specialty "Organic and Analytical Chemistry" in 2000 from Sofia University "St. Kliment Ohridski", Faculty of Chemistry. In 2007 defends a thesis for the educational and scientific degree Doctor of Chemistry (Organic Chemistry) code 01.05.03, VAK (Higher Attestation Commission)

Her professional career began in 2004, as a chemist in the Department of Organic Chemistry, Faculty of Chemistry, Sofia University "St. Kl. Ohridski". Since 2008, she has been a Senior Assistant, and from 2009 to the present, she is a Chief Assistant in the Department of Organic Chemistry and Pharmacognosy, Faculty of Chemistry, Sofia University "St. Kl. Ohridski".

In the period 2011-2013, Dr. Nevena Petkova conducted a long-term specialization at the 3B's Research Group - Biomaterials, Biodegradables and Biomimetics, Department of Polymer Engineering, University of Minho, Portugal, She specialized three times at the Central Research Laboratory, Department of Chemistry, University of Oxford, England as well as at the Max Planck Institute for Polymer Research, Mainz, Germany and in 2019 at BioNMR, University of Barcelona,

Spain. These specializations largely determined her successful development and establishment as a scientist in the field of organic chemistry, organic synthesis and analysis. Her scientific interests are related to the synthesis of organophosphorus compounds, strained cyclooctynes for click reactions, modified monosaccharides, and spectral characterization of organic compounds by one-dimensional and two-dimensional NMR techniques in solution and solid state.

2. General characteristics of the candidate's activities

➤ *Evaluation of the candidate's scientific and applied scientific activities*

Dr. Nevena Petkova-Yankova is a co-author of **22** scientific papers and **1** textbook, of which 20 publications are in journals, refereed and indexed in the global databases of scientific information Web of Science and Scopus, 1 in a Bulgarian journal and 1 in a scientific conference proceedings.

In the current competition, she participated with 16 scientific publications, which are in specialized scientific journals, refereed and indexed in Web of Science and Scopus. They have IF or SJR and fall into quartiles from Q1 to Q4 according to the grouping of scientific journals. They are distributed as follows: 8 articles are in journals with Q1, 2 articles are in journals with Q2, 3 of the articles are with Q3 and 3 with Q4. At the time of submission of the documents, a total of 49 citations (excluding self-citations) were noted on the scientific publications submitted for the competition, the h factor is 4. She participated in 93 international and national scientific forums with reports and posters.

I accept for evaluation all submitted scientific works. They fully meet the profile of the announced competition and show that the scientific activity of Ch. Asst. Prof. Dr. Nevena Petkova-Yankova is in the field of organic chemistry and organic synthesis. In 6 of the submitted publications she is the first author, in 7 she is the second author, which shows her significant contribution.

According to the requirements, she presented a habilitation thesis on the topic "Synthetic and theoretical studies on the reactivity of coumarin derivatives", which included research published in 4 scientific articles with a quartile of Q1. Dr. Nevena Petkova-Yankova has demonstrated excellent theoretical knowledge and experience in conducting research and competence in interpreting the results.

In the current competition, she participated with **546** points, which exceeds the required **510** points for candidates to occupy the academic position of "associate professor", according to the requirements of the DASRB and the regulations for acquiring scientific degrees and occupying academic positions at the Sofia University "Kl. Ohridski". The points are distributed as follows:

Indicator A1: *Dissertation for the award of the educational and scientific degree of "doctor".* The candidate, Ch. Assist. Prof. Dr. Nevena Petkova-Yankova, has successfully defended a dissertation on the topic "Molecular design of new methylenebisphosphonates containing coumarin and benzoxaphosphorine rings". (50 points).

Indicator group C.4 - *Habilitation work - scientific publications that are referenced and indexed in world-renowned databases of scientific information (Web of Science and Scopus).*

Chief Asst. Prof. Dr. Nevena Petkova-Yankova has presented a total of 4 publications with Q1. The points this group carries are 100 points. The criterion is met.

Indicator group D (D7).

Regarding this indicator, the candidate has submitted 12 publications of which 4 publications in Q1, 2 in Q2, 3 in Q3 and 3 in Q4. The total number of points that group D carries is 221. In this case, the criterion is also met.

Indicator group E. Citations.

In this competition, 35 citations were submitted, carrying 70 points, with which the respective indicator was fulfilled.

Indicator group G

The candidate has 105 points, with a required score of 70 points. The points for this indicator are formed as follows: h = 4, 2 new lecture courses introduced, member of a scientific team of 9 scientific projects. She was the supervisor of 3 successfully defended diploma theses, but they were not scored.

➤ ***Evaluation of the teaching activities of the candidate.***

The teaching activities of Chief Asst. Prof. Dr. Nevena Petkova-Yankova include conducting seminars and exercises in Organic Chemistry I and II for all specialties of the Faculty of Chemistry and Pharmacy and the Faculty of Biology of Sofia University "St. Kl. Ohridski". Exercises and seminars in "Organic Chemistry Part I" for foreign master's students in the specialty "Pharmacy" of the faculty of Chemistry and Pharmacy and modern techniques in NMR spectroscopy.

She has introduced 2 new lecture courses. She has developed and led a mandatory course in "Organic Chemistry Part II" for the Bachelor's degree program in "Chemistry and English", which started in the 2018/2019 academic year and an elective course for the Bachelor's degree program in "NMR Spectroscopy".

She is also assigned to teach lectures in Organic Chemistry II - Biology and Chemistry major, Bachelor's degree and Modern Techniques in NMR Spectroscopy, Bachelor's degree, 30 hours, elective course. She is a co-author of a textbook: "Laboratory Exercise Guide with a Collection of Problems in Organic Chemistry "for students of the specialty "Pharmacy", University Publishing House "St. Kliment Ohridski" - 2019. 3 diploma theses have been defended under her supervision.

3. Evaluation of contributions to scientific research

The candidate's scientific research is primarily focused on the synthesis and development of new methods for the preparation of coumarin and biscoumarin derivatives. Quantum-chemical calculations have been used to clarify the mechanisms and the influence of various factors on the course and selectivity of the studied reactions. By applying modern spectral methods, the

synthesized compounds have been proven and characterized. The scientific contributions from the research conducted can be summarized in two main directions, the more important of which are:

I. Synthetic research

- Heterocyclic methylenebisphosphonates have been synthesized by 1,3-dipolar cycloaddition of ethyl diazoacetate to 1,2-benzoxaphosphorine-3-phosphonates. It has been found that the reaction of salicylaldehydes with tetraethyl ester of methylenebisphosphonic acid, under Knoevenagel reaction conditions, gives the corresponding 1,2-benzoxaphosphorine-3-phosphonates in good yields.

The interaction of the diethyl ester of 2-oxo-2H-1-benzopyran-3-phosphonic acid with nitromethane under different reaction conditions has been studied (*publications 15 and 9*).

It has been established that in the absence of solvent a conjugate addition product of diethyl 4-(nitromethyl)-2-oxochroman-yl phosphonate is obtained.

The structures of the new compounds have been confirmed by spectroscopic and X-ray structural analysis.

- A new, effective method for the synthesis of 3,4-disubstituted pyrrolidine-2,5-diones from 3-substituted coumarins was developed (*publications 13 and 9*).

It was established that coumarins which contain electron withdrawing groups gave the expected pyrrolidine derivatives. Coumarins substituted with electron donating groups did not react at all.

- The reaction of 2-oxo-2H-1-benzopyran-3-phosphonic acid diethyl ester with organometallic compounds under heating and under ultrasound irradiation was studied (*publications 10 and 11*). It was found that the reaction of 3-phosphonocoumarin with organomagnesium reagents under ultrasound irradiation proceeds significantly more easily. Complete conversion of the starting material is observed, and the yields are high.

When reacting 3-diethylphosphonocoumarin with chloroacetic anhydride in the presence of metallic zinc under the action of ultrasound, a dimer of two identical coumarin fragments directly linked at the fourth carbon atom was isolated and characterized.

- A new method for the dimerization of 3-substituted coumarins with the use of ultrasonic radiation was developed, in which an increase in the speed and yield of the reaction is achieved.

It has been proven that the homodimerization reaction under ultrasound conditions in the presence of zinc and chloroacetane anhydride is applicable only to coumarins with an electron-withdrawing group in the 3-position. A mechanism of the dimerization reaction has been proposed.

- The behavior of 3-acetylcoumarin in the homodimerization reaction was studied. The reaction conditions for homodimerization were achieved under sonication using combination of zinc and metallic salt ($ZnCl_2$ or $Zn(OAc)_2$). The mechanism of the reaction was investigated. The relative stability of the possible intermediates has been compared, Theoretical results suggested that the radical mechanism is more favorable (*publication 5*).

- Factors affecting the reactivity of the ambident nucleophile in the tandem hydrogenation/alkylation reaction of 3-diethylphosphonocoumarin were investigated (*publications 7 and 9*). The effect of the organic solvent was also reported.

- The selectivity of the tandem reaction hydrogenation/phosphorylation of 3-diethylphosphonocoumarin under phase-transfer conditions was explored (*publication 3*). The change in the distribution of electron density in the coumarin ring was studied. It was found that the reaction proceeded with formation of two types of enol phosphates (O-phosphorylation products). The reaction conditions were optimized, which achieved high regioselectivity for O-phosphorylation and O-acylation.

- A simple method for the preparation of stable acylated enols of substituted 3,4-dihydrocoumarins was developed by working with an enantiomeric mixture of (4R,3R)- and (4S,3S)-ethyl-2-oxo-4-phenylchromane-3-carboxylate (*publication 2*). The O-acylated enol form (R/S)-ethyl-2-acetoxy-4-phenyl-4H-chromene-3-carboxylate is a new compound and its structure was characterized by NMR Spectroscopic techniques.

The preferred regioselectivity for O-acylation of the 3,4-dihydrocoumarin in the presence of substituent in the 4th position in the chroman ring was confirmed.

- A method for the preparation of heterocyclic methylenebisphosphonates by 1,3-dipolar cycloaddition of ethyldiazoacetate to 1,2-benzoxaphosphorinephosphonates was developed (*publication 14*). The relative configuration of some of the diastereoisomeric pyrazolines was proven by X-ray structural analysis.

- The possibilities of using 3-(ω -bromoacetyl)coumarin and its derivatives in Michaelis-Becker reactions have been investigated (*publication 6*). The reaction proceeds with the formation of highly reactive bromohydrins. It was found that the obtained bromohydrins with dialkylphosphites under interfacial catalysis gave a mixture of epoxyphosphonates and vinylphosphates.

- The reactivity of 3-substituted-6-bromocoumarins and 6-bromo-1,2-benzoxaphosphorines under the conditions of the Suzuki and Sonogashira reactions was studied. (*publication 4*). Two different approaches were used and the reaction conditions were optimized. The photophysical properties of the newly obtained compounds were studied using UV-VIS and fluorescence spectroscopy. It has been found that a phenyl substituent at the 6-position of the coumarin ring leads to a bathochromic shift in both the absorption and fluorescence spectra compared to the unsubstituted coumarin. In quantum chemical calculations, a good correlation between theoretical and experimental data has been observed.

- The characteristic rearrangement in 3-substituted coumarins associated with opening and a second transesterification of the formed intermediate has been reviewed (*publication 1*).

II. Quantum-chemical studies

- The spectral properties of some aryl-substituted 3-phosphonocoumarins have been investigated using quantum chemical methods. The influence of the substituent in the aryl residue

was determined. Structures with promising fluorescent properties have been synthesized under the conditions of Suzuki and Sonogashira reactions (*publ. 4*).

- The probable mechanisms for homodimerization of 3-acetylcoumarin have been investigated using quantum-chemical modeling. Based on these, the authors suggest that the most plausible reaction pathway involves the formation of biradicals from 3-acetylcoumarin, which later form dimers. The most optimal reaction conditions were found (*publ. 5*).

- Local reactivity descriptors, such as atomic charges, atomic electrostatic potential and atomic Fukui indices, which describe the degree of electronic localization (i.e. determine whether it is a soft or hard center) for a series of 3-substituted coumarin (2-oxo-2H-1-benzopyran) derivatives, have been calculated using density functional theory (DFT) and Möller-Plesset methods (MP2). Using X-ray photoelectron spectroscopy (XPS), the binding energies of the 1s levels of C and O have been experimentally measured and compared with the theoretically calculated values. The correlation between theoretical and experimental properties allows to trace the effect of electron-withdrawing substituents on the electrophilicity of a particular atomic center (*publ. 12*).

In addition to the described contributions in the two main directions, the candidate has also added a third direction, entitled "Other research" (direction III, *publications 16 and 8*).

The following can be noted as more important contributions here:

- A simple procedure for obtaining β -phenylglutamic acid esters by Michael addition of Schiff bases of glycine esters to cinnamic acid esters has been developed.

- Bioorthogonal click reactions have been used to track the temporal distribution of different glycans in hippocampal neurons of living mice during their in vitro maturation. The presented approach is biocompatible and does not affect glycan transport.

- The applicability of this strategy to tissue sections opens new opportunities for studying glycan dynamics under more complex physiological conditions.

4. Critical remarks and recommendations.

I have no critical remarks towards the candidate. The scientific and applied scientific works submitted for review correspond to the topic of the competition, contain sufficient analyses and author's assessments of the research results,

CONCLUSION

The documents and materials submitted for the competition by Chief Asst. Prof. Dr. Nevena Petkova-Yankova meet all the requirements of the DASRB, the Rules for the Application of the Development of Academic Staff in the Republic of Bulgaria Act, and the Rules set at the Sofia University, "St. Kliment Ohridski", for applying the Act aforementioned.

She has presented a sufficient number of scientific papers published in international specialized journals. The applicant's works have original scientific and applied contributions.

The scientific and pedagogical qualification of Dr. N. Petkova-Yankova is undoubted. The results achieved demonstrate the applicant's competence and research experience. This gives me a reason to give my positive assessment and to recommend the Academic Jury to render a positive decision on Chief Asst. Prof. Dr. Nevena Ivanova Petkova-Yankova filling the position of Associate Professor in the professional field 4.2, "Chemical Sciences" (Organic Chemistry-Organic Synthesis) for the needs of the Department of Organic Chemistry and Pharmacognosy, Faculty of Chemistry and Pharmacy, Sofia University "St. Kliment Ohridski".

Date: 15/05/2025

Reviewer:

/ Prof. Dr. Eng. Emilia Naydenova/