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PALLADIUM COMPLEX IMMOBILIZED ON MAGNETIC NANOPARTICLES AS AN EFFICIENT CATALYST FOR THE HECK REACTION

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PHAN THANH SON NAM, NGUYEN NGOC THUY HUONG
Ho Chi Minh City University of Technology, Vietnam

ABSTRACT

Cobalt superparamagnetic spinel ferrite ($CoFe_2O_4$) nanoparticles were synthesized following a microemulsion method, and functionalized via silane chemistry with 3-(trimethoxysilyl)-propylamine to create surface amino groups. The amino-functionalized magnetic nanoparticles were allowed to react with 2-hydroxybenzaldehyde or 2-acetyl pyridine to form immobilized bidentate ligands, which were complexed with palladium acetate, affording the immobilized palladium complex catalysts with a palladium loading of 0.26 mmol/g and 0.33 mmol/g (AAS), respectively. The catalyst was characterized by X-ray powder diffraction (XRD), transmission electron microscope (TEM), thermogravimetric analysis (TGA), Fourier transform infrared (FT-IR), and elemental analysis (EA). The immobilized palladium complex was used as an efficient heterogeneous catalyst for the Heck cross-coupling reaction of iodobenzene and styrene to form stilbene as the principal product. Recovery of catalyst was facilely achieved by simple magnetic decantation. The immobilized palladium complex catalyst could be reused without significant degradation in catalytic activity.

I - INTRODUCTION

Nanoparticles have emerged as efficient alternative support materials for homogeneous catalyst immobilization [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. The problem could be solved by using magnetic supports where the catalyst could be easily separated from liquid reaction media under an external magnetic field [3]. Recently, superparamagnetic spinel ferrite nanoparticles have been intensively investigated because of their remarkable electrical and magnetic properties, and wide practical applications, especially in biomedical diagnostics and in catalysis [4, 5].

Palladium-catalyzed Heck cross-coupling reactions have attracted significant interests as they represent key steps in the building of more complex molecules from simple precursors [6]. Their applications range from the synthesis of complex natural products to supramolecular chemistry and materials science and from fine chemical to the pharmaceutical industries [7]. Several catalyst systems have been developed for the Heck reactions however, the question of what is the best catalyst still remains unanswered even for the simplest cases, though studied in hundreds of works [8]. In this paper, we wish to report for the first time in Vietnam, to our best knowledge, the preparation of a palladium complex immobilized on superparamagnetic spinel ferrite nanoparticles and its application as an efficient catalyst for the Heck reaction of aryl iodides with styrene to form stilbenes as principal products. The magnetic catalyst could be facilely isolated from the reaction mixture by simple magnetic decantation, and reused without significant degradation in activity.

II - EXPERIMENTAL

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 hours 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. Transmission electron microscope (TEM) studies were performed using a JEOL JEM 1400, in which samples were dispersed on holey carbon grids for TEM observation. 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 10ºC/min under a nitrogen atmosphere. X-ray powder diffraction (XRD) patterns were recorded using CuK_{α} radiation source on a XPERT-PRO powder diffractometer.

GC-MS analyses were performed using an Agilent GC-MS 6890. GC analyses were performed using a Shimadzu GC-17A equipped with a FID detector and a 30 m × 0.25 mm × 0.25 μm DB-5 column. The temperature program for GC analyses heated samples from 60ºC to 140ºC at 10ºC/min, held at 140ºC for 1 min, from 140ºC to 300ºC at 50ºC/min, and held at 300ºC for 3 min.

2. Synthesis of amino-functionalized magnetic nanoparticles

Cobalt spinel ferrite ($CoFe_2O_4$) nanoparticles were synthesized following a microemulsion method [9]. $CoFe_2O_4$ nanoparticles (1.1 g) were dispersed in a mixture of ethanol and water (150 ml, 1:1 by volume). Ammonium hydroxide (15 ml, 25% v/v aqueous solution) was added, and the mixture was stirred vigorously at 60ºC for 24 hours. 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 (150 ml, 1:1 by volume), and sonicated for 30 min at room temperature. 3-(trimethoxysilyl)propylamine (1g) was then added, and the solution was heated at 60ºC with vigorous stirring for 24 hours. 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 (1.06 g).

3. Synthesis of palladium catalyst immobilized on magnetic nanoparticles

The amino-functionalized magnetic nanoparticles (0.40 g) was added to a round-bottom flask containing ethanol (99.5 %, 60 ml) and 2-hydroxybenzaldehyde (6 ml, 57 mmol) or 2-acetyl pyridine (4 ml, 36 mmol). The resulting mixture was sonicated for 5 minutes, and then heated at reflux with rapid stirring for 24 hours. After that, the reaction mixture was cooled to room temperature, washed with copious amounts of ethanol and *n*-hexane by magnetic decantation, and dried under vacuum at room temperature to yield the immobilized Schiff base (0.36 g). The immobilized Schiff base (0.30 g) was then added to the round-bottom flask containing the solution of palladium acetate (0.0286 g, 0.128 mmol) in acetone (50 ml). The mixture was then stirred vigorously at room temperature for 24 hours. The solid was then separated by magnetic decantation, washed with copious amounts of acetone and dried under vacuum at room temperature to yield the immobilized palladium catalyst (0.26 g).

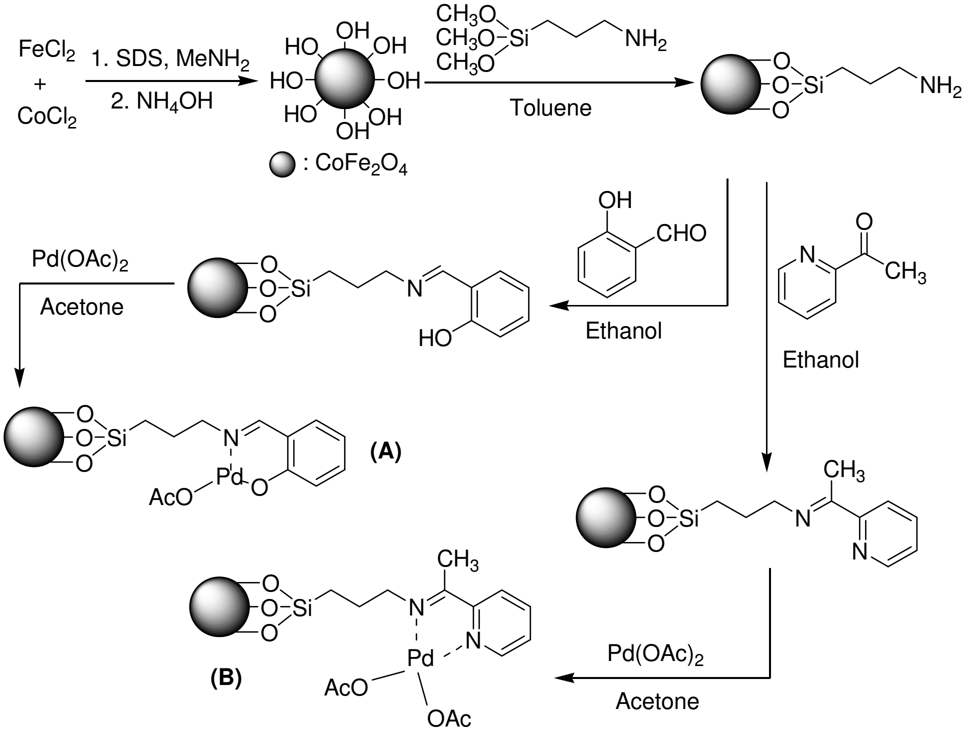
4. Catalysis studies

Unless otherwise stated, a mixture of iodobenzene (0.12 ml, 1.08 mmol), styrene (0.2

ml, 1.62 mmol), triethylamine (0.45 ml, 3.24 mmol), and hexadecane (0.12 ml, 0.41 mmol) as the internal standard in dimethylformamide (5 ml) were added to a round-bottom flask containing the required amount of the immobilized palladium 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. The organic components were extracted into diethylether, dried over Na_2SO_4 and analyzed by gas chromatography (GC) with reference to hexadecane. Product identity was also further confirmed by gas chromatography — mass spectroscopy (GC-MS), and also by using standard *trans*-stilbene and *cis*-stilbene (Sigma-Aldrich).

III - RESULTS AND DISCUSSION

Cobalt spinel ferrite ($CoFe_2O_4$) nanoparticles were synthesized following a microemulsion method [9]. 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 [10]. The hydroxyl groups on the surface of the magnetic nanoparticles were then enriched with an aqueous solution of ammonia, facilitating the surface modification step. The resulting nanoparticles were functionalized with 3-(trimethoxysilyl)propylamine to create surface amino groups, according to a slightly modified literature procedure [11]. The amino-functionalized magnetic nanoparticles were allowed to react with 2-hydroxybenzaldehyde or 2-acetyl pyridine to form immobilized bidentate ligands, which were complexed with palladium acetate using a literature procedure previously reported by Clark and co-workers, affording the immobilized palladium complex catalysts (catalyst A and catalyst B - scheme 1) [12].



Scheme 1: Synthesis of the immobilized palladium catalyst on magnetic nanoparticles

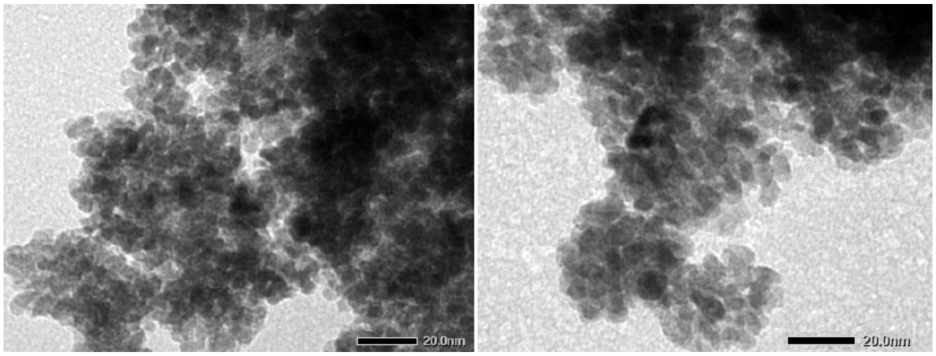


Figure 1: TEM micrographs of the catalyst A (left) and B (right)

The modified magnetic spinel ferrite nanoparticles were characterized by X-ray powder diffraction (XRD), transmission electron microscope (TEM), thermogravimetric analysis (TGA), Fourier transform infrared (FT-IR), and elemental analysis (EA). TEM studies showed an average diameter of approximately 8 - 10 nm for the particles (figure 1). Particle agglomeration was clearly observed for the magnetic nanoparticles, which was in good agreement with the literature [9, 11]. It should be noted that most oxide particles, regardless of composition, aggregate on TEM grids and the images do not imply that the nanoparticles aggregate similarly in solution. XRD studies showed that the magnetic nanoparticles are $CoFe_2O_4$ spinel ferrites, with XRD patterns being consistent with literature [3, 9, 11] (figure 2). No impurity peak was observed in the XRD diffractogram of the modified magnetic nanoparticles.

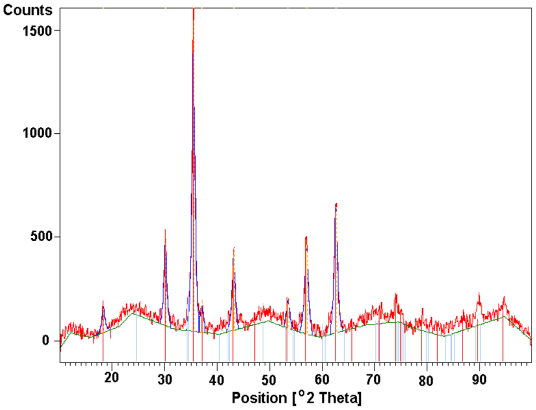


Figure 2: X-ray powder diffractogram of the functionalized magnetic nanoparticles

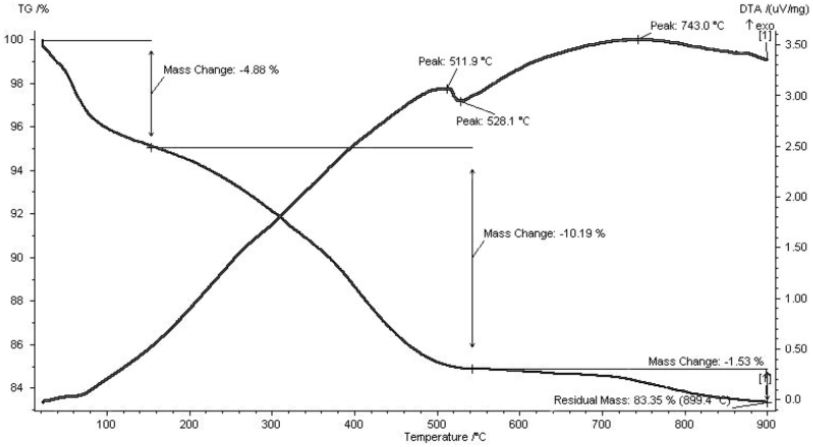


Figure 3: TGA graph of the immobilized bidentate iminopyridine ligand

TGA analysis of the amino-functionalized magnetic nanoparticles indicated that 0.7 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 particles. TGA analysis of the immobilized Schiff base exhibited a Schiff base loading of approximately 0.5 mmol/g for both cases (figure 3). As expected, EA analysis of the catalyst A, and catalyst B exhibited a palladium loading of 0.26 mmol/g, and 0.33 mmol/g (AAS), respectively. It should be noted that the metal loading of several immobilized palladium complex catalysts for cross-coupling reactions was reported to be in the range of 0.1 — 0.5 mmol/g [8]. 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 [13]. As the catalyst was designed for Heck reaction where a base was required, 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 Heck and the Suzuki reactions [13]. However, the effect of free amino groups on the activity of the catalyst still needs further investigation.

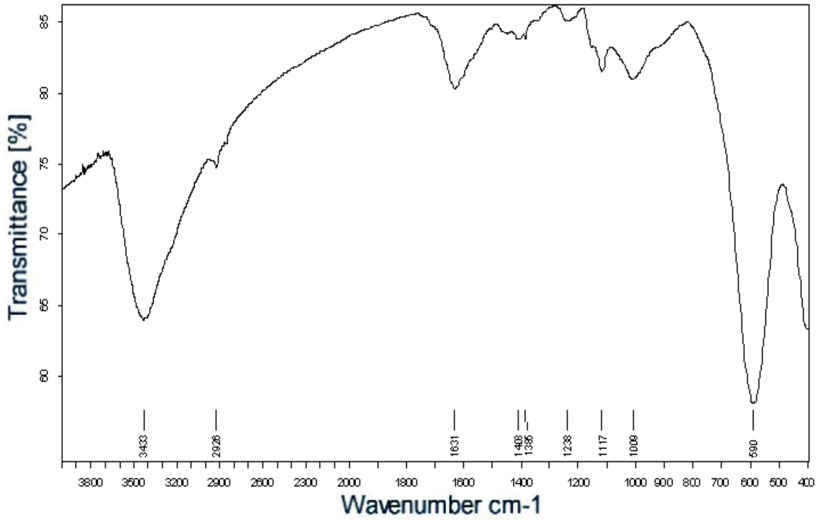
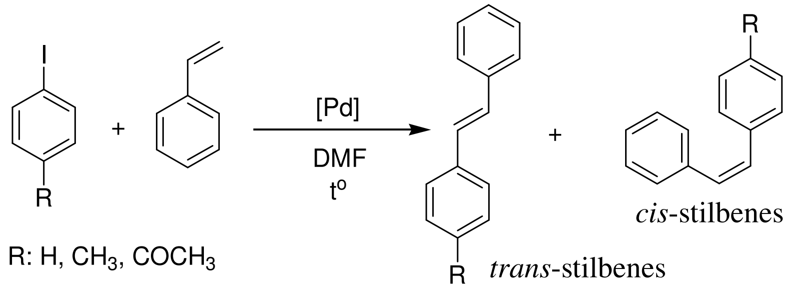


Figure 4: FT-IR spectrum of the catalyst B

FT-IR spectra of both the unfunctionalized and functionalized magnetic nanoparticles showed the presence of a Fe-O stretching vibration at approximately 590 cm^{-1}, an O-H stretching vibration due to physisorbed water and potentially surface hydroxyls near 3430 cm^{-1}, and an O-H deformation vibration near 1630 cm^{-1}, respectively. The significant features observed for the amine-functionalized nanoparticles, the immobilized Schiff base, and the immobilized palladium catalysts are the appearance of the peaks near 1110 cm^{-1} for Si-O stretching. For the immobilized ligands and the catalysts, there were also the appearance of the peaks near 2950 - 3050 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 (figure 4) [9]. However, the FT-IR spectra exhibited little meaningful data due to the low loading of the ligand and the palladium complex on the magnetic nanoparticles.



Scheme 2: The Heck reaction of aryl iodides and styrene using the palladium complex catalyst immobilized on the magnetic nanoparticles

The immobilized palladium complex catalyst (catalyst A) was assessed for its activity initially in the Heck reaction between iodobenzene and styrene to form *trans*-stilbene as the principal product and *cis*-stilbene as the minor product (scheme 2). As DMF is normally the solvent of choice for cross-coupling reactions [8], it was decided to carry out the Heck reaction in DMF at 120ºC, using 0.2 mol% of the catalyst A. It is generally accepted that a base is obviously necessary to neutralize the HI produced, and regenerate the active species to complete the catalytic cycle of the Heck reaction [8, 13]. Therefore, the effect of base on the reaction conversion was investigated, using three bases including Na_2CO_3,, CH_3COONa, and triethylamine (figure 5). The most commonly used base in the Heck reaction is Na_2CO_3, but stronger bases such as NaOH, K_3PO_4 and $Ba(OH)_2$ were previously reported to give better results in some cases. In this research, however, the Heck reaction using Na_2CO_3 afforded the coupling product in a significantly lower conversion than reactions using CH_3COONa and triethylamine as bases. After 6 hours, a conversion of only 18% was obtained for the case of Na_2CO_3, while reactions using CH_3COONa, and triethylamine proceeded with up to 62% and 100% conversions, respectively, being achieved under the same conditions. Indeed, triethylamine was previously employed as the base for several Heck cross-coupling reactions [13].

It was then decided to use triethylamine as the base for the Heck reaction in further studies. The effect of the reaction temperature was then investigated varying from 100ºC to 140ºC, using 0.2 mol% palladium catalyst A in DMF, and in the presence of triethylamine as the base. As expected, experimental results, showed that the higher the reaction temperature, the higher the reaction rate (figure 6). Increasing the temperature to 140ºC, more than 99% conversion was achieved after 2 hours. It was observed that the Heck reaction carried out at 100ºC proceeded with slower rate, with 63% conversion being obtained after 6 hours. Indeed, the temperature range of 80ºC to 140ºC has been the most commonly used for Heck transformation using different types of palladium catalysts [7, 8]. It should also be noted that DMF could decompose at its normal boiling point, therefore, Heck reactions in DMF should not be carried out at the temperature higher than 140ºC.

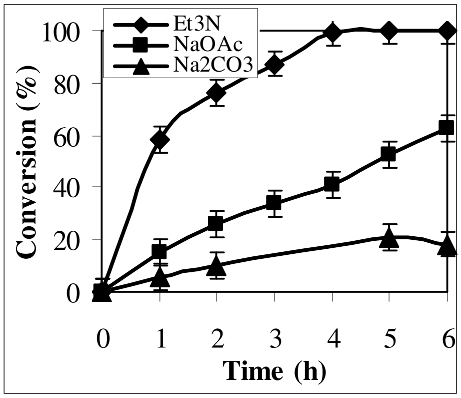


Figure 5: Effect of bases on reaction conversions

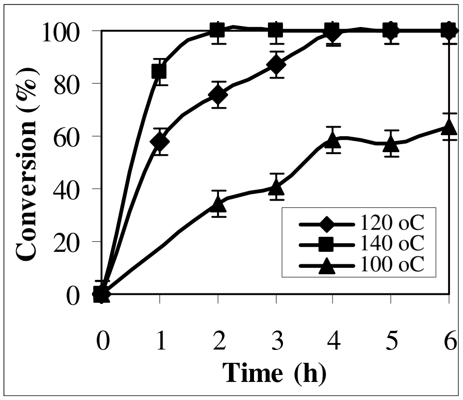


Figure 6: Effect of temperature on reaction conversions

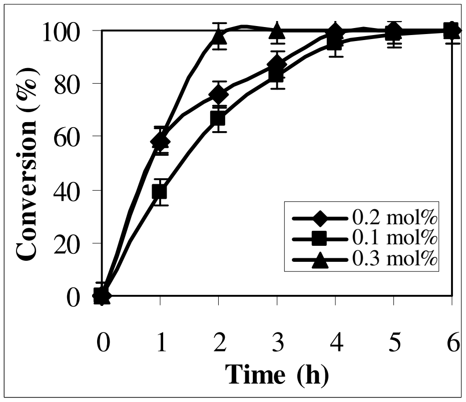


Figure 7: Effect of catalyst concentration on reaction conversions

With these results in mind, we therefore studied the effect of catalyst concentration on reaction conversions, using DMF as the solvent and triethylamine as the base at 120°C. As with previous reports, the higher the catalyst concentration was used, the higher the reaction rate was observed. Almost quantitative conversion of iodobenzene to stilbenes was achieved after 2 hours at the palladium concentration of 0.3 mol% relative to iodobenzene. Decreasing the catalyst concentration resulted in a drop in reaction rate, with 99% conversions being obtained after 4 hours and 6 hours at palladium concentrations of 0.2 mol% and 0.1 mol%, respectively (figure 7). The catalyst concentrations used in this study were comparable to those of several previous reports covering different aspects of the Heck reaction, where the palladium concentrations varied from less than 0.01 mol% to more than 1 mol%, depending on the nature of the catalysts as well as the substrates [7, 8, 13].

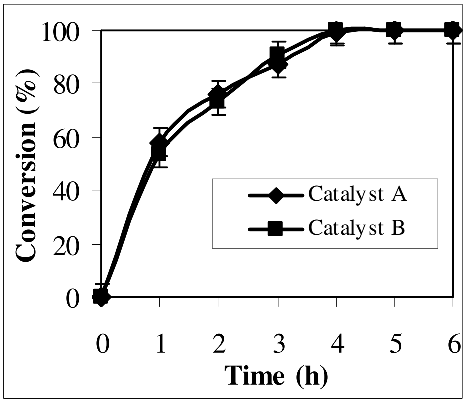


Figure 8: Conversions for the Heck reaction using catalyst A and catalyst B, respectively

It should be emphasized that for the Heck reaction, a small variation of substrate, structure, nature of base, ligands, temperature, pressure, etc. often leads to unpredictable results. Trends in reactivity and selectivity are uneven and often break when would not be expected. An obvious question of what is the best catalyst and procedure for the Heck reaction still remains unanswered even for the simplest cases, though studied in hundreds of works [8]. We therefore decided to investigate the difference in activity between the catalyst A and catalyst B in the Heck reaction of iodobenzene and styrene using 0.2 mol% palladium at 120°C. Experimental results showed that the activity of catalyst A and catalyst B was comparable, within experimental errors (figure 8). Indeed, Clark and co-workers previously immobilized these palladium complexes on silica gel and investigated their activity in the Heck reactions of several aryl halides and vinylic olefins [14]. However, the immobilization of these palladium complexes on superparamagnetic nanoparticles was not previously reported.

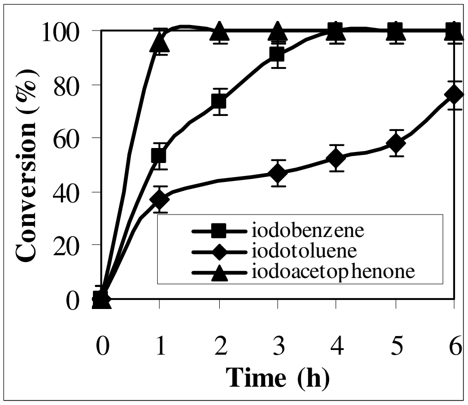


Figure 9: Effect of substituents on reaction conversions of iodobenzene derivatives

In order to investigate the effect of different substituents on reaction conversions, the study was then extended to the reaction of substituted iodobenzenes containing electron-donating (*i.e.* 4-iodotoluene) and electron-withdrawing (*i.e.* 4-iodoacetophenone) groups. Reactions were carried out using 0.2 mol% palladium of catalyst B at 120°C. It was observed that the reaction of 4-iodotoluene with styrene proceeded with slower rate than the Heck reaction of iodobenzene, with a total conversion of 75% being achieved after 6 hours (figure 9). As expected, the reaction rate of the Heck cross-coupling between 4-iodoacetophenone and styrene was higher than the case of iodobenzene, affording a total conversion of more than 99% after 1 hour. This result indicated that the Heck 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. It was also previously reported that the use of electron-withdrawing ring substituents normally lead to enhanced reactivity in palladium-catalyzed cross-coupling reactions [8, 13, 15]. The effect of substituents on reaction conversions of iodobenzene derivatives observed in this research was therefore in good agreement with the literature.

An important point concerning the use of a heterogeneous catalyst is its lifetime, particularly for industrial and pharmaceutical applications of the palladium-catalyzed Heck reaction. In the best case the catalyst can be recovered and reused before it eventually deactivates completely. At the same time, the catalyst recovery can also reduce the environmental pollution caused by heavy metals used in the catalyst system [16]. The immobilized palladium catalyst B was therefore investigated for recoverability and reusability in the Heck reaction of iodobenzene and styrene. After the reaction, an external magnetic field was applied on the outer surface of the glass reaction vessel containing the modified 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 magnetic nanoparticles stationary inside the vessel. The magnetic catalyst was washed with ethanol 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. Experimental results showed that catalyst B could be reused in further reaction without significant degradation in activity. A conversion of more than 99% was still achieved after 4 hours for the second run. As expected, the selectivity of the *trans*-isomer to the *cis*-isomer remained almost unchanged, being around 85% of *trans*-isomer and 15% of *cis*-isomer during the recycle of the catalyst.

IV - CONCLUSIONS

In summary, palladium complexes immobilized on cobalt superparamagnetic spinel ferrite ($CoFe_2O_4$) nanoparticles were synthesized. The immobilized palladium complexes were characterized by X-ray powder diffraction (XRD), transmission electron microscope (TEM), thermogravimetric analysis (TGA), Fourier transform infrared (FT-IR), and elemental analysis (EA). The immobilized palladium complex was used as an efficient heterogeneous catalyst for the Heck cross-coupling reaction of iodobenzene and styrene to form stilbene as the principal product. The most commonly used base in several Heck reactions, Na_2CO_3, was found to be almost ineffective for the reaction using the magnetic palladium catalyst. The Heck reaction of iodobenzene derivatives containing electron-donating and electron-withdrawing substituents with styrene could afford more than 99% conversions in the presence of triethylamine at 120 °C, and at the palladium loading of as low as 0.2 mol%. Recovery of catalyst was facilely achieved by simple magnetic decantation. The immobilized palladium complex catalyst could be reused 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.

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