

# Macroporous Polystyrene-Supported Palladium Catalyst Containing a Bulky *N*-Heterocyclic Carbene Ligand for Suzuki Reaction of Aryl Chlorides

Dong-Ho Lee,<sup>†</sup> Jong-Ho Kim,<sup>†,§</sup> Bong-Hyun Jun,<sup>†</sup> Homan Kang,<sup>‡</sup>  
Juyoung Park,<sup>†</sup> and Yoon-Sik Lee<sup>\*,†,‡</sup>

School of chemical and Biological Engineering, Seoul National University,  
Interdisciplinary Program in Nano-science and Technology, Seoul National University,  
Seoul 151-744, South Korea

yslee@snu.ac.kr

Received February 11, 2008

## ABSTRACT



Macroporous polystyrene (MPS)-supported 1-mesitylimidazolium chloride resin was prepared by reacting macroporous chloromethyl polystyrene with 1-mesitylimidazole as a supported *N*-heterocyclic carbene (NHC) precursor for the immobilization of a palladium catalyst. This MPS-supported NHC precursor readily formed a stable complex with Pd(OAc)<sub>2</sub>, which effectively catalyzed the Suzuki reaction of aryl iodide and bromides at room temperature and even aryl chlorides at elevated temperatures (100 °C). This catalyst showed reusability in the Suzuki reaction of aryl bromide.

The Suzuki reaction catalyzed by palladium is one of the most powerful routes for the formation of C(sp<sup>2</sup>)–C(sp<sup>2</sup>) bonds. This reaction has been used to make biaryl derivatives that are important intermediates in polymers, liquid crystals, pharmaceuticals, and herbicides.<sup>1,2</sup> From an industrial point of view, one of significant issue in the Suzuki reaction has focused on aryl chlorides because they are cheaper than aryl iodides and bromides and are readily available.<sup>3</sup>

Over the past few years, the Suzuki reaction of aryl chlorides were carried out successfully using homogeneous catalysts.<sup>4</sup> However, homogeneous catalysts have several problems, such as the need to separate and recycle the catalysts and the contamination from ligand residues in products. Therefore, a heterogeneous catalyst for the Suzuki reaction of aryl chlorides is still needed for industrial applications. Recently, several types of heterogeneous catalysts in the Suzuki reaction of aryl chlorides were reported using mesoporous silica-supported palladium catalysts,<sup>5</sup> Pd/C

<sup>†</sup> School of Chemical and Biological Engineering.

<sup>‡</sup> Interdisciplinary Program in Nano-science and Technology.

<sup>§</sup> Current address: Department of Chemical Engineering, Massachusetts Institute of Technology, Cambridge, MA 02139.

(1) (a) Miyaura, N.; Yanagi, T.; Suzuki, A. *Synth. Commun.* **1981**, *11*, 513. (b) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457. (c) Suzuki, A. *J. Organomet. Chem.* **1999**, *576*, 147.

(2) For recent reviews, see: (a) Bellina, F.; Carpita, A.; Rossi, R. *Synthesis* **2004**, 2419. (b) Pershichini, P. J. *Curr. Org. Chem.* **2003**, *7*, 1725. (c) Hassan, J.; Sevignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359. (d) Kotha, S.; Lashiri, S.; Kashinath, D. *Tetrahedron* **2002**, *58*, 9633.

(3) Review: (a) Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* **2002**, *41*, 4176. (b) Bedford, R. B.; Cazin, C. S. J.; Holder, D. *Coord. Chem. Rev.* **2004**, *248*, 2283.

(4) (a) Zapf, A.; Ehrentraut, A.; Beller, M. *Angew. Chem., Int. Ed.* **2000**, *39*, 4153. (b) Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* **1998**, *37*, 3387. (c) Stürmer, R. *Angew. Chem., Int. Ed.* **1999**, *38*, 3307. (d) Old, D. W.; Wolfe, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1998**, *120*, 9722. (e) Zhang, C.; Huang, J.; Trudell, M. L.; Nolan, S. P. *J. Org. Chem.* **1999**, *64*, 3804. (f) Bohn, V. P. W.; Gstottmayer, C. W. K.; Weskamp, T.; Herrmann, W. A. *J. Organomet. Chem.* **2000**, *595*, 186.

(5) (a) Yang, Q.; Ma, S.; Li, J.; Xiao, F.; Xiong, H. *Chem. Commun.* **2006**, 2495. (b) Trilla, M.; Pleixats, R.; Man, M. W. C.; Bied, C.; Moreau, J. J. E. *Tetrahedron Lett.* **2006**, *47*, 2399. (c) Sayah, R.; Glegola, K.; Framery, E.; Dufaud, V. *Adv. Synth. Catal.* **2007**, *349*, 373.

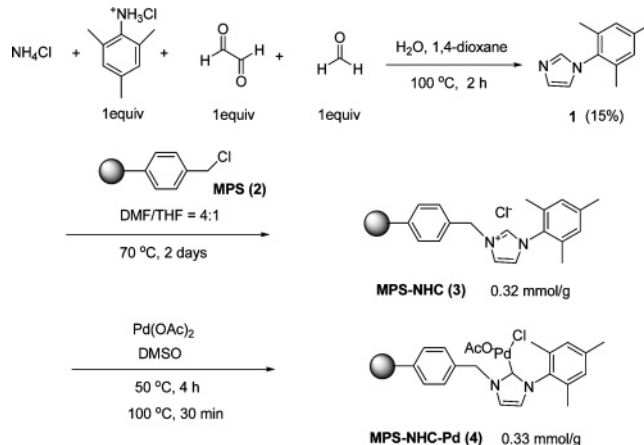
catalyst,<sup>6</sup> polymer-incarcerated palladium catalysts,<sup>7</sup> poly-urea-encapsulated palladium catalysts,<sup>8</sup> and dendrimer-supported palladium catalyst.<sup>9</sup> However, these systems catalyzed the Suzuki reaction of activated aryl chlorides but failed to work for deactivated aryl chlorides.

In order to carry out the Suzuki reaction of activated and deactivated aryl chloride, macroporous polystyrene (MPS) resin and bulky *N*-heterocyclic carbenes (NHC)s were used as a support and a ligand, respectively. MPS resin is an efficient support with a large surface area and high porosity. Therefore, MPS might solve the diffusion problem of reagents and solvents.<sup>10</sup> NHCs behave like typical  $\sigma$ -donor ligands in metal coordination chemistry. Moreover, NHCs have excellent air and moisture stability and have higher dissociation energies. Therefore, NHCs<sup>11–13</sup> can enhance the reactivity and stability of palladium catalysts compared with phosphines.<sup>14,15</sup> In particular, when bulky NHCs are used in the palladium catalyzed Suzuki reaction of aryl chlorides, its catalytic activity is enhanced by their steric and electronic effect.<sup>16</sup>

This paper reports that MPS-supported bulky NHC-palladium is an effective catalyst for the Suzuki reaction of both activated and deactivated aryl chlorides. This catalyst also showed outstanding reusability in the Suzuki reaction of aryl bromide.

As shown in Scheme 1, 1-(mesityl)imidazole was first synthesized to prepare the MPS-supported bulky *N*-hetero-

**Scheme 1.** Synthesis of Macroporous Polystyrene-Supported Bulky NHC–Pd Complex **4**



cyclic carbene palladium complex. In order to accomplish this, an ammonium chloride solution was added to a vigorously stirred solution of H<sub>2</sub>O and 1,4-dioxane at 100 °C containing paraformaldehyde, mesitylammonium salt, and glyoxal. This mixture was maintained at 100 °C for 2 h.<sup>17</sup> After the reaction was complete, the resulting 1-(mesityl)imidazole (**1**) was obtained in 15% yield. This ligand precursor has a bulky group that can enhance the catalytic activity in the Suzuki reaction. Next, a mixture of chloromethyl MPS resin (**2**) (0.7 mmol Cl/g) and compound **1** (3 equiv) in DMF/THF (4:1) were stirred at 70 °C for 2 days. After being cooled to room temperature, the reaction mixture was filtered, and the resin was washed thoroughly and dried to afford the MPS-supported 1-mesitylimidazolium chloride resin (**3**) with a 1-(mesityl)imidazolium loading of 0.32 mmol/g, as determined by the nitrogen content from elementary analysis. Based on the Cl contents, the reaction proceeded to 52% conversion.

In order to immobilize Pd on resin **3**, a mixture of resin **3** and Pd(OAc)<sub>2</sub> was stirred in DMSO at 50 °C for 4 h. The temperature was then increased to 100 °C, and the reaction was then allowed to proceed for a further 30 min at 100 °C, which led to the formation of a MPS-supported bulky NHC–Pd catalyst (**4**).<sup>18</sup>

After immobilizing the palladium, catalyst **4** was analyzed by inductively coupled plasma–atomic emission spectrometry (ICP–AES) and energy dispersive X-ray (EDX) to determine the amount of palladium bound to the ligand. The EDX spectra showed that palladium was only present in catalyst **4** with none detected in resin **3**. According to the loading levels of 1-(mesityl)imidazole on resin **3** (0.32 mmol IM/g) and Pd on catalyst **4** (0.33 mmol Pd/g), we indirectly

(6) (a) LeBlond, C. R.; Andrews, A. T.; Sun, Y.; Sowa, J. R. *Org. Lett.* **2001**, *3*, 1555. (b) Arvela, R. K.; Leadbeater, N. E. *Org. Lett.* **2005**, *7*, 2101.

(7) (a) Nishio, R.; Sugiura, M.; Kobayashi, S. *Chem. Asian J.* **2007**, *2*, 983. (b) Hagio, H.; Sugiura, M.; Kobayashi, S. *Org. Lett.* **2006**, *8*, 375. (c) Nishio, R.; Sugiura, M.; Kobayashi, S. *Org. Lett.* **2005**, *7*, 4831. (d) Okamoto, K.; Akiyama, R.; Kobayashi, S. *Org. Lett.* **2004**, *6*, 1987.

(8) (a) Lee, C. K. Y.; Holmes, A. B.; Ley, S. V.; McConvey, I. F.; Al-Duri, B.; Leeke, G. A.; Santos, R. C. D.; Seville, J. P. K. *Chem. Commun.* **2005**, 2175. (b) Ley, S. V.; Ramarao, C.; Gordon, R. S.; Holmes, A. B.; Morrison, A. J.; McConvey, I. F.; Shirley, I. M.; Smith, S. C.; Smith, M. D. *Chem. Commun.* **2002**, 1134.

(9) Garcia-Bernabe, A.; Tzchucke, C. C.; Bannwarth, W.; Haag, R. *Adv. Synth. Catal.* **2005**, *347*, 1389.

(10) (a) Hori, M.; Gravert, D. J.; Wentworth, P., Jr.; Janda, K. D. *Bioorg. Med. Chem. Lett.* **1998**, *8*, 2363. (b) Jang, H. S.; Chung, W. J.; Lee, Y. S. *Tetrahedron Lett.* **2007**, *48*, 3731.

(11) (a) Öfele, K. J. *Organomet. Chem.* **1968**, *12*, 11. (b) Wanzlick, H. J.; Schönherr, H. J. *Angew. Chem.* **1968**, *80*, 154. For a recent review, see: (c) Herrmann, W. A. *Angew. Chem., Int. Ed.* **2002**, *41*, 1290.

(12) (a) Weskamp, T.; Kohl, F. J.; Hieringer, W.; Gleich, D.; Herrmann, W. A. *Angew. Chem., Int. Ed.* **1999**, *38*, 2416. (b) Schwarz, J.; Böhm, V. P. W.; Gardiner, M. G.; Grosche, M.; Herrmann, W. A.; Hieringer, W.; Raudaschl-Sieber, G. *Chem. Eur. J.* **2000**, *6*, 1773.

(13) (a) Byun, J. W.; Lee, Y. S. *Tetrahedron Lett.* **2004**, *45*, 1837. (b) Kim, J. H.; Jun, B. H.; Byun, J. W.; Lee, Y. S. *Tetrahedron Lett.* **2004**, *45*, 5827. (c) Kim, J. H.; Kim, J. W.; Shokouhimehr, M.; Lee, Y. S. *J. Org. Chem.* **2005**, *70*, 6714. (d) Kim, J. W.; Kim, J. H.; Lee, D. H.; Lee, Y. S. *Tetrahedron Lett.* **2006**, *47*, 4745.

(14) (a) Cai, M.; Sha, J.; Xu, Q. J. *Mol. Catal. A Chem.* **2007**, *268*, 82. (b) Yu, H. W.; Tong, Q. S.; Peng, Y. R.; Jia, L.; Shi, J. C.; Jin, Z. L. *Chin. Chem. Lett.* **2007**, *18*, 37. (c) Leyva, A.; Garcia, H.; Corma, A. *Tetrahedron* **2007**, *63*, 7097.

(15) (a) Uozumi, Y.; Kimura, M. *Tetrahedron: Asymmetry* **2006**, *17*, 161. (b) Uozumi, Y.; Kikuchi, M. *Synlett* **2005**, 1775. (c) Hocke, H.; Uozumi, Y. *Tetrahedron* **2004**, *60*, 9297. (d) Uozumi, Y.; Tanaka, H.; Shibatomi, K. *Org. Lett.* **2004**, *6*, 281. (e) Uozumi, Y.; Nakai, Y. *Org. Lett.* **2002**, *4*, 2997. (f) Danjo, H.; Tanaka, D.; Hayashi, T.; Uozumi, Y. *Tetrahedron* **1999**, *55*, 14341. (g) Uozumi, Y.; Danjo, H.; Hayashi, T. *J. Org. Chem.* **1999**, *64*, 3384. (h) Uozumi, Y.; Watanabe, T. *J. Org. Chem.* **1999**, *64*, 6921. (i) Uozumi, Y.; Danjo, H.; Hayashi, T. *Tetrahedron Lett.* **1997**, *38*, 3557.

(16) (a) Walker, S. D.; Barder, T. E.; Martinelli, J. R.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2004**, *43*, 1871. (b) Kantchev, E. A. B.; Brien, C. J.; Organ, M. G. *Aldrichim. Acta* **2006**, *4*, 97.

(17) Gardiner, M. G.; Herrmann, W. A.; Reisinger, C.; Schwarz, J.; Spiegler, M. J. *Organomet. Chem.* **1999**, *572*, 239.


(18) Herrmann, W. A.; Schwarz, J.; Gardiner, M. G. *Organometallics* **1999**, *18*, 4082.

concluded that MPS-supported bulky NHC-palladium catalyst **4** was mostly a monodentate complex, as shown in Scheme 1. X-ray photoelectron spectroscopy (XPS) of catalyst **4** showed 336.5 eV (Pd 3d<sup>5</sup>) as the major peak and 337.7 eV as a minor peak, which corresponds to Pd(II) and PdCl<sub>2</sub> respectively.<sup>19</sup> Therefore, MPS-supported bulky NHC–Pd catalyst contained only Pd(II) with no Pd(0). It was concluded that the palladium was immobilized specifically to the imidazolium ligand in the forms of Pd(NHC)OAcCl (**4**, major) and Pd(NHC)Cl<sub>2</sub> (minor).

Field emission scanning electron microscopy (FE-SEM) showed that there were no morphological changes in MPS (**2**), MPS–NHC (**3**), and MPS–NHC–Pd (**4**), which confirms that the shape of the MPS resins had remained intact. Therefore, MPS–NHC–Pd is a rigid and stable complex. In addition, the surface area and porosity of compounds **2**, **3** and **4** were analyzed by BET. Although a series of reactions were performed on the MPS resins, the surface area (130–190 m<sup>2</sup>/g) and porosity (9.4–11.0 nm) of each resin were maintained.

The catalytic activity of catalyst **4** was examined for its ability to catalyze the Suzuki reaction of aryl chlorides with phenylboronic acid. In order to optimize the reaction conditions, the coupling of 4-chloroanisole (0.5 mmol) and phenylboronic acid (0.6 mmol) as a model reaction was carried out using catalyst **4** (2 mol %). Different bases were used to confirm the effect of the base in the Suzuki reaction of deactivated aryl chloride. As shown in Table 1, K<sub>2</sub>CO<sub>3</sub> as a

**Table 1.** Effect of Bases on the Suzuki Reaction of 4-Chloroanisole and Phenylboronic Acid<sup>a</sup>



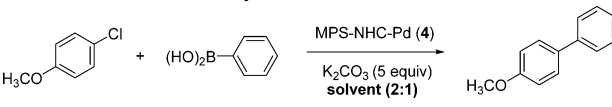
entry	base	time (h)	T (°C)	yield <sup>b</sup> (%)
1	CS <sub>2</sub> CO <sub>3</sub>	24	100	50
2	K <sub>3</sub> PO <sub>4</sub>	24	100	46
3	K <sub>2</sub> CO <sub>3</sub>	24	100	76
4	NaOH	24	100	30
5	<i>t</i> -BuOK	24	100	41
6	Na <sub>2</sub> CO <sub>3</sub>	24	100	51

<sup>a</sup> 4-Chloroanisole (0.5 mmol), phenylboronic acid (0.6 mmol), MPS–NHC–Pd (2 mol %), base (2.5 mmol), and DMF/water (2:1, v/v). <sup>b</sup> Isolated yield by column chromatography.

base gave the highest yield (76%) in the reaction of 4-chloroanisole with phenylboronic acid. The use of other bases resulted in lower yields due to their low activity.

The effect of various solvents was next investigated. According to the results shown in Table 2, a solution of DMF/water (2:1) gave an excellent yield (76%) in the

**Table 2.** Effect of the Solvents on the Suzuki Reaction of 4-Chloroanisole and Phenylboronic Acid<sup>a</sup>

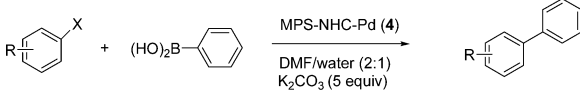


entry	solvent	time (h)	T (°C)	yield <sup>b</sup> (%)
1	DMF/water	24	100	76
2	DMA/water	24	100	40
3	dioxane/water	24	100	41
4	toluene/water	24	100	none
5	water	24	100	1

<sup>a</sup> 4-Chloroanisole (0.5 mmol), phenylboronic acid (0.6 mmol), MPS–NHC–Pd (2 mol %), K<sub>2</sub>CO<sub>3</sub> (2.5 mmol), and solvent (2:1, v/v). <sup>b</sup> Isolated yield by column chromatography.

reaction of 4-chloroanisole with phenylboronic acid for 24 h at 100 °C. A reaction also occurred using only water. However, there was poor yield due to the poor solubility of 4-chloroanisole in water and the decrease in the water compatibility of the MPS-supported bulky NHC–Pd catalyst (**4**).

**Table 3.** Suzuki Reaction of Aryl Halide, Including Aryl Chloride, with Phenylboronic Acid<sup>a</sup>



entry	R	X	time (h)	T (°C)	yield <sup>b</sup> (%)
1	<i>p</i> -COCH <sub>3</sub>	I	0.5	50	95
2	<i>p</i> -OCH <sub>3</sub>	I	0.5 (6)	50 (25)	99 (99)
3	<i>p</i> -COCH <sub>3</sub>	Br	1	50	94
4	<i>p</i> -OCH <sub>3</sub>	Br	1 (12)	50 (25)	97 (88)
5	<i>o</i> -OCH <sub>3</sub>	Br	1	50	85
6 <sup>c</sup>	<i>p</i> -COCH <sub>3</sub>	Cl	24	100	83
7 <sup>c</sup>	<i>p</i> -CN	Cl	24	100	71
8 <sup>d</sup>	<i>p</i> -NO <sub>2</sub>	Cl	24	100	82
9 <sup>c</sup>	<i>p</i> -OCH <sub>3</sub>	Cl	24	100	76
10 <sup>c</sup>	<i>p</i> -CH <sub>3</sub>	Cl	24	100	70
11 <sup>c</sup>	<i>o</i> -OCH <sub>3</sub>	Cl	24	100	58
12 <sup>e</sup>	<i>p</i> -OCH <sub>3</sub>	Cl	24	100	31

<sup>a</sup> Aryl halide (0.5 mmol), phenylboronic acid (0.6 mmol), MPS–NHC–Pd (1 mol %), K<sub>2</sub>CO<sub>3</sub> (2.5 mmol), and DMF/water (2:1, v/v). <sup>b</sup> Isolated yield by column chromatography. <sup>c</sup> Phenylboronic acid (0.8 mmol), MPS–NHC–Pd (2 mol %). <sup>d</sup> Phenylboronic acid (0.8 mmol), MPS–NHC–Pd (2 mol %), DMF/water (14:1, v/v). <sup>e</sup> 1-Methylimidazole was used as a ligand instead of 1-mesitylimidazole.

As shown in Table 3, the Suzuki reaction of various aryl halides, even aryl chloride, was examined under optimal reaction conditions to show the high catalytic activity of MPS-supported bulky NHC–Pd catalyst (**4**). The Suzuki reactions of deactivated aryl chloride including 4-chloroanisole and 4-chlorotoluene proceeded with high yields of 76% and 70%, respectively, at 100 °C (Table 3, entries 9 and

(19) (a) Kumar, G.; Blackburn, J. R.; Albridge, R. G.; Moddeman, W. E.; Jones, M. M. *Inorg. Chem.* **1972**, *11*, 296. (b) Kim, K. S.; Gossman, A. F.; Winogard, N. *Anal. Chem.* **1974**, *46*, 197. (c) Nyholm, R.; Martensson, N. *J. Phys. C* **1980**, *13*, L279.

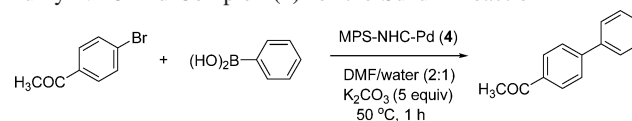
10). However, the Suzuki reaction of 2-chloroanisole, which may experience some steric effect, gave a somewhat lower yield of 58% (Table 3, entry 11). To the best of our knowledge, none of the known heterogeneous catalysts produced such high yields shown in the above Suzuki reaction of deactivated aryl chlorides. The Suzuki reaction of activated aryl chlorides with different substituents also gave good yields. (Table 3, entries 6–8). 4-Aminobiphenyl was obtained as a side product in the Suzuki reaction of 1-chloro-4-nitrobenzene in DMF/water (2:1) system. As the ratio of water was reduced to DMF/water (14:1), the side reaction was suppressed, and 4-nitrobiphenyl was obtained in 82% yield (Table 3, entry 8). In addition, the Suzuki reaction of aryl iodides and bromides produced excellent yields, regardless of the presence of activated, deactivated and steric substituents (Table 3, entries 1–5), even at room temperature (Table 3, entries 2 and 4).

In order to examine the effect of the bulkiness of the ligand, 1-methylimidazole and 1-mesitylimidazole were introduced to the catalyst system as ligands, respectively. When bulky 1-mesitylimidazole was used, a high yield was obtained compared with 1-methylimidazole. (Table 3, entries 9 and 12). Hence, the bulkiness of the ligand is an important factor for increasing the catalytic activity in the Suzuki reaction of aryl chlorides. Therefore, the MPS-supported bulky NHC–Pd catalyst (**4**) was confirmed to be an excellent catalyst showing high activity in the Suzuki reaction of aryl chlorides including deactivated chlorides.

The reusability of the MPS-supported bulky NHC–Pd catalyst (**4**) was examined in the Suzuki reaction of aryl bromides. As shown in Table 4, the catalytic activities (94%) and the initial loading levels of catalyst **4** (0.08 mmol/g) on the resin remained almost the same after being used five times. However, a small amount of palladium metal was detected from the filtrates after each run (3.0%, 1.1%, 1.2%, 1.4%, and 1.3%, by ICP-AES analysis). The leached Pd (homogeneous Pd) may not contribute a major role in their catalytic activity. Because all of the catalytic activity after each run looks similar even though the amount of leached palladium in the first cycle is higher than those of the other cycles.

In summary, MPS-supported 1-mesitylimidazolium chloride resin was prepared by reacting macroporous chlorom-

**Table 4.** Reusability of Macroporous Polystyrene-Supported Bulky NHC–Pd Complex (**4**) for the Suzuki Reaction<sup>a</sup>



recycle	first	second	third	fourth	fifth
yield <sup>b</sup> (%)	94	94	94	89	94

<sup>a</sup> 4-Bromoacetophenone (0.5 mmol), phenylboronic acid (0.6 mmol), MPS–NHC–Pd (1 mol %), K<sub>2</sub>CO<sub>3</sub> (2.5 mmol), DMF/H<sub>2</sub>O (2:1, v/v), 50 °C, and 1 h. <sup>b</sup> Isolated yield by column chromatography.

ethyl polystyrene with 1-(mesityl)imidazole as a supported NHC precursor for the immobilization of a palladium catalyst. The supported NHC precursor readily formed a stable complex with Pd(OAc)<sub>2</sub> and showed excellent catalytic activity in the Suzuki reactions of various aryl chlorides, bromides and iodides. Aryl chlorides with electron-donating groups were also converted to biaryl products in high yield. This MPS-supported bulky NHC–Pd catalyst showed reusability up to five times in the Suzuki reaction of aryl bromide.

**Acknowledgment.** This study was supported by the Nano Bioelectronics and Systems Research Center of Seoul National University, which is an ERC supported by the Korean Science and Engineering Foundation (KOSEF), and the Brain Korea 21 program supported by the Ministry of Education & Human Resources Development.

**Supporting Information Available:** Experimental procedure and characterization data (EDX, XPS, FE-SEM, BET) for MPS-supported *N*-heterocyclic carbene palladium catalyst, experimental procedure for the Suzuki reaction, and characterization data (<sup>1</sup>H NMR, GC–MS) for all of the products obtained from Suzuki reactions. This material is available free of charge via the Internet at <http://pubs.acs.org>.

OL8003047