

N-heterocyclic carbene–palladium complex immobilized on silica nanoparticles Recyclable catalyst for high yield Suzuki and Heck coupling reactions under mild conditions

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Received 30 November 2006; accepted 2 December 2006

Available online 8 December 2006

Abstract

N-heterocyclic carbene–palladium (NHC–Pd) complexes immobilized on ~10 nm silica nanoparticles were synthesized. Because of the very high surface area and small size, these nanoparticles remain suspended in a variety of solvents with the catalyst sites readily accessible to the reactants. The catalysts showed excellent activity towards Suzuki coupling reaction of different aryl iodides and bromides with phenyl boronic acid using isopropanol: H₂O as solvent. They were also effective for Heck coupling. The nano-sized particles can be easily recovered and repeatedly reused without loss of activity.

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Keywords: Palladium catalyst; Silica nanoparticles; Suzuki coupling; Heck coupling

1. Introduction

Carbon–carbon bond formation reactions, such as Suzuki and Heck coupling that are catalyzed by palladium complexes are used widely in a variety of synthetic and industrial applications [1–12]. However, the homogeneous catalysts that are often employed are difficult to separate and reuse. Polymer-supported recyclable heterogeneous catalysts have been employed [8–11]. In these cases, some of the catalytic sites are buried within the polymer matrix and cannot participate in the reactions. The use of palladium complex formed in situ on the surface of a silica gel for Heck reaction has also been reported [12]. Here, we report on Suzuki and Heck reactions catalyzed by *N*-heterocyclic carbene–palladium (NHC–Pd) complexes immobilized on ~10 nm silica nanoparticles. Because of the very high surface area and small size, these nanoparticles remain suspended in a variety of solvents with the catalyst sites readily

accessible to the reactants. Thus, they are effective catalysts for a wide range of substrates in benign non-conventional solvents, including water. Moreover, they are readily separated by filtration and can be reused repeatedly.

2. Experimental

2.1. Materials and instrumentation

N-imidazole was purchased from Acros Organics and all other chemicals and materials were purchased from Aldrich and used without further purification. All reactions were carried out under air unless otherwise stated. ¹H NMR spectra was recorded on Bruker DPX-300 spectrometer. The TEM images were taken with JOEL 1200EXII operating at 80 kV. The sample was prepared by depositing 4 μL of the compound dispersed in toluene on carbon coated copper grid (300 mesh). Leeman Labs PS3000UV inductively coupled plasma spectrophotometer was used to determine the amount of Pd on the catalysts.

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2.2. Preparation of 1-decyl-3-(triethoxysilyl propyl) imidazolium salts immobilized on silica nanoparticles

2.2.1. Synthesis of 1-decyl-3-(triethoxysilyl propyl) imidazolium chloride

The solution of imidazole (0.1 mol) in 80 mL THF was added drop wise to a slurry of NaH (0.12 mol) in 50 mL THF in a dry, inert atmosphere [13]. The mixture was stirred for 1 h at room temperature and a solution of tetrabutylammonium hydrogen sulfate (5 mmol) and decyl bromide (0.1 mol) in 50 mL THF was added. After stirring for 24 h, solids were filtered off and filtrate dried under vacuum. The product was purified by column chromatography using silica gel (0.035–0.070 mm, pore diameter 9 nm) and ethyl acetate. The resulting yields were in the range of 50–80%. A dry round bottomed flask with *n*-decyl imidazole (0.05 mol) and chloropropyl triethoxy silane (0.05 mol) was sealed and purged with N₂ for 20–25 min and then heated at 105 °C for 24 h. The resulting viscous liquid was washed with ether and dried under vacuum to give 71% of 1-decyl-3-(triethoxysilyl propyl) imidazolium chloride. Both *N*-decyl imidazole and the ionic liquid were characterized by using ¹H NMR spectroscopy.

N-decyl imidazole. ¹H NMR (CDCl₃, ppm): 7.38 (s, 1H), 6.96 (s, 1H), 6.82 (s, 1H), 3.85 (t, 2H), 1.69 (quintet, 2H), 1.18 (m, 14H), 0.80 (t, 3H).

1-Decyl-3-(triethoxysilyl propyl) imidazolium chloride. ¹H NMR (CDCl₃, ppm): 10.84 (s, 1H), 7.40 (s, 1H), 7.30 (s, 1H), 4.33 (m, 4H), 3.80 (q, 6H), 2.0 (m, 2H), 1.90 (m, 2H), 1.20 (m, 23H), 0.85 (t, 3H), 0.56 (t, 2H).

2.2.2. NHC precursor covalently bonded to silica nanoparticles

The 10.5 mL of Ludox colloidal silica (Ludox-SM, 30 wt.% SiO₂, particle size 7 nm, pH 10) was diluted to 60 mL with deionized water [14]. To this, 1-decyl-3-(triethoxysilyl propyl) imidazolium chloride in 15 mL MeOH (40 wt.%) was added. The white precipitate formed immediately was aged for 24 h with stirring at intervals. The precipitate was recovered by filtration washed with water, ethanol, and finally dried under vacuum.

Chloride ions were replaced by heating the white particles (2 g) with an excess of the corresponding sulfonate salt in water at 70 °C for 24 h. The particles were separated by filtration and washed with warm water, acetone and dried under vacuum to yield precursors **1** and **2**.

2.2.3. Preparation of silica supported *N*-heterocyclic carbene–Pd complex

Silica nanoparticle supported NHC precursor **1** or **2** (1 g) and Pd(OAc)₂ (230 mg) were mixed in 40 mL toluene and heated at 50 °C for 8 h. The light brown colored catalyst **3** or **4** formed was separated and washed thoroughly with acetone and dried under vacuum. The catalysts were obtained in quantitative yield.

The amount of palladium loading was analyzed by ICP-AES. The 50 mg of the catalyst was mixed with 8 mL of HCl:HNO₃ (3:1, v/v) and heated at 75 °C for 4 h. The resulting orange col-

ored solution was filtered, diluted to 50 mL with distilled water and analyzed.

2.3. General procedure for Suzuki coupling

Aryl halide (0.75 mmol), catalyst (2 mol.% Pd), phenyl boronic acid (0.9 mmol), Na₂CO₃ (3.75 mmol), IPA/H₂O (1:1, v/v) (10 mL) were mixed and heated at 50 °C for a specific period of time. Upon completion, catalyst was separated by filtration, and washed with 10 mL water. The product was extracted with ether, dried over anhydrous Na₂SO₄ and then solvent evaporated. The biaryl product was purified by flash chromatography and identified using ¹H NMR spectroscopy.

4-Phenyltoluene. ¹H NMR (CDCl₃, ppm): 7.50 (d, 2H), 7.41 (d, 2H), 7.35 (t, 2H), 7.25 (t, 1H), 7.18 (d, 2H), 2.30 (s, 3H).

Biphenyl-4-carbaldehyde. ¹H NMR (CDCl₃, ppm): 9.99 (s, 1H), 7.88 (d, 2H), 7.69 (d, 2H), 7.58 (d, 2H), 7.40 (m, 3H).

2.4. General procedure for Heck coupling

Aryl halide (0.75 mmol), catalyst (2 mol.% Pd), olefin (0.9 mmol), K₂CO₃ (0.9 mmol), Et₃N (0.9 mmol) and DMF (5 mL) were heated at 100 °C for a specific time. After the reaction was complete, catalyst was separated by filtration and washed with 10 mL water. The product was extracted with ether, dried over Na₂SO₄ and solvent evaporated. The cinnamate product was purified by column chromatography and identified by ¹H NMR spectroscopy.

n-Butyl cinnamate. ¹H NMR (CDCl₃, ppm): 7.60 (d, 1H), 7.46 (dd, 2H), 7.30 (t, 3H), 6.40 (d, 1H), 4.18 (t, 2H), 1.62 (quintet, 2H), 1.38 (m, 2H), 0.94 (t, 3H).

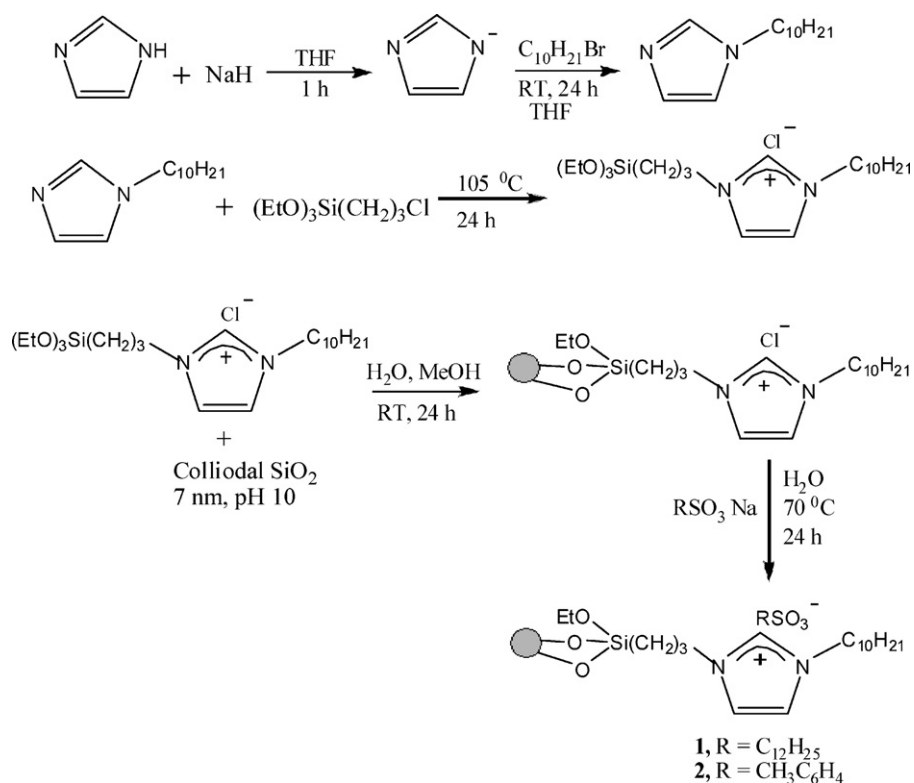
2.5. Procedure for recycling of the catalyst

4-Iodotoluene (0.75 mmol), catalyst **3** (2 mol.%), phenyl boronic acid (0.9 mmol), Na₂CO₃ (3.75 mmol), IPA/H₂O (1:1, v/v) (10 mL) were heated at 50 °C for 2 h. The catalyst was then separated by centrifuging at 750 rpm and then washed with 2 × 8 mL water, 8 mL acetone and dried at 50 °C for 4 h. The product was isolated by extraction with ether and purifying with flash chromatography. Recovered catalyst was reused for four more cycles of the same reaction.

3. Results and discussion

3.1. Preparation of 1-decyl-3-(triethoxysilyl propyl) imidazolium salts immobilized on silica nanoparticles

The synthesis of carbene ligand precursor is shown in Scheme 1. Imidazole was deprotonated by sodium hydride and then alkylated with decyl bromide in THF [13]. *N*-decyl imidazole was then quaternized with neat chloropropyl triethoxy silane. The resulting clear viscous ionic liquid 1-decyl-3-(triethoxysilyl propyl) imidazolium chloride was covalently linked with nano-sized silica support by condensation with surface silanol groups [14]. The chloride ions were subsequently replaced by either dodecane sulfonate or para-toluene sulfonate



Scheme 1. Synthesis of silica nanoparticle-immobilized NHC precursor.

ions by heating with corresponding sodium salt in aqueous medium to yield silica supported NHC precursor **1** and **2**. TEM image of the chloride analog of the precursor (Fig. 1) showed individual particles with an average diameter of 10 nm.

3.2. In situ preparation of silica supported *N*-heterocyclic carbene–Pd complex

The catalyst was synthesized by heating silica supported NHC precursor **1** or **2** with Pd(OAc)₂ in toluene at 50 °C for 8 h to obtain corresponding light brown colored catalyst **3** or **4** (Scheme 2). The amount of palladium in the catalysts was determined by inductively coupled plasma-atomic emission spectroscopy (ICP-AES). The loading level of Pd was found to be 0.239 and 0.235 mmol/g for catalyst **3** and **4**, respectively. Further, TEM images of **3** (Fig. 2) showed that the particles did not aggregate with the immobilization of the metal and the average diameter was measured to be 10 nm.

3.3. Heterogeneous Suzuki cross-coupling reaction

The catalytic activity of silica nanoparticle supported NHC–Pd complexes **3** and **4** were initially analyzed by reacting aryl iodides with phenyl boronic acid. The 2 mol.% of either catalyst **3** or **4** was used for the reaction and gave excellent yields within 2 h at 50 °C (Table 1). Typically, toxic organic solvents like DMF or NMP are employed in such coupling reactions. However, we employed a more benign solvent system: 1:1 (v/v) mixture of isopropanol (IPA) and water. The obtained yields

were at least as good as those obtained in traditional organic solvents [8].

The complex **3** was then chosen for the heterogeneous cross-coupling reaction of a range of aryl halides with PhB(OH)₂. Excellent yields were obtained in most of the cases (Table 2) including the substrates having electron withdrawing (entries 3, 8, 9) and electron donating (entries 4, 6, 7) functionalities. The catalyst was also active towards sterically hindered aryl

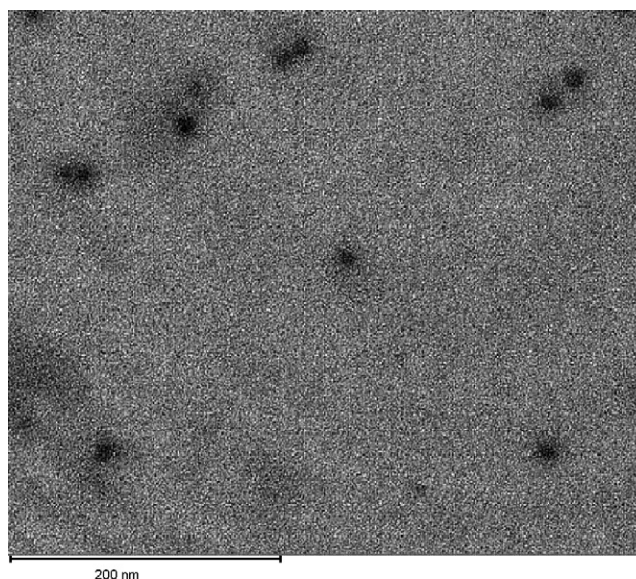
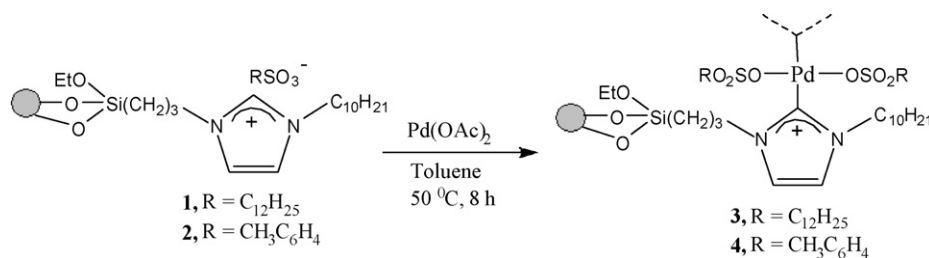
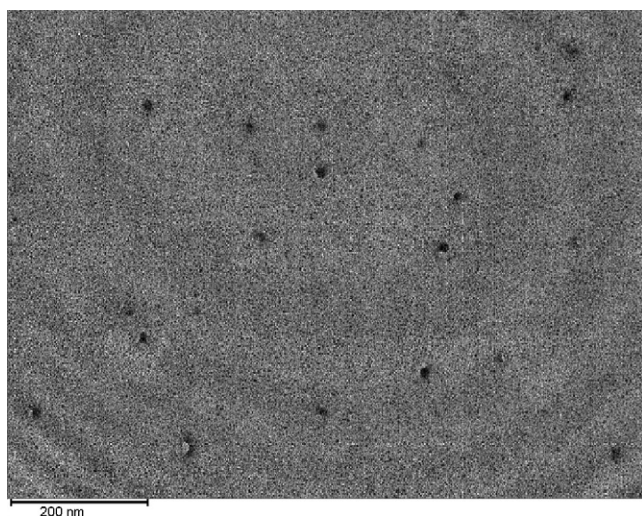


Fig. 1. TEM image of 1-decyl-3-(triethoxysilyl propyl) imidazolium chloride covalently linked to silica nanoparticles.



Scheme 2. Synthesis of silica supported NHC–Pd complex.

Fig. 2. TEM image of silica supported catalyst **3**.

bromide (entry 16). However, a low yield was obtained when chlorobenzene was used.

3.4. Heterogeneous Heck cross-coupling reaction

The ability of the nanoparticle-bound palladium species to catalyze Heck coupling was also examined. Aryl iodides with different functional groups were coupled with electron poor olefins like butyl acrylate and styrene at 100 °C using DMF as solvent. Excellent yields were obtained with *n*-butyl acrylate within 2 h using catalyst **4** (Table 3). Curiously, unlike the results

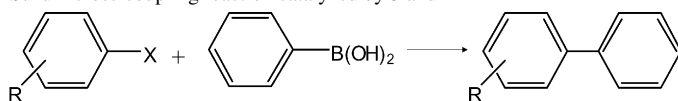
in the Suzuki coupling (Table 1), **3** was found to be significantly less reactive than **4**. Thus, **3** with dodecane sulfonate anion gave only 10% of *n*-butyl cinnamate while **4** with toluene sulfonate anion gave 99% of the product under similar conditions (entries 1, 2). With styrene, a high yield of product was formed only when catalyst and base were stirred for 15 min at 100 °C before the introduction of reactants. Bromobenzene failed to react even under the modified condition. Catalyst degradation was observed when water was used as a co-solvent; however, high yield was obtained in 24 h when pure IPA was the solvent (entry 6).

3.5. Reusability of silica supported catalyst

Easy recyclability and the prolonged retention of catalytic activity are very important for industrial applications. In order to check the reusability of the silica supported NHC–Pd complex, catalyst **3** was employed for the Suzuki coupling of 4-iodotoluene and phenyl boronic acid using 1:1 IPA:H₂O as solvent. In first cycle, 90% of 4-phenyl toluene was obtained. The nanoparticles were recovered by centrifugation, washed with water, acetone and dried at 50 °C for 4 h. The second cycle was started with the recovered catalyst and the process was repeated through five cycles without loss of productivity (Table 4).

Finally, in order to verify that both the metal and the *N*-heterocyclic carbene ligand are essential, the reaction of 4-iodotoluene with phenyl boronic acid was carried out in the presence of either the NHC precursor **1** or a mixture of *n*-octyl functionalized silica nanoparticles and Pd(OAc)₂, **5**. No product was formed with **1** while **5** formed 82% of the product in the first cycle. However, the yield decreased to only 39% in the sec-

Table 1
Suzuki cross-coupling reaction catalyzed by **3** and **4**^a



Entry	Aryl halide	Product	Yield (%) ^b [catalyst]
1			94 [3]
2			89 [4]
3			89 [3]
4			90 [4]

^a Conditions: Aryl halide (0.75 mmol), phenyl boronic acid (0.9 mmol), catalyst (2 mol.% Pd), Na₂CO₃ (3.75 mmol), IPA/H₂O (1:1, v/v) (10 mL), 50 °C, 2 h.

^b Isolated by column chromatography.

Table 2
Suzuki cross-coupling reaction of aryl halides with phenyl boronic acid catalyzed by **3**^a

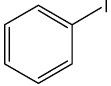
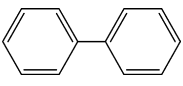
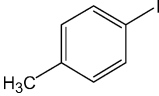
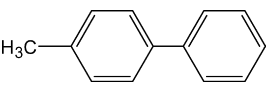
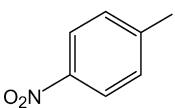
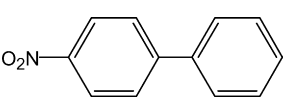
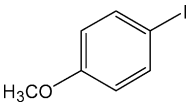
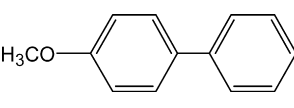
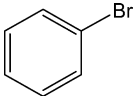
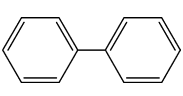
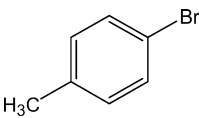
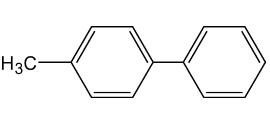
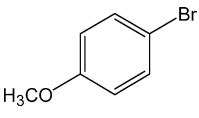
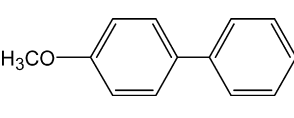
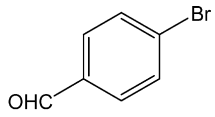
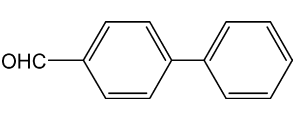
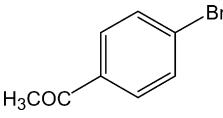
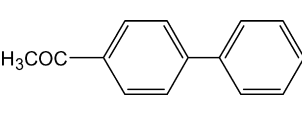
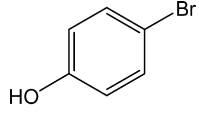
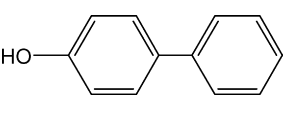
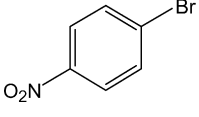
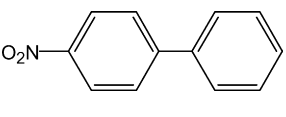
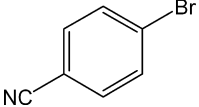
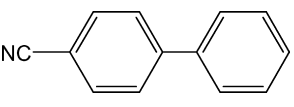
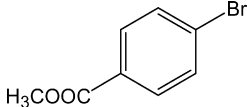
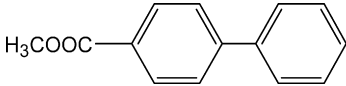
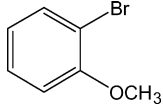
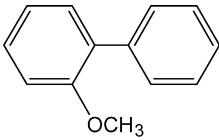
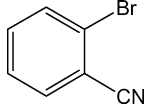
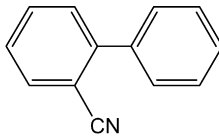
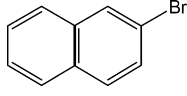
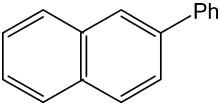
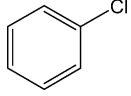
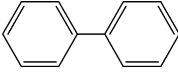
Entry	Aryl halide	Product	Time (h)	Yield (%) ^b
1			2	91 ^c
2			2	94
3			1	94 ^d
4			2	89
5			12	91
6			12	76
7			6	91
8			6	92 ^e
9			6	93
10			6	90
11			6	98
12			6	93

Table 2 (Continued)

Entry	Aryl halide	Product	Time (h)	Yield (%) ^b
13			6	88
14			12	93
15			6	92
16			12	82
17			11	29

^a Conditions: Aryl halide (0.75 mmol), phenyl boronic acid (0.9 mmol), **3** (2 mol.% Pd), Na₂CO₃ (3.75 mmol), IPA/H₂O (1:1, v/v) (10 mL), 50 °C.

^b Isolated by column chromatography.

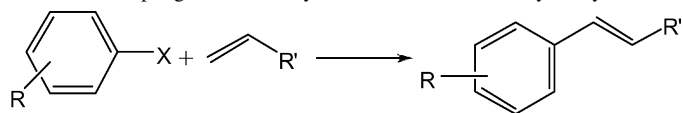
^c K₂CO₃ as base.

^d DMF solvent.

^e Determined by ¹H NMR spectroscopy (>95% purity).

Table 3

Heck cross-coupling reaction of aryl halides with olefins catalyzed by **4**^d



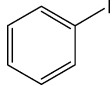
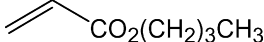
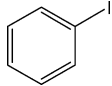
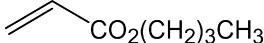
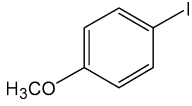
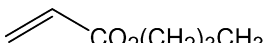
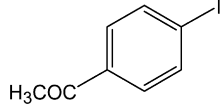
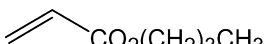
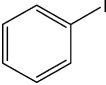
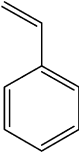
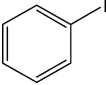
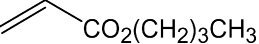
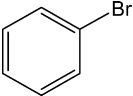
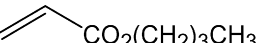
Entry	Aryl halide	Olefin	Time (h)	Yield (%) ^b
1			2	10 ^c
2			2	99
3			2	97
4			2	98 ^d

Table 3 (Continued)

Entry	Aryl halide	Olefin	Time (h)	Yield (%) ^b
5			4	94 ^e
6			24	85 ^f
7			24	–

^a Conditions: Aryl halide (0.75 mmol), olefin (0.9 mmol), **4** (2 mol.% Pd), K₂CO₃ (0.9 mmol), Et₃N (0.9 mmol), DMF (5 mL), 100 °C.

^b Isolated by column chromatography.

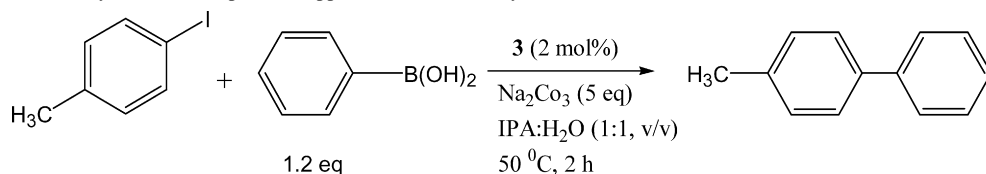
^c Catalyst **3** was used.

^d Determined by ¹H NMR spectroscopy (>95% purity).

^e K₂CO₃ (3.75 mmol).

^f IPA (5 mL), 70 °C.

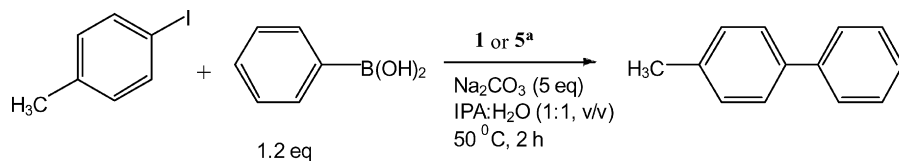
Table 4
Reusability of silica nanoparticle supported NHC–Pd catalyst



No. of run	Yield (%) ^a	Catalyst recovered (%)
1	90	85
2	90	98
3	92	98
4	95	97
5	91	91

^a Isolated by column chromatography.

Table 5
Suzuki coupling in the absence of metal or carbene species



Entry	Additives [no. of run]	Yield (%) ^b
1	1	–
2	5 [1]	82
3	5 [2]	39

^aThe 60 mg of either **1** or 4.5:1 (wt/wt) mixture of *n*-octyl functionalized SiO₂ and Pd(OAc)₂.

^b Isolated by column chromatography.

ond cycle, indicating significant loss of activity during recycling (Table 5).

4. Conclusion

In summary, we have described new heterogeneous NHC–Pd catalysts immobilized on nano-sized silica particles. The catalysts showed excellent activity towards Suzuki coupling reaction of different aryl iodides and bromides with phenyl boronic acid using IPA:H₂O as solvent. They were also effective for Heck coupling. The nano-sized particles can be easily recovered and repeatedly reused without loss of activity.

Acknowledgement

We thank the Department of Energy, Office of Basic Energy Sciences for funding.

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