O P I N I O N

by Prof. DSc. Panteley Petrov Denev, University of Food Technology - Plovdiv
on the dissertation for the award of the educational and scientific degree "Doctor"
in the field of higher education 4. Natural Sciences professional field 4.2. Chemical Sciences doctoral program "Analytical Chemistry"
Author: Dimitar Genchev Stoitsov
Topic: Application of NMR and vibrational spectra in confirming and revealing the structures of aromatic organic and organometallic coordination compounds
Scientific supervisors:
Prof. DSc.. Plamen Nikolov Penchev PU "Paisiy Hilendarski"
Assoc. Prof. Dr. Marin Neykov Marinov Agricultural University-Plovdiv

1. General presentation of the procedure and the doctoral student

This statement was prepared on the basis of order No. RD-22-1706/21.07.2025 of the rector of Plovdiv University "Paisiy Hilendarski", by which I was appointed a member of the scientific jury for ensuring a procedure for the defense of a dissertation on the topic "Relationship of NMR and vibrational spectra in confirming and revealing the structures of aromatic organic and organometallic coordination compounds" for the acquisition of the educational and scientific degree "doctor" in the field of higher education 4. Natural sciences; professional field 4.2. Chemical sciences; doctoral program "Analytical Chemistry". The author of the dissertation is Dimitar Genchev Stoitsov, a doctoral student in full-time education at the Department of "Analytical Chemistry and Computational Chemistry" with scientific supervisors Prof. Dr. Sc. Plamen Nikolov Penchev Plovdiv University "Paisiy Hilendarski" Assoc. Prof. Dr. Marin Neykov Marinov. Agrarian University-Plovdiv.

The doctoral student has submitted a set of materials under the procedure that meets all the requirements of the Act on the Development of the Academic Staff in the Republic of Bulgaria, the regulations for its implementation and is in accordance with Article 36 (1) of the regulations for the development of the academic staff of the University of Paisiy Hilendarski (dated 16.12.2024).

2. Relevance of the topic

The aim of the dissertation is to provide fully referenced NMR data, supported by partially referenced vibrational data, for new or known organic compounds of different classes, for which there are no or only partially and/or incorrectly referenced NMR and vibrational data in the literature.

For understanding the biological activity and action of organic compounds, confirmation and revelation of their structure is of particular importance. For this purpose, there are different approaches based on qualitative reactions, spectral analysis methods or a combination of both. The continuous development of instrumental analysis methods allows for the registration of a wide range of spectra, providing diverse information about the structure of organic compounds.

Complete and accurate NMR spectral assignments are intended not only to fill in the gaps and point out errors in the confirmation or discovery of certain structures, but also to assist in the development of NMR databases. The probability of finding fully assigned NMR data for structures of new or rare organic compounds is very small. For this reason, many NMR

spectroscopic techniques and computer programs for interpreting NMR spectra have been developed over the years to facilitate structure determination and significantly reduce human errors in interpreting NMR spectra. Such improvements in existing NMR reference databases and the creation of new databases providing fully and accurately assigned NMR data for structures are of particular interest to NMR spectroscopists.

3. Knowledge of the problem

Doctoral student Dimitar Stoitsov demonstrates in-depth knowledge of the topic related to the dissertation work. The dissertation cites 157 sources, a significant part of which were published in the last 10 years. The review covers summarized information about those types of NMR spectra that are used to confirm or reveal the molecular structures presented in the dissertation presentation, as well as some of their more common varieties. The structural information that a given type of NMR spectrum can provide about the connectivity and arrangement of atoms in the structure of the substance is examined first of all. Additionally, various factors influencing the shifts of the ^{1}H and ^{13}C signals are commented on.

In the dissertation, vibrational spectra were used as an aid to confirm the presence of certain functional groups in the confirmed and revealed structures. Therefore, a literature review was made of the frequency ranges of the vibrational bands of $–CH_3$, $–OCH_3$, $–CH_2$, aromatic CH and C=C bonds, –OH, C=O, C=S, NH and NH_2.

The review also provides general information on the classes of compounds (fluorenylspirohydantoins, naphthopyranones, pyrimidine complexes of Au(III) and Cu(II), dispiroimidazolidines, N-phenyl-2-(2,2,2-trichloroacetamido) benzamides and 1H-benzo[d]isoquinoline-1,3(2H)-diones) covered in the dissertation presentation, as well as on NMR software used in the confirmation and revelation of organic structures.

The sections in the literature review conclude with an analysis and summary of the literature, which proves that the doctoral student is capable of searching, systematizing, and critically analyzing scientific literature.

4. Research methodology

To achieve the goal set in the dissertation – providing fully referenced NMR for new or known organic compounds of different classes, for which there are no or only partially and/or incorrectly referenced NMR and vibrational data in the literature. To achieve the goal set, the doctoral student Dimitar Stoitsov has performed the following:

• familiarization with the features of these types of one-dimensional and two-dimensional NMR spectra that are covered in the dissertation and especially with the structural information that they can provide;

• familiarization with these classes of organic compounds included in the dissertation;

• full referencing of one-dimensional and two-dimensional NMR spectra, as well as partial referencing of some characteristic bands in FTIR, ATR and Raman spectra;

• simulation of NMR spectra with the MestreNova software and the Python package NMRSim of some three-, four- and five-spin systems of the type ABX, AA‘XX’, AA’BB’, AA‘MM‘X and AA’BB’X, which occur in some of the compounds;

• import of some of the assigned NMR data for fluorenylspirohydantoins and naphthopyranones into the NMRShiftDB database at the invitation of one of its creators, Stefan Kuhn, together with their structures and raw one-dimensional and two-dimensional NMR spectra.

The doctoral student Dimitar Stoitsov has mastered the methods used in the field of organic analysis and has acquired the knowledge and skills necessary for obtaining the educational and scientific degree "doctor".

5. Characteristics and evaluation of the dissertation work and contributions

The dissertation has an interdisciplinary nature. It is written on 144 pages and contains 38 tables and 27 figures. The bibliography covers 157 literary sources. The dissertation work includes the following sections: Introduction; Literature review entitled "A brief review of some one-dimensional and two-dimensional NMR spectra, characteristic vibrational intervals and classes of organic compounds"; Aim and objectives; Materials and methods; Results of spectral assignments; Conclusion and contributions; Literature. The predominant part (75 pages) has the section dedicated to the spectral assignments of the NMR spectral data, revealing and confirming the structures of the studied compounds. The conclusions and contributions are summarized as follows:

Enrichment of the available information with fully assigned NMR and partially assigned vibrational data for 23 organic compounds, 7 of which are verified to be novel. HOSE predictions of the ^{13}C chemical shifts of 14 of the confirmed organic structures are presented, respectively of the three naphthopyranones, the two ligands (2,4-dithiouracil and 2-thiouracil), the seven benzamide derivatives and the two 1H-benzo[d]isoquinoline-1,3(2H)-diones. The NMRShiftDB databases are enriched with the structures of fluorenylspirohydantoins and naphthopyranones along with their assigned ^{1}H and ^{13}C chemical shifts and 1H multiplicities.

Errors in the citation of NMR data presented in previous publications by other authors for four of the organic structures (5‘-oxospiro(fluorene-9,4‘-imidazolidine]-2’-thione, 2,4-dithiouracil, N-[(2H-1,3-benzodioxol-5-yl)methyl]-2-(2,2,2-trichloroacetamido)benzamide, 2-amino-1H-benzo[d]isoquinoline-1,3(2H)-dione) included in the dissertation have been corrected. It has been established that 4-(8-propyl-2,4-dithioxo-1,3-diazaspiro[4.5]decan-3-yl)spiro[1,5-dihydro-1,5-benzodiazepine-2,3'-indolin]-2'-one is in equilibrium with its tautomer.

6. Assessment of the publications and personal contribution of the doctoral student

Four scientific reports on the dissertation work have been presented, published in specialized and multidisciplinary international journals. Two of them in a second quarter journal (Q2) 2x20 issues, one in a Q4 journal 12 issues and one in a peer-reviewed but non-indexed journal – 10 issues. The total scientometric result of the published articles is 62 points, which exceeds the national minimum requirements for acquiring the ONS "doctor" and the requirements of the Regulations for the Development of the Academic Staff of PU- "Paisiy Hilendarski" (required 30 points). The doctoral student is the first author in two of the publications, has submitted documents for participation in one scientific conference and participation in one international scientific project. Dimitar Stoitsov has submitted a declaration that the results and contributions of the conducted dissertation research are original and have not been borrowed from research and publications in which he has no participation.

7. Abstract

The abstract is 34 pages long, written clearly and concisely, reflects the sequence of the research described in the dissertation and leads logically to the formulation of the main achievements of the doctoral student. Correct scientific language is used, and the discussed transformations and the obtained results are duly illustrated with 18 figures and 24 tables.

CONCLUSION

The dissertation contains scientific, scientifically-applied and applied results, which represent an original contribution to science and meet all the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria (ZRASRB). The Regulations for the Implementation of ZRASRB and the relevant Regulations of PU-..Paisiy Hilendarski". Dimitar Stoitsov demonstrates solid theoretical knowledge and practical skills in the analysis and structure of organic compounds, which shows that he has acquired the ability to

independently plan, conduct and report scientific research. Due to the above, I confidently give my positive assessment of the research, the achieved results and the declared contributions presented in the dissertation and the abstract and I propose to award the educational and scientific degree "doctor" to Dimitar Genchev Stoitsov in the field of higher education: 4. Natural Sciences, Mathematics and Informatics. Professional field 4.2. Chemical Sciences, doctoral program Analytical Chemistry.

Prepared the opinion:
15.08.2025 Prof. D.Sc. Panteley Denev