Pd Nanoparticles Incorporated in Highly Porous Hyper-Crosslinked Polystyrene as Effective Catalysts of Suzuki Cross-Coupling

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This paper describes synthesis of Pd-containing catalysts of Suzuki cross-coupling based on non-functionalized hyper-crosslinked polystyrene (HPS) at variation of Pd precursor nature ($PdCl_2$, $PdCl_2(CH_3CN)_2$ or $PdCl_2(PhCN)_2$). Relatively low affinity of Pd species to the chosen polymeric support was shown to be responsible for *in situ* formation of Pd nanoparticles and their aggregates. During the investigation of aryl halide nature, catalytic activity was shown to decrease in the following order: Br > I > Cl. Best results were obtained for the preliminarily reduced HPS-based sample synthesized while using $PdCl_2$ in the reaction between phenylboronic acid and 4-bromoanisole: more than 93% yield of cross-coupling product was achieved at mild reaction conditions (NaOH, 60°C, solvent ethanol-water mixture) using 0.8 mol.% of Pd.

1. Introduction

Suzuki cross-coupling in one of the most widespread method of biaryls formation using aryl halides and aryl boronic acids as substrates (Hajipour et al., 2014). Homogeneous palladium complexes are commonly used as catalysts for the Suzuki reaction providing high reaction rates and excellent yields of target products. However, last decades ligandless catalysts has been considered as an alternative to homogeneous ones since they can be easily separated from the reaction mixture and reused (Pagliaro et al., 2012). In the case of ligandless catalysts, the peculiarities of catalytic cycle of Suzuki cross-coupling (palladium changes reversibly its oxidation state from (II) to (0) and small palladium clusters, which are likely responsible for observed catalytic activity, can form Pd (0) nanoparticles (NPs) and vice versa) complicate the kinetic analysis of this reaction. Hence recently the term of "cocktail"-type catalytic systems was proposed to describe the behavior of majority of ligandless catalysts of Suzuki reaction (Eremin and Ananikov, 2017).

This paper is devoted to the study of Pd-containing catalysts based on non-functionalized hyper-crosslinked polystyrene (HPS) of MN270 type. It is noteworthy that the catalyst based on non-functionalized HPS and synthesized while using $PdCl_2(CH_3CN)_2$ as a precursor was found to be promising for the Suzuki reaction (88% yield of cross-coupling product was found in the reaction of 4-bromoanisole (4-BrAn) and phenylboronic acid (PBA) at mild conditions and in the absence of phase-transfer agents). However, the detailed investigation of ligandless catalysts based on MN270 was not carried out. It is noteworthy that for another HPS (MN100, bearing amino-groups) homogeneous reaction mechanism was proposed (Nemygina et al., 2018) in cross-coupling of 4-BrAn and PBA regardless of the nature of Pd precursor and the presence of Pd NPs (Nikoshvili et al., 2016). MN270 has twice higher specific surface area than MN100 (about 1400 m^2/g vs. 700 m^2/g) and is relatively more hydrophobic, thus in this work we aimed to find the influence of Pd precursor nature for MN270 in order to show how precursor-polymer combinations can affect the cross-coupling process.

2. Experimental

2.1 Materials

HPS Macronet MN270 (Purolite Int., UK) was washed with distilled water and acetone and dried under vacuum as described elsewhere (Sulman et al., 2012). 4-Methoxybiphenyl (4-MBP, >99%), 3-methoxybiphenyl (3-MBP, >96%) and 2-methoxybiphenyl (2-MBP, >98%) were purchased from Tokyo Chemical Industry Co. Ltd. 4-Bromoanisole (4-BrAn, ≥99%), 3-bromoanisole (3-BrAn, ≥98%), 2-bromoanisole (2-BrAn, 97%), 4-iodoanisole (4-IAn, 98%), 4-chloroanisole (4-ClAn, 99%), phenylboronic acid (PBA, 95%), diphenylamine (99%), biphenyl (99.5%), palladium(II)chloride (PdCl$_2$, 99%), bis(acetonitrile)palladium(II)chloride (PdCl$_2$(CH$_3$CN)$_2$, >99%), bis(benzonitrile)palladium(II)chloride (PdCl$_2$(PhCN)$_2$, 95%), tetrahydrofuran (THF, ≥99.9%), ethanol (EtOH, ≥99.8%), methanol (MeOH, 99.8%), sodium chloride (NaCl, ≥99%), sodium carbonate (Na$_2$CO$_3$, ≥99.5%) and sodium hydroxide (NaOH, ≥98%) were obtained from Sigma-Aldrich. All chemicals were used as received. Distilled water was purified with an Elsi-Aqua water purification system.

2.2 Catalyst synthesis

Series of Pd-containing HPS-based catalysts with calculated metal loading of 2 wt.% was synthesized via wet-impregnation method according to the procedure described elsewhere (Sulman et al., 2012). In a typical experiment, 1 g of pretreated, dried and crushed (<63 μm) granules of MN270 were impregnated with 2.8 mL of the THF solution of precursor (PdCl$_2$(CH$_3$CN)$_2$ or PdCl$_2$(PhCN)$_2$) of a certain concentration. The Pd-containing polymer was dried at 70°C, treated with 2.8 mL of Na$_2$CO$_3$ solution (concentration 0.07 mol/L) and dried until the constant weight was achieved. After that the catalyst was washed with distilled water till neutral pH and dried at 70°C.

In the case of PdCl$_2$, the synthesis procedure was similar, but the complex solvent THF/MeOH/H$_2$O was used (at a ratio of 8 : 1 : 1) instead of pure THF or pure water (Lyubimov at al., 2009). Besides, NaCl (1.6 molar excess with respect to palladium chloride) was added to the precursor solution in order to obtain Na$_2$PdCl$_4$ that has better solubility in comparison with pure PdCl$_2$.

Thus the following catalysts were synthesized (palladium content was confirmed by the XFA): Pd/MN270-1 (1.65 wt.% of Pd, precursor PdCl$_2$); Pd/MN270-2 (1.80 wt.% of Pd, precursor PdCl$_2$(CH$_3$CN)$_2$); Pd/MN270-3 (1.97 wt.% of Pd, precursor PdCl$_2$(PhCN)$_2$).

Besides, for all the synthesized catalyst, preliminarily reduction in hydrogen flow at 275°C for 2 h was carried out (the catalysts were designated as Pd/MN270-1-R, Pd/MN270-2-R and Pd/MN270-3-R, respectively).

2.3 Catalytic testing

Testing of HPS-based catalysts was carried out in a 60 mL shaker-type isothermal glass batch reactor at vigorous stirring (800 two-sided shaking per minute) at a temperature of 60°C. The total volume of liquid phase was 30 mL. EtOH/water mixture at the volumetric ratio of 5 : 1 was used as a solvent. NaOH was used as a base at the quantity of 1.5 mmol (equimolar to PBA). The choice of solvent and alkali metal compound was based on previous studies of HPS-based catalysts of Pd/MN100 series (Nemygina et al., 2016). In each experiment the quantity of aryl halide was equal to 1 mmol, 1.5 molar excess of PBA was used. Catalyst loading in each experiment was 50 mg. Before the catalyst addition in the reactor, in each experiment the blank test (duration of 60 min) was carried out in order to ensure that the reaction not proceeded at the absence of catalyst.

Samples of reaction mixture were periodically taken and analyzed via GC-MS (Shimadzu GCMS-QP2010S) equipped with a capillary column HP-1MS (30 m × 0.25 mm i.d., 0.25 μm film thickness). Helium was used as a carrier gas at pressure of 74.8 kPa and linear velocity of 36.3 cm/s. Oven temperature was programmed: 120°C (0 min) → 10°C/min (160°C) → 25°C/min (300°C) → 300°C (2.4 min). Temperature of injector, interface and ion source was 260°C, range from 10 up to 500 m/z. The concentrations of the reaction mixture components were calculated using the internal standard calibration method (diphenylamine was used as an internal standard).

Catalytic activity (R_0) was defined as a slope of the initial part on kinetic curves of aryl halide conversion vs. time: $R_0 = N_{ArHal} \times \tau^{-1} \times X$, where N_{ArHal} is quantity of aryl halide (μmol); X is conversion of aryl halide, and τ is the reaction time (s) for achieving of conversion X.

2.4 Catalyst characterization

Pd/HPS catalysts were characterized by X-Ray Fluorescence Analysis (XFA), X-Ray Photoelectron Spectroscopy (XPS) and Transmission Electron Microscopy (TEM).

XFA was carried out to determine the Pd content. It was performed with a Zeiss Jena VRA-30 spectrometer (Mo anode, LiF crystal analyzer and SZ detector). Analyses were based on the Co Kα line and a series of

standards prepared by mixing 1 g of polystyrene with 10-20 mg of standard compounds. The time of data acquisition was constant at 10 s.

XPS data were obtained using Mg Kα (hν = 1253.6 eV) radiation with ES-2403 spectrometer (Institute for Analytic Instrumentation of RAS, St. Petersburg, Russia) equipped with energy analyzer PHOIBOS 100-MCD5 (SPECS, Germany) and X-Ray source XR-50 (SPECS, Germany). All the data were acquired at X-ray power of 250 W. Survey spectra were recorded at an energy step of 0.5 eV with an analyzer pass energy 40 eV, and high resolution spectra were recorded at an energy step of 0.05 eV with an analyzer pass energy 7 eV. Samples were allowed to outgas for 180 min before analysis and were stable during the examination. The data analysis was performed by CasaXPS.

TEM characterization was provided using a JEOL JEM1010 instrument at electron accelerating voltage of 80 kV. Samples were prepared by embedding the catalyst in epoxy resin with following microtomming at ambient temperature. Images of the resulting thin sections (*ca*. 50 nm thick) were collected with the Gatan digital camera and analyzed with the Adobe Photoshop software package and the Scion Image Processing Toolkit.

3. Results and Discussion

Figure 1 shows TEM images of all the synthesized catalysts of Pd/MN270 series. In the case of catalysts containing $PdCl_2(CH_3CN)_2$ and $PdCl_2(PhCN)_2$, large irregular aggregates of NPs were formed after the Suzuki cross-coupling of 4-BrAn and PBA (Fig. 1 (b) and (c)), while in the case of the sample impregnated with $PdCl_2$, relatively narrower particle size distribution was observed (Fig. 1 (a)). Non-uniform distribution and presence of aggregates of Pd NPs after the Suzuki reaction can be explained by hydrophobic nature of the polymeric support and the absence of functional groups, which allows easy migration of Pd(II) species inside the MN270 matrix in contrast, for example, to more hydrophilic MN100 containing amino-groups, which was shown to allow formation of Pd NPs with mean diameters of about 4 nm and less pronounced aggregation after the cross-coupling of 4-BrAn and PBA (Nikoshvili et al., 2016). During this migration process, Pd(0) species, which are generated as a result of transmetalation step with PBA, form Pd_n clusters and NPs nucleating mainly in the HPS mesopores.

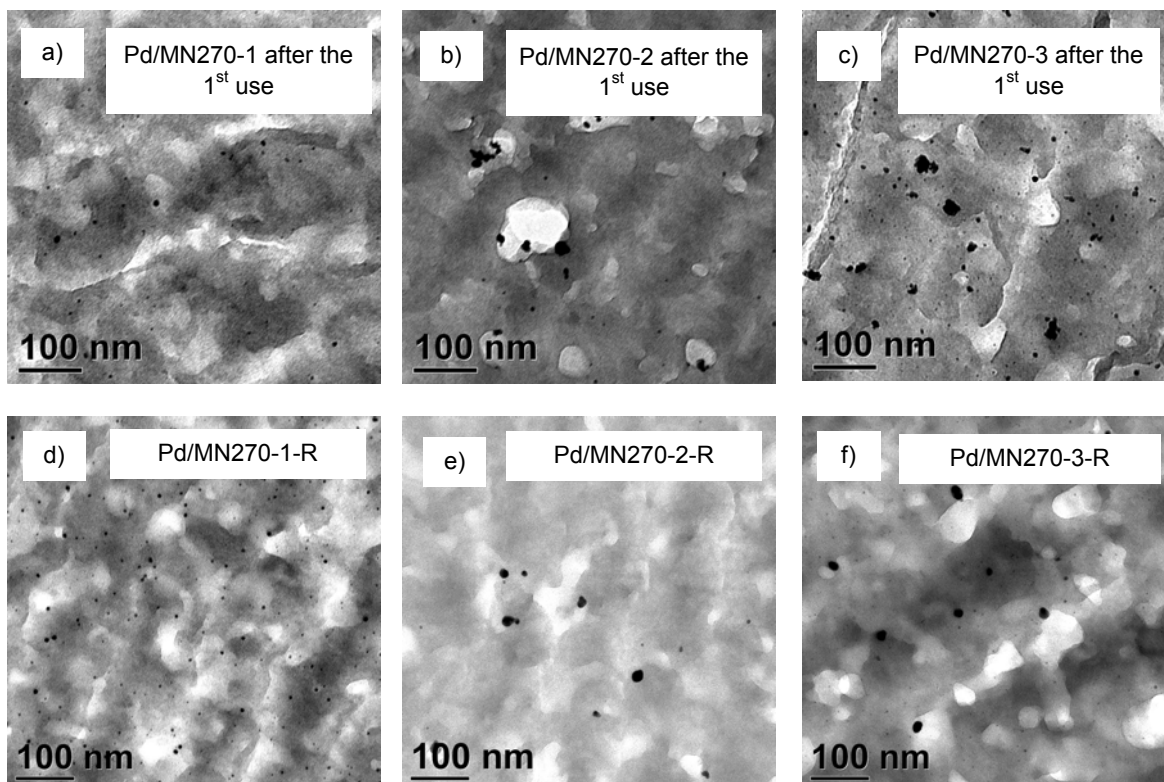*Figure 1: TEM images of Pd/MN270 samples (taken after the 1st run in Suzuki cross-coupling of 4-BrAn and PBA (a, b, c) and preliminarily reduced in H2 flow (d, e, f))*

Reduction of the as-synthesized samples of Pd/MN270 series allowed formation of well-defined NPs with mean diameter of about 4 nm in the case of Pd/MN270-1-R (Fig. 1 (d)), while in the case of Pd/MN270-2-R (Fig. 1 (e)) and Pd/MN270-3-R (Fig. 1 (f)) large aggregates (about 20 nm in diameter) were found.

XPS data revealed that the surface of freshly prepared catalysts of Pd/MN270 series contains chlorine, carbon, oxygen, nitrogen and palladium. According to the XPS data, the following values of binding energy (± 0.1 eV) of Pd $3d_{5/2}$ were found according to the high resolution spectra of Pd 3d: 338.6 eV (binding energy of Pd $3d_{5/2}$ in $PdCl_2(CH_3CN)_2$ and $PdCl_2(PhCN)_2$ was found to be equal to 338.7 eV); 336.3-336.6 eV (small clusters of Pd_n (n ≤ 13)) (Wu et al., 2009); 337.7 eV ($PdCl_2$); 335.0 eV (Pd NPs). The existence of $PdCl_2$ in the catalyst composition can be ascribed to the transformation of initial precursors ($PdCl_2(CH_3CN)_2$ or $PdCl_2(PhCN)_2$) during the catalyst synthesis.

It is noteworthy that high percentage of Pd(II) species (from about 18 at.% for Pd/MN270-2-R up to 50 at.% for Pd/MN270-1-R) was found on the surface of reduced catalysts according to the data of XPS, which shows the incomplete reduction of palladium during the treatment in hydrogen flow.

Thus it can be concluded that the synthesized HPS-based catalysts (both initial and reduced ones) can be considered as "cocktail" type systems containing multiple forms of Pd in the polymeric network, which can simultaneously catalyze the Suzuki reaction.

Precursor nature was investigated by the example of cross-coupling of 4-BrAn and PBA. The results of catalytic testing of both the initial samples and the samples reduced in hydrogen flow are presented in Table 1. It is noteworthy that for initial (unreduced) Pd/MN270 catalysts, the data on the mean diameter of Pd NPs are provided after the 1st run in Suzuki reaction.

Table 1. Influence Pd precursor nature on activity and selectivity of the catalysts of Pd/MN270 series

Sample designation	Mean diameter of Pd NPs, nm (TEM data)	Conversion of 4-BrAn, ± 0.5%*	Selectivity with respect to 4-MBP, ± 0.5%*	Yield of 4-MBP, ± 0.5%*	R_0, μmol(4-BrAn)/s
Pd/MN270-1	4.8 ± 3.0 nm	89.9	97.2	87.4	3.05
Pd/MN270-2	6.7 ± 2.5 nm and aggregates up to *ca.* 25 nm in size	89.3	98.4	87.9	4.48
Pd/MN270-3	5.2 ± 2.6 nm and aggregates up to *ca.* 30 nm in size	88.6	97.2	86.1	4.50
Pd/MN270-1-R	4.4 ± 1.7 nm	94.8	98.6	93.5	4.43
Pd/MN270-2-R	multimodal distribution with strongest mode at 8.5 ± 4.4 nm and aggregates up to *ca.* 22 nm in size	92.4	98.2	90.7	2.03
Pd/MN270-3-R	3.8 ± 1.1 nm and aggregates up to *ca.* 21 nm in size	81.2	97.9	79.5	0.89

*Calculated for the reaction time 1 h

As it can be seen (Table 1), in the case of initial catalysts of Pd/MN270 series the conversion of 4-BrAn reached after 1 h of reaction time slightly depends on the Pd precursor nature. Moreover, it seems that there is no dependence neither on the mean diameter of palladium NPs observed after the catalytic use in Suzuki reaction nor on the composition of catalyst surface obtained as a result of XPS. However, the initial slope of kinetic curves (R_0) is different (see Fig. 2 (a)): highest R_0 was found in the case of relatively more hydrophobic precursor – $PdCl_2(PhCN)_2$. This fact is likely due to the different mobility and distribution of Pd precursors inside the MN270, which correspondingly result to the different character (tendency to form irregular aggregates) and rates of Pd precipitation during transmetalation step.

In case of the catalysts preliminary reduced in H_2 flow, the best results regarding to the 4-MBP yield were observed for Pd/NM270-1-R (Fig. 2 (b)) synthesized while using $PdCl_2$ and containing more evenly distributed Pd NPs (see Fig. 1). If all other things are equal, the smaller the NPs the higher their ability to form homogeneous species during the oxidative addition and, consequently, the higher the initial reaction rate.

By the example of Pd/MN270-2 the influence of the type of aryl halide was studied (see Table 2). As it can be seen from the data obtained at variation of halogen type (Table 2, rows #1-3), the highest yield of 4-MBP (87.9%) was achieved for 4-BrAn, while the lowest one – for 4-ClAn (0.2%). In case of 4-IAn moderate activity

was found – conversion of 4-IAn was in 1.5-times lower in comparison with 4-BrAn (Table 2, rows #1), which is unusual for Suzuki cross-coupling, because, typically, catalytic activity increases in the following order: I > Br > Cl (Hajipour et al., 2014).
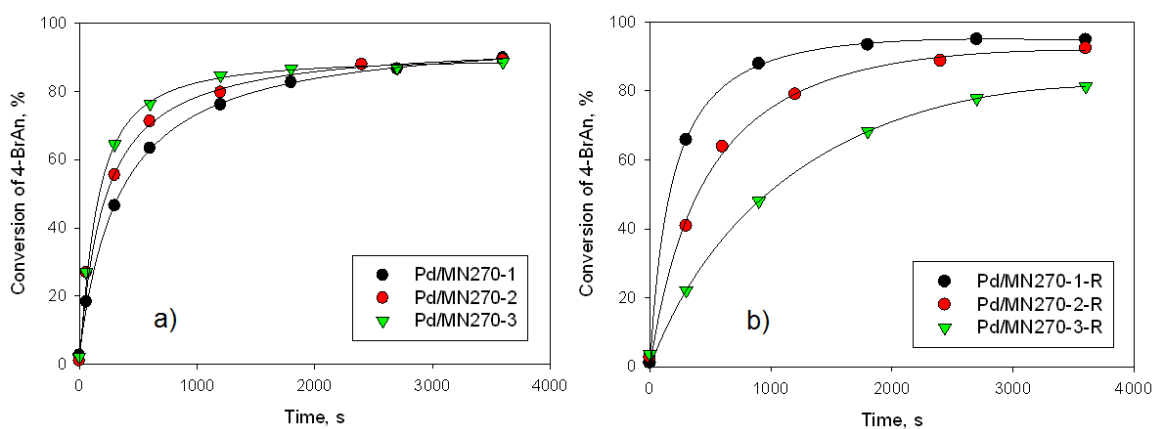

Figure 2: Influence of Pd precursor nature on kinetic curves obtained for the initial (unreduced) samples of Pd/MN270 series (a) and for the samples preliminarily reduced in H_2 flow (b)

Table 2. Cross-coupling of different aryl halides and PBA using Pd/MN270-2

N	Aryl halide	Conversion of aryl halide, ± 0.5%*	Selectivity with respect to cross-coupling product, ± 0.5%*	Yield of cross-coupling product, ± 0.5%*	R_0, µmol(aryl halide)/s
1	H₃CO——I	60.0	94.6	56.7	3.82
2	H₃CO——Cl	3.3	6.1	0.2	0.52
3	H₃CO——Br	89.3	98.4	87.9	4.48
4	H₃CO—— Br	17.4	52.0	9.1	1.87
5	H₃CO—— Br	28.4	92.7	26.3	3.23

*Calculated for the reaction time 1 h

This fact can be explained by the change of reaction mechanism (it should be noted that no other by-products, with the exception of biphenyl (result of PBA homocoupling), were found in the reaction mixture). Reactivity of different aryl halides is often caused by the change of rate-limiting step (Hirakawa et al., 2017). In most cases the oxidative addition of aryl halide is rate-limiting (Pudasaini and Janesko, 2011) resulting in strong dependence of observed reaction rate on concentrations of both palladium and aryl bromide. However, higher reactivity of aryl bromides in comparison with aryl iodides can be due to change of rate-limiting step from oxidative addition to transmetalation in the case of iodides, taking into account that the starting catalytic material (Pd/MN270-2) contains Pd(II) species.

In case of 4-ClAn the oxidative addition can be strongly suppressed, which can cause the aggregation of Pd(0) particles forming *in situ* quickly after the reaction start leading to extremely low catalytic activity and selectivity (Table 2).

Thus for bromides, which were most active in cross-coupling with PBA, the highest yield (87.9%) of the product (4-MBP) was found in case of 4-BrAn (Table 2, rows #3) that is likely due to the enrichment of the carbon atom bonded with bromine with electrons repulsed from *p*-substituent methoxy group. In case of 2-BrAn (Table 2, rows #5) the yield of 2-MBP was noticeably lower (26.3%) possibly due to the steric constraint of closely located bromine and methoxy group. Expectedly the lowest conversion was found while using 3-BrAn (17.4%), which was accompanied by low selectivity – yield of cross-coupling product (3-MBP) was only 9.1% (Table 2, rows #4).

4. Conclusions

Pd-containing catalysts based on non-functionalized HPS of MN270 type were shown to be promising for Suzuki cross-coupling reaction: about 90% conversion of 4-BrAn was achieved independent on the palladium precursor nature. In case of both initial (unreduced) and reduced samples homogeneous mechanism of Suzuki reaction was proposed with oxidative addition as a rate-limiting step. Study of the influence of aryl halide nature revealed that highest activity corresponds to aryl bromides rather than to aryl iodides. In case of aryl bromides the highest reaction rate was observed for 4-BrAn that is likely due to the electron repulsion from *p*-substituent methoxy group and the absence of steric constraints.

Acknowledgments

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