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Recyclable polymer-supported Pd catalysts for aryl amination reactions

Meritxell Guinó and King Kuok (Mimi) Hii*

Department of Chemistry, Imperial College London, South Kensington, London SW7 2AZ, UK

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Abstract—Polymer-supported palladium catalysts were prepared from three commercially available phosphine-functionalised polymers (PS-PR₂), Pd₂(dba)₃ and P(*t*-Bu)₃. Catalyst stability was investigated using VT ³¹P NMR spectroscopy. One of the catalysts can be reused in the amination of bromobenzene and chlorotoluene, up to three times, without loss in yield. Recyclability of the catalysts is dependent on the method of preparation and the nature of the polymer-bound phosphine. © 2005 Elsevier Ltd. All rights reserved.

1. Introduction

Phosphine-functionalised polymer resins are commonly used as a means of support, as well as a source of ligand in many catalytic reactions.¹ For example, diphenylphosphine functionalised polymer resins **1** and **3** (Fig. 1) have been used in the immobilisation of several palladium complexes for use as heterogeneous catalysts in Heck and Suzuki-Miyaura cross-coupling reactions.² In some cases, the recovered catalysts were reported to retain activity over several repeated experiments. Nevertheless, the scope of these supported catalysts is limited to fairly activated ArX substrates, where X = I, Br or OTf. Unless the aryl group contains electron-deficient substituents, reactions with aryl chlorides are generally difficult.^{2e}

Concurrent with the discovery of catalysts that can promote reactions with unactivated and/or sterically



Figure 1. Phosphine-functionalised polymer supports.

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demanding aryl bromides and chlorides,³ attempts were made to immobilise these catalysts onto solid supports. A number of these have been successful in catalytic reactions, but very often catalyst recovery and reuse were either not discussed⁴ or unsuccessful.⁵ The most successful catalyst in this regard is that reported by Parrish and Buchwald—polystyrene-supported dicyclohexylbiphenylphosphine **4** (Fig. 1) afforded catalysts that can promote aryl amination and Suzuki reactions, using aryl iodide, bromide or chloride as starting materials. The catalyst can be successfully recycled up to three times with no significant deterioration in performance.⁶ Although this is undoubtedly impressive, the preparation of phosphine-functionalised polymer resin **4** is by no means trivial.

In a previous letter, we described the ability of the phosphine-functionalised polymers 1-3 to capture the monoligated catalyst $[Pd{P(t-Bu)_3}]$.⁷ We speculate that this could also be exploited as a means of immobilising these catalytic species. The resultant supported complex could be catalytically active via two possible mechanisms: (i) The dissociation of the coordinatively unsaturated palladium species from the polymer support, thus effecting catalytic reactions in the homogeneous phase (Scheme 1, Eq. 1); or (ii) the dissociation of the tritert-butylphosphine ligand to generate the catalytically active palladium species, which could catalyse the reaction heterogeneously (Scheme 1, Eq. 2).8 If these processes could be effected reversibly, it may be possible to develop a new type of highly active and recoverable catalyst.

Keywords: Palladium; Polymer support; Aryl amination.

^{*} Corresponding author. Tel.: +44 20 7594 1142; fax: +44 20 7594 5804; e-mail: mimi.hii@imperial.ac.uk



Scheme 1. Dissociative pathways for polymer-bound palladium catalysts.

In both of the scenarios presented above, the coordination of the palladium complex to the tethered phosphine moiety on the polymer support will be an important factor in determining the catalyst's stability, reactivity and recyclability. Herein, we report the synthesis, characterisation and catalytic behaviour of palladium catalysts derived from $P(t-Bu)_3$ and three commercially available phosphine-functionalised polymer resins PS-TPP, PS-PCy₂ and PS-CH₂PPh₂.

2. Preparation of PS-Pd catalysts

Monoligated palladium catalysts are usually generated in situ by mixing a slightly sub-stoichiometric equivalent of $Pd_2(dba)_3$ precursor and $P(t-Bu)_3$. Under these conditions, the resultant mixture is likely to consist of a series of slowly equilibrating 12- and 14-electron complexes, $Pd(PR_3)$ and $Pd(PR_3)_2$, respectively (Scheme 2).⁹

With this in mind, two methods of preparing the polymer-bound palladium catalysts were employed (Scheme 2):⁹ In the first method (A), the polystyrene-resin was added to a THF solution containing a mixture of $Pd_2(dba)_3$ and $P(t-Bu)_3$ (Pd:P ratio of 1:0.8), which was stirred gently at room temperature overnight. In the alternate procedure (B), the mixture was heated at



Scheme 2. Preparation of polymer-supported Pd catalysts. Method A: THF, rt, overnight; Method B: THF, reflux, 5–14 h.

Table 1. Pd and P loadings of polymers prepared by different methods^a

80 °C, in an attempt to promote swelling and diffusion of reagents through the cross-linked polymer, as well as to facilitate the generation of the coordinatively unsaturated species. Additionally, to elucidate the role of the tri-*tert*-butylphosphine in these catalysts, $Pd_2(dba)_3$ was also supported onto **2** and **3** using method B, in the absence of the trialkylphosphine.¹⁰

The loading, as well as the metal-to-ligand ratio of the supported catalysts were determined using %Pd and %P analyses (Table 1). Using 1 as a support, there is a noticeable decrease in the Pd:P ratio upon heating the reaction mixture from 1:4 to 1:6.5 (entries 1 and 2). In comparison, the ratio was retained at 1:3 when polymer 3 was used (entries 3 and 4). This indicates that PS-TPP 1 does not coordinate strongly to palladium(0). Using polymer 2, an initially high Pd:P ratio was obtained (entry 5), which decreased to 1:3, obtained by heating the catalyst mixture for 14 h (entries 6 and 7). As this complex [Pd(PR₃){P(t-Bu)₃}] is the bulkiest, we attributed this to the slower diffusion, dissociation and/or accommodation of the palladium complex within the macroporous structure.¹¹

3. Variable temperature³¹ P NMR

To examine the release of palladium species into the homogeneous phase, VT $^{31}P-{}^{1}H$ spectra of the immobilised catalysts were recorded in toluene[d₈] using a normal (solution-phase) NMR probe, with resin beads swollen but suspended above the magnetic coil. The NMR spectra were recorded at 10 °C intervals between ambient temperature and 100 °C, and then in reverse back to room temperature. The liberation of any phosphorus-containing moieties into the solution phase would thus be indicated by the observation of corresponding resonance signals. Visual inspection of the NMR samples after these experiments could also reveal signs of catalyst decomposition, such as the development of colour (green or pink/red) and/or the formation of palladium black.

Substantial catalyst leaching and/or decomposition were observed for all the catalysts prepared at room temperature (method A). These were indicated visually, and/or

	÷					
Entry	PS	Method	T/h	Pd loading ^b	P loading ^c	Pd:P
1	TPP	А	14	0.43	1.77	1:4
2	TPP	В	5	0.22	1.43	1:6.5
3	CH ₂ PPh ₂	А	14	0.50	1.50	1:3
4	CH_2PPh_2	В	5	0.37	1.06	1:3
5	PCy ₂	А	14	0.52	0.17	3:1
6	PCy ₂	В	5	0.15	1.14	1:7.5
7	PCy ₂	В	14	0.36	1.04	1:3
8	$CH_2PPh_2^d$	В	14	0.53	2.61	1:5
9	PCy_2^d	В	14	0.56	2.42	1:4

^a Loading of commercial PS-TPP, PS-CH₂PPh₂ and PS-PCy₂ resins were 1.39, 1.37 and 1.24 mmol/g, respectively, as specified by the manufacturer. ^b mmol Pd/g, calculated from %Pd determined by ICP-AES analysis.

^c mmol P/g, calculated from %P determined by elemental analysis.

^d No $P(t-Bu)_3$ added.

by the observation of the emergence of 31 P resonances over the course of the VT experiment.

In contrast, catalysts prepared using method B were noticeably different. The PS-TPP supported catalyst showed a distinct δP resonance signal at +25 ppm even at room temperature, which persisted in solution over the VT experiment. With the sample containing PS-CH₂PPh₂, the emergence of this peak was only observed at 100 °C. Upon cooling to room temperature, the resonance signal disappeared, but the retrieved sample showed the deposition of palladium black, indicating that the decomposition is irreversible. Lastly, the catalyst generated from PS-PCy₂ (prepared by heating for 14 h) was found to be the most stable—no ³¹P resonance signals could be detected during the VT experiment. Furthermore, the solution remained colourless.

These VT ³¹P NMR experiments provided several valuable insights. Namely, they revealed that the stability of these PS-supported catalysts is not only dependent upon the nature of the phosphine moiety on these supports, but also on the way they are prepared. Furthermore, it suggested that catalysis is likely to occur heterogeneously (i.e., Scheme 1, Eq. 2), since we did not observe any reversible formation of palladium complexes in the homogeneous solution.

4. Catalytic behaviour

The catalytic activity of the supported catalysts was initially assessed in the arylamination reaction between bromobenzene and aniline (Scheme 3, Table 2).¹²

PhBr + PhNH₂
$$\frac{\text{PS-Pd} (2 \text{ mol}\%)}{t\text{-BuONa, toluene}}$$
 Ph₂NH
80 °C, 24 h

Scheme 3. Aryl amination of bromobenzene.

All of the polymer-bound catalysts exhibited catalytic behaviour at 80 °C, with bromobenzene being converted smoothly into diphenylamine. At the end of the reaction, each catalyst was recovered by filtration, rinsed and dried, before it was used in another reaction.

Catalysts derived from PS-TPP were catalytically active in the first cycle. Even though the sample prepared using method A had a higher %Pd, it afforded a lower % conversion than the catalyst prepared by heating (entries 1 vs 2). Both were completely inactive in the second catalytic cycle, even though there was a substantial amount of Pd present in the recovered resin (4.23%, entry 1), suggesting that the catalysts had become deactivated during the process.

The recovered catalyst derived from $PS-PPh_2$ contained a much reduced amount of palladium, which is attributed to the catalyst leaching during the first catalytic run. The recovered catalysts afforded good conversion in the second run (entries 3 and 4). Nevertheless, the products were found to contain some unidentified impurities, which could have arisen due to catalyst degradation.

In dramatic contrast, the catalyst prepared from PS- PCy_2 by method B (with prolonged heating) could be reused up to three times without compromising product formation and selectivity, while the samples prepared by method A, or method B with insufficient heating, were not recyclable (entries 5–7).

The trialkylphosphine ligand is clearly necessary, as the palladium catalysts generated from 2 and 3 with the metal precursor alone were not as catalytically active and were not reusable (entries 8 and 9).

The recyclability of the catalysts prepared from 2 is obviously dependent on the way they are prepared. We speculate that by heating the catalyst mixture, diffusion of the palladium complex to the binding sites within the polymer structure is thus promoted. Once there, the

Entry	PS	Method	T/h	First catalytic run		Second catalytic run		Third catalytic run	
				% Pd ^b	% Conversion ^c	% Pd ^b	% Conversion ^c	% Pd ^b	% Conversion
1	PS-TPP	А	14	4.62	72	4.23	0		
2	PS-TPP	В	5	2.33	95		0		
3	PS-PPh ₂	А	14	5.27	100	4.80	100 ^d		
4	PS-PPh ₂	В	5	3.89	100		100 ^d		
5	PS-PCy ₂	А	14	5.49	>95	4.96	0		
6	PS-PCy ₂	В	5	1.57	100		0		
7	PS-PCy ₂	В	14	3.87	100	3.69	100	3.22	100 ^e
8	PS-PPh ₂ ^f	В	14	5.62	>95		0		
9	PS-PCy ₂ ^f	В	14	5.97	64		0		

Table 2. Catalytic reactions with polymer-supported palladium catalysts^a

^a Reaction conditions: PS-Pd catalyst (2 mol %), bromobenzene (1 mmol), aniline (1 mmol), sodium *tert*-butoxide (1.5 mmol), toluene (2 mL), 80 °C, 24 h.

^bAs determined by ICP-AES analysis before the catalytic reaction/recovered from the previous reaction.

^c% conversion of bromobenzene as determined by GC.

^d Product contains by-products.

^e Reaction time: 36 h.

^f No $P(t-Bu)_3$ added.



Scheme 4. Aryl amination of an aryl chloride.

catalyst is effectively encapsulated within the crosslinked structure of the polymer, thus protected against atmospheric degradation, for example, during the recovery process, compared to catalysts bound on the surface. Other effects may also be exerted by the macroporous structure, such as the 'confinement effect',¹³ which could control the rate of diffusion of tri-*tert*-butylphosphine from the reactive site, thus enhancing stability.

Despite the great number of solid-supported palladium catalysts reported in the literature, very few are able to catalyse the reaction of aryl chlorides. With this in mind, the most active catalyst identified from the above study was used to catalyse the addition of morpholine to the relatively unactivated aryl halide substrate, 4-chlorotoluene (Scheme 4). Gratifyingly, the reaction proceeded under relatively mild reaction conditions. Furthermore, the catalyst could be reused, and product yield remained unaffected over two runs.

In summary, we have synthesised a new class of supported PS-Pd-P(t-Bu)₃ catalysts from readily available phosphine and polymer supports. The catalysts were active in the aryl amination reaction, and the stability and recyclability were dependent on the nature of the polymer-supported phosphine moiety, as well as on the way they are prepared. The palladium catalyst immobilised with the dicyclohexylphosphine-functionalised support displayed the best turnovers, and preliminary studies showed that it can be used to catalyse amination reactions of aryl bromides and chlorides, and can be reused up to three times with no apparent loss in catalyst activity. We are currently investigating the nature of the palladium catalyst present in these polymer resins in greater detail. Further applications in other palladiumcatalysed processes will be reported in due course.

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- Method A: PS-PCy₂ (1.24 mmol/g, 500 mg, 0.62 mmol), Pd₂(dba)₃ (214 mg, 0.207 mmol), P(*t*-Bu)₃ (10 wt% in hexane, 0.670 mL, 0.33 mmol) and anhydrous THF (10 mL) were placed in a round bottom flask under an atmosphere of N₂. The mixture was swirled in an orbital shaker at rt overnight. The beads were filtered off, transferred to a sintered Alltech tube and washed with acetone/CH₃OH/H₂O (1:1:1) (5 mL × 5), acetone/CH₃OH (1:1) (5 mL × 5), acetone (5 mL × 5), ethyl acetate (5 mL × 5), CH₂Cl₂ (3 mL × 5) and finally HPLC-grade pentane (5 mL × 5). The dark-coloured beads were then dried under vacuum at 50 °C for 2 h.

Method B: PS-PCy₂ (1.24 mmol/g, 300 mg, 0.372 mmol), Pd(dba)₂ (143 mg, 0.248 mmol) and P(*t*-Bu)₃ (10% wt in hexane, 400 μ L, 0.198 mmol) and anhydrous THF (8 mL) were placed in a Radley's carousel reaction tube under an atmosphere of N₂. The mixture was heated at 80 °C overnight. After cooling, the beads were stirred for a further 2 h and then collected into a sintered (Alltech) tube and subjected to washings as stated in the previous method. The dark brown beads were dried under vacuum at 50 °C for 2 h.

- 11. During the reviewing process, one referee commented on some unusual values presented in Table 1—entries 5 (low P loading), 8 and 9 (high P loadings)—compared to original loading of the polymer beads (given in footnote 'a'). We do not have a reasonable explanation for this at this juncture. Given that the elemental analyses were carried out, in duplicate, by professional services on the same batch of resins, we have no reason to doubt their accuracy. One possibility is that the loading values provided by the commercial supplier were erroneous. The coordination sphere of immobilised Pd is currently being examined by other techniques, and results will be reported in due course.
- 12. Reactions were performed in parallel in a Radley's 12placed reaction carousel. Typical catalytic procedure: A reaction tube was charged with bromobenzene (106 μ L, 1.0 mmol), aniline (91 μ L, 1.0 mmol), sodium *tert*-butoxide (150 mg, 1.5 mmol) and the appropriate catalyst (2 mol%). Anhydrous toluene (2 mL) was added and the reaction mixture was stirred at 80 °C for 24 h. The progress of the reaction was monitored by GC.
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