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# Amphiphilic polymer supported *N*-heterocyclic carbene palladium complex for Suzuki cross-coupling reaction in water

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**Abstract**—We synthesized amphiphilic polymer-supported *N*-heterocyclic carbene (NHC) precursor resins by loading polyethylene glycol (PEG) containing imidazolium groups on Merrifield resin. These PS–PEG–NHC precursor resins were compatible with water and readily formed a stable complex with palladium. These PS–PEG–NHC–Pd catalysts showed excellent catalytic activity for Suzuki cross-coupling reactions of various aryl iodides and bromides with phenylboronic acid in water than the previously described polystyrene based catalysts. In addition, the PS–PEG–NHC–Pd catalysts continued to provide excellent catalytic activity in Suzuki cross-coupling reactions after five consecutive recycles.

*N*-Heterocyclic carbenes (NHCs) have attracted a great deal of interest as transition metal ligands in the area of organic and inorganic chemistry ever since they were first discovered by Öfele and Wanzlick[1] in the late 1960s. These NHCs have the same σ-donor and exhibit low π-acceptor ability as phosphine in terms of their metal coordination chemistry.[2] Recently, the NHC ligands have also shown to have excellent air and moisture stability and higher dissociation energies than those of other ligands quantified by theoretical calculations for different metals.[3] Therefore, they have been applied to many organic reactions that use the transition metal catalysts as efficient ligands. There have been many successful demonstrations of homogeneous catalysis using NHCs as ligands for transition metals.[4] These homogeneous catalyst systems, however, have basic problems in terms of the separation and recycling of the catalysts. In addition, these systems induced contamination of the ligand residue in the products. Therefore, the development of a polymer-supported and insoluble transition metal catalyst has attracted a great deal of attention in organic chemistry. The heterogeneous catalysis system have several advantages, such as fast recovery and simple recycling of the catalysts by filtration (a process that prevents the contamination of the ligand and decreases environmental pollution caused by residual metals in the wastes).[5] Several kinds of polymer-supported NHC-transition metal complexes have been designed so far.[6,7]

In addition, organic reactions conducted in an aqueous phase have drawn much attention recently because of the advantages as an eco-friendly and economic process using water as a non-toxic solvent.[8] Uozumi's group has done a thorough investigation amphiphilic ArgoGel (polystyrene–*g*-polyethylene glycol resin)-supported phosphine–palladium complex for aqueous phase organic reaction.[9] We have previously reported regarding the polystyrene-based NHC–Pd catalysts which exhibited excellent catalytic activity for Suzuki reactions in a mixture of organic solvents and water. However, the polystyrene-based NHC–Pd catalysts yielded poor results for the Suzuki reactions only conducted in water.[7]

Therefore, in this letter, we report on the use of amphiphilic polystyrene–*g*-polyethylene glycol–NHC(PS–PEG–NHC) precursor resins that were prepared from Merrifield resin and the subsequent application of the PS–PEG–NHC–Pd complex to a heterogeneous Suzuki cross-coupling reaction in water.

As detailed in Scheme 1, we first synthesized two types of imidazoliums using different units of PEG (PEG 200, PEG 600) as NHC precursors. The PEGs were mono-tosylated in 45% and 47% yield following which the mono-tosylated PEGs were reacted with 1-methyl

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*Keywords*: *N*-Heterocyclic carbene (NHC); Suzuki reaction; Aqueous phase reaction; Palladium; Heterogeneous catalyst.

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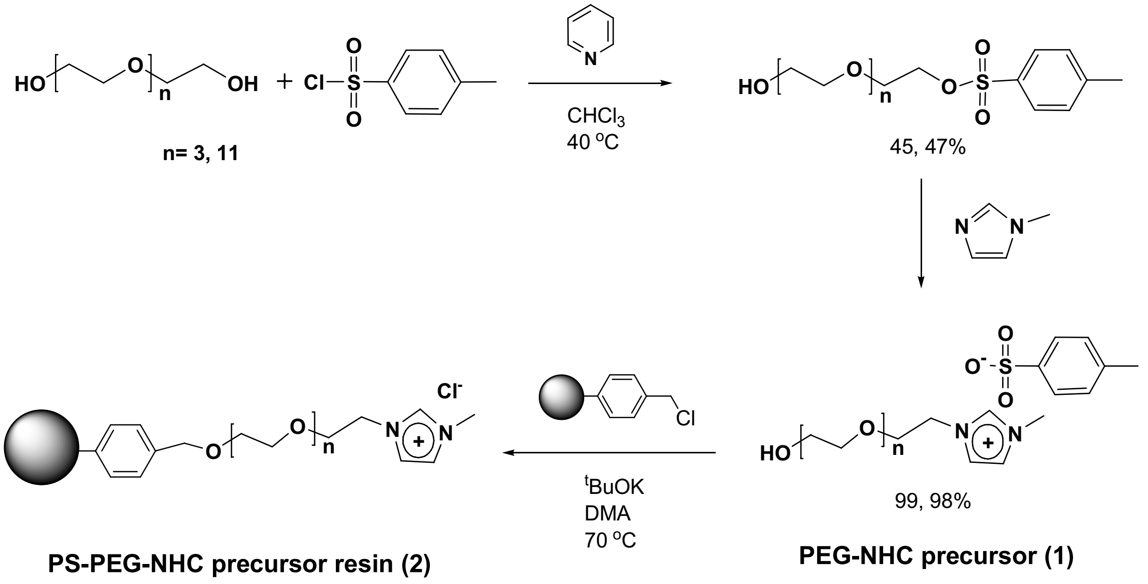


**Scheme 1.** Synthesis of PS–PEG–NHC precursor resins.

imidazole for 24 h at 70 °C. The final imidazolium (PEG–NHC) precursors (**1**) were obtained in excellent yields (PEG 200–NHC; 99%, PEG 600–NHC; 98%). We obtained the PS–PEG–NHC precursor resins (**2**) by loading the PEG–NHC precursors on Merrifield resin, as shown in Scheme 1. The loading levels of imidazolium depended on the molecular weight of the PEG (PS–PEG 200–NHC precursor resin; 0.87 mmol/g, PS–PEG 600–NHC precursor resin; 0.54 mmol/g). The conversion of functional groups on the Merrifield resins was estimated to be 80% based on the weight increase of the resin.

As the length of PEG chain on the resins increased, their swelling volumes increased in polar solvents such as water and MeOH and decreased in non-polar solvents such as MC and THF (Fig. 1). In contrast to the conventional polystyrene-based polymeric supports, PS–PEG–NHC precursor resins were water-compatible. Palladium was then immobilized on the PS–PEG–NHC precursor resins using potassium tertiary butoxide as a base for the in situ deprotonation of imidazolium salts (Scheme 2).[10,11] When the quantity of the base increased, the loading level of palladium also increased (shown in Table 1). We confirmed that palladium was immobilized specifically at the C2 position of the imidazolium on the bead using IR spectroscopy. Before the immobilization of palladium, we could observe a strong band of quaternary imidazolium on the bead at 1157 $cm^{-1}$ in the IR spectrum.[12] However, it decreased, and the band of alkene at 1665 $cm^{-1}$ became stronger after the immobilization of palladium.

Both the PS–PEG 200–NHC–Pd and PS–PEG 600–NHC–Pd catalysts were investigated for the Suzuki reaction in water in order to confirm the effects of PEG length. As shown in Table 2, PS–PEG 600–NHC–Pd provided an excellent yield (91%), indicating that PEG 600 would be suitable for rendering the water-compatibility to a polystyrene-based resin. For any potential industrial applications of a heterogeneous Suzuki cross-coupling reaction, the lifetime of the PS–PEG

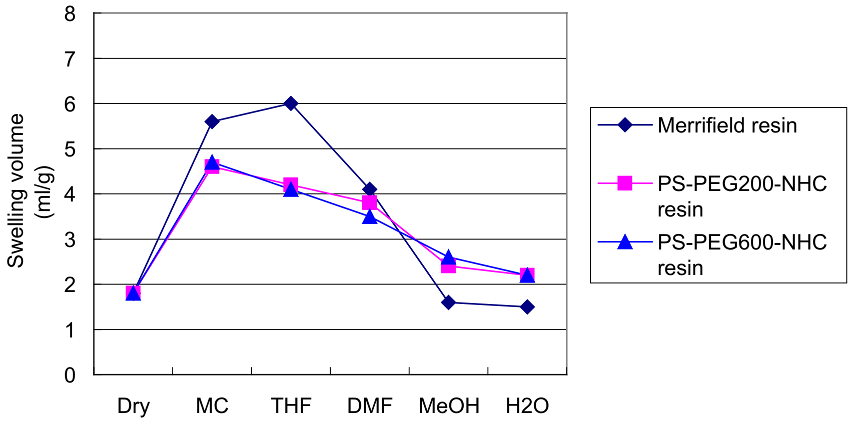
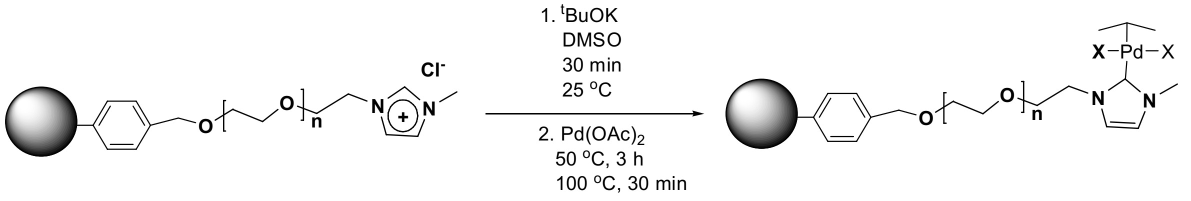


**Figure 1.** Swelling properties of PS–PEG–NHC precursor resins.



**PS-PEG-NHC precursor resin (2)**

**PS-PEG-NHC-Pd complex (3)**

**Scheme 2.** Immobilization of palladium on PS–PEG–NHC precursor resins.

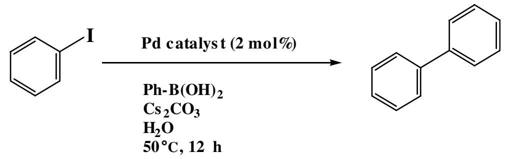
**Table 1.** Immobilization of palladium on the NHC precursor resin[b]

| MW of PEG | $^t$BuOK (mmol) | Loading level of imidazolium (mmol/g) | Loading level of Pd (mmol/g)[a] |
|---|---|---|---|
| 200 | 0.52 | 0.87 | 0.012 |
| 200 | 1.04 | 0.87 | 0.11 |
| 600 | 0.65 | 0.54 | 0.05 |

[a] Analyzed by ICP-AES (inductively coupled plasma-atomic emission spectrometry).

[b] 1 g of PS–PEG–NHC precursor resins was used.

**Table 2.** Suzuki reaction of iodobenzene with Ph–B$(OH)_2$ in water[a]



| Entry | MW of PEG in Pd catalyst | Loading level of Pd (mmol/g) | Isolated yield (%)[b] |
|---|---|---|---|
| 1 | 200 | 0.11 | 57 |
| 2 | 600 | 0.05 | 91 |

[a] All of the reactions were carried out with the mole ratio of Ph–I:Ph–B$(OH)_2$:$Cs_2CO_3$:Pd = 1:1.3:5.0:0.02.

[b] Isolation yields were calculated from the mass of the biphenyl product after separation using column chromatography.

600–NHC–Pd catalyst and its reusability would be the most important factors. Therefore, the catalyst (2 mol % Pd) was repeatedly used five times in the reaction of iodobenzene and phenylboronic acid in water for 12 h at 50 °C (shown in Table 3). In this exercise, the PS–PEG 600–NHC–Pd catalyst continued to provide excellent catalytic activity.

To extend the scope of the heterogeneous reaction, the Suzuki cross-coupling reaction of various aryl iodides and bromides with phenylboronic acid was examined under very mild conditions as detailed in Table 4.[13]

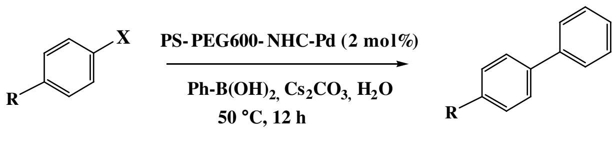
**Table 3.** Reusability test of the PS–PEG 600–NHC–Pd complex[a]

| The number of recycle | 1st | 2nd | 3rd | 4th | 5th |
|---|---|---|---|---|---|
| Isolated yield (%)[b] | 91 | 88 | 87 | 84 | 82 |

[a] All of the reactions were carried out with the mole ratio of Ph–I:Ph–B$(OH)_2$:$Cs_2CO_3$:Pd = 1:1.3:5.0:0.02. 12 h, 50 °C.

[b] Isolation yields were calculated from the mass of the biphenyl product after separation using column chromatography.

**Table 4.** Suzuki reactions of various aryl halides and phenylboronic acid with the PS–PEG 600–NHC–Pd complex in water[a]



| Entry | *R* | *X* | Isolated yield (%)[d] |
|---|---|---|---|
| 1 | H | I | 91 |
| 2[c] | OH | I | 99 |
| 3[b] | OMe | I | 76 |
| 4[b] | $COCH_3$ | I | 99 |
| 5[b] | $NO_2$ | I | 90 |
| 6[b] | H | Br | 97 |
| 7[c] | CHO | Br | 99 |

[a] All of the reactions were carried out with the mole ratio of RPh–X:Ph–B$(OH)_2$:$Cs_2CO_3$:Pd = 1:1.3:5.0:0.02.

[b] 2 v/v % DMF was used for solving the substrate.

[c] 5 v/v % DMF was used for solving the substrate.

[d] Isolation yields were calculated from the mass of the biphenyl product after separation using column chromatography.

All of the aryliodides and arylbromides were converted to the corresponding biaryls with excellent yields within 12 h at 50 °C, regardless of the substituents. As mentioned above, the PS–PEG 600–NHC–Pd catalyst was so effective that all of the aryl iodides and bromides were converted very rapidly to the corresponding products in water and under mild reaction conditions.

In conclusion, we have prepared amphiphilic PS–PEG–NHC precursor resins by loading PEG containing imidazolium group on Merrifield resin. These PS–PEG–NHC precursor resins readily formed a stable complex with palladium and the resulting PS–PEG–NHC–Pd catalysts showed excellent catalytic activity for the Suzuki reaction in water. This polymer-supported catalyst demonstrated outstanding reusability for the Suzuki cross-coupling reaction.

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## References and notes

1. (a) Öfele, K. *J. Organomet. Chem.* **1968**, *12*, 42–43; (b) Wazlick, 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*, 1290–1309.
2. (a) Öfele, K.; Herrmann, W. A.; Mihalios, D.; Elison, M.; Herdtweck, E.; Scherer, W.; Mink, J. *J. Organomet. Chem.* **1993**, *459*, 177–184; (b) Herrmann, W. A.; Öfele, K.; Elison, M.; Kühn, F. E.; Roesky, P. W. *J. Organomet. Chem.* **1994**, *480*, c7–c9.
3. (a) Weskamp, T.; Kohl, F. J.; Hieringer, W.; Gleich, D.; Herrmann, W. A. *Angew. Chem., Int. Ed.* **1999**, *38*, 2416–2419; (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*, 1773–1780.
4. (a) Grasa, G. A.; Viciu, M. S.; Huang, J.; Zhang, C.; Trudell, M. L.; Nolan, S. P. *Organometallics* **2002**, *21*, 2866–2873; (b) Lebel, H.; Janes, M. K.; Charette, A. B.; Nolan, S. P. *J. Am. Chem. Soc.* **2004**, *126*, 5046–5047; (c) Gstöttmayr, C. W. K.; Böhm, V. P. W.; Herdtweck, E.; Grosche, M.; Herrmann, W. A. *Angew. Chem., Int. Ed.* **2002**, *41*, 1363–1365; (d) Chen, A. C.; Ren, L.; Decken, A.; Crudden, C. M. *Organometallics* **2000**, *19*, 3459–3461; (e) Sato, Y.; Sawaki, R.; Mori, M. *Organometallics* **2001**, *20*, 5510–5512; (f) Andrus, M. B.; Song, C. *Org. Lett.* **2001**, *3*, 3761–3764.
5. (a) McNamara, C. A.; Dixon, M. J.; Bradley, M. *Chem. Rev.* **2002**, 3275–3300; (b) Leadbeater, N. E.; Marco, M. *Chem. Rev.* **2002**, 3217–3274; (c) Uozumi, Y. *Top. Curr. Chem.* **2004**, *242*, 77; (d) Bergbreiter, D. E. *Top. Curr. Chem.* **2004**, *242*, 113.
6. (a) Schwarz, J.; Böhm, V. P. W.; Gardiner, M. G.; Grosche, M.; Herrmann, W. A.; Hieringer, W.; Raudaschl-Sieber, G. *Chem. Eur. J.* **2000**, *6*, 1773–1780; (b) Schürer, S. C.; Gessler, S.; Buschmann, N.; Blechert, S. *Angew. Chem., Int. Ed.* **2000**, *39*, 3898–3901; (c) Mayr, M.; Mayr, B.; Buchmeiser, M. R. *Angew. Chem., Int. Ed.* **2001**, *40*, 3839–3842.
7. (a) Byun, J. W.; Lee, Y. S. *Tetrahedron Lett.* **2004**, *45*, 1837–1840; (b) Kim, J. H.; Jun, B. H.; Byun, J. W.; Lee, Y. S. *Tetrahedron Lett.* **2004**, *45*, 5827–5831; (c) Kim, J. H.; Kim, J. W.; Shokouhimehr, M.; Lee, Y. S. *J. Org. Chem.* **2005**, *70*, 6714–6720.
8. (a) Herrmann, W. A.; Kohlpaintner, C. W. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1524–1544; (b) Lindström, U. M. *Chem. Rev.* **2002**, 2751–2772.
9. (a) Uozumi, Y.; Danjo, H.; Hayashi, T. *Tetrahedron Lett.* **1998**, *39*, 8303–8306; (b) Uozumi, Y.; Danjo, H.; Hayashi, T. *J. Org. Chem.* **1999**, *64*, 3384–3388; (c) Uozumi, Y.; Nakai, Y. *Org. Lett.* **2002**, *4*, 2997–3000; (d) Uozumi, Y.; Kikuchi, M. *Synlett* **2005**, 1775–1778.
10. (a) Amyes, T. L.; Diver, S. T.; Richard, J. P.; Rivas, F. M.; Toth, Krisztina *J. Am. Chem. Soc.* **2004**, *126*, 4366–4374; (b) 1.0 g of PS–PEG–NHC precursor resin (0.54 mmol/g imidazolium) and potassium tertiary butoxide (1.2 equiv, 73 mg) were mixed and stirred in DMSO (40 mL) for 30 min at room temperature. Pd(OAc)$_2$ (0.5 equiv, 60 mg) was dissolved in DMSO (10 mL) by using sonicator and then added into the dispersion of PS–PEG–NHC resin. The resulting dispersion was stirred for 3 h at 50 °C. After the temperature was increased to 100 °C, the resin mixture was stirred for further 30 min. The PS–PEG–NHC–Pd was washed with DMSO (20 mL × 3), DMF (20 mL × 3), THF (20 mL × 3), distilled water (20 mL × 5), 1 *N*-HCl / THF (20 mL × 5), methanol (20 mL × 5) and dried under reduced pressure.
11. (a) Herrmann, W. A.; Schwarz, J.; Gardiner, M. G.; Spiegler, M. *J. Organomet. Chem.* **1999**, *575*, 80–86; (b) Douthwaite, R. E.; Haüssinger, D.; Green, M. L. H.; Silcock, P. J.; Gomes, P. T.; Martins, A. M.; Danopoulos, A. A. *Organometallics* **1999**, *18*, 4584–4590; (c) Weskamp, T.; Kohl, F. J.; Hieringer, W.; Gleich, D.; Herrmann, W. A. *Angew. Chem., Int. Ed.* **1999**, *38*, 2416.
12. Petrak, K.; Degen, I.; Beynon, P. *J. Polym. Sci.* **1982**, *20*, 783–793.
13. The PS–PEG 600–NHC–Pd complex (0.05 mmol/g Pd, 200 mg) was suspended in a mixture of phenylboronic acid (84 mg, 0.65 mmol) and Cs$_2$CO$_3$ (820 mg, 2.5 mmol) in distilled water (4 mL), and then aryl halide (0.5 mmol) was added to the mixture. The resulting dispersion was stirred for 12 h at 50 °C. The catalyst was filtered and washed with distilled water and diethyl ether. The product was extracted with diethyl ether and purified by column chromatography. The yield was calculated from the mass value of the product after isolation with column chromatography.