

## STATEMENT

from prof. Lily Plamenova Peikova, PhD

for the acquisition of the educational and scientific degree "Doctor" of MPharm Tania Nedelcheva Dimova, PhD student in full-time study, doctorate program "Pharmaceutical Chemistry", field of higher education 7. "Health and Sport" and professional field 7.3. "Pharmacy", "New aromatic iodo-derivatives - synthesis, structure, properties", Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Medical University (MU) – Varna.

MPharm Tania Dimova acquired the educational and qualification degree "Master of Pharmacy" at the Faculty of Pharmacy, Medical University - Sofia in 2010. In 2020 she was enrolled as a full-time PhD student in the Department of Pharmaceutical Chemistry at the Faculty of Pharmacy, Medical University - Varna. She acquired a specialization in "Drug Technology with Biopharmaceutics" from MU-Varna in 2020. MPharm Tanya Dimova has been an assistant since 2011 and chief assistant since 2019 at MU-Varna, Faculty of Pharmacy, Department of Pharmaceutical Chemistry.

The dissertation thesis includes 101 pages, 10 tables, 29 figures and 75 diagrams. 213 literature sources are cited.

The scope and scientific hypothesis are in the field of organic synthesis, structure, and property analysis of aromatic iodo- and bromo-derivatives. The topic is dissertable. The synthetic part of the research is focused on optimizing the synthetic methods known in the literature for the preparation of halogenoarenes. Many experiments have been performed under different reaction conditions and reagents, and the optimal conditions of iodination with  $I_2/AgNO_3$  in methanol have been established. The yields were quantitative. Spectral methods were used to characterize the structure of the halogenoarenes ( $^1H$  NMR, ATR-FTIR, UV and Raman). Potassium bromate in sulfur/acid environment was used in the synthesis of the bromoarenes. Two new compounds, 2-bromo-6-iodo-3,4,5-trimethoxybenzoic acid (BrITMBA) and 2-(2-iodo-3,4,5-trimethoxyphenyl)acetic acid (ITMPhAA) were also obtained. The synthesis of BrITMBA was done in two steps: the first is bromination ( $KBrO_3/H_2SO_4$ ) followed by iodination ( $I_2/AgNO_3$  in methanol). The crystal structure of (BrITMBA) was studied and proved by SC-XRD. The special arrangement of the molecules is related to the translation of catenary chains.

The crystallization and crystal structures of 2,6-diiodo-3,4,5-trimethoxybenzoic acid (DITMBA), 2,6-dibromo-3,4,5-trimethoxybenzoic acid (DBrTMBA), and 2-bromo-3,4,5-trimethoxybenzoic acid (BrTMBA) were studied in detail. SC-XRD, Raman and UV analyses were used, and the results show that DITMBA crystallizes as a toluene solvatomorph and on a non-solvated cathemer. The compound DITMBA was also screened for *in vitro* cytotoxicity and phototoxicity. The results showed that it had no photoinduced toxicity against the test cell line BALB/3T3 clone A31. The sodium salt of this compound has potential application in contrast-enhanced mammography. The standard used in practice is Omnipaque.

#### Scientific research work

The results of the thesis were published in four scientific journals, two of which are in refereed and indexed in world-renowned databases of scientific information, and the other two publications are in non-refereed peer-reviewed journals. The PhD student participates in the team of a scientific project on the topic of the PhD thesis funded by the Science Fund of MU-Varna.

The Abstract book completely covers the thesis.

#### Conclusion

The thesis of MPharm Tania Dimova meets the requirements of the Regulations for the Development of the Academic Staff at MU-Varna and the Minimum Scientific and Metric Requirements of MU-Varna and fully meets the requirements of the PhD program in Pharmaceutical Chemistry. The aim is precise, the experimental work is sufficient, the conclusions meet the tasks. The contributions are of fundamental and scientifically applied nature.

I propose to award the educational and scientific degree "Doctor" to MPharm of MPharm Tania Nedelcheva Dimova.

Предлагам да се присъди образователната и научна степен "Доктор" на маг.фарм. Таня Неделчева Димова.

My assessment is convincingly POSITIVE.

18.01.2024

Reviewer:

Заличено на основание чл. 5,  
§1, б. „В“ от Регламент (ЕС)  
2016/679

(prof. Peikova, PhD)