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# Modified mesoporous materials as Pd scavengers and catalyst supports\*

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*Abstract*: The use of mesoporous molecular sieves (MMSs) modified by mercaptopropyl trimethoxysilane (MPTMS) to scavenge Pd is described. The ordered mesoporous material displays excellent ability to remove Pd from organic and aqueous solutions. After only one treatment, a 500-ppm solution of  $PdCl_2$  in water can be reduced to 1 ppb. In addition, the resulting material is an effective, leach-proof catalyst for the Suzuki–Miyaura and Mizoroki–Heck reactions. Thus, the Suzuki–Miyaura reaction can be conducted in water at 80 °C with as little as 3 ppb Pd leaching. Hot filtrations and three-phase tests confirm that the catalyst acts without leaching Pd from the surface.

*Keywords*: palladium; ordered materials; coupling reactions; heterogeneous; SBA-15; micelle-templated materials.

## INTRODUCTION

The development of heterogeneous Pd catalysts for industrially important reactions, such as coupling reactions, is a long-standing goal in organic chemistry because of the significant contamination problems posed by Pd in the pharmaceutical industry [1]. Thus, a variety of strategies have been employed to immobilize Pd for recovery and reuse [2]. The most commonly employed heterogeneous Pd catalyst is undoubtedly Pd on carbon. Much like Pd on silica, Pd/C is believed to act as a reservoir of soluble Pd, which is the true catalytic species [3]. Arai [4–7] and Kohler [8–10] independently and convincingly demonstrated that reactions with these catalysts proceed via Pd that has leached from the surface. By determining the Pd content of the solution during reaction, a direct correlation between soluble Pd and reaction conversion was demonstrated. These studies also illustrated the important effect known as redeposition [11], where soluble metal present in solution redeposits on the support at the end of the reaction. This effect is often observed indirectly, since reactions that do not proceed to completion are more prone to Pd contamination.

The redeposition of Pd is likely tied to the consumption of aryl halide at the end of the reaction. There is considerable evidence that the cause of Pd leaching, in addition to simple ligand breakdown, is the oxidative addition of the aryl halide to Pd(0) forming soluble ArPdX species [2,12]. Thus, when the aryl halide is no longer present, the Pd does not have any ligands to solubilize it, causing redeposition on the support. This hypothesis has support from the work of Reetz and Westermann [12], who

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showed that Pd nanoparticles can be dissolved by treatment with aryl iodides, resulting in production of species with a general structure of either ArPdI or  $[ArPdI_3]^{2-}$ .

In addition to the use of Pd supported directly on inorganic supports such as carbon and silica, virtually all common ligands for transition metals including phosphines, carbenes, amines, sulfides, thiols, pyridines, nitriles, and polyenes have been employed in an attempt to immobilize Pd [2,13]. A significant drawback of all of these methods is the need to independently prepare modified ligands in order to introduce a second, remote site for attachment of the ligand to the support of interest. This dramatically increases the effort required to prepare the supported catalyst, but the direct mimicry of solution-phase ligands is the most intuitively satisfying approach to the design of supported catalysts. Despite this fact, the large majority of these catalysts has also been shown to be merely reservoirs of soluble, ligand-free Pd [2].

An interesting case is that of multidentate charged ligands, including palladacycles and pincer ligands such as **1** and **2**, which can be modified and immobilized on a solid support (Chart 1). The high catalytic activity of these structures, both in solution and on support, raised considerable debate about the possibility of a Pd(II)–Pd(IV) catalytic cycle [14–16] in order to account for catalysis via an intact Pd–ligand complex. Despite the very high activity of these catalysts, with turnover numbers (TONs) of up to  $10^{10}$  reported, careful studies by several groups have shown definitively that all palladacycles [17–22] and pincer complexes [2,23–26] act by slow release of ligand-free Pd. The high catalytic activity is proposed to come from the fact that Pd is released into solution slowly and at very low concentrations, where it is stable toward decomposition by agglomeration to Pd black or other metallic forms of Pd.



Chart 1 Palladacycle and pincer-type Pd catalysts.

The concept of the slow release of catalytically active Pd has been exploited by de Vries et al. (Scheme 1) [27–30]. In this approach, no effort is made to contain the Pd, but rather Pd nanoparticles are treated under conditions where slow release of Pd into solution creates a highly active catalyst. In this approach, higher catalytic activity is observed when low concentrations of Pd are employed since this shifts the equilibrium away from the Pd nanoparticles and toward soluble Pd species. Depending on the ability of the organic product in question to absorb the Pd, this may be a good approach to catalysis with Pd since only very low levels of Pd are released into solution. In a similar vein, Gladysz commented that developing a catalyst with high turnover frequency (TOF), in other words, one that functions at low loadings, is a more important and likely more attainable goal than developing catalysts that are truly heterogeneous [31].

Other nontraditional methods to support Pd include the use of microencapsulated or microencarcerated Pd by Kobayashi et al. [32,33] and the use of polyoxometallates as supports by Ley et al. [34], although the latter has been clearly shown by Ley and Smith [35] to be a reservoir for soluble Pd.

Thus, with the prospects for the preparation of truly heterogeneous supported Pd catalysts seeming particularly bleak, we embarked on a study of the ability of thiol-modified mesoporous molecular sieves (MMSs) to act as scavengers of Pd left behind after coupling reactions. During this study, we also found that the scavenged material, which employs a simple, cheap, commercially available thiol ligand, provides what appears to be a leach-proof heterogeneous catalyst [36].



Scheme 1 Generation of soluble Pd from Pd nanoparticles, c.f. deVries et al. [29].

## **RESULTS AND DISCUSSION**

#### Palladium scavenging

MMSs are silicaceous materials prepared by hydrolysis and surfactant-templated condensation of silica monomers such as Si(OEt)<sub>4</sub>, among others (Scheme 2) [37]. After removal of the surfactant, the resulting materials have high long-range order with cubic, hexagonal, or lamellar space groups. The most appealing feature of the materials from our perspective is their large, monodisperse pores (20–300 Å) and their high surface areas, up to 2000 m<sup>2</sup>/g. These characteristics provide the possibility of tethering large complexes to the surface and providing access to these complexes through the large pores. Many different surfactants can be employed to produce these materials, but the ones we have employed are block-copolymer-based since these give materials with the greatest hydrothermal stability, thickest walls, and large pores on the order of 70–100 Å.



Scheme 2 Preparation of MMSs by surfactant-templating and functionalization of their surfaces.

The inspiration to employ thiol-modified molecular sieves as Pd scavengers came from the work of Fryxell [38] and Pinnavaia [39], who independently showed that these materials were extremely effective at scavenging mercury from simulated waste water. Relative to amorphous silica modified with the same thiol (mercaptopropyl trimethoxysilane, MPTMS **3**), the mesoporous material had a greater capacity, which was attributed to improved access of the solution to all of the thiols [39]. The two groups used different approaches for the immobilization of the thiol on the surface, co-condensation and post-synthesis grafting (Scheme 3).

Pinnavaia and Mercier used the co-condensation method in which the MPTMS is added directly to the synthesis mixture along with  $Si(OEt)_4$  and the surfactant P123 (Pluoronic-123) [40]. Liu and Fryxell introduced the thiol by exposing the mesoporous silicate first to water to form a hydration layer, and then to MPTMS [38]. Using this method, very high loadings of thiol were obtained since co-condensation likely occurred in the hydration layer as well as directly with the surface. Both materials were shown to be highly effective at adsorbing mercury from aqueous solutions in the presence of a variety of other common contaminants such as sodium. Following on this work, Walcarius and others have carried out a series of detailed studies aimed at elucidating the effect of the support and the various conditions on the uptake of mercury into mesoporous silicates [41,42]. C. M. CRUDDEN et al.



Scheme 3 Functionalization routes for the preparation of metal scavengers.

Within the context of this work, we prepared thiol-modified mesoporous materials by the grafting technique, although prehydration of the surface was not employed, and so thiol loadings on the order of 2 mmol/g were obtained [36]. As shown in Fig. 1, the resulting mesoporous silicate (MMS-SH) was much more effective at removing Pd from solution than unfunctionalized MMSs, Montmorillonite clay, and amorphous silica gel surface modified with MPTMS (SiO<sub>2</sub>–SH).





This latter material was the closest to the mesoporous silicate in terms of effectiveness, and so its scavenging ability is compared with the mesoporous silicate in Table 1 and Fig. 2. The uptake of Pd in the +2 oxidation state was on the same order of magnitude for high initial loadings of Pd. Thus, at 1500–2000 ppm Pd, both materials absorbed on the order of 90 % of the Pd charge. However, starting with a Pd concentration of 1000 ppm or less, the mesoporous material had a definite advantage over the amorphous silica, absorbing over 99.9 % of all Pd present and leaving the solution at less than 1 ppm Pd. By comparison, a solution with the same initial Pd concentration treated with amorphous silica-thiol still had 67 ppm Pd present. Although some of this difference is attributable to the higher loading of thiol on the mesoporous material compared with amorphous silica (2.2 mmol/g compared with 1.3 mmol/g), the amorphous silica thiol does not achieve the same magnitude of Pd scavenging until very low initial concentrations of Pd are employed (ca. 100 ppm, entry 7, Table 1).

Entry	Initial [Pd]	After treatment; mesoporous silica <sup>b</sup>		After treatment; amorphous silica <sup>c</sup>	
	(ppm)	[Pd] (ppm)	% removed	[Pd] (ppm)	% removed
1	2120	152	92.85	193	90.93
2	1590	111	93.05	142	91.10
3	1060	0.908	99.91	67.42	93.66
4	848	0.0052	99.9994	4.17	99.51
5	530	0.0011	99.9998	1.16	99.78
6	265	0.0005	99.99998	-	_
7	106	0.00037	99.9996	0.0024	99.998
8	530 <sup>d</sup>	0.12 <sup>e</sup>	99.977	_	_
9	530 <sup>d</sup>	0.096 <sup>b</sup>	99.982	_	-

able i Scavenging of i u with unor-functionalized mesoporous and amorphous sineates.	<b>Fable</b>	1 Scavenging	of Pd with	thiol-functionalized	mesoporous and a	umorphous silicates. <sup>a</sup>
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<sup>a</sup>Aqueous solutions of  $PdCl_2$  (10 mL) treated with 100 mg of silicate for 1 h with stirring unless otherwise noted.

<sup>b</sup>Grafted mesoporous silica with MPTMS loading of 2.2 mmol/g.

<sup>c</sup>Grafted amorphous silica with a loading of 1.3 mmol/g.

 ${}^{d}\textrm{Pd}(\textrm{OAc})_{2}$  in THF was employed in place of  $\textrm{PdCl}_{2}$  in water.

eThiol-containing mesoporous silica prepared by co-condensation with loading of 1.0 mmol/g.



Fig. 2 Scavenging of Pd using thiol-modified MMSs with detection via atomic absorption.

The increased effectiveness of the mesoporous scavenger at <1000 ppm initial concentration may be attributed to the ratio of sulfur on support to Pd in solution. Under scavenging conditions (100 mg of material used to treat 10 mL of solution for 1 h), the S:Pd ratio is exactly 2:1 at 1000 ppm. From this, we infer that this ratio is the most effective at removing Pd. Obviously, the material has a greater overall capacity based on the results with 2000 ppm, but for complete Pd removal, the 2:1 ratio seems optimum.



Fig. 3 Scavenging of Pd using thiol-modified MMSs with detection via ICPMS.

The magnitude of the scavenging power of the material is illustrated by the results at  $[Pd]_{init}$  of 500 ppm, where the solution after scavenging contained only 1.1 ppb, corresponding to a 500 000-fold reduction in Pd content after only one treatment (Fig. 3). By comparison, amorphous silica treatment left the solution at 1 ppm, 1000 times more concentrated than the solution treated with the mesoporous scavenger.

Mesoporous materials in which the thiol was incorporated by a co-condensation method were also prepared and tested (Table 1, entry 8). These materials showed a remarkable ability to take up Pd. In tetrahydrofuran (THF), where the uptake is overall less efficient, the so-called "sol-gel-incorporated" material converted a 500-ppm solution to a 120-ppb solution, corresponding to an overall 99.977 % removal of Pd. The grafted thiol described in Table 1 took up 99.982 % of Pd, resulting in a 96-ppb solution. Remarkably, the sol-gel-incorporated material had a loading of 1 mmol/g compared to the grafted at 2.2 mmol/g. Thus, despite having less than half the thiol content, the sol-gel material had virtually the same activity as a scavenger.

In addition to scavenging Pd in the +2 oxidation state, scavenging of Pd(0) is also important since Pd is often in this state during and after coupling reactions. Thus, solutions of two common Pd(0) sources, Pd(dba)<sub>2</sub> and Pd(PPh<sub>3</sub>)<sub>4</sub>, were treated with the thiol-modified mesoporous silicate. Although Pd(dba)<sub>2</sub> was effectively taken up by the scavenger (500 ppm was reduced to 0.2 ppm corresponding to removal of 99.96 %), Pd(PPh<sub>3</sub>)<sub>4</sub> was not. Treatment with the ordered silicate left 116 ppm of Pd in solution and amorphous silica left 211 ppm. In these last cases, the scavenging solution turned dark brown/black upon addition of the thiol, indicating that an unwanted reaction had taken place, which may explain the ineffectiveness of the scavenger.

Thus, with the exception of removing  $Pd(PPh_3)_4$ , our scavenger appears to be competitive with Smopex<sup>TM</sup> fibers [43], and have significant advantages over polystyrene-based scavengers such as MP-TMT (macroporous polystyrene-2,4,6-trimercaptotriazine) [44] where long reaction times (up to 32 h) and excesses of scavengers are required [1].

## CATALYSIS

Having demonstrated that thiol-modified mesoporous materials are able to absorb significant quantities of Pd from solution, we then examined the ability of these materials to actually catalyze coupling reactions after adsorption of Pd. Although thiols and sulfur-containing ligands are often believed to be poisons for Pd [45], the reaction proceeded cleanly in water, DMF, or mixtures of the two solvents, *without leaching discernable amounts of Pd* [36]. As shown in Table 2, the reaction between 4-bromoacetophenone and phenylboronic acid [46] in water was complete after 5 h and the resulting solution contained only 3 ppb of Pd after filtration through a Teflon filter. Since the concentration of Pd in the resulting solution is dependent on the amount of solvent, the Pd leaching is also given as a percentage of the initially added Pd. In this case, 0.001 % of the initially added 1 % of Pd leached from support. This corresponds to a total of approximately 1  $\mu$ g of Pd.

Table 2 Suzuki–Miyaura coupling with mesoporous and amorphous silica-SH·Pd.

$R \xrightarrow{X} + PhB(OH)_2 \xrightarrow{Silica-SH-Pd}_{K_2CO_3} \xrightarrow{Ph}_{R} \xrightarrow{Ph}_{(eq. 1)}$						
Entry	Substrate (R, X)	Silica source	Conditions	Solvent	Conversion (yield), (%)	Pd leaching (%, ppm) <sup>b</sup>
1	CH <sub>3</sub> CO, Br	mesoporous	5 h, 80 °C	H <sub>2</sub> O	99 (98)	0.001, 0.003
2	CH <sub>3</sub> CO, Br	mesoporous	2 h, 100 °C	H <sub>2</sub> O	97	0.04, 0.09
3	H, Br	mesoporous	8 h, 80 °C	DMF/H <sub>2</sub> O <sup>c</sup>	99	0.009, 0.02
4	CH <sub>3</sub> CO, Br	mesoporous	8 h, 80 °C	H <sub>2</sub> O <sup>2</sup>	99 (97)	0.04, 0.09
5	H, Čl	mesoporous	24 h, 80 °C <sup>d</sup>	H <sub>2</sub> O	93 (80)	0.019, 0.08
6	CH <sub>2</sub> CO, Br	mesoporous	8 h, 80 °C	DMF	96 (94)	0.35, 0.75
7	$CH_3CO, Br$	amorphous	8 h, 80 °C	DMF	33 (31)	0.61, 1.30

<sup>a</sup>Unless otherwise noted, reaction conditions are: 1 % cat. 8 h, 80 °C. Conversions and yields are determined by GC vs. internal standard unless otherwise noted.

<sup>b</sup>As a % of the initially added Pd, and the ppm of the filtrate, determined by ICPMS.

<sup>c</sup>DMF/H<sub>2</sub>O in a 20:1 ratio.

<sup>d</sup>2 % catalyst.

As shown in Table 2, the amount of Pd that leaches during reactions in water or DMF/water, is relatively consistent between 0.019 at the highest and 0.001 ppb at the lowest (entries 1–5). Higher leaching was observed in pure DMF (entry 6), but still less than 1 ppm was observed in solution. Amorphous silica functionalized with MPTMS had significantly lower activity than the ordered silicate, entry 7.

Table 3 shows the substrate scope for the reaction, including the fact that aryl chlorides react, albeit at higher temperatures (100  $^{\circ}$ C) and longer reaction times.

In addition to being active for the Suzuki–Miyaura reaction, the thiol-modified material was also an active catalyst for the Mizoroki–Heck reaction as shown in Table 4. We examined both the thiolmodified material described above and a material prepared by grafting aminopropyl triethoxysilane on the surface of the silicate. Although this material absorbed Pd and generated an active catalyst (entries 4 and 5), Pd leaching was severe. After the reaction, the solution contained 35 ppm of Pd, which corresponded to over 10 % of the initially added Pd. In contrast, the thiol-modified material left only ca. 0.2 ppm of Pd in solution at the end of the coupling reaction.

Various forms of Pd could be used to load the silicates with little effect on the catalytic activity, Table 5. The low yield observed in entry 2 using  $PdCl_2$  as the Pd source was due to its low solubility in THF. When water was employed as the solvent to load the Pd, high activity was observed in the result-

Entry	Substrate	Solvent	Conv. (yield), %
1	4-chlorobenzene	DMF	(67) <sup>b</sup>
2	4-chloroacetophenone	H <sub>2</sub> O	99 (96) <sup>b</sup>
3	3-bromopyridine	DMF/H <sub>2</sub> O	99 (98)
4	4-bromotoluene	$DMF/H_2O$	(82) <sup>b</sup>
5	4-bromoanisole	H <sub>2</sub> O	99 (96) <sup>b</sup>
6	4-bromobenzaldehyde	H <sub>2</sub> O	99 (97) <sup>b</sup>

Table 3 Substrate scope for the Suzuki-Miyaura coupling.<sup>a</sup>

<sup>a</sup>Reactions performed using phenyl boronic acid (1.5 equiv) at 90 °C for 15 h with 1 % catalyst, and at 100 °C for 24 h with 2 % catalyst for chloroarenes. <sup>b</sup>Isolated yields.

Table 4 Thiol-modified Pd catalysts for the Mizoroki-Heck reaction.<sup>a</sup>

	R +	Ph MMS-XH•Pd NaOAc, DMF 120 °C, 15 h Pt	R	(eq. 2)
Entry	Substrate (R/X)	Catalyst (loading)	Conversion (yield), (%)	Pd leaching (ppm)
1	H/Br	MMS-SH·Pd (1 %) <sup>b</sup>	98 (95)	<2 <sup>c</sup>
2	COMe/Br	MMS-SH·Pd (0.5 %)	99 (96)	0.23 <sup>d</sup>
3	COMe/Br	Reuse (entry 3, 0.5 %)	98 (93)	0.27 <sup>d</sup>
4	H/I	MMS-NH <sub>2</sub> •Pd (1 %)	99 (96)	n.d.
5	H/Br	$MMS-NH_2^{-} \cdot Pd (1.5 \%)$	99 (97)	35°

<sup>a</sup>Unless otherwise noted, reaction conditions are: 120 °C, 1 mmol of halide, 1.5 mmol olefin, 2 mmol NaOAc, DMF, 15 h.

<sup>b</sup>MMS = mesoporous molecular sieve.

<sup>c</sup>Determined by atomic absorption.

<sup>d</sup>Determined by ICPMS.

**Table 5** Effect of Pd source on reactivity in the

 Suzuki–Miyaura coupling.<sup>a</sup>

Entry	Pd Source	Solvent <sup>b</sup>	Yield (%) <sup>c</sup>
1	$Pd(OAc)_2$	THF	96
2	PdCl <sub>2</sub>	THF	1
3	$PdCl_{2}$	H <sub>2</sub> O	78
4	Pd(dba) <sub>2</sub>	TĤF	66

<sup>a</sup>For the reaction of 4-bromoacetophenone with the pinacol ester of phenyl boronic acid under conditions outlined in Table 1.

<sup>b</sup>Solvent employed for loading the material with Pd. <sup>c</sup>GC yield vs. internal standard.

ing materials. Interestingly, somewhat lower activity was observed when  $Pd(dba)_2$  was employed as the Pd source. Since Pd is already in the (0) oxidation state, one might expect that the reaction would be more efficient. Although we are currently examining these different materials to determine whether or not there is a difference in the kinetics of the reaction at low conversion [i.e., the presence or absence of an induction period for the Pd(II) vs. Pd(0) species], these results imply that reduction to Pd(0) is not a difficult process under our reaction conditions.

#### Leach-proof Pd catalysts

### **POSITION OF THIOL**

In order to determine whether there is any difference in reactions taking place on the interior thiols compared to the exterior thiols, we are investigating the effect of introducing a protecting group on the exterior of the mesoporous silicate before extracting the polymeric template. After removing the template, the thiol is introduced to the interior of the silicate. Materials prepared in this way were treated with Pd, and the resulting complex was active for the coupling of 4-bromoacetophenone and the pinacol ester of phenyl boronic acid. Current studies are directed toward assessing the leaching and Pd mobility in these materials to more completely determine the effect of confinement.

## **HETEROGENEITY TESTS**

In order to determine whether or not the catalyst, or a portion thereof, is truly heterogeneous, we have performed a number of heterogeneity tests [36]. Firstly, Pd leaching was assessed during the reaction to determine whether or not there is a spike in Pd content of the solution, and this was found not to be the case. The Pd level of the solution was found to be the same within error when the reaction was stopped at 42 and 62 % conversion in water, and similarly at 22, 56, and 98 % conversions in DMF/water with phenyl boronic acid as the coupling partner.

As a second test, a series of hot filtrations were performed to look for the presence of soluble, catalytically active Pd species. In the first experiment, the reaction was allowed to proceed for 3 h before being split into two fractions, one containing the suspended catalyst and the other filtered to remove any solid catalyst. The reaction was run in DMF in the glove box to prevent any difficulties with oxygenpromoted deactivation of the catalyst. If the catalyst is truly heterogeneous, filtration should remove all of the catalyst, and the conversion in the filtered flask should not increase past the point of the split. This sequence, shown as the first entry in Fig. 4, indicated that very little activity remained in the filtered solution. At the time of the filtration, the conversion was 29 %. After an additional 5 h, the reaction containing the suspended catalyst went on to 95 % conversion, while the portion that had been filtered progressed only an additional 1 to 30 %.

However, concern about the solubility of some of the reagents,  $PhB(OH)_2$  and  $K_2CO_3$  in pure DMF, caused us to repeat the same reaction scheme in DMF/H<sub>2</sub>O, 4/1 in case these critical reagents were removed during the filtration. In 4/1 DMF/H<sub>2</sub>O, an additional 5 % reaction was observed in the filtered portion. In a final experiment (designated by an asterisk in Fig. 4),  $PhB(OH)_2$  and  $K_2CO_3$  were added to the second flask prior to filtration of the reaction mixture. This experiment also gave rise to an increase in conversion of between 4 and 5 %. These results indicate the presence of small amounts of active catalyst in the solution phase. However concern over the fast re-precipitation of Pd which would invalidate these types of tests [2,7,11] led us to perform a three-phase test as described below.

Three-phase tests are among the most definitive tests for catalysis by soluble, leached Pd species [47,48], but the manner in which they are performed is critical for correct interpretation. The test involves chemically tethering one of the two reactants, usually the aryl halide, to an insoluble support, which forms one of the three phases. The second phase is then the catalyst, which is immobilized on a different support, and the third phase is the solution, which contains all other necessary reagents. It is here where the nature in which the test is performed becomes critical.

As noted previously, Arai [4–7] and Kohler [8–10,49] demonstrated that it is likely exposure to the aryl halide that initiates dissolution of Pd from support by oxidative addition to form an aryl Pd(II) species. Reetz et al. also demonstrated that treatment of Pd nanoclusters with stoichiometric amounts of aryl iodides causes dissolution of the nanoparticles and formation of what is believed to be either ArPdI or  $[ArPdI_3]^{2-}$  [12]. Thus, it is critical in the three-phase test to either (1) immobilize the aryl boronic acid and use a soluble aryl halide; or (2) add soluble aryl halide to the reaction mixture in addition to the supported aryl halide. This latter method adds the additional check that the generation of



Fig. 4 Hot filtration tests for determination of heterogeneity.

an active catalyst can be assessed by the presence of product resulting from reaction of the soluble aryl halide.

An example of the effect of addition of soluble reagents to the three-phase test can be found in a publication by Davies et al., who were investigating the methoxy carbonylation of vinyl bromide **3** catalyzed by Pd/C (eq. 4) [50]. Large amounts of Pd (200 ppm) were found in the product of the reaction and analysis of the reaction mixture after simple filtration indicated that 25 % of the initially added Pd had leached.



A three-phase test was devised to determine whether the leached Pd was in fact responsible for the observed catalytic activity. Thus, an aryl iodide was tethered to a Novosyn TGR resin and the resulting supported iodide **5** was subjected to the reaction conditions. Using Pd/C as the catalyst, no reaction was observed on support, seemingly indicating that the reaction was truly heterogeneous (eq. 5) [50].



However, when the same reaction was performed *in the presence of added soluble bromide* **3**, quantitative conversion of supported aryl iodide **5** was observed, indicating that a homogeneous catalyst had been generated (eq. 6). Like bromide **3**, iodobenzene was also effective at solubilizing Pd from the support and affecting complete conversion of the supported iodide **5**. Thus, the importance of adding soluble aryl halide during this test cannot be overstated.



Following on these results, and those of Corma et al. [18,51], we prepared supported aryl halides by reaction of the corresponding 4-haloaroyl chlorides with silica gel that had been functionalized with aminopropyl triethoxysilane. The resulting amides were then subjected to the reaction conditions in the presence of soluble aryl halide: 4-bromoacetophenone or 4-chloroacetophenone (Scheme 4). After reaction, the soluble fraction was analyzed for the expected coupling product **6**, providing evidence that an active catalyst had been generated and the solid was treated with 2 M NaOH in EtOH/H<sub>2</sub>O to affect hydrolysis of the amide bond. The presence of compound **7** would then indicate coupling from leached Pd, while **8** is indicative of unreacted supported aryl halide.



Scheme 4 Three-phase test to determine extent of heterogeneity.

As shown in Table 6, in the case of 4-chloroacetophenone, no coupling was detected on support, indicating that an active catalytic species had not leached from support. In the case of 4-bromoacetophenone, under our standard conditions, only 50 % conversion was obtained in solution, which we attributed to decreased efficiency stirring in the presence of large amounts of silica-supported reagent. Under these conditions, trace amounts of coupling on support were in fact observed, indicating that some active Pd had leached from support. The reaction was repeated a second time and left for 13 h instead of the usual 5–8 h. Under these conditions, the reaction in solution went to complete conversion and 7 % of the supported aryl bromide was also observed to couple with PhB(OH)<sub>2</sub>.

Substrate Conditions	но Каказана		
X = Cl 100 °C, 24h	100	0	80 % yield
X = Br 80°C, 5 h	97	3	50 % yield
X = Br 80 °C, 13 h	93	7	97 % yield

Table 6 Three-phase test for the Suzuki–Miyaura coupling.

These results indicate that under the conditions employed, the reaction appears to proceed predominantly on support, with a small amount of active Pd leaching from the surface. An alternative explanation is that Pd does leach from the surface, but is contained within the pores of the silicate where it is recaptured before escaping the channels. This may explain the importance of having excess thiol on support relative to Pd. Positional grafting of the thiol within the channels of the silicate is currently being attempted in our lab, which will hopefully provide insight into this possibility.

## CATALYST STRUCTURE

One thing that does appear to be critical in terms of leaching of Pd is the ratio of sulfur to Pd. All of the results described herein employ catalysts that have an S to Pd ratio of between 2-4:1. At lower ratios, we have observed Pd agglomeration on the external surface of the silicate by HAADF (high-angle annular dark field) TEM, which is not seen at higher ratios of S to Pd. If the Pd is able to form large clusters, it follows that the Pd is likely mobile and free to enter solution. Thus, we are currently examining the effect of S:Pd loading in more detail. This is particularly important in view of the recent report of Davis et al. [52], who used a similar material with a S:Pd ratio of 1.6:1 and observed leaching of Pd in solution on the order of 12 ppm for the Heck coupling of iodobenzene with *n*-butylacrylate. It is important to note that iodides were used in this latter study instead of bromides, and it is entirely likely that iodides promote leaching more effectively than bromides or chlorides. Because of their sensitivity to very low levels of Pd, Jones has recommended the use of bromides in the study of new catalysts [2]. However, work by Davis et al. clearly shows that the catalyst prepared under their conditions does leach Pd, in contrast to the conditions we have employed [52]. Similarly, Shimizu has prepared a thiol-modified material based on FSM and has shown that like ours, it does not appear to leach Pd [53]. In this case, the thiol to Pd ratio was close to 3:1, so once again an excess of thiol was employed on support. Whether or not this thiol functions as an internal scavenger, or whether it somehow stabilizes the Pd is yet unclear.

One critical effect of the thiols does seem to be controlling the mobility of the supported Pd. Shimizu demonstrated that Pd grafted on materials *without* thiols was significantly more mobile, as observed in the formation of nanoparticles of increasing size, and larger amounts of leaching [53]. Thus, a catalyst prepared by adsorbing Pd on thiol-modified mesoporous materials such as FSM was observed to have very small nanoparticles on the surface after being used in the Mizoroki–Heck reaction. No such particles were observed in the case of the Suzuki–Miyaura reaction. Contrast this with the case of FSM-supported Pd without the benefit of thiol ligation, where large Pd nanoparticles were observed on the surface of the material and Pd leaching was much more significant. Pd supported on zeolite Y had the highest level of leaching, and the largest nanoparticles were observed after reaction, on the order of 40 nm. Interestingly, the nature of the material had an effect as well since Pd was observed to have

slightly greater mobility on thiol-modified amorphous silica compared to on mesoporous silica [53]. This also correlates with greater leaching in the case of the Heck reaction (0.23 % of initially adsorbed Pd for thiol-modified silica vs. 0.01 % for thiol-modified FSM).

## CONCLUSIONS

In conclusion, we have shown that simple, commercially available thiols can be tethered to mesoporous silica and the resulting material used as a scavenger for Pd in various forms. The modified silica is extremely effective as a scavenger, reducing the Pd content of solutions by a factor of up to 500000. Remarkably, the resulting Pd-encapsulated material is able to catalyze the Suzuki–Miyaura and Mizoroki–Heck reactions without leaching appreciable quantities of Pd. Several heterogeneity tests, including a hot filtration and a three-phase test, indicated that only a small amount of catalysis was occurring from leached species. Although these tests do not allow us to rule out a mechanism where small quantities of Pd escape from the surface and are confined within the pores where they can be recaptured, the TEM results of Shimizu et al. indicate that the thiol ligand restricts the mobility of surface-bound Pd. Studies are currently underway to address the effect of the inner surface of the material, which we hope will shed light on the question of the true heterogeneity of the reaction.

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