

Polymethyl methacrylate micro-spheres supported palladium: A new catalyst for Heck and Suzuki reactions

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Received 7 August 2007; received in revised form 12 October 2007; accepted 17 October 2007

Available online 23 October 2007

Abstract

Polymethyl methacrylate (PMMA) micro-spheres, a kind of commercially available polymeric material was treated with PdCl₂ and formaldehyde giving a reagent with a palladium loading of 0.79 (wt.%). The Pd-PMMA catalyzed the highly efficient Heck and Suzuki reactions. The reactions can be performed under ligand-free conditions in an air atmosphere. The palladium catalyst is easily separated and can be reusable with negligible leaching of palladium.

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Keywords: PMMA; Palladium catalyst; Heck reaction; Suzuki reaction

1. Introduction

Heck and Suzuki reactions are powerful methods for C–C bond formation [1–5]. They can be used in the synthesis of a variety of compounds, including heterocycles, several natural products and pharmaceuticals [1–5]. Traditionally, palladium-catalyzed Heck and Suzuki reactions often require relatively large amounts of catalysts, which have to be removed from the reaction product. In recent years, various homogeneous palladium catalysts have been developed for the efficient Heck and Suzuki cross-coupling reactions. However, homogeneous palladium has several shortcomings such as limited reusability, which impacts cost and palladium contamination in the product [6]. Therefore, removal of residual palladium is a challenging task for chemists and a topic of enormous importance in the pharmaceutical industry that involves palladium-catalyzed process [7]. Many methods have been introduced to address the palladium contamination issue, which include palladium-containing perovskites [8], palladium supported on various materials such as carbon [9], zeolites [10], silica [11,12], sepiolites [13,14],

polyionic gels [15] and hydrotalcite [16]. Although the palladium level in the product was lower in these systems when compared to homogeneous, the systems exhibit generally lower activity and the activity of the catalysts decreases gradually in the recycled systems because the palladium leaches away from their supports [17].

Polymer-supported organotransition metal catalysts offer several significant advantages in synthetic and industrial chemistry; among these, the ease of separation of catalyst from the desired reaction products and the ease of recover and reuse of the catalyst are most important. Various polymer-supported palladium catalysts for the Heck and Suzuki cross-coupling reaction have been reported [6,18–36]. However, most of them are related to the Pd(II) complexes in combination with triarylphosphines, sterically demanding trialkylphosphines, statically demanding *N*-heterocyclic carbenes or ligands, and in many cases residual palladium in the product was still under the level that satisfies specifications required by regulators. To our knowledge, the use of polymer-supported Pd(0) catalysts for efficient C–C couplings has not been exploited well until recently [17,37,38]. When compared with the most frequently used expensive palladium catalysts (e.g., Pd(PPh₃)₄, (PPh₃)₂PdCl₂, Pd(OAc)₂/PPh₃, etc.), polymer-supported Pd(0) catalysts have an economic advantage and hence remain attractive in large or industrial scale applications.

Polymethyl methacrylate (PMMA) is a kind of commercially available polymeric material. PMMA micro-spheres with

Abbreviations: SEM, scanning electron microscope; ICP, inductively coupled plasma; TLC, thin layer chromatography; PMMA, polymethyl methacrylate; DMF, dimethyl formamide; NEt₃, triethylamine; EtOAc, ethyl acetate.

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narrow size distribution can be obtained by dispersion polymerization [39,40]. There are functional groups on the surface of PMMA, which can adsorb noble metal hydronium. Homogeneous size of micrometer is favorable to recycle of the catalyzer [39,40]. As a part of our studies to explore palladium-catalyzed cross-coupling reactions, we decided to use the palladium adsorbed on micrometer PMMA micro-spheres as a catalyst in Heck and Suzuki cross-coupling reactions.

2. Experimental

2.1. General remarks

^1H NMR spectra were characterized with a Bruker Advance RX300 spectrometer. Mass and GC analyse were performed on a Saturn 2000GC/MS instrument. Field-emission scanning electron microscope (SEM) photograph were recorded with a LEO1530VP instrument. Inductively coupled plasma (ICP) spectra were measured on an Ultima2C apparatus. Micrometer PMMA micro-spheres was commercially obtained from Zongyan Chemical Co. of Suzhou. Commercially available reagents were used without further purification. Pd contents were measured by ICP analysis method after the reaction mixture was filtered, then diluted with water, extracted with ether, dried, and concentrated to dryness.

2.2. Preparation of Pd-PMMA

PdCl_2 (0.27 g, 1.5 mmol) was dissolved in 20% hydrochloric acid (40 ml). Then PMMA micro-spheres (15 g) were added. After vigorous stirring at 90°C for 2 h, 35% formaldehyde (5 ml) was added. Then, the mixture was stirring at 90°C for 1 h. The mixture was cooled to 15°C and the pH was adjusted to 6 by using 30% sodium hydroxide solution. After stirring at 15°C for 30 min, the mixture was allowed to stand for *ca.* 2 h without stirring. Then the deposit was separated and washed with water ($20\text{ ml} \times 3$) and toluene ($20\text{ ml} \times 2$). The isolated solids was dried at 120°C for 24 h in vacuum to give a gray solid (15.13 g). The solid contained 0.79% Pd by weight based on the ICP analysis.

2.3. Typical procedure for Heck reaction with Pd-PMMA

Styrene (6 mmol) was added to a mixture of Pd-PMMA (1.29 g, 1% Pd) and DMF (5 ml) in a glass flask under vigorous stirring. After 5 min, iodobenzene (5 mmol) and NEt_3 (7.5 mmol) were introduced into the flask. After stirring at 100°C for 2 h, the mixture was cooled and the catalyst was filtered. The filtrate was diluted with water (5 ml) and extracted with ether ($10\text{ ml} \times 2$). The combined organic extracts were dried over Na_2SO_4 and evaporated under vacuum to give a crude product (examined for Pd). The crude product was subjected to column chromatography on silica gel with hexane and EtOAc (9:1, v/v) as eluent to give *trans*-stilbene product (0.87 g, 95%). The product was characterized by GC/MS and ^1H NMR.

2.4. Typical procedure for Suzuki reaction with Pd-PMMA

Bromobenzene (5 mmol) was added to a mixture of Pd-PMMA (1 g, 1% Pd) and DMF (5 ml) in a glass flask under vigorous stirring. After 10 min, phenylboronic acid (7.5 mmol) and a solution of K_3PO_4 (2.66 g, 10 mmol) in water (5 ml) were introduced into the flask. After stirring at 95°C for 2.5 h, the mixture was cooled and the catalyst was filtered. The filtrate was diluted with an aqueous KOH (10 ml, 10%) and extracted with ether ($10\text{ ml} \times 2$). The combined organic extracts were dried over Na_2SO_4 and evaporated under vacuum to give a crude product (examined for Pd). The crude product was subjected to column chromatography on silica gel with petroleum ether and EtOAc (25:1, v/v) as eluent to give biphenyl product (0.67 g, 87%). The product was characterized by GC/MS and ^1H NMR.

2.5. Typical procedure for catalyst recycling

After the reaction as described above, the mixture was allowed to stand for *ca.* 30 min without stirring at room temperature, and then filtered. The solids were washed with water ($5\text{ ml} \times 3$) and toluene ($5\text{ ml} \times 3$). The catalyst isolated was dried at 120°C for 24 h in vacuum. The resulting catalyst was ready for further runs in Heck reaction and Suzuki reactions.

3. Results and discussion

Palladium can be easily loaded onto PMMA by stirring a solution of PdCl_2 and PMMA micro-spheres and then reduction with formaldehyde at elevated temperature. After filtration and washing, the catalyst was dried and the content of palladium confirmed by weight and analysis. The SEM photograph of the catalyst was shown in Fig. 1. From the figure, we can clearly see that palladium was absorbed onto the PMMA micro-spheres.

We first examined the palladium-catalyzed Heck coupling of aryl halides with various Heck acceptors, such as styrene, alkyl acrylate and propenyl cyanide. In a typical experiment, a base (1.5 equiv.) was added and the mixture was heated at 100°C

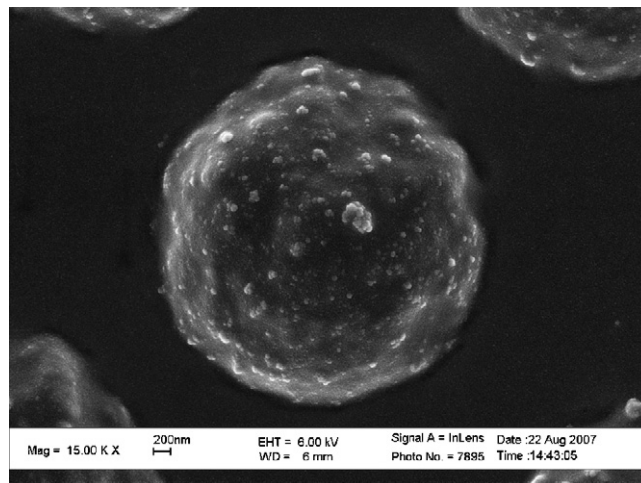


Fig. 1. The SEM photograph of Pd-PMMA catalyst.



Scheme 1. Pd-PMMA catalyzed Heck reactions.

Table 1
Pd-PMMA catalyzed Heck reactions^a

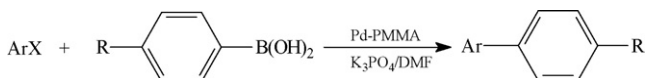
Entry	ArX	R	Time (h)	Yield (%) ^b
1	PhI	Ph	2	95
2	2-CH ₃ PhI	Ph	2	94
3	4-CH ₃ PhI	Ph	2	92
4	4-NO ₂ PhI	Ph	3	51
5	PhBr	Ph	6	89
6	4-CH ₃ OPhBr	Ph	7	92
7	4-NO ₂ PhBr	Ph	8	84
8	PhBr	CO ₂ CH ₃	10	73
9	PhBr	CO ₂ C ₄ H ₉	10	71
10	PhI	CN	3	82
11	PhBr	CN	10	75
12	4-NO ₂ PhCl	Ph	16	41

^a The reaction condition: halobenzene, 5 mmol; olefins, 6 mmol; Pd-PMMA, 1–1.58 g (1 wt.% of Pd with respect to the substrate); DMF, 5 ml; NEt₃, 7.5 mmol; 100 °C.

^b Isolated yields.

(Scheme 1). The course of the reaction was followed by TLC. As depicted in Table 1, Pd-PMMA demonstrated good activity. Reactions of iodobenzene and iodotoluene with styrene provided high yields in rather short time. However, 4-nitroiodobenzene had the yield of 51%, the side reaction was dehalogenation. Aryl bromides either with electron-donating or electron-withdrawing functional groups afforded good yields. The coupling of methyl and butyl acrylate with bromobenzene gave the corresponding product in 73 and 71% yield, respectively. Propenyl cyanide afforded required conversion to the coupling product. However, in the case of 4-nitrochlorobenzene, reaction only gave the corresponding product in 41% yield due to dehalogenation and high activation energy of C–Cl bond.

The Suzuki coupling reaction shown in Scheme 2 was then conducted in the presence of Pd-PMMA. The representative results are shown in Table 2. The Pd-PMMA also had high catalytic activity for Suzuki couplings. In all cases, no ligand was required for coupling reaction to occur. Couplings of aryl bromides with aryl boronic acids occurred readily with Pd-PMMA using K₃PO₄ as a base and a water/DMF mixture. Notably, 85% yield was obtained in the reaction of 4-fluorobromobenzene with phenylboronic acid. Aryl bromides containing electron-donating groups required longer reaction time to obtain good yields. For the electron-rich aryl chloride of 4-chlorophenol, the catalyst was inefficient, and the conversion of 4-chlorophenol was as low as 5%. The coupling was unsatisfactory even for the electron-deficient aryl chloride of 4-chloroacetophenone.



Scheme 2. Pd-PMMA catalyzed Suzuki reactions.

Table 2
Pd-PMMA catalyzed Suzuki reactions^a

Entry	ArX	R	Time (h)	Yield (%) ^b
1	PhBr	H	2.5	87
2	4-NO ₂ PhBr	H	2.5	92
3	4-CH ₃ COPhBr	H	2.5	98
4	4-CHOPhBr	H	3	91
5	4-FPhBr	H	3.5	85
6	4-CH ₃ PhBr	H	5	81
7	4-CH ₃ OPhBr	H	6	78
8	2-CH ₃ OPhBr	H	6	83
9	PhBr	CH ₃	2.5	91
10	PhBr	Cl	3	89
11	4-CH ₃ COPhCl	H	8	53
12	4-HOPhCl	H	12	5

^a The reaction condition: halobenzene, 5 mmol; aryl boronic acid, 7.5 mmol; Pd-PMMA, 1–1.29 g (1 wt.% of Pd with respect to the substrate); K₃PO₄, 10 mmol; H₂O, 5 ml; DMF, 5 ml; 95 °C.

^b Isolated yields.

Hot filtration method was performed in the coupling reaction of iodobenzene with styrene: a process was started as for a standard reaction. In the other process, the reaction mixture was filtered after 20 min of reaction process, and Pd-PMMA was separated from the system. The reaction system was not broken down by the filtration and the filtrate was returned to the flask and compared to the standard one. The course of the reaction was monitored by GC. Fig. 2 clearly showed that the catalytic activity of the filtrate was highly affected by the removal of the solid-supported palladium. The yield after 40 min is 54%, which is almost similar with the yield observed immediately after the filtration. The reactions proceeded interruptedly, stopping at around 55% conversion. These results may mean that the reaction is taking place with supported Pd.

Attempts were made to recycle the catalytic system. The reaction of bromobenzene with styrene and phenylboronic acid under the conditions mentioned above were run for four

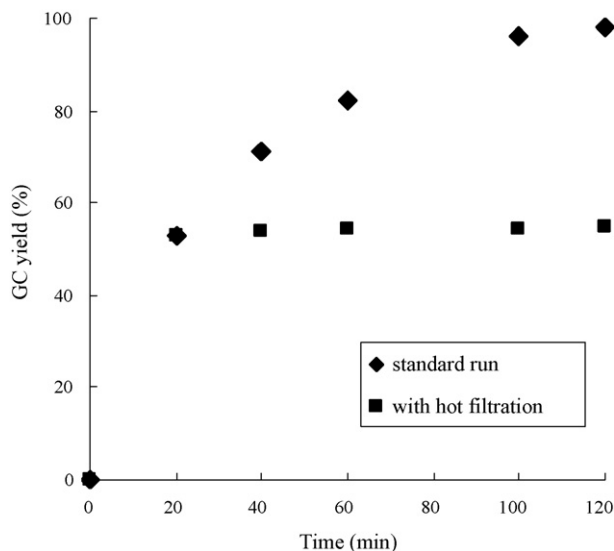
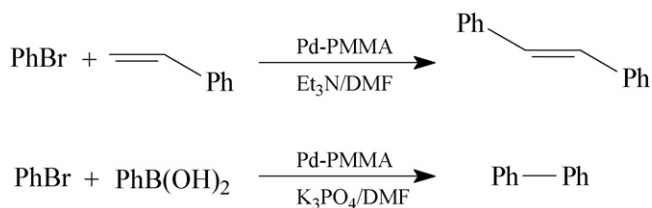


Fig. 2. Residual activity after hot filtration after 20 min reaction vs. a standard catalyst run.



Scheme 3. Recycling of the catalyst in Heck and Suzuki reactions.

Table 3
Recycling of the catalyst in Heck and Suzuki reaction

Cycles	Yield (%)		Pd leaching (ppm)	
	Heck	Suzuki	Heck	Suzuki
1	89	87	2.0	3.4
2	88	85	3.2	5.1
3	85	85	3.8	5.6
4	83	83	5.1	7.8

consecutive cycles, respectively (Scheme 3), furnishing the corresponding stilbene with 89, 88, 85 and 83% isolated yields and biphenyl with 87, 85, 85 and 83% isolated yields. No noticeable loss of activity was observed as noted by yield. In each iteration, the catalyst from reaction was filtered off, washed and reused without concern for exposure to air. As is shown in Table 3, palladium leaching from the catalyst is negligible with each cycle. The results demonstrate the Pd-PMMA catalyst may have practical utility.

4. Conclusion

In conclusion, Pd-PMMA was found to be an interesting and highly efficient catalyst for both Heck and Suzuki cross-coupling reactions. The reactions can be carried out under ligand-free conditions in an air atmosphere. The catalyst performed is easily separated and can be reusable with negligible leaching of palladium.

Acknowledgment

We thank the Nature and Science Foundation of Jiangsu Province (BK2007592) for financial support.

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