Reusable, Highly Active Heterogeneous Palladium Catalyst by Convenient Self-Encapsulation Cross-Linking Polymerization for Multiple Carbon−Carbon Cross-Coupling Reactions at ppm to ppb Palladium Loadings

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Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201400520.

Abstract: Designing reusable high-performance heterogeneous palladium (Pd) catalysts *via* convenient, economic synthesis is of great importance to the industrial applications of various carbon-carbon cross-coupling reactions. We demonstrate herein a convenient one-pot self-encapsulation synthesis of a heterogeneous Pd catalyst [Pd@PDEB, PDEB = poly(1,3-diethynylbenzene)] directly from commercially available, economic precursors. In the synthesis, the formation of the cross-linked polymer networks and Pd encapsulation are accomplished simultaneously, turning a homogeneous Pd polymerization catalyst into the heterogeneous cross-coupling catalyst. As a unique, practical heterogeneous catalyst, Pd@PDEB shows remarkably high activity, high reusability, and high versatility towards at least four types of cross-coupling reactions (Suzuki–Miyaura, Stille, allylic arylation, and Mizoroki–Heck reactions) with even difficult reactants (aryl chlorides and heteroaryl halides) under aerobic conditions with Pd loadings down to ppm or even ppb levels. Evidences from hot filtration and 3-phase tests demonstrate the heterogeneous nature of the catalyst with very low Pd leaching and negligible contributions of leached homogeneous Pd species towards the coupling reactions.

Keywords: allylic arylation; cross-coupling reactions; heterocycles; heterogeneous catalysis; Mizoroki–Heck reaction; palladium; self-encapsulation; Stille reaction; Suzuki–Miyaura reaction

Introduction

Pd-catalyzed carbon-carbon cross-coupling reactions play a vital role in modern organic synthesis by enabling many important chemical transformations.[1–8] Due to the high cost of Pd as well as environmental and product safety issues, the development of reusable, highly active heterogeneous Pd catalysts is crucial to the industrial applications of these coupling reactions since homogeneous Pd-based catalysts are often difficult for recovery and reuse.[9–20] Besides high activity and reusability with low Pd leaching, heterogeneous Pd catalysts are also required to have convenient economic syntheses, as well as versatility in catalyzing multiple types of coupling reactions, in order for practical industrial applications.[21] Numerous heterogeneous Pd catalysts have been developed with the use of various inorganic or polyme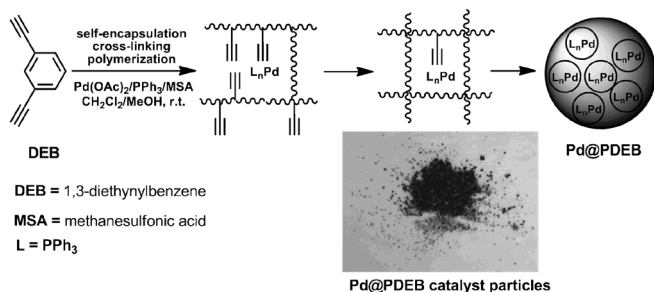r supports through different Pd immobilization/encapsulation strategies.[9–20] In particular, a few notable heterogeneous Pd catalysts have been demonstrated to exhibit high reusability and high activity requiring Pd loadings at as low as parts per million (ppm) to parts per billion (ppb) levels in selected reactions.[22–34] However, the majority of the heterogeneous catalysts developed thus far require multistep syntheses, including special, sophisticated syntheses and/or functionalization of the inorganic/polymer support and catalyst immobilization/encapsulation, which is often impractical for industrial applications. Meanwhile, most catalysts were only demonstrated to catalyze only one or two types of reactions. Commercially available catalysts, such as Pd on carbon and polyurea-encapsulated Pd[35,36] are often restricted in catalyst activity and/or applicability. There is thus a scarcity of practical, high-performance heterogeneous Pd catalysts with combined convenient synthesis, high activity, high reusability, and high versatility.

Tackling this, we report herein the convenient, one-step, one-pot synthesis of a unique heterogeneous catalyst with Pd self-encapsulated within cross-linked polymer networks from commercially available inexpensive precursors. This versatile reusable heterogeneous catalyst is demonstrated to facilitate multiple types of coupling reactions, including the Suzuki–Miyaura, Stille, allylic arylation, and Mizoroki–Heck reactions, at high activity with Pd loadings down to as low as ppm or even ppb levels relative to reactants.

Results and Discussion

Self-Encapsulation Synthesis of Pd@PDEB

The heterogeneous catalyst herein, Pd@PDEB, was synthesized simply by one-step cross-linking polymerization of a difunctional acetylenic monomer, 1,3-diethynylbenzene (DEB) with Pd(OAc)$_2$/triphenylphosphine/methanesulfonic acid (Pd:PPh$_3$:DEB = 1:6:10) as the *in situ* generated cationic Pd(II) catalyst at room temperature. We designed this synthetic strategy by taking advantage of the unique dual functions of the Pd-based catalyst in catalyzing both alkyne polymerization and cross-coupling reactions. Traditionally, diphosphine-ligated Pd(OAc)$_2$ has often been used for the catalytic chain-growth polymerization of acetylenic monomers, such as acetylene, phenylacetylene and DEB.[37–39] When designing the synthetic strategy herein, we purposely used PPh$_3$ in lieu of diphosphine as the ligand for Pd(OAc)$_2$, considering that PPh$_3$ is a classical, efficient, inexpensive ligand extensively used to formulate highly active Pd catalysts for various coupling reactions. We discovered that the cross-linking polymerization of DEB occurred nearly quantitatively in spite of PPh$_3$ being a monophosphine ligand. In the polymerization, the insoluble cross-linked polymer [Poly(DEB)] yielded with the PPh$_3$-ligated Pd species self-encapsulated simultaneously into the tightly cross-linked polymer network by physical entrapment and/or coordination to pendant alkyne groups (see Scheme 1). The catalytic synthesis of the cross-linked polymer support and Pd encapsulation are thus accomplished concurrently in one step, with the homogeneous PPh$_3$-ligated Pd polymerization catalyst successfully turned into an encapsulated heterogeneous cross-coupling catalyst. Although conceptually similar, self-supporting strategies have been previously used by both others[40] and our group[41,42] for the synthesis of polymer-supported Pd catalysts for cross-coupling reactions, the convenient synthesis herein with the sole use of inexpensive commercially available precursors and, more importantly, the outstanding catalytic performance of Pd@PDEB to be shown below make this catalyst system distinct.

Following extensive washing, the heterogeneous Pd catalyst was obtained as black particles (average particle size around 0.4 mm, see Figure S1 in the Supporting Information) with nearly quantitative Pd encapsulation (95%, with a Pd content of 5.1 wt% or 0.5 mmol g^{-1}). X-ray photoelectron spectroscopy (XPS) of the heterogeneous catalyst reveals 3$d_{3/2}$ and 3$d_{5/2}$ peaks of Pd at 340.7 and 335.5 eV (see Figure 1), respectively. These peaks indicate that the encapsulated Pd species in Pd@PDEB were present primarily as Pd(0) (typically with 3$d_{5/2}$ peak at *ca.* 334.6–335.7 eV) since Pd(II) species have higher binding energies with the 3$d_{5/2}$ peak typically in the range of 336–339 eV.[43] Nevertheless, Pd(0) nanoparticles were found to be absent in the catalyst (see Figure S2 in the Supporting Information) by examination with transmission electron microscopy (TEM). Clearly, the original PPh$_3$-ligated Pd(II) species were reduced to ligated Pd(0) species during the polymerization and/or postpolymerization treatment, which were uniformly dispersed within polymer matrix without aggregation. With XPS, the presence of P in Pd@PDEB was also confirmed with a P/Pd molar ratio of 0.7:1.

Scheme 1. One-step synthesis of heterogeneous Pd@PDEB *via* self-encapsulation cross-linking polymerization of 1,3-diethynylbenzene.
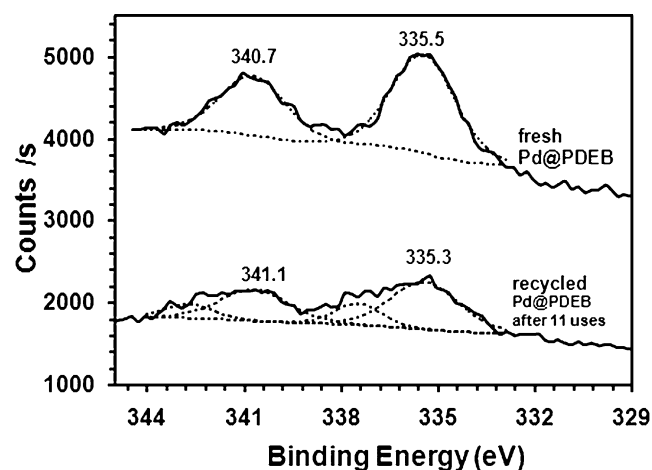

Figure 1. XPS spectra of Pd for fresh Pd@PDEB and the recycled catalyst after 11 uses in the Suzuki–Miyaura reaction of PhI and PBA.

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Suzuki–Miyaura Reactions

The catalytic performance of Pd@PDEB in the Suzuki–Miyaura, Stille, allylic arylation, and Mizoroki–Heck reactions was individually evaluated. All the reactions were undertaken under air. The Suzuki–Miyaura reactions between various aryl halides (ArX) and arylboronic acids were carried out at 100 °C in water as the environmentally benign solvent (see Table 1). No phase-transfer agent was used in all the reactions with iodobenzene (PhI) and aryl bromides. In the reactions with aryl chlorides, tetra-n-butylammonimum bromide (TBAB) was needed to enhance catalyst activity. In the case with PhI (runs SM1 and SM2), quantitative reactions occurred even at the very low Pd loading of 1 mol ppm and 300 mol ppb, respectively, yielding high turnover numbers (TON, 1×10^6 and 3.2×10^6, respectively) and high turnover frequencies (TOF, 1×10^5 and 6.67×10^4 h^{-1}, respectively). These TON and TOF values are well comparable to the highest (TON: 3.57×10^6; TOF: 1.19×10^5 h^{-1}) reported in the literature for the Suzuki–Miyaura reactions of aryl iodides facilitated with heterogeneous catalysts. The highest values were achieved by Uozumi et al.[24] with their self-assembled poly(imidazole-Pd) heterogeneous catalyst but in the presence of a phase-transfer agent that is known to increase catalytic activity.

The reaction between bromobenzene (PhBr) and phenylboronic acid (PBA) was carried out with Pd@PDEB at different Pd loadings within 1–100 mol ppm (see runs SM3–7). The TON and TOF were up to 1×10^6 and 5×10^4 h^{-1}, respectively, achieved at the lowest Pd loading of 1 mol ppm (run SM3). The activity of Pd@PDEB was much higher than that of the classical homogeneous Pd(OAc)$_2$/PPh$_3$ (1:2) counter

Table 1. Suzuki–Miyaura reactions catalyzed with Pd@PDEB.[a]
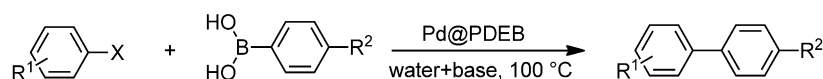
Run	X	R^1	R^2	Pd[b] [mol ppm]	Time [h]	Conversion [%]	TON [$\times 10^4$]	TOF [$\times 10^4$ h^{-1}]
SM1	I	H	H	1	10	>99	100	10.0
SM2	I	H	H	0.3	48	97	320	6.67
SM3	Br	H	H	1	20	>99	100	5.00
SM4	Br	H	H	5	6	85	17	2.83
SM5[c]	Br	H	H	5	48	2	0.4	0.01
SM6	Br	H	H	10	6	>99	10	1.67
SM7	Br	H	H	100	1.5	>99	1	0.67
SM8	Br	4-CN	H	100	2	>99	1.0	0.50
SM9	Br	4-COMe	H	100	2	>99	1.0	0.50
SM10	Br	4-NO$_2$	H	100	3	81	0.8	0.27
SM11	Br	2-Me	H	100	6	92	0.9	0.15
SM12	Br	3-Me	H	100	6	>99	1.0	0.17
SM13	Br	4-Me	H	100	6	>99	1.0	0.17
SM14	Br	4-OMe	H	100	6	>99	1.0	0.17
SM15	Br	naphthalene[d]	H	100	6	91	0.9	0.15
SM16	Br	4-NH$_2$	H	100	10	92	0.9	0.09
SM17	Br	4-OH	H	100	24	67	0.7	0.03
SM18	Br	mesitylene[e]	H	100	24	87	0.9	0.04
SM19	Br	H	OMe	100	1	>99	1.0	1.00
SM20	Br	H	COMe	100	2	>99	1.0	0.50
SM21	Br	4-Me	COMe	100	6	>99	1.0	0.17
SM22	Cl	4-COMe	H	100	28	93	0.9	0.03
SM23	Cl	4-CN	H	100	20	>99	1.0	0.05
SM24	Cl	H	H	100	28	>99	1.0	0.04
SM25	Cl	4-Me	H	100	40	80	0.8	0.02
SM26	Cl	4-OMe	H	100	40	87	0.8	0.02

[a] *Other reaction conditions:* [ArX]:[R$_2$-PBA]:[base] = 1:1.3:1.5; [ArX] = 0.6 mmol mL^{-1}; K$_2$CO$_3$ was the base in the reactions with PhI or ArBr, and CsF was the base in the reactions with ArCl; TBAB was used in the reactions with ArCl ([TBAB]:[ArCl] = 1:1).
[b] Pd molar loading relative to ArX.
[c] A control run using homogeneous Pd(OAc)$_2$/PPh$_3$ (1:2).
[d] 1-Bromonaphthalene as reactant.
[e] 2-Bromomesitylene as reactant.

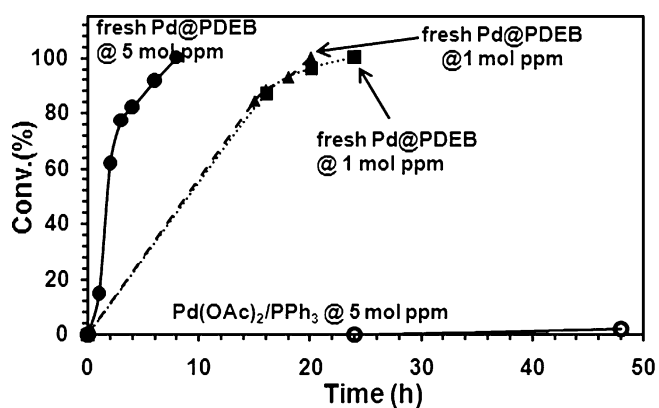**These are not the final page numbers! ↗↗**

Figure 2. Conversion curves of PhBr in Suzuki–Miyaura reactions of PhBr with PBA catalyzed with fresh Pd@PDEB at 5 mol ppm (run SM4 in Table 1) and 1 mol ppm of Pd (run SM3), recycled Pd@PDEB (after 11 uses in Suzuki–Miyaura reaction of PhI and PBA, see Section "Reusability Tests") at 1 mol ppm, and homogeneous Pd(OAc)$_2$/PPh$_3$ at 5 mol ppm (run SM5).

catalyst. At the same Pd loading of 5 mol ppm, a PhBr conversion of 85% was achieved at 6 h with Pd@PDEB (run SM4) whereas only negligible conversion (2%) was observed even after 48 h in the control run (run SM5) with the homogeneous catalyst (see Figure 2 for a comparison of their conversion curves). The low activity with the homogeneous catalyst should be attributed most likely to its quick decomposition to form inactive aggregated Pd(0) particles. At the Pd loading of 100 mol ppm, Pd@PDEB also successfully effected quantitative or nearly quantitative reactions of other activated or deactivated aryl bromides with PBA (runs SM8–18). In comparison, relatively higher TOF values were observed with the activated electron-deficient aryl bromides (4-bromobenzonitrile, 4-bromoacetophenone, and 1-bromo-4-nitrobenzene in runs SM8–10) than with the electron-rich deactivated ones (2-, 3-, and 4-bromotoluene, 4-bromoanisole, 1-bromonaphthalene, 4-bromoaniline, 4-bromophenol, and sterically hindered 2-bromomesitylene in runs SM11–18). Similarly, quantitative yields were also achieved in the reactions of PhBr or 4-bromotoluene with activated or deactivated substituted PBAs (runs SM19–SM21).

Compared to aryl iodides and bromides, aryl chlorides are much more difficult to activate, but are highly desired since they are readily available and inexpensive.[44] The coupling reactions of aryl chlorides with heterogeneous catalysts have often been challenging. Pd@PDEB was found herein to be highly efficient in catalyzing the coupling of several aryl chlorides (including the deactivated 4-chlorotoluene and 4-chloroanisole) with PBA at a Pd loading of 100 mol ppm (runs SM22–SM26). Nearly quantitative conversions were obtained in all cases with TOF up to 5×

10^2 h^{-1}, which is among the highest reported in the literature for the Suzuki–Miyaura coupling of aryl chlorides with heterogeneous catalysts.[9]

We also investigated the performance of Pd@PDEB in catalyzing Suzuki–Miyaura reactions involving heteroaryl halides and/or heteroarylboronic acids, which are even more challenging yet very important for medicinal and agrochemical applications.[45] Quite a few homogeneous Pd catalysts have been developed for the versatile Suzuki–Miyaura reactions of heteroaryl compounds, but with the typical requirement of high Pd loadings (1–4 mol%).[46–56] Heterogeneous Pd catalysts, however, have only been reported in very limited cases for such reactions at the requirement of high Pd loadings (0.5–3 mol%).[57–62] Herein, we have found that Pd@PDEB is highly efficient in catalyzing the reactions of representative heteroaryl halides (2-bromopyridine, 3-bromothianaphthene, and 2-chloropyridine, see Table 2) with PBA or a typical heteroarylboronic acid, 3-thienylboronic acid. Quantitative conversions were reached in the reactions of 2-bromopyridine/3-bromothianaphthalene with PBA or 3-thienylboronic acid at the Pd loading of 50 mol ppm, rendering high TONs of 2×10^4 and TOFs from 2.5×10^3 to 3.3×10^3 h^{-1} (runs SM28, SM29, SM31 and SM32). At the further reduced Pd loading of 10 mol ppm, high biaryl yields were still maintained in the reactions (runs SM27 and SM30) of the heteroaryl bromides with PBA, with enhanced TONs (8.7×10^4 and 10^5, respectively) and TOFs (4.4×10^3 and 5×10^3 h^{-1}, respectively). At high Pd loadings (1,000 or 5,000 mol ppm), quantitative conversions were achieved in the reactions with the more challenging 2-chloropyridine (runs SM33–SM35), confirming the high efficiency of Pd@PDEB in catalyzing the reactions with less active heteroaryl chlorides. On the basis of these results, Pd@PDEB is one of very few heterogeneous Pd catalysts reported to date that can efficiently facilitate Suzuki–Miyaura reactions of heteroaryl compounds while at comparable or even higher activities.[57–62]

Stille Reactions

Stille reactions of aryl/heteroaryl bromides or chlorides with organotin compounds (see Table 3) were performed with Pd@PDEB at 100°C. At the Pd loading of 50 mol ppm, the reactions (runs St1–St6) of various aryl bromides with Ph$_4$Sn proceeded nearly quantitatively. A higher TOF (2.5×10^3 h^{-1}) was achieved with the activated aryl bromides (4-bromobenzonitrile and 4-bromoacetophenone in runs St5 and St6) than with PhBr or deactivated aryl bromides (in runs St1–St4). The reactions between 4-bromoacetophenone and various organotin compounds (runs St7–St9) were also performed at 50 mol ppm of Pd, with high

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Table 2. Suzuki–Miyaura reactions of different heteroaryl compounds catalyzed with Pd@PDEB.[a]
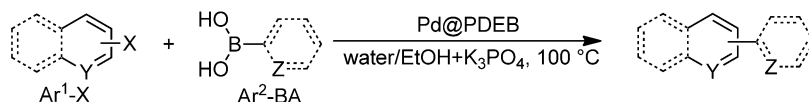
Run	Ar¹-X	Ar²-BA	Pd[b] [mol ppm]	Time[h]	Conversion [%]	TON [×10³]	TOF [×10³ h⁻¹]
SM27		—B(OH)₂	10	20	87	87	4.4
SM28	(2-bromopyridine)	—B(OH)₂	50	8	>99	20	2.5
SM29		(thiophene)—B(OH)₂	50	6	>99	20	3.3
SM30		—B(OH)₂	10	20	>99	100	5
SM31	(3-bromobenzothiophene)	—B(OH)₂	50	8	>99	20	2.5
SM32		(thiophene)—B(OH)₂	50	8	>99	20	2.5
SM33		—B(OH)₂	1000	36	94	0.94	0.026
SM34	(2-chloropyridine)	—B(OH)₂	5000	24	>99	0.2	0.008
SM35		(thiophene)—B(OH)₂	5000	20	>99	0.2	0.01

[a] *Other reaction conditions:* water/ethanol mixture (v/v = 2:1) as solvent, [Ar¹X]:[Ar²BA]:[K₃PO₄] = 1:1.3:1.5; [Ar¹X] = 0.6 mmol mL⁻¹.
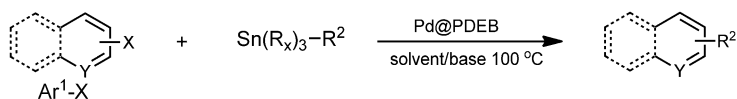
[b] Pd molar loading relative to Ar¹X.

conversions achieved. By comparing TOF values, the reactivity of the organotin compounds decreases by following the commonly observed order: $Me_4Sn > Ph_4Sn \approx$ 2-(tributylstannyl)thiophene $> Bu_4Sn$. With the most active pair of 4-bromoacetophenone and Me_4Sn, the coupling was accomplished quantitatively (runs St10 and St11) even at the low Pd loadings of 10 and 1 mol ppm, respectively. In particular, to the best of our knowledge, the TON and TOF values (1×10^6 and 5×10^4 h⁻¹, respectively) achieved at 1 mol ppm Pd are the highest ever reported for the Stille reactions with heterogeneous catalysts.[9,10] Pd@PDEB also efficiently catalyzed the quantitative reactions (runs St12–St15) of two heteroaryl bromides, 2-bromopyridine and 3-bromothianaphthalene, with Ph_4Sn or 2-(tributylstannyl)thiophene, but at the requirement of higher Pd loadings of 100 and 1000 mol ppm, respectively. This makes it within the very limited heterogeneous catalysts that have been reported to effectively facilitate Stille reactions of heteroaryl compounds.[60,63] Meanwhile, at the Pd loading of 5,000 mol ppm, Pd@PDEB also efficiently catalyzed the Stille reactions of three aryl chlorides with Me_4Sn (runs St16–St18), giving high conversions. It is thus also one of the very few heterogeneous Pd catalysts reported to effect the Stille reactions of unreactive aryl chlorides.[63–66]

Allylic Arylation Reactions

Allylic arylation reactions between allylic acetates and tetraarylborates/PBA were further carried out with Pd@PDEB at different Pd loadings (Table 4). Compared to aryl-aryl coupling, allylic arylation (i.e., allyl-aryl coupling)[67–71] is less studied yet more challenging and often requires a large amount (1–10 mol%) of catalyst, with the rare exception of Uozumi's heterogeneous poly(imidazole-Pd) catalyst that can catalyze allylic arylation at as low as 0.8 mol ppm of Pd.[23,24] From runs A1–A4, the reaction between cinnamyl acetate and sodium tetraphenylborate (NaBPh₄) proceeded quantitatively at as low as 1 mol ppm Pd with TON and TOF up to 9.4×10^5 and 3.4×10^4 h⁻¹, respectively, which are close to the highest values (TON: 1.25×10^6; TOF: 1.04×10^5 h⁻¹) reported by Uozumi et al.[23,24] Similarly, the reactions (runs A5–A7) between cinnamyl acetate and PBA also proceeded successfully but at slightly lowered TOFs. Meanwhile, quantitative conversions were also achieved in the reactions (runs A8–A11) of less reactive prenyl acetate with NaBPh₄ or PBA at the Pd loadings down to as low as 10 mol ppm.

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Table 3. Stille reactions catalyzed with Pd@PDEB.[a]

$$Ar^1\text{-}X + Sn(R_x)_3\text{-}R^2 \xrightarrow[\text{solvent/base 100 °C}]{\text{Pd@PDEB}} \text{product}$$

| Run	Ar¹-X	$(R_x)_3$Sn-R²	Pd[b] [mol ppm]	Time [h]	Conversion [%]	TON [×10³]	TOF [×10³ h⁻¹]
St1	Ph–Br	Sn(Ph)₄	50	20	95	19	1
St2	Me–C₆H₄–Br	Sn(Ph)₄	50	28	83	17	0.6
St3	MeO–C₆H₄–Br	Sn(Ph)₄	50	28	93	19	0.7
St4	1-naphthyl–Br	Sn(Ph)₄	50	28	90	18	0.6
St5	NC–C₆H₄–Br	Sn(Ph)₄	50	8	>99	20	2.5
St6	(O=)C(CH₃)–C₆H₄–Br	Sn(Ph)₄	50	8	>99	20	2.5
St7	(O=)C(CH₃)–C₆H₄–Br	Sn–(C₄H₉)₄	50	20	>99	20	1
St8	(O=)C(CH₃)–C₆H₄–Br	thienyl-Sn-(C₄H₉)₃	50	8	97	19	2.4
St9	(O=)C(CH₃)–C₆H₄–Br	Sn–(CH₃)₄	50	4	>99	20	5
St10	(O=)C(CH₃)–C₆H₄–Br	Sn–(CH₃)₄	10	6	>99	100	17
St11	(O=)C(CH₃)–C₆H₄–Br	Sn–(CH₃)₄	1	20	>99	10³	50
St12	2-pyridyl–Br	Sn(Ph)₄	1000	28	>99	1	0.04
St13	benzothiophen-3-yl–Br	Sn(Ph)₄	100	20	>99	10	0.5
St14	2-pyridyl–Br	thienyl-Sn-(C₄H₉)₃	1000	20	>99	1	0.05
St15	benzothiophen-3-yl–Br	thienyl-Sn-(C₄H₉)₃	100	20	>99	10	0.5
St16	Ph–Cl	Sn–(CH₃)₄	5000	40	>99	0.2	0.005
St17	(O=)C(CH₃)–C₆H₄–Cl	Sn–(CH₃)₄	5000	28	96	0.2	0.007
St18	NC–C₆H₄–Cl	Sn–(CH₃)₄	5000	20	93	0.2	0.01

[a] *Other reaction conditions:* [ArX]=0.6 mol/L. [ArX]:[R²-Sn(R$_x$)₃]:[base]=1:1.2:1.5. In the reactions with aryl bromides/ chlorides, NMP was used as solvent with KF as base. In others with heteroaryl bromides (St12-St15), NMP/ethanol mixture (v/v=1:2) was used as solvent with K_3PO_4 as base.

[b] Pd molar loading relative to ArX.

Mizoroki–Heck Reactions

Pd@PDEB also successfully facilitated the Mizoroki–Heck reactions of various aryl halides with *n*-butyl acrylate or styrene (see Table 5). Quantitative conversion was reached in the coupling of PhI with *n*-butyl acrylate (run MH1) at the low Pd loading of 10 mol ppm at 100 °C, giving high TON of 1×10^5 and TOF of 2.1×10^3 h⁻¹. Although these TON and TOF values are lower than the highest ones reported in Yamada's most recent paper (TON$=2\times10^6$ and TOF$=40\times10^3$ h⁻¹),[72] they are still among the highest values

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Table 4. Allylic arylation reactions catalyzed with Pd@PDEB.[a]
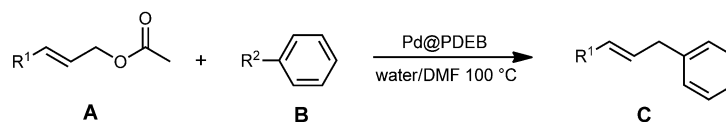
Run	A	B	Pd[b] [mol ppm]	C	Time [h]	Conversion [%]	TON [$\times 10^4$]	TOF [$\times 10^3$ h^{-1}]
A1			100		1	>99	1	10
A2		Na$^+$ B(Ph)$_4^-$	50		2	>99	2	10
A3			10		4	>99	10	25
A4			1		28	94	94	34
A5			50		4	>99	2	5
A6		—B(OH)$_2$	10		8	>99	10	13
A7			1		28	68	68	24
A8		Na$^+$ B(Ph)$_4^-$	50		2	>99	2	10
A9			10		8	94	9.4	12
A10		—B(OH)$_2$	50		6	92	1.8	3
A11			10		20	>99	10	5

[a] *Other reaction conditions:* H$_2$O/DMF at 1/1 vol. ratio was used as the solvent; [allylic acetate (A)] = 0.6 mol/L. In reactions using NaBPh$_4$, [A]:[NaBPh$_4$] = 1:1.3. In reactions using PBA, KF was applied as the base, [A]:[PBA]:[KF] = 1:1.3:1.5.
[b] Pd molar loading relative to allylic acetate.

Table 5. Mizoroki–Heck reactions catalyzed with Pd@PDEB.[a]
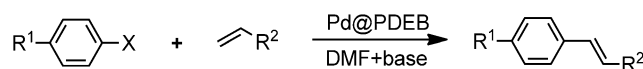
Run	R^1	X	R^2	Pd[b] [mol ppm]	Time [h]	Conversion [%]	TON [$\times 10^3$]	TOF [h^{-1}]
MH1	H	I	CO$_2$Bu	10	48	>99	100	2083
MH2	H	Br	CO$_2$Bu	1000	8	>99	1	125
MH3	H	Br	CO$_2$Bu	100	20	89	8.9	445
MH4	COMe	Br	CO$_2$Bu	1000	2	>99	1	500
MH5	COMe	Br	CO$_2$Bu	100	20	96	9.6	480
MH6	COMe	Br	Ph	1000	2	94	0.94	475
MH7	COMe	Br	Ph	100	48	96	9.6	200
MH8	CN	Br	CO$_2$Bu	1000	4	>99	1	250
MH9	naphthalene[c]	Br	CO$_2$Bu	1000	20	>99	1	50
MH10	COMe	Cl	Ph	10000	3	>99	0.10	33
MH11	CN	Cl	Ph	10000	3	>99	0.10	33
MH12	Me	Cl	Ph	10000	40	86	0.09	2

[a] *Other reaction conditions:* [ArX] = 0.6 mmol mL^{-1}. For run MH1 with PhI, [PhI]:[alkene]:[Et$_3$N] = 1:1.5:1.5 and T = 100 °C. For runs MH2-MH9 with ArBr, [ArBr]:[alkene]:[K$_2$CO$_3$] = 1:1.5:1.5 and T = 130 °C. For runs MH10–MH12 between ArCl and styrene, [ArCl]:[St]:[NaOH] = 1:3:3 and T = 150 °C.
[b] Pd molar loading relative to ArX.
[c] 1-Bromonaphthalene as reactant.

reported for heterogeneous catalyzed Mizoroki–Heck reactions under similar conditions.[9,10] For aryl bromides, a higher reaction temperature of 130 °C and an enhanced Pd loading (100 or 1,000 mol ppm; runs MH2–MH9) were found necessary in order to obtain high TOF. Again, the activated aryl bromides were more reactive than PhBr and deactivated ones, with TON up to 9,600 and TOF up to 500 h^{-1} achieved. In addition, the catalyst also efficiently facilitated the reactions (runs MH10–MH12) of aryl chlorides with styrene but under more critical reaction conditions (i.e., 1 mol% of Pd loading at 150 °C with NaOH as base).

High conversions (86 or $> 99\%$; TOF $= 2$–$33\ h^{-1}$) were achieved in the reactions with both activated 4-chloroacetophenone and 4-chlorobenzonitrile, and de-activated 4-chlorotoluene. This ranks Pd@PDEB within the very limited heterogeneous catalysts that have been reported to effectively facilitate the Mizoroki–Heck reaction of aryl chlorides.[65,73–76] All the Mizoroki–Heck reaction products herein were featured with pure E-selectivity with no/negligible Z-isomers observed.

Reusability Tests

With the demonstrated high activity and high versatility of Pd@PDEB in catalyzing the above four types of cross-coupling reactions, we subsequently investigated its reusability as well as catalyst leaching in the reactions undertaken in different media. We first carried out the Suzuki–Miyaura reaction of PhI and PBA in water at the high Pd loading of 1,000 mol ppm at 100 °C for 11 cycles by recovering and reusing the same catalyst for additional 10 times. During the whole reusability test, the catalyst retained well its particle morphology without pulverization (see Figure S1 in the Supporting Information for an optical image) due to its tightly cross-linked structures, thus facilitating easy recovery. High conversions, although with a slight gradual decrease (from > 99 to 85% in 11th cycle) after the first three cycles, were maintained in all the cycles at the same reaction time of 1 h (see Figure 3).

The leaching of Pd was found to be marginal (see Table S1 in Supporting Information for detailed results). The concentration of the leached Pd in the reaction solution was generally below 0.5 ppm (i.e.,
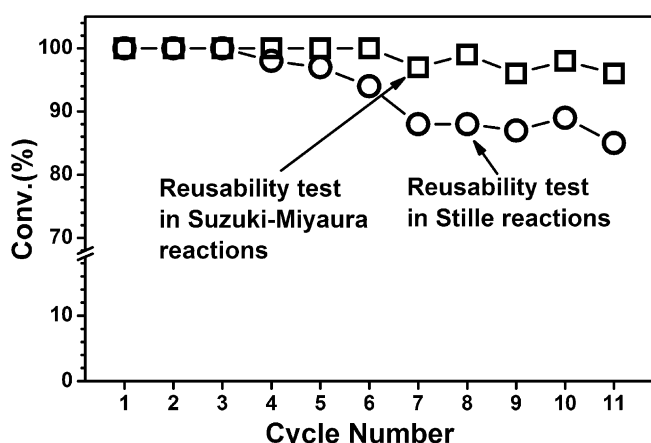
0.8% of total Pd) in each cycle, except for cycles 1 (0.94 ppm; 1.4% of total Pd) and 4 (1.12 ppm; 1.8% of total Pd). In total, only 5.3% of the Pd leached out in the 11-cycle reactions. The catalyst recovered from the 11-cycle reusability test was further used to catalyze the reaction between PhBr and PBA at a Pd loading of 1 mol ppm. Compared to the fresh catalyst at the same reaction time of 24 h, the recovered catalyst exhibited similar activity and conversion curve, with the same TON of 1×10^6 and only a slight decrease in TOF from 5×10^4 to $4.2 \times 10^4\ h^{-1}$ (see Figure 2). XPS analysis of the recycled catalyst recovered from the 11-cycle reusability test indicates the broadening in the $3d_{3/2}$ and $3d_{5/2}$ peaks of Pd with the appearance of Pd(II) species at higher binding energies (see Figure 1), indicating the oxidation of some Pd(0) species to Pd(II) during the coupling reactions. While absent in the fresh catalyst, Pd(0) nanoparticles were, however, observed in the recycled catalyst under TEM (see Figure S2 in the Supporting Information for an image), indicating the presence of dynamic Pd dissolution/redeposition during the reactions.[77]

Similarly, another 11-cycle reusability test was performed on the Stille reaction of 4-bromoacetophenone with Bu_4Sn at 1,000 mol ppm Pd loading in NMP at 100 °C. Again, quantitative conversions (see Figure 3) were achieved in all cycles at a fixed reaction time of 12 h. The concentrations of leached Pd in the reaction solutions were slightly higher compared to those in water media, but were still around or below 1 ppm in each cycle (see Table S2 in the Supporting Information for details). In total, 11.7% of Pd leached out in all the 11 cycles. The enhanced Pd leaching in these Stille reactions relative to that in the above aqueous-phase Suzuki–Miyaura reactions is suspected to result from the use of organic NMP as the solvent since the hydrophobic cross-linked PDEB polymer matrix can be better swollen in NMP, which facilitates the diffusive leaching of Pd species. The recycled catalyst recovered from the reusability test also behaved similarly as the fresh catalyst in the Stille reaction between 4-bromoacetophenone and Bu_4Sn at the Pd loading of 50 mol ppm (identical conditions as run St7), with a conversion of 94% achieved relative to $> 99\%$ with the fresh catalyst. These tests confirm the excellent reusability of Pd@PDEB as well as its low Pd loss during the reactions.

Hot Filtration and 3-Phase Tests

To elucidate the contributions of leached homogeneous Pd species towards the reactions, hot filtration tests[77–83] were carried out in both the Suzuki–Miyaura reaction of PhI with PBA and Stille reaction of 4-bromoacetophenone with Me_4Sn catalyzed with fresh Pd@PDEB at the same Pd loading of 1,000 mol

Figure 3. Conversion *vs.* cycle number in the reusability tests of Pd@PDEB in the Suzuki–Miyaura reaction of PhI with PBA (100 °C, reaction time $= 1$ h, Pd loading $= 1,000$ mol ppm), and the Stille reaction of 4-bromoacetophenone with Bu_4Sn (100 °C, reaction time $= 12$ h).

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ppm. The former reaction mixture was hot filtered after reaching a conversion of 71% at 20 min to remove the heterogeneous catalyst. The conversion of PhI in the filtered solution was found to remain at *ca.* 71% in spite of additional 24 h at 100°C (see Figure 4). On the contrary, the conversion reached >99% within 40 min in the control run without involving hot filtration. The latter Stille reaction mixture was hot filtered after reaching a conversion of 68% at 1.5 h. The conversion of the aryl bromide in the filtered solution increased slightly to 78% after additional 22 h at 100°C, whereas >99% of conversion was reached only after 2 h in the control run without hot filtration (see Figure 4). Although they cannot completely exclude the contribution of leached homogeneous Pd species, these tests indicate that the small percentage of leached homogeneous Pd species have only small contributions towards the reactions.[14,23,24,77–83]

In addition to the hot filtration tests, we also carried out 3-phase tests to further verify the heterogeneous nature of catalytically active species in the coupling reactions with fresh Pd@PDEB. 3-phase tests, which entail anchoring one of the reactants onto a solid support, have been a useful technique in the determination of heterogeneity in cross-coupling reactions facilitated with solid-supported Pd catalysts.[77,81,84,85] In the tests, no transformation should occur with the anchored reactant if the cross-coupling reactivity results completely from the heterogeneous Pd species embedded in Pd@PDEB. On the other hand, if the leached homogeneous Pd species have some activity, the anchored reactant will be converted to some degree. We designed two 3-phase tests for the Stille and Mizoroki–Heck reactions, respectively, undertaken in organic media, with the use of a mesoporous silica-supported aryl iodide (SBA-ArI, see
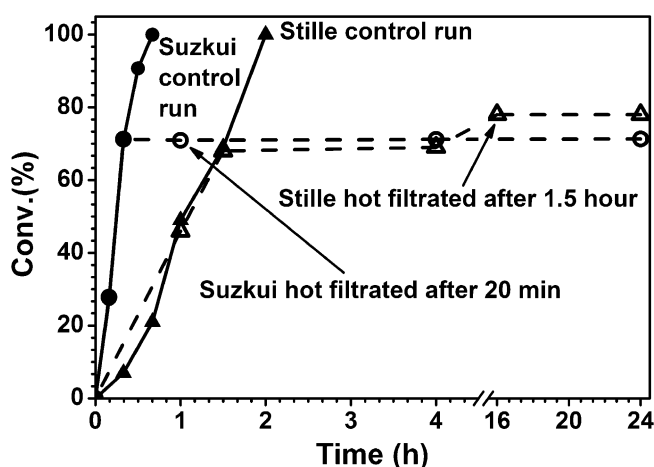
Scheme S1 in the Supporting Information) as a part of the aryl halide in the reactions. In each test, 4-bromoacetophenone (in Stille reaction with Me$_4$Sn) or 4-iodoacetophenone (in Mizoroki–Heck reaction with *n*-butyl acrylate) was used as the homogeneous aryl halide with the addition of 10 mol% heterogeneous SBA-ArI. In the tests, the heterogeneous aryl iodide has similar or even higher reactivity relative to the homogenous aryl halide. Both reactions were undertaken at a high Pd loading of 1,000 mol ppm at 100°C.

No appreciable conversion of SBA-ArI was observed in both reactions when the homogeneous aryl halide reached a high conversion of 72 and 88% in the Stille and Mizoroki–Heck reactions, respectively. Considering that most of the cross-coupling reactions in this work were performed with Pd@PDEB at Pd loadings less than 1,000 mol ppm, the 3-phase tests, in combination with the above hot filtration tests, support that Pd@PDEB is a heterogeneous catalyst and the leached homogeneous Pd species only have a small contribution compared to the immobilized Pd species. This differentiates it from many heterogeneous Pd catalysts reported in the literature where the leached homogeneous Pd species are in fact the true ones responsible for the reactions.[77–85] Nevertheless, one exception should be noted with the recycled catalysts, particularly those after many cycles of reuse. Given the presence of Pd nanoparticles in the recycled catalysts as shown in Figure S2 (Supporting Information), we expect that the contribution of leached homogeneous Pd species towards the reactions should become increasingly pronounced with increased reuse.

Conclusions

We have presented herein a simple, convenient, economic, and practical synthesis of the heterogeneous Pd@PDEB catalyst *via* one-pot self-encapsulation cross-linking polymerization with the sole use of commercially available inexpensive precursors. It shows high catalytic activity and high versatility in catalyzing four types of cross-coupling reactions under aerobic conditions even with difficult reactants like aryl chlorides and heteroaryl halides at Pd loadings down to ppm or even ppb levels. The best catalyst activities achieved herein are highest or among the highest reported with heterogeneous catalysts for the four types of reactions. The catalyst is also air- and water-stable, and is featured with excellent reusability and low Pd loss. With its overall performance, the catalyst competes well and performs even better than the best heterogeneous catalysts reported in the literature for coupling reactions. The outstanding combined features also make the catalyst highly promising for

Figure 4. Conversion curves in the hot filtration tests in Suzuki–Miyaura reaction of PhI with PBA and Stille reaction of 4-bromoacetophenone with Me$_4$Sn.

broad industrial applications. The continued study on the broader scope of the catalyst to other reaction substrates and other types of coupling reactions will be on the way.

Experimental Section

Materials

All manipulations were performed in air unless otherwise noted. In order to avoid the influence of any residual Pd species adsorbed on the surface, all the glassware and magnetic stirring bars used for cross-coupling reactions were pre-treated with aqua regia, washed with distilled water, and then dried in an oven. Palladium(II) acetate [Pd(OAc)$_2$, 98%] were obtained from Strem Chemicals and used as received. HPLC-grade CH$_2$Cl$_2$ (99.5%, Fisher Scientific) was deoxygenated and dried by using a solvent purification system (Innovative Technology) before use. Methanol (ACS reagent grade, Fisher Scientific) was dried over 3 Å/5 Å molecular sieves before use. Deionized water (DW) was obtained from a Barnstead/Synbron Nanopure II water purification system. A palladium atomic absorption standard solution (contain 1011 ppm of Pd in 5.1 wt% HCl) was purchased from Aldrich and stored at 4 °C in the fridge. N,N-dimethylformamide (DMF, certified ASC grade), tetrahydrofuran (THF, certified), hydrochloric acid (35–38 wt% in water), KF (certified ACS, granular powder), K$_3$PO$_4$ (certified ACS, granular powder) and K$_2$CO$_3$ (certified ACS, granular powder) were received from Fisher Scientific and used without further purification. Mesoporous silica SBA-15 was purchased from Claytec Inc., and was vacuum dried at 160 °C for 8 h before use. Other chemicals or solvents, including 1-methyl-2-pyrrolidinone (NMP, ReagentPlus), CsF (> 99%) 1,3-diethynylbenzene (DEB, 96%), methanesulfonic acid (MSA, 99.5%), triphenylphosphine (PPh$_3$, 99%), iodobenzene (PhI, 98%, Aldrich), bromobenzene (PhBr, 99%), 1-bromo-4-nitrobenzene (99%), 4-bromobenzonitrile (99%), 4-bromoaniline (97%), 4-bromophenol (99%), 4-bromoacetophenone (98%), 4-bromoanisole (99%), 4-bromotoluene (98%), 2-bromotoluene (99%), 3-bromotoluene (98%), 2-bromomesitylene (98%), 1-bromonaphthalene (97%), 2-bromopyridine (99%), 3-bromothianaphthalene (95%), 4′-bromoacetophenone (98%), tetra-n-butylammonium bromide (TBAB, ACS reagent, > 98%), chlorobenzene (PhCl, ReagentPlus), 4-chloroacetophenone (97%), 4-chlorotoluene (98%), 4-chloroanisole (99%), 4-chlorobenzonitrile (99%), 2-chloropyridine (99%), 4-methoxyphenylboronic acid (≥ 95%), 4-acetylphenylboronic acid, 4-pyridinylboronic acid (90%), 3-thienylboronic acid (≥ 95%), cinnamyl acetate (99%), n-butyl acrylate (BA, > 99%), styrene (99%), triethylamine (Et$_3$N, 99%), phenylboronic acid (PBA, > 97%), sodium tetraphenylborate (NaBPh$_4$, ACS reagent), prenyl acetate (≥ 98%), 2-(tributylstannyl)thiophene (97%), tetrabutyltin (Bu$_4$Sn, 93%), tetraphenyltin (Ph$_4$Sn, 97%), tetramethyltin (Me$_4$Sn, 95%), 3-aminopropyltrimethoxylsilane (97%), ethanol (reagent grade), nitric acid (HNO$_3$, 70%), and hydrogen peroxide (H$_2$O$_2$, 50 wt% in water), were all purchased from Aldrich and used as received.

Characterization and Measurement

Proton nuclear magnetic resonance (^{1}H NMR) spectra of the reaction mixtures and products were all obtained on a Bruker AV500 spectrometer (500 MHz) at ambient temperature with CDCl$_3$ as solvent. Atomic absorption (AA) analyses were performed on a Perkin–Elmer Precisely AAnalyst 400 spectrometer equipped with a Pd element lamp (max. 30 mA, Perkin–Elmer). The data were collected with the WinLab32 software (Perkin–Elmer). The blank solution for the preparation of all solutions in AA analysis was composed of 11.1 vol% THF, 6.7 vol% HCl and 3.4 vol% H$_2$O$_2$ in deionized water. For all the analyses, a calibration curve was first generated with Pd standard solutions at different concentrations (with [Pd] in the range of 0.25–10 mg L^{-1}). X-ray photoelectron spectroscopy (XPS) measurements of the heterogeneous Pd catalysts were carried out on a Thermo Scientific Theta Probe XPS spectrometer (ThermoFisher). A monochromatic Al K$_\alpha$ X-ray source was used, with a spot area of 400 μm. The samples were run in a standard mode, i.e., all angles collected (60° angular acceptance) for the survey spectra, and for the region spectra. Transition electron microscopy (TEM) images were collected on a JEOL 2010F field emission electron microscope operated at 200 keV.

Synthesis of Heterogeneous Catalyst Pd@PDEB by Self-Encapsulation Catalytic Cross-Linking Polymerization of DEB

Pd(OAc)$_2$ (89 mg, 0.4 mmol), PPh$_3$ (0.62 g, 2.4 mmol), DEB (0.5 g, 4 mmol), CH$_2$Cl$_2$ (1 mL), and MeOH (0.2 mL) were mixed in a 20-mL glass vial under N$_2$ protection. Then one drop MSA (*ca.* 0.05 mL) was added. The system changed to dark red immediately following the addition of MSA and gradually became cloudy within the first hour of polymerization. Visible insoluble particles formed throughout the polymerization process. The polymerization lasted for 18 h at room temperature under N$_2$ protection. At the end, the black insoluble cross-linked polymer particles were collected by filtration and washed with a large amount of DMF then methanol to remove unreacted monomer, non-encapsulated Pd catalysts and PPh$_3$ before being dried at 60 °C for 24 h to afford the heterogeneous Pd catalyst, Pd@PDEB; yield: 0.79 g.

To determine the Pd content and the percentage of Pd encapsulation in the resultant Pd@PDEB, 5.8 mg of the sample were burned off at 1000 °C in air and then extracted with HCl/HNO$_3$/H$_2$O$_2$ (v/v/v = 3:1:0.5, total volume 2.3 mL × 10) mixture. A mixture of HCl/H$_2$O$_2$ (v/v = 1:1; 5 mL) was added before the final solution was diluted to 30 mL. Two mL of the resulting extract solution were taken out and further diluted to 3 mL with blank solution. The resulting solution was determined to have a Pd concentration of 6.6 ppm on the basis of AA analysis, which gives the Pd content of 5.1 wt% or 0.5 mmol g^{-1} in Pd@PDEB, and the percentage of Pd encapsulation of 95.3%. Figure S1 (Supporting Information) shows the optical microscopy image of the fresh Pd@PDEB catalyst as well as that of the recycled catalyst after the 11-cycle reusability test for the Suzuki–Miyaura reaction of PhI and PBA in water at 100 °C (see the reusability test section). Figure S2 (Supporting Information) shows the TEM images of both fresh and recycled catalysts.

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Suzuki–Miyaura Reactions Catalyzed with Pd@PDEB

The following is a typical procedure (run SM7 in Table 1) for the Suzuki–Miyaura reactions of arylboronic acid with iodobenzene or different aryl bromides. PhBr (0.39 g, 2.5 mmol), PBA (0.40 g, 3.3 mmol), Pd@PDEB (0.5 mg, containing 0.25 µmol of Pd), K_2CO_3 (0.52 g, 3.8 mmol), and water (4 mL) were combined in a clean test tube having a magnetic stirring bar. The test tube was sealed and placed in an oil bath set at 100 °C. The reaction solution was monitored with ^{1}H NMR spectroscopy to determine the conversion. At completion of the reaction, the mixture was cooled to room temperature and washed with ethyl acetate 3 times (2 mL×3) to extract the organic product. The insoluble Pd@PDEB was picked out easily from the reaction solution with the use of tweezers.

For the Suzuki–Miyaura reactions of PBA with different aryl chlorides, the following is a typical procedure (run SM22 in Table 1). PBA (0.10 g, 0.8 mmol), Pd@PDEB (0.12 mg, containing 0.06 µmol of Pd), CsF (0.14 g, 0.92 mmol), and water (1.5 mL) were combined in a clean test tube having a magnetic stirring bar. The mixture was heated at 100 °C until PBA and CsF were dissolved. Then 4-chloroacetophenone (0.095 g, 0.6 mmol) and TBAB (0.20 g, 0.6 mmol) were added to the system. The test tube was then sealed and placed in an oil bath preheated to 100 °C. At the completion of the reaction, the mixture was cooled to room temperature and diluted with ethyl acetate (1 mL) and water (4 mL). The insoluble Pd@PDEB was picked out. The organic layer was separated and aqueous layer was further washed with ethyl acetate (3×1 mL) to extract the organic product and any unreacted precursors.

For the Suzuki–Miyaura reactions of different heteroaryl halides (runs in Table 2), the following is a typical procedure (run SM29 in Table 2). 2-Bromopyridine (0.095 g, 0.6 mmol), 3-thienylboronic acid (0.102 g, 0.8 mmol), Pd@PDEB (0.06 mg, containing 0.03 µmol of Pd), K_3PO_4 (0.191 g, 0.9 mmol), and water/ethanol mixture (v/v=2:1, 1 mL) were combined in a clean test tube having a magnetic stirring bar. The test tube was sealed and placed in an oil bath set at 100 °C. At the completion of the reaction, the mixture was cooled to room temperature and washed with ethyl acetate/water 3 times to extract the organic product.

Stille Reactions Catalyzed with Pd@PDEB

A typical procedure (run St7 in Table 3) for Stille reactions of different aryl halides with various tin compounds is as follows. Pd@PDEB (0.06 mg, containing 0.03 µmol of Pd), 4-bromoacetophenone (0.12 g, 0.6 mmol), Bu_4Sn (0.25 mL, *ca.* 0.8 mmol), KF (52 mg, 0.9 mmol), and NMP (1 mL) were combined in a clean test tube having a magnetic stirring bar. The sealed test tube was placed in an oil bath set at 100 °C and stirred for a predetermined reaction time. The conversion of aryl halide and the yield of the product were monitored with ^{1}H NMR spectroscopy. At the end of the reaction, the insoluble salts/Pd@PDEB mixture and organic solution were separated by filtration. Water was used to wash off the inorganic salts and Pd@PDEB was recovered.

For the Stille reactions of different heteroaryl halides, the following is a typical procedure (run St12 in Table 3). 2-Bromopyridine (0.095 g, 0.6 mmol), Ph_4Sn (0.342 g, *ca.*

0.8 mmol), Pd@PDEB (1.2 mg, containing 0.6 µmol of Pd), K_3PO_4 (0.191 g, 0.9 mmol), and NMP/ethanol mixture (v/v= 1:2, 1 mL) were combined in a clean test tube. The test tube was sealed and placed in an oil bath set at 100 °C. At the completion of the reaction, the mixture was cooled to room temperature and washed with ethyl acetate/water 3 times to extract the organic product. The insoluble Pd@PDEB was recovered.

Allylic Arylation Reactions Catalyzed with Pd@PDEB

A typical procedure (run A5 in Table 4) for allylic arylation reactions with different allylic acetates is as follows. Pd@PDEB (0.06 mg, contain Pd 0.03 µmol), cinnamyl acetate (0.1 g, 0.6 mmol), PBA (0.1 g, 0.8 mmol), KF (52 mg, 0.9 mmol), DMF (0.5 mL), and water (0.5 mL) were combined in a clean test tube having a magnetic stirring bar. The sealed test tube was placed in an oil bath set at 100 °C and stirred for a predetermined reaction time. The conversion of acetate and the yield of the product were monitored with ^{1}H NMR spectroscopy. At the end of the reaction, the insoluble salts/Pd@PDEB mixture and organic solution were separated by filtration. Water was used to wash off the inorganic salts and Pd@PDEB was recovered.

Mizoroki–Heck Reactions Catalyzed with Pd@PDEB

A typical procedure (run MH2 in Table 5) for the Mizoroki–Heck reactions of aryl bromides with different alkenes carried out with Pd@PDEB is as follows. Pd@PDEB (5 mg, containing Pd 2.5 µmol), PhBr (0.39 g, 2.5 mmol), *n*-butyl acrylate (0.48 g, 3.8 mmol), K_2CO_3 (0.52 g, 3.8 mmol), and DMF (4 mL) were combined in a clean test tube having a magnetic stirring bar. The sealed test tube was placed in an oil bath set at 130 °C and stirred for 8 h. At the end of the reaction, the insoluble salts/Pd@PDEB mixture and organic solution were separated by filtration. Water was used to wash off the inorganic salts and Pd@PDEB was recovered.

For the Mizoroki–Heck reactions of different aryl chlorides with styrene, the following is a typical procedure (run MH10 in Table 4). 4-Chloroacetophenone (0.095 g, 0.6 mmol), styrene (0.187 g, 1.8 mmol), NaOH (72 mg, 1.8 mmol), Pd@PDEB (12 mg, containing 6 µmol of Pd) and DMF (1 mL) were combined in a clean test tube having a magnetic stirring bar. The sealed test tube was placed in an oil bath set at 150 °C and stirred for a predetermined reaction time. The conversion of the aryl chloride and the yield of the product were monitored with ^{1}H NMR spectroscopy. At the end of the reaction, the insoluble salts/Pd@PDEB mixture and organic solution were separated by filtration. Water was used to wash off the inorganic salts and Pd@PDEB was recovered.

Reusability Tests

The reusability test in the Suzuki–Miyaura reaction of PhI and PBA was performed with Pd@PDEB at the Pd loading of 1,000 mol ppm at 100 °C in water ([PhI]/[PBA]/[K_2CO_3]/ [Pd]=1:1.3:1.5:0.001, [PhI]=0.6 mol/L, 4 mL water). The same heterogeneous catalyst was used for 11 identical reactions with 10 times of recycling. In each reaction, the system

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was cooled down to room temperature at the completion of the reaction. The heterogeneous catalyst was then picked out from the reaction solution with tweezers and washed with acetone for 4 times before being dried. The dried catalyst was reused for the next cycle of reaction with the same amount of reactants and solvent. In each reaction, the final reaction solution was concentrated to 3 mL and the Pd concentration in the solution was determined with AA spectroscopy. Table S1 (Supporting Information) lists the detailed reaction results. The catalyst recovered after the 11th reaction above was characterized with XPS (Figure 1) and TEM (Figure S2, Supporting Information). The catalyst recovered after the 11th reaction was further used to catalyze the Suzuki–Miyaura reaction of PhBr with PBA at the Pd loading of 1 mol ppm relative to PhBr (i.e., the same condition as run SM3 with fresh Pd@PDEB).

The reusability test in Stille reaction of 4-bromoacetophenone with Bu$_4$Sn was undertaken at the Pd loading of 1,000 mol ppm (reaction conditions: [aryl bromide]/[Bu$_4$Sn]/[KF]/[Pd] = 1:1.2:1.5:0.001, [aryl bromide] = 0.6 mol/L, 1 mL NMP as solvent at 100°C). The same heterogeneous catalyst was used for 11 identical reactions with 10 times of recycling. A similar procedure as above was used, with detailed reaction results listed in Table S2 (Supporting Information). The recycled catalyst recovered from this reusability test was further used to catalyze another Stille reaction of 4-bromoacetophenone with Bu$_4$Sn under the same condition (i.e., Pd loading of 50 mol ppm; 20 h of reaction) as run St7 to examine its performance after reusability test. The conversion of 4-bromoacetophenone was 94% (TON = 19,000; TOF = 940 h^{-1}) with the recycled catalyst as opposed to >99% with the fresh catalyst.

Hot Filtration Tests

The test in the Suzuki–Miyaura reaction of PhI with PBA was performed as follows. Two parallel reactions were undertaken under identical conditions ([PhI]/[PBA]/[K$_2$CO$_3$]/[Pd] = 1:1.3:1.5:0.001, [PhI] = 0.6 mol/L, 4 mL water as solvent, 100°C). In one reaction, the liquid phase was hot filtered quickly with a Teflon syringe filter (0.2 μm pore size) after 20 min of reaction (PhI conversion: 71%). The resulting hot filtrate was immediately transferred to a new sealed test tube set at 100°C for continuous reaction. The reaction was monitored with ^{1}H NMR for 24 h. The other reaction as the control run was terminated at 40 min when the conversion of PhI reached >99%.

In the second test, two parallel Stille reactions of 4-bromoacetophenone with Me$_4$Sn were performed similarly under identical conditions ([ArBr]/[Me$_4$Sn]/[KF]/[Pd] = 1:1.2:1.5:0.001, [ArBr] = 0.6 mol/L, 1 mL of NMP as solvent at 100°C). The control run was terminated at 2 h when the ArBr conversion reached ≥99%, whereas the liquid phase of the other reaction was hot filtrated after 1.5 h of reaction (ArBr conversion: 68%) to remove the heterogeneous catalyst and was continuously monitored for total 24 h.

Synthesis of SBA-ArI for 3-Phase Tests

A similar procedure used by Jones et al.[81] was employed for the synthesis of heterogeneous mesoporous silica SBA-supported aryl iodide, SBA-ArI (see Scheme S1 in the Suppoorting Information). An aryl iodide-containing trimethoxysilane compound (**1** in Scheme S1, Supporting Information) was first synthesized by reacting 4-iodoacetophenone (1.35 g, 5.5 mmol) and 3-aminopropyltrimethoxylsilane (0.895 g, 5 mmol) in 20 mL dry MeOH under reflux at 75°C for 20 h. After being cooled to room temperature, MeOH was evaporated under reduced pressure and the product was extracted with CH$_2$Cl$_2$. The mixture was then concentrated and washed with cold hexane to afford **1**; yield: 1.87 g (92%). ^{1}H NMR (CDCl$_3$): δ = 0.78 (m, 2H, −CH_2Si), 1.84 [m, 4H, −(CH_2)$_2$CH$_2$Si], 2.07 [s, 3H, N=C(*Me*)], 3,34–3.52 [m, 9H, −Si(O*Me*)$_3$], 7.44–7.63, (m, 4H, Ar*H*).

Subsequently, **1** (1.63 g, 4 mmol) was added into a toluene (20 mL) suspension of dry mesoporous silica SBA-15 (1.0 g) and the mixture was stirred at 70°C for 24 h under N$_2$ protection. After cooling to room temperature, the mixture was filtered and the solid was washed with CH$_2$Cl$_2$ then hexane. After being dried under high vacuum at 80°C overnight, the SBA-supported aryl iodide (SBA-ArI) was obtained as white powder; yield: 1.258 g; aryl iodine content (based on TGA analysis): 22 wt%.

3-Phase Tests

3-Phase tests using immobilized aryl halide SBA-ArI were performed for both Stille reaction and Mizoroki–Heck reaction. All the liquid reagents and solvents involved were dried with 4 Å molecular sieves before use to avoid possible hydrolysis of SBA-ArI. For the 3-phase test of the Stille reaction, 4-bromoacetophenone (0.24 g, 1.2 mmol), Me$_4$Sn (0.26 g, 1.6 mmol), KF (0.104 g, 1.8 mmol), SBA-ArI (0.15 g, containing *ca.* 0.12 mmol ArI), Pd@PDEB (2.4 mg, 1.2 μmol), and NMP (1 mL) were combined in a clean test tube having a magnetic stirring bar. The test tube was sealed and placed in an oil bath set at 100°C. After 1.5 hour of reaction, Pd@PDEB was picked out with tweezers and the insoluble SBA-ArR was recovered by filtration and washed with a large amount of dry DMF/THF to remove all the soluble small molecules. Subsequently, SBA-ArR was hydrolyzed with 1 mol/L HCl solution overnight and extracted by ethyl acetate (2 mL×3). The solvent was then removed and the resulting compound **2** by hydrolysis (see Scheme S1 in the Supporting Information) was characterized by NMR.

For the 3-phase test of the Mizoroki–Heck reaction, 4-iodoacetophenone (0.295 g, 1.2 mmol), *n*-butyl acrylate (0.23 g, 1.8 mmol), Et$_3$N (0.18 g, 1.8 mmol), SBA-ArI (0.15 g, containing *ca.* 0.12 mmol ArI), Pd@PDEB (2.4 mg, 1.2 μmol), and DMF (1 mL) were combined in a clean test tube having a magnetic stirring bar. The test tube was sealed and placed in an oil bath set at 100°C. After 2 hour of reaction, Pd@PDEB was picked out with tweezers and the insoluble SBA-ArR was recovered by filtration and washed with large amount of dry DMF/THF to remove all the soluble small molecules. Subsequently, SBA-ArR was hydrolyzed and the product was characterized by NMR to determine the conversion of the heterogeneous aryl iodide. Table S3 (Supporting Information) summarizes the conversion data of both homogeneous aryl halide and the heterogeneous aryl iodide in the two 3-phase tests. In both tests, negligible conversion of the heterogeneous aryl iodide was observed.

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Acknowledgements

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Reusable, Highly Active Heterogeneous Palladium Catalyst by Convenient Self-Encapsulation Cross-Linking Polymerization for Multiple Carbon−Carbon Cross-Coupling Reactions at ppm to ppb Palladium Loadings

Adv. Synth. Catal. **2014**, *356*, 1 – 15

Zhongmin Dong, Zhibin Ye*

highest TON = 3.2 million
highest TOF = 10^5 h^{-1}
in coupling reactions

Pd/PPh$_3$
self-encapsulation cross-linking polymerization

heterogeneous self-encapsulated Pd catalyst

Stille
Suzuki–Miyaura
arylation
Mizoroki–Heck

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