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Practical Preparation Method of Polymer-Incarcerated (PI) Palladium Catalysts Using Pd(II) Salts

Hiroyuki Hagio, Masaharu Sugiura, and Shū Kobayashi*

Graduate School of Pharmaceutical Sciences, The University of Tokyo, The HFRE Division, ERATO, Japan Science and Technology Agency (JST), Hongo, Bunkyo-ku, Tokyo 113-0033, Japan

skobayas@mol.f.u-tokyo.ac.jp

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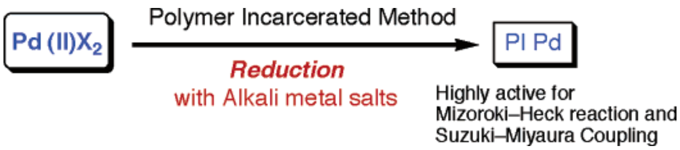
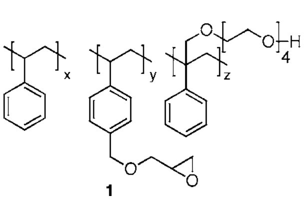
ABSTRACT



Polymer-incarcerated (PI) palladium catalyst was practically prepared from inexpensive Pd(II) salts and a polystyrene-based copolymer under reducing conditions. Remarkable effects of alkali metal salts on the palladium loading were observed. PI Pd thus prepared showed high catalytic activity in Mizoroki–Heck reactions and Suzuki–Miyaura couplings with a range of substrates including an aryl chloride. In all cases, the Pd catalyst was recovered quantitatively without leaching, and reused several times without significant loss of activity.

Palladium catalysts find widespread utility in a variety of transformations in organic synthesis.[1] However, they are often expensive, are air-sensitive, and cannot be recovered sufficiently. To address these issues, immobilization of Pd catalysts on inorganic solid supports[2] or organic polymers[3,4] have been studied, although recovery and reuse were not efficient in many cases. Recently, we developed a new immobilization method of Pd catalysts using copolymer **1** or **2**, the so-called "polymer-incarcerated (PI)" method (Scheme 1).[5] This method is based on microencapsulation[6] and cross-linking. Tetrakistriphenylphosphine palladium(0) ($Pd(PPh_3)_4$) was successfully immobilized by this method to form phosphine-free polymer-incarcerated Pd(0) (PI Pd).[5] Although it was thought that a ligand exchange from phosphine to copolymers would be the key to successful



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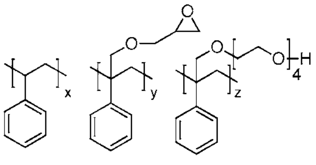

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(1) (a) Tsuji, J. *Palladium Reagents and Catalysts*; Wiley: Chichester, 1995. (b) *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., Ed.; John Wiley and Sons: New York, 2002. (c) Stahl, S. S. *Angew. Chem., Int. Ed.* **2004**, *43*, 3400.

(2) (a) Choudary, B. M.; Madhi, S.; Chowdari, N. S.; Kantam, M. L.; Streedhar, B. *J. Am. Chem. Soc.* **2002**, *124*, 14127. (b) Kwon, M. S.; Kim, N.; Park, C. M.; Lee, J. S.; Kang, K. Y.; Park, J. *Org. Lett.* **2005**, *7*, 1077. (c) Kim, N.; Kwon, M. S.; Park, C. M.; Park, J. *Tetrahedron Lett.* **2004**, *45*, 7057.

(3) (a) Chauhan, B. P.; Rathore, J. S.; Chauhan, M.; Krawicz, A. *J. Am. Chem. Soc.* **2003**, *125*, 2876. (b) Biffs, A.; Zecca, M.; Basato, M. *J. Mol. Catal. A: Chem.* **2001**, *173*, 249.

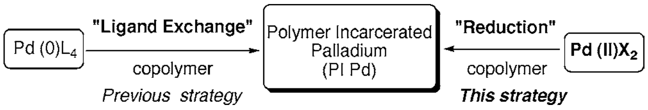
(4) Recently, immobilized Pd catalysts using effective dendrimers, multilayer polyelectrolyte films, and ionic liquids have been reported. (a) Ooe, M.; Murata, M.; Mizugaki, T.; Ebitani, K.; Kaneda, K. *J. Am. Chem. Soc.* **2004**, *126*, 1604. (b) Chechik, V.; Crooks, R. M. *J. Am. Chem. Soc.* **2000**, *122*, 1243. (c) Kidambi, S.; Dai, J.; Li, J.; Bruening, M. L. *J. Am. Chem. Soc.* **2004**, *126*, 2658. (d) Huang, J.; Jiang, T.; Gao, H.; Han, B.; Liu, Z.; Wu, W.; Chang, Y.; Zhao, G. *Angew. Chem., Int. Ed.* **2004**, *43*, 1397. (e) Dupont, J.; Fonseca, G. S.; Umpierre, A. P.; Fichtner, P. F. P.; Teixeira, S. R. *J. Am. Chem. Soc.* **2002**, *124*, 4228.

(5) (a) Akiyama, R.; Kobayashi, S. *J. Am. Chem. Soc.* **2003**, *125*, 3412. (b) Okamoto, K.; Akiyama, R.; Kobayashi, S. *J. Org. Chem.* **2004**. *69*, 2871. (c) Okamoto, K.; Akiyama, R.; Kobayashi, S. *Org. Lett.* **2004**, *6*, 1987. (d) Okamoto, K.; Akiyama, R.; Yoshida, H.; Yoshida, T.; Kobayashi, S. *J. Am. Chem. Soc.* **2005**, *127*, 2125.

(6) For reviews, see: Kobayashi, S.; Akiyama, R. *Chem. Commun.* **2003**, 449.

10.1021/ol052310y CCC: $33.50

Scheme 1. Two Strategies for the Polymer-Incarcerated Method



immobilization (Scheme 1, previous strategy), four triphenylphosphine moieties were lost during the preparation. We envisaged that PI Pd could be altenatively prepared from inexpensive Pd(II) salts under suitable reduction conditions (Scheme 1, this strategy). As a consequence, a new practical immobilization method of Pd was achieved. Remarkable effects of alkali metal salts on palladium immobilization and high catalytic activity were observed.

Initially, immobilization of palladium nitrate ($Pd(NO_3)_2$) using copolymer **2** was investigated according to the general PI procedure (Scheme 2, Table 1, entry 1). However, serious leaching of Pd occurred, and immobilization was unsuccessful. Therefore, immobilization of Pd(II) without reduction seemed to be difficult. Then, immobilization of Pd via reduction of $Pd(NO_3)_2$ or palladium acetate ($Pd(OAc)_2$) in THF under atmospheric hydrogen was tested. However, immobilization failed, and precipitation of Pd-black was observed. Meanwhile, it was recently reported that Pd(0) nanoparticles were formed via thermal decomposition of $Pd(OAc)_2$ without any additional reducing agents.[7] We therefore expected that use of copolymer **2** might enable immobilization of Pd(0) nanoparticles. Thus, a solution of $Pd(OAc)_2$ and copolymer **2** in THF was heated at 66 °C for 3 h (entry 2), gradual color change (orange to dark brown) was observed, and palladium was successfully immobilized, although the loading level was low (entry 2).[8–10] Encouraged by this result, we investigated immobilization of $Pd(NO_3)_2$ by adding 1 or 2 equiv of sodium acetate (entries 3 and 4). Interestingly, not only did immobilization occur, but also significant increases of the loading levels were observed (vs entry 2). It was speculated that sodium nitrate produced during the formation of $Pd(OAc)_2$ might assist the immobilization.[11,12]

Scheme 2. Preparation of Polymer-Incarcerated Palladium

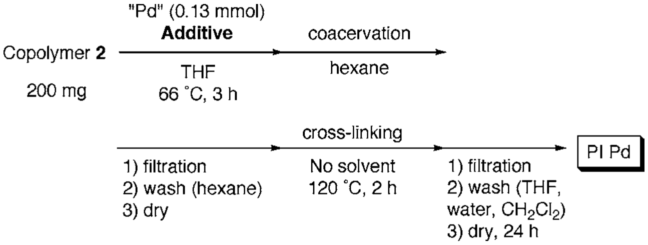


Table 1. Effect of Pd Sources and Salts

entry	"Pd"	additive	yield (mg)	loading (mmol/g)[b]	PI Pd
1[a]	$Pd(NO_3)_2$		112	0	
2[a]	$Pd(OAc)_2$		189	0.19 (28%)	**A**
3	$Pd(NO_3)_2$	NaOAc (2 equiv)	169	0.44 (57%)	**B**
4	$Pd(NO_3)_2$	NaOAc (1 equiv)	166	0.63 (80%)	**C**
5	$Pd(OAc)_2$	$NaNO_3$ (2 equiv)	184	0.34 (48%)	**D**
6	$Pd(OAc)_2$	NaCl (2 equiv)	187	0.31 (45%)	**E**
7	$Pd(OAc)_2$	NaOAc (2 equiv)	165	0.50 (63%)	**F**
8	$Pd(NO_3)_2$	KOAc (2 equiv)	177	0.71 (96%)	**G**
9	$Pd(NO_3)_2$	LiOAc (2 equiv)	209	0.41 (66%)	**H**

[a] Immobilization of Pd using reduction of Pd(II) in THF under H_2 (1 atm) at room temperature was also unsuccessful. [b] Determined by XRF analysis. Percentages of Pd loaded are shown in parentheses.

Indeed, when sodium nitrate was added to $Pd(OAc)_2$, the loading level was increased (entry 5). Addition of sodium chloride or sodium acetate to $Pd(OAc)_2$ was also found to enhance the loading level (entries 6 and 7). Then, we investigated the effect of metal ions on loading level (entries 3, 8, and 9). It turned out that the loading level was increased dramatically when potassium acetate was used, whereas lithium acetate showed almost the same loading level as that of sodium acetate.[13] The effect of those salts is likely an electrostatic stabilization;[11] the precise mechanism is as yet unclear. This is the first example of the preparation of polymer-incarcerated (PI) palladium using a reduction strategy.

Next, we focused on the application of these catalysts, PI Pd **A**−**H**, to the Mizoroki−Heck reaction[7a,14] of iodobenzene (**1a**) with ethyl acrylate (**2a**) as a model reaction (Table 2).

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(7) (a) Reetz, M. T.; de Vries, J. G. *Chem. Commun*. **2004**, 1559. (b) Reetz, M. T.; Maase, M. *Adv. Mater*. **1999**, *11*, 773. (c) Reetz, M. T.; Helbig, W.; Quaiser, S. A.; Stimming, U.; Breuer, N.; Vogel, R. *Science* **1995**, *267*, 367.

(8) It was observed by transmission electron microscope (TEM) analysis that the size of immobilized palladium particles was less than 1.5 nm and Pd dispersed uniformly on the polymer.

(9) Immobilization of Pd nanoparticles in the presence of tetrabutylammonium bromide (1 equiv) was also effective [yield 206 mg, 0.45 mmol/g (70%)]. However, reactivity of this catalyst in Heck reaction of iodobenzene and ethyl acrylate was low (49% yield).

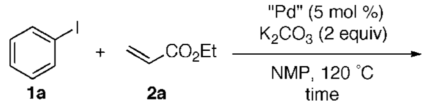
(10) This observation suggested that formation of Pd(0) from Pd(II) and subsequent stabilization by the polymer might be the key to the success of the current immobilization method.

(11) It has been reported that ionic compounds such as those containing halides, carboxylates, or polyoxoanions might form an electrical double layer around the metal particles to suppress aggregation of metals. (a) Finke R. G. In *Metal Nanoparticles: Synthesis, Characterization and Application*; Feldheim, D. L., Foss, C. A., Jr., Eds.; Marcel Dekker: New York, 2002; Chapter 2, pp 17−54. (b) Labib, M. E. *Colloids Surf*. **1988**, *29*, 293. For reviews, see: (a) Roucoux, A.; Schulz, J.; Patin, H. *Chem. Rev*. **2002**, *102*, 3757. (b) Aiken, J. D., III; Finke, R. G. *J. Mol. Catal. A* **1999**, *145*, 1.

(12) Immobilization of $Pd_2(dba)_3$ using the previous PI method (ligand exchange from dba to the polymer) in the absence of tetrabutylammonium salts (1 equiv) was unsuccessful, while addition of the ammonium salts enabled immobilization of $Pd_2(dba)_3$. Considering the role of the ammonium salts as stabilizers for Pd(0), our initial success in the immobilization of $Pd(PPh_3)_4$ suggested the effect of phosphine ligands as stabilizers as well. Synthesis of Pd nonoparticles stabilized by phosphine ligands has recently been reported; see: (a) Son, S. U.; Jang, Y.; Yoon, K. Y.; Kang, E.; Hyeon, T. *Nano Lett*. **2004**, *4*, 1147. (b) Jansat, S.; Gomez, M.; Philippot, K.; Muller, G.; Guiu, E.; Claver, C.; Castillon, S.; Chaudret, B. *J. Am. Chem. Soc.* **2004**, *126*, 1592. (c) Tamura, M.; Fujihara, H. *J. Am. Chem. Soc.* **2003**, *125*, 15742. (d) Narayanan, R.; El-Sayed, M. A. *J. Am. Chem. Soc.* **2003**, *125*, 8340.

(13) Transmission electron microscope (TEM) analysis showed that the size of Pd particles of PI Pd **G** and **H** are 3−5 nm.

Table 2. Heck Reaction of Iodobenzene (**1a**) with Ethyl Acrylate (**2a**); Comparison of Catalytic Activity[a]



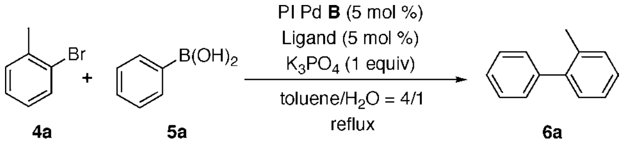
entry	"Pd"	time (h)	yield (%)[b]		
			first	second	third
1	PI Pd **A**	1	83 (nd)[c]	46 (nd)	
2	PI Pd **B**	1	92 (nd)	40 (nd)	40 (nd)
3	PI Pd **B**	2	94 (nd)	90 (nd)	93 (nd)
4	PI Pd **C**	1	57 (nd)		
5	PI Pd **D**	1	quant (nd)		
6	PI Pd **E**	1	86 (nd)	40 (nd)	45 (nd)
7	PI Pd **F**	1	67 (nd)		
8	PI Pd **G**	1	72 (nd)		
9	PI Pd **H**	1	65 (nd)	33 (nd)	

[a] Reaction conditions: 1.0 equiv of iodobenzene (**1a**), 1.5 equiv of ethyl acrylate (**2a**), 2.0 equiv of K_2CO_3, 5 mol % of PI Pd, NMP, 120 °C, 1 h. [b] Determined by GC analysis. [c] Leaching of Pd was measured by XRF analysis. nd = not detected (<0.94%).

When PI Pd **A**, **B**, **D**, or **E** was used as a catalyst, desired product **3a** was obtained in good to high yield without any leaching of Pd (entries 1, 2, 3, 5, and 6). It is noteworthy that these catalysts were recovered quantitatively by simple filtration and high yields were obtained even after the third use, though a prolonged reaction time, 2 h, was required to complete the reaction (entries 2 and 3).[15] On the other hand, reactivity was moderate when PI Pd **C**, **F**, **G**, or **H** was used as a catalyst (entries 4, 7, 8, and 9).

Next PI Pd **B** was applied to Suzuki−Miyaura coupling reactions[16] of 2-bromotoluene (**4a**) with phenylboronic acid (**5a**). The reaction proceeded smoothly in toluene−H_2O (4/1) in the presence of tris(*o*-methoxyphenyl)phosphine ligand[5c] to afford the desired product **6a** in high yield (Table 3, entry 1). It was confirmed by XRF analysis that leaching of Pd did not occur during the reaction. In addition, these catalysts were recovered quantitatively by simple filtration and high yields were obtained even after the third use. On the other hand, addition of triphenylphosphine as a ligand was not effective, and leaching of Pd was observed (entry 2).

Table 3. Suzuki−Miyaura Coupling of 2-Bromotoluene (**4a**) with Phenylboronic Acid (**5a**)

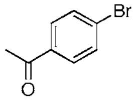
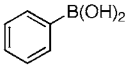
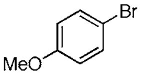
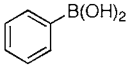
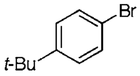
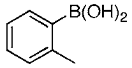
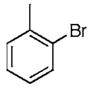
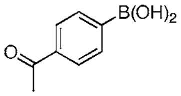
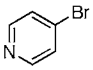
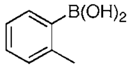
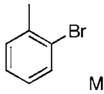
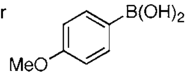
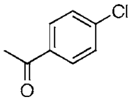
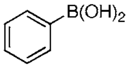


entry	ligand	time (h)	yield (%)[a]		
			first	second	third
1	$P(o\text{-}MeOC_6H_5)_3$	4	95 (nd)[b]	93 (nd)	93 (nd)
2	PPh_3	2	50 (5.7%)		

[a] Isolated yield. [b] Leaching of Pd was measured by XRF analysis. nd = not detected (<0.94%).

We then surveyed the substrate scope of PI Pd **B**-catalyzed Suzuki−Miyaura couplings of other aryl halides with arylboronic acids (Table 4). Both electron-rich and -deficient aryl halides were reactive, and the desired coupling products were obtained in high yields without leaching of the Pd (entries 1−7). It is noteworthy that the reaction proceeded

Table 4. PI Pd (**B**)-Catalyzed Coupling of Various Substrates[a]

entry	aryl halide	boronic acid	yield (%)[b]	leaching (%)[c]
1			quant	nd
2			96	nd
3			quant	nd
4			97	nd
5[d]			quant	nd
6			quant	nd
7[e]			95	nd

[a] Reaction conditions: 1.0 equiv of aryl halide, 1.5 equiv of boronic acid, 1.0 equiv of K_3PO_4, 5 mol % of $P(o\text{-}MeOC_6H_4)_3$, 5 mol % of Pl Pd **B** (0.44 mmol/g), toluene−H_2O (4/1), reflux, 2 h. [b] Isolated yield. [c] Measured by XRF analysis. nd = not detected (<0.94%). [d] K_3PO_4 (2.0 equiv) was used. [e] 2-(Dicyclohexylphosphino)biphenyl was used as a ligand. Reaction time was 6 h.

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(14) For reviews, see: (a) Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev.* **2000**, *100*, 3009. (b) Heck, R. F. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 4, pp 833−863. (c) De Meijere, A.; Braese, S. In *Transition Metal Catalyzed Reactions*; Davies, S. G., Murahashi, S.-I., Eds.; Blackwell Science: Oxford, 1999. (d) Link, J. T.; Overman, L. E. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: New York, 1998, pp 231−269.

(15) Aggregation of the Pd cluster was observed after the first use (entries 2 and 3). However, no further aggregation was confirmed after the second and the third use. Partial loss of the catalytic activity after the first use might be attributed to this aggregation. PI Pd **H** also showed the same tendancy as PI Pd **B** (see Supporting Inforamtion).

(16) For reviews, see: (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457. (b) Suzuki, A. *J. Organomet. Chem.* **1999**, *576*, 147. (c) Suzuki, A. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, Germany, 1998; p 49. (d) *Organometallics in Synthesis*: *A Manual*; Schlosser, M., Ed.; Miley: West Sussex, U.K., 1995. (e) Stanforth, S. P.; *Tetrahedron* **1998**, *54*, 263. (f) Thompson, L. A.; Ellman, J. A. *Chem. Rev.* **1996**, *96*, 555. (g) Hassan, J.; Sevignon, M.; Gozzi, C.; Schultz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359.

well even with an aryl chloride in the presence of 2-(dicyclohexylphosphino)biphenyl as a ligand,[17] even though Suzuki-Miyaura coupling of aryl chlorides is generally thought to be difficult.[18−20] As shown in this example, one advantage of this phosphine-free PI Pd over other polymer-supported Pd catalysts is that various ligands can be utilized depending on the reactions.

In summary, we have demonstrated that immobilization of palladium catalysts was successful by reducing Pd(II) salts in the presence of copolymer **2**. A remarkable effect of alkali metal salts on Pd loading level was observed. Although the role of these salts is unclear at this stage, this is the first example of polymer-incarcerated (PI) palladium using a reduction strategy. The Pd catalysts thus prepared showed high activity in Mizoroki−Heck reactions, and recovery and reuse were achieved without significant loss of catalytic activity and leaching of Pd. In addition, this catalyst also showed high activity in Suzuki−Miyaura coupling reactions not only of aryl bromides but also of an aryl chloride without leaching of Pd. We believe that this method further extends the possibilities of our immobilization method as well as the utility of immobilized catalysts. Elucidation of the immobilization mechanism as well as the application of this catalyst to other reactions are now in progress.

Acknowledgment. This work was partially supported by Grant-in-Aid for Scientific Research from the Japan Society of the Promotion of Sciences (JSPS).

Supporting Information Available: Experimental details and spectral data of products. This material is available free of charge via the Internet at http://pubs.acs.org.

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(17) Wolfe, J. P.; Singer, R. A.; Yang, B. H.; Buchwald, S. L. *J. Am. Chem. Soc*. **1999**, *121*, 9550.

(18) Shaughnessy, K. H.; Booth, R. S. *Org. Lett*. **2001**, *3*, 2757.

(19) Recently, biphastic Suzuki−Miyaura coupling of aryl chlorides using MeOPEG-supported palladium phosphine complexes was reported, see: Heiden, M. A. D.; Plenio, H. *Chem. Eur. J*. **2004**, *10*, 1789.

(20) When tris(*o*-methoxyphenyl)phosphine ligand was used, product was obtained in 17% yield.