STATEMENT

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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 **Irena Bocheva Zagranyarska** (Scientific Jury according to order № PA-09-180/03.07.2020 of the Director of IOCCP-BAS).

Topic: "Stereoselective synthesis of functionalized chiral amino alcohols – configuration and application"

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

The dissertation of Assistant Professor Irena Zagranyarska aims to perform stereoselective transformations and obtaining of multifunctional chiral compounds. This kind of compounds find application in various fields, e.g. in the development of drug candidates, materials science, etc. In the dissertation, for some of the compounds obtained, is studied the opportunity to serve as precatalysts for enantioselective addition of diethylzinc to aldehydes, which is the test reaction for applicability.

Two types of transformations are used in the dissertation, leading to compounds with suitable structure for use in the test addition reaction. Chiral amino alcohols and their sulfur-containing analogues have been obtained by the addition of suitable organometallic reagents to (-)-menthone with high stereoselectivity. The main direction in synthetic aspect is the use of the chiral analogue of 2-naphthol, deoxo-isoequyleneine in the three-component Betty condensation. The task is to study in first order the applicability of deoxy-isoequyleneine as a naphthol component in the Betty reaction and to synthesize a series of chiral aminomethylnaphthols by varying the aldehyde component.

Within the dissertation the stereoselectivity of the synthetic transformations performed was studied and a series of chiral amino alcohols and their analogues were isolated. Testing the compounds as precatalysts for the enantioselective addition of diethylzinc to aldehydes shows that some of the

synthesized compounds are highly effective catalysts (isolation of products with up to 98% enantiomeric excess).

In her work Irena Zagranyarska applies the available physicochemical methods for characterization of the obtained compounds. An NMR approach to determine the configuration of newly formed stereogenic center has been demonstrated, which is unambiguously confirmed by the structures determined by X-ray diffraction.

During the experimental elaboration of the dissertation Irena Zagranyarska mastered all the necessary skills that are expected for independent work. The results achieved with respect to Betty condensation are a definite contribution of the dissertation and can be used in future experimental developments.

As the second scientific supervisor of the dissertation Irena Zagranyarska I can share the good impressions from her work, as well as from the preparation and summarization of the obtained experimental results.

The observed technical omissions and errors in the dissertation do not substantially change the quality of the dissertation, so I will not discuss them.

Conclusion

The dissertation of Assistant Professor Irena Bocheva Zagranyarska 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 Irena Bocheva Zagranyarska in the field of higher education: "Natural sciences, mathematics and informatics", professional field 4.2 . “Chemical Sciences”, Scientific specialty “Organic Chemistry”.

04.09.2020 г. Prof. DSc Vladimir Dimitrov