Pure Appl. Chem., Vol. 79, No. 9, pp. 1553–1559, 2007.
doi:10.1351/pac200779091553

Highly active organosilane-based *N*-heterocyclic carbene-palladium complex immobilized on silica particles for the Suzuki reaction*

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Abstract: 1-Methyl-3-(3-trimethoxysilylpropyl)imidazolium chloride, [TMSPIM][Cl^-], was synthesized as a precursor of *N*-heterocyclic carbene (NHC), which can be coordinated with palladium to give an organosilane-based bidentic NHC-Pd complex. The organosilane-based NHC-Pd complex was immobilized covalently on silica particles (NHC-Pd/silica) and then characterized by field emission/scanning electron microscopy (FE/SEM), transmission electron microscopy (TEM), Fourier transform infrared spectroscopy (FTIRS), and inductively coupled plasma/atomic emission spectroscopy (ICP/AES). The Suzuki reaction was performed as a model reaction to examine the catalytic activity of NHC-Pd/silica. NHC-Pd/silica exhibited excellent performance in the Suzuki reaction of various aryl halide derivatives (except for aryl chloride derivatives) with phenylboronic acid *under mild conditions* (room temperature and short reaction time). Moreover, the catalyst was recycled several times without any significant loss of catalytic activity in the Suzuki reaction.

Keywords: *N*-heterocyclic carbene; Suzuki reaction; palladium; silica; organosilane.

INTRODUCTION

N-heterocyclic carbenes (NHCs) have emerged as an important research field since Öfele [1] disclosed originally in 1968. NHCs can be prepared in situ from the corresponding ionic liquids and readily coordinated with various transition metals affording stable and effective NHC-metal complexes. NHCs are very strong σ donors and show higher dissociation energies than phosphine ligands for a broad range of metals, so they do not easily dissociate from the metal center [2]. As with other ligands, NHCs can also stabilize catalytically relevant intermediates via electronic and steric effects [3]. Moreover, of particular importance is the fact that NHCs are reliable and user-friendly due to air- and moisture-stability [4].

NHC-metal complexes are effective catalysts in many useful transformations, such as Suzuki, Heck, and Sonogashira coupling and aryl amination by NHC-Pd complexes [5], arylation and alkenylation of aldehyde by NHC-Rh complexes [6], olefin metathesis, metathesis cross-coupling and hydroformylation by NHC-Ru complexes [7], and Kumada coupling by NHC-Ni complexes [8]. Among the above-mentioned complexes, NHC-Pd complexes have been examined as the most significant catalysis

*Paper based on a presentation at the 12th International Conference on Polymers and Organic Chemistry 2006 (POC'06), 2–7 July 2006, Okazaki, Japan. Other presentations are published in this issue, pp. 1471–1582.
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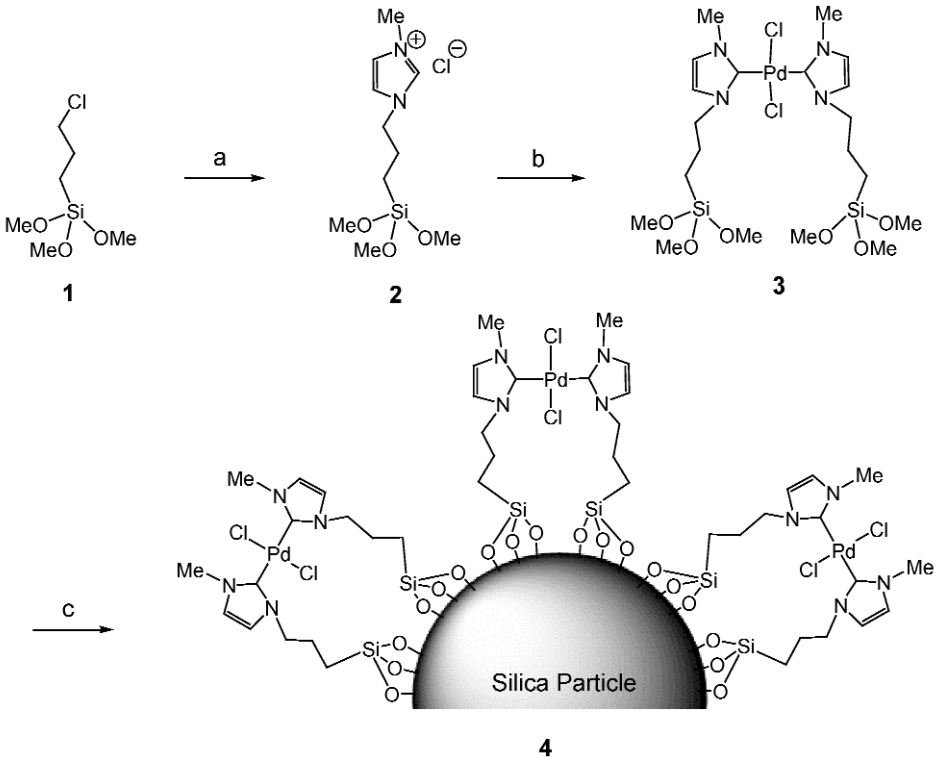
in both homogeneous and heterogeneous reactions. In particular, the use of heterogeneous NHC-Pd complexes is expanding due to their easy handling, little ligand contamination, and economic efficiency. NHC-Pd complexes have mainly been immobilized on polystyrene-based supports through several immobilization methods. Herrmann's group synthesized a bidentic NHC-Pd complex in solution and then immobilized it on Wang resin, which was successfully applied to the Heck reaction of aryl bromides [9]. Luo's group prepared a polystyrene-based Pd catalyst with another bidentic NHC-Pd complex for the Suzuki reaction. In this case, they anchored a bis-imidazolium precursor, which was synthesized in solution, on Merrifield resin and then treated the resin with $Pd(OAc)_2$ [10]. Our group has also developed several polymer supports immobilized with NHC-Pd complex, and they exhibited excellent catalytic performance in the Suzuki and Heck reactions [11].

Organosilanes have been used as a linker or coupling agent that can covalently connect a catalyst to an oxide support because they have functionalities at both end-sides. A number of organosilane-based ligands containing amine, imine, thiol, or phosphorous donors were coordinated with metals and immobilized on the oxide supports [12]. Organosilane-based imidazolium ions (ionic liquids) were also synthesized and applied as precursors of NHC-metal complexes as well as the ionic liquid-matrix (ILM). NHC-Ru complex on mesoporous silica was reported as a catalyst for olefin metathesis [13]. Moreover, NHC-Pd complex/ILM on silica particles was reported as a recoverable catalyst in Heck reactions [14]. In this case, a small amount of NHC-Pd complex was surrounded by an excess ionic liquid, but the effects of the ILM environment on the reactivity of the corresponding reactions were not mentioned in detail.

This report describes the preparation of silica immobilized with organosilane-based bidentic NHC-Pd complex (NHC-Pd/silica), which does not contain ILM completely, and demonstrates their effectiveness in the Suzuki reaction *under mild conditions*. Organosilane-based NHC-Pd complex was synthesized and in situ anchored on silica particles. When the catalysts were applied to Suzuki reaction, the reaction proceeded smoothly without difficulties, affording biphenyl products in high yield. In particular, the catalyst was recycled several times in the Suzuki reaction without significant loss of catalytic activity and showed reasonable turnover number (TON) and turnover frequency (TOF) values, under mild reaction conditions.

PREPARATION OF BIDENTIC NHC-Pd COMPLEX IMMOBILIZED ON SILICA PARTICLE

As shown in Scheme 1, 1-methyl-3-(3-trimethoxysilylpropyl)imidazolium chloride ([TMSPIM][Cl^-], **2**) was first synthesized as a precursor to the carbene ligand. To accomplish this, 3-chloropropyltrimethoxysilane (CPTS, **1**) was reacted with 1-methylimidazole at 80 °C for 24 h. The resulting [TMSPIM][Cl^-] (**2**) was obtained as a brown-colored paste in 98 % yield. To get organosilane-based NHC-Pd complex (**3**) with a bidentic structure, [TMSPIM][Cl^-] (**2**) (1 mol equiv) was allowed to react with $Pd(OAc)_2$ (0.6 mol equiv) in dimethylsulfoxide (DMSO) at 50 °C for 4 h and then at 100 °C for 0.5 h under a nitrogen atmosphere. We confirmed through ^1H NMR that the coordinating reaction progressed completely without any imidazolium ion left unreacted. The peak at 9.847 ppm, which corresponds to the chemical shift of C2 proton of [TMSPIM][Cl^-] (**2**), disappeared clearly after the reaction [15]. Then, organosilane-based NHC-Pd complex (**3**) was immobilized on silica (MERCK, 230–400 mesh) through condensation between silanol and alkoxy silane groups of (**3**). Organosilane-based NHC-Pd complex (**3**) dissolved in DMSO was mixed with silica particles and stirred at 50 °C for 24 h. A dark yellow-colored solid catalyst with an irregular shape (NHC-Pd/silica, **4**) was obtained (Figs. 1a,b) with the Pd loading level of 86 μmol/g. According to inductively coupled plasma/atomic electron microscopy (ICP/AEM) (Pd quantification) and elemental analysis (nitrogen quantification) together with C=C stretching peak of NHC at 1639 cm^{-1} in IR spectroscopy, we confirmed that [TMSPIM][Cl^-] (**2**) completely formed bidentic NHC-Pd complex without any ILM layer left on silica. Additionally, as shown in Fig. 1c, the immobilization of organosilane-based NHC-Pd complex (**3**) was confirmed by detecting Pd and Cl species using energy-dispersive X-ray (EDX) spectroscopy.



Scheme 1 Preparation of organosilane-based NHC-Pd complex (**3**) and NHC-Pd/silica (**4**). (a) 1-methyl imidazole, 80 °C, 24 h; (b) $Pd(OAc)_2$, DMSO, 50 °C, 4 h, and then 100 °C, 0.5 h; (c) silica particles (38~60 µm), 50 °C, 24 h.

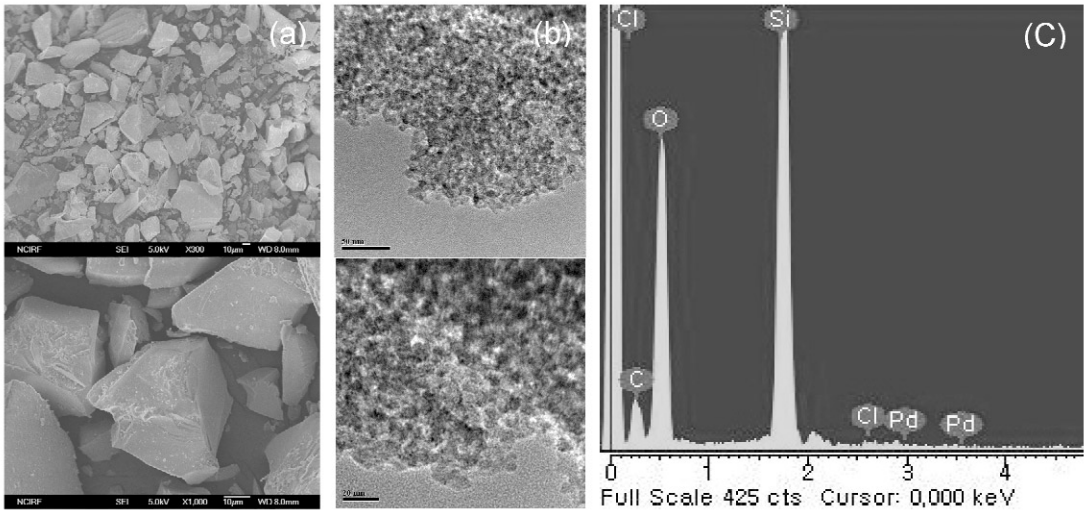


Fig. 1 (a) FE/SEM, (b) TEM images, and (c) EDX spectra of NHC-Pd/silica, **4**.

HETEROGENEOUS SUZUKI REACTION UNDER MILD CONDITIONS

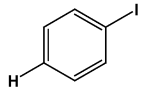
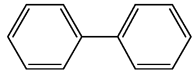
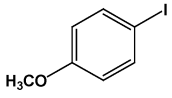
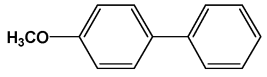
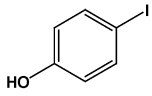
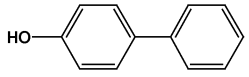
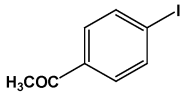
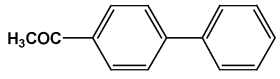
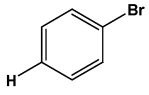
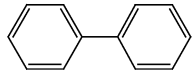
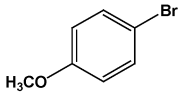
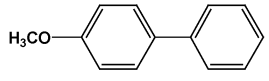
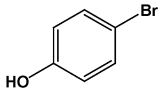
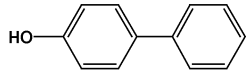
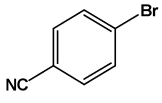
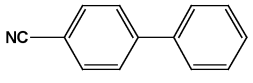
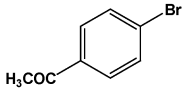
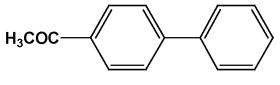
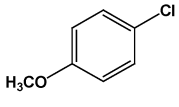
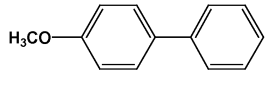
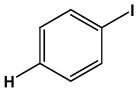
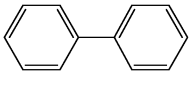
The heterogeneous NHC-Pd/silica (**4**) was applied to the Suzuki reaction between various aryl halides and phenylboronic acid at room temperature (RT) using DMF/H_2O (1:1) as the solvent system, which was used as the optimal solvent system in our previous study with polystyrene resin-based NHC-Pd complex but not optimized here.

Ten kinds of aryl halides were selected according to the reactivity of halogen groups (–I, –Br, and –Cl) and different substituents of electron-donating or -withdrawing properties (–OH, $COCH_3$, etc). Phenylboronic acid was fixed as the count part of the coupling reaction. Then, the catalytic activity of the heterogeneous NHC-Pd/silica (**4**) was examined. As shown in Table 1, the heterogeneous NHC-Pd/silica (**4**) showed excellent catalytic activity in all cases except for aryl chloride. In the case of aryl iodide and bromide, the Suzuki reaction proceeded smoothly within 2 h at RT regardless of the electronic properties of substituents and the reactivity of halogen groups. The isolated yields of corresponding biaryls were commonly >98 %. However, in the case of aryl chloride, the heterogeneous NHC-Pd/silica (**4**) was not effective under these conditions used in this study. Further studies of the Suzuki reaction of aryl chloride using heterogeneous NHC-Pd/silica are currently underway.

In the development of heterogeneous catalysts, *reusability* is one of the important factors in determining their potential value as an industrial catalyst. Moreover, the effectiveness of the heterogeneous catalysis is expressed as the well-known TON or TOF as a performance barometer. In these respects, reusability, TON, and TOF of the heterogeneous NHC-Pd/silica (4) was examined.

The catalyst was used four times in the Suzuki reaction between bromobenzene and phenylboronic acid in DMF/H_2O (1:1) at RT for 2 h. As shown in Table 2, the catalytic activity was maintained at an excellent level and the coupling yields were >95 % for four turns, which means that leaching of the coordinated Pd from the catalyst barely occurred. To obtain TON and TOF, the catalytic activity was evaluated by lowering the amount of the catalysts from 0.5 to 0.005 mol % under identical conditions to that used in the reusability tests. With 0.005 mol % of the catalyst, the Suzuki reaction proceeded with an isolated yield up to 32 % for 24 h. Therefore, TON and TOF were calculated to be 6400 and 267, respectively (Table 3). These might be reasonable values corresponding to mild reaction conditions. We concluded that the heterogeneous NHC-Pd/silica catalyst revealed excellent performance and reusability in the Suzuki reaction.

Table 1 Heterogeneous Suzuki reaction of aryl iodide, bromide and chloride with phenylboronic acid at RT for 2 h.[a]

Entry	Aryl halide	Product	Yield (%[b])
1			99
2			98
3			> 99
4			98
5			99
6			98
7			99
8			> 99
9			98
10			7
11[c]			87

[a]Aryl halides (1 mmol), phenylboric acid (1.2 mmol), NHC-Pd/Silica (86 μmol/g, 0.5 mol %), K_2CO_3 (3 mmol), and DMF/H_2O (1:1), RT, 2 h.
[b]Isolated by column chromatography.
[c]The reaction was carried out in water for 12 h.

Table 2 Reusability of the heterogeneous NHC-Pd/silica (**4**) in Suzuki reaction.[a]

Recycles	1st	2nd	3rd	4th
Yield (%)[b]	99	96	95	95

[a]Bromobenzene (1 mmol), phenylboronic acid (1.2 mmol), NHC-Pd/silica (86 μmol/g, 0.5 mol %), K_2CO_3 (3 mmol), and DMF/H_2O (1:1), RT, 2 h.
[b]Isolated by column chromatography.

Table 3 TON and TOF of the heterogeneous NHC-Pd/silica (**4**) in Suzuki reaction.[a]

Entry	Catalyst (mol %)	Yield (%)[a]	TON	TOF (h^{-1})
1[b]	0.5	99	198	99
2[c]	0.05	78	1560	65
3[c]	0.005	32	6400	267

[a]Isolated by column chromatography.
[b]Iodobenzene (1 mmol), phenylboronic acid (1.2 mmol), NHC-Pd/silica (86 μmol/g, 0.5 mol %), K_2CO_3 (3 mmol), and DMF/H_2O (1:1), RT, 2 h.
[c]Iodobenzene (1 mmol), phenylboronic acid (1.2 mmol), NHC-Pd/silica (86 μmol/g, 0.5 mol %), K_2CO_3 (3 mmol), and DMF/H_2O (1:1), RT, 24 h,
[d]Iodobenzene (1 mmol), phenylboronic acid (1.2 mmol), NHC-Pd/silica (86 mmol/g, 0.5 mol %), K_2CO_3 (3 mmol), and DMF/H_2O (1:1), RT, 24 h.

CONCLUSIONS

Organosilane-based bidentic NHC-Pd complex was synthesized from organosilane-based ionic liquid precursor and immobilized on silica particles covalently. This heterogeneous NHC-Pd/silica showed high catalytic activity in the Suzuki reaction of various aryl halides (except for aryl chlorides) with phenylboronic acid *under mild conditions* (RT and 2 h). In addition, the heterogeneous NHC-Pd/silica catalyst was reusable, which might be a good property for industrial applications.

ACKNOWLEDGMENT

This work was supported by the Nano Systems Institute-National Core Research Center (NSI-NCRC) program of the Korea Science and Engineering Foundation (KOSEF), Korea.

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15. ^{1}H NMR analysis was in situ carried out without the isolation of NHC-Pd complex because the coordinating reaction proceeded in DMSO-d_6 solvent.