

Palladium nanoparticles supported on modified polystyrene resin as a polymeric catalyst for Sonogashira–Hagihara coupling reactions

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Abstract: Pd(0) nanoparticles supported on modified crosslinked polystyrene were synthesized and characterized. Crosslinked polystyrene was reacted with trioxane and chlorotrimethylsilane in the presence of SnCl₄ to form Merrifield resin. The Merrifield resin was then converted to polymer-bound β-aminoalcohol and subsequently to β-aminophosphinite ligand. This polymeric ligand was reacted with PdCl₂ to obtain a polymeric Pd(0) complex. The TEM image of the Pd catalyst showed good dispersion of catalytic sites. The Pd catalyst exhibits excellent activity and stability in copper-free Sonogashira–Hagihara cross-coupling reactions under aerobic conditions. This protocol can be applied efficiently to the coupling reactions of chloro- as well as iodo- and bromo-arenes. The catalyst can be reused several times without any considerable decrease in its activity.

Key words: Merrifield support, palladium nanoparticle, Sonogashira coupling

1. Introduction

The Sonogashira–Hagihara coupling reaction is the most powerful method in organic synthesis for the production of arylalkyne compounds from terminal alkynes and aryl halides directly.^{1–4} The traditional procedure for the Sonogashira reaction employs a homogenous Pd-complex of phosphine as a catalyst, copper iodide salt as a cocatalyst, and a large amount of amine as a solvent or cosolvent.⁵

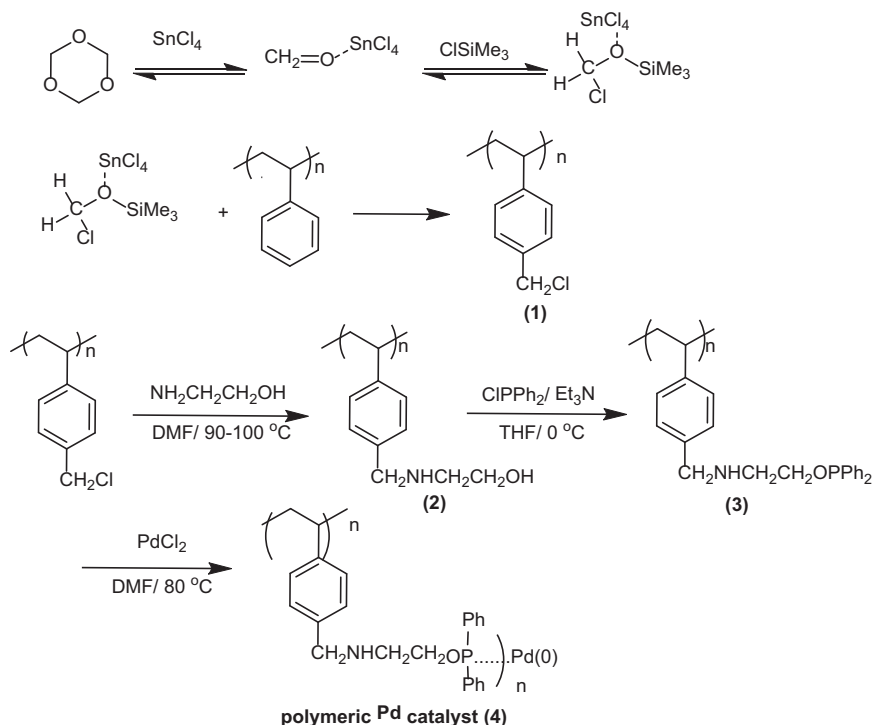
In recent years, many improvements have been made to the Sonogashira reaction. Using copper salts as cocatalyst sometimes leads to the homo-coupling reaction of terminal alkynes (Glaser-type reaction) upon exposure of the explosive copper-acetylide intermediate in the presence of air or other oxidizing agents.^{6–8} Therefore, numerous improved copper-free methodologies are reported to eliminate the copper salt from the reaction.^{9–11} Other improved methodologies include the use of palladium nanoparticles as a catalyst due to their large surface area.¹² Furthermore, the high cost of the precious palladium catalysts has led to the development of supported Pd nanoparticles that can be recovered from the reaction mixtures.¹³ In this regard, palladium nanoparticles immobilized on silica,^{14,15} metal oxides and double hydroxides layers,^{16,17} carbon nanotubes,^{18,19} and different organic^{20,21} and bio-organic polymers²² have been reported. Despite the fact that the Sonogashira coupling reaction has been intensively studied, there are only a few examples of heterogeneous palladium nanoparticle catalyst systems for the Sonogashira coupling of aryl chlorides that can act under copper-free conditions.²³ Thus, the study of new types of polymer-supported palladium nanoparticle catalysts that might be suitable for the copper-free Sonogashira reaction of all aryl halides, especially less active ones, has practical significance.

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In continuation of our previous studies on the introduction of different supports for palladium nanoparticles,^{24–27} we recently introduced novel Pd(0) nanoparticles supported on modified Merrifield resin as a catalyst for the Heck and Suzuki coupling reactions.²⁸ Herein, we present a new application of this catalyst for the efficient copper-free Sonogashira reaction of different aryl halides including chloroarenes.

2. Results and discussion

The heterogeneous Pd catalyst was designed by the sequence of reactions given in the Scheme. Merrifield resin (**1**) was prepared by the reaction of crosslinked polystyrene (2%) with trioxane and chlorotrimethylsilane in the presence of SnCl₄ as Lewis acid in chloroform.²⁹ Polymer-bound β-aminoalcohol (**2**) was synthesized by nucleophilic substitution of Merrifield resin with β-aminoalcohol. The modified polymer was then converted to β-aminophosphinite ligand (**3**) by the reaction with ClPPh₂ in THF at 0 °C. The phosphorous content of the ligand (**3**) was determined by iodometric titration and was found to be 1.6 mmol/g. The obtained polymeric ligand (**3**) was reacted with palladium(II) chloride in DMF to obtain the polymeric Pd(0) complex (**4**). The Pd capacity of the catalyst was determined by elemental analysis. ICP analysis revealed that the complex contained an average of 0.19 mmol Pd/g of the catalyst. The XRD pattern of the Pd catalyst showed the crystallographic planes of Pd(0) nanoparticles in (111), (200), (220), and (311). The transmission electron microscope (TEM) image of the Pd catalyst shows Pd particles dispersed in the polymer matrix with a size in the range of 10–30 nm.²⁸



Scheme. Synthesis of modified Merrifield resin-supported Pd nanoparticles.²⁸

The activity of this polymeric Pd catalyst was investigated for the Sonogashira coupling reaction. To optimize the reaction conditions, we chose iodobenzene and phenylacetylene as model coupling partners. Among the different bases (K₂CO₃, Et₃N, NaOAc, and KF) and different solvents (NMP, DMF, CH₃CN, EtOH, H₂O,

and THF) that were explored for this reaction, Et₃N and THF proved to be the best. In all, 0.5 mol % of polymeric catalyst and 2.0 equiv. of Et₃N in THF at 100 °C were found to be an optimum catalyst system.

By employing the optimized catalytic conditions, different aryl halides were coupled with phenylacetylene to produce the desired products in moderate to good yields. The results are tabulated in Table 1. Electron-deficient bromides coupled with phenylacetylene (Table 1, entries 5–7). In addition, the reaction of phenylacetylene with aryl bromides and iodides bearing electron-releasing substituent was carried out successfully. 4-Iodoanisole, 4-bromoanisole, 4-bromotoluene, 2-bromotoluene, and 3-bromotoluene were completely converted to the coupled products after 4, 4.5, 6, 10, and 16 h, respectively (Table 1, entries 2, 4, and 8–10). Less reactive aryl chlorides have not been employed much in palladium-catalyzed coupling reactions because the oxidative addition of the C–Cl bond to Pd(0) species is usually difficult.^{30,31} In our catalytic system, chloroarenes coupled with phenylacetylene in the presence of tetrabutylammonium bromide (TBAB) as an additive (Table 1, entries 11–15). Although the effect of TBAB in the coupling reactions is not completely clear, it has a promoting effect in the regeneration of zerovalent palladium by reductive elimination of Pd(II) compound in the presence of base.^{32,33}

Furthermore, we examined recycling of the catalyst in the reaction of iodobenzene with phenylacetylene as a model reaction. The catalyst was recycled for five cycles in this reaction to record a TON of 806 in total and average TOF (h⁻¹) of 42. The yield of the product decreased from 88% for the first run to 72% for the fifth run as shown in Table 2. To find the amount of palladium leaching in our system, the filtrate of a model reaction between iodobenzene and phenylacetylene was analyzed by ICP in five repeating cycles. The results showed that palladium leaching was negligible.

Supplementary data (¹H and ¹³C NMR spectra of coupling products) are available on the journal's website.

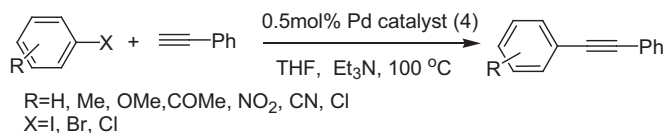
3. Experimental


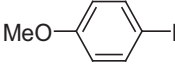
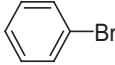
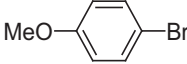
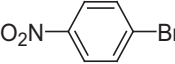
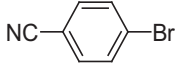
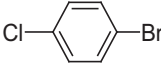
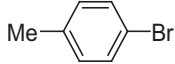
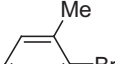
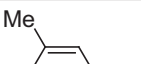
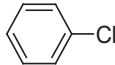
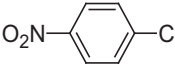
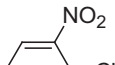
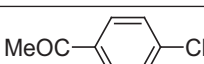
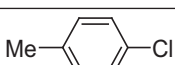
3.1. General

Substrates were purchased from Aldrich, Fluka, and Merck. All products were characterized by comparison of their FT-IR and NMR spectra and physical data with those reported in the literature. All yields refer to the isolated products. Progress of the reactions was followed by TLC on silica-gel Polygram SILG/UV 254 plates or by GC on a Shimadzu model GC 10-A instrument with a hydrogen flame ionization detector. IR spectra were run on a Shimadzu FT-IR 8300 spectrophotometer. The ¹H NMR and ¹³C NMR spectra were recorded on a Bruker Avance DPX instrument (250 MHz). The Pd analysis and leaching test were carried out by an inductively coupled plasma analyzer (ICP-OES) (Varian, Vista-Pro).

3.2. Preparation of the supported palladium catalyst

The polymer-supported palladium catalyst was prepared as described in our previous paper.²⁸ Trioxane (10 mmol) and chlorotrimethylsilane (30 mmol) were dissolved in chloroform (10 mL). Then 2% cross-linked polystyrene (1 g) and SnCl₄ (4.3 mmol) were added to the solution and the mixture was stirred at 0 °C for 30 min and then for 2 h at rt. The obtained Merrifield resin was filtered, washed, and dried under reduced pressure. Chloromethylated resin (1 g) was then suspended in DMF (10 mL) and to this were added ethanolamine (4 mmol) and triethylamine (4 mmol). The mixture while stirred was heated at 90–100 °C for 17 h. It was filtered, washed, and dried under vacuum. In the next step, polystyrene immobilized β-aminoalcohol (1 g) and

Table 1. Sonogashira–Hagihara coupling reaction of phenylacetylene with different aryl halides. ^a

Entry	Aryl halides	Products	Time (h)	Yield (%) ^b
1		1a	2.5	88
2		1b	4	78
3		1a	5	73
4		1b	4.5	78
5		1c	3.5	83
6		1d	4	85
7		1e	4	80
8		1f	6	81
9		1g	10	65
10		1h	16	62
11		1a	13	55 ^c
12		1c	7	58 ^c
13		1i	10	53 ^c
14		1j	9	55 ^c
15		1f	15	50 ^c

^a Molar ratio of the reagents ArX:phenylacetylene:Et₃N:palladium catalyst = 1.0:1.2:2.0:0.005. Reaction conditions: THF, 100 °C.

^b Isolated yields.

^c With additional tetrabutylammonium bromide (0.05 mmol)

Table 2. Recycling of Pd catalyst for the Sonogashira coupling reaction of iodobenzene with phenylacetylene.^a

Entry	Cycle	Time (h)	Isolated yield (%)	TON ^b	TOF (h ⁻¹) ^c
1	1st	2.5	88	176	70.4
2	2nd	3	88	176	58.7
3	3rd	4.5	80	160	35.5
4	4th	6	75	150	25
5	5th	7	72	144	20.6
TON for 5 runs 806 Av. TOF (h ⁻¹) 42					

^a Reaction conditions: molar ratio of iodobenzene:phenylacetylene:Et₃N:Pd catalyst = 1.0:1.2:2.0:0.005 in THF at 100 °C. All reactions were carried out with 100% conversion of iodobenzene.

^b TON = mmol of products/mmol of Pd catalyst

^c TOF = TON/time

triethylamine (4.6 mmol) were suspended in THF (10 mL) at 0 °C. A solution of chlorodiphenylphosphine (4.6 mmol) in THF (2 mL) was added dropwise over 20 min while stirring. The reaction mixture was then stirred for an additional 10 h at rt, and filtered. The obtained polystyrene supported phosphinite ligand (1 g) was treated with a solution of PdCl₂ (0.8 mmol) in DMF (15 mL) at 100 °C for 18 h. The polymeric Pd catalyst was filtered, washed, and dried under reduced pressure. ICP analyses revealed that the complex contained an average of 0.19 mmol of palladium/g of polymeric catalyst.

3.3. General procedure for the Sonogashira–Hagihara coupling reaction

In a round-bottomed flask equipped with a condenser and stirrer, a mixture of phenylacetylene (1.2 mmol, 0.13 mL), aryl halide (1.0 mmol), Pd catalyst (0.5 mol %), and Et₃N (2.0 mmol, 0.24 mL) in THF (20 mL) was heated at 100 °C. Progress of the reaction was monitored by TLC or GC. After completion of the reaction, the mixture was filtered and the residue was diluted with EtOAc and the organic layer was washed with water (20 mL) and brine (20 mL). The organic phase was dried over Na₂SO₄ and evaporated under vacuum. The mixture was then purified by column chromatography over silica gel using petroleum ether/ethyl acetate or recrystallization with CHCl₃ to afford a product with high purity. The identity of the products was determined by comparison of their FT-IR, ¹H NMR, ¹³C NMR, and physical data with those of the authentic samples.

3.4. Reuse of the catalyst

After completion of a coupling reaction, the catalyst was isolated by filtration. Then the isolated catalyst was washed with THF, acetone, and water and dried under vacuum. The resulting solid catalyst was charged into another batch for repeating cycles.

3.5. Conclusion

We have shown the applicability of a new palladium catalyst based on modified Merrifield resin carrying phosphinite ligand as an efficient catalyst for the copper-free Sonogashira reaction. Either electron-rich or electron-poor aryl bromides and iodides gave the desired product. Inactive aryl chlorides in the presence of TBAB coupled successfully. Recyclability of the catalyst without considerable loss of activity and low palladium leaching from the support are other characteristics of the process.

Acknowledgment

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References

1. Sonogashira, K. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F.; Stang, P. J., Eds. Wiley-VCH: New York, NY, USA, 1998, pp. 203–230.
2. Miyaura, N. *Cross-Coupling Reactions*; Springer: Berlin, Germany, 2002.
3. Chinchilla, R.; Najera, C. *Chem. Rev.* **2007**, *107*, 874–922.
4. Chinchilla, R.; Najera, C. *Chem. Soc. Rev.* **2011**, *40*, 5084–5121.
5. Thorand, S.; Krause, N. *J. Org. Chem.* **1998**, *63*, 8551–8553.
6. Glaser, C. *Ber. Dtsch. Chem. Ges.* **1869**, *2*, 422–424.
7. Li, J. H.; Liang, Y.; Wang, D. P.; Liu, W. J.; Xie, Y. X.; Yin, D. L. *J. Org. Chem.* **2005**, *70*, 2832–2834 and references cited therein.
8. Yang, F.; Cui, X.; Li, Y.; Zhang, J.; Ren, G.; Wu, Y. *Tetrahedron* **2007**, *63*, 1963–1969.
9. Bakherad, M.; Keivanloo, A.; Bahramian, B.; Mihanparast, S. *Tetrahedron Lett.* **2009**, *50*, 6418–6420.
10. Lu, N.; Chen, Y. C.; Chen, W. S.; Chen, T. L.; Wu, S. J. *J. Organomet. Chem.* **2009**, *694*, 278–284.
11. Suzuka, T.; Okada, Y.; Ooshiro, K.; Uozomi, Y. *Tetrahedron* **2010**, *66*, 1064–1069.
12. Jiang, J. Z.; Wei, Y. A.; Cai, C. *J. Colloid Interf. Sci.* **2007**, *312*, 439–443.
13. Karimi, B.; Behzadnia, H.; Farhangi, E.; Jafari, E.; Zamani, A. *Curr. Org. Synth.* **2010**, *7*, 543–567.
14. Kim, N.; Kwon, M. S.; Park, C. M.; Park, J. *Tetrahedron Lett.* **2004**, *45*, 7057–7059.
15. Lin, B. N.; Huang, S. H.; Wu, W. Y.; Mou, C. Y.; Tsai, F. Y. *Molecules* **2010**, *15*, 9157–9173.
16. Choudary, B. M.; Madhi, S.; Chowdari, N. S.; Kantam, M. L.; Sreedhar, B. *J. Am. Chem. Soc.* **2002**, *124*, 14127–14136.
17. Phan, N. T. S.; Le, H. V. *J. Mol. Catal. A: Chem.* **2011**, *334*, 130–138.
18. Zhou, L.; Jiang, H. F. *Tetrahedron Lett.* **2007**, *48*, 8449–8452.
19. Likhari, P. R.; Sughas, M. S.; Roy, M.; Roy, S.; Kantam, M. L. *Helv. Chim. Acta* **2008**, *91*, 259–264.
20. Li, P.; Wang, L.; Li, H. *Tetrahedron* **2005**, *61*, 8633–8640.
21. Cheng, L.; Hong, S.; Zhou, X.; Zhou, Z.; Hou, H. *Catal. Commun.* **2008**, *9*, 2221–2225.
22. Firouzabadi, H.; Iranpoor, N.; Ghaderi, A. *Org. Biomol. Chem.* **2011**, *9*, 865–871.
23. Ye, Z. W.; Yi, W. B. *J. Fluorine Chem.* **2008**, *129*, 1124–1128.
24. Tamami, B.; Ghasemi, S. *J. Mol. Catal. A: Chem.* **2010**, *322*, 98–105.
25. Tamami, B.; Allahyari, H.; Ghasemi, S.; Farjadian, F. *J. Organomet. Chem.* **2011**, *696*, 594–599.
26. Tamami, B.; Allahyari, H.; Farjadian, F.; Ghasemi, S. *Iran. Polym. J.* **2011**, *20*, 699–712.
27. Tamami, B.; Farjadian, F. *J. Iran. Chem. Soc.* **2011**, *8*, 77–88.
28. Tamami, B.; Nowroozi Dodeji, F. *J. Iran. Chem. Soc.* **2012**, *9*, 841–850.
29. Itsuno, S.; Uchikoshi, K.; Ito, K. *J. Am. Chem. Soc.* **1990**, *112*, 8187–8188.
30. Selvakumar, K.; Zapf, A.; Beller, M. *Org. Lett.* **2002**, *4*, 3031–3033.
31. Kohler, K.; Kkleist, W.; Prockl, S. S. *Inorg. Chem.* **2007**, *46*, 1876–1883.
32. Jeffery, T. *Tetrahedron Lett.* **1985**, *26*, 2667–2670.
33. Jeffery, T. *Tetrahedron* **1996**, *52*, 10113–10130.