

Captured and Cross-Linked Palladium Nanoparticles

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Palladium is among the most popular transition metals in modern organic synthesis and widely used for a significant number of synthetic transformations.¹ However, its use is often complicated by issues surrounding the separation of the palladium and ligands from the desired product while reuse, ideally without loss of catalytic activity, becomes a major practical and economic issue with respect to large-scale applications.

The most generally utilized methods for immobilization are physical adsorption of palladium onto a support such as charcoal, silica, or alumina,² but over the past few years, a number of groups have immobilized a variety of palladium catalysts onto a range of other insoluble supports, most notably polymers. For example palladium has been coordinated through resin-bound ligands;³ Uozumi et al reported that palladium metal (Pd(0)) could be dispersed on amphiphilic resins as nanoparticles when palladium acetate (Pd(II)), coordinated by resin-bound phosphine ligands, was reduced,⁴ while a number of passive encapsulation methods have been developed with various palladium species trapped within polymers via the interaction between palladium and the polymer backbone.⁵ However, questions must always be raised as to whether the supported palladium is truly heterogeneous or just a precursor of a homogeneous catalyst, and many results have shown that palladium-catalyzed reactions with supported palladium progress predominantly via homogeneous palladium, which "leaches" out of the support.⁶ This loss of palladium from encapsulated supports prompted us to exploit a simple alternative means to "entrap" palladium by extensive cross-linking on a well-defined commercial solid-phase synthesis resin (PS-PEG), which offers excellent mechanical properties, comes in a variety of sizes, and offers compatibility with a range of solvents.

In this report we show that soluble Pd(OAc)₂ can enter swollen resins and that amino groups on the resin can be "tied and tangled" by cross-linking, allowing permanent capture of the palladium on the resin without the assistance of any resin-bound ligand or stabilizer prior to conversion to stable palladium "nanoparticles". The resin of choice was a PS-PEG-based material, which is a well-defined material, with good handling properties and with broad solvent and pH compatibility. The resulting supported palladium was found to be highly effective for heterogeneous Suzuki coupling reactions in water, could be handled in air without precautions, and be reused without significant loss of activity.

The cross-linked resin-captured palladium (XL-RC Pd) was readily prepared by treating a mixture of aminomethylated TentaGel resin with palladium acetate (10 wt % of resin) in toluene at 80 °C for 10 min and then room temperature for 2 h to afford a brown-colored resin-captured palladium acetate. At this stage the resin was filtrated and then treated with 10% hydrazine hydrate in

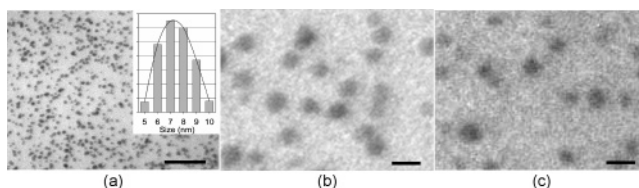


Figure 1. TEM images of cross-sectional resin beads of (a) XL-RC Pd, magnified by approximately 5×10^4 (scale bar: 100 nm) and size distribution of Pd nanoparticles; (b) original XL-RC Pd; and (c) XL-RC Pd after six reuses. Magnified by approximately 3×10^6 (scale bar: 10 nm).

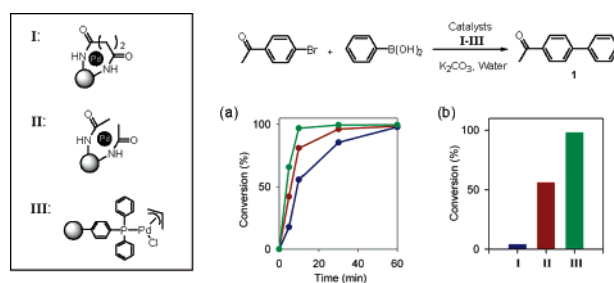


Figure 2. (a) Kinetic profiles of each supported catalyst and (b) the conversion yields following the filtration test: Catalyst **I** (blue), **II** (red), **III** (green).

methanol to give Pd(0), which at this time was black due to the trapped palladium nanoparticles, while IR analysis indicated the absence of acetate peaks (see Supporting Information).⁷ The resulting resin was cross-linked with succinyl chloride to fix the captured palladium. TEM images showed that Pd(0) nanoparticles, with an average size of 7.4 ± 1.4 nm in diameter, had formed in the resin (Figure 1).

The resulting XL-RC Pd (**I**) was then compared to acetylated resin-captured palladium without cross-linking (**II**) and palladium coordinated by resin-bound phosphine ligands (**III**) in a number of investigations to look at the relative levels of homogeneous versus heterogeneous catalysis (Figure 2).

In solution-phase aqueous Suzuki reactions,⁸ all three catalysts produced the desired biaryl product **1** in yields greater than 95% after 2 h at 80 °C, although kinetic profiles showed **I** had a slightly slower rate than that of the other catalysts (Figure 2a). To verify the amounts of active Pd species in solution during the reaction, a filtration test was carried out.^{6c} Each supported Pd catalyst was placed in water at 80 °C for 20 min and filtered off, and the still-hot filtrate was immediately used for a Suzuki cross-coupling reaction. The filtrate from **II** and **III** afforded conversions of 52% and 98%, respectively while **I** gave just 4% conversion (Figure 2b). The Pd content in the filtrate from **I** was 0.09 ppm based on elemental analysis using ICP-OES. The above results strongly suggest that minimal amounts of palladium were released into

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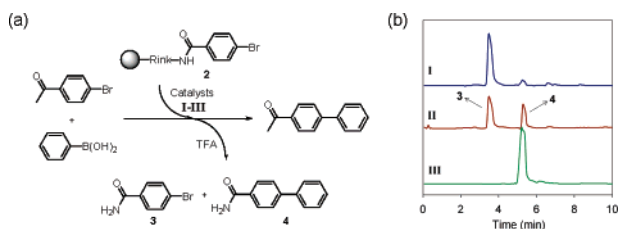


Figure 3. (a) Three-phase test methodology and (b) HPLC traces of the solid-phase Suzuki coupling products by Pd leached from the supported catalysts.

Table 1. Aqueous Suzuki Couplings with XL-RC Pd

$\text{R}_1\text{-C}_6\text{H}_4\text{-X} + \text{R}_2\text{-C}_6\text{H}_4\text{-B(OH)}_2 \xrightarrow{\text{Conditions}^a} \text{R}_1\text{-C}_6\text{H}_4\text{-C}_6\text{H}_4\text{-R}_2$									
entry st	R ₁	R ₂	X	yield ^b (%)	entry	R ₁	R ₂	X	yield ^b (%)
1	4-CH ₃ CO	H	Br	98	7	2,4-diCH ₃ O	H	Br	63
2 ^c	4-CH ₃ CO	H	Br	99	8	4-CH ₃	CH ₃ O	Br	82
3	4-NO ₂	H	Br	93	9	2-CH ₃	CH ₃ O	Br	62
4	4-CH ₃	H	Br	83	10	4-CH ₃ O	CH ₃ O	Br	91
5	2-CH ₃	H	Br	72	11	4-CH ₃ CO	H	Cl	25
6	4-CH ₃ O	H	Br	94	12	4-CH ₃	H	Cl	14

^a Aryl halide (0.5 mmol), boronic acid (0.75 mmol), K₂CO₃ (1.5 mmol), XL-RC Pd (10 mol % of aryl halide), water (2 mL), 80 °C, 4–16 h. ^b Isolated yield. ^c Microwave, 120 °C, 10 min.

solution, with the resin cross-linking suppressing the leaching of palladium from the support. This was confirmed by carrying out a solid-phase Suzuki coupling reaction with each of the three catalysts in a three-phase test (see Figure 3a).^{6a} In this case reaction would only be expected on the resin-bound 4-bromobenzamide **2** if palladium was leached into solution during the solution-phase reaction (to increase the robustness of this experiment reactions were carried out for 16 h at 80 °C). Complete conversion occurred with **III**, and 43% of the biaryl product **4** was obtained with **II**; however, only 5% of **4** was generated with **I** (Figure 3b).

Aqueous Suzuki couplings between a range of aryl bromides (which are preferred to aryl iodides due to economic concerns despite reduced reactivity) and aryl boronic acids were performed with both activated and deactivated aryl bromides and afforded good yields of products. Microwave conditions were also investigated (120 °C, SmithSynthesier), and the former overnight reaction could be accomplished within 10 min. However, the XL-RC Pd did not have any reasonable activity with aryl chlorides under these conditions (Table 1). The XL-RC Pd could be recycled six times without loss of catalytic activity, with recovery by simple filtration and washing, and gave excellent yields, with no special precautions needed with respect to handling (in air). In particular, no noticeable change in the size of Pd nanoparticles was observed by TEM after recycling (Figure 1c and see Supporting Information).

The XL-RC Pd was employed in Suzuki reactions of sulfophthalein dyes (required for sensor array-type applications) where palladium contaminants can cause serious problems in the optical properties of final product.⁹ Expectedly, the XL-RC Pd afforded the desired products without contamination and with yields comparable to those found under more conventional conditions (Table 2).

In summary, cross-linked resin-captured palladium catalysts were prepared and applied to Suzuki cross-couplings in water. These

Table 2. Suzuki Couplings with Sulfophthalein Dyes with XL-RC Pd

	R ₁	R ₂	yield ^a (%)
bromophenol blue	Br	H	41 (33)
bromocresol purple	Me	H	57 (56)
bromothymol blue	<i>i</i> -Bu	Me	28 (25)

^a Substrate (0.5 mmol), carboxyphenyl boronic acid (0.6 mmol), K₃PO₄ (1.5 mmol), XL-RC Pd (10 mol % of aryl halide), water (5 mL), microwave, 120 °C, 10 min. ^b Based on the isolated yield of the monosubstituted product and compared with yields obtained using (Pd(OAc)₂) in parentheses.

supported catalysts are predominantly heterogeneous in nature and could be recycled without loss of activity.

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Supporting Information Available: Detailed experimental procedures of TEM analysis, various tests, aqueous Suzuki coupling and their characterization data, IR spectra, SEM, TEM of XL-RC Pd. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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