STATEMENT

Prof. Vladimir Dimitrov, Institute of Organic Chemistry
with Centre of Phytochemistry (IOCCP-BAS), BAS; 1113 Sofia, Acad. G. Bonchev Str., Bl. 9

Subject: Dissertation for awarding the educational and scientific degree 'Doctor' in the field of higher education "Natural Sciences, Mathematics and Informatics", professional field 4.2. "Chemical Sciences", Scientific specialty "Organic Chemistry", presented by **Krassimira Petkova Dikova** (Scientific Jury according to order № PA-09-179 / 03.07.2020 of the Director of IOCCP-BAS).

Topic: " Betty-condensation – an instrument for preparation of chiral aminomethylnaphthols"

Supervisors:
• Prof. Vladimir Dimitrov, IOHCF-BAS
• Assoc. Prof. Dr. Kalina Kostova, IOHCF-BAS

The dissertation of Assistant Professor Krassimira Dikova is in the field of stereoselective organic synthesis. The main goal is to realize a rational synthesis of enantiomerically (diastereoisomerically) pure polyfunctional compounds, which have structure and properties allowing to be applied as ligands in metal catalyzed enantioselective processes.

The main goal of the dissertation is the application of the three-component Beti-condensation to obtain a series of chiral compounds. For this purpose, an approach is chosen in which aldehydes containing the metallocene component as well as condensed aromatic systems or their analogues are used for the aldehyde component. For the naphthol component, 2-naphthol and 3-methoxy-2-naphthol were used, for the chiral amino component (S)-phenylethylamine or (S)-leucinol. In the process of her experimental activity Assistant Professor Dikova optimized procedures for obtaining aminomethylnaphthols in very good yields. Extraordinary high selectivity was found for the metallocene-containing compounds, leading to the isolation of only one of the possible diastereoisomers. In the other aminomethylnaphthols, high diastereoselectivity is observed, and the diastereoisomers formed in unequal amounts are isolated in pure form. It should be noted that Assistant Professor Dikova demonstrated high experimental skills in optimizing synthetic procedures and isolating pure diastereoisomers. In subsequent experiments, the isolated aminomethylnaphthols were transformed into the corresponding dihydrooxazines with the aim of reducing them to give N-

methyl substituted aminomethylnaphthols. These experiments have not been successful, but the isolated oxazines have served well in determining the configuration of the new stereogenic centers.
Assistant Dikova skillfully applies physical methods for structural characterization of the synthesized compounds. A significant contribution is the application of NMR approach to determine the relative configuration of the newly formed stereogenic centers, which in the presence of known chirality in the amine component of the structures, leads to the determination of the absolute configuration of the isolated compounds. The absolute configurations determined by this approach were confirmed by X-ray diffraction analysis.

Parts of the synthesized and isolated compounds have been used as ligands for the enantioselective addition of diethylzinc to aldehydes, some of which have shown a high degree of asymmetric induction.
It makes a good impression that Krassimira Dikova works precisely and the results obtained support the well-made interpretation. The experimental data and the generalizations made about the mechanism of Betty condensation are a definite contribution to the dissertation and can be used in future experimental developments.

As the scientific supervisor of Krassimira Dikova, I would like to express my satisfaction with the persistence in her work, with which she achieved excellent synthetic results.
There are technical omissions and errors in the dissertation, which I will not comment on here, because they do not substantially change the quality of the dissertation.

Conclusion

The dissertation of Assistant Professor Krassimira Petkova Dikova contains sufficient scientific and applied results, which have an original contribution and meet the requirements set out in the Law for Development of the Academic Staff in the Republic of Bulgaria (ZRASRB), the Regulations for the Implementation of the ZRASRB and the relevant Regulations of IOCCP-BAS.
Therefore, I confidently give my positive assessment of the results achieved in the dissertation and propose to the scientific jury to award the educational and scientific degree "Doctor" to Krassimira Petkova Dikova in the field of higher education: "Natural sciences, mathematics and informatics", professional field 4.2 . “Chemical Sciences”, Scientific specialty “Organic Chemistry”.

3.09.2020 г. Prof. DSc Vladimir Dimitrov