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REVIEW OF PHD THESIS ENTITLED „DNA-SUPPORTED PALLADIUM AND ITS APPLICATION IN CROSS-COUPLING AND CARBONYLATION REACTIONS" SUBMITTED BY MR. MEHMET MART

Modern trends in the development of the chemical industry consist in introducing to the European and world markets the manufacture of high value-added compounds (mainly so-called *fine chemicals*) which play a significant role in the organic synthesis during the production of pharmaceuticals, agrochemicals, cosmetics, liquid crystals, and ligands. Examples of compounds of this type are aryl and biaryl derivatives such as acids, amides, and ketones that are obtained in the reactions of coupling and carbonylation. The catalysts for the processes of this type are, to a large extent, palladium compounds. Commonly used are homogeneous catalysts, however, despite their high catalytic activity, possibility of applying low concentrations, as well as considerably shorter induction periods, the tendency is observed to apply heterogeneous catalysts because they offer the possibility of separation from post-reaction mixtures and reuse. However, this trend is developing not only for economic reasons but also for application ones because the presence of metals, even in trace amounts, is impermissible in many products. Many research groups, including those in industrial centres, conduct intense studies aimed at developing more effective catalytic systems, both using diverse palladium precursors (one of the variants is the application of metallic palladium in the form of nanoparticles) and new supports to enable easy isolation from post-reaction mixtures and to maintain high catalytic activity even after multiple use.

The subject area of the doctoral dissertation, prepared under the supervision of Professor Anna Trzeciak, concerned the synthesis of new palladium catalysts immobilized on DNA support and the study of their catalytic activity for the reactions of cross-coupling and carbonylation. The research presented in the PhD thesis rests closely in the area of studies conducted by Professor Trzeciak's research group which is renowned in the world for many of its spectacular achievements.

Mr. Mehmet Mart presented his doctoral dissertation in the form of a guidebook to a monothematic cycle of four publications containing a short description of the most important results obtained while conducting his doctoral research. The results of the mentioned research were published in 2018-2021 in good scientific journals from the JCR list: Catalysts (IF=3.520) and Molecular Catalysis (3.687). It is worth mentioning that in all the publications the PhD candidate is the first of two or three co-authors. It should be noted that Mr. Mart took part in all stages of the study: in the construction of the whole work, in the research on synthesis and characterization of new catalytic systems, as well as on their application in the reactions of cross-coupling and carbonylation. Positions of the journals in which Mr. Mart's papers were published are high and all papers were peer-reviewed, therefore my role as a reviewer of the submitted guidebook and attached publications is, in this case, considerably limited.

The author of the dissertation began the guidebook with a short theoretical introduction in which he paid attention to the essence and innovativeness of his PhD study. He presented therein mechanistic aspects of the most important reactions of cross-coupling (Suzuki-Miyaura coupling) and carbonylation (aminocarbonylation, Sonogashira synthesis of β-enaminones) in the presence of palladium as a catalyst. Moreover, he presented foregoing applications of DNA as a support for catalysts. The interest in this untypical support appeared relatively recently but at present several effective catalytic systems, in which it participates, are known. The doctoral candidate clearly defined the aim of his dissertation, namely the synthesis of DNA-supported palladium catalysts and studies of their activity in cross-coupling and carbonylation reactions. An inherent element of the studies was also the determination of the stability of the developed catalysts and the possibility of their multiple use.

During his doctoral research, Mr. Mart synthesised and applied seven Pd/DNA catalysts. The differences in the syntheses consisted in the application of various palladium precursors ($Pd(OAc)_2$ or $PdCl_2$), DNA with different molecular weights, different reducing agents (EtOH or hydrazine), as well as different temperature and time of impregnation. The obtained catalysts were characterised by different analytical techniques (FT-IR, XRD, XPS, TEM, ICP-AES). In Table 1 (in the guidebook) palladium contents in the catalysts were shown. I assume that they represent the total content, however, I would like to ask how was it determined? Should this content correlate (to a certain extent) with the amount of introduced precursor?

The aforementioned catalysts were employed in the reactions whose results are the subject of four publications constituting the dissertation. The first of them concerns Suzuki-Miyaura cross-coupling. At the first stage, studies were carried out of coupling of various aryl bromides with phenylboronic acid catalysed by different catalysts (C1-C4), and the most effective catalyst was selected for further research. However, I do not understand why the selected catalyst was C2 and not C1, although the C1 enabled to obtain the highest yield. Admittedly, it was found during the experiments that the reaction conditions result in a fast reduction in palladium oxidation state and the amount of Pd(0) rises, thereby the catalytic activity increases. At the same time, it was found that the amount of Pd(0) in the initial catalyst C1 was twice as low as that in the catalyst C2. However, this could be expected because the amount of Pd(0) has been increasing during the reaction, particularly that the yields were the highest in the case of C1. To my mind, this is why it would be worth a while to check it in the remaining coupling reactions. In the case of the studied catalyst C2, the possibility of its multiple use (5-7 times) was found. I wish to ask whether after the mentioned 5-7 uses no more reactions were carried out even if the catalyst was still active? And maybe the catalyst lost its activity? And if yes, what was the reason for the deactivation?

The second paper concerns aminocarbonylation of iodobenzene with different aromatic and aliphatic amines. In the latter case, the study was performed only in the presence of the catalyst C1, albeit for the first time the reactions were conducted in the aqueous medium. Additionally, CO gas and $Mo(CO)_6$ were compared as the sources of CO. The obtained results confirmed the high activity of the catalyst C1 in aminocarbonylation with the participation of aromatic amines and primary aliphatic amines. In the latter case, the reactions in which $Mo(CO)_6$ was employed proceeded with higher selectivity compared to those in which CO gas was used. Moreover, the catalyst could be turned back and used four times, while maintaining a high yield of the reaction.

The third paper concerns carbonylative Sonogashira coupling. In the study, Pd/DNA catalysts were employed for the first time (they differed in the DNA used; strictly speaking in its molecular weight) and compared to the commercially available catalysts. The solvent effect on the course of the process was found. In the case of the reaction carried out in the DMF medium, various alkynones were formed with high yields, whereas in the aqueous medium diaryl alkynes were selectively formed. It has been also found that contrary to the high stability of Pd/DNA catalysts, observed in the reactions described in publications 1 and 2, in the case of Sonogashira reaction the leaching was considerably greater. However, the addition of free DNA causes an improvement in the stabilization of leached Pd nanoparticles and prevents deactivation.

In the fourth paper, the results of the study on β-enaminones synthesis were presented. The latter reaction is a tandem reaction that consists of alkynone formation via carbonylative Sonogashira coupling and oxidative dealkylation of aliphatic tertiary amines. This is a very interesting presentation of a highly effective one-pot method of β-enaminones synthesis that was reported for the first time. Also, in this case, the Pd/DNA catalysts showed not only high activity but also the capability of being used several times without the loss of activity.

All results presented in the aforementioned publications, proved that palladium nanoparticles immobilised on biopolymer (DNA) are active and selective catalysts for cross-coupling and carbonylation. Mr. Mart's papers contain elements of scientific novelty about synthetic (a number of derivatives including many new ones) and catalytic (the selection of an effective catalyst) aspects. The dissertation provided novelty also as concerns mechanistic aspects (mechanisms of several studied reactions were proposed) and optimization aspects (the choice of suitable conditions for conducting several reactions). As I have already mentioned at the beginning of my opinion, the reviewer's role, in this case, is limited because all the publications were already subjected to evaluation in the course of the editorial process. In addition to four papers published within his dissertation, the doctoral candidate is also a co-author of three other papers.

Summing up, I can say that the dissertation submitted to the reviewing process, is an example of a well, reliably done work. Its concept is mature and well-conceived. The developed catalytic systems and conditions of conducting coupling and carbonylation processes make it possible to selectively obtain a whole range of new derivatives with considerably higher yields and under milder conditions. The doctoral candidate proved his ability to conduct research work and showed good command of analytical methods. He also rightly draws conclusions based on the obtained experimental results. Based on the above, I evaluate the dissertation as very good and in my opinion, Mr. Mart's dissertation complies with the requirements for PhD theses. Therefore, I am applying to the Council of Scientific Discipline, Faculty of Chemistry of Wrocław University, for the acceptance of the PhD thesis and the admission of Mr. Mehmet Mart to further stages of the PhD procedure.

Moreover, taking into consideration that the PhD candidate fulfilled an extensive research programme, showed high competencies, both in planning experiments and interpreting results, as well as concluding, I believe that Mr. Mart deserves to be awarded a PhD degree with distinction.

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