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Advanced heterogeneous Pd catalysts for the Suzuki–Miyaura reaction with aryl bromides

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The set of heterogeneous Pd catalysts containing different forms of Pd ($PdCl_4^{2-}$ or Pd^0) was prepared by chemical modification and laser electrodispersion using two types of supports, namely, SiO_2 modified by ionic liquid and γ-Al_2O_3. Testing of the synthesized catalysts in the Suzuki–Miyaura reaction with aryl bromides pointed out the possibility to achieve the prominent TOF and TON values. The dependencies of TOF on the catalyst loading indicate that only a fraction of loaded Pd was involved in the catalysis.

- ✓ Not only heterogeneous catalyst, but also **truly heterogeneous catalysis**
- ✓ ‘Ligand-free’ Suzuki–Miyaura reaction
- ✓ High values of TON and TOF
- ✓ Air stable catalyst

Keywords: Suzuki–Miyaura reaction, palladium, heterogeneous catalysts, kinetics, reaction mechanism, ionic liquids.

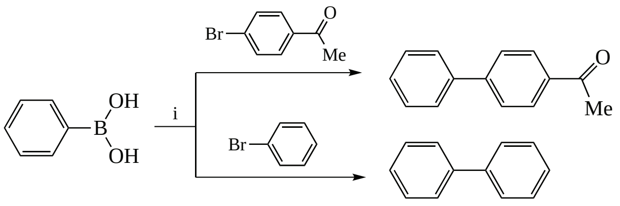
Dedicated to Prof. Irina P. Beletskaya for her outstanding contribution in catalysis on the occasion of her anniversary.

The Suzuki–Miyaura reaction with formation of unsymmetric biaryls is a demand process in modern fine organic synthesis.[1–4] Obviously, heterogeneous catalysts are highly desirable for industrial application due to their easy removing and possible recycling after the reaction completion. To the moment, the widest range of heterogeneous catalysts have been developed for the Suzuki–Miyaura reaction (see recent reviews[5,6]). However, in general catalytic activity obtained with heterogeneous precursors turns to be lower than that for homogeneous ones. Moreover, the mechanistic data resulted from larger complexity of the studies of heterogeneous systems are still not sufficient. These circumstances make the development and study of heterogeneous precursors possessing high catalytic activity to be an urgent task.

The way for Pd anchoring on the heterogeneous support is one of the key factors dramatically influencing the efficiency of heterogeneous catalysis in cross-coupling reactions.[5–7] In this work, we developed three types of heterogeneous Pd catalysts differing in the Pd state (Pd^0 and Pd^{II}), Pd content, and the type of Pd anchorage (chemical anchoring using ionic liquid (2.3 Pd/SiO_2-IL, hereinafter number indicates Pd containing in the catalyst), impregnation with the following reduction (0.05- and 0.1 Pd/Al_2O_3-Imp), or laser electrodispersion (LED) (0.03 Pd/Al_2O_3-LED) were tested in the Suzuki–Miyaura under competition of two aryl bromides (Scheme 1).[†] The detailed experimental procedures for the synthesis of catalysts, catalytic reactions techniques, and the analysis of the catalysts and the reaction mixtures are included in Online Supplementary Materials (Section S1). The extensive description of the precursor characterization was published earlier.[8]

The competitive variant of the Suzuki–Miyaura reaction (see Scheme 1) was chosen to simultaneously obtain data on the catalytic activity (characterized by TOF) and stability (characterized by TON),[9] and the reaction differential selectivity (estimated as the ratio of two competitive product formation rates).[10] Two aryl bromides, *i.e.*, 4-bromoacetophenone and bromobenzene possessing comparable reactivity, were chosen as good compromise between easily converted aryl iodides and non-reactive aryl chlorides.

Preliminarily we compared catalytic performance of the above-mentioned synthesized catalysts with routinely used in the Suzuki–Miyaura reaction homogeneous $PdCl_2$ and



[Pd] = Pd/Al_2O_3-LED, Pd/Al_2O_3-Imp, Pd/SiO_2-IL, Pd/C, $PdCl_2$

Scheme 1 *Reagents and conditions*: i, [Pd] (catalyst precursor), NaOAc, DMF, 140 °C.

[†] In catalytic Suzuki–Miyaura reaction, competing 4-bromoacetophenone and bromobenzene (5 mmol each), and naphthalene (GC internal standard, 1 mmol) were dissolved in DMF (5 ml). The solution was placed in a 25 ml one-necked round bottom flask equipped with a magnetic stir bar and a septum inlet containing phenylboronic acid (5 mmol), NaOAc (6.5 mmol), and Pd precursor (5.6×10^{-4}–0.8 μmol of Pd, 1.12×10^{-5}–1.6×10^{-2} mol%) under air. The reaction was initiated by placing the reactor in a pre-heated oil bath (140 °C) with stirring (480 rpm), and the processing was performed for 7–8 h. Samples for GC analysis were taken using a syringe with a steel needle at specified reaction times.

heterogeneous 4 Pd/C (Section S2, Table S1). It was revealed that under moderate Pd loading (0.8 μmol, 0.016 mol%) TOF values (calculated as [sum moles of products formed from competing aryl bromides] per [mol of Pd]·[min]) were substantially higher than those with 4 Pd/C, and were comparable or even two times higher (for 2.3 Pd/SiO_2-IL) if compared with homogeneous $PdCl_2$. As for the catalyst stability, for all catalysts TON values ([sum moles of products formed from competing aryl bromides] per [mol of Pd]) exceeded the corresponding ones for both reference samples (see Table S1). Therefore, we decided to test the performance of the synthesized Pd catalyst in the experiments where Pd loading was considerably lower. As it follows from Figure 1, the synthesized Pd catalysts demonstrated different trends of maximum TOF and TON on Pd loading depending on the catalyst nature. For the samples prepared using γ-Al_2O_3 by impregnation (0.1 Pd/Al_2O_3-Imp and 0.05 Pd/Al_2O_3-Imp) or LED (0.03 Pd/Al_2O_3-LED), TOF and TON values were slightly sensitive to the total Pd loading under its moderate values, but considerably grew with continued decrease in the loading of Pd. The decrease in loading of 0.03 Pd/Al_2O_3-LED to 5.6×10^{-4} μmol of Pd (that corresponded to applying of one granule of the catalyst) led to outstanding values of TOF (2.4×10^4 min^{-1}) and TON (6.6×10^4, see Figure 1). The rest values of TOF and TON for 0.05- and 0.1 Pd/Al_2O_3-Imp and 2.3 Pd/SiO_2-IL were substantially lower while they were obtained under higher Pd loading. The mostly close TON value (6.5×10^3) was achieved using 0.1 Pd/Al_2O_3-Imp [see Figure 1(*b*), 0.08 μmol of Pd]. In accordance with the very recent study,[11] the obtained TON values corresponded to 'advanced heterogeneous catalytic system' and indicated the prospects of the synthesized heterogeneous catalysts for Suzuki–Miyaura catalysis.

The observed TOF and TON dependencies on Pd loading were not unexpected. Similar tendencies were reported earlier for the cross-coupling reactions by several groups.[9,11–13] The observation of TOF increasing with decreasing catalyst loading indicates an increase in the fraction of active catalyst and is usually interpreted as the evidence for homogeneous catalysis;[12,14] however, alternative hypotheses were proposed for similar 'inverse' TOF dependences observed in heterogeneously-catalyzed hydrogenation using the catalytic systems like 'transition metal precursor + nanoparticles' stabilizer'.[15,16] Nevertheless, in accordance with the mostly accepted viewpoint,[12,14] such TOF pattern is resulted from more successive competition between the homogeneously catalyzed catalytic cycle and agglomeration of dissolved Pd complexes with the formation of inactive heterogeneous phase. It needs to be emphasized that when TOF and TON values are calculated, the question always raises about the actual amount of a catalyst that the reaction rate (for TOF) or product yield (for TON) should be related to. It is clear, that to obtain true values of TOF and TON instead apparent ones,[15] this amount should be the amount of active catalyst, $[Cat]_1$, equation (1), that is unknown in most cases. Moreover, the thesis about the *in situ* formation of several forms of catalyst including inactive ones from catalyst precursor during any catalytic reaction is undoubted, and it was repeatedly evidenced in the cross-coupling reactions (see reviews[14,17,18]). It can be easily demonstrated that passing of apparent TOF (TOF_{app}) dependence on catalyst loading through a maximum strongly supports the speculation that only a fraction of loaded Pd is catalytically active. Accepting that TOF_{app} is calculated as the sum reaction rate related to the total catalyst concentration, it can be presented as follows:

$$TOF_{app} = \frac{k_{app}[Cat]_1}{[Cat]_\Sigma}, \qquad (1)$$

where k_{app} is the apparent rate constant, $[Cat]_1$ is the *true* amount of active catalyst, $[Cat]_\Sigma$ is the sum catalyst concentration determined by its total loading in the reactor.

If one accepts that all catalyst loaded is active, *i.e.*, $[Cat]_\Sigma = [Cat]_1$, TOF value will be true (not apparent), and, in accordance with equation (2), TOF_{true} will be equal to the rate constant of the reaction. In this situation, the equation (2) for TOF_{true} does not contain catalyst amount at all and, therefore, TOF_{true} should not be dependent on the catalyst loading:[15]

$$TOF_{true} = \frac{k_{app}[Cat]_1}{[Cat]_1} = k_{app}. \qquad (2)$$

Considering that a fraction of inactive catalyst presents in the catalytic system in any case,[11,12,17,18] *i.e.*, $[Cat]_1 < [Cat]_\Sigma$, the TOF_{true} will always be higher than TOF_{app} estimated with sum catalyst loading (see Figure 1). Therefore, 'inverse' TOF_{app} dependence on catalyst loading or its passing through a maximum strongly supports the statement that only a portion of loaded Pd is catalytically active.

The obtained data on the catalytic activity were analyzed considering the distinction between synthesized Pd catalysts and their changes after the reaction completion (Section S3). The structure of the catalysts used in this work was studied in detail by TEM, XPS, and TPR.[8] According to these data, fresh 2.3 Pd/SiO_2-IL contained palladium mainly in the form of $PdCl_4^{2-}$ that may be easily reduced. Both fresh samples of Pd/Al_2O_3-Imp and 0.03 Pd/Al_2O_3-LED included predominantly Pd^0 nanoparticles. The comparison of SEM micrographs of the fresh and spent 2.3 Pd/SiO_2-IL (Figure 2) shows that the catalyst surface becomes less uniform after the reaction, which may be associated with its partial destruction and the formation of a layer of catalytic reaction products. In accordance with SEM-EDA (Table S2), the atomic ratio of Pd to Si decreases

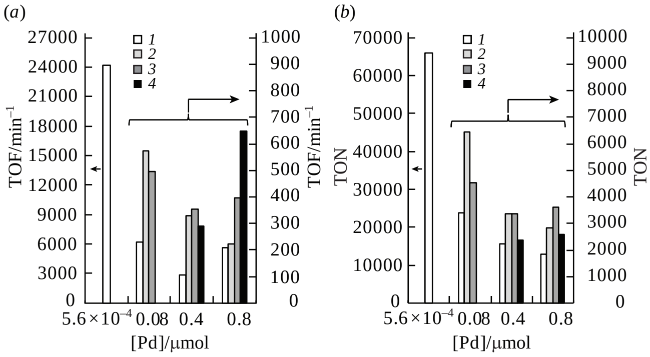


Figure 1 (*a*) TOF and (*b*) TON values obtained in the Suzuki–Miyaura reaction (see Scheme 1) using different Pd catalysts in loading range 5.6×10^{-4}–0.8 μmol of Pd: (*1*) 0.03 Pd/Al_2O_3-LED, (*2*) 0.1 Pd/Al_2O_3-Imp, (*3*) 0.05 Pd/Al_2O_3-Imp, (*4*) 2.3 Pd/SiO_2-IL.

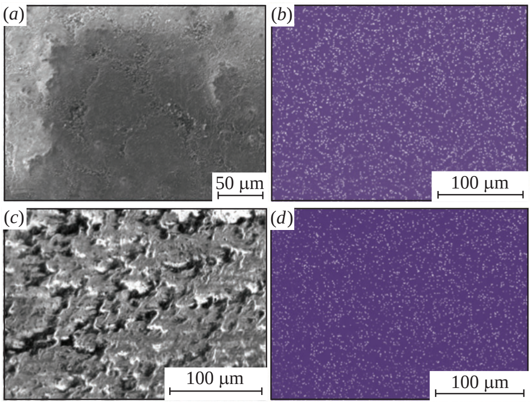


Figure 2 (*a*, *c*) SEM images and (*b*, *d*) EDA Pd mappings of fresh and spent 2.3 Pd/SiO_2-IL, respectively.

only slightly from 0.011 to 0.009, which indicates that the active phase is predominantly retained on the surface of SiO_2-IL with possible negligible leaching to the solution phase (Figure S3). However, the atomic ratio of Cl to Pd after the reaction is reduced from 5.7 to 2.2, which may be due to the Pd reduction being inherent step of the catalytic reaction. The distribution of palladium on the surface of 2.3 Pd/SiO_2-IL changed after catalytic tests (Figures S3 and S4). Instead of the uniform Pd distribution in the fresh sample, aggregates of dark nanoparticles corresponding to the appearance of metallic palladium were clearly visible in the image of the spent catalyst. There were no such particles in the images of the initial sample, where Pd was anchored on the surface in the highly dispersed ionic form. The appearance of metal particles in the TEM images (Figure S4) and the analysis of the electronic structure of palladium in spent catalysts by XPS (Table S3) confirm these conclusions. The easy reduction of Pd^{II} under the action of nitrogen-containing components of the catalyst (see Section S1.2 for 2.3 Pd/SiO_2-IL) under spectra registration probably leads to an overestimated content of the component corresponding to the metallic palladium in XPS data. The TEM images of the spent after catalysis samples 0.03 Pd/Al_2O_3-LED [Figure S5(*b*)] and 0.1 Pd/Al_2O_3-Imp [Figure S6(*b*)] indicate that highly dispersed Pd particles are uniformly distributed on the alumina surface. However, according to XPS data (Figure S7 and Table S3), part of the palladium becomes oxidized after the reaction.

In can be concluded that initially different catalysts become structurally similar after the catalytic reaction completion. Therefore, both the modes of TOF and TON values and the changes in heterogeneous catalyst morphology agreed with each other and were indicative of occurrence of Pd transformations during the Suzuki–Miyaura reaction.[19] However, any changes of the structure of heterogeneous Pd catalyst as a result of the catalytic reaction do not mean its proceeding on the surface and are only indicative for Pd interconversions with the formation of several potentially active Pd forms. To resolve possible participation in the Suzuki–Miyaura catalysis of homogeneous Pd formed likely by leaching (even in negligible amounts, Table S2)[9,12] and heterogeneous Pd (either in the form of started precursors or as particles formed from leached by agglomeration) we analyzed the phase trajectories of competing reaction when various heterogeneous and homogeneous catalysts were used (see Online Supplementary Materials, Section S2).[10,20] The changes of the phase trajectories indicated the change of the differential selectivity of competing aryl bromides observed when different Pd catalysts were used (Figures S1 and S2). This pattern unambiguously pointed to the catalysis proceeding on the surface of Pd metal particles (including nanoparticles)[10,20] because the type of heterogeneous Pd precursor cannot influence the origin of leached Pd^0 and Pd^{II} molecular species, and if such species are exclusively responsible for activity, the corresponding phase trajectories (*i.e*. differential selectivity) should not change.[18] Note that the distinctions between the phase trajectories obtained with various precursors were more pronounced for the experiments with lower Pd loading (Figure S2 for 0.08 μmol of Pd *vs*. Figure S1 for 8 μmol of Pd). In any case, even at higher Pd loading phase trajectories obviously changed when different Pd catalysts were used, pointing to involvement of aryl bromides into Suzuki–Miyaura reaction products in considerable extend through heterogeneous pathway, as minimum, using the Pd catalysts discussed. This result agreed with the above proposal that only a part of catalyst loaded was active, and less reactive catalyst (or inactive, in utmost case) can be the leached Pd along with probably inaccessible Pd in catalysts depth.

To conclude, the set of heterogeneous Pd catalysts were prepared *via* the treatment of SiO_2 modified by ionic liquid and γ-Al_2O_3 by impregnation or LED. Application of the catalysts in the Suzuki-Miyaura reaction under ‘ligand-free’ conditions allowed achieving prominent TOF and TON values relating to ‘advanced heterogeneous catalytic systems’[11] and exceeding the corresponding values even for a homogeneous precursor. Taking into account the patterns of TOF, TON, and the differential selectivity of competing Suzuki–Miyaura reaction, the true heterogeneous catalysis mechanism can be proposed as the main way for the substrates conversion under the conditions applied.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2023.02.009.

References

1 A. B. Pagett and G. C. Lloyd-Jones, in *Organic Reactions*, ed. S. E. Denmark, Wiley, 2019, vol. 100, pp. 547–619.
2 I. P. Beletskaya, F. Alonso and V. Tyurin, *Coord. Chem. Rev.*, 2019, **385**, 137.
3 S. Kyushin, H. Fujii, K. Negishi and H. Matsumoto, *Mendeleev Commun.*, 2022, **32**, 87.
4 V. A. Egorov, L. S. Khasanova, F. A. Gimalova, A. N. Lobov, D. V. Ishmetova, V. A. Vakhitov and M. S. Miftakhov, *Mendeleev Commun*., 2022, **32**, 183.
5 S. Vásquez-Céspedes, R. C. Betori, M. A. Cismesia, J. K. Kirsch and Q. Yang, *Org. Proc. Res. Dev.*, 2021, **25**, 740.
6 D. Roy and Y. Uozumi, *Adv. Synth. Catal.*, 2018, **360**, 602.
7 P. P. Mpungose, Z. P. Vundla, G. E. M. Maguire and H. B. Friedrich, *Molecules*, 2018, **23**, 1676.
8 A. F. Schmidt, A. A. Kurokhtina, E. V. Larina, N. A. Lagoda, D. A. Yavsin, S. A. Gurevich, V. M. Zelikman, I. N. Krotova, T. N. Rostovshchikova and I. G. Tarkhanova, *Kinet. Catal*., 2023, **64**, in press (*Kinet. Katal*., 2023, **64**, DOI: 10.31857/S0453881123010082).
9 I. P. Beletskaya and A. V. Cheprakov, *Chem. Rev.*, 2000, **100**, 3009.
10 A. F. Schmidt, A. A. Kurokhtina and E. V. Larina, *Catal. Sci. Technol.*, 2014, **4**, 3439.
11 D. B. Eremin, A. S. Galushko, D. A. Boiko, E. O. Pentsak, I. V. Chistyakov and V. P. Ananikov, *J. Am. Chem. Soc.*, 2022, **144**, 6071.
12 A. H. M. de Vries, J. M. C. A. Mulders, J. H. M. Mommers, H. J. W. Henderickx and J. G. de Vries, *Org. Lett.*, 2003, **5**, 3285.
13 A. F. Schmidt, A. Al Halaiqa and V. V. Smirnov, *Synlett*, 2006, **18**, 2861.
14 A. F. Schmidt and A. A. Kurokhtina, *Kinet. Catal.*, 2012, **53**, 714 (*Kinet. Katal*., 2012, **53**, 760).
15 A. B. Crooks, K. H. Yih, L. Li, J. C. Yang, S. Özkar and R. G. Finke, *ACS Catal*., 2015, **5**, 3342.
16 N. I. Skripov, L. B. Belykh, T. P. Sterenchuk, A. S. Levchenko and F. K. Schmidt, *Kinet. Catal.*, 2021, **62**, 299 (*Kinet. Katal*., 2021, **62**, 245).
17 D. B. Eremin and V. P. Ananikov, *Coord. Chem. Rev.*, 2017, **346**, 2.
18 A. Biffis, P. Centomo, A. del Zotto and M. Zecca, *Chem. Rev.*, 2018, **118**, 2249.
19 L. A. Bulygina, N. S. Khrushcheva, K. A. Lyssenko and A. S. Peregudov, *Mendeleev Commun.*, 2022, **32**, 331.
20 A. F. Schmidt, A. A. Kurokhtina and E. V. Larina, *Kinet. Catal.*, 2019, **60**, 551 (*Kinet. Katal.*, 2019, **60**, 555).

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