

Silica-acac-supported palladium nanoparticles as an efficient and reusable heterogeneous catalyst in the Suzuki–Miyaura cross-coupling reaction in water

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Abstract. Supported Pd nanoparticles on acetyl acetone modified silica gel was prepared and its catalytic application in the Suzuki–Miyaura reaction of various aryl halides with phenylboronic acid was investigated. The reaction was carried out in water as solvent under green conditions in the presence of NaHCO₃ as the base. The catalyst was characterized by a combination of powder XRD, XPS, TEM and SEM. The catalyst is not sensitive to air and moisture, so reactions were carried out without using inert atmosphere. The catalyst can be reused up to six times without significant loss of catalyst activity. The cumulative turnover number (TON) over six runs is 13525.

Keywords. Supported palladium nanoparticles; Suzuki–Miyaura reaction; aryl halide; phenylboronic acid; heterogeneous catalyst.

1. Introduction

The Suzuki–Miyaura cross-coupling reaction is an important method for aryl–aryl bond formation, using aryl halides and phenylboronic acids.^{1–3} Significant studies that had been done in this area in the last decade are derived from numerous advantages of this reaction such as high stability of organoboranes towards air and moisture, low toxicity associated with boron compounds, mild and easy reaction conditions, use of aqueous inorganic bases and coupling of steric hindered substrates.^{4–6} The Pd-catalysed Suzuki reactions are well-known as influential methods to construct C–C bond in modern chemical transformations,^{7–9} and have found extensive use as much as of the utility of its products in the synthesis of natural products, pharmaceutical intermediates, agrochemical drug, advanced materials and liquid crystals.^{10–15}

In spite of the fact that homogeneous palladium catalysts based on various Pd complexes along with some ligands^{16–18} or free of ligands,^{19,20} have been extensively used for Suzuki reaction, an outstanding disadvantage of these procedures is the difficulty in recovering and reusing the expensive catalyst. Overcoming this drawback using heterogeneous palladium catalysts

could be an attractive method since the heterogeneous catalysts can be easily separated from the reaction mixture.^{21–23} Thus, many studies have been concerned with the development of palladium catalysts, including immobilizing palladium complexes or nanoparticles on several supports.^{24–35} In the case of silica-supported palladium nanoparticles, several amorphous and porous supports have been used for Suzuki reaction.^{36–47}

Recently, many studies have been devoted to the development of milder reaction conditions, and water has been currently used as a benign solvent in the Suzuki reaction.^{48–53} Water has obvious advantages as a solvent in organic synthesis, since it is the most abundant and inexpensive liquid on earth. Also, it is eco-friendly, nontoxic, and non-flammable solvent.^{54,55} Herein, we report a new heterogeneous and reusable catalyst for Suzuki–Miyaura cross-coupling reaction in water. The catalyst is not sensitive to air and displays high efficiency for biaryl synthesis. Moreover, this heterogeneous catalyst performed up to six runs without significant loss of activity.

2. Experimental

All starting materials were purchased from Merck and used without further purification. ¹H and ¹³C NMR

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spectra were recorded on a Bruker 300 spectrometer using TMS as an internal standard in CDCl_3 and FT-IR spectra were obtained as KBr pellets on a JASCO 680-PLUS spectrophotometer. The XPS spectra were obtained by X-ray photoelectron spectroscopy, Twin Anode X-Ray Source Systems (X-Ray 8025-Bestes). Also we used GC (BEIFIN 3420 Gas Chromatograph equipped with a Varian CP SIL 5CB column – 30 m, 0.32 mm, 0.25 μm) for examination of reactions conversions. X-ray powder diffraction (XRD) were obtained by Philips X'Pert PRO over the 2θ range from 10–100° at the rate of 2.58°/min, using Cu-K α radiation ($\lambda = 1.54060 \text{ \AA}$). Sizes of the synthesized particles were observed using transmission electron microscope (TEM, HITACHI H-700H) at an accelerating voltage of 150 kV. Samples were prepared by placing drops of diluted ethanol dispersed of catalyst particles on the surface of copper grids and evaporation.

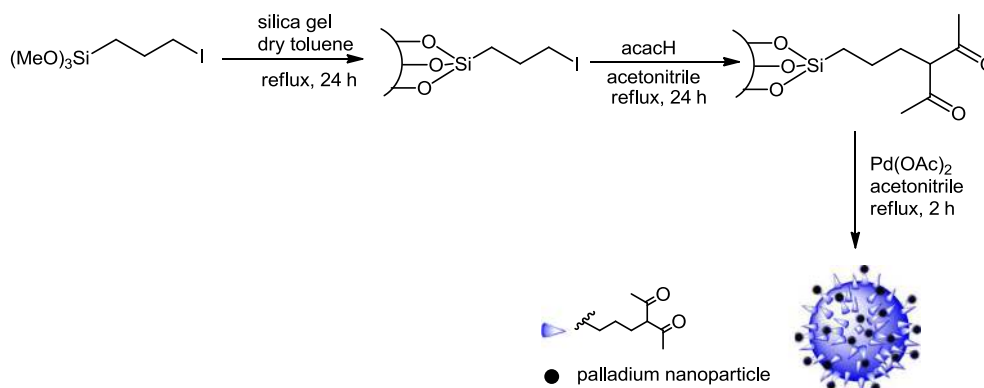
2.1 General procedure for the Synthesis of the silica-acac-supported palladium nanoparticles

Initially, to prepare activated silica, silica gel 60 (5 g) was soaked in concentrated HCl overnight and then re-suspended in deionized water several times until the pH of the filtrate was higher than 6. The acid-treated silica gel was dried at 150°C overnight and cooled in a desiccator. To prepare 3-iodopropyl trimethoxysilane-supported silica gel, activated silica gel (5 g) was suspended in solution of 3-iodopropyl trimethoxysilane (5 mmol) in toluene. The suspension was refluxed for 24 h. After cooling, the particles were collected by filtration and exhaustively washed with ethanol, and dried under reduced pressure to give iodopropyl-silica gel. Iodoropropyl-silica gel re-suspended in 30 mL acetonitrile and 5 mmol (0.50 g) acetyl acetone and 5 mmol (0.69 g) K_2CO_3 were added and refluxed for

24 h. The solids were washed with water and soxhlated with ethanol for 5 h and dried under reduced pressure. Finally, the resulting solid was stirred with acetonitrile in the presence of 0.05 g of $\text{Pd}(\text{OAc})_2$ and after washing the solids by acetonitrile, the Pd(II)-acac-supported silica refluxed in acetonitrile to form a black solid. The black solid was washed with acetone and dried under vacuum at room temperature to obtain the desired catalyst. The Pd-amount was 0.04 mmol/g (4.26 mg/g) determined using AAS.

2.2 General procedure for the Suzuki reaction of aryl halides with phenylboronic acid

A mixture of the appropriate aryl halide (1 mmol), phenylboronic acid (1.2 mmol), SiO_2 -acac-PdNPs catalyst (10 mg, 0.0004 mmol, 0.04 mol%), NaHCO_3 (2 mmol) was added to water (3 mL) in a round-bottom flask equipped with condenser and refluxed under heating conditions in reflux temperature. The mixture was stirred continuously during the reaction. After the reaction was completed (monitored by TLC, 90/10 hexane/EtOAc), the mixture was cooled to room temperature and the catalyst was separated by filtration, washed thrice with water and acetone and allowed to dry at room temperature for 30 min under vacuum for the next run. The reaction mixture was poured into a separating funnel and water (20 mL) and n-hexane (10 mL) were added and extracted for thrice. The combined organic phases were dried over CaCl_2 , filtered, and the solvent was evaporated. The residue was the products which were various biaryls. In some cases, the residue was purified by column chromatography (silica gel 60, EtOAc: n-hexane 10:90). All the products were known and characterized by melting point, IR and ^1H NMR spectroscopy and were compared with authentic samples. The data were found to be identical to those reported in the literature.



Scheme 1. Synthetic route for preparation of the catalyst.

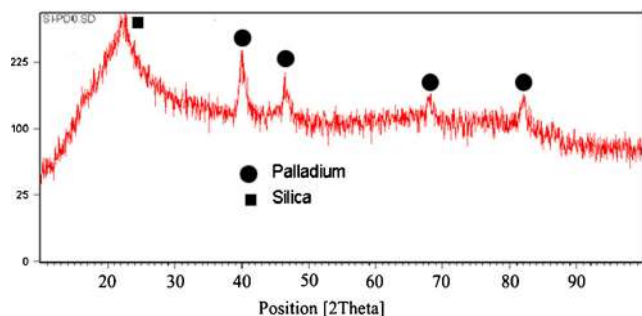


Figure 1. Powder X-ray diffraction (XRD) pattern of palladium nanoparticles supported on silica.

3. Results and discussion

Synthetic route for preparation of the catalyst is shown in scheme 1. The catalyst is represented as SiO_2 -acac-PdNPs. In this study, we utilize acetonitrile as reducing agent for reduction of palladium(II) to palladium(0) nanoparticles. As Susharina and co-workers mentioned earlier on the oxidation of acetonitrile by using platinum catalysts, oxidation of acetonitrile in the presence of oxygen leads to formation of CO_2 , H_2O , N_2 and NO_x at high temperatures.⁵⁶ As we did not observe any changes in GC chromatograms (FID detector) of acetonitrile (HPLC grade) after and before reduction of palladium, we believe that the formation of these products may be probable during reduction of palladium with acetonitrile.

Characterization of heterogeneous catalyst was studied using XRD, XPS, SEM and TEM analysis. Results indicate that palladium content of the catalyst is 0.04 mmol/g (4.26 mg/g). As shown in figure 1, XRD pattern of catalyst that matched well with that of it (Reference code: 00-005-0681) shows the presence of metallic palladium phases (2 theta = 40.1, 46.5, 68.0 and 86.0) and amorphous silica (2 theta = 22.0) and is consistent with the metallic palladium(0) data in the literature.⁵⁷ Also, we can see that no characteristic peaks of impurities were observed. Results from XRD indicate that palladium nanoparticles have been successfully immobilized on the surface of silica-acac.

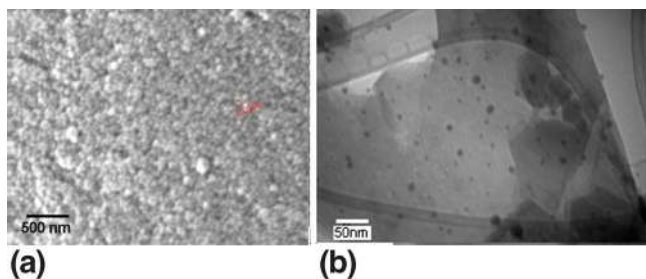


Figure 2. (a) SEM and (b) TEM images of the palladium nanoparticles supported on the surface of silica gel.

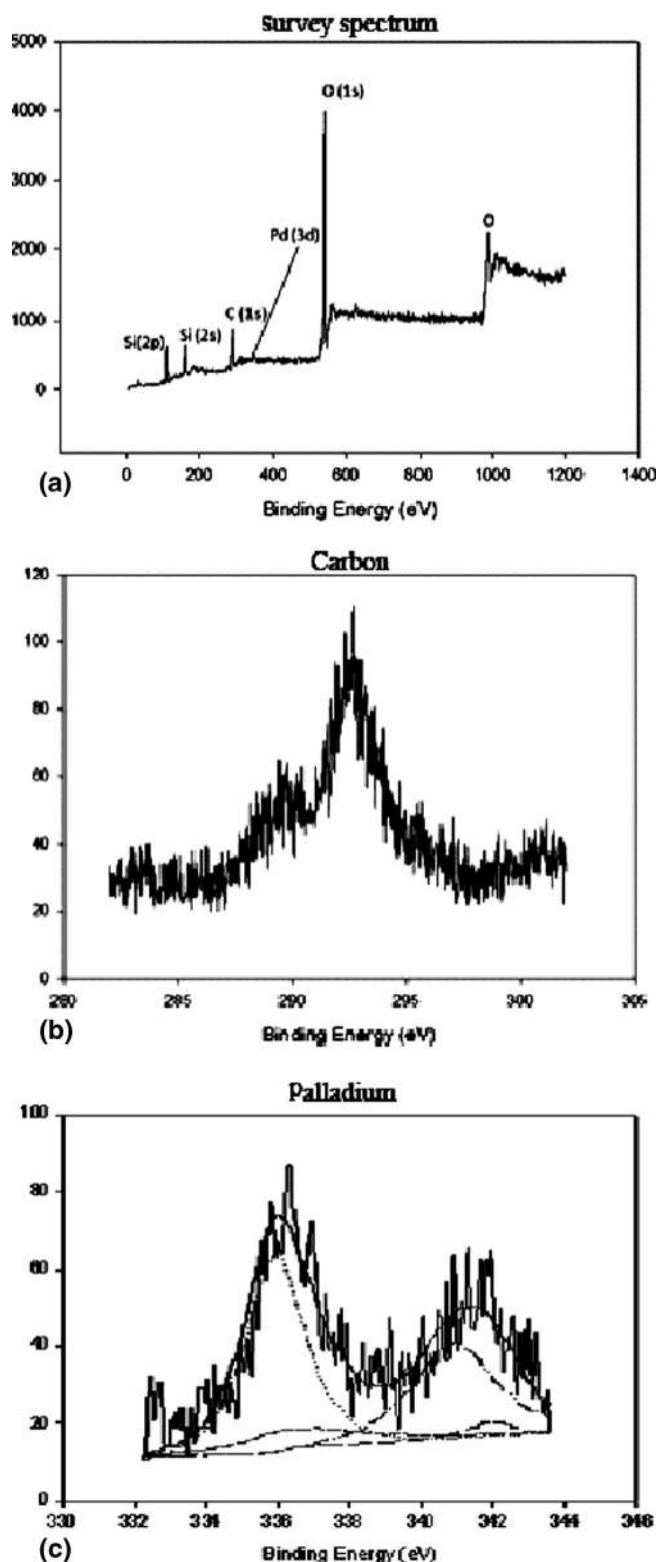
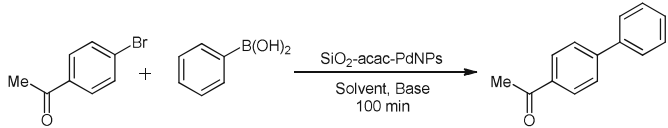


Figure 3. XPS spectra of the catalyst: (a) survey spectrum, (b) C_{1s} , and (c) Pd_{3d} .

The SEM image (figure 2a) in accordance with broad peak of silica in XRD spectra, shows that the catalyst was almost amorphous. Dark spots in the TEM image (figure 2b) indicate the presence of palladium nanoparticles in the range of 6–12 nm.

Table 1. Optimization of base and solvent for the Suzuki reaction of 4-bromoacetophenone with phenylboronic acid.^a


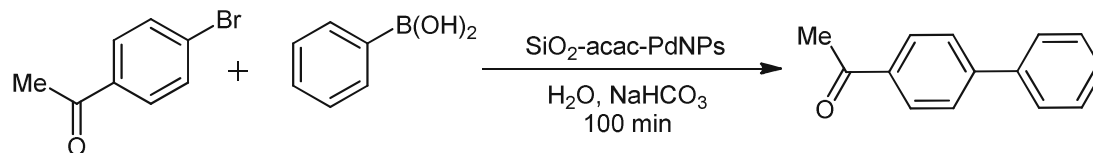
Entry	Base	Solvent	Conversion(%) ^b
1	NaHCO ₃	EtOH	85
2	NaHCO ₃	MeOH	87
3	NaHCO ₃	H ₂ O	90
4	NaHCO ₃	DMF	60
5	NaHCO ₃	NMP	25
6	NaHCO ₃	CH ₃ CN	50
7	NaHCO ₃	Dioxane	10
8	Na ₂ CO ₃	H ₂ O	40
9	NaOH	H ₂ O	0
10	Et ₃ N	H ₂ O	0
11	Na(OAc)	H ₂ O	20
12	K ₂ CO ₃	H ₂ O	30

^aReaction conditions: 4-bromoacetophenone (1 mmol), phenylboronic acid (1.2 mmol), 20 mg catalyst, various bases and solvents

^bGC conversion

The catalyst was also characterized by XPS analysis, and the results are shown in figure 3. Figure 3a shows the survey spectrum of catalyst and it is obvious that C and Pd were present in the catalyst. Figure 3b illustrates the C_{1s} spectrum, in which the peak centred at 293 eV is attributed to C species, which originated from the acac and propyl groups, suggesting that organic moieties existed in the surface of the catalyst. From figure 2c, it can be seen that the Pd_{3d} spectrum could be

resolved into two spins – orbit pairs with 3d_{5/2} binding energies of 336 and 337 eV. Peak binding energies of 336 eV (Pd_{3d_{5/2}}) and 341.0 eV (Pd_{3d_{3/2}}) correspond to fully reduced palladium, while the peaks at 337 and 342.1 eV are assigned to the palladium(II) species, which may result from incomplete reduction of palladium. It can be seen from the XPS spectrum that most of Pd²⁺ was reduced to Pd⁰ because the area of the peak of Pd²⁺ ion was relatively small.

Table 2. Optimization of base and catalyst concentration for the Suzuki reaction of 4-bromoacetophenone with phenylboronic acid.^a

Entry	Cat.(mg)	Base (mmol)	Conversion (%) ^b
1	5	2	80
2	10	2	> 99
3	20	2	> 99
4	40	2	100
5	10	1	65
6	10	2	99
7	10	4	99

^aReaction conditions: 4-bromoacetophenone (1 mmol), phenylboronic acid (1.2 mmol), water (1.5 ml), reflux

^bGC conversion

In order to optimize the reaction conditions, the reaction in various solvents in the presence of different bases was tried. Initially, the Suzuki reaction conditions were optimized for the reaction of 4-bromoacetophenone and phenylboronic acid in the presence of various solvents and bases using 20 mg of catalyst. According to data present in table 1, water was the most efficient solvent and NaHCO_3 was chosen as the best base for this reaction (table 1, entry 3).

The concentration of base and catalyst was also optimized by employing various amounts of base and catalyst for the reaction of 4-bromoacetophenone and phenylboronic acid, using 10 mg (0.0004 mmol, 0.04 mol% Pd) of catalyst and 2 equivalents of base gave the best results (table 2, entry 2). The catalyst was completely stable and thus the reactions could be carried out without using inert atmosphere. These reaction conditions were applied in the Suzuki reaction of different types of aryl halides with phenylboronic acids under reflux conditions (table 3).

As demonstrated in table 3, the catalyst can be used for cross-coupling reaction of aryl iodides, bromides and even less reactive aryl chlorides under heating conditions in reflux temperature, and they were transformed to the corresponding coupled products in good to excellent yields in short reaction times. However, aryl chlorides were reacted more slowly in comparison to the iodides and bromides derivatives. Reactions were performed with both electron-donating and electron-withdrawing groups and the results are demonstrated in

table 3, the reaction did not show any significant sensitivity to electronic effects. Also, selectivity of the catalyst was examined by using ortho-, meta- and para-bromochlorobenzene (table 3, entries 4–6); in each case, only Br as the better leaving group was substituted and “Cl did not enter the reactions;” this means that the reaction acts chemo-selectively and in comparison to Cl, Br is a better leaving group.

In addition, we found that most hindered aryl halides usually produce corresponding biaryls in longer reaction times and lower yields. To show the effect of steric hindrance in the Suzuki coupling reaction and applicability of the catalyst for sterically hindered aryl halides, we tried the coupling of 1-bromo-2-nitrobenzene, 2-bromo toluene and 2, 6-dimethyl bromobenzene and found that the reaction of these compounds took place in longer times (entries 17, 22 and 23).

Recycling of the catalyst was examined for the coupling reaction of iodobenzene with phenylboronic acid under optimized reaction conditions (iodobenzene (0.25 mmol), phenylboronic acid (0.3 mmol), NaHCO_3 (0.5 mmol), catalyst (0.04 mol%) and water 3 ml) in reflux temperature. After the first run of the catalyst, the reaction mixture was allowed to cool to room temperature and the catalyst was separated by filtration, washed with H_2O and acetone (thrice) and allowed to dry at room temperature for 30 min under vacuum. The recycled catalyst was reused under the same reaction conditions. The catalyst could be recycled four times

Table 3. Suzuki reaction of aryl halides with phenylboronic acid in water at reflux temperature^a.

Entry	ArX	Product	Time (min)	Yield (%)
1				
	TON ^b	TOF/h ^c		
Run 1	2350	392	6	94
Run 2	2375	396	6	95
Run 3	2300	383	6	92
Run 4	2250	375	6	90
Run 5	2200	314	7	88
Run 6	2050	292	7	82
Total TON	13525			

Table 3. (continued)

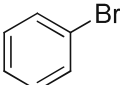
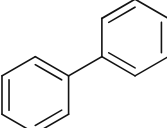
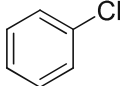
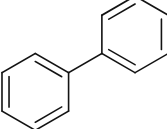
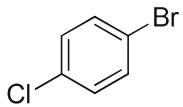
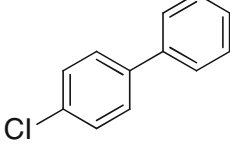
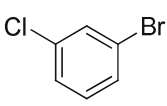
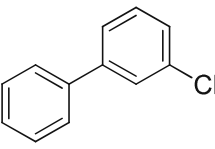
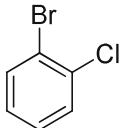
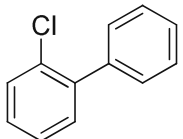
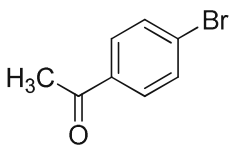
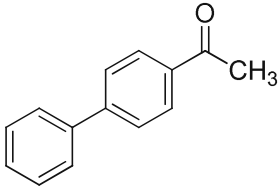
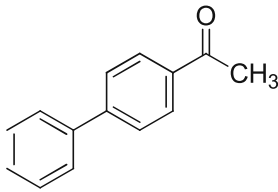
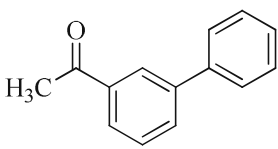
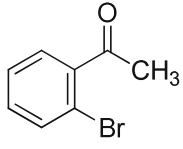
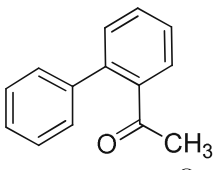
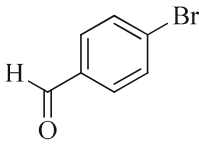
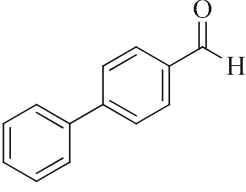
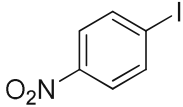
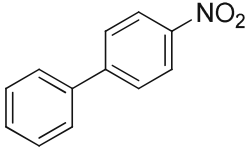
Entry	ArX	Product	Time (min)	Yield (%)
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3			20	84
4			6	90
5			7	91
6			8	85
7			50	92
8			95	87
9			125	58
10			20	91
11			17	89

Table 3. (continued)

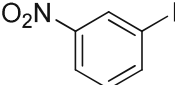
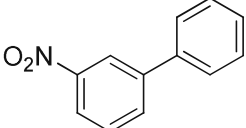
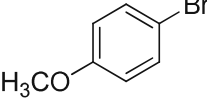
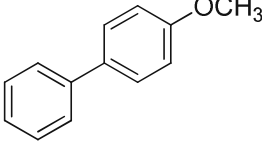
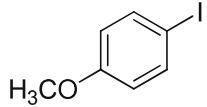
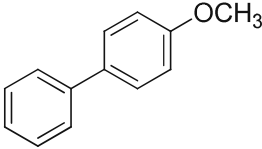
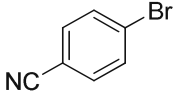
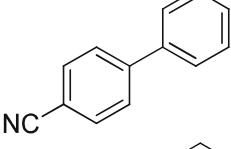
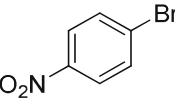
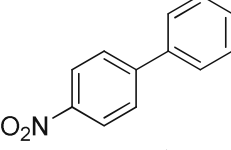
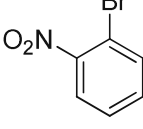
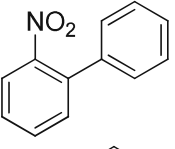
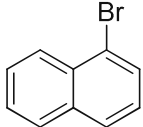
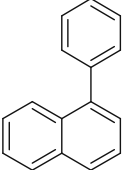
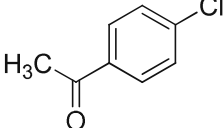
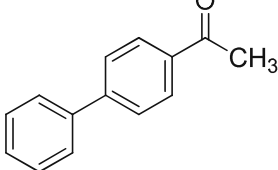
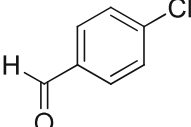
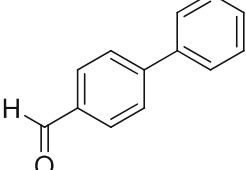
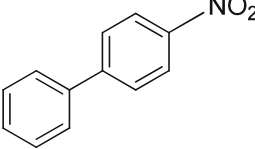
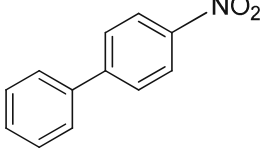
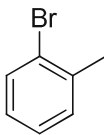
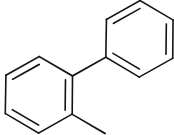
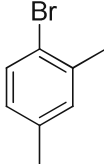
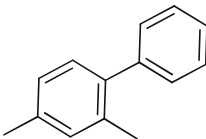
Entry	ArX	Product	Time (min)	Yield (%)
12			19	90
13			13	91
14			10	92
15			45	94
16			45	91
17			6 h	80
18			4 h	93
19			17	88
20			12	86
21			15	87

Table 3. (continued)

Entry	ArX	Product	Time (min)	Yield (%)
22			8 h	71
23			9.5 h	66

^aReaction conditions: aryl halide (1 mmol), phenylboronic acid (1.2 mmol), base (2 mmol), 10 mg catalyst and 3 ml water as solvent

^bTON (turnover number) = product (mmol)/catalyst (mmol)

^cTOF (turnover frequency) = TON/reaction time (h)

with essentially no loss in activity, even after recycling six times, yield of product could still be obtained at 82% (table 3, entry 1). The cumulative turnover number (TON) over six runs was 13525. We performed the FT-IR analysis for studying the fate of acac in the catalyst after six catalytic runs. The FT-IR spectra clearly showed the absorption bands of acac and confirmed that acac is still present on the catalyst surface.

4. Conclusion

In summary, we found that palladium nanoparticles could be stably immobilized onto the surface of ligand-modified silica gel, and thus could act as highly active and reusable catalyst for promoting the Suzuki–Miyaura cross-coupling reaction of various aryl halides with phenylboronic acids to produce the corresponding products in excellent yields with high chemo-selectivity and acceptable reaction times.

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References

- Das P, Sharma D, Shil A K and Kumar A 2011 *Tetrahedron Lett.* **52** 1176
- Miyaura N and Suzuki A 1995 *Chem. Rev.* **95** 2457
- Ikegami S and Hamamoto H 2009 *Chem. Rev.* **109** 583
- Amoroso F, Colussi S, zotto A D, Llorca J and Trovarelli A 2011 *Catal. Commun.* **12** 563
- John A, Shaikh M M and Ghosh P 2010 *Inorg. Chim. Acta* **363** 3113
- Alonso F, Beletskaya I P and Yus M 2008 *Tetrahedron* **64** 3047
- Wang J, Song G and Peng Y 2011 *Tetrahedron Lett.* **52** 1477
- Zarei A, Khazdooz L, Hajipour A R, Rafiee F, Azizi G and Abrishami F 2012 *Tetrahedron Lett.* **53** 406
- Kitamura Y, Sakurai A, Udzu T, Maegawa T, Monguchi Y and Sajik H 2007 *Tetrahedron* **63** 10596
- Wang J, Seefeld M A and Luengo J 2011 *Tetrahedron Lett.* **52** 6346
- Hargreaves S L, Pilkington B L, Russell S E and Worthington P A 2000 *Tetrahedron Lett.* **41** 1653
- Phakhodee W, Toyoda M, Chou C M, Khunnawutmanotham N and Isobe M 2011 *Tetrahedron* **67** 1150
- Afonso A, Feliu L and Planas M 2011 *Tetrahedron* **67** 2238
- Borhade S R and Waghmode S B 2011 *Beilstein J. Org. Chem.* **7** 310
- Yang H, Han X, Li G and Wang Y 2009 *Green Chem.* **11** 1184
- Fleckenstein C A and Plenio H 2010 *Chem. Soc. Rev.* **39** 694
- Marion N and Nolan S P 2008 *Acc. Chem. Res.* **41** 1440
- Amatore C and Jutand A 1998 *Coord. Chem. Rev.* **178** 511
- Molander G A and Biolatto B 2003 *J. Organomet. Chem.* **68** 4302
- Kabalka G W, Namboodiri V and Wang L 2001 *Chem. Commun.* 775
- Molander G A and Biolatto B 2002 *Org. Lett.* **4** 1867
- Yang J, Li P and Wang L 2011 *Synthesis* 1295
- Chen W, Li P and Wang L 2011 *Tetrahedron* **67** 318
- Senapati K K, Roy S, Borgohain C and Phukan P 2012 *J. Mol. Catal. A: Chem.* **352** 128
- Zhao H, Peng J, Xiao R and Cai M 2011 *J. Mol. Catal. A: Chem.* **337** 56
- Li L, Shi J L and Yan J N 2004 *Chem. Commun.* **17** 1990
- Artok L and Bulut H 2004 *Tetrahedron Lett.* **45** 3881
- Corma A, Iborra S, Xamena F X L, Monton R, Calvino J J and Prestipino C 2010 *J. Phys. Chem.* **C114** 8828

29. Tao R, Miao S, Liu Z, Xie Y, Han B, An G and Ding K 2009 *Green Chem.* **11** 96
30. Costa N J S, Kiyohara P K, Monteiro A L, Coppel Y, Philippot K and Rossi L M 2010 *J. Catal.* **276** 382
31. Zhang F, Jin J, Zhong X, Li S, Niu J, Li R and Ma J 2011 *Green Chem.* **13** 1238
32. Cirtiu C M, Dunlop-Briere A F and Moores A 2011 *Green Chem.* **13** 288
33. Senapati K K, Roy S, Borgohain C and Phukan P 2012 *J. Mol. Catal. A: Chem.* **352** 128
34. Polshettiwar V and Varma R S 2009 *Org. Biomol. Chem.* **7** 37
35. Gruber-Woelfler H, Radaschitz P F, Feenstra P W, Haas W and Khinast J G 2012 *J. Catal.* **286** 30
36. Das D D and Sayari A 2007 *J. Catal.* **246** 60
37. Gude K and Narayanan R 2011 *J. Phys. Chem.* **C115** 12716
38. Fihri A, Cha D, Bouhrara M, Almana N and Polshettiwar V 2012 *ChemSusChem* **5** 85
39. MacQuarrie S, Nohair B, Horton J H, Kaliaguine S and Crudden C M 2010 *J. Phys. Chem.* **C114** 57
40. Wang L and Cai C 2009 *J. Mol. Catal. A: Chem.* **306** 97
41. Yang H, Han X, Lia G and Wang Y 2009 *Green Chem.* **11** 1184
42. Karimi B, Elhamifar D, Clark J H and Hunt A J 2010 *Chem. Eur. J.* **16** 8047
43. Ungureanu S, Deleuze H, Babot O, Achard M-F, Sanchez C, Popa M I and Backov R 2010 *Appl. Catal. A: General* **390** 51
44. Iranpoor N, Firouzabadi H, Motevalli S and Talebi M 2012 *J. Organomet. Chem.* **708–709** 118
45. Iranpoor N, Firouzabadi H, Safavi A, Motevalli S and Doroodmand M M 2012 *Appl. Organometal. Chem.* **26** 417
46. Budroni G, Corma A, García H and Primo A 2007 *J. Catal.* **251** 345
47. Xu Y, Zhang Z, Zheng J, Du Q and Li Y 2013 *Appl. Organometal. Chem.* **27** 13
48. Polshettiwar V, Hesemann P and Moreau J E 2007 *Tetrahedron* **63** 6784
49. Ohtaka A, Tamaki Y, Igawa Y, Egami E, Shimomura O and Nomura R 2010 *Tetrahedron* **66** 5642
50. Dupuis C, Adiey K, Charruault L, Michelet V, Savignac M and Genet J P 2001 *Tetrahedron Lett.* **42** 6523
51. Leadbeater N E 2005 *Chem. Commun.* 2881
52. Moore L R and Shaughnessy K H 2004 *Org. Lett.* **6** 225
53. Arcadi A, Cerichelli G, Chiarini M, Correa M and Zorzan D 2003 *Eur. J. Org. Chem.* **10** 4080
54. Lamblin M, Nassar-Hardy L, Hierso J C, Fouquet E and Felpin F X 2010 *Adv. Synth. Catal.* **352** 33
55. Pawar S S, Uppalla L S, Shingare M S and Thore S N 2008 *Tetrahedron Lett.* **49** 5858
56. Susharina T L, Kerzhentsev M A, Pod'yacheva O Yu and Ismagilov Z R 1986 *React. Kinet. Catal. Lett.* **31** 27
57. Martinez S, Vallribera A, Cotet C L, Popovici M, Martin L, Roig A, Moreno-Manas M and Molins E 2005 *New J. Chem.* **29** 1342