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Intensification of Pd-catalyzed Suzuki Cross-coupling: Influence of Second Metal Addition, Reactor Type and Visible Light Irradiation

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This work is devoted to the synthesis of Pd- and Au-containing mono- and bimetallic catalysts based on hypercrosslinked polystyrene (HPS) and study of their catalytic properties in Suzuki cross-coupling of 4-bromoanisole (4-BrAn) and phenylboronic acid (PBA). Series of HPS-based catalysts were synthesized at variation of Pd content and tested in Suzuki cross-coupling of 4-BrAn and PBA in a batch mode at ambient pressure while using ethanol/water mixture as a solvent and NaOH as a base. The highest catalytic activity was observed for Au-Pd/HPS catalyst containing 1.15 wt.% of Pd and 1.80 wt.% of Au andreduced with aqueous solution of $NaBH_4$ (more than 98 %of 4-BrAn conversion was achievedfor 3 h of reaction time). Selectivity was higher than 98 % with respect to 4-methoxybiphenyl (4-MBP). Thus HPS-supported bimetallic palladium catalysts were found to be promising (active, selective) and simple in preparation for the Suzuki cross-coupling at mild temperatures along with the absence of the necessity to use phase-transfer agents.

1. Introduction

The Suzuki cross-coupling reaction between aryl halides and arylboronic acids is one of the most common and effective methods for the synthesis of biaryls, which are important intermediates in the synthesis of pharmaceuticals, ligands and polymers (Jung et al., 2010).

Traditionally, the Suzuki reaction is carried out using palladium complexes containing phosphorus- and nitrogen-based ligands as catalysts. The activity and selectivity of homogeneous catalysts can be easily optimized by modifying the metal center with various organic ligands, so the development of new ligands attracts great attention of researchers. However, most of these ligands are expensive, which significantly limits their use in industry (Pan et al., 2008). In addition, the main disadvantage of homogeneous palladium catalysts is the difficulty of their separation from reaction products for reuse (additional methods such as chromatography, crystallization or treatment with activated carbon are required) (Sołoducho at al., 2013). These disadvantages can be overcome by using heterogeneous or quasi-homogeneous palladium catalysts, since they can be easily separated from the reaction mixture and reused (Pagliaro et al., 2012). However, despite the advances made in some cases, a general drawback of all catalytic systems developed up to date for this reaction is the loss of catalytic activity as a result of palladium leaching from catalysts (Cantillo and Kappe, 2014).

Recently, scientists are increasingly focusing on gold nanoparticles (NPs) as catalysts for conducting various organic reactions. Due to the fact that Au (I) is isoelectronic with Pd (0), gold NPs can also catalyze the Suzuki reaction (Li et al., 2010). In this case, as in the case of palladium, both homogeneous gold complexes and heterogeneous catalysts on different supports can participate in the reaction (Corma and Garcia, 2008). It should be noted that the size of gold NPs plays an important role while carrying out the Suzuki reaction: the smaller the diameter of Au NPs, the more active the catalyst (Mondal et al., 2015). The size of gold NPs can be controlled by changing the Au/support weight ratio (Li et al., 2010) as well as by varying the temperature of catalyst

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calcination (Dumbre et al., 2013). As in the case of palladium catalysts, the Suzuki reaction on Au-containing catalysts can proceed according to either homogeneous (Han et al., 2009) or heterogeneous (Shah and Kaur, 2014) mechanisms depending on the catalyst selected.

In addition to monometallic Au-containing catalysts, bimetallic (Au-Pd) systems can also be used in the Suzuki reaction (Heugebaert et al., 2012). Bimetallic catalytic systems are more active, selective and stable in comparison with monometallic analogues. For example, the catalytic behavior of bimetallic Pd/Au NPs in the Suzuki cross-coupling reaction was investigated (Nasrollahzadeh et al., 2015). Scanning electron microscopy showed that in this catalyst, palladium NPs were located on the surface of gold particles. Under optimal conditions, a combination of various aryl iodides and arylboronic acids containing electron-donor and electron-acceptor groups was studied. In all cases, the yield of cross-coupling products was from 86 up to 90 %. Developed catalyst was stable for four repeated runs (Nasrollahzadeh et al., 2015). Improvement of activity while introducing gold in a catalyst composition is most likely due to the change in the electronic structure of the catalytically active metal (Pd) as well as to the formation of small palladium NPs and structural changes in the catalyst (Speziali et al., 2013).

This work is devoted to the synthesis of mono- (Pd, Au) and bimetallic (Au-Pd) HPS-based catalysts and study of their catalytic properties in Suzuki cross-coupling of 4-BrAn and PBA to obtain 4-MBP. In previous studies (Nikoshvili et al., 2016), HPS-supported monometallic Pd-containing catalysts were shown to be simple in preparation and promising for the Suzuki cross-coupling: more than 94 %yield of 4-MBP for less than 1 h of reaction duration was achieved. Micro-meso-porous structure, huge surface area and aromatic nature of HPS were found to favour the formation of small Pd_n clusters and NPs after the reduction in hydrogen flow, which were responsible for observed catalytic activity. However, after three consecutive runs the activity of Pd/HPS catalysts decreased by about 20 %, which was due to the homogeneous pathway of Suzuki reaction resulting in redistribution of palladium inside the pores of developed catalysts and leaching of palladium-containing species into the reaction solution (Nikoshvili et al., 2016). It is expected that new bimetallic Au-Pd/HPS catalysts will possess higher activity and stability in comparison with monometallic palladium catalysts.

2. Experimental

2.1 Materials

HPS was purchased from Purolite Int. (U.K.) as Macronet MN100. 4-BrAn (≥98 %) was purchased from Merck KGaA. 4-MBP (>99 %) was purchased from Tokyo Chemical Industry Co. Ltd. PBA (95 %), diphenylamine (99 %), biphenyl (99.5 %), $PdCl_2(CH_3CN)_2$ (>99 %), THF (≥99.9 %), EtOH (≥99.8 %), Na_2CO_3 (≥99.5 %), $NaBH_4$(≥96 %) and NaOH (≥98 %) were obtained from Sigma-Aldrich. Gold(III) chloride hydrate ($HAuCl_4*nH_2O$, 48.95 % of Au) was purchased from JSC “Aurat” (Russia). All chemicals were used as received. Distilled water was purified with an Elsi-Aqua water purification system.

2.2 Catalyst synthesis

The monometallic Au- and Pd-containing HPS-based catalysts were synthesized via wet-impregnation method according to the procedure described elsewhere (Nemygina et al., 2016). In a typical experiment, 1 g of pretreated, dried and crushed (<63 μm) granules of HPS were impregnated with 2.8 mL of the THF solution of metal precursor ($PdCl_2(CH_3CN)_2$ or $HAuCl_4$) of a certain concentration. Resulting Au- or Pd-containing polymer was dried at 70 °C, treated with 2.7 mL of Na_2CO_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 again at 70 °C.

All synthesized monometallic catalysts were reduced either in a hydrogen flow (100 mL/min) at 300 °C during 3 h or with aqueous solution of $NaBH_4$ (concentration 0.1 mol/L).

Bimetallic catalysts were synthesized by the sequential wet-impregnation method: freshly prepared gold-containing catalyst was reduced in hydrogen flow (100 mL/min) at 300 °C during 3 h and then $PdCl_2(CH_3CN)_2$ was impregnated and treated (washed and dried) as described above.

The resulting catalysts are summarized in Table 1.

2.3 Catalytic testing

Testing of HPS-based catalysts was carried out at 60°C in temperature-controlled glass batch reactors of two types: (i) shaker-type reactor and (ii) reactor with magnetic stirrer. In the reactor of (i) type the total volume of liquid phase was 30 mL. EtOH/water mixture (5:1) was used as a solvent and NaOH (1.5 mmol) was used as a base. In each experiment the quantity of 4-BrAn was equal to 1 mmol, 1.5 molar excess of PBA was used. Catalyst loading was 50 mg in each experiment. In the reactor of (ii) type, the amount of substrates, base, catalyst and volume of the liquid phase were twice lower, which was due to the less volume of (ii) reactor. Thus, the concentrations of all the reaction components were equal in both reactors while maintaining the same substrate-to-catalyst ratio. Reaction duration was 3 h.

Table 1: Synthesized mono- and bimetallic HPS-based catalysts

Sample designation	Au content, ± 0.05 wt.%	Pd content, ± 0.05 wt.%
Au/HPS	1.75	none
Pd/HPS-1	none	1.16
Au-Pd/HPS-1	1.80	1.15
Pd/HPS-2	none	0.85
Au-Pd/HPS-2	2.35	0.70
Pd/HPS-3	none	0.52
Au-Pd/HPS-3	2.15	0.35

Samples of reaction mixture were taken and analyzed via GC-MS (Shimadzu GCMS-QP2010S) equipped with a capillary column HP-1MS (100 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 was defined as $R = N_{4\text{-}BrAn} \times N_{Pd}^{-1} \times \tau^{-1} \times X$, where $N_{4\text{-}BrAn}$ and N_{Pd} are number of moles of 4-BrAn and Pd, respectively; X is conversion of 4-BrAn, and τ is the reaction time for achieving of conversion X.

3. Results and discussion

The effect of reduction method (in H_2 flow or with aqueous solution of $NaBH_4$) was studied (see Figure 1) while using shaker-type glass batch reactor.

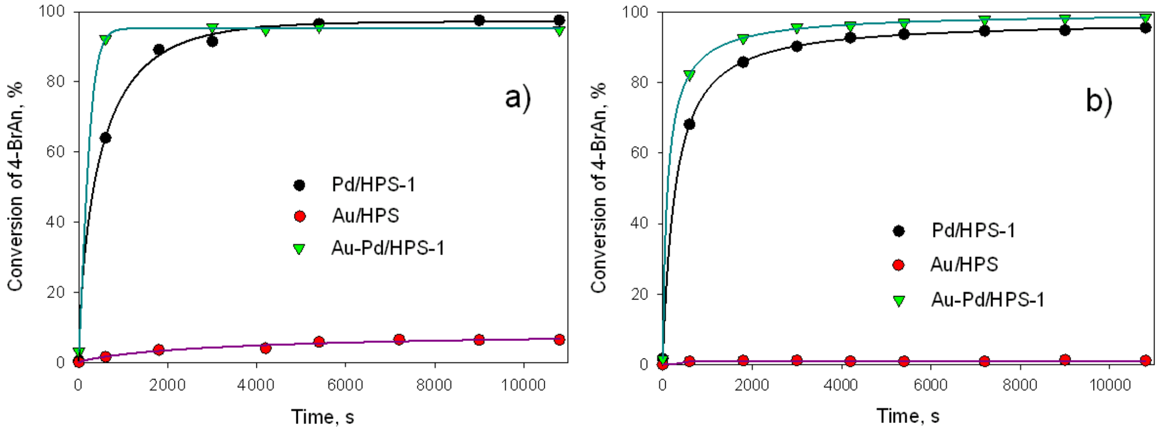

Figure 1: Results of testing of mono- (Au and Pd) and bimetallic (Au-Pd) catalysts at variation of reduction method, in H_2 flow (a) or with aqueous solution of $NaBH_4$ (b), using the reactor of (i) type

It is obvious (Figure 1) that conversion of 4-BrAn is extremely low while using Au/HPS catalyst (7.8 % in case of reduction with H_2 and 0.9 %in case of reduction with $NaBH_4$). Pd/HPS-1 catalyst revealed equal conversion of 4-BrAn (about 96.0 %) regardless of the reduction method. High activity of palladium catalyst is likely due to the fact that small NPs and Pd_n clusters were formed during the reduction (Nikoshvili et al., 2016). In the case of bimetallic catalyst, highest activity was found (conversion of 4-BrAn 99.0 %) for the sample reduced with $NaBH_4$. Moreover, regardless of the reduction method, bimetallic Au-Pd/HPS-1 was more active at the beginning of the reaction in comparison with Pd/HPS-1.

The results of testing mono- and bimetallic catalysts at variation of palladium content in the reactor of (i) type are presented in Table 2 and Figure 2 (it is noteworthy that all the samples were reduced with $NaBH_4$). For catalysts with palladium content of less than 1 wt.% an obvious positive effect of gold on catalyst activity was found: the initial reaction rate (designated as R – maximum activity) was more than order of magnitude higher in the case of bimetallic samples in comparison with monometallic ones. The sample Au-Pd/HPS-1 with highest

Pd content was an exception likely due to the formation of bulk Pd phase instead of thin shell, which resulted in behavior similar to Pd/HPS-1.

Table 2: Results of testing mono- and bimetallic catalysts at variation of palladium content

Catalyst	Conversion of 4-BrAn, %	Yield of 4-MBP, %	Maximum activity, R, h^{-1}	Synergy coefficient, Z
Pd/HPS-1	95.6	94.5	750	
Au-Pd/HPS-1	98.5	97.1	914	1.2
Pd/HPS-2	26.7	26.4	50	
Au-Pd/HPS-2	94.5	93.4	1018	20.3
Pd/HPS-3	26.3	26.0	75	
Au-Pd/HPS-3	73.3	72.4	824	11.0

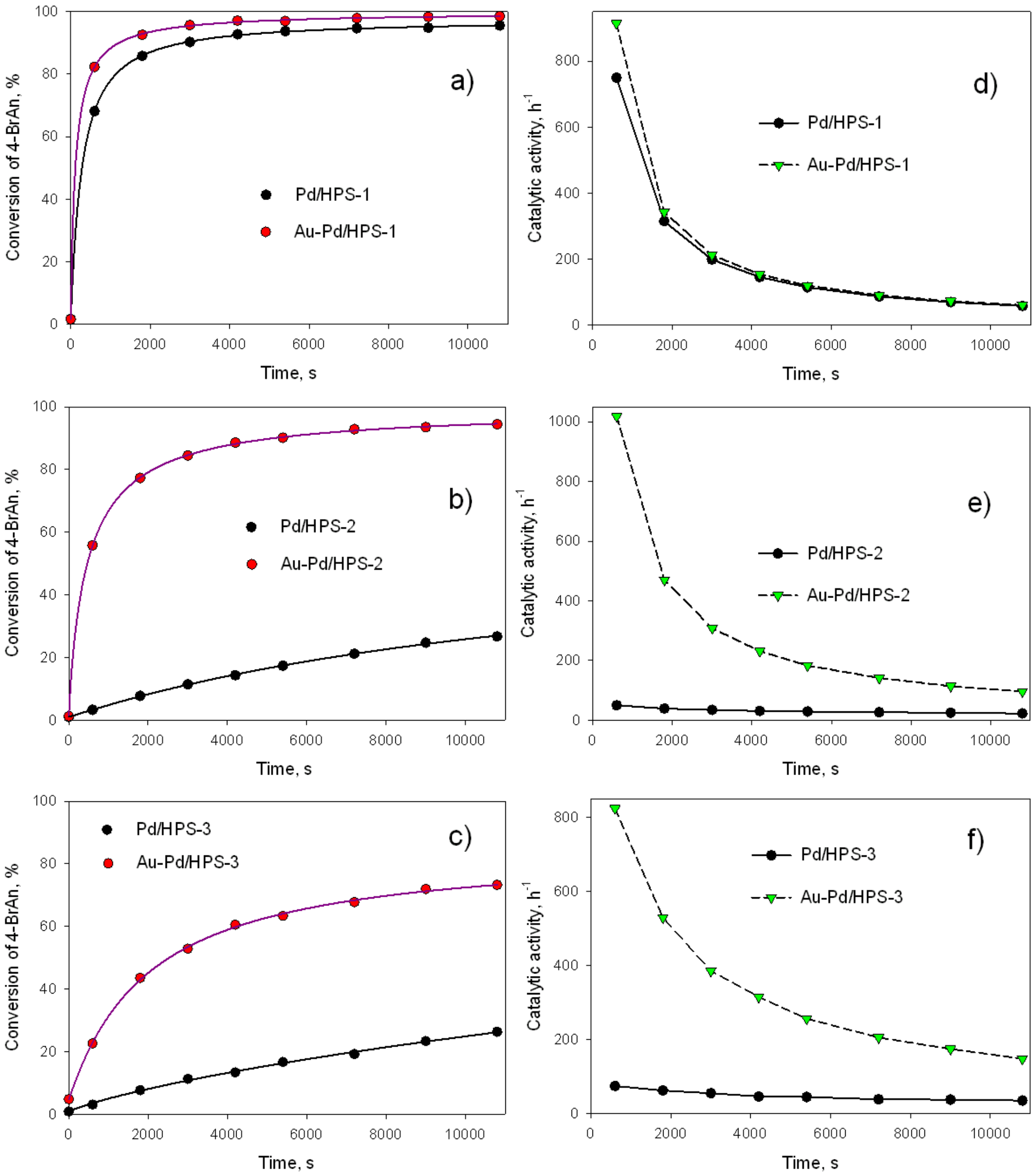

Figure 2: Influence of Pd content on catalytic activity of mono- and bimetallic HPS-based samples

It is noteworthy that for catalysts with Pd content of 0.35 wt.% and 0.70 wt.% about 3-fold increase of the yield of 4-MBP was observed compared tothe corresponding monometallic samples.

Thus the emerging synergistic effect occurred in bimetallic catalysts presumably having defined core-shell structure. In this connection, the synergy coefficients (Z) were calculated for the maximum observed activity *R* (Figure 2d-f) of palladium in mono- and bimetallic samples (since the Au/HPS activity was very low, it was not taken into account while calculating Z).

Figure 3 shows TEM image of Au-Pd/HPS-1 sample reduced with $NaBH_4$ (a) and comparison of NP size distribution for all the synthesized bimetallic catalysts (b).

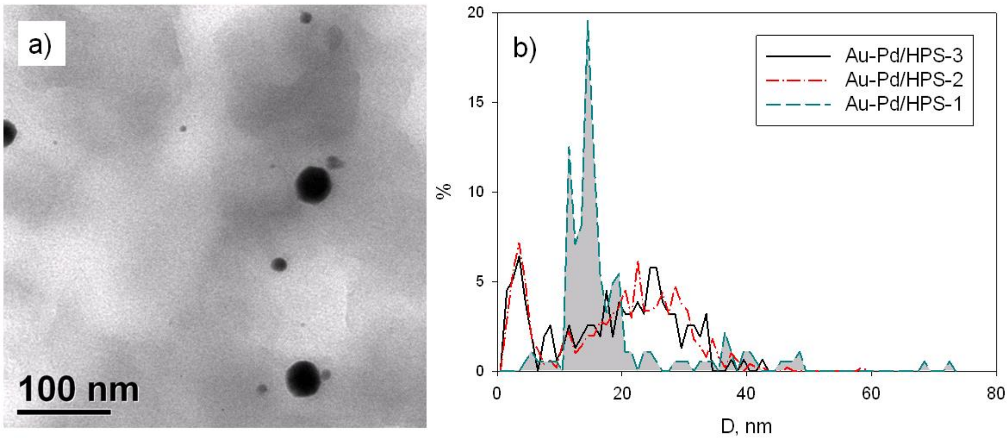

Figure 3: TEM image of Au-Pd/HPS-1 (a) and NP size distribution for the bimetallic HPS-based catalysts (b)

As shown in the Figure 3, for all three bimetallic catalysts the fraction of small NPs with diameters less than 10 nm was present. These small NPs could be explained either by Au-Pd core-shell NPs or by pure palladium particles, which were not interact with the surface of gold NPs during the catalyst synthesis. NPs with diameters higher than 10 nm were proposed to have bimetallic core-shell structure. Obviously, structures of Au-Pd/HPS-2 and Au-Pd/HPS-3 samples are similar.

One can be assumed that the decrease of Pd content in bimetallic samples may result in the thinning of Pd shell. In the case of Au-Pd/HPS-1 with highest palladium content, the properties of Pd shell were likely similar to that of bulk Pd NPs and thus almost no synergy effect was observed for this sample from the presence of Au in the catalyst composition.

The influence of the reactor type was also investigated for Au-Pd/HPS-3 catalyst reduced with $NaBH_4$. It was found (Figure 4) that in the case of (i) reactor (shaker-type) with extremely high intensity of stirring (more than 800 two-sided shaking per minute) the conversion of 4-BrAn achieved for 3 h was in 1.3 times higher in comparison with common glass batch reactor (ii) with magnetic stirrer (stirring rate 600 rpm).

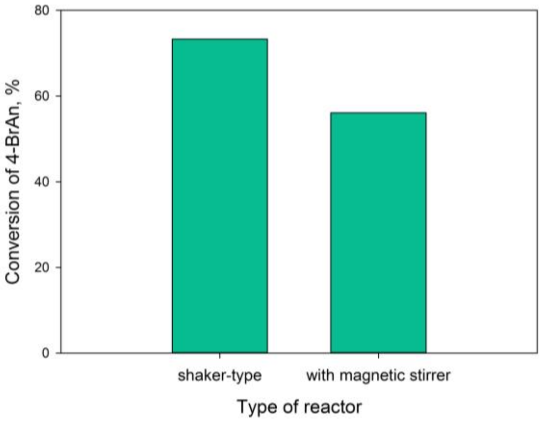

Figure 4: Influence of the reactor type on conversion of 4-BrAn

It is noteworthy that both experiments were carried out in the dark. However, while conducting the experiment in (ii) reactor under the visible light irradiation (300 W filament lamp was used) the same conversion of 4-BrAn was obtained as in the reactor of (i) type working in the dark.

4. Conclusions

HPS-supported mono- and bimetallic Au- and Pd-containing catalysts were found to be promising (active and selective) and simple in preparation for the Suzuki cross-coupling at mild temperatures along with the absence of the necessity to use phase-transfer agents. At mild reaction conditions (temperature 60°C, 1.5 mmol of NaOH, solvent EtOH/water mixture at volumetric ratio of 5:1), 98.5 % conversion of 4-BrAn was achieved after 3 h of Suzuki reaction in shaker-type reactor for bimetallic 1.80 %-Au-1.15 %-Pd/HPS catalyst preliminarily reduced with $NaBH_4$. The results of testing mono- and bimetallic catalysts at variation of palladium content revealed that gold has positive effect on catalytic activity.For bimetallic catalysts with palladium content of 0.35 wt.% and 0.70 wt.% approximately 3-fold increase the yield of 4-MBP was found in comparison with corresponding monometallic Pd samples.

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