

**STATEMENT**  
**on the competition for the academic position Associate Professor**  
**Scientific direction 4.2. Chemical Sciences**  
**(Organic Chemistry – Chemistry of Heterocyclic Compounds)**  
**at Sofia University “St. Kliment Ohridski” – Faculty of Chemistry and Pharmacy**  
**announced in „ДБ“, No 105, 11.12. 2020**

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Assistant Professor Dr Nikola Tomov Burdzhiev is the sole candidate in this competition.

The candidate Nikola T. Burdzhiev graduated in 2002 the Faculty of Chemistry and Pharmacy at Sofia University “St. Kliment Ohridski”, acquiring bachelor's degree in Organic Chemistry. In 2007 he successfully defended his doctoral thesis on “ Polyfunctional piperidinones and pyrrolidinones - synthetic and chromatographic studies” and was awarded the PhD degree in Organic Chemistry again at the Faculty of Chemistry and Pharmacy, SU “ Kl. Ohridski”.

**Report on the fulfilment of the minimal criteria**

The topic of the Habilitation thesis of Dr. Nikola T. Burdzhiev is "Polyfunctional heterocyclic compounds - synthetic and spectral studies". It is based on 6 scientific publications presenting the synthesis and characterization of polyfunctional heterocyclic nitrogen-containing compounds with potential biological activity. The quartiles of these publications are as follow: one is Q1, three are Q2 and two are Q4.

In addition to the Habilitation thesis, presented scientific publications are 13 in number and also concern both the synthesis of new heterocyclic compounds with probable biological activity and spectral characterization of heterocyclic compounds with potential application in practice. Ten of them are in journals with impact factor (IF), being categorized as follow: three are in Q1, four are in Q2, one is in Q3, two are in Q4. The other three papers are published in journals with impact rank (SJR). Citations presented for the competition are 54, though in Scopus they are 132.

Dr. Burdzhiev has pointed participation in eight projects funded by programs of the SU and the National Science Foundation, in one of which he is a leader, and in the other seven - a participant.

***Educational and pedagogical activity:*** Dr. Burdzhiev has been appointed as Senior Assistant in Organic Chemistry at the Department of Organic Chemistry and Pharmacognosy of the Faculty of Chemistry and Pharmacy at Sofia University in 2008 to 2010. Since 2010 until now he is Assistant Professor in Organic chemistry at the same Department. During this period he has taught exercises, seminars and also lectures for bachelor students in the following subjects: • Organic Chemistry II; • Structure and biological activity of organic compounds; • Chemistry of heterocyclic compounds. He was co-supervisor of 3 and the only supervisor of 4 diploma theses, all of them successfully defended. He is a co-author of three manuals booklets: "Manual for laboratory exercises and problems in Organic chemistry“ for students studying Pharmacy and "National Olympiad in Chemistry and Environmental Protection (2000-2019).Questions and Problems“ - Part 1 and Part 2. All three were issued in 2019.

On the basis of data presented above Dr Nikola Burdzhiev's scientific output fully complies with both the requirements for holding the academic position „Associate Professor“ in the field 4.2. Chemical Sciences, stated in The Law for the Development of the Academic Staff in the Republic of Bulgaria, and the additional criteria of Sofia University “St. Kliment Ohridski”.

### **Scientific research activity**

The candidate summarizes his contributions in the following three scientific fields:

#### ***1. Synthesis of heterocyclic compounds by reactions of cyclic anhydrides and subsequent modifications in order to obtain compounds with potential biological activity***

The publications here reveal the synthesis of new biologically active compounds containing heterocycles. The selected synthetic approaches are based on studies traditionally developed in the department and concern compounds with stereogenic centers.

- The main syntheses are based on reactions of N-benzylidenebenzylamine with succinic, glutaric and diglycol anhydride, correspondingly obtaining oxopyrrolidine, oxopiperidine and oxomorpholine carboxylic acids.
- In some of the products, the carboxylic group has been transformed to a peptide bond either by a direct acylation of an amino-group or after conversion to an amino group (applying Hofmann or Curtius rearrangement) and subsequent condensation with another carboxyl group. Some of the newly synthesized pseudopeptides and piperazine products have shown antihistamine activity, and other representatives have revealed potential ACE inhibitory activity.
- The interaction of cyclic imines with monocyclic anhydrides as a one-step pathway to the benzo [a] quinolizidine system and its bioisosteric O and S analogs has been considered, which is extremely easy for researchers, as commonly multistage methods for preparing heterocycles have been used.
- The reactivity of 1- ( $\omega$ - (N-acylated amino) alkyl)-3,4-dihydroisoquinolines to homophthalic anhydride was studied. The role of the easy enolysis of the anhydride in the reaction under milder conditions was observed even when the imines were inhibited and a putative mechanism was stated.
- Tetrahydroisoquinolines containing indole, phthalimide and imidazole moieties with potential antiaromatase activity were synthesized. The use of ultrasound has also been shown to shorten the reaction time in the Mitsunobu reaction used to introduce the phthalimide fragment.

**Contributions** here are related to both conducting syntheses and isolation of the target products, and monitoring of the steric course of the reactions carried out. In many cases, studies have been performed to determine the ratios of the configurational isomers of the target product. Various NMR spectral techniques and sometimes X-ray diffraction analysis have been used to establish the structure and relative configuration of the newly obtained compounds.

#### ***2. Synthesis and spectral characterization of heterocyclic compounds with potential application in practice***

Here again several directions are pointed:

- Compounds that change their optical properties when complexed with metal ions can be used for metal ion sensors or optical switches. To this end, new derivatives of 2-acetyl-1,3-indandione with 4-(1,4,7,10-tetraoxa-13-azacyclopentadecan-13-yl)benzaldehyde and 4-hydroxy-1-naphthaldehyde with 4-(1,4,7,10-tetraoxa-13-azacyclopentadecan-13-yl)aniline have been synthesised. The condensation reaction itself and the influence of a number of metal ions ( $K^+$ ,  $Na^+$ ,  $Mg^{2+}$ ,  $Si^{2+}$  и  $Ba^{2+}$ ) have been carefully studied. IR, NMR and X-ray diffraction analysis were used for characterization.

- A new "green" approach has been developed targeting preparation of a square acid dye from square acid and two equivalents of 1,3,3-trimethyl-2-methyleneindoline in an ethyl L-lactate solvent. The target dye was obtained in only 4 minutes with a very good yield, and its structure and purity were proved by NMR spectroscopy and mass spectrometry.

- A novel compound: 3'-amino-4-thio-1H-tetrahydropyranspiro-5'-hydantoin has been synthesised and two of its complexes with Pd (II) and Pd (IV) have shown cytotoxicity on five human tumor cell lines in *in-vitro* experiments.

### 3. Spectral properties of heterocycles used in practice

It concerns practical applications of spectroscopy, generally NMR, in several directions:

- Solubilisation of very sparingly water-soluble biologically active substances containing heterocycles has been studied. Itraconazole has been tested and its solubility in aqueous solutions with anionic single chain surfactants at pH = 3 has been demonstrated.  $^1H$  NMR spectroscopy analysis has shown that Itraconazole was protonated at two places - at the N-atom of the piperazine ring attached to the phenoxide portion of the molecule and at a second place at the N-atom of the triazole moiety, which explains the strong interaction with the surfactant.

- Identification of synthetic cannabinoids such as 5-ADB (methyl(S)-3,3-dimethyl-2-[1-(5-fluoropentyl)-1H-indazole-3-carboxamido] butanoate) and FU B-AMB(ethyl(S)3-methyl-2[1-(4-fluorobenzyl)-1H-indazole-3-carboxamido] butanoate)by GC-MS,  $^1H$  and  $^{19}F$  NMR. These substances mimic the psychoactive effect of tetrahydrocannabinol, but in case they are used as substitutes for cannabis, can cause death.

- The use of copper isotopes in modern synthetic and nuclear chemistry, with potential application in the diagnosis and treatment of cancer.

**Additional qualifications and specializations:** The candidate has additional qualifications and several short-term specializations (one to two months) in renowned foreign universities: University of Oxford, Oxford, UK (2015); Max-Planck-Institut für Polymerforschung, Mainz, Germany (2018) and Universitat de Barcelona, Barcelona, Spain (2019).

Dr. Burdzhiev was awarded the Badge of Honor of the Sofia University "St. Kliment Ohridski" Second degree, 2018.

It should be noticed, that in addition to his knowledge and experience in synthetic organic chemistry, Dr. Burdzhiev is familiar to the application of NMR techniques, so to study molecule structures and processes in organic chemistry.

## CONCLUSION

The documents and materials presented by Dr. Nikola Burdzhiev meets the requirements of the Law for the Development of the Academic Staff in the Republic of Bulgaria, the Regulations for its application, the Regulations for its application at Sofia University and the requirements of Faculty of Chemistry and Pharmacy at Sofia University.

The publications co-authored by Dr. Burdzhiev have been highly praised by the scientific community and cited accordingly. The total Hirsch index (H-factor) of Dr. Burdzhiev 's scientific output is 8 (SCOPUS database).

Based on the overall research and teaching activities, I recommend to the honourable members of the Scientific Jury to prepare a report proposal to the Scientific Council of the Faculty of Chemistry and Pharmacy, Assistant Professor Dr. Nikola Tomov Burdzhiev to be elected for the academic position of "Associate Professor" at the Faculty of Chemistry and Pharmacy, in the professional field 4.2. Chemical Sciences (Organic chemistry - Chemistry of heterocyclic compounds).

14.04.2021 г.

Daniela S. Tsekova