

# Reduced Graphene Oxide-Supported CuPd Alloy Nanoparticles as Efficient Catalysts for the Sonogashira Cross-Coupling Reactions

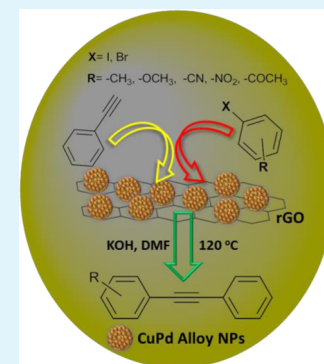
Sümeyra Diyarbakir, Hasan Can, and Önder Metin\*

Department of Chemistry, Faculty of Science, Atatürk University, 25240 Erzurum, Turkey

## S Supporting Information

**ABSTRACT:** Monodisperse CuPd alloy nanoparticles (NPs) were prepared by using a typical high-temperature organic solution phase protocol comprising the coreduction of copper(II) acetylacetonate and palladium(II) acetylacetonate by morpholine–borane complex in oleylamine and 1-octadecene solution at 80 °C. The presented synthesis protocol allows us to control the composition of CuPd alloy NPs by simply tuning the initial ratio of metal precursors and the Cu-rich Cu<sub>75</sub>Pd<sub>25</sub> NPs and Pd-rich Cu<sub>32</sub>Pd<sub>68</sub> were synthesized besides the Cu<sub>48</sub>Pd<sub>52</sub> NPs. Transmission electron microscopy studies revealed that most of the CuPd alloy NPs are polyhedral with an average diameter of 3.0 ± 0.3 nm. The alloy structure of CuPd NPs was confirmed by the detailed X-ray diffraction and X-ray photoelectron spectroscopy analysis. As-prepared CuPd NPs were deposited on reduced graphene oxide (rGO) by using a liquid self-assembly method (rGO-CuPd) and used as catalysts in the Sonogashira cross-couplings of various aryl iodides or bromides and phenyl acetylene under the optimized reaction conditions. Among the three compositions of CuPd alloy NPs tested in the Sonogashira couplings, the rGO-Cu<sub>48</sub>Pd<sub>52</sub> gave the best yields in shorter reaction times and therefore it was used for further coupling reactions. The results demonstrated that rGO-Cu<sub>48</sub>Pd<sub>52</sub> were efficient catalysts for the Sonogashira reaction of various aryl halides with phenylacetylene. The coupling reactions proceeded smoothly with both electron-rich and electron-deficient aryl iodides and aryl bromides, affording the desired biaryl products in high yields. This is the first example of the employment of monodisperse CuPd alloy NPs with composition control in the Sonogashira cross-coupling reactions.

**KEYWORDS:** CuPd, alloy nanoparticles, composition control, reduced graphene oxide, heterogeneous catalyst, Sonogashira cross-coupling



## INTRODUCTION

Aryl alkynes that are found in numerous natural products are versatile intermediates in the synthesis of various agrochemicals, medicines, and functional organic molecules.<sup>1</sup> Although there are many routes for the construction of substituted aryl alkynes, the Sonogashira cross-coupling reaction of terminal alkynes with aryl halides has become the most efficient one.<sup>2</sup> Aryl-substituted alkynes can be routinely prepared by Sonogashira coupling reactions in the presence of a palladium catalyst and a copper cocatalyst in an amine as the solvent to obtain a good yield.<sup>3,4</sup> However, the use of Cu as a cocatalyst raises several drawbacks such as generation of homocoupling products of the terminal alkyne along with the desired coupling product and the use of an extra environmentally unfriendly chemical (CuX).<sup>5</sup> Therefore, remarkable efforts have been dedicated to develop Sonogashira cross-coupling procedures that are utilizable in the absence of copper additives, so-called copper-free Sonogashira coupling.<sup>6–8</sup> Those copper-free Sonogashira coupling reactions are generally performed in the presence of an excess amount of amine either as base or even as solvent, which decreases the environmental/economic impact of the methodology. In this regard, a Sonogashira cross-coupling protocol that allows the exclusion of copper additives and excess use of amine is highly desirable.

On the other hand, the use of a palladium catalyst is indispensable for the Sonogashira cross-coupling reactions like all other coupling reactions.<sup>9,10</sup> After careful examination of the literature about the Sonogashira coupling reactions, it can be easily seen that mostly palladium complexes in the presence of various ligands have been employed as homogeneous catalysts.<sup>11</sup> Although those homogeneous catalysts showed notable activities, the use of homogeneous catalysts has numerous drawbacks such as the difficulty in the separation of the reaction product from the catalyst, nonreusability, and instability in air.<sup>12</sup> Because sustainable chemistry encompasses the use of reusable catalysts, the search for the heterogeneous catalysts to replace the homogeneous ones is a key issue. In this respect, the use of transition metal nanoparticles (NPs) as catalysts in the coupling reactions has appeared to be a promising solution because they combine the advantages of homogeneous and heterogeneous catalysts, so-called semiheterogeneous catalysts.<sup>13,14</sup> Recently, a variety of Pd NPs were reported to be highly active and reusable catalysts in the Sonogashira coupling reactions.<sup>15</sup> Although some of these Pd NPs showed high efficiencies in the absence of a CuX cocatalyst, others

Received: November 7, 2014

Accepted: January 16, 2015

Published: January 16, 2015

provided low efficiencies even in the presence of amine additives.<sup>16–18</sup> The bimetallic alloy NPs comprising a noble metal and a first-row transition metal such as iron, cobalt, nickel, and copper show an enhancement in the catalytic properties owing to the synergistic effects between the two distinct metals.<sup>19</sup> Therefore, the use of a bimetallic alloy NP catalyst comprising both Pd and Cu metals on its surface will be beneficial for the Sonogashira couplings to obtain high yields. Besides this advantage, CuPd alloy NPs are cost-effective catalysts compared to monometallic Pd NPs due to Pd metal being used less. In recent years, several bimetallic Pd NPs have been tested as catalysts in the Sonogashira couplings including Ni/Pd core/shell NPs,<sup>20</sup> Pd–Co bimetallic nanospheres,<sup>21,22</sup> PdCo alloy NPs,<sup>23,24</sup> Pd–Cu mixed NPs,<sup>25</sup> and nano-Pd/PdO/Cu system.<sup>26</sup> In a very recent study, Gao et al. reported Pd/Cu nanoalloys supported on montmorillonite as the catalysts for the Sonogashira couplings of aryl iodide and various alkynes.<sup>27</sup> However, there is no example of the use of reduced graphene oxide-supported CuPd alloy NPs with the perfect alloy structure and composition-control synthesis in the Sonogashira coupling reactions of phenyl acetylene and various aryl halides including iodides and bromides.

We report herein for the first time the employment of monodisperse CuPd alloy NPs supported on reduced graphene oxide (rGO) as catalysts for the Sonogashira couplings of phenyl acetylene and various aryl iodides and bromides under mild conditions. Monodisperse CuPd alloy NPs were synthesized by our established procedure comprising the coreduction of copper(II) acetylacetonate and palladium(II) acetylacetonate by morpholine–borane complex in oleylamine and 1-octadecene solution at 80 °C.<sup>28</sup> As-synthesized CuPd alloy NPs were deposited on rGO (rGO-CuPd) via the liquid-phase self-assembly method<sup>29,30</sup> before their use as catalysts for the Sonogashira couplings. Colloidal CuPd alloy NPs and rGO-CuPd catalysts were characterized by transmission electron microscopy (TEM), powder X-ray diffraction (XRD), X-ray photoelectron spectroscopy (XPS), and inductively coupled plasma atomic emission spectroscopy (ICP-MS). Composition of the CuPd alloy NPs could be controlled by simply tuning the ratio of metal precursors. Among the three compositions (Cu<sub>75</sub>Pd<sub>25</sub>, Cu<sub>48</sub>Pd<sub>52</sub>, and Cu<sub>32</sub>Pd<sub>68</sub>) tested in the Sonogashira couplings, the Cu<sub>48</sub>Pd<sub>52</sub> provided the best performance in terms of both chemical yields of the desired products and reaction time under the optimized reaction conditions. rGO-Cu<sub>48</sub>Pd<sub>52</sub>-catalyzed Sonogashira couplings were studied on various aryl iodides or bromides and phenyl acetylene under the optimized reaction conditions and all the desired coupling products were obtained by high chemical yields reaching up to 96% in short reaction times.

## EXPERIMENTAL SECTION

**Materials.** Copper(II) acetylacetonate (Cu(acac)<sub>2</sub>, 97%), palladium(II) acetylacetonate (Pd(acac)<sub>2</sub>, 99%), morpholine–borane complex (MB, 97%), oleylamine (OAm, >70%), 1-octadecene (ODE, 90%), hexane (97%), ethanol (99%), potassium permanganate (KMnO<sub>4</sub>, >99%), sodium nitrate (NaNO<sub>3</sub>, >99%), and dimethylformamide (DMF, >99%) were all purchased from Sigma-Aldrich. Natural graphite flakes (average particle size, 325 mesh) and all the organic compounds used in the Sonogashira coupling reactions were purchased from Alfa-Aesar and used as-received. Hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>, 30%) and sulfuric acid (H<sub>2</sub>SO<sub>4</sub>, 95–98%) were purchased from Merck. Deionized water was distilled by a water purification system (Milli-Q System).

**Instrumentation.** Transmission electron microscopy (TEM) images were obtained by FEI Technai G<sup>2</sup> Spirit BiO(TWIN) at 120 kV. XRD patterns were recorded on a Rigaku Miniflex diffractometer with Cu K $\alpha$  radiation (30 kV, 15 mA,  $\lambda = 1.54051 \text{ \AA}$ ) over a  $2\theta$  range from 5° to 90° at room temperature. Elemental analysis measurements were carried out on a PerkinElmer NexION ICP-MS after each sample was completely dissolved in aqua-regia (HCl/HNO<sub>3</sub>; 3/1 v/v ratio). X-ray photoelectron microscopy studies were performed by PHI Versaprobe 5000 Scanning XPS with a monochromatic Al K $\alpha$  source. <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on a Bruker Avance DPX 400 MHz spectrometer.

**Synthesis of Reduced Graphene Oxide (rGO).** rGO was prepared by using a well-established protocol including two steps: (i) synthesis of graphite oxide via modified Hummer's method<sup>31</sup> and (ii) reduction of graphene oxide by refluxing its DMF solution for 6 h.<sup>32,33</sup> The details of the rGO synthesis procedure and the characterization of rGO can be found in our recent reports.<sup>34</sup>

**Synthesis of CuPd Alloy Nanoparticles.** CuPd alloy NPs were prepared by using our reported protocol.<sup>28</sup> In a typical synthesis of Cu<sub>48</sub>Pd<sub>52</sub> alloy NPs, 0.30 mmol of Cu(acac)<sub>2</sub> and 0.30 mmol of Pd(acac)<sub>2</sub> were dissolved in 3 mL of OAm. This solution was then injected into a mixture of morpholine–borane (1.5 mmol), OAm (3 mL), and ODE (7 mL) at 80 °C. The resulting mixture was subsequently raised to 100 °C and kept at this temperature for 1 h. Finally, the NPs were washed in a mixture of acetone and ethanol and centrifuged two times at 9000 rpm for 12 min before redispersing them in hexane. With use of the current protocol, Cu<sub>32</sub>Pd<sub>68</sub> alloy NPs were synthesized by using 0.15 mmol of Cu(acac)<sub>2</sub> and 0.35 mmol of Pd(acac)<sub>2</sub>; Cu<sub>75</sub>Pd<sub>25</sub> alloy NPs were prepared by using 0.3 mmol of Cu(acac)<sub>2</sub> and 0.1 mmol of Pd(acac)<sub>2</sub>. Additionally, monometallic Pd NPs were prepared by using the same protocol, but in the absence of Cu(acac)<sub>2</sub>.

**Assembly of CuPd Alloy NPs on rGO.** To use CuPd alloy NPs as catalysts in the Sonogashira coupling reactions, they were deposited on rGO by using a liquid self-assembly method.<sup>29,30</sup> In a typical procedure, 80 mg of rGO was dispersed in 40 mL of ethanol and 20 mL of hexane and then 40 mg of hexane dispersion of CuPd alloy NPs were added into the rGO dispersion. Next, the resulted mixture was sonicated for 1 h. To separate the rGO-CuPd catalysts from the solution, the mixture was centrifuged at 7500 rpm for 10 min after the ethanol addition and then dried by vacuuming.

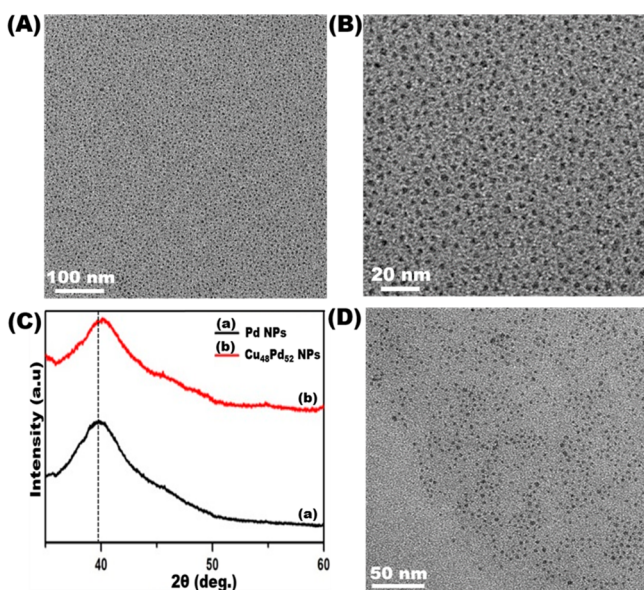
**General Procedure for the rGO-CuPd-Catalyzed Sonogashira Couplings.** In a typical procedure, 10 mg of rGO-CuPd catalyst, aryl halide (1 mmol), phenyl acetylene (1 mmol), and KOH (2 mmol) were well-dispersed in 5 mL of DMF in a 25 mL round-bottom flask in air. Then the mixture was heated up to 120 °C in an oil bath and kept at this temperature for 1 h under vigorous stirring. Next, the resulted mixture was filtrated by washing ethyl acetate or dichloromethane to separate the catalyst. The organic material in the eluent was washed seven times by dichloromethane and water to remove DMF. The resulted mixture was dried by the addition of Na<sub>2</sub>SO<sub>4</sub> and purified by the addition of dichloromethane following evaporation by a rotary evaporator.

**Reusability of rGO-CuPd Catalysts in the Sonogashira Coupling Reactions.** A typical Sonogashira coupling of phenyl acetylene and iodo toluene was initiated as described in the section General Procedure for the rGO-CuPd-Catalyzed Sonogashira Couplings. After the completion of the reaction,

the rGO-CuPd catalyst was separated from the reaction mixture via simple centrifugation at 7500 rpm and washed several times with dichloromethane and dried under vacuum. Next, another typical coupling reaction was started by using the recovered rGO-Cu<sub>48</sub>Pd<sub>52</sub> catalyst as described in the section entitled General Procedure for the rGO-CuPd-Catalyzed Sonogashira Couplings. This process was repeated by five runs.

## RESULTS AND DISCUSSION

Monodisperse CuPd NPs were prepared by using a surfactant-assisted organic solution phase protocol comprising the coreduction of Cu(acac)<sub>2</sub> (0.3 mmol) and Pd(acac)<sub>2</sub> (0.3 mmol) by MB in OAm and ODE solution at 80 °C.<sup>28</sup> In the protocol, MB served as a mild-reducing agent and OAm and ODE were used as a surfactant and solvent, respectively. The synthesis protocol gave the Cu<sub>48</sub>Pd<sub>52</sub> NPs that is determined by ICP-MS analysis. The current synthesis protocol allows us to have composition control over the CuPd NPs by simply tuning the initial ratio of metal precursors. The Cu-rich Cu<sub>75</sub>Pd<sub>25</sub> NPs and Pd-rich Cu<sub>32</sub>Pd<sub>68</sub> were synthesized besides the Cu<sub>48</sub>Pd<sub>52</sub> NPs (see Figure S1 for the representative TEM images of colloidal Cu<sub>32</sub>Pd<sub>68</sub> and Cu<sub>75</sub>Pd<sub>25</sub> NPs). The size and shape of Cu<sub>48</sub>Pd<sub>52</sub> NPs were analyzed by TEM (Figure 1A,B). As clearly seen from



**Figure 1.** (A,B) Representative TEM images of as-prepared Cu<sub>48</sub>Pd<sub>52</sub> NPs at different magnifications, (C) XRD patterns of colloidal Pd and Cu<sub>48</sub>Pd<sub>52</sub> NPs taken from their hexane dispersion, and (D) a representative TEM image of rGO-Cu<sub>48</sub>Pd<sub>52</sub> catalyst taken from the ethanol solution.

the TEM images taken at different magnifications, most of the Cu<sub>48</sub>Pd<sub>52</sub> NPs are polyhedral with an average diameter of  $3.0 \pm 0.3$  nm with a standard deviation of 10%, which indicates the monodisperse particle size distribution. XRD patterns of the Pd and Cu<sub>48</sub>Pd<sub>52</sub> NPs assemblies (Figure 1C) show a typical (111) and (200) diffractions of the face-centered cubic phase with the small shift in the (111) plane of Cu<sub>48</sub>Pd<sub>52</sub> NPs indicating its solid-solution (alloy) structure. As-prepared Cu<sub>48</sub>Pd<sub>52</sub> NPs were deposited on rGO by using a liquid self-assembly method.<sup>29,30</sup> Figure 1D shows a representative TEM image of rGO-Cu<sub>48</sub>Pd<sub>52</sub> catalysts taken from the ethanol dispersion (see Figure S2 for the additional TEM images of rGO-Cu<sub>48</sub>Pd<sub>52</sub>

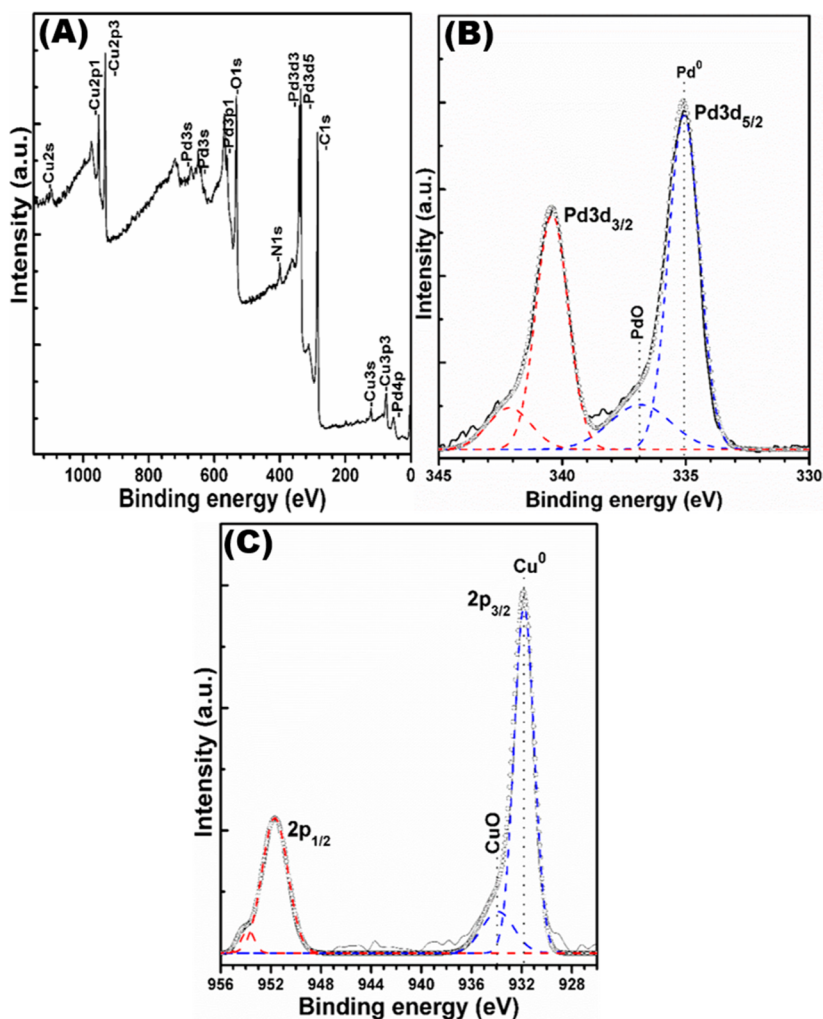
catalysts). As clearly seen from Figure 1D and Figure S2, the Cu<sub>48</sub>Pd<sub>52</sub> alloy NPs were well-dispersed on rGO nanosheets by preserving their particle size distribution without any aggregates formation. The ICP-MS analyses performed on different rGO-Cu<sub>48</sub>Pd<sub>52</sub> samples revealed that the catalysts contain approximately 13 wt % metal.

XPS measurements were performed on rGO-Cu<sub>48</sub>Pd<sub>52</sub> catalysts to investigate their surface composition and to find the chemical state of the metals on their surface. Figure 2A shows the XPS survey spectrum of rGO-Cu<sub>48</sub>Pd<sub>52</sub> catalyst that reveals the existence of C, N, Cu, Pd, and O elements in the sample. The Cu/Pd atomic ratio at the rGO-CuPd catalyst surface was measured to be 3.7/4.2, which is consistent with the alloy composition determined by ICP-MS. Figure 2B shows the deconvoluted high-resolution XPS spectrum for Pd 3d core level with two major peaks at 335.1 and 340.4 eV, which are corresponding to the Pd 3d<sub>5/2</sub> and Pd 3d<sub>3/2</sub>, respectively. The binding energy difference between the major peaks is 5.3 eV. It is concluded by the detailed examination of the deconvoluted XPS spectra that Pd was found mostly in the zerovalent state (335.1 eV, 89%), but a small portion of PdO was detectable in the sample (336.9 eV, 11%). In the case of Cu on the surface of rGO-Cu<sub>48</sub>Pd<sub>52</sub> catalyst (Figure 2C), it was found mostly in the metallic state (931.8 eV, 91%), but there was also a small amount of CuO detected in the sample (934 eV, 9%). Moreover, a shift of 0.8 eV to lower binding energy observed on the Cu 2p<sub>3/2</sub> peak (931.9 eV) compared to the reference data (932.62 eV)<sup>35</sup> indicates alloying of Cu and Pd.

After the detailed characterization of rGO-Cu<sub>48</sub>Pd<sub>52</sub>, they were tested as catalysts in the Sonogashira coupling reactions. The rGO-Cu<sub>48</sub>Pd<sub>52</sub> catalyzed Sonogashira coupling reactions were initially optimized by screening various bases, solvents, catalyst loadings, and temperatures in the coupling reaction of iodo toluene and phenyl acetylene. The results have been depicted in Table 1. As seen from Table 1, KOH provided the best yield (95%) among a variety of bases (K<sub>2</sub>CO<sub>3</sub>, KOH, NaOH, and Na<sub>2</sub>CO<sub>3</sub>) tested in the Sonogashira coupling reaction. Among the solvents tested (DMF, H<sub>2</sub>O, DMSO, and DMF/H<sub>2</sub>O mixture (v/v = 3/2)), the best yield (95%) was obtained by using DMF as the solvent. In the presence of different catalyst loadings (5, 10, and 15 mg), 10 mg of rGO-Cu<sub>48</sub>Pd<sub>52</sub> was found to be the optimum loading. Finally, the Sonogashira coupling reactions were performed at various temperatures (50, 80, 100, and 120 °C) and 120 °C was concluded to be the optimal one. Upon these results, the optimized reaction conditions for rGO-Cu<sub>48</sub>Pd<sub>52</sub>-catalyzed Sonogashira reactions were found to be KOH as base, DMF as solvent, 10 mg of rGO-Cu<sub>48</sub>Pd<sub>52</sub> as catalyst, and 120 °C as the temperature and were used for further coupling reactions.

Employing the optimized reaction conditions, we next studied the composition effect on the performance of rGO-Cu<sub>48</sub>Pd<sub>52</sub> catalysts in the Sonogashira cross-coupling reaction of 4-iodo-toluene with phenyl acetylene and the results were depicted in Table 2. Among the three compositions tested (Cu<sub>32</sub>Pd<sub>68</sub>, Cu<sub>48</sub>Pd<sub>52</sub>, and Cu<sub>75</sub>Pd<sub>25</sub>), the rGO-Cu<sub>48</sub>Pd<sub>52</sub> provided the best performance in terms of the product yield and reaction time in the Sonogashira couplings under the optimized reaction conditions. Therefore, it was decided that the rGO-Cu<sub>48</sub>Pd<sub>52</sub> catalyst should be used for further coupling reactions.

The optimized conditions were then applied to the Sonogashira couplings of various aryl iodides/bromides and phenyl acetylene and the results were depicted in Table 3.



**Figure 2.** (A) XPS survey spectra, (B) deconvoluted high-resolution XPS spectrum of Pd 3d core-level, and (C) deconvoluted high-resolution XPS spectrum of Cu 2p core-level for rGO-Cu<sub>48</sub>Pd<sub>52</sub> catalyst.

**Table 1. Optimization Experiments for the rGO-Cu<sub>48</sub>Pd<sub>52</sub>-Catalyzed Sonogashira Couplings of 4-Iodo-toluene and Phenyl Acetylene**

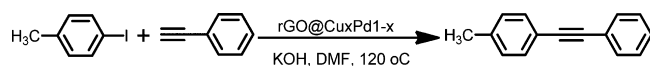


| base                            | solvent               | temperature (°C) | catalyst amount | time (h) | yield <sup>a,b</sup> (%) |
|---------------------------------|-----------------------|------------------|-----------------|----------|--------------------------|
| K <sub>2</sub> CO <sub>3</sub>  | DMF                   | 120              | 10 mg           | 1        | 50                       |
| KOH                             | DMF                   | 120              | 10 mg           | 1        | 95                       |
| Na <sub>2</sub> CO <sub>3</sub> | DMF                   | 120              | 10 mg           | 1        | 30                       |
| NaOH                            | DMF                   | 120              | 10 mg           | 1        | 60                       |
| KOH                             | DMSO                  | 120              | 10 mg           | 1        | 55                       |
| KOH                             | DMF                   | 120              | 10 mg           | 1        | 95                       |
| KOH                             | water                 | 120              | 10 mg           | 1        | 66                       |
| KOH                             | DMF/water (v/v = 3/2) | 120              | 10 mg           | 1        | 75                       |
| KOH                             | DMF                   | 50               | 10 mg           | 1        |                          |
| KOH                             | DMF                   | 80               | 10 mg           | 1        | 40                       |
| KOH                             | DMF                   | 100              | 10 mg           | 1        | 60                       |
| KOH                             | DMF                   | 120              | 10 mg           | 1        | 95                       |
| KOH                             | DMF                   | 120              | 5 mg            | 1        | 50                       |
| KOH                             | DMF                   | 120              | 10 mg           | 1        | 95                       |
| KOH                             | DMF                   | 120              | 15 mg           | 1        | 95                       |

<sup>a</sup>Reaction conditions: 4-iodo-toluene (1 mmol), phenyl acetylene (1 mmol), base (2 mmol), and solvent (5 mL). <sup>b</sup>Isolated yield.

The results demonstrated that rGO-Cu<sub>48</sub>Pd<sub>52</sub> were efficient catalysts for the Sonogashira reaction of various aryl halides

with phenylacetylene. All the coupling reactions proceeded smoothly with both electron-rich and electron-deficient aryl

**Table 2. Composition-Control Experiments for the rGO-Cu<sub>x</sub>Pd<sub>1-x</sub>-Catalyzed Sonogashira Couplings of 4-Iodo-toluene and Phenyl Acetylene**

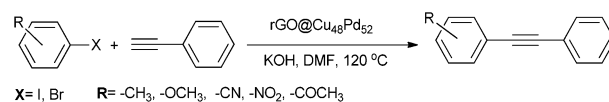
| composition                       | time (h) | yield <sup>a,b</sup> (%) |
|-----------------------------------|----------|--------------------------|
| Cu <sub>32</sub> Pd <sub>68</sub> | 1        | 50                       |
| Cu <sub>48</sub> Pd <sub>52</sub> | 1        | 95                       |
| Cu <sub>75</sub> Pd <sub>25</sub> | 1        | 30                       |

<sup>a</sup>Reaction conditions: iodo benzene (1 mmol), phenyl acetylene (1 mmol), rGO-Cu<sub>x</sub>Pd<sub>1-x</sub> (10 mg), KOH (2 mmol), and DMF (5 mL).

<sup>b</sup>Isolated yield.

iodides and aryl bromides, affording the desired biaryl products in high yields (Table 3, entries 1–11). First, the Sonogashira

couplings of aryl iodides with phenylacetylene were tested and all the biphenylacetylene products were obtained by yields higher than 90% in 1 h (Table 3, entries 1–6). As expected, the aryl iodides bearing electron-donating groups (–CH<sub>3</sub>, –OCH<sub>3</sub>) provided lower yields compared to those possessing electron-withdrawing groups (–NO<sub>2</sub>, –CN) due to the increase in the electron density of aromatic ring that makes it difficult to remove iodo from the substrate (Table 3, entries 2 and 3). On the other hand, the rGO-Cu<sub>48</sub>Pd<sub>52</sub>-catalyzed Sonogashira couplings worked also for the aryl bromides whose coupling reactions are known to be more difficult compared to aryl iodides. Electron-poor and electron-rich aryl bromides (Table 3, entries 7–12) were successfully coupled to biphenylacetylene derivatives with the yields higher than 70% in 5 h. It is noteworthy to mention that we also tested the several aryl

**Table 3. rGO-Cu<sub>48</sub>Pd<sub>52</sub>-Catalyzed Sonogashira Couplings of Various Aryl Halides and Phenyl Acetylene**

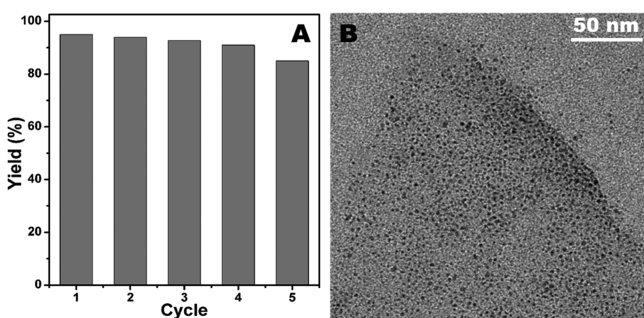
| Entry | Aryl halide | Product | Time (h) | Yield <sup>a],[b]</sup> (%) |
|-------|-------------|---------|----------|-----------------------------|
| 1     |             |         | 1        | 93                          |
| 2     |             |         | 1        | 90                          |
| 3     |             |         | 1        | 89                          |
| 4     |             |         | 1        | 94                          |
| 5     |             |         | 1        | 96                          |
| 6     |             |         | 5        | 83                          |
| 7     |             |         | 5        | 74                          |
| 8     |             |         | 5        | 71                          |
| 9     |             |         | 5        | 70                          |
| 10    |             |         | 5        | 88                          |
| 11    |             |         | 5        | 93                          |
| 12    |             |         | 5        | 89                          |

<sup>a</sup>Reaction conditions: iodo benzene (1 mmol), phenyl acetylene (1 mmol), rGO-Cu<sub>48</sub>Pd<sub>52</sub> (10 mg), KOH (2 mmol), and DMF (5 mL). <sup>b</sup>Isolated yield.

chlorides by the Sonogashira coupling reactions, but no product was obtained with yields higher than 15% in 24 h.

To exhibit the high catalytic activity of rGO-supported  $\text{Cu}_{48}\text{Pd}_{52}$  alloy NPs in the Sonogashira couplings, the monometallic Pd NPs were also synthesized by using the same recipe of  $\text{Cu}_{48}\text{Pd}_{52}$  alloy NPs but in the absence of  $\text{Cu}(\text{acac})_2$  and then supported on rGO. The rGO-Pd catalysts were tested in the Sonogashira coupling of 4-iodo-toluene and phenyl acetylene under the optimized reaction conditions and the respective coupling product was obtained by the yield of only 25% in 1 h. This result clearly reveals that the alloying of Pd with Cu enhances its activity in the Sonogashira coupling reactions, dramatically owing to the synergistic effects between the Pd and Cu. Moreover, it is noteworthy to mention that rGO might also have a role in the high activity of  $\text{Cu}_{48}\text{Pd}_{52}$  alloy NPs in the Sonogashira reactions as we demonstrated in our recent studies.<sup>30,36,37</sup> The role of rGO in the catalytic reactions is ascribed to its very good properties for dispersing and stabilizing the NPs, to the more favorable accessibility of reagent molecules to active centers due to its 2D configuration, and to the intimate interaction between the NPs and graphene which leads to efficient electron transfer and/or mass transport between the support and the catalyst. Additionally, the rGO used in this study was prepared by the reduction of graphene oxide in DMF solution. Therefore, a small portion of the functional groups ( $-\text{COOH}$ ,  $-\text{OH}$ , and epoxide) still remained in the rGO structure, which makes it more dispersible in polar solvents such as DMF in this study. The higher dispersion of support materials makes the CuPd alloy NPs and aromatic compounds interaction more facile along with the defects of rGO that makes the  $\pi-\pi$  interactions.

The reusability is a key property for a heterogeneous catalyst that should be studied. In this regard, we performed a reusability test for the rGO- $\text{Cu}_{48}\text{Pd}_{52}$  catalysts in the Sonogashira couplings of 4-iodo-toluene and phenyl acetylene under the optimized conditions. The rGO- $\text{Cu}_{48}\text{Pd}_{52}$  catalysts were stable during the catalytic reaction and easily separated by centrifugation from the reaction solution at the end of the reaction. A new batch of coupling reactions was started by using the separated rGO- $\text{Cu}_{48}\text{Pd}_{52}$  catalysts and this process was continued up to the five cycles. Figure 3A shows the cycle



**Figure 3.** (A) Cycle number versus percentage yield graph for the five runs reusability test of rGO- $\text{Cu}_{48}\text{Pd}_{52}$  catalysts in Sonogashira couplings of 4-iodo-toluene and phenyl acetylene; (B) a representative TEM image of rGO- $\text{Cu}_{48}\text{Pd}_{52}$  catalysts after the five runs reusability test.

number versus percentage yield for the five runs reusability test of rGO- $\text{Cu}_{48}\text{Pd}_{52}$  catalysts in the Sonogashira coupling. As seen by Figure 3A, the rGO- $\text{Cu}_{48}\text{Pd}_{52}$  catalysts were still active and provide 83% yield in 1 h after five runs. Moreover, no important change was observed in the morphology of

rGO- $\text{Cu}_{48}\text{Pd}_{52}$  catalysts after the five runs, which is concluded by the TEM image given in Figure 3B.

To elucidate whether rGO- $\text{Cu}_{48}\text{Pd}_{52}$  is the real catalyst or just serves as the source for the Cu(II) or Pd(II) ions that leaches out into the solution to form the active catalyst species, a hot filtration test was performed. The Sonogashira coupling of 4-iodo-toluene and phenyl boronic acid was studied as the test reaction for the filtration test. Once 30% of the reaction was completed (followed by TLC), the rGO- $\text{Cu}_{48}\text{Pd}_{52}$  catalysts were separated by centrifugation and the reaction was then continued without catalysts in the reaction flask for an additional 1 h at 120 °C. There was no noticeable biaryl formation determined that reveals the amount of Pd leaching out was negligible and the catalyst was indeed heterogeneous in nature.

As we mentioned in the Introduction, many Pd NPs have been tested as catalysts for the Sonogashira coupling reactions. Therefore, to evaluate the efficiency of rGO- $\text{Cu}_{48}\text{Pd}_{52}$  catalyzed Sonogashira coupling reactions, the catalytic system was compared with several Pd nanocatalysts. The in situ generated montmorillonite nanopores-stabilized Pd NPs were tested in the Sonogashira coupling of iodo benzene with phenyl acetylene in the presence of  $\text{Et}_3\text{N}$  as base and the respective coupling products were obtained by 90% yield in 3 h,<sup>38</sup> whereas the same coupling product yielded 95% within 1 h in the presence of rGO- $\text{Cu}_{48}\text{Pd}_{52}$  catalysts (Table 3, entry 1). In another example, MOF-5-supported Pd NPs were tested in the Sonogashira coupling of 4-iodo-toluene with phenyl acetylene and gave 90% yield within 3 h,<sup>39</sup> while the same coupling products were obtained by 95% yield in 1 h by our catalytic system (Table 3, entry 2). In another study, polypyrrole globules-encapsulated Pd NPs were tested in the Sonogashira coupling of *p*-nitro iodo-benzene with phenyl acetylene and the respective coupling product yielded 85% in 4 h,<sup>40</sup> but our catalytic system gave the same coupling product with 96% in 1 h (Table 3, entry 4). These results clearly indicate that rGO- $\text{Cu}_{48}\text{Pd}_{52}$  is a highly efficient catalyst for the Sonogashira cross-coupling reactions.

## CONCLUSIONS

We have demonstrated for the first time that monodisperse CuPd alloy NPs supported on rGO can successfully be employed as catalysts in the Sonogashira cross-coupling reactions under mild/aerobic conditions. A variety of aryl iodides or bromides were successfully coupled to the biphenylacetylene derivatives with high yields via rGO- $\text{Cu}_{48}\text{Pd}_{52}$ -catalyzed Sonogashira cross-coupling reactions. The better yields and shorter reaction times were provided by the rGO- $\text{Cu}_{48}\text{Pd}_{52}$  catalyst compared to other alloy compositions and monometallic Pd NPs, indicating that alloying of Cu and Pd at optimum atomic ratio forms a highly active catalyst in the Sonogashira coupling reactions owing to the synergistic effects between the Pd and Cu metals. The catalytic method presented here has obvious advantages such as being recyclable, easy to operate, and environmentally friendly over the conventional Sonogashira couplings in which mostly homogeneous Pd complexes are used as catalyst in the presence of CuX and amine additives. We believe that the method presented here will open new perspectives to organic chemists for the application of rGO-CuPd catalysts in various metal-catalyzed organic reactions.

## ASSOCIATED CONTENT

### Supporting Information

Additional characterization data for the catalysts (Figures S1 and S2) and  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra of the coupling products. This material is available free of charge via the Internet at <http://pubs.acs.org/>.

## AUTHOR INFORMATION

## Corresponding Author

\*E-mail: ometin@atauni.edu.tr; ondermetin1981@hotmail.com.

## Notes

The authors declare no competing financial interest.

## ACKNOWLEDGMENTS

The partial financial support by Turkish Academy of Science Young Scientist Program (TUBA-GEBIP) and Atatürk University Scientific Research Project Council (Project No: 2013/88) are greatly acknowledged.

## REFERENCES

- (1) Stang, P. J.; Diederich, F. *Modern Acetylene Chemistry*; Wiley-VCH: Weinheim, Germany, 1995.
- (2) Sonogashira, K. Development of Pd-Cu Catalyzed Cross-Coupling of Terminal Acetylenes with  $sp^2$ -Carbon Halides. *J. Organomet. Chem.* **2002**, *653*, 46–49.
- (3) Sonogashira, K. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, Germany, 1998; pp 203–229.
- (4) Sonogashira, K. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E.-i., Ed.; Wiley-VCH: New York, 2002; p 493.
- (5) Siemsen, P.; Livingston, R. C.; Diederich, F. Acetylenic Coupling: A Powerful Tool in Molecular Construction. *Angew. Chem., Int. Ed.* **2000**, *39*, 2632–2657.
- (6) Fukuyama, T.; Shinmen, M.; Nishitani, S.; Sato, M.; Ryu, I. A. Copper-Free Sonogashira Coupling Reaction in Ionic Liquids and Its Application to a Microflow System for Efficient Catalyst Recycling. *Org. Lett.* **2002**, *4*, 1691–1694 and references therein.
- (7) Mery, D.; Heuze, K.; Astruc, D. A Very Efficient, Copper-Free Palladium Catalyst for the Sonogashira Reaction with Aryl Halides. *Chem. Commun.* **2003**, *2003*, 1934–1935.
- (8) Alonso, D. A.; Naejra, C.; Pacheco, M. C.  $C(sp^2)$ - $C(sp)$  and  $C(sp)$ - $C(sp)$  Coupling Reactions Catalyzed by Oxime-Derived Palladacycles. *Adv. Synth. Catal.* **2003**, *345*, 1146–1158.
- (9) Hassan, J.; Seignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. Aryl–Aryl Bond Formation One Century after the Discovery of the Ullmann Reaction. *Chem. Rev.* **2002**, *102*, 1359–1470.
- (10) Tykwinski, R. R. Evolution in the Palladium-Catalyzed Cross-Coupling of  $sp$ - and  $sp^2$ -Hybridized Carbon Atoms. *Angew. Chem., Int. Ed.* **2003**, *42*, 1566–1568.
- (11) Rafael, C.; Carmen, N. The Sonogashira Reaction: A Booming Methodology in Synthetic Organic Chemistry. *Chem. Rev.* **2007**, *107*, 874–922.
- (12) Cole-Hamilton, D. J. Homogeneous Catalysis—New Approaches to Catalyst Separation, Recovery, and Recycling. *Science* **2003**, *299*, 1702–1706.
- (13) Astruc, D. In *Nanoparticles and Catalysis*; Astruc, D., Ed.; Wiley-VCH Verlag GmbH & Co. KGaA: Weinheim, Germany, 2008; pp 1–48.
- (14) Zahmakıran, M.; Özkar, S. Metal Nanoparticles in Liquid Phase Catalysis; From Recent Advances to Future Goals. *Nanoscale* **2011**, *3*, 3462–3481.
- (15) Balanta, A.; Godard, C.; Claver, C. Pd Nanoparticles for C–C Coupling Reactions. *Chem. Soc. Rev.* **2011**, *40*, 4973–4985.
- (16) Singh, A. S.; Shendage, S. S.; Nagarkar, J. M. Palladium Supported on Zinc Ferrite: An Efficient Catalyst for Ligand Free C–C and C–O Cross Coupling Reactions. *Tetrahedron Lett.* **2013**, *54*, 6319–6323.
- (17) Khalafi-Nezhad, A.; Panahi, F. Immobilized Palladium Nanoparticles on a Silica-Starch Substrate (PNP–SSS): As an Efficient Heterogeneous Catalyst for Heck and Copper-Free Sonogashira Reactions in Water. *Green Chem.* **2011**, *13*, 2408–2415.
- (18) Moussa, S.; Siamaki, A. R.; Gupton, B. F.; El-Shall, M. S. Pd-Partially Reduced Graphene Oxide Catalysts (Pd/PRGO): Laser Synthesis of Pd Nanoparticles Supported on PRGO Nanosheets for Carbon–Carbon Cross Coupling Reactions. *ACS Catal.* **2012**, *2*, 145–154.
- (19) Wang, D.; Li, Y. Bimetallic Nanocrystals: Liquid-Phase Synthesis and Catalytic Applications. *Adv. Mater.* **2011**, *23*, 1044–1060.
- (20) Son, S. U.; Jang, Y.; Park, J.; Na, H. B.; Park, H. M.; Yun, H. J.; Lee, J.; Hyeon, T. Designed Synthesis of Atom-Economical Pd/Ni Bimetallic Nanoparticle-Based Catalysts for Sonogashira Coupling Reactions. *J. Am. Chem. Soc.* **2004**, *126*, 5026–5027.
- (21) Li, Y. G.; Zhou, P.; Dai, Z. H.; Hu, Z. X.; Sun, P. P.; Bao, J. C. A Facile Synthesis of PdCo Bimetallic Hollow Nanospheres and Their Application to Sonogashira Reaction in Aqueous Media. *New J. Chem.* **2006**, *30*, 832–837.
- (22) Li, H.; Zhu, Z.; Liu, J.; Xie, S.; Li, H. Hollow Palladium-Cobalt Bimetallic Nanospheres as an Efficient and Reusable Catalyst for Sonogashira-Type Reactions. *J. Mater. Chem.* **2010**, *20*, 4366–4370.
- (23) Feng, Y.-S.; Lin, X.-Y.; Hao, J.; Xu, H.-J. PdCo Bimetallic Nanoparticles Supported on PPI-Grafted Graphene as an Efficient Catalyst For Sonogashira Reactions. *Tetrahedron* **2014**, *70*, 5249–5253.
- (24) Ahmad, S.; Mojtaba, M. PdCo Bimetallic Nanoparticles Supported on PPI-Grafted Graphene as an Efficient Catalyst for Sonogashira Reactions. *J. Mater. Chem. A* **2013**, *1*, 9303–9311.
- (25) Wei, X.; Yuanlong, S.; Menghan, G.; Weiqiang, Z.; Ziwei, G. Montmorillonite Supported Pd/Cu Bimetallic Nanoparticle Catalyzed Sonogashira Coupling. *Chin. J. Org. Chem.* **2013**, *33*, 820–826.
- (26) Korzec, M.; Bartczak, P.; Niemczyk, A.; Szade, J.; Kapkowski, M.; Zenderowska, P.; Balin, K.; Lelatko, J.; Polanski, J. Bimetallic Nano-Pd/PdO/Cu System as a Highly Effective Catalyst for the Sonogashira Reaction. *J. Catal.* **2014**, *313*, 1–8.
- (27) Xu, W.; Sun, H.; Yu, B.; Zhang, G.; Zhang, W.; Gao, Z. Sonogashira Couplings on the Surface of Montmorillonite-Supported Pd/Cu Nanoalloys. *ACS Appl. Mater. Interfaces* **2014**, *6*, 20261–20268.
- (28) Ho, S. F.; Mendoza-Garcia, A.; Guo, S.; He, K.; Su, D.; Liu, S.; Metin, Ö.; Sun, S. A General Approach to Monodisperse MPd (M = Co Cu) Alloy Nanoparticles and Their Catalysis for Electrooxidation of Formic Acid. *Nanoscale* **2014**, *6*, 6970–6973.
- (29) Guo, S.; Sun, S. FePt Nanoparticles Assembled on Graphene as Enhanced Catalyst for Oxygen Reduction Reaction. *J. Am. Chem. Soc.* **2012**, *134*, 2492–2495.
- (30) Metin, Ö.; Ho, S. F.; Alp, C.; Can, H.; Mankin, M. N.; Gültekin, M. S.; Chi, M.; Sun, S. Ni/Pd Core/Shell Nanoparticles Supported on Graphene as a Highly Active and Reusable Catalyst for Suzuki-Miyaura Cross-Coupling Reaction. *Nano Res.* **2013**, *1*, 10–18.
- (31) Hummers, W. S.; Offeman, R. E. Preparation of Graphitic Oxide. *J. Am. Chem. Soc.* **1958**, *80*, 1339–1339.
- (32) Kovtyukhova, N. I.; Ollivier, P. J.; Martin, B. R.; Mallouk, T. E.; Chizhik, S. A.; Buzaneva, E. V.; Gorchinskiy, A. D. Layer-by-Layer Assembly of Ultrathin Composite Films from Micron-Sized Graphite Oxide Sheets and Polycations. *Chem. Mater.* **1999**, *11*, 771–778.
- (33) Ai, K. L.; Liu, Y. L.; Lu, L. H.; Cheng, X. L.; Huo, L. H. A Novel Strategy for Making Soluble Reduced Graphene Oxide Sheets Cheaply by Adopting an Endogenous Reducing Agent. *J. Mater. Chem.* **2011**, *21*, 3365–3370.
- (34) Metin, Ö.; Kayhan, E.; Özkar, S.; Schenieder, J. J. Palladium Nanoparticles Supported on Chemically Derived Graphene: Highly Active and Reusable Catalyst for the Dehydrogenation of Ammonia Borane. *Int. J. Hydrogen Energy* **2012**, *37*, 8161–8169.
- (35) Powell, C. J. Recommended Auger Parameters for 42 Elemental Solids. *J. Electron Spectrosc. Relat. Phenom.* **2012**, *185*, 1–3.
- (36) Gökusu, H.; Ho, S. F.; Metin, Ö.; Korkmaz, K.; Mendoza-Garcia, A.; Gültekin, M. S.; Sun, S. Monodisperse NiPd Alloy Nanoparticles Catalyzed Reduction of Nitro and Nitrile Compounds via a Tandem Reaction of Hydrolysis of Ammonia Borane/Hydrogenation. *ACS Catal.* **2014**, *4*, 1777–1782.
- (37) Gökusu, H.; Can, H.; Şendil, K.; Gültekin, M. S.; Metin, Ö. Reduced Graphene Oxide Supported CoPd Nanoalloys Catalyzed

Tandem Ammonia Borane Dehydrogenation and Hydrogenation of Aromatic Nitro, Nitrile and Carbonyl Compounds. *Appl. Catal., A* **2014**, *488*, 176–182.

(38) Borah, B. J.; Dutta, D. K. In Situ Stabilization of Pd<sup>0</sup>-Nanoparticles into the Nanopores of Modified Montmorillonite: Efficient Heterogeneous Catalysts for Heck and Sonogashira Coupling Reactions. *J. Mol. Catal. A: Chem.* **2013**, *366*, 202–209.

(39) Gao, S.; Zhao, N.; Shu, M.; Che, S. Palladium Nanoparticles Supported on MOF-5: A Highly Active Catalyst for a Ligand- and Copper-free Sonogashira Coupling Reaction. *Appl. Catal., A* **2010**, *388*, 196–201.

(40) Magdesieva, T. V.; Nikitin, O. M.; Zolotukhina, E. V.; Zinovieva, V. A.; Vorotyntsev, M. A. Palladium–Polypyrrole Nanoparticles-Catalyzed Sonogashira Coupling. *Mendeleev Commun.* **2012**, *22*, 305–306.