A water-compatible, highly active and reusable PEG-coated mesoporous silica-supported palladium complex and its application in Suzuki coupling reactions†‡

Qing Yang,[ab] Shengming Ma,*[a] Jixue Li,[b] Fengshou Xiao*[b] and Hai Xiong[a]

Received (in Cambridge, UK) 16th December 2005, Accepted 3rd February 2006
First published as an Advance Article on the web 4th May 2006
DOI: 10.1039/b605733k

A highly active heterogeneous palladium catalyst was prepared from coated mesoporous materials which contain a layer of readily available PEG with a labile coordinating ability for palladium. The aqueous suspension of the catalyst may be reused several times by simple extraction of the aqueous reaction mixture with ether to remove the product.

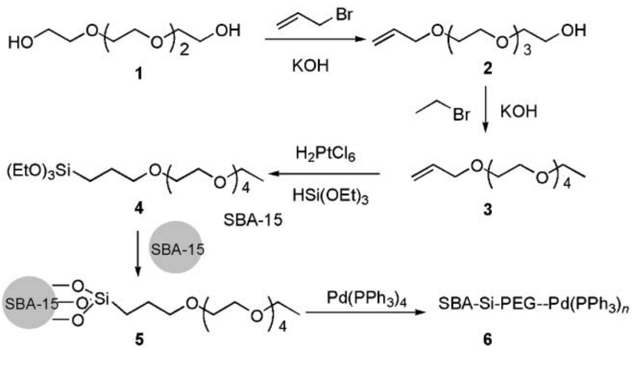
One of the most successful stories of organometallic chemistry is its application in homogeneous catalysis, demonstrating tunable reactivity and selectivity due to the diversity of the metal(s) and the ligand(s) in organometallic catalysts. However, after homogeneous organometallic catalysis, the final products are always contaminated with metallic species due to the leaching of the catalyst; this being a very serious problem in industry, especially the pharmaceutical industry. Palladium-catalyzed coupling reactions,[1–3] Heck reactions,[4–6] Sonogashira couplings[7] and Tsuji–Trost allylations[8] have become very important organic transformations in modern synthetic organic chemistry. However, they usually suffer from the high loading of the palladium catalyst. In most cases, up to 5 mol% of catalysts have to be used, which may have a very serious negative impact on their possible industrial applications. Thus, the development of supported palladium catalysts showing a much higher catalytic activity without leaching is highly desirable. Generally, Pd catalysts can be successfully supported on organic materials such as core-shell block copolymers,[9,10] ligand-incorporated polymers[11,12] and dendrimers.[13] Pd catalysts can also be supported on inorganic materials such as zeolites,[14] carbon,[12,15] hydroxides,[16] amorphous silicates,[17] and mesoporous silica.[18–22] We proposed that if mesoporous silica[23,24] is coated with a layer of a molecule containing functionalities (L) with labile coordinating ability, it may be an excellent supporting material for any metallic complex (MY_n). In this paper, we wish to report the realization of such a concept by the production of a highly active mesoporous silica-supported palladium catalyst, which has shown high activity in Suzuki coupling reactions in water.

As shown in Scheme 1, tetra(ethylene glycol) (**1**) was allylated in the presence of KOH to afford alcohol **2**, which was followed by etherification with EtBr to afford allyl ether **3**. Pt-catalyzed hydrosilylation of **3** with $HSi(OEt)_3$ afforded the organosilane **4**, which was used for grafting onto the surface of SBA-15 to support the Pd catalyst.

Mesoporous silica SBA-15 was synthesized according to the reported procedure using tri-block P123 as a template under acidic conditions.[24] After coating with organosilane **4**, the mesoporous silica **5** was treated with a 5×10^{-3} M solution of $Pd(PPh_3)_4$ in THF with stirring. After 10 h, the mixture was filtered and washed with THF to afford the supported catalyst **6** (Scheme 1). The Pd% in this supported catalyst was 0.050 mmol g^{-1} (0.53% by wt), as determined by ICP, and the P% in this supported catalyst was 0.017 mmol g^{-1} (0.0522% by wt), as determined by high performance ion chromatography (HPIC), indicating that the number of PPh_3 units per Pd in the supported catalyst was very limited (P/Pd = 1/3).

The transmission electron microscopy (TEM) images of catalyst **6**, shown in Fig. 1, provide a direct observation of the morphology and distribution of the palladium in the catalyst. Obviously, a hexagonally packed pore structure was found in catalyst **6**. Comparing the TEM images of SBA-15[24] with those of **6**, it can be concluded that no bulk aggregation of the metal on the surface could be found, indicating that the Pd was finely dispersed on the walls of the PEG-coated SBA-15.

The prepared catalyst was used to catalyze Suzuki coupling reactions that may have high industrial potential.[25] Due to the hydrophilic nature of PEG, we wished to consider the possibility of conducting Suzuki coupling reactions in water. Among the bases



Scheme 1 Synthesis of mesoporous silica-supported catalyst **6**.

---

[a] *State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Lu, Shanghai, 200032, P. R. China. E-mail: masm@mail.sioc.ac.cn; Fax: (+86) 21-6416-7510*
[b] *State Key Laboratory of Inorganic Synthesis and Preparative Chemistry, Jilin University, Changchun, 130012, P. R. China. E-mail: fsxiao@mail.jlu.edu.cn; Fax: (+86) 431-5168590*

† Electronic Supplementary Information (ESI) available: Experimental procedures and characterization data of all new compounds. See DOI: 10.1039/b605733k

‡ This article is an updated version of DOI: 10.1039/b517862b which was published as an Advance Article on the web on 22nd February 2006 and retracted by the authors on 13th March 2006.

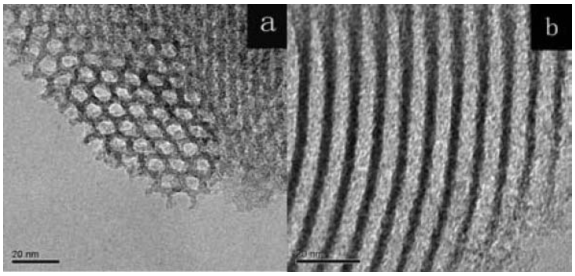


Fig. 1 TEM images of SBA–Si–PEG–Pd$(PPh_3)_n$ **6**.

tested (K_2CO_3, $CsCO_3$, Et_3N, KOH and K_3PO_4), K_3PO_4 was the best, affording **9a** in 90% yield at 50 °C. When the reaction was conducted at 30 °C, the yield of **9a** was lower. No obvious improvement was observed when the reaction was conducted at 70 or 100 °C.

Thus, the scope of the Suzuki coupling reaction was studied by conducting it in water at 50 °C using K_3PO_4 as the base. Some typical results are listed in Table 1. It can be concluded that (1) the scope of the reaction is broad: both aryl halides and aryl boronic acids with electron donating or withdrawing groups can be used; (2) sterically hindered aryl halides and boronic acids can also be used (Table 1, entries 4, 11 and 12); (3) in most of cases, the reaction with 0.1 mol% catalyst can afford the products in fairly good yields, the catalyst loading can even be reduced to 0.01 or 0.001 mol% (Table 2); (4) even phenyl bromide (Table 1, entry 2) and the very unreactive phenyl chloride with SPhos[26,27] (Table 1, entry 3) can be applied.

It is well known that $Pd(PPh_3)_4$ is unstable, losing catalytic activity upon exposure to air. However, it was quite a surprise for us to observe that the supported catalyst **6** is still effective even after exposure to air for 6 weeks, and that the reaction can be conducted in the open air without any obvious loss of activity with a yield of 86% (0.01 mol% of Pd, 50 °C, 24 h). In comparison, when the $Pd(PPh_3)_4$-catalyzed reaction was conducted in air, the coupling product **9a** was formed in a much lower yield of 60% (1.5 mol% of Pd, 50 °C, 72 h).

Table 1 The SBA–Si–PEG–Pd$(PPh_3)_n$-catalyzed Suzuki coupling of various substrates[a]

$$\underset{\mathbf{7}}{R^1{-}X} + \underset{\mathbf{8}}{R^2{-}B(OH)_2} \xrightarrow[K_3PO_4\cdot 3H_2O,\ H_2O,\ 50^{\circ}C,\ 10\ h]{\mathbf{6}\ (0.1\ mol\%)} \underset{\mathbf{9}}{R^1{-}R^2}$$

Entry	Halide (**7**) R^1–X	Boronic acid (**8**) R^2	Yield[b] (%)
1	C_6H_5I	p-$MeOC_6H_4$	88 (**9a**)
2[c]	C_6H_5Br	p-$MeOC_6H_4$	87 (**9a**)
3[d]	C_6H_5Cl	p-$MeOC_6H_4$	84 (**9a**)
4[e]	2,6-$Me_2C_6H_3I$	p-$MeOC_6H_4$	86 (**9b**)
5	p-$MeOC_6H_4I$	Ph	82 (**9a**)
6	o-$MeO_2CC_6H_4I$	Ph	95 (**9c**)
7	(Z)-$EtO_2CC_2H_2I$	Ph	90 (**9d**)
8	o-HOC_6H_4I	Ph	98 (**9e**)
9	p-$O_2NC_6H_4Br$	Ph	81 (**9f**)
10	o-NCC_6H_4Br	Ph	83 (**9g**)
11	o-NCC_6H_4Br	o-$MeOC_6H_4$	89 (**9h**)
12	o-$MeO_2CC_6H_4I$	o-$MeOC_6H_4$	89 (**9i**)
13[f]	o-$MeO_2CC_6H_4I$	p-$CF_3C_6H_4$	86 (**9j**)

[a] The reactions of 0.3 mmol of **7**, 1.2 equiv. of **8**, 2.0 equiv. of K_3PO_4 and 0.1 mol% of **6** in H_2O (3 mL) were conducted at 50 °C for 10 h. [b] Isolated yield. [c] Reaction was conducted at 90 °C for 10 h using 2 equiv. of bromide with 0.5 mol% of **6**. [d] Reaction was conducted using 2 equiv. of chloride at 60 °C for 10 h with 0.5 mol% of **6** and 1 mol% of SPhos. [e] 1 mol% of **6** and 2 mol% of PPh_3 were used. [f] Reaction time 20 h.

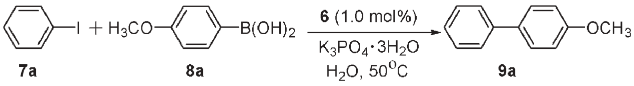
Table 2 Suzuki couplings catalyzed by SBA–Si–PEG–Pd$(PPh_3)_n$ at lower catalyst loadings[a]

$$\underset{\mathbf{7}}{R^1{-}X} + \underset{\mathbf{8b}}{PhB(OH)_2} \xrightarrow[K_3PO_4\cdot 3H_2O,\ H_2O,\ 50^{\circ}C]{\mathbf{6}\ (0.01\text{-}0.001mol\%)} \underset{\mathbf{9}}{R^1{-}Ph}$$

Entry	Halide (**7**)	Catalyst (**6**) loading (mol%)	Time/h	Yield[b](%)
1	o-NCC_6H_4Br	0.01	48	78 (**9g**)
2	o-HOC_6H_4I	0.01	24	98 (**9e**)
3	o-HOC_6H_4I	0.001	24	98 (**9e**)
4	o-$MeO_2CC_6H_4I$	0.005	72	66 (**9c**)

[a] The reactions of 1.0 equiv. of **7**, 1.2 equiv. of **8** and 2.0 equiv. of K_3PO_4 in H_2O were conducted at 50 °C. [b] Isolated yield.

Table 3 The reuse of SBA–Si–PEG–Pd$(PPh_3)_n$ **6**[a]



Run	1	2	3	4	5
Yield[b] (%)	91	92	91	91	89
Leaching of Pd[c]	nd	nd	nd	nd	nd

[a] The reactions of 0.3 mmol of **7**, 1.2 equiv. of **8**, 2.0 equiv. of K_3PO_4 and 1.0 mol% of **6** in H_2O (3 mL) were conducted at 50 °C for 10 h. [b] Isolated yield. [c] After ether extraction to remove the product, the ether was removed by evaporation, and the sample was submitted to ICP for determination of the extent of leaching of Pd to the organic layer. nd = not detected by ICP.

In addition, due to the hydrophilic nature of the supported catalyst, after ether extraction to remove the product, the catalyst in water could be reused without any obvious loss of the activity (Table 3). Leaching of the Pd into the organic layer after the reaction, which was determined by ICP, was not observed.

In conclusion, we have designed and prepared a new palladium catalyst supported on PEG-modified mesoporous silica that is still catalytically active after exposure to air for up to 6 weeks and shows very high catalytic activity in Suzuki coupling reactions. Its stability towards air may be due to the mesoporous structure. An aqueous suspension of the catalyst may be reused several times by simple extraction of the aqueous reaction mixture with ether to remove the product. No leaching of the catalyst to the organic layer was observed. Further studies in the application of this catalyst to other organic reactions are now being conducted in our laboratory.

Notes and references

1 N. Miyaura and A. Suzuki, *Chem. Rev.*, 1995, **95**, 2457.
2 *Metal-Catalyzed Cross-Coupling Reactions*, ed. A. de Meijere and F. Diederich, Wiley-VCH, Weinheim, 2004.
3 J. Tsuji, *Palladium Reagents and Catalysts*, Wiley, Chichester, 2nd edn, 2004.
4 R. F. Heck, *Comprehensive Organic Synthesis*, ed. B. M. Trost and I. Fleming, Pergamon, Oxford, 1991, vol. **4**, pp. 3881.
5 A. W. Cabri and I. Candiani, *Acc. Chem. Res.*, 1995, **28**, 2.

6 A. de Meijer and F. E. Meyer, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 2379.

7 N. Miyaura and A. Suzuki, *Chem. Rev.*, 1995, **95**, 2457.

8 B. M. Trost and T. R. Verhoeven, *J. Am. Chem. Soc.*, 1978, **100**, 3435.

9 For a review of heterogeneous Pd catalysts, see: H.-U. Blaser, A. Indolese, A. Schnyder, H. Steiner and M. Studer, *J. Mol. Catal. A: Chem.*, 2001, **173**, 3.

10 (*a*) R. Akiyama and S. Kobayashi, *J. Am. Chem. Soc.*, 2003, **125**, 3412; (*b*) K. Okamoto, R. Akiyama, H. Yoshida, T. Yoshida and S. Kobayashi, *J. Am. Chem. Soc.*, 2005, **127**, 2125.

11 (*a*) N. E. Leadbeater and M. Marco, *Chem. Rev.*, 2002, **102**, 3217; (*b*) C. A. McNamara, M. J. Dixon and M. Bradley, *Chem. Rev.*, 2002, **102**, 3275.

12 A. L. Dantas Ramos, P. da Silva Alves, D. A. G. Aranda and M. Schmal, *Appl. Catal., A*, 2004, **277**, 71.

13 R. van Heerbeek, P. C. J. Kamer, P. W. N. M. van Leeuwen and J. N. H. Reek, *Chem. Rev.*, 2002, **102**, 3717.

14 (*a*) L. Djakovitch and P. Rollet, *Adv. Synth. Catal.*, 2004, **346**, 1782; (*b*) K. Okumura, K. Nota, K. Yoshida and M. Niwa, *J. Catal.*, 2005, **231**, 245.

15 (*a*) M. Lysén and K. Köhlera, *Synlett*, 2005, **11**, 1671; (*b*) R. K. Arvela and N. E. Leadbeater, *Org. Lett.*, 2005, **7**, 2101.

16 (*a*) K. Mori, K. Yamaguchi, T. Hara, T. Mizugaki, K. Ebitani and K. Kaneda, *J. Am. Chem. Soc.*, 2002, **124**, 11572; (*b*) B. M. Choudary, S. Madhi, N. S. Chowdari, M. L. Kantam and B. Sreedhar, *J. Am. Chem. Soc.*, 2002, **124**, 14127.

17 M. K. Richmond, S. L. Scott and H. Alper, *J. Am. Chem. Soc.*, 2001, **123**, 10521.

18 For vapor grafting, see: (*a*) C. P. Mehnert and J. Y. Ying, *Chem. Commun.*, 1997, 2215; (*b*) C. P. Mehnert, D. W. Weaver and J. Y. Ying, *J. Am. Chem. Soc.*, 1998, **120**, 12289.

19 B. F. G. Johnson, S. A. Raynor, D. S. Shephard, T. Mashmeyer, J. M. Thomas, G. Sankar, S. Bromley, R. Oldroyd, L. Gladden and M. D. Mantle, *Chem. Commun.*, 1999, 1167.

20 For grafting *via in situ* reduction, see: L. Li, J.-L. Shi and J. Yan, *Chem. Commun.*, 2004, 1990.

21 For a recent mercaptopropyl-modified mesoporous silica-supported Pd(OAc)$_2$, see: C. M. Crudden, M. Sateesh and R. Lewis, *J. Am. Chem. Soc.*, 2005, **127**, 10045.

22 E. Paetzold, G. Oehme, H. Fuhrmann, M. Richter, R. Echelt, M.-M. Pohl and H. Kosslick, *Microporous Mesoporous Mater.*, 2001, **44–45**, 517.

23 C. T. Kresge, M. E. Leonowicz, W. J. Roth, J. C. Vartuli and J. S. Beck, *Nature*, 1992, **359**, 710.

24 D. Zhao, J. Feng, Q. Huo, N. Melosh, G. H. Fredrickson, B. F. Chmelka and G. D. Stucky, *Science*, 1998, **279**, 548.

25 (*a*) A. M. Rouhi, *Chem. Eng. News*, 2004, **82**, 36, 49; (*b*) A. M. Rouhi, *Chem. Eng. News*, 2004, **82**, 36, 66; (*c*) For a recent review on Suzuki coupling, see: A. Suzuki, *Chem. Commun.*, 2005, 4759.

26 (*a*) S. D. Walker, T. E. Barder, J. R. Martinelli and S. L. Buchwald, *Angew. Chem., Int. Ed.*, 2004, **43**, 1871; (*b*) T. E. Barder, S. D. Walker, J. R. Martinelli and S. L. Buchwald, *J. Am. Chem. Soc.*, 2005, **127**, 4685.

27 For recent reports on the activation of aryl chlorides, see: (*a*) N. Hadei, E. A. B. Kantchev, C. J. O'Brien and M. G. Organ, *Org. Lett.*, 2005, **7**, 1991; (*b*) L. Ackermann and R. Born, *Angew. Chem., Int. Ed.*, 2005, **44**, 2444.