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# Superparamagnetic nanoparticles-supported phosphine-free palladium catalyst for the Sonogashira coupling reaction

Nam T.S. Phan*, Ha V. Le

*Department of Chemical Engineering, HCMC University of Technology, VNU-HCM, 268 Ly Thuong Kiet, District 10, Ho Chi Minh City, Viet Nam*

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ABSTRACT

Superparamagnetic nanoparticles were synthesized following a microemulsion method, and functionalized with Schiff-base groups on the surface to form immobilized bidentate ligands. The functionalized nanoparticles were complexed with palladium acetate, affording the immobilized palladium complex catalyst with a palladium loading of 0.24 mmol/g. The catalyst was characterized by X-ray powder diffraction (XRD), scanning electron microscopy (SEM), transmission electron microscopy (TEM), vibrating sample magnetometry (VSM), thermogravimetric analysis (TGA), Fourier transform infrared (FT-IR), atomic absorption spectrophotometry (AAS), and nitrogen physisorption measurements. The immobilized palladium complex was used as an efficient catalyst for the Sonogashira reaction of iodobenzene and phenylacetylene to form diphenylacetylene as the principal product without added phosphine ligands. Recovery of catalyst was facilely achieved by simple magnetic decantation. The immobilized palladium complex catalyst could be reused several times without significant degradation in catalytic activity. No contribution from homogeneous catalysis of active palladium species leaching into reaction solution was detected.

## 1. Introduction

The immobilization of homogeneous catalysts to facilitate easy catalyst recovery and recycling, as well as product separation is a longstanding pursuit of catalysis science [1]. When the size of the support material is decreased to nanometer scale, the activity of nanoparticle-supported catalysts could be significantly improved, compared to homogeneous catalysts immobilized on conventional support matrices [2]. However, in this case, facile separation and recycling of nanoparticle materials from reaction media still remains a challenge [3]. This issue can be addressed by using superparamagnetic supports, allowing the catalyst to be easily separated from the liquid reaction media with application of an external magnetic field [4,5]. Recently, superparamagnetic nanoparticles have been intensively investigated because of their promising properties, and hence their potential applications in several fields [6–10]. In the field of catalysis, superparamagnetic nanoparticles have been utilized as catalyst supports for organic transformations such as olefin hydroformylation [11], alcohol hydrogenation [12], olefin hydrogenation [13], Suzuki and Heck cross-coupling reactions [14–17], Sonogashira and Carbonylative Sonogashira reactions [14,18], Knoevenagel condensation [3], asymmetric hydrogenation [19], dehalogenation [20], oxidation [21,22], ring-opening polymerization of epsilon-caprolactone [23], as well as supports for biocatalysts [24–27] with high activity and selectivity.

The Sonogashira cross-coupling of aryl halides with terminal alkynes has been employed for the synthesis of several compounds bearing an internal alkyne moiety, including biologically active molecules and functional polymers [28–30]. Toxic and expensive homogeneous palladium phosphine complexes, which are rarely recoverable without elaborate and wasteful procedures [31], have been used as catalysts for the Sonogashira reaction. Phosphines could be a more serious economical burden than even the palladium itself in some cases [32]. From an economic and environmental standpoint, it is desirable to use solid catalyst without the use of hazardous phosphine additives as a greener alternative to conventional homogeneous processes [32]. Indeed, phosphine-free Sonogashira coupling processes under homogeneous as well as heterogeneous conditions have been reported [33–38]. In this paper, we wish to report the Sonogashira reaction of iodobenzene with phenylacetylene using palladium catalyst immobilized on superparamagnetic nanoparticles without added phosphine ligands. The magnetic catalyst could be facilely isolated from the reaction mixture by simple magnetic decantation, and could be reused without significant degradation in activity.

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* Corresponding author. Tel.: +84 838222447.
*E-mail address:* ptsnam@hcmut.edu.vn (N.T.S. Phan).

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## 2. Experimental

### 2.1. Materials and instrumentation

Chemicals were purchased from Sigma-Aldrich, Fisher, and Merck and used as received without further purification unless otherwise noted. Distilled water was purged with nitrogen for 2 h prior to use. A Fischer Scientific FS60H was used to sonicate samples. Fourier transform infrared (FT-IR) spectra were obtained on a Bruker TENSOR37 instrument with samples being dispersed on potassium bromide pallets. Magnetic properties were measured with a PPMS 6000 vibrating sample magnetometer (VSM) at 305 K. Samples were sonicated in dimethylformamide for 30 min before measurements were taken. Scanning electron microscopy studies were conducted on a JSM 740 Scanning Electron Microscope (SEM). Transmission electron microscopy studies were performed using a JEOL JEM 1400 Transmission Electron Microscope (TEM) at 100 kV. The samples were dispersed on holey carbon grids for TEM observation. Nitrogen physisorption measurements were conducted using a Quantachrome 2200e system. Samples were pretreated by heating under vacuum at 150 °C for 3 h. Elemental analysis with atomic absorption spectrophotometry (AAS) was performed on an AA-6800 Shimadzu. X-ray powder diffraction (XRD) patterns were recorded using a Cu K$\alpha$ radiation source on a D8 Advance Bruker powder diffractometer.

A Netzsch Thermoanalyzer STA 409 was used for simultaneous thermal analysis combining thermogravimetric analysis (TGA) and differential thermal analysis (DTA) with a heating rate of 10 °C/min in air. Gas chromatographic (GC) analyses were performed using a Shimadzu GC 17-A equipped with a flame ionization detector (FID) and an DB-5 column (length = 30 m, inner diameter = 0.25 mm, and film thickness = 0.25 μm). The temperature program for GC analysis heated samples from 60 to 140 °C at 10 °C/min and held them at 140 °C for 1 min; then heated them from 140 to 300 °C at 50 °C/min and held them at 300 °C for 3 min. Inlet and detector temperatures were set constant at 300 °C. *n*-Hexadecane was used as an internal standard to calculate reaction conversions. GC–MS analyses were performed using a Hewlett Packard GC-MS 5972 with a RTX-5MS column (length = 30 m, inner diameter = 0.25 mm, and film thickness = 0.5 μm). The temperature program for GC–MS analysis heated samples from 60 to 280 °C at 10 °C/min and held them at 280 °C for 2 min. Inlet temperature was set constant at 280 °C. MS spectra were compared with the spectra gathered in the NIST library.

### 2.2. Synthesis of superparamagnetic nanoparticles

Superparamagnetic nanoparticles were synthesized following a microemulsion method [3,39]. Cobalt (II) chloride (0.9 g, 6.9 mmol) and iron (II) chloride (1.9 g, 14.9 mmol) were mixed in an aqueous solution (500 ml). An aqueous surfactant solution of sodium dodecyl sulfate (SDS) (12.9 g, 38.3 mmol) in deionized water (500 ml) was added, and the mixture was stirred at room temperature for 30 min to form a mixed micellar solution of $Co(DS)_2$ and $Fe(DS)_2$. The mixture was then heated to 55–65 °C. A solution of methylamine (300 ml, 40%, w/w aqueous solution) in deionized water (700 ml) was heated to the same temperature and rapidly added to the surfactant mixture. Black nanoparticles were precipitated. After the reaction mixture was stirred vigorously for 3 h, the nanoparticles were isolated by centrifugation and washed with copious amounts of deionized water, ethanol, and hexanes by magnetic decantation. The final product was dried in air at 50 °C overnight to yield superparamagnetic cobalt spinel ferrite nanoparticles (1.5 g).

### 2.3. Synthesis of amino-functionalized magnetic nanoparticles

The superparamagnetic nanoparticles (2.2 g) were dispersed in a mixture of ethanol and water (300 ml, 1:1 by volume). Ammonium hydroxide (35 ml, 25%, v/v aqueous solution) was added, and the mixture was stirred vigorously at 60 °C for 24 h. The nanoparticles were washed with copious amounts of deionized water, ethanol, and *n*-hexane via magnetic decantation. The resulting product was redispersed in a mixture of ethanol and water (300 ml, 1:1 by volume), and sonicated for 30 min at room temperature. 3-(Trimethoxysilyl)propylamine (2 g) was then added, and the solution was heated at 60 °C with vigorous stirring for 36 h. The final product was washed with copious amounts of deionized water, ethanol, and *n*-hexane by magnetic decantation, and dried under vacuum at room temperature overnight to yield amino-functionalized magnetic nanoparticles (1.71 g).

### 2.4. Synthesis of palladium catalyst immobilized on magnetic nanoparticles

The amino-functionalized magnetic nanoparticles (1.71 g) were added to a round-bottom flask containing ethanol (99.5%, 250 ml) and 2-acetyl pyridine (17 ml, 150 mmol). The resulting mixture was sonicated for 30 min, and then heated at reflux with rapid stirring for 36 h. After that, the reaction mixture was cooled to room temperature, and the solid was separated by magnetic decantation. The magnetic solid was then redispersed in ethanol, and sonicated for 30 min at room temperature. The product was then separated by magnetic decantation, and dried under vacuum at room temperature to yield the immobilized Schiff base (1.49 g). The immobilized Schiff base (1.49 g) was added to the round-bottom flask containing the solution of palladium acetate (0.1585 g, 0.70 mmol) in acetone (240 ml). The mixture was then stirred vigorously at room temperature for 36 h. The solid was separated by magnetic decantation, redispersed in acetone, sonicated for 30 min at room temperature, and then separated by magnetic decantation. The magnetic catalyst was washed with copious amounts of acetone and dried under vacuum at room temperature to yield the immobilized palladium catalyst (1.41 g).

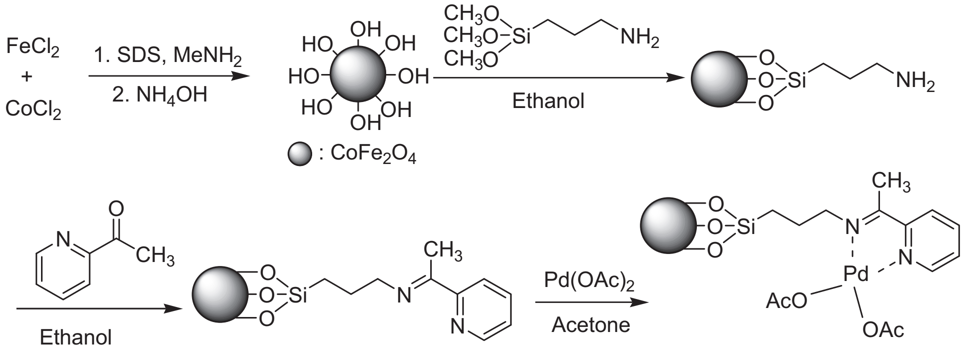
### 2.5. Catalytic studies

Unless otherwise stated, a mixture of iodobenzene (0.12 ml, 1.08 mmol), phenylacetylene (0.18 g, 1.65 mmol), $K_3PO_4$ (0.8628 g, 3.24 mmol), and *n*-hexadecane (0.12 ml) as the internal standard in dimethylformamide (5 ml) were added to a round-bottom flask containing the required amount of the immobilized palladium catalyst and copper (I) iodide co-catalyst. The flask was heated at the required temperature with magnetic stirring. Reaction conversions were monitored by withdrawing aliquots (0.1 ml) from the reaction mixture at different time intervals, and quenching with water (1 ml). The organic components were extracted into diethylether (2× 2 ml), dried over $Na_2SO_4$ and analyzed by gas chromatography (GC) with reference to *n*-hexadecane. Product identity was also further confirmed by gas chromatography–mass spectroscopy (GC–MS).

## 3. Results and discussion

### 3.1. Catalyst synthesis and characterization

Superparamagnetic nanoparticles were synthesized following a microemulsion method developed by Zhang and co-workers [3,39]. AAS analysis of the nanoparticles indicated a Co:Fe molar ratio of 1:2.08, corresponding to the $CoFe_2O_4$ structure. Indeed, the synthesis of $Co_xFe_{3-x}O_4$ superparamagnetic nanoparticles (where



**Scheme 1.** Synthesis of the palladium catalyst immobilized on superparamagnetic nanoparticles.

$x = 0.4–1$) were mentioned in the literature [40]. It was previously reported that magnetic nanoparticles synthesized in basic aqueous media are covered with a number of hydroxyl (–OH) groups, due to the adsorption of hydroxyl groups and protons ($H^+$) on the bare atoms of the metal and oxygen, respectively [41]. The hydroxyl groups on the surface of the magnetic nanoparticles were then enriched with an aqueous solution of ammonia, facilitating the surface modification step [3]. The resulting nanoparticles were functionalized with 3-(trimethoxysilyl)propylamine to create surface amino groups, according to a slightly modified literature procedure [42]. The amino-functionalized magnetic nanoparticles were allowed to react with 2-acetyl pyridine to form immobilized Schiff base bidentate ligands, which were complexed with palladium acetate, affording the immobilized palladium complex catalyst (Scheme 1). Indeed, Clark and co-workers previously prepared similar Schiff base bidentate ligands immobilized on amino-functionalized silica and amino-modified starch, respectively. It was reported that immobilized palladium catalysts prepared by the complexation of these immobilized Schiff base ligands with palladium acetate exhibited high activity in several palladium-catalyzed organic transformations [43,44]. The use of superparamagnetic nanoparticles as catalyst supports would offer advantages in catalyst separation and recycling over silica-based catalysts.

The immobilized palladium complex catalyst was then characterized using a variety of different techniques. Magnetization curves measured at 305 K showed that the immobilized palladium catalyst was almost superparamagnetic (Fig. 1). SEM (Fig. 2) and TEM (Fig. 3) studies showed diameters of approximately 30–40 nm for the superparamagnetic nanoparticles. However, particle agglomeration was clearly observed in the material, and the primary particle size was likely closer to 5–10 nm in diameter. It should be noted that most oxide particles, regardless of composition, aggregate on TEM grids and the TEM images do not imply that the nanoparticles aggregate similarly in solution [3]. Nitrogen physisorption measurements of the superparamagnetic nanoparticles gave BET surface areas of 150 $m^2/g$ and no mea-

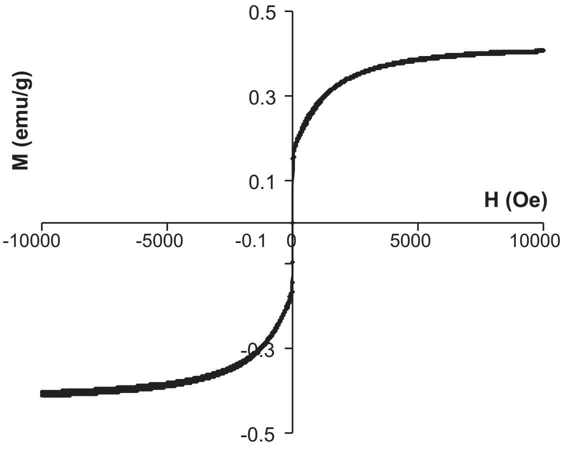


**Fig. 1.** Magnetization curves for the immobilized palladium catalyst measured at 305 K.

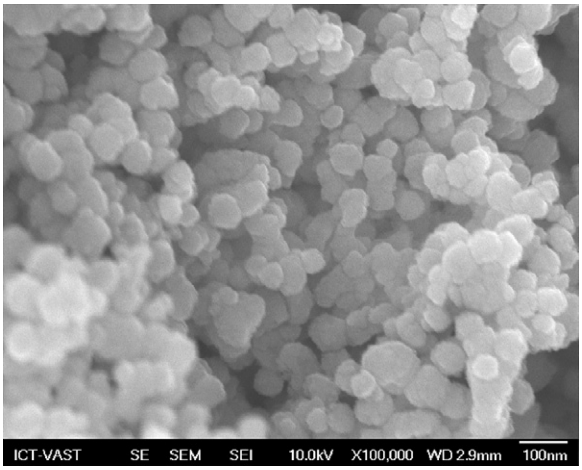


**Fig. 2.** SEM micrograph of the functionalized superparamagnetic nanoparticles.

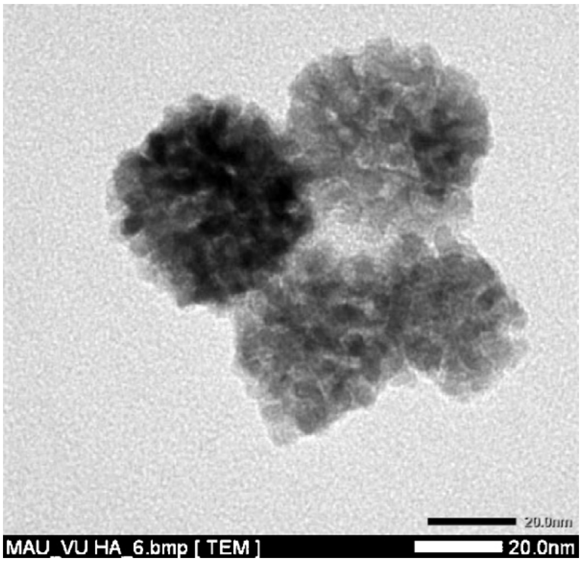


**Fig. 3.** TEM micrograph of the functionalized superparamagnetic nanoparticles.

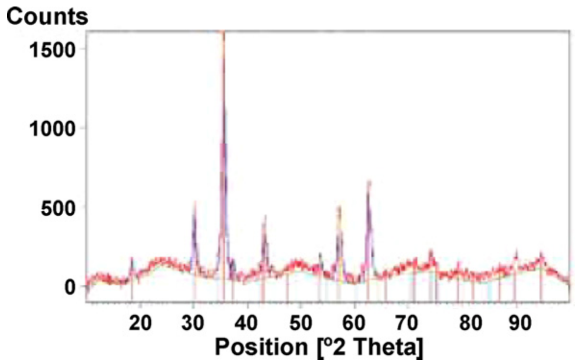


**Fig. 4.** X-ray powder diffractogram of the immobilized palladium catalyst.

surable mesoporosity, which was in good agreement with the literature where BET surface areas could range from 120 $m^2$/g to 200 $m^2$/g [4,6]. XRD patterns of the superparamagnetic nanoparticles were consistent with literature, with no impurity peak being observed [4,6,41] (Fig. 4).

FT-IR spectra of both the unfunctionalized and functionalized magnetic nanoparticles showed the presence of an Fe–O stretching vibration at approximately 590 $cm^{-1}$, an O–H stretching vibration due to physisorbed water and potentially surface hydroxyls near 3400 $cm^{-1}$, and an O–H deformation vibration near 1630 $cm^{-1}$, respectively [3,41,42]. The significant features observed for the amine-functionalized nanoparticles, the immobilized Schiff base, and the immobilized palladium catalyst were the appearance of the peaks near 1015 $cm^{-1}$ for Si–O stretching. For the immobilized ligand and the catalyst, there were also the appearance of the peaks near 2950 $cm^{-1}$ due to the –$CH_2$ and aromatic C–H stretching vibrations, and the presence of the imine C=N stretching vibration near 1600 $cm^{-1}$ which was overlapped with the O–H deformation vibration (Fig. 5) [41,42]. TGA analysis of the amino-functionalized magnetic nanoparticles indicated that 0.65 mmol/g of the amine was immobilized on the particles. This amine loading was also supported by the elemental analysis result of the nitrogen content on the nanoparticles. TGA analysis of the immobilized Schiff base ligand exhibited a Schiff base loading of approximately 0.50 mmol/g. It should also be noted that the TGA analysis of the unfunctionalized particles exhibited a significant weight loss below 200 °C due to the physisorbed water (Fig. 6).

XRD and FT-IR results gave little meaningful data for the palladium immobilization due to the low loading of the metal on the magnetic support. As the superparamagnetic nanoparticles were black, it was impossible to observe the changes on the surface of the particles using electron microscopy techniques. Therefore, proof that the palladium could be immobilized onto the magnetic nanoparticles came from the AAS data of the catalyst, from the magnetic decantation experiment which showed little leaching of the palladium from the solid catalyst into solution during the course of the reaction, and from the fact that the catalyst could be recovered and reused in further reactions without a significant degradation in catalytic activity. AAS analysis of the immobilized palladium complex exhibited a palladium loading of 0.24 mmol/g. It should be noted that the metal loading of several immobilized palladium complex catalysts for cross-coupling reactions was previously reported to be in the range of 0.1–0.5 mmol/g [32]. It was previously found that higher palladium loading was unnecessary as increasing the catalyst loading on the solid support to over 0.5 mmol/g could make a number of active sites inaccessible to the reactants [45]. As the catalyst was designed for the Sonogashira reaction where a base was required in the catalytic cycle, it was unnecessary to block the free amino groups on the surface of the catalyst. Indeed, it was previously reported that the presence of an amine could increase the stability of the palladium catalyst in the Suzuki and the Heck reactions [32,46]. However, the effect of free amino groups present in the immobilized palladium catalyst on the catalytic activity in the Sonogashira reaction still needs further investigation.

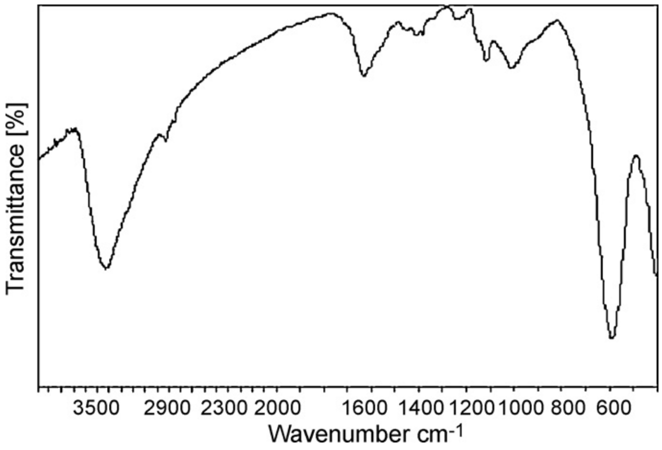


**Fig. 5.** FT-IR spectrum of the immobilized palladium catalyst.

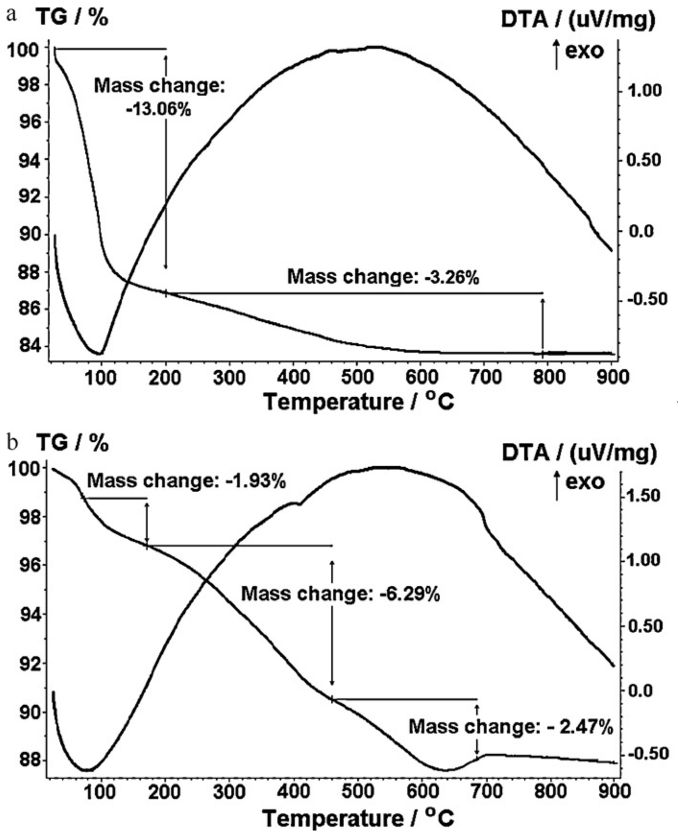
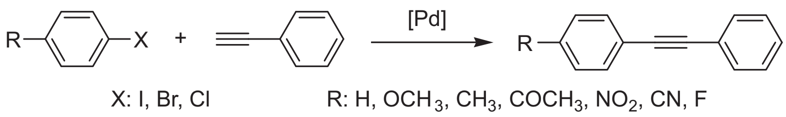


**Fig. 6.** TGA graphs of the unfunctionalized superparamagnetic nanoparticles (a) and immobilized Schiff base ligand (b).

### 3.2. Catalytic studies

The immobilized palladium complex catalyst was assessed for its activity initially in the Sonogashira reaction between iodobenzene and phenylacetylene to form diphenylacetylene as the principal product (Scheme 2). As DMF is normally the solvent of choice for cross-coupling reactions [32], it was decided to carry



**Scheme 2.** The Sonogashira reaction of aryl halides and phenylacetylene using the palladium complex catalyst immobilized on the superparamagnetic nanoparticles.

out the Sonogashira reaction in DMF at 80 °C, using 1 mol% of the immobilized palladium catalyst in the presence of CuI (molar ratio of Pd:Cu = 1:1) and piperidine as additives. Under this condition, a reaction conversion of 93% was achieved after 6 h, without added phosphine ligands. It should be noted that several catalyst systems for the Sonogashira reaction required the presence of toxic and expensive phosphines [47,48]. Indeed, phosphine-free Sonogashira reactions have been investigated using palladium–nitrogen complexes, carbene–palladium complexes, palladacycle catalysts, and ligand-free palladium catalysts [33,47,49]. It is generally accepted that a base is obviously necessary to neutralize the hydrogen halide produced as the byproduct in the catalytic cycle of the Sonogashira reaction. The base is also required for the generation of the alkynyl copper intermediate in the catalytic cycle, allowing the transmetallation step to occur [47]. It was also observed that non-functionalized superparamagnetic nanoparticles exhibited no activity in the reaction, indicating the necessity of the catalyst immobilization.

It was therefore decided to investigate the effect of bases on the reaction conversion, having carried the reaction in the presence of $K_3PO_4$, $K_2CO_3$, triethylamine, and piperidine, respectively. Triethylamine was effectively employed in several Sonogashira processes using homogeneous palladium phosphine complexes as catalysts [50,51]. In this research, however, the Sonogashira reaction using the immobilized palladium catalyst in the presence of triethylamine occurred with significant slower rate than that of reactions using piperidine and $K_3PO_4$, respectively. Reaction conversions of only 38% and 42% were observed after 6 h for the case of triethylamine and $K_2CO_3$, respectively. Piperidine and $K_3PO_4$ were shown to be the most effective base for the Sonogashira reaction using the palladium complex catalyst immobilized on the functionalized superparamagnetic nanoparticles, with conversions of 92% and 93% being achieved after 2 h, respectively (Fig. 7). It was therefore decided to use $K_3PO_4$ for the reaction in further experiments.

The temperature range from 50 °C to 140 °C has been the most commonly used for Sonogashira transformations using different types of palladium catalysts. Indeed, it was previously reported that the Sonogashira reaction using phosphine-based catalysts could also occur at room temperature [47]. The effect of temperature on the reaction conversion was therefore addressed. The Sonogashira reaction was carried out in DMF using 1 mol% palladium catalyst, and in the presence of CuI (molar ratio of Pd:Cu = 1:1) at 80 °C, 70 °C, and 60 °C, respectively. Experimental results showed that a reaction conversion of 93% was achieved after 2 h at the reaction temperature of 80 °C. As expected, decreasing the reaction temperature from 80 °C to 70 °C resulted in a drop in the conversion of iodobenzene, though a conversion of 92% was achieved after 3 h. The reaction at 60 °C still afforded 90% conversion although a longer reaction time was required (6 h) (Fig. 8). The most effective temperature range for the Sonogashira reaction using the immobilized palladium catalyst in this research was in good agreement with the literature.

The effect of catalyst concentration on the reaction conversion was then studied, using DMF as the solvent and $K_3PO_4$ as the base at 70 °C. As with previous reports, the higher the catalyst concentration was used, the higher the reaction rate was observed. It was observed that 98% conversion was achieved after 4 h at the palladium concentration of 0.5 mol%. The catalyst concentrations used in this study were comparable to those of several previous reports covering different aspects of the Sonogashira reaction, where the palladium concentrations varied from less than 0.5 mol% to more than 5 mol%, depending on the nature of the catalysts as well as the substrates [47]. Interestingly, it was found that increasing the palladium concentration from 0.5 mol% to 1 mol% enhanced the reaction rate in the first 3 h. However, the reaction using 1 mol% reached 92% after 3 h and the conversion did not increase any further, while the reaction using 0.5 mol% palladium proceeded up to 99% conversion after 4 h (Fig. 9). This could be rationalized based on the fact that the homo-coupling of phenylacetylene increased significantly at 1 mol% catalyst, leaving no phenylacetylene for the cross-coupling reaction. It was therefore decided to use 0.5 mol% catalyst for further experiments.

It was previously reported that the rate of the Sonogashira reaction could be significantly accelerated in the presence of CuI as a co-catalyst [47,50,51]. The transmetallation of copper acetylide to the palladium has been believed to be the rate determining step in the Sonogashira catalytic cycle [52]. However, copper-free Sonogashira transformation could still occur, though under much harsh

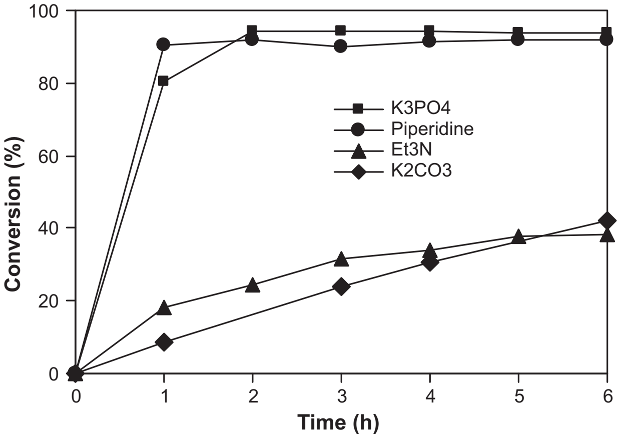


**Fig. 7.** Effect of different bases on reaction conversions.

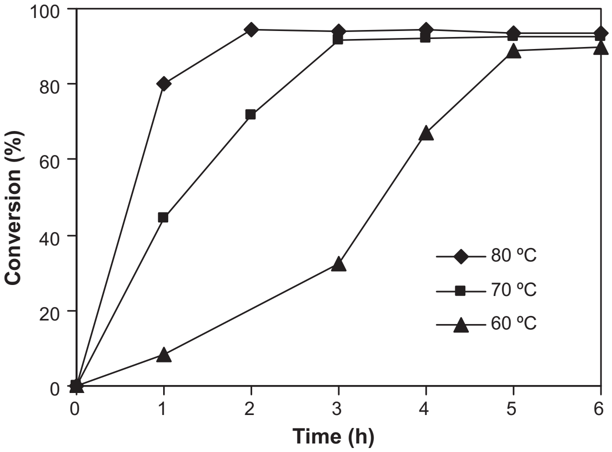


**Fig. 8.** Effect of temperature on reaction conversions.

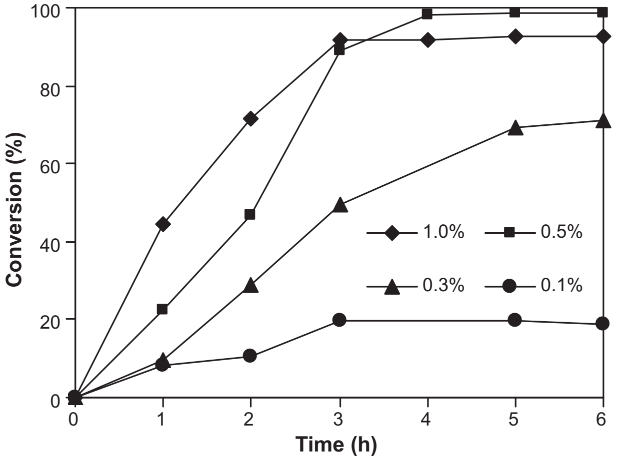


**Fig. 9.** Effect of catalyst concentration on reaction conversions.

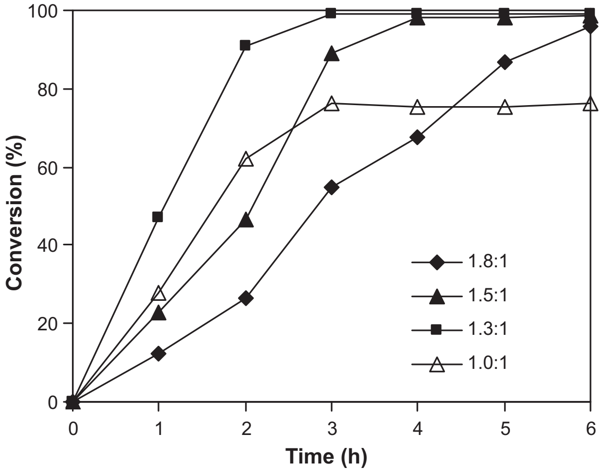


**Fig. 11.** Effect of phenylacetylene:iodobenzene molar ratio on reaction conversions.

conditions. Indeed, both copper- and copper-free catalytic cycles for the Sonogashira reaction were previously proposed in the literature [47]. We therefore decided to investigate the effect of CuI on the Sonogashira reaction using the immobilized palladium catalyst. The Sonogashira reaction was carried out in DMF at 70 °C in the presence of 0.5 mol% palladium catalyst, using Pd:Cu molar ratio of 1:2, 1:1, 1:0,5 and 1:0, respectively. It was found that a reaction conversion of 27% was achieved after 6 h in the absence of CuI, while conversions of 84% and 99% were obtained at Pd:Cu molar ratio of 1:0.5, 1:1 and 1:2, respectively (Fig. 10). It was therefore decided to use the Pd:Cu molar ratio of 1:1 at 0.5 mol% palladium catalyst for further studies.

With these results in mind, we then decided to investigate the effect of reagent molar ratio on the reaction conversion. The Sonogashira reaction was previously carried out at phenylacetylene:aryl halide molar ratio in the range of 1.2:1 to 2:1, depending on substrate structure and the nature of the catalyst [53,54]. Interestingly, in this research, it was found that increasing the phenylacetylene:iodobenzene molar ratio from 1.3:1 to 1.5:1 or 1.8:1 resulted in a significant drop in reaction rate (Fig. 11). The reason for this behavior was that the formation of polymer or oligomer by-products from excess phenylacetylene would deposit on the surface of the nanoparticles, deactivating the activity of the immobilized palladium catalyst. However, the reaction using one equivalent of phenylacetylene reached 77% conversion after 3 h and the conversion did not increase any further. This could be explained based on the homo-coupling by-reaction of phenylacetylene, leaving no phenylacetylene for the cross-coupling reaction. It was also observed that the Sonogashira reaction using the immobilized palladium catalyst should be carried out using the $K_3PO_4$:iodobenzene molar ratio in the range of 2:1 to 3:1. The reaction using one equivalent of $K_3PO_4$ afforded only 40% conversion after 6 h (Fig. 12). Indeed, it was previously reported that the Sonogashira reaction normally requires at least two equivalents of a base [53,54].

When using a supported catalyst, a crucial issue is the possibility that some of active sites could migrate from the solid support to the liquid phase and that these leached species could become responsible for a significant part of the catalytic activity [3]. After the catalyst was separated from the reaction mixture using a small permanent magnet, the solution was analyzed by AAS. The palladium concentration in the solution was observed to be as low as 1.3 ppm. Indeed, a small amount of palladium was previously detected in the solution of the Carbonylative Sonogashira reaction using a palladium catalyst immobilized onto superparamagnetic nanoparticles [18]. A minimal loss of palladium into solution was previously observed for the palladium catalyst supported onto superparamagnetic nanoparticles in the Suzuki and Heck reactions [17]. However, it was also reported that no palladium was detected in the reaction solution for other superparamagnetic nanoparticles-supported palladium catalysts [16,20]. In order to determine if leaching was a problem, an experiment was performed to estimate the contribution of leached palladium to the catalytic activity by

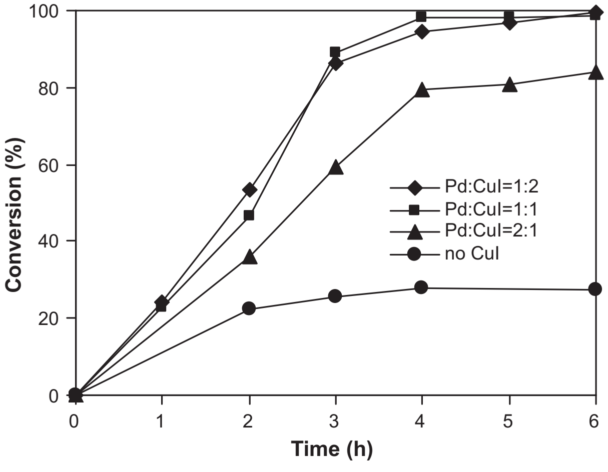


**Fig. 10.** Effect of Pd:Cu molar ratio on reaction conversions.

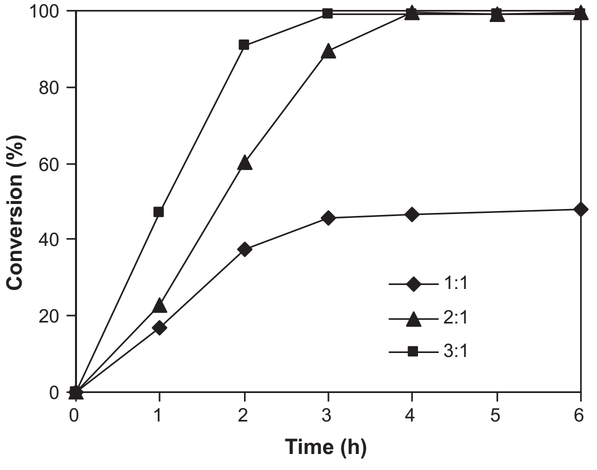


**Fig. 12.** Effect of base:iodobenzene molar ratio on reaction conversions.

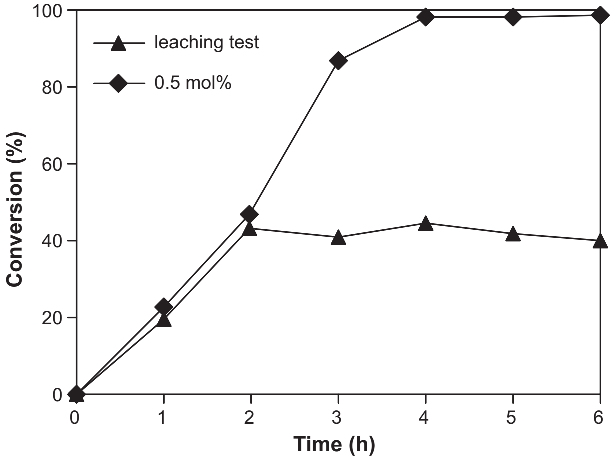


**Fig. 13.** Leaching test indicated no contribution from homogeneous catalysis of palladium leaching into reaction solution.

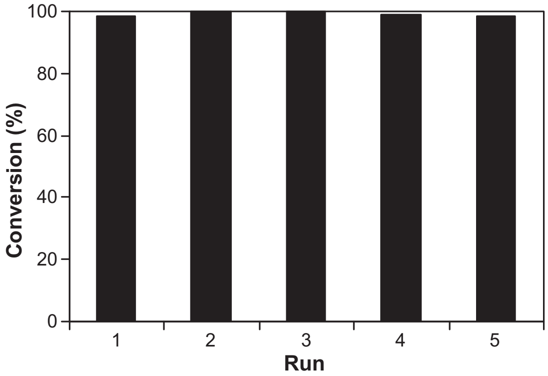


**Fig. 14.** Catalyst recycling studies.

performing a magnetic decantation during the course of the reaction to remove the solid catalyst. If the catalytic reaction continued this would indicate that the active species was leached palladium rather than the solid catalyst. The organic phase was separated from the solid catalyst after 2 h reaction time by magnetic decantation, having used 0.5 mol% fresh catalyst at 70 °C. The reaction solution was transferred to a new reactor vessel, and stirred for an additional 4 h at 70 °C with aliquots being sampled at different time intervals, and analyzed by GC. The data from GC determinations gave quantitative information about residual, catalytically active acid in solution. Within experimental error, no further reaction was observed, proving that there was no contribution from leached palladium and that conversion was only being possible in the presence of the magnetic palladium catalyst (Fig. 13). However, further studies are needed to elucidate the real active species in the Sonogashira reaction using this catalyst system.

Another point of great concern for most of anchored catalysts is the ease of separation as well as the deactivation and reusability of the catalyst. The immobilized palladium catalyst was therefore investigated for recoverability and reusability over five successive runs. After each run using 0.5 mol% catalyst (Pd:Cu molar ratio of 1:1) at 70 °C for 6 h, an external magnetic field was applied on the outer surface of the glass reaction vessel containing the magnetic nanoparticles using a small permanent magnet. The reaction solution was then easily removed from the reaction vessel by decantation while the external magnet held the superparamagnetic nanoparticles stationary inside the vessel. The magnetic catalyst was washed with deionized water, acetone and *n*-hexane to remove any physisorbed reagents, dried under vacuum at room temperature overnight, and reused in further reactions under identical conditions to the first run. It was found that the activity of the magnetic catalyst decreased after the first run. Interestingly, if the recovered catalyst was treated in DMF at 120 °C for 15 min and then reused in further reaction at 70 °C, the catalytic activity could remain almost the same over five successive runs, with 99% conversion still being achieved in run 5 (Fig. 14).

The study was then extended to the Sonogashira reaction of substituted iodobenzenes containing electron-donating (*i.e.* 4-iodotoluene) and electron-withdrawing (*i.e.* 4-iodoacetophenone) groups. It was observed that the reaction of 4-iodotoluene with phenylacetylene proceeded with significantly slower rate than the case of iodobenzene, with a total conversion of only 70% being achieved after 6 h (Fig. 15). As expected, the reaction rate of the Sonogashira reaction between 4′-iodoacetophenone and phenylacetylene was higher than the case of iodobenzene, affording a total conversion of more than 99% after 1 h. This result indicated that the Sonogashira reaction using the immobilized palladium catalyst was favored by electron-withdrawing groups on benzene ring, while electron-donating groups slowed down the cross-coupling processes. Indeed, the presence of electron-withdrawing groups in the arylhalide normally enhance the reaction rate in several palladium-catalyzed cross-coupling transformations [32]. However, Liu and co-workers previously reported high yields for the Sonogashira reaction of both electron-poor and electron-rich aryliodides with phenylacetylene, though no kinetic data was provided [50].

The Sonogashira reactions of bromobenzene derivatives with phenylacetylene using the immobilized palladium catalyst were also investigated. The reason for this trend is that iodoarene derivatives are normally significantly more expensive than bromoarenes, while chloroarenes require lowest cost and therefore they are the most desirable starting materials [32]. Chloroarenes are unreactive in most cases, though the Sonogashira reactions of activated chloroarene (*i.e.* containing strong electron-withdrawing groups) could be successful by using special catalyst systems. In this study, it was observed that the reaction of bromobenzene with phenylacetylene proceeded with significantly slower rate than the case of iodobenzene, with a conversion of 38% being achieved after 6 h (entry 1, Fig. 16). It should be noted that chlorobenzene was inactive in the reaction with phenylacetylene, and the product was detected only in trace amounts. Indeed, chloroarenes were previously reported to be inactive for several palladium-catalyzed cross-coupling reactions [32]. As expected, it was found that the presence of electron-withdrawing

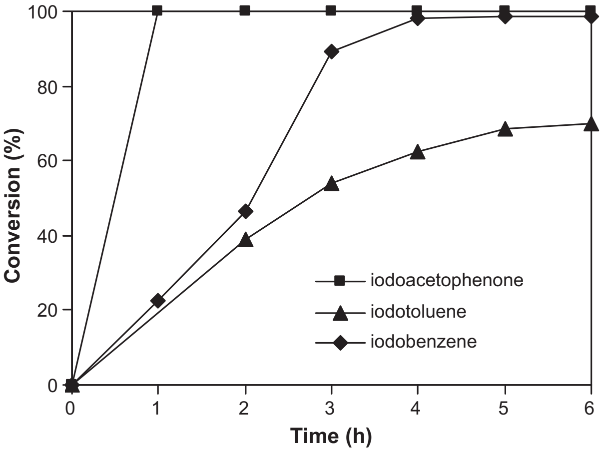


**Fig. 15.** Effect of substituents on reaction conversions.

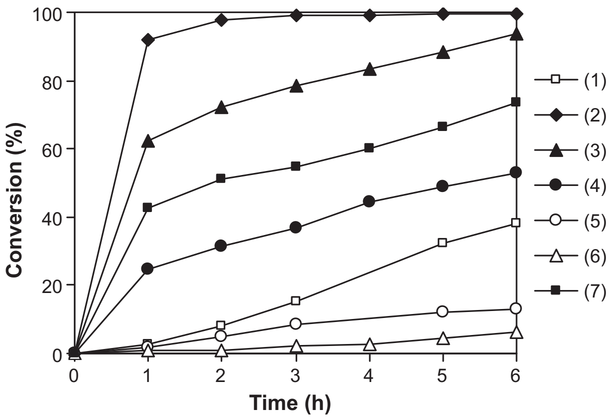


**Fig. 16.** Effect of arylbromide on reaction conversions: bromobenzene (1), 4-bromonitrobenzene (2), 4-bromobenzonitrile (3), 4-bromoflorobenzene (4), 4-bromotoluene (5), 4-bromomethoxybenzene (6), and 4′-bromoacetophenone (7).

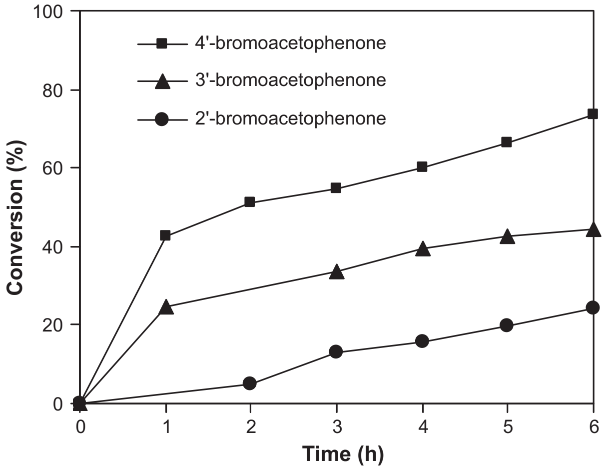


**Fig. 17.** Effect of bromine substitution position on reaction conversions.

groups on benzene ring significantly accelerated the Sonogashira reaction using the immobilized palladium catalyst. The Sonogashira reactions of 4-bromonitrobenzene, 4-bromobenzonitrile, 4′-bromoacetophenone, and 4-bromoflorobenzene afforded conversions of 99% (entry 2), 93% (entry 3), 73% (entry 7), and 53% (entry 4, Fig. 16), respectively, after 6 h. Electron-donating groups slowed down the reaction, with 13% and 6% conversions being observed for the Sonogashira reaction of 4-bromotoluene (entry 5), and 4-bromomethoxybenzene (entry 6, Fig. 16), respectively. Interestingly, the Sonogashira reaction using the immobilized palladium catalyst offered a selectivity for 4′-bromoacetophenone over the corresponding 3′- and 2′-isomer. The reaction of the 4-isomer could proceed to 73% conversion, while a conversion of 44% was obtained for the case of the 3-isomer. Furthermore, 75% unreacted starting material in the case of the 2-isomer led us to believe that this was a rate limited selectivity based on the increased steric bulk at the 2-position inhibiting substitution (Fig. 17) [45].

## 4. Conclusions

In summary, palladium complex immobilized on superparamagnetic nanoparticles was synthesized, and characterized by XRD, VSM, TEM, TGA, FT-IR, and elemental analysis. The immobilized palladium complex was used as an efficient catalyst for the Sonogashira reaction of iodobenzene and phenylacetylene to form diphenylacetylene as the principal product without added phosphine ligands. Recovery of catalyst was facilely achieved by simple magnetic decantation. The immobilized palladium complex catalyst could be reused several times without significant degradation in catalytic activity. Our results here demonstrate the feasibility of applying magnetic nanoparticles as catalyst supports for immobilizing homogeneous catalysts. The unique properties of the particles such as nanometer-sized, magnetic, and facilely functionalized via silane chemistry, offer potential advantages over conventional catalyst support materials, and would be interested to the chemical industry. Current research in our laboratory has been directed to the design and immobilization of several catalysts on superparamagnetic nanoparticles for a wide range of organic transformations.

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