COMMUNICATION www.rsc.org/chemcomm | ChemComm

Entangled palladium nanoparticles in resin plugs†

Romain Najman,[a] Jin Ku Cho,[a] Andrew F. Coffey,[b] John W. Davies[b] and Mark Bradley*[a]

Received (in Cambridge, UK) 3rd August 2007, Accepted 11th September 2007
First published as an Advance Article on the web 4th October 2007
DOI: 10.1039/b711978j

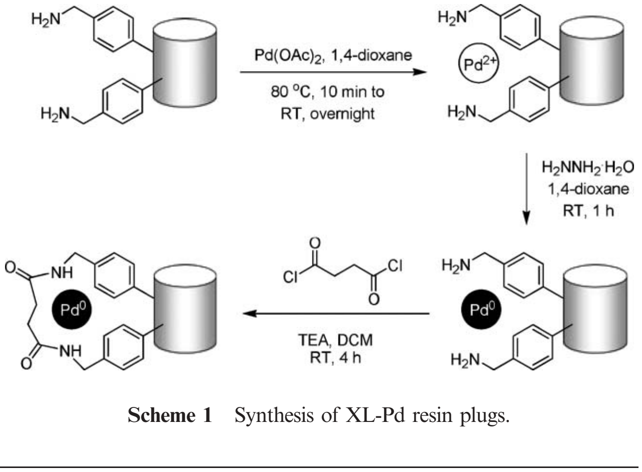
Palladium nanoparticles were entrapped within resin plugs and used in a range of ligand-free cross-coupling reactions; the convenient modular format of the resin plug enhanced resin handling and allowed the catalysts to be easily recovered and multiply reused.

The interest in transition metal-catalysed reactions in organic synthesis and specifically in palladium-catalysed cross-couplings continues to grow.[1] Considering both environmental and economic issues, there is a need for palladium catalysts that can be easily recovered, generate highly pure products and that generate few catalyst-based contaminants. Over recent years efforts have been expended in the area of palladium immobilisation, with a number of insoluble supports developed to address the concerns of recovery and reusability. Traditionally, palladium metal has been adsorbed onto inorganic supports such as silica or alumina,[2] but more recently polymer-supported palladium catalysts have been devised *via* immobilisation of a ligand and subsequent metal coordination to form an anchored complex.[3] However, this technique involves the use of expensive ligands and problems of leaching associated with these supported homogeneous catalysts have been reported. Other methods have been developed by Akiyama and Kobayashi[4] and Ley *et al.*[5] to encapsulate palladium catalysts by "polymer incarceration" and interfacial polymerisation respectively. Pre-formed resin beads offer an attractive alternative, with advantages associated with their commercial availability and mechanical stability as well as a substantial knowledge associated with their use. Following studies on polymer-supported catalysts,[6] we wish to report here the entanglement of palladium nanoparticles into resin plugs (resin beads sintered and embedded within inert high-density polyethylene to give a modular cylindrical support)[7] and the catalytic activity of these "cross-linked(XL)-Pd plugs" in Suzuki–Miyaura,[8] Sonogashira–Hagihara[9] and Heck–Mizoroki reactions.[10]

The palladium-captured cross-linked-resin plugs were readily prepared *via* a 3-step procedure:[11] (1) palladium loading (achieved by heating a mixture of the Polymer Laboratories aminomethylstyrene resin plugs and palladium acetate in 1,4-dioxane at 80 °C); (2) palladium nanoparticle generation by 10% hydrazine-mediated reduction in 1,4-dioxane and (3) cross-linking and entanglement with succinyl chloride (Scheme 1). Controlling the amount of $Pd(OAc)_2$ added allowed Pd-resin plugs with various metal loadings to be prepared (0.8 to 98 μmol/plug). Palladium levels in the plugs were determined by inductively coupled plasma atomic emission spectroscopy (ICP-AES), see ESI for details.†

Analysis of the resulting plugs (Fig. 1) revealed a core-shell structure, with black resin beads loaded with palladium being located predominantly at the edges of the plug [Fig. 1(b)]. Within the beads themselves [Fig. 1(c) and 1(d)] microscopic analysis showed a palladium nanoparticle gradient with tiny nanoparticles observed at the edge of the beads [Fig. 1(e) and 1(f)], presumably due to rapid reduction at the edge. Transmission electron microscopy (TEM) gave an average size for the palladium particles as approximately 7 nm at the edge, moving to progressively larger nanoparticles towards the middle of the bead itself (approximately 25–70 nm), where various "shapes" (*e.g.* triangular, cubic, rhomboidal, diamond, trapezium, pentagon) were observed for the palladium particles [Fig. 1(g–m)], suggesting that the polymer scaffolds could offer an interesting approach to the control of nanoparticle architectures. The thickness of the whole palladium-filled layer inside a bead was around 30 μm.

The ability of the palladium-loaded plugs to catalyse C–C bond forming reactions and their recyclability were assessed in 3 major classes of couplings, *i.e.* the Suzuki–Miyaura, Sonogashira–Hagihara and Heck–Mizoroki reactions (Table 1). The results show that resin plug-entangled palladium nanoparticles were good catalysts for the three cross-coupling reactions, giving good yields and purities. Moreover, they could be reused multiple times with no major loss of activity, with recovery by simple filtration and washing and with no precautions taken to prevent exposure to oxygen or moisture. Their efficiency in cross-coupling reactions was further investigated using a broader range of substrates of varying electron density (Table 2).‡



Scheme 1 Synthesis of XL-Pd resin plugs.

---

[a] *School of Chemistry, The University of Edinburgh, The King's Buildings, West Mains Road, Edinburgh, UK EH9 3JJ.*
E-mail: Mark.Bradley@ed.ac.uk; Fax: +44 (0)131 650 6453;
Tel: +44 (0)131 650 4820
[b] *Polymer Laboratories Ltd., Essex Road, Church Stretton, UK SY6 6AX. Fax: +44 (0)1694 722 171; Tel: +44 (0)1694 723 581*

† Electronic supplementary information (ESI) available: Detailed experimental procedures of XL-Pd resin plug preparation and TEM analysis, Suzuki–Miyaura, Sonogashira–Hagihara and Heck–Mizoroki couplings, characterisation data of the products. See DOI: 10.1039/b711978j

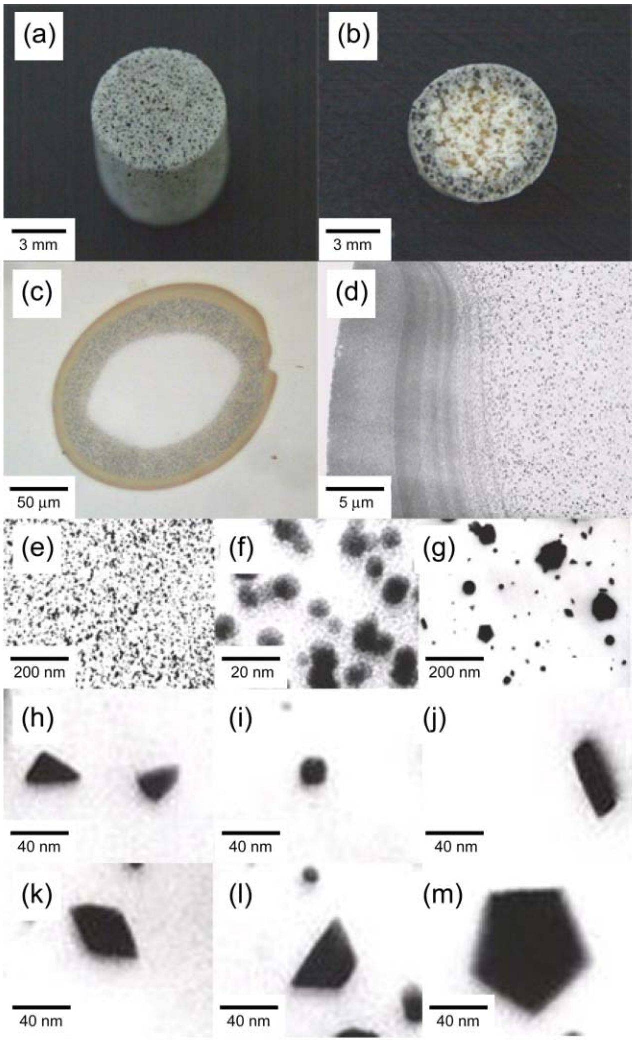
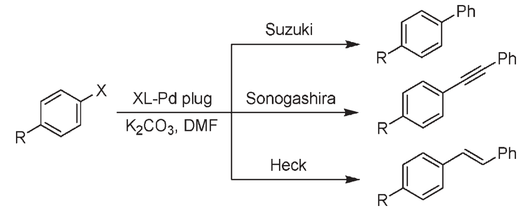


Fig. 1 (a) Optical image of a cross-linked (XL)-Pd containing resin plug; (b) optical image of the top of a XL-Pd resin plug; (c) optical microscope image (low magnification) of a single bead from within the plug that has been sliced; (d–m) TEM images showing: (d). the interior of a sliced bead; (e) outer layer (× 40 000); (f) magnified view of outer layer (× 400 000); (g) inner layer (× 40 000); (h) magnified view (× 400 000) of inner layer showing triangular; (i) cubic; (j) rhomboidal; (k) diamond; (l) trapezium; and (m) pentagon shapes of palladium particles.

Table 1 Cross-linked-Pd plugs in Suzuki, Sonogashira and Heck cross-couplings and their recyclability



Recycle		1	2	3	4
Isolated yield (%)	Suzuki[a]	92	96	87	92
	Sonogashira[a]	73	74	73	72
	Heck[b]	92	83	81	79[c]

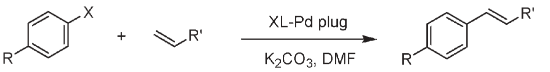
[a] Reaction conditions: substrate $[X = Br, R = NO_2]$ (1.0 mmol), phenylboronic acid or phenylacetylene (1.5 mmol), K_2CO_3 (3.0 mmol), XL-Pd plug (9.8 mol%), DMF (4 mL), air, 80 °C. [b] Reaction conditions: substrate $[X = I, R = H]$ (1.0 mmol), styrene (1.5 mmol), K_2CO_3 (1.5 mmol), XL-Pd plug (0.08 mol%), DMF (5 mL), air, 115 °C. [c] The amount of Pd in solution at the 5th run was determined by ICP-AES to be 0.37 ppm.

Table 2 Pd plugs catalytic activity in Suzuki, Sonogashira and Heck cross-couplings of aryl iodides[a]

			Isolated yield (%)		
Entry	X	R	Suzuki[b]	Sonogashira[b]	Heck[c]
1	I	OMe	91	77	91
2	I	CF_3	81	87	95
3	I	NO_2	99	92	97
4	I	Me	91	88	97
5	I	H	86	85	95

[a] Reaction conditions: aryl iodide (1.0 mmol), coupling partner (1.5 mmol), K_2CO_3 (1.5 mmol), XL-Pd plug, DMF (5 mL), air, 115 °C. [b] Phenylboronic acid or phenylacetylene, 2.8 mol% of XL-Pd plug. [c] Styrene, 0.6 mol% of XL-Pd plug.

Table 3 Various Heck reactions with XL-Pd plugs[a]



Entry	X	R	R′	Isolated yield (%)
1	I	H	Ph	92
2	I	H	C_5H_4N	97
3	I	OMe	CO_2Me	93
4	I	OMe	$CO_2{}^tBu$	79
5	I	OMe	C_5H_4N	97
6	I	OMe	Ph	91
7	Br	OMe	Ph	4

[a] Reaction conditions: aryl halide (1.0 mmol), alkene (1.5 mmol), K_2CO_3 (1.5 mmol), XL-Pd plug (0.08 mol%), DMF (5 mL), air, 115 °C.

Results were very consistent with reactions achieved with high yields and purities regardless of the substituents on the aromatic ring and again with all reactions run in air. Pd resin plugs with low Pd loadings were evaluated in Heck–Mizoroki reactions using substituted alkenes and haloarenes as summarised in Table 3. Substrates such as 4-iodoanisole underwent coupling reactions with acrylic esters (Table 3, entries 3 and 4) and aryl alkenes (Table 3, entries 5 and 6) in excellent yields, however the corresponding bromo derivatives proved difficult to couple to phenylacetylene under these conditions (Table 3, entry 7).

In summary, palladium nanoparticles, entangled in a convenient modular resin format, were prepared. The resin plug-supported Pd catalysts were successfully employed to perform Suzuki–Miyaura, Sonogashira–Hagihara and Heck–Mizoroki cross-couplings without the need of any precautions to avoid oxygen exposure and could be recycled without a major drop in efficiency. The preparation of the nanoparticles also led to some unusual shapes of palladium nanoparticle such as trapeziums and pentagons, presumably as the result of isolation mediated by the polymer within the resin bead during nanoparticle growth.

We would like to thank the EPSRC for funding and Dr Anton Page (Southampton General Hospital) for providing microscopic analysis.

Notes and references

‡ **Typical procedure for palladium-catalysed chemistries using XL-Pd resin plug**. *Synthesis of 4-methoxybiphenyl via Suzuki–Miyaura cross-coupling*. To a solution of 4-methoxyphenyl iodide (1.0 mmol) in DMF (5 mL) was added phenylboronic acid (183 mg, 1.5 mmol, 1.5 equiv.), K_2CO_3 (207 mg, 1.5 mmol, 1.5 equiv.) and 1 Pd plug catalyst (30 µmol, 3 mol%). The reaction mixture was heated at 115 °C under magnetic stirring. The Pd plug was removed from solution with tweezers, washed with DCM (10 × 6 mL) and dried in the vacuum oven at room temperature for 48 h. The reaction mixture was diluted in DCM (100 mL) and washed with 1 M HCl (pH 7). The aqueous phase was extracted with DCM (3 × 50 mL). The combined organic phases were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to yield the final product as a white solid (167 mg, 91%).

1 For reviews, see: (*a*) K. C. Nicolaou, P. G. Bulger and D. Sarlah, *Angew. Chem., Int. Ed.*, 2005, **44**, 4442; E. Negishi and L. Anastasia, *Chem. Rev.*, 2003, **103**, 1979; (*b*) C. A. McNamara, M. J. Dixon and M. Bradley, *Chem. Rev.*, 2002, **102**, 3275.

2 (*a*) C. M. Crudden, M. Sateesh and R. Lewis, *J. Am. Chem. Soc.*, 2005, **127**, 10045; (*b*) B. M. Choudary, S. Madhi, N. S. Chowdari, M. L. Kantam and B. Sreedhar, *J. Am. Chem. Soc.*, 2002, **124**, 14127.

3 (*a*) F.-T. Luo, C. Xue, S.-L. Ko, Y.-D. Shao, C.-J. Wu and Y.-M. Kuo, *Tetrahedron*, 2005, **61**, 6040; (*b*) Y. Uozumi and Y. Nakai, *Org. Lett.*, 2002, **4**, 2997; (*c*) C. A. McNamara, F. King and M. Bradley, *Tetrahedron Lett.*, 2004, **45**, 8239.

4 R. Akiyama and S. Kobayashi, *J. Am. Chem. Soc.*, 2003, **125**, 3412.

5 C. Ramarao, S. V. Ley, S. C. Smith, I. M. Shirley and N. DeAlmeida, *Chem. Commun.*, 2002, 1132.

6 B. Atrash, J. Reader and M. Bradley, *Tetrahedron Lett.*, 2003, **44**, 4779.

7 B. Atrash, M. Bradley, R. Kobylecki, D. Cowell and J. Reader, *Angew. Chem., Int. Ed.*, 2001, **40**, 938.

8 (*a*) N. Miyaura, T. Yanagi and A. Suzuki, *Synth. Commun.*, 1981, **11**, 513; (*b*) F. Bellina, A. Carpita and R. Rossi, *Synthesis*, 2004, 2419.

9 (*a*) K. Sonogashira, Y. Thoda and N. Hagihara, *Tetrahedron Lett.*, 1975, **16**, 4467; (*b*) R. R. Tykwinski, *Angew. Chem., Int. Ed.*, 2003, **42**, 1566.

10 (*a*) T. Mizoroki, K. Mori and A. Ozaki, *Bull. Chem. Soc. Jpn.*, 1971, **44**, 581; (*b*) R. F. Heck and J. P. Nolley, Jr., *J. Org. Chem.*, 1972, **37**, 2320; (*c*) I. P. Beletskaya and A. V. Cheprakov, *Chem. Rev.*, 2000, **100**, 3009.

11 J. K. Cho, R. Najman, T. W. Dean, O. Ichihara, C. Muller and M. Bradley, *J. Am. Chem. Soc.*, 2006, **128**, 6276.