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Immobilization of $Pd(OAc)_2$ in Ionic Liquid on Silica: Application to Sustainable Mizoroki–Heck Reaction

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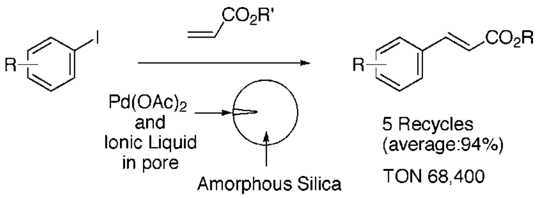
ABSTRACT



Palladium acetate was supported on amorphous silica with the aid of an ionic liquid, $[bmim]PF_6$. The immobilized catalyst was highly efficient in promoting the Mizoroki–Heck reaction without a ligand in *n*-dodecane for at least six reuses, in 89∼98% yields. The TON and TOF reached 68 400 and 8000, respectively.

The Mizoroki−Heck reaction[1] has been one of the most fundamental Pd-catalyzed carbon−carbon bond-forming reactions. Since its invention, numerous efforts have been devoted to further development of the reaction because of its usefulness and especially the wide applicability to various substrates. Recent developments in this area enabled the introduction of various new ligands,[2] new bases,[3] new techniques such as microwave[4] or ultrasonic irradiation,[5] and so on.[3] Another current interest is the development of environmentally as well as economically benign reaction conditions due to the high price of Pd. Since a homogeneous Pd catalyst easily loses catalytic activity, forming Pd clusters, a heterogeneous catalyst is desirable[6] especially for recycling, though it is not always as reactive compared to homogeneous catalysts.

To satisfy both recyclability and reactivity, immobilization of a reactive homogeneous catalyst was devised to bind the Pd catalyst on a polymer.[7] A more facile method is to immobilize the catalyst in a liquid phase by dissolving it into a nonvolatile and nonmixing liquid such as PEG.[8] From such a standpoint, a room-temperature ionic liquid[9] is expected to be a candidate as a support of the catalyst[10] due

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Table 1. Optimization of Reaction Conditions Employing Supported Pd Catalyst

entry	R′	Pd source	base	solvent	temp (°C)	time (h)	yield (%)[e]
1	Me	Pd Black	Et_3N	*n*-dodecane	120	7	31
2	Me	$Pd(PPh_3)_4$	Et_3N	*n*-dodecane	120	7	59
3	Me	$Pd(OAc)_2$	Et_3N	*n*-dodecane	120	7	59
4[a]	Me	$Pd(OAc)_2$	Et_3N	toluene	120	17	64
5	cyclohexyl	$Pd(OAc)_2$	K_2CO_3	*n*-dodecane	120	11.5	21
6	Me	$Pd(OAc)_2$	Et_3N	methylcyclohexane	100	5	22
7	Me[b]	$Pd(OAc)_2$	Et_3N	*n*-octane	120	7	68
8[c]	Me	$Pd(OAc)_2$	Et_3N	*n*-octane	120	5	51
9[c]	Me	$Pd(OAc)_2$	Et_3N	*n*-dodecane	120	5	51
10	cyclohexyl	$Pd(OAc)_2$	Et_3N	*n*-dodecane	120	16.5	75
11[d]	cyclohexyl	$Pd(OAc)_2$	Et_3N	*n*-dodecane	150	15.5	99
12	cyclohexyl	$Pd(OAc)_2$	*n*-Bu_3N	*n*-dodecane	150	15	96

[a] $Pd(OAc)_2$ dissolved from silica surface in toluene layer. [b] Performed with 2 equiv of acrylate. [c] Sodium *m*-diphenylphosphinobenzene-sulfonate was added. [d] Reaction was carried out in a sealed tube at 150 °C. [e] Yield is for isolated pure product and is based on iodobenzene **1a**.

to its nonlipophilic and nonhydrophobic nature. However, there are two major drawbacks, i.e., the higher cost of ionic liquids for larger scale use and the higher viscosity in handling as a liquid support.

Another option is to immobilize the catalyst on a solid-phase such as silica, which is chemically and mechanically stable. Williams et al.[6b,e] reported immobilization of $Pd(PPh_3)_4$ on reversed-phase silica beads, which exhibited high efficiency in Pd-catalyzed reactions in aqueous media, while Mehnert et al.[11] demonstrated immobilization of a rhodium catalyst in $[bmim]PF_6$ on a silica surface. Our recent interest in the development of sustainable organic reactions in an ionic liquid by homogeneous as well as heterogeneous catalysts[10c,12] led us to investigate a facile immobilization of the Pd catalyst in an ionic liquid in silica pores for use in sustainable Mizoroki−Heck reactions with high efficiency and recyclability. Immobilization of the Pd catalyst on silica with the aid of an ionic liquid should provide the following features: (1) stabilization of the Pd catalyst, (2) inexpensive immobilization without using expensive coupling reagents or a large amount of ionic liquid, and (3) accumulation of Pd on silica to facilitate catalytic reaction.

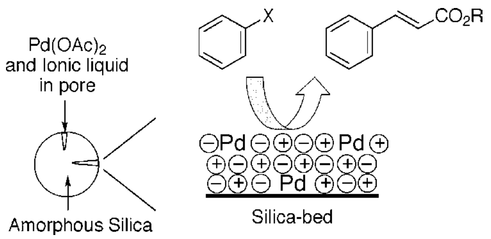

Figure 1.

The procedure of immobilization is quite simple.[13] A suspension of spherical amorphous silica in a solution of $Pd(OAc)_2$ in $[bmim]PF_6$ and THF was evaporated to dryness to afford a powdery and free-flowing immobilized catalyst. Among the ionic liquids tested, $[bmim]PF_6$ was better to at holding $Pd(OAc)_2$ than [bmim]Br, $[bmim](CF_3SO_2)_2N$, or $[hmim]PF_6$.

According to scanning electron microscopy (SEM), the shape of the immobilized catalyst was round (×1700). In contrast to the original unsupported silica, primary particles were observed clearly in a magnified picture (×70 000). This result indicates that ionic charges exist on the round surface or in pores of the primary silica particles. Electron X-ray microanalyses (EPMA) showed that phosphorus, fluorine, and Pd distributed on the surface of silica uniformly. By atomic force microscopy (AFM), a smooth surface of the supported silica was observed compared to that of unsupported silica (see Supporting Information). These results along with the dry character of the catalyst suggest that solution of $Pd(OAc)_2$ in an ionic liquid exists in the pores of silica. In a similar manner, $Pd(PPh_3)_4$ and Pd black were immobilized according to the procedure, though Pd/C and

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(13) **Representative Procedure for Catalyst Preparation.** To a stirred solution of $Pd(OAc)_2$ (690 mg) in $[bmim]PF_6$ (1 g) and THF (10 mL) was added silica powder (10 g, spherical for flash column chromatography, diameter = 40−50 μm, pore size = 5−7 nm, pore volume = 0.80−1.00 mL/g, surface area = 600−700 m^2/g). After being stirred for 90 min, THF was evaporated to dryness in vacuo to give a light brown dry powder that was rinsed with diethyl ether until the diethyl ether layer became colorless and then dried in vacuo. The amount of $Pd(OAc)_2$ supported was 560 mg (0.25 mmol/g) based on weight gain.

$PdCl_2(PPh_3)_2$ could not be immobilized due to negligible solubility of the catalysts in $[bmim]PF_6$ and THF.

By employing a reaction of iodobenzene **1a** and acrylate **2** as a probe, the reaction conditions were optimized. To prevent removal of the ionic liquid layer from the silica, the reaction was carried out in a hydrocarbon solvent. The results are compiled in Table 1.

Among Pd sources, $Pd(OAc)_2$ was chosen for further reactions due to the lack of phosphine ligand, stability, and economy since $Pd(OAc)_2$ and $Pd(PPh_3)$ showed similar activities (entries 2 and 3). Triethylamine was a superior base to potassium carbonate (entries 3 and 5). Reuse of the catalyst was difficult in hot toluene due to solubility of the ionic liquid (entry 4). Addition of sodium *m*-diphenylphosphinobenzenesulfonate did not show significant improvement (entries 8 and 9). With cyclohexyl acrylate **2** ($R' = C_6H_{11}$), the yield was improved to a certain degree (entry 10). When the reaction temperature was raised to 150 °C in a sealed tube, the reaction proceeded almost quantitatively (entry 11). Finally, the optimized reaction condition was obtained using tri-*n*-butylamine as a base (entry 12) in an open vessel.

The catalyst was easily reused up to three times as shown in Table 2 without taking any precautions after taking up the supernatant *n*-dodecane layer. A decrease of the catalytic activity was observed after three cycles, in which the free-flowing nature of the catalyst was lost. This result might arise from covering the silica surface with the resulting tributylammonium iodide, which could not be removed due to its insolubility in *n*-dodecane. This shortcoming was solved by washing the catalyst with dilute aqueous sodium hydroxide to retrieve the catalytic activity[14] as shown in entry 6, Table 2.

Table 2. Recycling of the Immobilized Catalyst

entry[a]	cycle	yield (%)
1	1	96
2	2	98
3	3	96
4	4	90
5	5	89
6[b]	6	93

[a] Reaction was carried out under the optimized reaction conditions as described in Table 1, entry 12. [b] Catalyst was washed with dilute aqueous NaOH.

According to the optimized reaction conditions in entry 12, Table 1,[15] the Mizoroki−Heck reaction with several aryl halides **1** was examined, and some representative results are listed in Table 3. Not only aryl halides **1b**−**e** having electron-withdrawing substituents (entries 1−4) but also **1f**−**h** having electron-donating substituents (entries 5−7) provided coupling products **3** in satisfactory yields. In entry 7, a certain amount of reduction occurred. In the reaction of iodobenzene **1a** and cyclohexyl acrylate **2**, the turnover number (TON) and turnover frequency (TOF) reached 68 400 and 8000 (h^{-1}), respectively (Table 4, entry 4), which are quite high values among other heterogeneous Pd catalysts,[6c] except for recently developed polymer-bound catalysts.[7b] By recycling

Table 3. Mizoroki−Heck Reaction with Various Aryl Halides **1** with Cyclohexyl Acrylate **2**

entry[a]	**1**	time (h)	**3** yield (%)[b]
1	**1b**	1.3	82
2	**1c**	5.0	68
3	**1d**	1.3	81
4	**1e**	2.0	86
5	**1f**	2.5	96
6	**1g**	2.0	85
7	**1h**	2.0	59[c]
8	**1i**	2.5	88
9[d]	**1a**	6.0	60

[a] Reaction was carried out under the optimized reaction condition as described in Table 1, entry 12. [b] Yield is for isolated pure product and is based on aryl halide **1**. [c] Product **3** was accompanied with vanillin in 17% yield. [d] Styrene was used instead of acrylate **2**.

Scheme 1

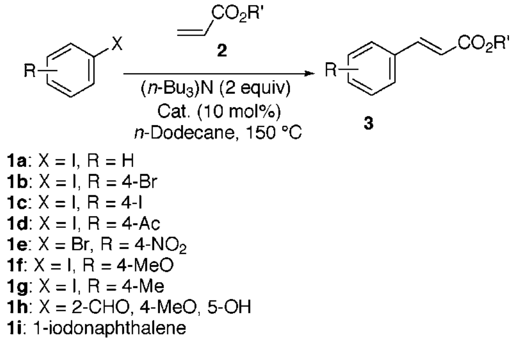

Table 4. Performance of the Immobilized Catalyst

entry	catalyst (equiv)	time (h)	yield (%)	TON	TOF (h^{-1})
1	0.0103	5.5	91	8800	1600
2	0.0053	6.0	96	18 000	3000
3	0.0024	8.0	91	38 000	4800
4	0.0013	8.5	94	68 400	8000

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[15] **Representative Procedure for Mizoroki−Heck Reaction.** To a suspension of the immobilized catalyst (400 mg, 0.1 mmol as $Pd(OAc)_2$) in *n*-dodecane (2 mL) were added iodobenzene **1** (112 mg, 1 mmol), cyclohexyl acrylate **2** (189 mL, 1.2 mmol), and tri(*n*-butyl)amine (279 mL, 2 mmol) under a nitrogen atmosphere. The suspension was heated at 150 °C until disappearance of iodobenzene **1** by GLC monitoring. After being cooled to room temperature, the *n*-dodecane layer was passed through a silica column with the aid of *n*-hexane to remove *n*-dodecane. Subsequently, the product was eluted with *n*-hexane−ethyl acetate. The *n*-hexane−ethyl acetate eluent was evaporated to dryness to give a residue that was purified by medium-pressure LC (eluent = ethyl acetate/*n*-hexane 1:20) to afford cyclohexyl cinnamate **3** (234 mg, 98%). The catalyst was reused intact for the next reaction without any pretreatment.

the catalyst, the TON could be multiplied. The higher concentration (3.4 M) of $Pd(OAc)_2$ in the pores distributed on the wide surface area might provide the remarkably high efficiency.

The supernatant *n*-dodecane layer was filtered through a membrane filter (pore diameter: 7 μm) after the reaction was complete, and the mixture was analyzed by ICP, in which 0.24 ppm of Pd was found in the layer when 10 mol % $Pd(OAc)_2$ was used in the reaction; that is, less than 0.24% Pd was dissolved from the silica support. The level of leaching is quite reasonable compared to other heterogeneous catalysts[6b,d] supported on solid.

In summary, we have demonstrated an environmentally benign, economically friendly, and sustainable ligandless Mizoroki−Heck reaction of aryl halides **1** employing Pd-$(OAc)_2$ supported in an ionic liquid layer in silica pores. The immobilization was simple without requiring any multistep operations or expensive coupling reagents. The catalyst immobilized in this way was air-stable and thermally stable to allow easy use and storage without any precautions, which would enable wide application in various Pd-catalyzed reactions.

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Supporting Information Available: Copies of EPMA, SEM, and AFM pictures of Pd-supported and unsupported silica before use, SEM and EPMA pictures of the catalyst after six cycles, ^{1}H NMR spectra of the products **1a** −**i**, and a representative experimental procedure of the catalyst preparation and Mizoroki−Heck reaction. This material is available free of charge via the Internet at http://pubs.acs.org.

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