OPINION
by Assoc. Prof. Georgi Dobrikov, PhD - member of the Scientific Jury,
appointed by Order RD-09-179/03.07.2020
by a competition for taking the academic position "**PhD**",
professional field "4.2. Chemical Sciences,
Candidate (single): Krassimira Petkova Dikova

Krassimira Petkova Dikova has been working for over 15 years in the Laboratory of Organic Synthesis and Stereochemistry (OSS) at IOCCP-BAS, for which period she has participated in a number of projects, mainly related to the pharmaceutical industry. He currently holds the position of "assistant" at the same laboratory. She presents her dissertation work as a doctoral student in independent training with supervisors Prof. Vladimir Dimitrov and Assoc. Prof. Dr. Kalina Kostova. It is aimed at protection from the colloquium "Natural and synthetic biologically active compounds" at IOCCP-BAS on June 23, 2020.

The dissertation is presented on 165 pages, includes 34 tables, 10 figures and 76 diagrams. The main sections are seven and include: Introduction, Objectives and Tasks, Literature Review, Results and Discussion, Conclusions, Experimental Part and Literature. It is preferable to number the figures, diagrams and tables separately for each section. The bibliography includes 165 literature sources, arranged in a single numbering. The results are reflected in 2 scientific publications and are presented at 11 scientific forums, with 1 citation. The quantity and quality of the work done is more than enough for the formation of a completed dissertation, the main points of which can be summarized as follows:

- Realization of three component condensation of Betti-type using ferrocene- and ruthenocenecarbaldehyde, as well as aromatic aldehydes 1-pyrenecarbaldehyde and 2-fluorenecarbaldehyde, as aldehyde components in the reaction with 2-naphthol or 3-methoxy-2-naphthol as naphthol components, and (S)-phenylethylamine or (S)-leucinol as the amino-component, respectively;
- Study of the diastereoselectivity of the condensation reaction and isolation of the obtained diastereoisomers in pure form. Determination of their structure and properties using NMR spectroscopy, mass spectrometry, specific angle of rotation, elemental analysis and other methods of characterization;
- The configuration determination of the newly formed stereogenic center within the synthesized compounds using modern NMR techniques and X-ray diffraction analysis;
- Application of the newly obtained diastereoisomerically pure aminomethylnaphthols as catalysts in the model reaction for enantioselective addition of diethylzinc to aldehydes;
- Study of the efficiency of the natural alkaloids quinine and (-)-ephedrine, the aminoalcohol (S)-prolinol, as well as the aminoacids L-proline, and L-phenylalanine as chiral catalysts for the enantioselective addition of diethylzinc to ferrocenecarbaldehyde, for preparation of chiral non-racemic ferrocene alcohols.

Critical remarks and recommendations

Krassimira Dikova has many years of experience in the laboratory "OSS" at IOCCP-BAS and shows diligence and precision in performing its tasks, which I have witnessed over the years. But I have a critical remark about her, not so directly related to her dissertation. As it is known, the legislation in Bulgaria does not offer administrative independence to doctoral students. However, the development of a scientific one is envisaged in order to acquire the qualities necessary for career growth. According to my personal observations, she had much more time than usual to complete a dissertation. During this time, she should have a tendency to be independent, to diversify her scientific research, and to initiate scientific discussions with her colleagues, which I have not noticed. Such circumstances do not help to develop her scientific career towards habilitation.

My notes and questions on the dissertation are mostly grammatical and stylistic. For example, the distances between figures and texts above and below them are often unnecessarily large. The same goes for too wide rows in some tables. On page 10 it is written "In this paper we will look at some features of…", and on page 12 - "In this review we will analyze…". Similar expressions are available elsewhere in the dissertation. It is desirable to use mainly the present tense and impersonal verb forms. I.e. the relevant texts should look like this: "Some features of… are considered in this paper" and "In this review is analyzed…". On page 16 it says "Fülöp and co-workers successfully use ammonium carbamate and ammonium bicarbonate (as ammonium sources)…". The correct one is "as sources of ammonia." The phrase "ionic salts" on page 24 seems wrong to me. It is better to write "metal salts". On page 68, the purification of ferrocene aminonaphthol 4-6 is discussed. Has column chromatography been tried using basic Al2O3? It is particularly suitable for substances sensitive to acidic environments and oxidation. Rotation angle and melting point data for connection 4-7 are available on page 70. It is not necessary to have these data right here, provided that they are not commented on, nor are they important evidence for the successful synthesis of 4-7. There are more such examples on pages 75, 78, 82, 83, 85, 86, 89 and 90. On page 82, weight is mentioned along with yield, which is meaningless in the specific place. In view of a clearer structure of the results obtained, all attempts for aminomethylation of aminonaphthols, although unsuccessful, are better separated into a separate but more compact subheading. Tables 4-5 to 4-9 mention secondary alcohols of unknown configuration (apparently no literature data are available). Why aren't their esters made with enantiomerically pure carboxylic acid, in order to possibly isolate pure diastereoisomers and clarify their configuration?

I also have a recommendation regarding unpublished results of the dissertation. I would advise future publications to be entirely published in foreign referenced and indexed Q-factor journals, even if additional experiments are required. The achieved results (and the topic in general) do not suggest that journals such as "Proceedings of the Bulgarian Academy of Sciences" and "Bulgarian Chemical Communications" are suitable for this purpose. These journals have never been able to reach and maintain the required level internationally over the years.

Conclusion

The dissertation is based on extensive experimental material, part of which has not yet been published. A number of novel compounds have been prepared, purified and characterized in enantiomerically pure form. Some compounds have been used as ligands in the asymmetric addition of diethylzinc to aldehydes, and the degree of enantioselectivity achieved is moderate to high (up to 93% ee).

The presented dissertation results represent an original contribution to science and comply with the requirements of the Law for the Development of the Academic Staff in the Republic of Bulgaria (ZRASRB), the Regulations for application of ZRASRB and the respective Rules of BAS. The abstract clearly and concisely reflects the results described in the dissertation. The doctoral student also satisfies all the specific requirements of the Regulations for the conditions and the order for acquiring scientific degrees and for holding academic positions in IOCCP-BAS.

Despite the expressed critical remarks, the provided materials give me grounds to express a positive opinion on the presented dissertation and I propose to the esteemed scientific jury to award the educational and scientific degree "Doctor" to Krassimira Petkova Dikova.

Sofia, 11 August 2020 Assoc. Prof. Georgi Dobrikov