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The first heterogeneous Sonogashira coupling reaction of aryl halides with terminal alkynes catalyzed by diatomite-supported palladium(II) salophen complex

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We report here our observation that, using appropriate reaction conditions, the Sonogashira reaction can be performed without the need for copper catalyst and solvent. Our approach involves the use of diatomite-supported palladium(II) salophen complex as a catalyst and triethylamine as a base. The methodology works, to differing extents, for aryl iodides and bromides. This heterogeneous catalyst can be reused at least five times without any decrease in activity. Copyright © 2011 John Wiley & Sons, Ltd.

Keywords: copper- and solvent-free; supported catalyst; Sonogashira coupling; aryl halides

Introduction

The palladium-catalyzed sp^2 – sp Sonogashira coupling reaction of terminal alkynes with aryl halides[1–5] is one of the most valuable methods for the synthesis of arylated alkynes. A number of studies have been reported on homogeneously catalyzed reactions.[6] In Sonogashira coupling reaction, copper salts usually play an important role in assisting the oxidative addition of acetylene to palladium metal. This method has drawbacks, though, including waste production and the necessity of separation after the reaction. Recently, some successful examples of copper-free homogeneous Sonogashira coupling reactions have been reported for the reduction of the drawbacks for the use of copper salts.[7–11]

Two complications with the Sonogashira couplings is that the reaction needs degassed solvents, and that it has to be carried out under an inert atmosphere.[12,13] This is particularly inconvenient when the reactions are carried out in multiple vessels for library generation. Therefore, the development of a convenient method is an important objective in this effort. From the standpoint of environmentally benign organic synthesis, the development of highly active and easily reusable immobilized catalysts and a solvent-free medium are of great interest to chemists.[14,15] Moreover, there have been many efforts on the development of copper-free methodologies.[16–21] So far, polymer-supported palladium catalysts have successfully been used for the Heck, Suzuki and Sonogashira reactions, among others.[22] Recently, Zhang and co-workers[23] reported that the Pd nanoparticles immobilized on natural diatomite are highly active for Heck and Suzuki reactions and can be recovered and reused many times. However, to the best of our knowledge, there has been no general study of the Sonogashira coupling reaction catalyzed by diatomite-supported palladium complex catalyst described to date.

Diatomite ($SiO_2 \cdot nH_2O$) or diatomaceous earth is a siliceous rock made up largely from the skeletons of aquatic plants called diatoms.[6] Owing to the extremely porous structure, low density and high surface area of diatomite, it is possible to use it for the adsorption of organic and inorganic chemicals. Furthermore, these unique properties have led to its applications as filtration media in a number of industries. The diatom shell, which is composed of amorphous silica, has properties such as high porosity with strong adsorbance ability and excellent thermal resistance.[24–27]

As part of our continuing interest in heterogeneous palladium-catalyzed Sonogashira coupling reactions,[28,29] we report herein our results demonstrating that the Sonogashira coupling of various aryl halides with terminal acetylenes proceeds in the presence of a diatomite-supported palladium(II) salophen complex under copper-and solvent-free conditions.

Results and Discussion

The synthesis of the diatomite-supported Pd(II) salophen complex was carried out using a slight modification of the procedure previously reported for the synthesis of diatomite-supported Mn(II) salophen.[30] Specifically, 2.0 g of diatomite was added to 100 ml of ethanol, together with 10.0 mmol of $PdCl_2(PhCN)_2$. After the mixture was refluxed for 6 h, 10.0 mmol of salophen was added to the suspension, and the mixture was further refluxed for 12 h. Then the mixture was cooled to room temperature, filtered and washed with ethanol. The catalyst was then obtained by drying the solid under vacuum at 100 °C for 12 h (Scheme 1).

A new heterogeneous catalyst has been prepared by salophen ligand diffusion in Pd(II)-modified diatomite. The palladium

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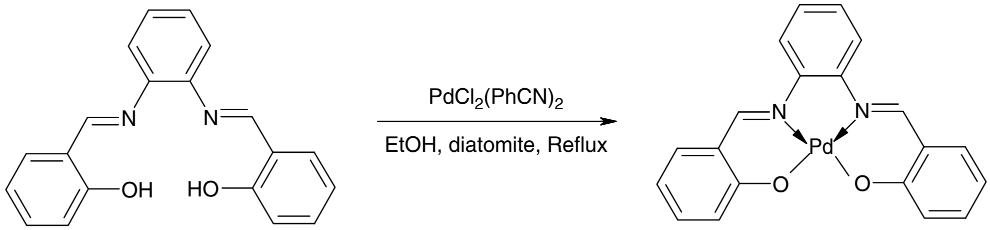


Scheme 1. Preparation of the diatomite-supported Pd(II) salophen complex.

Table 1. Copper-free Sonogashira reaction of phenylacetylene with iodobenzene[a]

Entry	Solvent	Base	Yield[b] (%)
1	CH_3CN	Et_3N	86
2	CH_3CN	DIEA[c]	42
3	CH_3CN	Pyrrolidine	80
4	CH_3CN	Pyridine	70
5	CH_3CN	Piperidine	84
6	1,4-Dioxane	Et_3N	77
7	1,4-Dioxane	Diea	57
8	1,4-Dioxane	Pyrrolidine	64
9	1,4-Dioxane	Pyridine	69
10	1,4-Dioxane	Piperidine	61
11	THF	Et_3N	83
12	THF	DIEA	78
13	THF	Pyrrolidine	70
14	THF	Pyridine	68
15	THF	Piperidine	85
16	NMP	Et_3N	76
17	NMP	DIEA	68
18	NMP	Pyrrolidine	90
19	NMP	Pyridine	55
20	NMP	Piperidine	65

[a] Reaction conditions: phenylacetylene (1.5 mmol), iodobenzene (1.0 mmol), diatomite–Pd(II) salophen (0.3 mol%), base (2.0 mmol), solvent (2 ml), 5 h, room temperature, aerobic conditions.
[b] GC yield.
[c] Diisopropylethylamine.

Table 2. Copper-free Sonogashira reaction of phenylacetylene with iodobenzene[a]

Entry	Base	Catalyst (mol%)	Time (h)	Yield[b] (%)
1	DIEA	0.3	5	94
2	Et_3N	0.3	5	97
3	Pyrrolidine	0.3	5	93
4	Pyridine	0.3	5	92
5	Et_2NH	0.3	5	89
6	$BuNH_2$	0.3	5	88
7	$PrNH_2$	0.3	5	85
8	$EtNH_2$	0.3	5	87
9	Ethanolamine	0.3	5	83
10	KOH	0.3	5	92
11	K_2CO_3	0.3	5	90
12	Cs_2CO_3	0.3	5	78
13	Et_3N	0.4	3	97
14	Et_3N	0.2	10	94
15	Et_3N	0.1	15	92

[a] Reaction conditions: phenylacetylene (1.5 mmol), iodobenzene (1.0 mmol), base (2.0 mmol), room temperature, aerobic conditions.
[b] GC yield.

content of diatomite-supported Pd(II) salophen, which was determined by inductively coupled plasma (ICP), was obtained to be 3.38%. A comparison of the FT-IR spectra of the encapsulated complex with that of the ‘free complex’ indicates the presence of the complex inside the diatomite cavities and pores.

The IR spectra of diatomite show major adsorption bands at 3436, 1637, 1087, 796, 625, 526 and 471 cm^{-1}. The band at 3436 cm^{-1} is due to the free silanol group (Si–O–H), the band at 1637 cm^{-1} represents H–O–H bending vibration of water, the band at 1087 cm^{-1} reflects the siloxane (–Si–O–Si–) group stretching and the bands at 526 and 471 cm^{-1} are attributed to the Si–O–Si bending vibration.

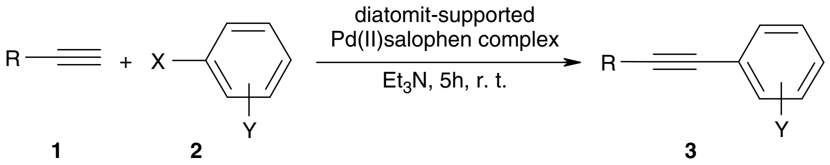
The IR spectra of [Pd(salophen)]-diatomite show major bands at 3050 (Carom–H), 1610 (C=N), 1570, 1530, 1100 and 790 cm^{-1}, which are absent in the diatomite. The IR spectra of complex show a shift in the υC=N to a lower frequency compared with free ligand because of coordination of azomethine nitrogen to the palladium, which indicates the formation of Pd(II) salophen complex.

The coupling of phenyacetylene with iodobenzene was initially studied as a model reaction. The reaction conditions were systematically optimized, and the results are presented in Table 1. It was found that the best system for the reaction was NMP in combination with pyrrolidine, which delivered a 90% yield of diphenylacetylene within 5 h when 0.3 mol% of diatomite-supported Pd(II) salophen complex was used (Table 1, entry 18). It is interesting that the highest yield of product was obtained when the reaction was performed under solvent-free conditions (Table 2). As shown in this table, when the reaction of phenylacetylene with iodobenzene was performed with Et_3N as base, an excellent 97% yield of the product was obtained (entry 2). Increasing the amount of palladium catalyst shortened the reaction time but did not increase the yield of diphenylacetylene (entry 13). A low palladium concentration led to a long reaction time (entry 14).

After the optimized conditions were found, we explored the general applicability of the diatomite-supported Pd(II) salophen complex, as a catalyst for copper- and solvent-free coupling of different alkynes **1** with aryl iodides and bromides **2** containing electron-withdrawing or donating substituents. The results are tabulated in Table 3.

The coupling of phenylacetylene with iodobenzene took place smoothly at room temperature in the presence of Et_3N (2 mmol) and 0.3 mol% palladium of the diatomite-supported Pd(II) salophen complex to give a good yield of diphenylacetylene (entry 1).

Table 3. Copper- and solvent-free Sonogashira reactions of terminal alkynes with aryl halides[a]



Entry	R	X	Y	Yield (%)[b]
1	Ph	I	H	97 (96)[c]
2	Ph	I	4-NO_2	98
3	Ph	I	4-Cl	94
4	Ph	I	4-Br	93
5	Ph	I	4-MeO	96
6	*n*-C_4H_9	I	H	95
7	*n*-C_4H_9	I	4-NO_2	98
8	*n*-C_4H_9	I	4-Cl	92
9	*n*-C_4H_9	I	4-Br	94
10	*n*-C_4H_9	I	4-MeO	96
11	CH_2OH	I	H	94
12	CH_2OH	I	4-MeO	93
13	CH_2OH	I	4-MeCO	95
14	Ph	Br	H	95
15	Ph	Br	4-NO_2	98
16	Ph	Br	3-NO_2	98
17	Ph	Br	4-CN	97
18	Ph	Br	4-F	96
19	Ph	Br	4-MeO	74
20	*n*-C_4H_9	Br	H	82
21	*n*-C_4H_9	Br	4-NO_2	97
22	*n*-C_4H_9	Br	4-F	94
23	*n*-C_4H_9	Br	4-MeO	84
24	CH_2OH	Br	H	96
25	CH_2OH	Br	4-NO_2	98
26	CH_2OH	Br	4-MeO	87

[a] Reaction conditions: **1** (1.5 mmol), **2** (1.0 mmol), [diatomite–Pd(II) salophen] (0.003 mmol), Et_3N (2 mmol), 5 h, room temperature, aerobic conditions.
[b] GC yield.
[c] Third cycle.

The Sonogashira reactions of electron-rich aryl iodides with terminal alkynes proceeded smoothly to give the corresponding coupling products in high yields (entries 5, 10 and 12). Unsurprisingly, *p*-nitroiodobenzene was found to be the most reactive amongst the aryl iodides studied (entries 2 and 7). As expected, aryl iodides with electron-withdrawing groups reacted faster than aryl iodides possessing electron-donating groups to give the desired products in high yields.

To extend the scope of our work, we next investigated the coupling of various aryl bromides with terminal alkynes. As expected, aryl iodides were more reactive than aryl bromides. However, as shown in Table 3, high catalytic activity was observed in the coupling of inactivated aryl bromides such as *p*-nitrobromobenzene (entries 15, 21 and 25) as well as activated *p*-nitroiodobenzene (entries 2 and 7). Moreover, *m*-nitroiodobenzene, *p*-bromobenzonitrile and *p*-fluorobromobenzene, having electron-deficient aromatic rings, also underwent the Sonogashira coupling with terminal alkynes under similar conditions to afford the corresponding products in excellent yields (entries 16, 17, 18 and 22), although the electron-rich bromoarene showed lower reactivity under similar conditions (entries 19, 23 and 26). The feasibility of recycling the diatomite-supported Pd(II) salophen complex was also examined. We presented the experimental results on the recycling of the supported Pd on a model reaction of phenylacetylene with iodobenzene. After each round, the supported catalyst was recovered by simple centrifugation and used directly for the next round of the reaction without further manipulation. The diatomite-supported Pd(II) salophen complex exhibited only a marginal loss in activity to achieve similar results after the third cycle (Table 3, entry 1).

Conclusion

In summary, we presented a new supported catalyst in which the Pd(II) salophen complex was immobilized on widespread natural diatomite by a simple procedure. The catalyst showed high activity for copper-free Sonogashira coupling reaction of alkynes with halobenzenes, and could be recovered easily and reused many times. This novel supported catalyst is air-stable, and all the reactions can be conducted in air. All these virtues indicate that the diatomite-supported catalyst has potential applications.

Experimental Section

All materials were commercial reagent grade. Alkyne and arylhalide compounds were obtained from Merck or Fluka. Diatomite sample was supplied as a natural resource from Tabriz, Iran.

Typical Procedure for the Preparation of Diatomite-supported Pd(II) Salophen Complex

To a 250 ml round-bottom flask equipped with a magnetic stirrer bar, and containing EtOH (100 ml) were added 2.0 g of dried diatomite and 10.0 mmol (0.383 g) of $PdCl_2(PhCN)_2$, and the reaction mixture was refluxed for 6 h. Then 10.0 mmol (0.318 g) of salophen was added to the suspension, and the mixture was further refluxed for 12 h. The resulting product was filtered, washed with ethanol, and dried at 100 °C for 12 h to give diatomite-supported Pd(II) salophen complex.

General Procedure for the Sonogashira Reaction Catalyzed by Diatomite-supported Pd(II) Salophen Complex

An aryl halide (1.0 mmol) and a terminal alkyne (1.5 mmol) was added to a mixture of diatomite-supported Pd(II) salophen complex (0.3 mol%) and base (2 mmol) in a glass flask under vigorous stirring. The mixture was stirred at room temperature for 5 h under aerobic conditions. Upon completion of the reaction, the reaction mixture was dissolved in chloroform (10 ml). The palladium catalyst was recovered by simple centrifugation, and reused in the next run. The chloroform solution was washed with water (10 ml) and dried over $MgSO_4$, and toluene (1.0 mmol) was added as internal standard for GC analysis. After GC analysis, the solvent was removed under vacuum, leaving the crude product.

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