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Palladium tetrazole–supported complex as an efficient catalyst for the Heck reaction

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Abstract A tetrazole-supported polymeric ligand has been synthesized. The palladium complex derived from the polymeric material has been evaluated as a catalyst for the Heck reaction of aryl iodides and bromides with styrene to provide the corresponding products in high yields. The reaction proceeded smoothly in the presence of 1 mol% with respect to Pd of catalyst in DMF at 125 or 140 °C within 1–3 h. Recycling studies showed that the catalyst can be readily recovered and reused for several times without significant loss of catalytic activity.

Introduction

Palladium-catalyzed cross-coupling reactions have been recognized as powerful synthetic tools and a major area of interest in multiple organic transformations for academic and industrial processes [1]. The cross-coupling reaction of aryl halides with styrene, i.e., the Heck reaction, is among the most commonly used methods for C–C bond formation and widely applied to organic and fine chemical synthesis [2, 3]. In the past few years, various ligands such as phosphorus ligands [4], N-heterocyclic carbenes [5], P,O-based ligands [6], thiosemicarbazones [7] and bis(thiourea) ligands [8] have been used to prepare catalytic palladium species. However, homogeneous processes suffer from the problems of separation from the reaction mixture, reuse of expensive palladium catalysts and palladium contamination in the products. In addition, most of the available ligands for Heck reactions are undesirable for industrial chemistry because of their toxicity, high price and air-sensitivity.

In this regard, stable, reusable and active catalysts anchored to solid supports are of current interest. Many organic and inorganic supports such as activated carbon, zeolites, metal oxides, clays, organic polymers, mesoporous silica and capsules have been used in the preparation of novel catalytic systems [9–17]. Among these, organic polymers offer different ways of metal attachment to the polymer matrix via covalent or non-covalent bonding, through hydrogen bonding, as well as through ionic, hydrophobic or fluorous interactions [18]. Correspondingly, palladium complexes anchored on polymers with Schiff bases [19], N-heterocyclic carbene groups [20, 21] and dendrimers [22] have been described recently.

In recent years, N-donor ligands, such as imidazole or tetrazole derivatives, have attracted the interest of synthetic organic chemists. As examples, Welton and co-workers have reported on the Suzuki coupling reaction catalyzed by $(CH_3CN)_2PdCl_2$-imidazole and its derivatives [23]. Gupta and co-workers [24] have reported on the homogeneous Heck reaction catalyzed by a tetrazole palladium ligand. In continuation of our work on the development of heterogeneous palladium catalysts for C–C bond formation reactions, we have investigated whether a tetrazole functionalized polymer-supported palladium complex could catalyze the coupling reaction efficiently. We were able to use this catalyst for room temperature Suzuki cross-coupling reactions in our previous study [25]. In this paper, we report on the use of this catalyst for the Heck reaction (Scheme 1). As we expected, the catalyst exhibited excellent catalytic activity and stability in the Heck reaction. Furthermore, the catalyst can be readily recovered by simple filtration and reused several times with only slight decrease in its activity.

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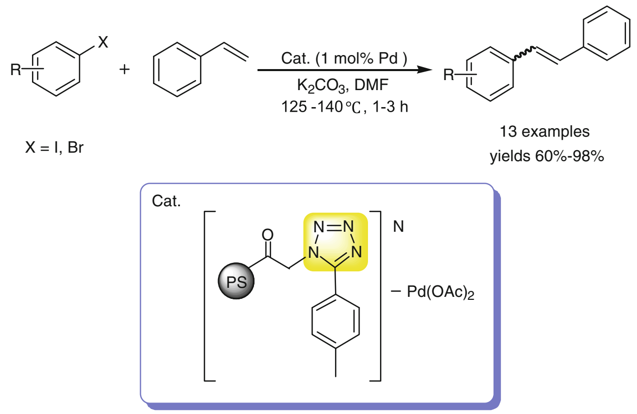


Scheme 1 Palladium tetrazole–supported complex for the Heck reaction

Experimental

All of the reagents and solvents were commercial products. Chloroacetylated polystyrene (7% divinylbenzene, 1.8 mmol/g of Cl, grain size range: 240–280 μm, surface area: 32 m^2 g^{-1}, pore diameter: 80–100 Å, total pore volume: 0.11 cm^3 g^{-1}) was obtained from Nanjing Microspheres Co., Ltd. (Nanjing, China). IR spectra were recorded as KBr disks with a Shimadzu IRPrestige-21 FT-IR spectrometer. Elemental analyses were performed on a Vario EL III recorder. Scanning electron microscopy (SEM) analyses were performed on a JEOL JSM-6380LV instrument. ^{1}H NMR spectra were measured with a Bruker Avance III 500 analyzer. GC–MS analyses were performed on a Saturn 2000 GC/MS instrument. Palladium content of the catalyst was measured by inductively coupled plasma (ICP) on a Perkin-Elmer 5300DV analyzer.

Preparation of the palladium tetrazole–supported complex

The palladium tetrazole–supported complex was prepared in three steps from chloroacetylated polystyrene resin as reported in the literature [25] (Scheme 2).

Preparation of 5-(p-tolylene)-1H-tetrazole

A mixture of 4-tolunitrile (4.68 g, 0.04 mol), sodium azide (2.86 g, 0.044 mol) and ammonium chloride (2.35 g, 0.044 mol) in DMF (20 ml) was stirred and heated at 100 °C for 18 h. After being allowed to cool to room temperature, the mixture was poured into ice water and acidified with aq HCl (6 N) to pH 2–3. The precipitate was filtered off, washed several times with H_2O and further purified by crystallization to afford the desired product.

Preparation of the polymer-supported tetrazole ligand

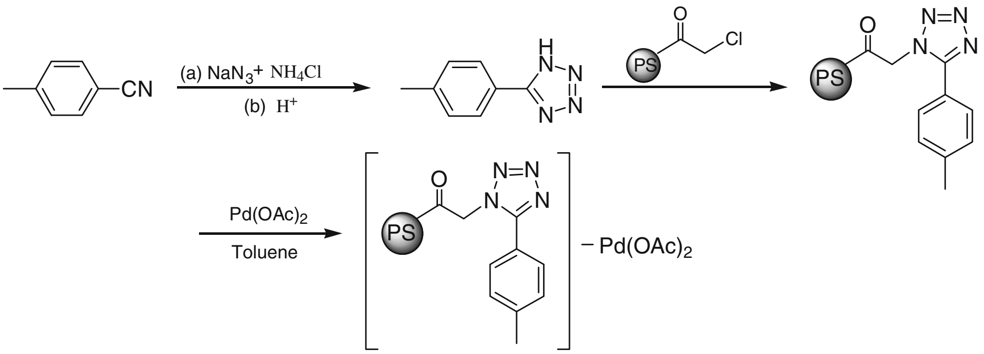
Pre-washed chloroacetylated styrene–divinylbenzene copolymer beads (0.5 g, 0.9 mmol of Cl) were swollen in 10 ml of DMF for about 12 h. 5-(*p*-tolylene)-1H-tetrazole (0.16 g, 1.0 mmol) was added and the mixture was stirred at 50 °C for 24 h in the presence of NaH (0.029 g, 1.2 mmol). The color of the beads changed from brown to yellow. The beads were then filtered off, washed with distilled water and methanol, respectively, and dried at 80 °C under vacuum overnight. The tetrazole unit content of the beads was 1.46 mmol g^{-1} according to the results of elemental analyses.

Preparation of the catalyst

The functional beads (0.2 g) were swollen in toluene (5 ml) for about 2 h. The catalyst was then prepared in toluene using 1.2 equiv. of $Pd(OAc)_2$ per tetrazole unit. The mixture was stirred at 30 °C for about 24 h, and the resulting beads were filtered off, washed with methanol and dried at 100 °C under vacuum overnight. The content of palladium was 0.76 mmol/g as determined by ICP.

General procedure for the Heck reaction

In a typical reaction, a mixture of aryl halide (1.0 mmol), styrene (1.5 mmol), K_2CO_3 (2.0 mmol), DMF (6 ml) and catalyst (1 mol% with respect to Pd) was stirred at



Scheme 2 Preparation of palladium tetrazole–supported complex

125–140 °C for a certain time as the reaction was monitored by GC. After the completion of the reaction, the mixture was cooled to room temperature. The solid catalyst was separated by filtration, washed with water to remove base and salt and finally with dichloromethane to remove adsorbed organic substrate and dried under vacuum for the next cycle. The filtrate was diluted with water followed by extraction with dichloromethane. The combined organic phase was washed with brine and dried over anhydrous Na_2SO_4. The solvent was removed and the crude products were purified by flash chromatography with *n*-hexane/EtOAc as eluent to afford the corresponding products. All the products were known compounds and were identified by comparison with their physical and spectroscopic data with those of authentic samples.

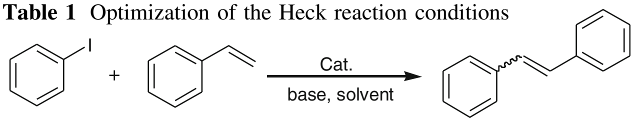
Results and discussion

Optimization of the reaction conditions

Initially, the Heck reaction of iodobenzene and styrene was chosen as a model reaction. Various parameters including bases, solvents and loadings of the catalyst were screened to optimize the reaction conditions (Table 1). Base plays a significant role in both the rate and product distribution of the Heck reaction. Hence, K_2CO_3, NaOAc, NaOH, K_3PO_4, NEt_3 and diisopropylethylamine (DIPEA) were all investigated as bases. K_2CO_3 was found to be the most effective base, as shown in Table 1, entries 1–6. Slightly lower yields and selectivities were obtained when K_3PO_4 and NaOH were used as base (Table 1, entries 2, 3). When the organic bases NEt_3 and DIPEA were used, moderate yields were obtained but longer reaction times were required (Table 1, entries 4, 5). However, NaOAc gave lower yields than other bases, even when 5 h reaction times were used (Table 1, entry 6).

Next, the effects of different solvents were studied. According to publications from Hartwig and co-workers [26], Zapf and Beller [27], and Böhm and Herrmann [28], polar, aprotic solvents tend to give the best results for Heck coupling. Among the evaluated polar and non-polar solvents, DMF was the most productive (Table 1, entry 1). Lower catalyst activities were found in other solvents such as DMAc, DMSO, CH_3CN and toluene (Table 1, entries 7–10). We further evaluated the effects of temperature on the reaction. As illustrated in Table 1, entries 11, 12, reducing the amount of the catalyst led to a decrease in the yields. Thus, we selected K_2CO_3 as the base, DMF as solvent and 1 mol% with respect to Pd of catalyst as the best conditions for the Heck reaction.

Table 1 Optimization of the Heck reaction conditions



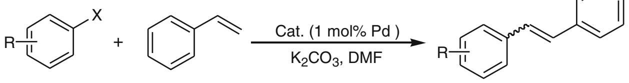
Entry	Solvent	Base	T (°C)	Time (h)	All yield (%)[a]	E/Z[b]
1	DMF	K_2CO_3	125	1	98	87:13
2	DMF	NaOH	125	1	96	86:14
3	DMF	K_3PO_4	125	1	97	84:16
4	DMF	DIPEA	125	3	72	82:18
5	DMF	NEt_3	125	3	81	71:29
6	DMF	NaOAc	125	5	46	88:12
7	DMAc	K_2CO_3	125	3	73	83:17
8	DMSO	K_2CO_3	125	3	90	78:22
9	CH_3CN	K_2CO_3	81	5	35	81:19
10	Toluene	K_2CO_3	110	5	Trace	–
11	DMF	K_2CO_3	100	5	92	80:20
12	DMF	K_2CO_3	80	5	73	84:16

Reaction conditions: iodobenzene (1.0 mmol), styrene (1.5 mmol), K_2CO_3 (2.0 mmol); catalyst (1 mol%) in 6 ml solvent

[a] Isolated yield

[b] The ratio of E/Z was determined by GC of the crude reaction mixture

Table 2 Heck reaction of aryl halides and styrene



Entry	X	R	T (°C)	Time (h)	All yield (%)[a]	E/Z[b]
1	I	H	125	1	98	87:13
2	I	*p*-NO_2	125	1	97	85:15
3	I	*p*-Me	125	1	98	83:17
4	I	*m*-Me	125	1	96	86:14
5	I	*o*-Me	125	1	95	85:15
6	Br	H	140	3	90	90:10
7	Br	*p*-NO_2	140	3	87	93:7
8	Br	*p*-CHO	140	3	89	77:23
9	Br	*p*-COMe	140	3	95	92:8
10	Br	*p*-Cl	140	3	93	90:10
11	Br	*p*-Me	140	5	60	78:22
12	Br	*p*-OMe	140	5	67	86:14
13	Br	*o*-Me	140	5	70	90:10
14	Cl	H	140	8	14	84:16
15	Cl	*p*-NO_2	140	8	51	80:20
16	Cl	*p*-CH_3	140	8	3	–

Reaction conditions: aryl halides (1.0 mmol), styrene (1.5 mmol), K_2CO_3 (2.0 mmol); catalyst (1 mol%) in 6 ml DMF

[a] Isolated yield

[b] The ratio of E/Z was determined by GC of the crude reaction mixture

Heck reaction of aryl halides with styrene catalyzed by the supported catalyst

Encouraged by the efficiency of the reaction protocol described earlier, we investigated the substrate scope. As can be seen in Table 2, a range of aryl iodides and bromides were found to give the desired products in high yields. Aryl iodides with electron-withdrawing or electron-donating groups underwent efficient couplings with styrene for reaction times of 1 h at 125 °C (Table 2, entries 1–5). As for aryl bromides, satisfactory yields were obtained when the reaction was carried out for 3 h at 140 °C. Aryl bromides with electron-withdrawing groups in the *para* positions reacted smoothly, while aryl bromides with electron-donating groups in the *para* and *ortho* positions were less reactive (Table 2, entries 7–13). We also examined whether aryl chlorides were active for the Heck reaction. However, unsatisfactory yields were obtained even after prolonged reaction times at 140 °C (Table 2, entries 14–16).

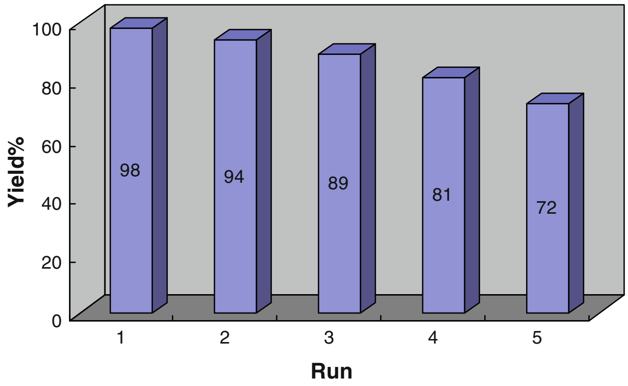


Fig. 1 Recycling experiment

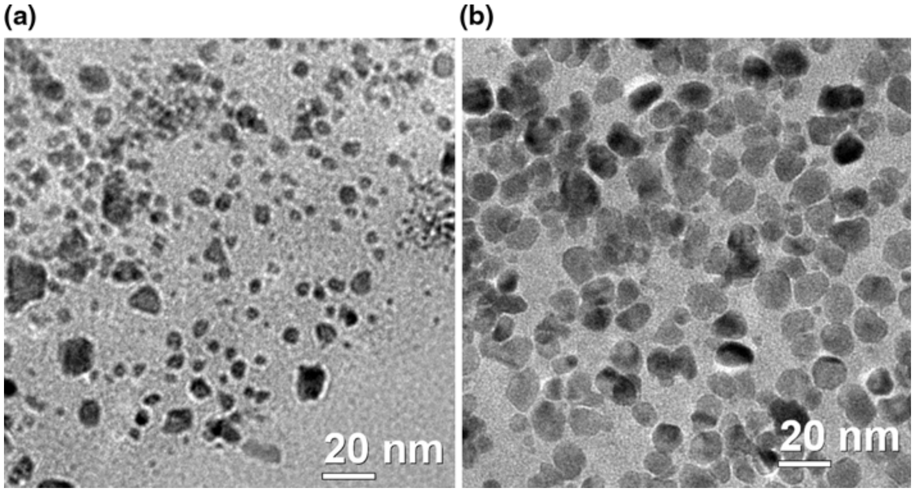
Reusability of the catalyst

The reusability of the catalyst is a very important theme, especially for commercial applications. Therefore, the recovery and reusability of the catalyst were investigated using the reaction of iodobenzene with styrene as a model system. After the reaction was completed, the mixture was cooled to room temperature. The solid catalyst could be separated readily from the reaction mixture by filtration. The recycled catalyst was then used in the model reaction under the same conditions, giving 94, 89, 81 and 72% yields in successive experiments (Fig. 1). ICP analysis showed that leaching of palladium from the polymer was 3–5% after five cycles. TEM analyses of the recovered catalyst were also performed. The TEM analysis of the structure of the catalyst was used to gain information on the Pd of the catalyst after the reaction, in terms of the nanoparticle size and shape. We found that the size of the palladium nanoparticles inside the beads had increased from 2 to 5 nm for the first run to 15–20 nm for the fifth run (Fig. 2). Therefore, the slight decrease in catalytic activity in subsequent runs may be due to passivation of the nanocluster surface [29].

Hot filtration experiments

Although extensive studies have been carried out to elucidate the true catalytic species in the heterogeneous Pd-catalyzed Heck reaction, it is still unclear in many cases whether the reaction takes place on the surfaces of the solid Pd catalyst [30] or whether the active catalysts are Pd species leached out from the support, which simply acts as a reservoir of Pd [31]. Thus, a hot filtration test was carried out, using the reaction of bromobenzene with styrene as a model reaction. After 20 min of reaction time, the solid catalyst was separated by hot filtration and the hot filtrate was further reacted with fresh K_2CO_3 at 140 °C for an

Fig. 2 TEM images of **a** recovered catalyst after first run for the Heck reaction; **b** recovered catalyst after fifth run for the Heck reaction



additional 1 h. After the reaction, samples of the reaction mixture were analyzed by GC. It was found that the reaction continues after removing the catalyst and the yield of product was from 56 to 78%. This might be explained by a "release and recapture" mechanism, as described in previous literature [32].

Conclusion

In conclusion, we have successfully applied a palladium tetrazole–supported complex in the Heck reaction. The catalyst exhibits high activity, affording a diverse range of products in good to excellent yields. Furthermore, the catalyst is stable to the reaction conditions and can be recycled, albeit with a slow progressive decrease in activity. The easy separation and availability make such supported palladium catalysts an interesting alternative to homogeneous catalysts.

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