REFEREE REPORT

by **Assoc. Prof. Dr. Yulian Dimitrov Zagranyarski**

Sofia University "St. Kliment Ohridski", Faculty of Chemistry and Pharmacy, member of the scientific jury, according to order № RD-09-291/28.09.2020 of the Director of IOCCP-BAS, of a dissertation paper to award the academic and scientific degree Doctor in the field of higher education 4. Natural sciences, mathematics and informatics professional field 4.2. Chemical sciences, professional field "Organic Chemistry"

of **assistant Zhanina Stoyanova Petkova**

PhD student at IOCCP-BAS

Topic: SYNTHETIC APPROACHES TOWARDS CHIRAL AND BIOLOGICALLY ACTIVE COMPOUNDS

Scientific advisers: Prof. DSc. Vladimir Dimitrov

Assist. Prof. Dr. Malinka Stoyanova

The dissertation of assistant Zhanina Stoyanova Petkova has a fundamental and applied character in the field of organic synthesis and stereochemistry. The dissertation clearly outlines two main objectives, namely: 1) preparation of new diphenylphosphine derivatives of chiral phenylsulfonamides to be used as P,O-ligands in palladium-catalyzed allyl substitution; 2) preparation of a series of enantiomerically pure camphane-based *β*-aminoalcohols and study of their *in vitro* anti-tuberculosis activity.

A huge amount of synthetic work has been done, which is clearly described and systematized. In the course of the work, a synthetic approach was developed for the synthesis of chiral diphenylphosphine substituted sulfonamides. Sulfonamides were prepared using a variety of chiral amines, as well as by performing a targeted ortho-lithium reaction and then introducing appropriate electrophiles. The catalytic properties of the synthesized chiral compounds such as P,O-ligands in palladium-catalyzed allyl substitution and in the *Suzuki-Miyaura* reaction were studied.

A series of novel chiral *β*-amino alcohols was prepared and structurally characterized by the aminolytic opening of the vinyl-substituted camphane epoxy ring with suitable secondary

amines. The resulting β-amino alcohols were tested for *in vitro* anti-tuberculosis activity using the *Canetti* method. The cytotoxic activity of some of the synthesized compounds was evaluated.

In the experimental part of the dissertation, all synthetic procedures are described in detail, as well as the spectral characteristics of the obtained compounds. All newly synthesized compounds were characterized by NMR spectroscopy, mass spectrometry, melting points, specific angle of rotation and elemental analysis.

The abstract of the dissertation is 58 pages long, accurately and correctly reflecting the content of the dissertation and is written in accordance with the approved rules.

The scientific results in the dissertation of assistant Zhanina Petkova are formed in three scientific articles published in journals with an impact factor (*Tetrahedron Letter*s **2014**, Q2, IF = 2.38; *European Journal of Medicinal Chemistry*, **2014**, Q1, IF = 3.54; *Monatshefte für Chemistry* **2018**, Q2, IF = 1.50). The first publication in Tetrahedron Letters was cited three times and the publication in the European Journal of Medicinal Chemistry had 12 notable citations. Some of the results of the dissertation were promoted at a total of 13 conferences with posters and reports. From the presented list, it is clear that eight of the participations are at international conferences, four of which are learned forums abroad - Italy, Scotland, Slovakia and Northern Macedonia. The publications of assistant Zhanina Petkova are collective, as she is the first author in two of the publications and the second in one of the publications, which shows the significant contribution of the doctoral student.

I have no significant remarks on the dissertation. There are some minor technical omissions that I will not comment on, as they do not substantially change the quality of the dissertation.

Conclusion

Zhanina Petkova's dissertation fully meets the requirements of the Law for the Development of the Academic Staff in the Republic of Bulgaria (LDASRB), the Regulations for its application (LDASRB) and the Regulations for the conditions and procedures for acquiring scientific degrees and holding academic positions at BAS and IOCCP-BAS. The presented materials and dissertation results significantly exceed the specific requirements for obtaining the scientific and educational degree "Doctor" in the field of organic synthesis.

All of the above and primarily the contributions of the dissertation and the obtained results give me a reason to fully recommend to the esteemed scientific jury to award assistant Zhanina

Stoyanova Petkova educational and scientific degree "Doctor" in higher education. education 4. Natural sciences, mathematics and informatics, professional field 4.2. Chemical sciences.

Sofia, 10.11.2020 Prepared the opinion: ……

/Assoc. Prof. Dr. Yulian Zagranyarski/