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Warsaw, May 24th 2022

**Reviewer's Report on the Thesis entitled Applications of α - α Coupling
and α - α Bridging in the Synthesis of Electron-Deficient Oligopyrroles"
by Ms. Liliia Moshniaha**

The doctoral dissertation by Ms. Lilia Moshniaha has been carried out at the Faculty of Chemistry of the University of Wrocław under the scientific supervision of prof. dr hab. Marcin Stępień. It formally consists of 11 chapters. They deal with research objectives; an extensive (over 50 pages long) literature review; the main research part split to two main topics - bridged azacoronenes via electrophilic condensations with aldehydes and synthesis of bipyrrrole derivatives via double C-H bond activation; an experimental part presenting the methodological approaches with technical details; presentation of main conclusions; and a list of references. The latter is very impressive as it refers to 388 articles. It finishes with a list of abbreviations; specification of the contributions of the author and her co-workers; acknowledgements of the agencies financing the project; and a list of publications of the author. The overall presentation exceeds 190 pages. In my opinion, abstracts in both Polish and English are currently missing, but I expect that they are being prepared as additional material (supplement). The dissertation is written in very concise way, although it well balances the literature review and highly impressive novel experimental work. It is important to acknowledge that the essential part has been published in a recent *Chemical Reviews* paper (2022) on *Recent advances in heterocyclic nanographenes and other polycyclic heteroaromatic compounds* and two original papers in the *Journal of the American Chemical Society* (2020) on *Aromatic nanosandwich obtained by σ -dimerization of a nanographeneoid π -radical* and *Beilstein Journal of Organic Chemistry* (2020) on *Bipyrrrole boomerangs via Pd-mediated tandem cyclization-oxygenation. Controlling reaction selectivity and electronic properties*. In the latter ones, the Doctoral Student is the first author. Importantly, Ms. Moshniaha is an author of two other papers published in *Chemistry – A European Journal* (2018) and *Journal of Organic Chemistry* (2018). They are also thematically related to the current work.

Reading this doctoral dissertation work was a real intellectual pleasure for me. Heterocyclics are arguably the most interesting systems amongst aromatics (or, more

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generally, systems with π -electron delocalization) where, due to almost unlimited combinations of carbon, hydrogen and heteroatoms an inexhaustible number of novel compounds can (theoretically) be devised with almost any required physicochemical property. Even more, due to the enormously rapid development of organic synthesis methods, it might be expected that any molecular target is limited solely by the researcher's fantasy. Although not all synthetic dreams have been achieved in this doctoral project, the obtained systems were perhaps even more interesting ones than those originally devised. The properties of the most interesting systems have been characterized with a variety of physicochemical tools including X-ray diffraction, NMR analyses, electrochemical properties, absorbance spectroscopy, ESR methods, fluorescence, ESR spectra and also theoretical ones with use of high-level DFT calculations (including also time-dependent DFT) to find the most stable conformers and to perform frontier molecular orbital analyses. However, it is fair to note that the scope of this work is far more general. The real value of this work is a comprehensive examination of different synthetic approaches with application of α - α coupling and α - α bridging in the synthesis of electron-deficient oligopyrroles, revealing their advantages, but also showing possible shortcuts and limitations. Generally, two groups of systems - extended azacoronenes and bipyrrrole derivatives via double C-H bond activation - are examined. The findings, in my opinion, are very important and I consider this work to be a valuable contribution to the development of Organic Chemistry.

The literature part is a very comprehensive introduction to the subject of the work. The introductory part is devoted to importance and significance of the heteroaromaticity field with a particular attention paid to fused, large polycyclic systems and their applications in organic electronics and more generally in material science. The next parts are devoted to synthetic strategies and the role of palladium in the synthesis of polycyclic heteroaromatics. Cyclizations based on oxidative, reductive and transition-metal catalyzed protocols are among the most fundamental methods in organic chemistry. Their rapid improvement has an impact not only on the variety of structural motifs but also on their availability. Application to annulative techniques enabling the building of complex targets via several components which are a significant alternative to direct cyclizations. From this perspective, palladium-catalyzed C-H bond activation is of special interest. It has many practical advantages such as relatively easy formation of π -conjugated systems from simple substrates; softer reaction conditions; tolerance of diverse functional groups; and generally higher yields. Application of this approach has been very fruitful and enabled the synthesis of diverse planar, curved, twisted or highly strained π -conjugated polycycles in last decades. The last part of the literature part is devoted to azacoronenes and related structures. Again, this is a very well written part of the thesis showing high proficiency of the Student. Personally, I am impressed by the variety of systems discussed, including highly strained molecules with helical motives or azulene fragment. The synthetic routes, with a special contribution from the Supervisor's group, are well presented.

The objectives of the work deal with an expansion of chemistry of polycyclic heteroaromatics. The main issues include: applicability of the hexapyrrolylbenzene–aldehyde condensation reaction; the possibility of modification of the azacoronene core; palladium-induced double C–H bond activation process; tandem palladium-catalyzed reactions for the synthesis of fused oligopyrroles; and last but not least, methods for the synthesis of new (chiral) dyes and fluorescent materials.

The first part of the project is devoted to the synthesis of azacoronenes *via* electrophilic condensations with aldehydes and subsequent oxidative fusion of the resulting condensation products. In my opinion, both unsuccessful and successful attempts can be considered as very important, as they indicate the limitations/perspectives of this kind of approach. As real progress has been obtained in the case of a system denoted as 53.1, which was a precursor of an unexpected dimeric structure 55.1. The latter has been intensively investigated to study its molecular shape (with use of X-ray diffraction), stable conformers (by molecular modelling, but also NMR experiments in solution), its fluorescent properties, UV-vis absorption spectra, electrochemical behavior (voltammetric analysis, cyclic voltammograms) electronic properties and dissociation process. The crystal structure of the system is very intriguing, as two macrocyclic parts interact with each other with van der waals interactions and, due to steric repulsion, the single CC bond which links them is much elongated to 1.64Å. Each monomeric fragment is considerably distorted as a result of steric congestion of the outer NMI fragments and contacts the other subunits. Interestingly, the subunits differ by relative helicities, which means that they are stereochemically incompatible in the solid state. Theoretical modelling revealed that none of the parts were the lowest energy conformers, but this can be attributed both to strong intramolecular interactions (with the other part) and crystal packing forces. The system has C₁ symmetry but no further information about the crystal system is given in the thesis (however, it can be found in the related paper). The elongated C-C linking bond is very weak, which suggests the possibility of radical formation. This aspect has been thoroughly studied. The switching between the radical and its σ -dimer is regulated by a balance of π -conjugative stabilization and internal strain. The 56.1* can be relatively easily formed and its properties have been also well investigated. It exhibits substantial spin delocalization and spontaneously dimerizes into a stable σ -dimer that is photochemically cleavable. There's a successful transformation into ketone 56.2, the properties of which were also intensively analyzed. A further step led to multiple bridged azacoronenes. Four further interesting systems were obtained: 57.1, 57.2, 57.3 and 57.4. By optimizing the reaction conditions (due to reversible bridge formation), it was possible obtain all these compounds in different ratios, even exclusively 57.4, a six-fold condensed target system. Both 57.1 and 57.4 have been analyzed by XRD, but in the latter case the crystals were not stable enough to collect high quality data and well-refine the structure. Only the packing along [010] direction is shown. Due to lack of strong hydrogen bonds, the structure is mostly stabilized by van der waals interactions. Again, the details of the analysis could be presented, at least giving the most essential data like space

group or final refinement parameters. The systems were further physicochemically characterized. Due to their rather low stabilities, reliable fluorescence quantum yields were not obtained. Using an alternative strategy of quadruple-bridged HPB, the author managed to obtain two further compounds: 59.2 and 59.3; however, they were not further exploited.

The second part of the dissertation is devoted to an exploration of the Pd(II) induced double C–H bond activation approach in the synthesis of highly-conjugated oligopyrrole systems. The reaction conditions were carefully optimized to improve its practical feasibility. A large number of systems were obtained which differ in shape; push-pull properties of chromophores; mutual orientations; and length of the linker. In this group of compounds, bipyrrrole boomerangs are especially interesting. They are twisted and two of them are extremely efficient fluorophores. In my opinion, the structural solid state chemistry of these compounds could be very interesting, in particular taking into account the possibility of crystallization in Sohncke groups.

The doctoral thesis work was prepared with a high level of proficiency, both in terms of editing and graphics. The analyses, including the literature review, although detailed, are described in an excellent way using a concise scientific language. In my opinion, it is a fully professional monograph. I highly appreciate the way that the synthetic routes and molecular graphs are presented. The (expected) systems which could not be obtained were marked as somewhat transparent. The enumeration of the systems has been made in a very useful way, but sometimes it is not very consistent, for example using TT^H and 68.1 in one Scheme (Scheme 68). The list of references is vast, but I could not find both 2020 papers of the Author referring to the current work. In the X-ray crystallography part of the Experimental chapter, the references to the crystal structures are missing (only one refers to a paper by Sheldrick). In a few cases, the literature references dealing with earlier achievements direct a Reader to more recent articles, as exemplified by the 1950s' carcinogenesis topic (Harvey, 1991). Of course taking into account the extent of the literature contributions a reasonable choice had to be made. Concerning possible typographical errors, I think that the “vapor fusion method” used for crystallization meant rather “vapor diffusion method” which is an often-used method in crystallography. All tables were prepared with great care and only the units of concentration of the starting materials were not given. Although the list of abbreviations is almost complete, I found HPB, a very basic one, missing. I would also highly appreciate a short summary at the end of the most important chapters describing the results obtained by the Author.

Summing up: I am fully convinced that Ms. Liliia Moshniaha's doctoral dissertation contains important elements of scientific novelty. The doctoral student has well-defined the research problem and well-planned it and performed quite excellent research. Her commitment to the work is particularly impressive. Not only has she carried out the synthesis, purification and analysis of all new compounds and prepared the majority of previously known intermediates, she also did most of spectroscopic experiments including NMR measurements

(including also NMR-controlled titrations), irradiations, measurements at different temperatures, and UV-vis-NIR or UV-vis experiments. Additionally, she obtained crystals for XRD analyses and prepared solutions for fluorescence measurements. Importantly, she also performed all DFT modeling and analyzed the data.

The doctoral thesis by Ms Liliia Moshniaha easily meets all formal conditions of the current act on the Academic Degrees and Titles of Republic of Poland. Therefore it is my great pleasure to recommend that the Scientific Council of the Chemistry Discipline at the University of Wrocław should admit her to further stages of the doctoral dissertation process. Because of the very high scientific value of the dissertation, the extensive scope of the research, its complexity and the mature, and very significant scientific achievements of the doctoral student presented in her papers published in excellent journals, I also recommend that the Council should award a distinction for this dissertation.



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