Supported Ultra Small Palladium on Magnetic Nanoparticles Used as Catalysts for Suzuki Cross-Coupling and Heck Reactions

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Abstract: Application of transition metal nanoparticles as catalysts for organic transformations has been attracting wide interest as nanoparticle-based catalytic systems might exhibit superior catalytic activities than the corresponding bulk materials. However, the main difficulty is that such small particles are almost impossible to separate by conventional means, which can lead to the blocking of filters and valves by the nanoparticle catalyst. We have conveniently prepared ultra small palladium(0) particles (less than 1 nm) on magnetic nanoparticle supports, in which immobilized auxiliaries are used as stabilizing ligands. These catalysts were active for Suzuki cross-coupling and Heck reactions giving isolated yields of 83% and 56%, respectively. In addition, the catalyst can be easily separated using a magnet and reused several times with sustained activity.

Keywords: C−C coupling; Heck reaction; magnetic nanoparticle support; palladium; phosphorylation

Introduction

It is well-known that catalytic Suzuki cross-coupling and Heck reactions are very important and powerful chemical methods for the formation of C−C bonds.[1,2] Many review articles regarding catalytic C−C coupling reactions have been recently published, both in journals and books.[3–5] Although the technology involved has been widely explored and well-developed, there is still a desire to discover new methodologies for C−C cross-coupling reactions, especially for economically and industrially attractive issues such as low catalyst amounts, high yields, and reliable and reproducible yields. It is worthy of note that most of the catalytic C−C cross-coupling reactions so far reported are ligand-based reactions.[5] One main disadvantage of that approach is that extra steps are needed for attaching and removing the ligands. In addition, removal of the leached metals in the reaction solution is also critical to reduce the toxicity. So, recycling both ligand and metal is highly desirable for (a) reducing raw material costs, and (b) engineering a "greener" process *via* reduction of the amount of waste chemicals for disposal, yielding less metallic pollution to both products and environment.

To overcome this problem, both palladium complexes and metal particles, which are the most popular catalysts in Suzuki cross-coupling and Heck reactions, have been immobilized on various supports.[6] As well, nanochemistry, especially nanoscale-sized metal particles, has also been widely explored as a potential solution, utilizing the unique chemical and physical properties of nanoparticles.[7,8] With the development of nanochemistry it has been possible to prepare "soluble" analogues of heterogeneous catalysts, materials that might have properties intermediate between those of bulk and single particles due to high surface areas and high densities of active sites.[9,10] The application of transition metal nanoparticles as catalysts for organic transformations has been attracting wide interest as nanoparticle-based catalytic systems can exhibit superior catalytic activities than the corresponding bulk materials.[11] In general, the preparation and stabilization of metallic nanoparticles with controlled sizes and compositions, such as alloys or core-shell particles, are critical and
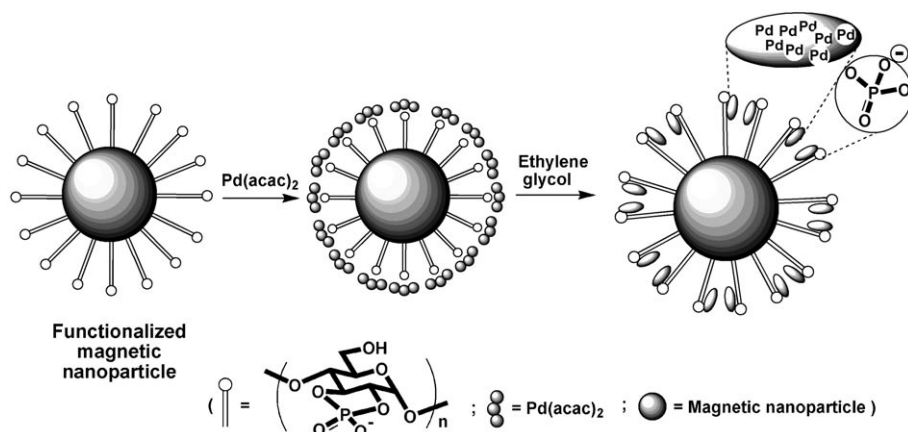
Scheme 1. Synthesis of magnetic nanoparticle supported palladium nanoparticles.

challenging.[12] It is believed that the particle size is closely related to and a function of the preparation process used.[13] To sustain activity, it is important to stabilize catalytic metallic nanoparticles because the nanoparticles tend to aggregate to form larger, bulk particles and therefore reduce, or even lose, their catalytic nature. Typical methods to stabilize metallic nanoparticles in solution can include electrostatic or steric protection.[14] However, the recycle problem must be addressed before nanocatalytic processes can be scaled-up, due to the fact that nanoparticles, which include nano-scaled metal catalysts and supports, are difficult to separate from the reaction mixture.

Currently, a method used to address this problem is through the use of magnetic nanoparticles, a route that has attracted wide research interest for its unique physical properties.[15] It has been reported that magnetic nanoparticles can be used as catalyst supports for many organic reactions such as hydroformylation, Knoevenagel reaction, and olefin polymerization to mention but a few examples.[16–26] Herein, we report the use of modified magnetic nanoparticles as catalyst vehicles to support palladium nanoparticles useful in Suzuki cross-coupling and Heck coupling reactions. The new catalyst system can be well-dispersed in the reaction medium, easily recovered from reaction mixture, and reused several times without significant losses in performance.

Results and Discussion

In this paper, commercially-available magnetic nanoparticles with a mean diameter of 100 nm were enriched with phosphate functional groups on the surface and used as a catalyst support. After reaction with phosphorus oxychloride and neutralization with basic aqueous solution, the surface of the magnetic nanoparticle was successfully enriched with phosphate

functional groups *via* formation of $C_{Starch}O-P$ bonds (Scheme 1).[27] Despite no obvious changes in the IR spectra (Figure 1), the modification was confirmed by the TGA results which showed an increased amount of residue (70.3 wt%) compared with residue from the purchased magnetic support (68.4 wt%) (Figure 2). The phosphate modification did not cause aggregation of the magnetic nanoparticles and the particle size was sustained as shown by TEM after our process step (see Supporting Information). The palladium complex $Pd(acac)_2$ was successfully absorbed on the support surface by electrostatic interaction. After further reduction using glycol under an argon atmosphere (Scheme 1), well-dispersed nanoscale palladium particles were obtained. The supported catalyst can be homogeneously dispersed in deionized water to produce a black "solution" [see Figure 3 (top)]. In the IR spectrum of supported palladium nanoparticles (Figure 2), no absorptions due to those typically seen with the acac ligand were found, thus confirming that the acac ligands in $Pd(acac)_2$ have
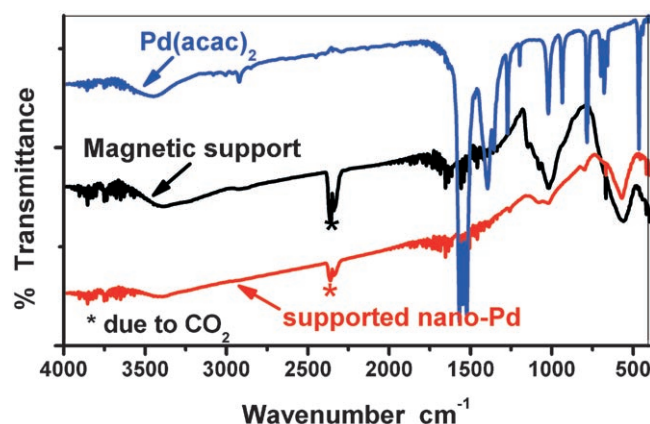
Figure 1. IR spectra of phosphate group-enriched magnetic nanoparticles, $Pd(acac)_2$ and supported nano-Pd.
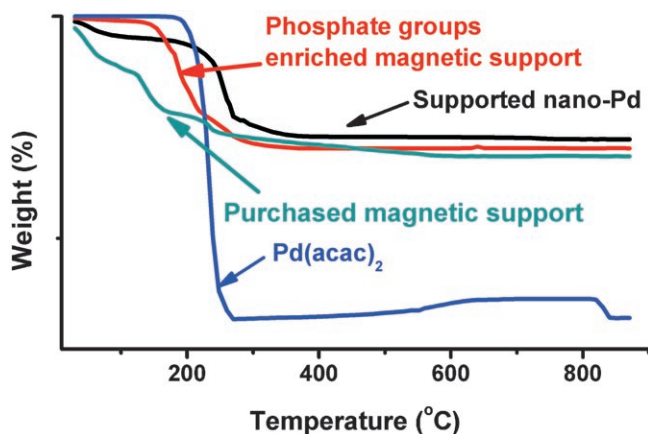
Figure 2. TGA spectra of purchased magnetic support, phosphate group-enriched magnetic support, Pd(acac)$_2$ and supported nano-Pd.

been cleanly removed after the reduction process. The IR spectrum of supported nano-Pd is similar to the spectrum of the phosphate group-enriched supported magnetic nanoparticles.

As one can see from the TGA curves (Figure 2), after supporting palladium the amount of residue increased up to 71.8 wt% compared with residue from the phosphate group-enriched magnetic support (70.3 wt%) and purchased magnetic support (68.4 wt%). These results are consistent with ICP results showing that a loading amount of 0.32 mmol Pd/g (magnetic support) has been achieved. In addition, the color of the phosphate group-enriched magnetic nanoparticles dispersed in aqueous phase has changed dramatically from red-brown (before) to black (after) as the palladium nanoparticles are loaded [see Figure 3 (top)]. The magnetic nanoparticle-supported nano-Pd has also been analyzed using TEM (Figure 4). In the TEM images, only magnetic particle cores with an average of *ca.* 5 nm are shown; no other particles are found. This is a significant indication that the prepared Pd nanoparticles are less than 1 nm in diameter and thus cannot be detected by the TEM method. Combining all the analytical information, we conclude that palladium nanoparticles with a particle size of less than 1 nm have been successfully loaded onto a magnetic support. To investigate the chemical oxidation state of the supported palladium species, the synthesized catalyst was analyzed using XPS. The XPS spectrum (see Figure 5) shows typical Pd(0) absorptions at 335.30 and 340.50 eV for 3d$_{5/2}$ and 3d$_{3/2}$, respectively, with a $\Delta = 5.2$ eV, which is consistent with the literature for Pd(0).[28]

The prepared magnetic nanoparticle-supported palladium nanoparticle materials have been tested as catalysts in the Suzuki cross-coupling and Heck coupling reactions, respectively. For the Suzuki cross-coupling reaction, the model reaction of bromobenzene and
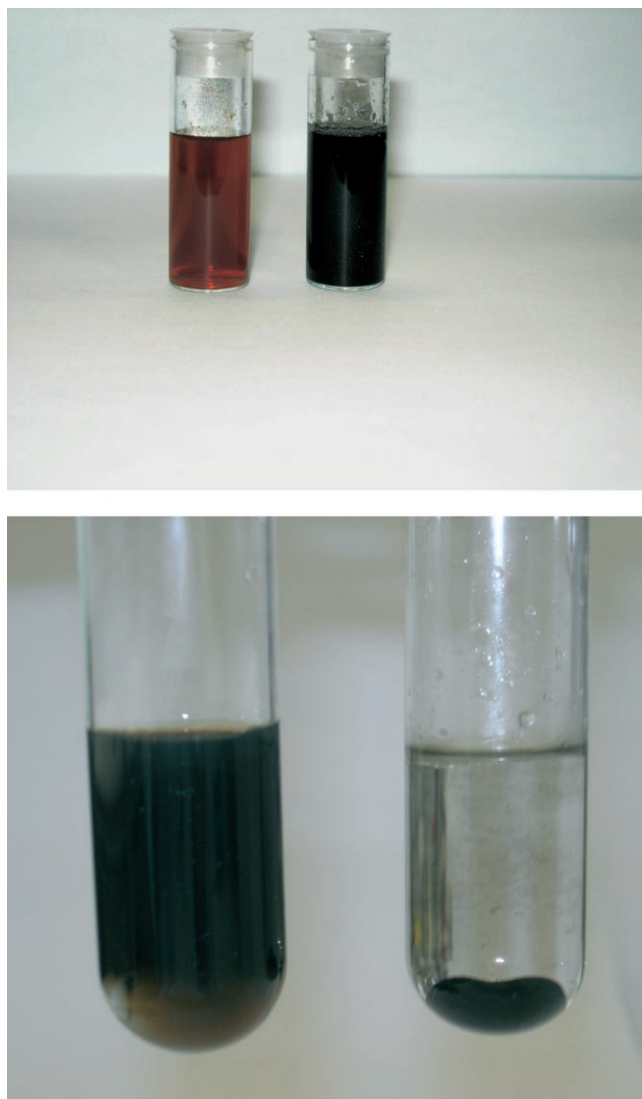

Figure 3. (*Top*) Aqueous solution of phosphate group enriched magnetic nanoparticle (*left*) and with supported nano Pd (*right*). (*Bottom*) Stirred (*left*) and stationary (*right*) reaction mixture.

phenylboronic acid was explored. In this reaction, oxygen-free deionized water was used as reaction medium to form a three-phase system consisting of an aqueous solution of potassium carbonate and phenylboronic acid, an oil phase of bromobenzene, and the supported nano-Pd(0) catalyst. The catalyst is effective in the environmentally benign system reaching a satisfactory yield of 83%. It should be pointed out that our catalyst is ferromagnetic and can easily be separated from the reaction mixture by simple magnetic attraction. Under our conditions, the supported catalysts were attracted onto the surface of the magnetic stirring bar when the reaction mixture was kept in a stationary condition by stopping stirring [see Figure 3 (right)]. As such, the product mixture could be easily collected by decantation. The catalyst could be reused at least 3
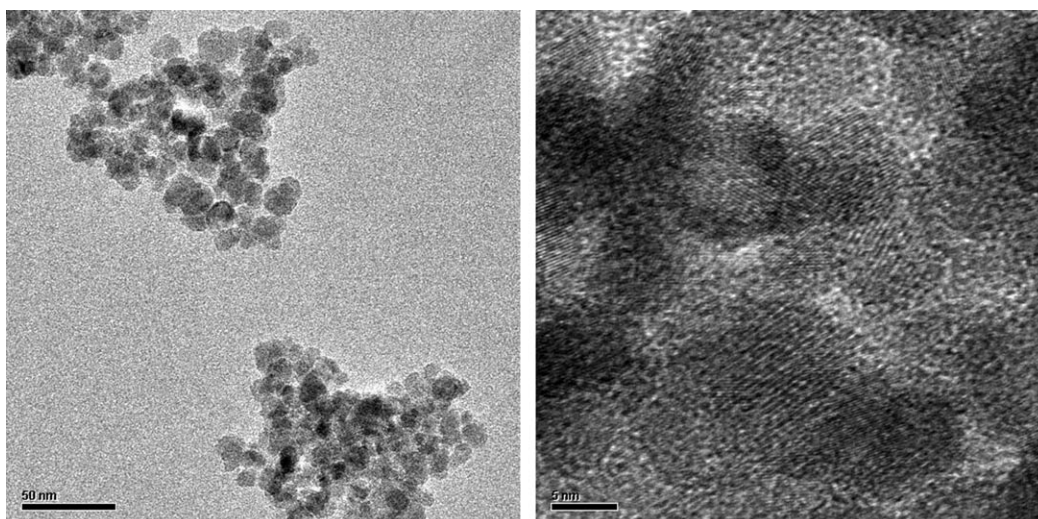
Figure 4. TEM images of catalyst.
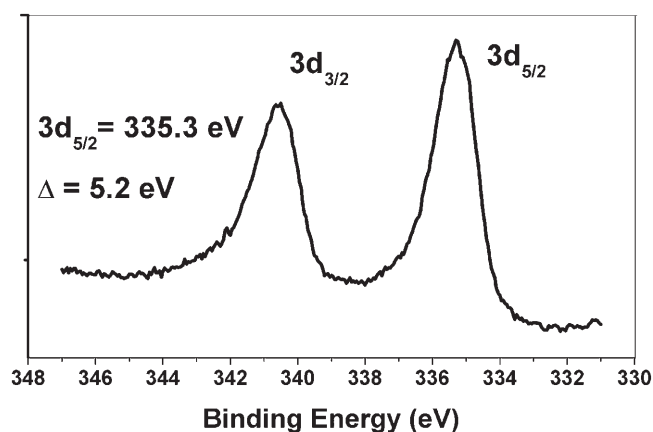
Figure 5. XPS spectra of supported nano-Pd, indicating reduction to Pd(0).

times without showing any obvious decrease of catalytic performance. Despite the good yield of 83%, our environmentally benign catalyst system cannot compare with the classic homogeneous catalysts in efficiency. However, the magnetic nanoparticle supported nano-Pd(0) catalysts are more active than the magnetic nanoparticle supported homogeneous catalysts using N-heterocyclic carbene-coordinated Pd complexes.[21] The lower interaction chance of reactants in the three-phase reaction mixture and relatively strong electrostatic interaction might contribute to lowering the efficiency of the catalyst.[29] In addition, after 3 runs, no obvious aggregation of Pd on the support surface to form visible nanoparticles was observed; only magnetic particle cores were observed using TEM with the oxidation state of Pd(0) confirmed by XPS analysis (see Supporting Information).

In a classic Heck coupling reaction of bromobenzene and styrene, *N,N*-dimethylformamide was used as solvent to increase the solubility of the organic reagents. After reaction and product purification using thin layer chromatography (TLC), *trans*-stilbene (based on NMR spectra, see Supporting Information) was isolated as the major product in 56% yield. Similarly, the catalyst particles could be recovered by magnetic attraction, followed by washing with organic phase and water to remove the organic reagents and sodium acetate. As above, the recycled catalyst could be reused at least 5 times under our conditions without losing activity. The concentrations of leached Pd in the filtrate plus wash solution obtained from the above reactions are less than 5.0 ppm based on ICP results. It should be noted that our catalyst system is more efficient for Heck reactions than other supported nano-Pd(0) on different supports (such as MgO, TiO_2, and ZrO_2) which achieved less than 50% conversions.[30]

To confirm that the high activity originated from the supported palladium and not from leached Pd, contrasting experiments have been investigated under the same conditions in an aqueous solution obtained from the filtrate and wash solution of catalyst. After similar purification processes, the products from Suzuki cross-coupling reactions were obtained in only *ca.* 5% isolated yield. The results confirmed that the supported palladium magnetic nanoparticles provide the high catalytic activity, and not any leached palladium. At present, the true mechanism regarding our catalysts is still unclear and related studies are underway in our laboratory using on-line IR technology.

Conclusions

In conclusion, we have demonstrated that palladium nanoparticles supported on the magnetic nanoparti-

cles derived using phosphate functional groups are effective for both Suzuki cross-coupling and Heck coupling reactions. The supported catalysts can be well-dispersed in both aqueous and organic phase to produce a pseudo-homogeneous catalyst system. Additionally, the unique catalyst can be easily separated from the reaction mixture and products by simple magnetic attraction.

Experimental Section

General Remarks

All operations were performed under an argon atmosphere with glove box or standard Schlenk line techniques. The purchased magnetic support ($50 \, mg \, mL^{-1}$, 100 nm, magnetic iron oxides matrixed with starch) was provided by chemicell GmbH. Other reagents were supplied from Sigma–Aldrich Pte. Ltd., and used as received. ^1H and ^{13}C NMR were recorded on a Bruker Fourier-Transform multinuclear spectrometer operating at 400 and 100.6 MHz, respectively, relative to an external Me_4Si (TMS) standard. Infrared (IR) spectra were measured using a BIO-RAD spectrophotometer using KBr pellets. ICP analysis was determined using a VISTA-MPX, CCD Simultaneous ICP-OES analyzer. The TGA analyses were carried out on a SDT 2960 Simultaneous DSC-TGA analyzer. Transmission electron microscopy (TEM) measurements were carried out on a JEOL Tecnai-G^2, FEI analyzer operating at 200 kV. X-Ray photoelectron spectrometery (XPS) was performed with an ESCALAB 250 analyzer.

Surface Enrichment of Phosphate Functional Groups on the Magnetic Support

A literature method was used to immobilize phosphate groups by the reaction of phosphorus oxychloride with hydroxy groups in the starch matrix covering the surface of the magnetic nanoparticles.[27] Briefly, in the glove box, with vigorous magnetic stirring, 1000 mg (large excess) of $POCl_3$ was slowly added to a solution of 500 mg magnetic nanoparticles suspended in 20.0 mL of anhydrous benzene. After stirring for 3 h at room temperature, the reaction mixture was removed from the glove box and collected with a magnet to gather the magnetic nanoparticles, which were then further washed with 2×10 mL portions of anhydrous benzene to remove unreacted phosphorus oxychloride. The magnetic material was then redispersed in 10 mL deionized water, neutralized with 1 N aqueous NaOH to about pH 8.0, collected with a magnet, and washed with 2×5 mL portions of oxygen-free, deionized water. The obtained sample of magnetic nanoparticles enriched with phosphate functional groups was subjected to analysis by TEM and TGA, respectively.

Synthesis and Characterization of Nano-Pd Supported Magnetic Nanoparticles

Under an argon atmosphere, 10 mL of an aqueous solution ($50 \, mg \, mL^{-1}$) of the above prepared phosphate functional group-enhanced magnetic nanoparticles were added to an aqueous solution of 100 mg $Pd(acac)_2$ in 10 mL of deionized

water. The mixture was stirred at room temperature for 2 h. The red-brown magnetic support was filtered and washed with methanol (2×10 mL) and dimethylformamide (2×10 mL) in sequence. The treated magnetic support was redispersed in 10 mL dimethyl sulfoxide followed by addition of 5 mL ethylene glycol. The obtained mixture was heated to 150 °C, which gave a black color to the supported Pd catalyst. The Pd nanoparticle modified magnetic support was washed with deionized water and collected with a magnet. The loading amount of 0.32 mmol of Pd/g was found by ICP analysis. The product was also subjected to further characterization using TGA, TEM, IR, and XPS.

Catalyzed Suzuki Cross-Coupling Reaction

Bromobenzene (0.5 mmol), phenylboronic acid (1.0 mmol), potassium carbonate (1.5 mmol), and Pd-containing catalyst (0.05 mmol based on Pd) were added to a 25-mL round-bottom flask equipped with a magnetic stirring bar. 5 mL of deionized and oxygen-free water were added and the reaction mixture was stirred at 80 °C for 5 h. After the reaction, the Pd-containing catalyst was separated with a magnet and washed with diethyl ether (2×10 mL) followed by deionized and oxygen-free water (2×10 mL). The collected Pd-containing catalyst was dried and reused for the next run. The aqueous phase was extracted with diethyl ether (2×20 mL) and the combined organic phases were concentrated and purified with thin layer chromatography (TLC, SiO_2) to produce biphenyl; yield: 64.0 mg (83 %).

Catalyzed Heck Coupling Reaction

Bromobenzene (0.5 mmol), styrene (1.0 mmol, 2 equivs.), sodium acetate (1.3 mmol, 2.6 equivs.), and Pd-containing catalyst (0.05 mmol) were added to a 25-mL round-bottom flask equipped with a magnetic stirring bar. 8 mL of N,N-dimethylformamide were added and the reaction mixture was stirred at 140 °C for 4 h. After the reaction, the reaction mixture was cooled to room temperature, separated and purified following a similar procedure as the product purification and catalyst recycling used in catalyzed Suzuki cross-coupling reaction, to produce stilbene; yield: 50.5 mg (56 %).

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