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Polystyrene-anchored Palladium(II) Complex as an Efficient and Reusable Catalyst for Suzuki Cross-coupling Reaction in Water Medium

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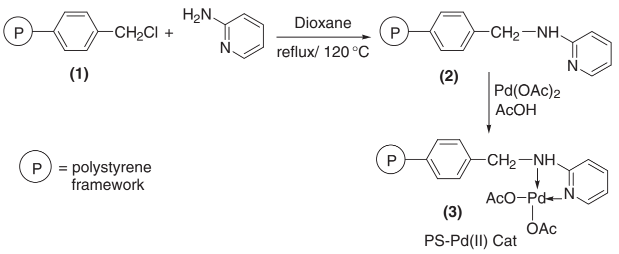
A new polystyrene-anchored palladium(II) catalyst has been prepared and characterized by conventional spectroscopic methods and elemental analyses. The catalyst was found to be highly effective for the Suzuki cross-coupling reactions of aryl halides with arylboronic acid in water medium under phosphine-free reaction conditions. The optimal reaction conditions of the coupling were determined. The present heterogeneous Pd(II) catalyst was reusable as well as air-stable to allow easy use.

Transition metal catalyzed coupling reactions have contributed greatly to the straightforward and facile construction of carbon–carbon bonds.[1–3] Among them, the Suzuki–Miyaura coupling reaction of aryl halides with arylboronic acids is one of the most powerful tools for the synthesis of biaryl derivatives.[4–7] Among the reasons for its appeal are the commercial availability of a large range of boronic acids, the ease with which these reagents can be handled and their high functional group compatibility. Significance progress in this area has been achieved with a variety of palladium catalyst.[8–13] Various homogeneous as well as heterogeneous Pd catalysts have been proposed for the Suzuki coupling, the latter recognized clearly as more advantageous with respect to cost, ease of handling, reusability, and selectivity and purity of obtained products.[14–19] Different materials have been employed as supports including mesoporous silicas,[20] activated carbons,[21] polymers,[22] zeolites,[23] and hydrotalcite.[24] Organic polymer supports can induce specific control over the catalytic and complexing ability of the ligand. Palladium coordinating with functionalized polymer ligands is increasingly attracting attention in recent time because of their fascinating molecular topologies and their application potential in developing new catalytic materials. Polystyrene is one of the most widely employed macromolecular supports. Very recently our group has reported the synthesis of Pd(II) compound anchored on functionalized polystyrene and its efficient use as a heterogeneous catalyst for various organic reactions.[25–29]

Although the Suzuki cross-coupling reactions catalyzed by the polymer-anchored palladium complexes in organic solvents is well-developed, its potential utility in water is largely limited. Recently, the use of water as an environmentally benign solvent has received considerable attention from the view point of green chemistry.[30–33] The organic solvents, which are usually used as the reaction media, often creat a great deal of safety, health, and environmental issues due to their flammability, toxicity, and volatility. The use of water in transition metal catalyzed reactions has become popular because water-base synthetic processes are inherently safer as well as being inexpensive. Furthermore, the use of water-insoluble metal complexes allows an easy separation and the products can be isolated easily by extraction.



Scheme 1. Synthesis of polymer-anchored Pd(II) complex.

Herein, we report an effective catalyst system composed of a palladium complex with polystyrene support. The aim of our studies is to evaluate the effect of this new heterogeneous palladium catalyst on the reactivity in the Suzuki cross-coupling reactions and to further determine the extent of their recovery and recycling in water.

The synthesis of the polymer-supported palladium(II) complex was accomplished according to Scheme 1. The polymer-anchored ligand **2** was prepared according to a literature method.[34] First, the chloromethylated polystyrene **1** (1 g) was reacted with 2-aminopyridine (3 mL) in dioxane (10 mL) under reflux condition for 48 h to afford polymer-anchored 2-aminopyridine ligand **2**. In the next step, polymer-anchored ligand (1 g) subsequently reacted with palladium acetate (0.5 g) in acetic acid (10 mL) at 80 °C for 10 h to generate the corresponding polystyrene-supported palladium(II) complex **3**.

The characterization of the catalyst was done on the basis of elemental analysis, IR spectroscopy, thermogravimetric analysis, and scanning electron microscopy. The complete incorporation of organic substructure in the material was confirmed by elemental analyses. The metal content in the catalyst determined by atomic absorption spectroscopy suggested 4.37 wt % metals loading in the immobilized palladium complex. The mode of attachment of 2-aminopyridine and metal onto the polymeric support was confirmed by IR spectral bands. The pure chloromethylated polystyrene beads show a sharp characteristic IR peak at 1266 cm^{-1}(ν: CH_2Cl group in polymer). The disappearance of the peak at 1266 cm^{-1} and the appearance of a strong band in the region 1650–1660 cm^{-1} due to *sec*-amine (–NH) stretching vibration confirmed the attachment of 2-aminopyridine with chloromethylpolystyrene. The polymer-anchored ligand exhibited medium to broad intensity bands in the region 3100–3500 cm^{-1} which may be assigned to the NH stretching as well as the –CH stretching mode of the pyridine. Pyridyl ring breathing vibrations were observed as strong bands in the region 1400–1600 cm^{-1}.[35] Slight shifting of these bands toward lower frequency in the palladium complex suggests possible coordination through the nitrogen of the pyridine ring. More conclusive information on the coordination of the ligand

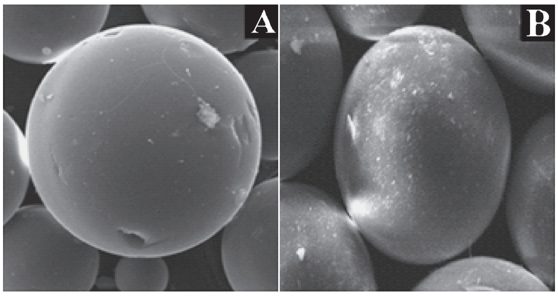
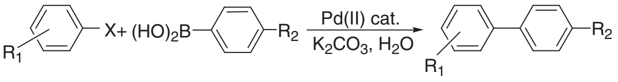


Figure 1. SEM images of polymer-anchored ligand (A) and polymer-anchored Pd(II) complex (B).



Scheme 2. Suzuki cross-coupling reaction.

Table 1. Effect of temperature, base, and solvent on the Suzuki cross-coupling reaction[a]

Entry	Temp/°C	Base	Solvent	Yield[b]/%
1	25	K_2CO_3	H_2O	11
2	50	K_2CO_3	H_2O	57
3	**75**	$\mathbf{K_2CO_3}$	$\mathbf{H_2O}$	**98**
4	75	Na_2CO_3	H_2O	76
5	75	Na_2HPO_4	H_2O	67
6	75	KOH	H_2O	45
7	75	NaO*t*-Bu	H_2O	32
8	75	Et_3N	H_2O	41
9	75	K_2CO_3	DMF	98
10	75	K_2CO_3	MeCN	56
11	75	K_2CO_3	Toluene	23
12	75	—	H_2O	0

[a]Reaction conditions: Bromobenzene (1.0 mmol), phenylboronic acid (1.2 mmol), base (2.0 mmol), and Cat. (1.0 mol % of Pd). [b]Yield was determined by GC analysis.

to the central metal ion comes from the new bands due to ν(Pd–N) = 565 cm^{-1} (pyridine nitrogen),[36] ν(Pd–N) = 455 cm^{-1} (secondary nitrogen),[37] and ν(Pd–Cl) = 330 cm^{-1}.[38]

Scanning electron micrographs for a single bead of polymer-anchored ligand and Pd(II) complex were recorded to understand the morphological changes occurring at the polymer surface. As shown in Figure 1, more roughness appeared on the surface of the ligand after introduction of metal. From EDX analysis (Figure 2 in Supporting Information (SI)[41]) it is seen that only C and Cl was present in ligand while polymer-anchored metal complex contained metal along with C and Cl suggested the formation of metal complex with anchored ligand. The complex is insoluble in all common organic solvents and thermally stable up to 360 °C above which there is a continuous weight loss which extends to 600 °C (Figure 3, SI[41]).

In order to evaluate the catalytic activity of the present polystyrene-supported palladium(II) complex, the Suzuki cross-coupling reaction of aryl halides with arylboronic acids was studied (Scheme 2). The optimization of the reaction conditions was carried out with bromobenzene and phenylboronic acid as model substrates and influence of various parameters such as metal precursors, solvent, base, temperature, and time were examined (Table 1). Various palladium precursors such as $Pd(OAc)_2$, $Pd(PhCN)_2Cl_2$, and $PdCl_2$ were screened. However, $Pd(OAc)_2$ was found to be most effective providing 98% yield of desired product. Solvent effect on the activity of the present catalyst was surveyed with different polar and nonpolar solvent. The reaction was more favorable in polar solvents like water and DMF (Table 1, Entries 3 and 9) as compared to nonpolar solvent such as toluene (Table 1, Entry 11). The complex is very stable in oxygen and moisture and no change of its composition as well as activity was observed when it was exposed to air and water in the Suzuki reaction. From a greener point of view water was used as solvent for further studies. This coupling reaction was found to be highly sensitive to the reaction temperature. At lower temperatures (25–50 °C) only low to moderate yield was obtained (Table 1, Entries 1 and 2). A reaction temperature of 75 °C was found to be optimal for the model reaction (Table 1, Entry 3). The impact of various bases on the efficiency of this process was studied because the nature of the base is known to be crucial in this type of coupling reaction. A control experiment indicated that the coupling reaction did not occur in the absence of base (Table 1, Entry 12). Various inorganic and organic bases such as Na_2CO_3, K_2CO_3, Na_2HPO_4, KOH, Et_3N, and NaO*t*-Bu were examined. The best performance was observed with K_2CO_3 (Table 1, Entry 3). Other inorganic bases like Na_2CO_3, Na_2HPO_4, and KOH gave reasonable conversions leading to 45% to 76% yields (Table 1, Entries 4–6). The yield was noticeably low when organic bases such as Et_3N and NaO*t*-Bu were employed (Table 1, Entries 7 and 8). The quantity of K_2CO_3 was also found to be important. The base–substrate molar ratio of 2:1 was found to be ideal for present catalytic system.

Under the optimized reaction conditions so far developed for bromobenzene and phenylboronic acid, we extended this procedure to a variety of aryl halides and arylboronic acids as shown in Table 2. Both aryl iodides (Table 2, Entries 1–6) and aryl bromides (Table 2, Entries 7–12 and 17) gave good to excellent yields of coupled product. Notably, the less reactive and less expensive phenyl chloride also showed moderate reactivity in the presence of catalyst (Table 2, Entries 13 and 14). No reaction occurred in the absence of catalyst. Various electron-donating and electron-withdrawing groups such as Me, OMe, NO_2, COMe, and CHO on aryl halide were well tolerated to give the desired biaryl in good yields. As expected, the reaction rates of electron-deficient aryl halides were faster than those of electron-rich aryl halides. Hence, the cross-coupling reactions of electron-rich aryl halides required a slightly longer reaction time to achieve highest yield. 2-Substituted aryl halides gave the desired products in lower yields than 4-substituted aryl halides probably due to steric hindrance (Table 2, Entry 8). The catalytic system also worked efficiently for the coupling of heteroaryl halides furnishing desired product in good yields (Table 2, Entry 17). The reaction of 4-methyl or 4-acetyl boronic acid with bromobenzene also provided the corresponding biaryls in high yields (Table 1, Entries 15 and 16).

Many efficient heterogeneous catalysts have been reported for the Suzuki cross-coupling reaction in water medium.[39,40] Comparison of the catalyst with previously reported systems reveals that the present system gives better yields than other catalysts.

Table 2. Suzuki cross-coupling reaction of haloarenes in water[a]

Entry	Haloarenes	Boronic acids	Time /h	Yields[b] /%
1	$4\text{-NO}_2\text{–C}_6\text{H}_4\text{–I}$	$\text{C}_6\text{H}_5\text{–B(OH)}_2$	6	99 (95)
2	$4\text{-COCH}_3\text{–C}_6\text{H}_4\text{–I}$	$\text{C}_6\text{H}_5\text{–B(OH)}_2$	6	99 (96)
3	$4\text{-OCH}_3\text{–C}_6\text{H}_4\text{–I}$	$\text{C}_6\text{H}_5\text{–B(OH)}_2$	8	97 (90)
4	$4\text{-CH}_3\text{–C}_6\text{H}_4\text{–I}$	$\text{C}_6\text{H}_5\text{–B(OH)}_2$	8	95 (89)
5	$4\text{-CHO–C}_6\text{H}_4\text{–I}$	$\text{C}_6\text{H}_5\text{–B(OH)}_2$	8	92 (85)
6	$\text{C}_6\text{H}_5\text{–I}$	$\text{C}_6\text{H}_5\text{–B(OH)}_2$	6	98 (95)
7	$4\text{-NO}_2\text{–C}_6\text{H}_4\text{–Br}$	$\text{C}_6\text{H}_5\text{–B(OH)}_2$	6	99
8	$2\text{-NO}_2\text{–C}_6\text{H}_4\text{–Br}$	$\text{C}_6\text{H}_5\text{–B(OH)}_2$	12	87 (81)
9	$4\text{-COCH}_3\text{–C}_6\text{H}_4\text{–Br}$	$\text{C}_6\text{H}_5\text{–B(OH)}_2$	6	97
10	$4\text{-OCH}_3\text{–C}_6\text{H}_4\text{–Br}$	$\text{C}_6\text{H}_5\text{–B(OH)}_2$	10	94
11	$4\text{-CH}_3\text{–C}_6\text{H}_4\text{–Br}$	$\text{C}_6\text{H}_5\text{–B(OH)}_2$	10	93
12	$\text{C}_6\text{H}_5\text{–Br}$	$\text{C}_6\text{H}_5\text{–B(OH)}_2$	8	98 (96)
13	$4\text{-COCH}_3\text{–C}_6\text{H}_4\text{–Cl}$	$\text{C}_6\text{H}_5\text{–B(OH)}_2$	24	75
14	$\text{C}_6\text{H}_5\text{–Cl}$	$\text{C}_6\text{H}_5\text{–B(OH)}_2$	24	56
15	$\text{C}_6\text{H}_5\text{–Br}$	$4\text{-COCH}_3\text{–C}_6\text{H}_4\text{–B(OH)}_2$	8	98 (94)
16	$\text{C}_6\text{H}_5\text{–Br}$	$4\text{-CH}_3\text{–C}_6\text{H}_4\text{–B(OH)}_2$	8	95 (92)
17	2-Bromopyridine	$\text{C}_6\text{H}_5\text{–B(OH)}_2$	12	92 (83)

[a] Reaction conditions: haloarenes (1 mmol), arylboronic acid (1.2 mmol), K_2CO_3 (2 mmol), Cat. (1 mol % of Pd), water (6.0 mL), and 75 °C. [b] Yield of product was determined by GC and GC-MS analysis using dodecane as internal standard. Isolated yields are given in parentheses. Products were identified by comparison of their IR, GC-MS, and ^{1}H NMR spectral data with those reported in literature.

A long catalyst lifetime and the ability to easily recycle the catalyst are highly desirable for industrial applications. The recycling efficiency of the present catalyst was investigated in the coupling reaction of 4-bromoanisole with phenylboronic acid. After each run the catalyst was recovered by simple filtration, washed, dried under vacuum, and then reused in the following runs. The catalytic activity of the present catalyst remained almost unchanged over five cycles (Figure 4, SI[41]). Furthermore, after separation of the catalyst, analysis of the filtrate by atomic absorption indicated that no palladium metal had leached out from the catalyst surface. The filtered solution did not exhibit any further reactivity. IR spectrum of the reused catalyst confirmed that no catalyst deterioration occurred during reaction. These studies clearly demonstrated that palladium was intact to a considerable extent with the heterogeneous support and there is no considerable amount of leaching during reactions.

In summary, we have developed a new Pd-catalyzed cross-coupling reaction using polystyrene-anchored palladium(II) complex which proceeds in water medium under aerobic conditions. The present system is highly air- and moisture-stable and the catalyst can be synthesized readily from inexpensive and commercially available starting materials. A broad range of functional groups are tolerated in this cross-coupling and high yield of coupled product were obtained. Utilization of this catalyst in various other organic transformations is in progress.

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