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Synthesis of diethyl 2-(aryl)vinylphosphonate by the Heck reaction catalysed by supported palladium catalysts

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ABSTRACT

The synthesis of diethyl 2-(aryl)vinylphosphonate through direct Heck coupling reaction of the diethyl vinylphosphonate with aryl or heteroaryl halides catalysed by solid materials ($[Pd(NH_3)_4]$/NaY, Pd/C, PdO/SiO_2) is reported. After optimising the reaction conditions (1.3 mol% $[Pd(NH_3)_4]$/NaY, DMF, K_2CO_3, 110–140 °C), various aryl and heteroaryl halides were engaged in this reaction leading in all cases good to high yields. Interestingly, when using activated aryl bromides the palladium loading could be lowered to only 0.25 mol%. While highly active when coupling aryl iodides (i.e. only 0.15 mol% required), the PdO/SiO_2 catalyst was found to be inactive when considering aryl bromides. Deep study of this catalytic material revealed that in the case of aryl bromides, absence of *in situ* reduction of the catalyst precursor prevents the cross-coupling reaction with this latter material.

1. Introduction

Vinylphosphonates are valuable compounds due to their widespread applications in organic synthesis [1]. Among them, 2-(aryl)vinylphosphonates constitute a particularly interesting group known as starting material for the synthesis of pharmaceutically relevant molecules like metabolites, anticancer, antiviral drugs, immunosuppressives, insecticides, antibacterial and antifungal [2–7]. These building blocks are also involved in the preparation of flame retardant [8,9] or polymer, fuel and lubricant additives [10]. Some of them were also evaluated for their own pharmaceutical activity [11,12].

Owing their relevance, several methodologies to synthesise these compounds have been reported. Organometallic approaches include the *syn*-addition of organocuprates to 1-alkynylphosphonates [13,14], *anti*-hydrotelluration of 1-alkynylphosphonates [15], the formation of titanacycles from 1-alkynylphosphonates [16,17], the reaction of α-stannylated phosphonates with aldehydes to give *E*/*Z* mixtures [18], hydrozirconation of alkynes followed by phosphorylation [19,20], and olefin metathesis [21]. These methods are sometimes difficult to handle and often intolerant towards sensitive functional groups. Furthermore, the reagents are not always readily accessible. As alternatives α-lithiation of β-oxy or β-thio vinylphosphonates [22], NaH catalysed olefination of benzenesulfinylmethylphosphonates [23] and addition of sodium organyl chalcogenolates to 1-alkynylphosphonates were reported [24]. However, in practice these methods led to formation of regio- and stereoisomers mixture.

To overcome these limitations palladium catalysed procedures including, the Heck reactions using aryl halides [25–28] or aryldiazonium salts [29], the reactions between vinyl bromides and dialkylphosphonates[30] or the Suzuki-type coupling of boronic acids with vinylphosphonates were reported [31–33]. Generally good yields and high selectivities were achieved; however, these procedures were limited to few examples or remained linked to the preparation of the reagents.

In our ongoing researches related to the Heck cross-coupling [34–43], we reported a direct synthesis of 2-(aryl)vinylphosphonates from commercially available reagents applicable to a wide range of substrates [44]. However the methodology thus achieved was limited to the use of homogeneous catalysts as severe limitations in terms of Heck-product yields were observed when using heterogeneous palladium materials.

With the aim of resolving these issues (i.e. low activity, lack of recycling, selectivity...), we undertook a study focused on the use of heterogeneous palladium catalysts for cross-coupling diethyl

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vinylphosphonate with aryl and heteroaryl halides which results are reported here.

2. Experimental section

All glassware was base-, acid- and water-washed and oven dried. Toluene and heptane were freshly distilled under argon over sodium before use. The zeolite NaY was purchased from Sigma–Aldrich Chemical (LZ-Z-52) and dried under 5×10^{-2} mm Hg at 120 °C for 48 h before use.

The catalytic reactions were carried out in pressure sealed tubes under air. The qualitative and quantitative analysis of the reactants and the products was made by Gas Chromatography. Conversions and yields were determined by GC based on the relative area of GC-signals referred to an internal standard (biphenyl) calibrated to the corresponding pure compound.

Pd/C (Pd/C 5%wt, 55% water, 36% Pd-dispersion, only $\mathrm{Pd^{(II)}}$-species through TPR and XPS analyses) catalyst was obtained from EVONIK. The $[Pd(NH_3)_4]$/NaY catalyst was prepared according the procedure previously reported [34,37]. The palladium content determinations of the heterogeneous catalyst were performed by ICP-AES spectroscopy from a solution obtained by treatment of the catalysts with a mixture of HBF_4, HNO_3 and HCl in a Teflon reactor at 180 °C.

Transmission electron microscopy (TEM) was carried out on a JEOL 2010 microscope with an instrumental magnification of 50 000× to 100 000× and an acceleration voltage of 200 kV. The point-to-point resolution of the microscope was 0.19 nm and the resolution between lines was 0.14 nm. The microscope is equipped with an EDX link ISIS analyser from Oxford instruments. Energy-dispersive X-ray microanalysis (EDX) was conducted using a probe size of 25–100 nm to analyse grains of the phases. The powder samples were directly deposited on holey-carbon coated copper grid. XPS measurements were recorded on an AXIS ULTRA DLD from KRATOS ANALYTICAL spectrometer equipped with a dual anode (Mg and Al Kα source) and a high power Al monochromator. The measurements of the binding energies were referred to the characteristic C1s peak of the carbon fixed at the generally accepted value of 285.0 eV. X-ray powder diffraction (XRD) data were acquired on a Bruker D5005 diffractometer using Cu Kα monochromatic radiation ($\lambda = 1.054184$ Å). Liquid NMR spectra were recorded on a BRUKER AC-250 spectrometer. All chemical shifts were measured relative to residual ^{1}H or ^{13}C NMR resonances in the deuterated solvents: $CDCl_3$, δ 7.26 ppm for ^{1}H, 77.0 ppm for ^{13}C; DMSO, δ 2.50 ppm for ^{1}H, 39.5 ppm for ^{13}C. Melting points were determined in open capillary tubes and were uncorrected. Flash chromatography was performed at a pressure slightly greater than atmospheric pressure using silica (Merck Silica Gel 60, 230–400 mesh). Thin layer chromatography was performed on Fluka Silica Gel 60 F_{254}. GC analyses were performed on a HP 4890 chromatograph equipped with a FID detector, a HP 6890 autosampler and a HP-5 column (cross-linked 5% Phenyl-Methylsiloxane, 30 m × 0.25 mm i. d. × 0.25 μm film thickness). Nitrogen was used as carrier gas. The mass spectra were obtained on a Shimadzu GC-MS-QP2010S equipped with a Sulpelco SLB-5MS column (95% methylpolysiloxane + 5% phenylpolysiloxane, 30 m × 0.25 mm × 0.25 μm) with He as carrier gas. The experimental error was estimated to be $\Delta_{rel} = \pm 5\%$.

2.1. Preparation of the catalysts

2.1.1. Procedure for the preparation of the $[Pd(NH_3)_4]$/NaY [34]

A 0.1 M ammonia solution of $[Pd(NH_3)_4]Cl_2$ – prepared from $PdCl_2$ and a commercial ammoniac solution – (5 mL/g zeolite, corresponding respectively approximately to 5%wt Pd in the final catalyst) was added drop wise to a suspension of the zeolite NaY in bidistilled water (100 mL/g zeolite). The mixture was stirred for 24 h at rt and the exchanged zeolite was filtered off and washed until no trace of chloride was detected in the filtrate ($AgNO_3$ test). Then the zeolite was allowed to dry at room temperature to give the $[Pd(NH_3)_4]$/NaY as a slightly yellow material. The AAS gave 5.1 ± 0.2%wt Pd.

2.1.2. Procedure for the preparation of the Pd/SiO_2

Silica Aerosil 200 was added in water (100 mL/g SiO_2) in a round bottle flask under vigorous stirring. After 2 h water was evaporated. The silica was then dried in air at 120 °C, then slightly crushed and sifted. For the following experiment, we selected the particle sizes 40–60 mesh (250–400 nm) that allow easy handling of the material.

A solution of $Pd(acac)_2$ in toluene (made from 2.8 g of $Pd(acac)_2$ in 40 mL of toluene) was added to 10 g of agglomerated silica. The mixture was then stirred for 1 h at room temperature (r.t.) under argon, before the toluene is evaporated to give a slightly yellow material. This was calcinated under air flow (100 mL/min) at 300 °C for 5 h to give the desired PdO/SiO_2 catalyst as a brown material. AAS determination gave 8.7 ± 0.1%wt Pd. TEM analyses showed that the particle size average 5–10 nm.

2.1.3. Preparation of the palladacycle catalyst $\{Pd[P(o\text{-}C_6H_5CH_3)_2(C_6H_5CH_2)][OCOCH_3]\}_2$ [45]

$Pd(OAc)_2$ (4.5 g, 20 mmol) was dissolved in freshly distilled toluene (500 mL) under argon to give a reddish brown solution. Tri(*o*-tolyl)phosphine (8.0 g, 26.3 mmol) was added under argon. The resulted mixture was shortly (1 min) heated at 50 °C then rapidly cooled to room temperature to give a bright orange solution. The volume was reduced under vacuum to about 1/3 (160 mL) and freshly distilled hexane (500 mL) was added which causes the palladacycle to precipitation. After filtration and drying under vacuum the palladium complex was recrystallised from toluene/hexane to give the product as a microcrystalline yellow compound in 83% yield. Spectroscopic data were in accordance with literature.

2.1.4. General procedure for the catalytic tests under Heck conditions

0.6 mmol of aryl halide, 0.6 mmol of diethyl vinylphosphonate, 0.6 mmol of K_2CO_3 and 2 mol% of Pd-catalyst were introduced in a pressure tube. 6 mL of DMF were added and the reactor was then placed in a pre-heated oil bath at 110–140 °C for 4–24 h under vigorous stirring and then cooled to room temperature before the reaction mixture was analysed by GC. At completion of the reaction, the mixture was diluted with 100 mL of water and the resulting mixture was extracted with 4× 20 mL CH_2Cl_2. The combined organic layers were dried over $MgSO_4$ and evaporated. The residue was then purified by flash chromatography on silica gel eluting with petroleum-ether/ethylacetate (9:1) [46] except for the anthracyl derivative that was obtained by crystallisation from a mixture CH_2Cl_2/pentane (1:2).

2.1.5. GC analysis

3 mL of the reaction mixture was sampled and quenched with 3 mL of water in a test tube. The mixture was extracted with 2 mL of CH_2Cl_2 and the organic layer was filtered through a $MgSO_4$ pad. The resulting dry organic layer was then analysed by GC.

2.1.6. Characterisations of organic compounds

All compounds were characterised through MS spectra obtained from GC–MS. Additionally, isolated products were fully characterised through ^{1}H, ^{13}C and ^{31}P NMR and melting point. All compounds gave satisfactory data compared to reported literature [26,44,47–51].

3. Results and discussions

3.1. Catalysts

Several palladium(II)-based heterogeneous catalysts were evaluated within this study. The $[Pd(NH_3)_4]$/NaY (noticed within the text [Pd]/NaY) was prepared by ion-exchanged from NaY zeolite with a 0.1 M ammonia solution of $[Pd(NH_3)_4)]Cl_2$ following previously described procedure [34,37]. The Pd/SiO_2 catalysts was prepared by impregnation of agglomerated Aerosil by a solution of $Pd(acac)_2$ in toluene followed by calcination under air flow. These home made catalysts were compared to the commercially available Pd/C (Pd/C 10%wt on dry basis, 52% water, low reduction degree [i.e. almost exclusive $Pd^{(II)}$] and high palladium dispersion) [52]. This latter catalyst is characterised by its low reduction degree and high water content (52%).

Linked to our previous report [44], all heterogeneous palladium materials were comparatively evaluated to the homogeneous Herrmann–Beller palladacycle that was prepared following reported procedure [45].

3.2. Initial studies

Initially, heterogeneous palladium catalysts were evaluated for the cross-coupling reactions of iodo- and bromobenzene under the previously optimised conditions (1 mmol ArX, 1 mmol diethylvinylphosphonate, 1 equiv. 2 mol% [Pd], 3 mmol K_2CO_3, DMF [30 mL], 110–140 °C, up to 24 h) [44].

The results reported in Table 1 show that all heterogeneous catalysts exhibit high activity at 140 °C, given generally, in short reaction time, quantitative conversions of the aryl halides toward the expected compounds (entries 1, 4, 8). Regarding these results, further optimisation was related to improving the catalyst loading, the temperature and the reaction time. Using the Pd/C catalyst, the reaction temperature could be decreased to 110 °C without strong alteration of the catalyst's performances (entries 1 and 2). Additionally, the catalysts loading could be decreased up to 0.4 mol%; however under these conditions 24 h were required in order to achieve full conversion (entry 3). The [Pd]/NaY showed approximately the same tendencies (entries 4–6); however as observed in Table 1 decreasing the temperature affects more strongly the catalyst performances as the reaction time should be increased from 1.5 h at 140 °C to 8 h at 110 °C to achieve complete conversion. However, at very low catalyst loading (i.e. 0.25 mol%), this catalyst is as efficient as the Pd/C, leading to full conversion within 24 h at 110 °C. The case of the Pd/SiO_2 is somewhat surprising as long reaction time is required to achieve complete conversion whatever the reaction temperature (i.e. 120 °C or 140 °C, entries 8 and 9) that can be related to the low palladium loading used here (0.15 mol%). However, for this catalyst we noticed that higher palladium loading resulted generally in lower conversions for any reasons (i.e. 47% conversion of iodobenzene observed at 140 °C when using 2 mol% [Pd], Table 1, entry 7) as previously described by Huang et al. [53].

As expected bromobenzene exhibited lower reactivity than iodobenzene as at 140 °C *ca.* 40% yields were obtained using either the Pd/C or the [Pd]/NaY as catalyst (Table 1, entries 10 and 11). In any case, bromobenzene reacted at temperature below than 140 °C.

Whatever the reaction conditions used here, all reaction sets gave the expected 2-(phenyl)vinylphosphonate as exclusive *trans*-derivative; no *cis*-derivative neither dehalogenation toward benzene was observed.

In order to gain better insights on the activity of such heterogeneous catalysts using aryl bromides we evaluated the Heck reaction between the 2-bromonaphtalene, known for its higher reactivity, and the diethyl vinylphosphonate (Table 2). As previously observed, almost all catalysts, except the Pd/SiO_2, gave good yields in the target compound. As previously described the good activity of the [Pd]/NaY catalyst allowed both to decrease the palladium loading down to 0.25 mol%; however with longer reaction time (i.e. 24 h). Optimising the reaction temperature revealed that 120 °C appeared to be optimal giving full conversion in only 4 h. Apparently, according to previous reports [37,43], such a temperature allows efficient activation of the catalyst compared to results achieved at 110 °C (i.e. initiation of the dissolution/redeposition process; known also as reversible leaching) limiting also its deactivation by formation of palladium aggregates that is not the case by working at 140 °C, temperature at which black palladium was observed.

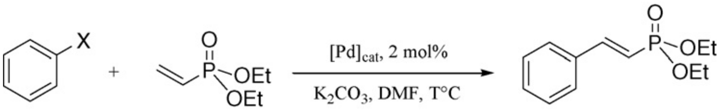
3.3. Kinetic studies

In order to compare homogeneous and heterogeneous catalysts in this reaction, kinetic experiments were performed at different temperatures.

The evolution of the conversion of 2-bromonaphtalene with time was determined at 110 °C, 120 °C and 140 °C with different palladium catalysts (i.e. Herrmann–Beller palladacycle, Pd/C and [Pd]/NaY; Fig. 1a, b and c, respectively). The activity of the catalysts and the induction period were determined for each reaction conditions (Table 3).

At 140 °C (Fig. 1a) it is clear that the heterogeneous [Pd]/NaY has similar activity than the homogeneous Herrmann–Beller palladacycle (i.e.: [Pd]/NaY: $Ai_2 = 28.8\ mmol/g_{Pd}$ min *versus* homogeneous

Table 1
Heck arylation of diethyl vinylphosphonate with iodo- or bromobenzene.[a]

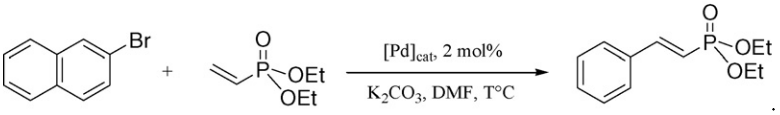


Entry	X	Catalyst	[Pd] (mol%)	*T* (°C)	Time (h)	Yield (%)[b]
1	I	Pd/C	2	140	6	100
2		Pd/C	2	110	8	100
3		Pd/C	0.4	110	24	92
4		[Pd]/NaY	1.3	140	1.5	100
5		[Pd]/NaY	1.3	110	8	100 [72]
6		[Pd]/NaY	0.25	110	24	100
7		Pd/SiO_2	2	140	24	47
8		Pd/SiO_2	0.15	140	16	100
9		Pd/SiO_2	0.15	120	24	100
10	Br	Pd/C	2	140	4	42
11		[Pd]/NaY	1.3	140	4	36

[a] Reaction conditions: 3 mmol PhX, 3 mmol diethyl vinylphosphonate, 3 mmol K_2CO_3, 30 mL DMF.

[b] Yields were determined by GC with an internal standard (diethylene glycol di-*n*-butyl ether) ($\Delta rel = \pm 5\%$). [Isolated yields] are reported in brackets.

Table 2
Heck arylation of diethyl vinylphosphonate with bromonaphtalene.[a]



Entry	Catalyst	[Pd] (mol%)	T (°C)	Time (h)	Conv.(%)	Yield (%)[b]
1	Pd/C	2	140	6	100	85
2	[Pd]/NaY	1.3	140	6	100	100
3	[Pd]/NaY	1.3	110	24	83	80
4	[Pd]/NaY	1.3	120	4	100	100 [74]
5	[Pd]/NaY	0.25	140	24	100	100
6	Pd/SiO_2	2	140	24	12	10
7	Pd/SiO_2	0.15	140	24	0	–
8	Pd/SiO_2	2	120	24	15	13

[a] Reaction conditions: 3 mmol PhX, 3 mmol de diethyl vinylphosphonate, 3 mmol K_2CO_3, 30 mL DMF.

[b] Yields were determined by GC with an internal standard (biphenyl) (Δrel = ±5%). In some cases (entries 1 and 3) dehalogenation was observed. [Isolated yields] are reported in brackets.

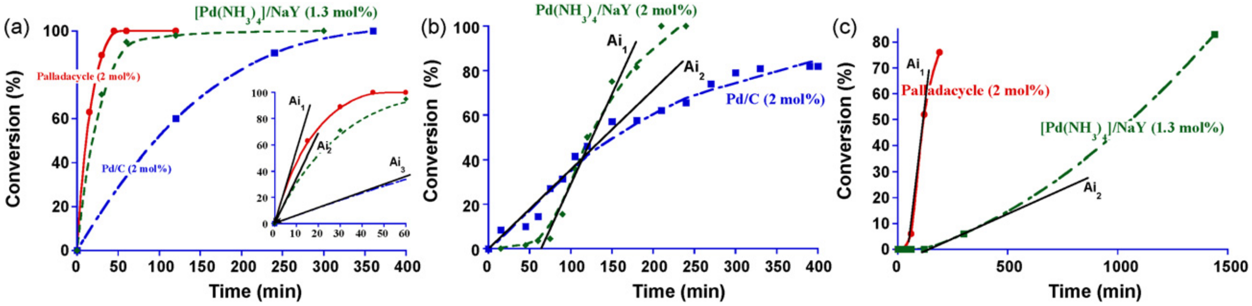


Fig. 1. Conversions *versus* the time for the coupling reaction of 2-bromonaphtalene with the diethyl vinylphosphonate using the Herrmann's palladacycle" (●); the [Pd]/NaY (♦); and the Pd/C (■) catalysts. Reaction conditions: 3 mmol 2-bromonaphtalene, 3 mmol diethyl vinylphosphonate, x mol% [Pd], 3 mmol K_2CO_3, 30 mL DMF at (a) 140 °C; (b) 120 °C; and (c) 110 °C.

palladacycle: $Ai_1 = 29.2\ mmol/g_{Pd}\ min$). Such observations were already made several times in the literature [41]. As predictable from previous reports [43], the heterogeneous [Pd]/NaY catalyst is clearly more active than the commercial Pd/C 10%wt (i.e. $Ai_3 = 2.6\ mmol/g_{Pd}\ min$).

As expected, by decreasing the reaction temperature the activity of the different catalysts was lowered and at 120 °C both heterogeneous catalyst exhibited close initial activities (i.e. 2.4 and 1.7 $mmol/g_{Pd}$ min for the [Pd]/NaY and the Pd/C, respectively) (Fig. 1b). It is important to note that for both pre-catalysts an induction period was observed before the catalyst being active. While this period was very short for the Pd/C (<5 min), the highest activity was reached only after *ca.* 60 min for the [Pd]/NaY. Both catalysts led finally to full conversions after 20 h and 4 h, respectively.

Decreasing further the reaction temperature to 110 °C resulting in strong decrease of the activity of the [Pd]/NaY catalyst (i.e. 0.2 $mmol/g_{Pd}$ min) while the induction period increase considerably (*ca.* 90 min). Whatever, after 48 h full conversion of the 2-bromonaphtalene was achieved with this heterogeneous catalyst. On the other hand, at this temperature, the homogeneous palladacycle exhibited higher activity (i.e. 2.6 $mmol/g_{Pd}$ min) with low induction period (*ca.* 15 min) leading to full conversion of the substrate after 24 h.

As previously suggested, these results confirmed that the heterogeneous [Pd]/NaY catalyst requires an optimum reaction temperature (i.e. 120 °C) in order to attain high activity (see Fig. 1c), at least competitive with that of homogenous catalysts. Otherwise the reaction time became longer favouring side reactions like dehalogenation (i.e. in this case, *ca.* 8% at reaction completion after 48 h *versus* 2% for the homogeneous palladacycle). It is supposed that this temperature is necessary to dissolve palladium species in the reaction medium according to the well-documented dissolution–redeposition mechanism [43].

Interestingly, we compared the activity of the different catalysts involved here at different reaction temperature (Table 3; Fig. 1). Data clearly indicates that the homogenous palladacycle is more active than any other heterogeneous catalysts whatever the reaction temperature. While the Pd/C catalyst never showed activation period, its activity remained below than that of the [Pd]/NaY that had to be activated upon temperature. Its induction period clearly depended on the applied reaction temperature (i.e. 0 min at 140 °C; 20 min at 120 °C and 90 min at 110 °C) that however did not affect its efficiency and full conversions were achieved in 3 h, 4 h and 24 h, respectively.

To summarise, solid catalysts can be alternatively used for Heck coupling of diethyl vinylphosphonate with aryl iodides and bro-

Table 3
Comparing catalyst performances at various reaction temperatures for the Heck reaction of bromonaphtalene with diethyl vinylphosphonate.

Catalyst	140 °C		120 °C		110 °C	
	A(i) ($mol/g_{[Pd]}$ min)	Induction time	A(i) ($mol/g_{[Pd]}$ min)	Induction time	A(i) ($mol/g_{[Pd]}$ min)	Induction time
Palladacycle	29.2	0	–	–	2.6	15 min
[Pd]/NaY	28.8	0	2.4	20 min	0.2	90 min
Pd/C	2.6	0	1.7	<5	–	–

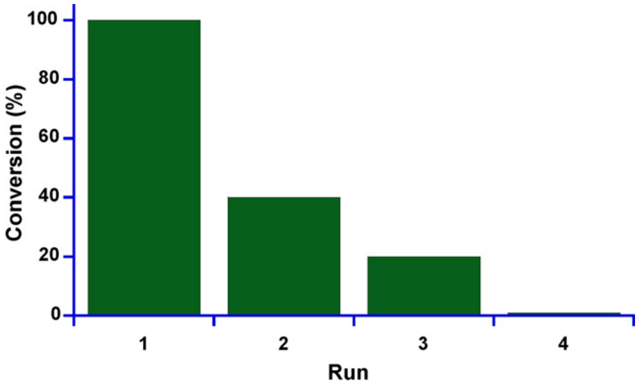


Fig. 2. Conversions for the coupling reaction of 2-bromonaphtalene with the diethyl vinylphosphonate using the [Pd]/NaY upon recycling. Reaction conditions: 3 mmol 2-bromonaphtalene, 3 mmol diethyl vinylphosphonate, 1.3 mol% [Pd], 3 mmol K_2CO_3, 30 mL NMP, 140 °C.

mides. However, it is clear that the reaction occurs in homogeneous phase by dissolution of palladium in the solvent [43] and that exchanged zeolite exhibited the best activity for this reaction.

3.4. Leaching and recycling

Regarding the general applicability of this methodology, we attempted to recycle the heterogeneous Pd/C and [Pd]/NaY catalysts for the coupling reaction of 2-bromonaphtalene and diethyl vinylphosphonate under optimised reaction conditions (2 mol% [Pd], DMF, K_2CO_3, 140 °C) over 24 h. After the first run of the catalyst, the reaction mixture was allowed to cool to room temperature and the catalyst was separated by centrifugation, washed twice with DMF and allowed to dry at room temperature overnight. The recycled palladium catalyst was then used without any regeneration under the same reaction conditions as the fresh catalyst. Whatever the nature of the catalysts, all attempts to reuse the catalytic material failed leading to only to the production of naphthalene issued from dehalogenation of the substrate that is probably due to the formation of large inactive palladium aggregates as previously reported under similar reaction conditions [54].

To get better insights, we run the coupling reaction under alternative conditions (2 mol% [Pd], NMP, K_2CO_3, 140 °C, 6 h) under which the [Pd]/NaY heterogeneous catalysts showed good recyclability [34,41]. While the fresh catalyst led to quantitative conversions, the reused catalysts gave 40%, 20% and 0% conversions (respectively for the 2nd, 3rd, 4th – Fig. 2). These results confirm that deactivation of the catalyst occurred during the reactions, while less pronounced than in DMF. Such deactivation of the catalyst upon recycling may have several origins: (a) mass loss during catalyst separation and washing; (b) formation of low active palladium aggregates; (c) salts precipitation upon cooling preventing therefore efficient catalysts (re)activation through the dissolution process. To date, we cannot discard with certitude one or the other hypothesis; however strongly support the last postulate as mass loss, nor palladium agglomeration, were generally not observed previously under such protocols. On the contrary, salts precipitation preventing efficient activation of the recycled catalysts was previously reported [55].

Leaching is often observed when supported palladium catalysts are used in such cross-coupling reactions [43,56]. Several methodologies are commonly used [43,57], the hot-filtration method, when applied with care, provides quick and reliable information about leaching. The procedure (see Section 2) was applied to [Pd]/NaY after 30 min reaction corresponding to *ca.* 20% conversion (Fig. 3). Comparing a standard run (in presence of solid material) to the hot-filtration run clearly showed further product formation after removal of the heterogeneous catalyst, up to a conversion of 60% after 3 h. These data clearly indicate that active palladium species are dissolved during the reaction. The differences in performances observed between the runs with and without the solid material can be related to: (1) the lack of continuous palladium source due to the removal of the material; (2) deactivation of the dissolved palladium species to less active colloids or palladium black; or (3) to the removal of the contribution of a heterogeneous catalysis to the overall conversion (which we consider as an unlikely or very minor factor) [43].

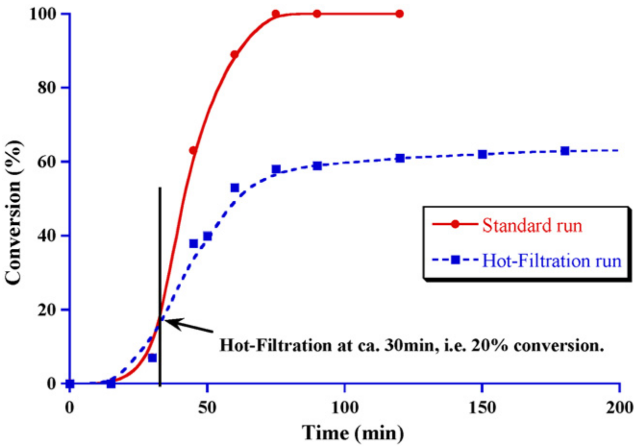


Fig. 3. Residual activity of [Pd]/NaY after hot filtration (■, dotted line) *versus* standard catalytic run (●, solid line). Reaction conditions: 3 mmol 2-bromonaphtalene, 3 mmol diethyl vinylphosphonate, 1.3 mol% [Pd], 3 mmol K_2CO_3, 30 mL NMP, 140 °C.

While palladium amount reached *ca.* 13 ppm during the reaction it decreased below 3 ppm after cooling, and no palladium contamination could be detected in isolated compounds.

3.5. Pd/SiO$_2$: a case of study

The results observed while using the Pd/SiO_2 were quite surprising as this catalyst was previously reported to be particularly efficient in the Heck reaction of bromobenzene with styrene [54], and poorly active when considering aryl iodides.

In order to understand deeper the phenomenon observed when engaging the Pd/SiO_2 in the Heck arylation of diethyl vinylphosphonate with iodo-, bromobenzene or 2-bromonaphtalene we performed catalysts characterisation before and after a catalytic run. Several techniques were used for this purpose (XRD, XPS and TEM).

XRD analysis of the fresh catalyst indicates that the immobilised palladium phase corresponds to crystalline palladium oxide because it has the major diffraction peak of 2θ at 33.94° with an average particle size of 6 nm (Fig. 4) [58]. XPS analysis of this catalyst exhibit a peak at 336.7 eV attributed to Pd^{2+}-species (i.e. a signal at *ca.* 335.1 eV is expected for $Pd^{(0)}$-species as measured for the reduced sample (Table 4)) [59–61] as amorphous palladium oxide (Fig. 5). These data were further confirmed by TEM of the fresh catalyst that clearly shows particles with an average size of 6–10 nm (Fig. 6) which diffractogram exhibits lattice fringes at 2.56 Å and 2.53 Å corresponding respectively to (1 0 1) and (0 −1 −1) crystallographic planes of palladium oxide.

XRD analysis of the catalyst used in the coupling reaction of iodobenzene with diethyl vinylphosphonate revealed that the initial supported palladium species were reduced to metallic palladium as the pattern shows characteristic peaks of face-centered cubic (fcc) crystalline palladium of 2θ = 40.12°, 46.86° and 68.12° corresponding respectively to Pd planes (1 1 1), (2 0 0) and (2 2 0)

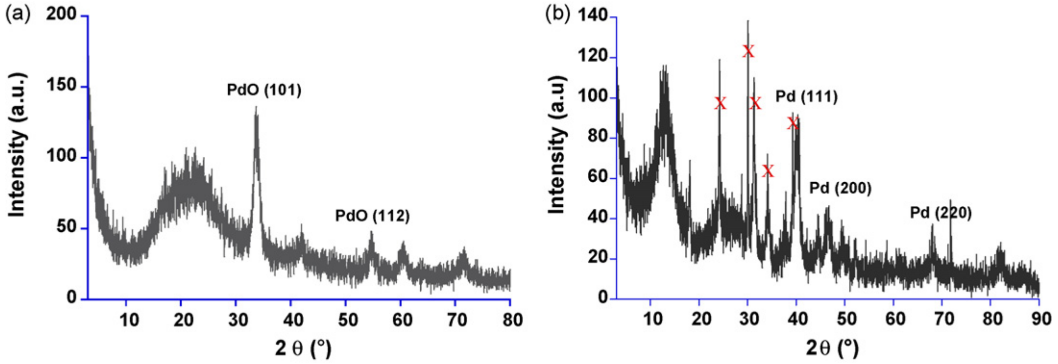


Fig. 4. XRD of the Pd/SiO_2 catalysts: (a) fresh catalyst, (b) catalyst used for the coupling reaction of iodobenzene with diethyl vinylphosphonate (X: contamination of the sample by $KHCO_3$ is observed).

Table 4
XPS data for fresh and used PdO/SiO_2 material. Comparison with a reduced Pd/SiO_2.

Material	Binding energy for Pd $3d_{5/2}$ (eV) [%]		
	$Pd^{(II)}$	$Pd^{(0)}$	Metallic palladium
Fresh Pd/SiO_2	336.5 [87]	335.5 [13][a]	–
Pd/SiO_2 used with C_6H_5I	336.4 [12]	335.3 [25]	334.2 [63][b]
Pd/SiO_2 used with $C_{10}H_7Br$	336.8 [21] and 335.9 [68]	334.6 [11][a]	–
Reduced Pd/SiO_2[c]	336.6 [19]	335.1 [81]	–

[a] Partial reduction due to electron beam.

[b] Metallic palladium described as palladium alloys or foils [61].

[c] Pd/SiO_2 catalyst was reduced under hydrogen flow (120 mL/min) at 300 °C for 5 h.

[58] (Fig. 4b). The reduction of the initial Pd(II) to Pd(0) was further confirmed by XPS recording (Fig. 7, Table 4) that show a peak at 335.3 eV together with a peak at 334.2 eV corresponding to palladium species at oxidation state (0) like in palladium alloys and metallic palladium (i.e. large agglomerates) [60]. TEM analyses agree with these interpretations showing palladium particles with an average size of 5–10 nm those diffractograms confirm the oxidation sate (0) (Fig. 8).

These results were compared to that obtained with the Pd/SiO_2 used in the coupling reaction of 2-bromonaphtalene with diethyl vinylphosphonate for which the conversion of the aryl halide was low (i.e. <15%). Noticeably in XRD spectra of the used catalysts, no peaks could be correlated with the presence of palladium at oxidation state (0); rather than data indicate the presence of crystalline palladium oxide like in fresh material (i.e. characteristic peak of (1 0 1) plane of $2\theta = 33.94°$). These observations were further con-

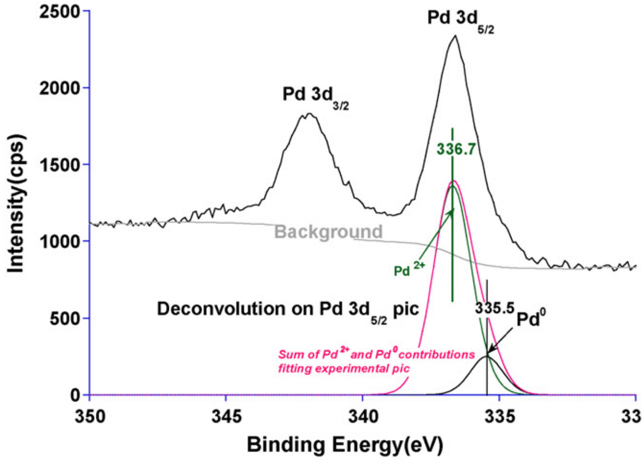


Fig. 5. XPS of the fresh Pd/SiO_2 catalyst. Deconvolution of the Pd$3d_{5/2}$ exhibits value at 336.7 eV (87%) and 335.5 eV (13%). The last is probably related to partial reduction under electron beam.

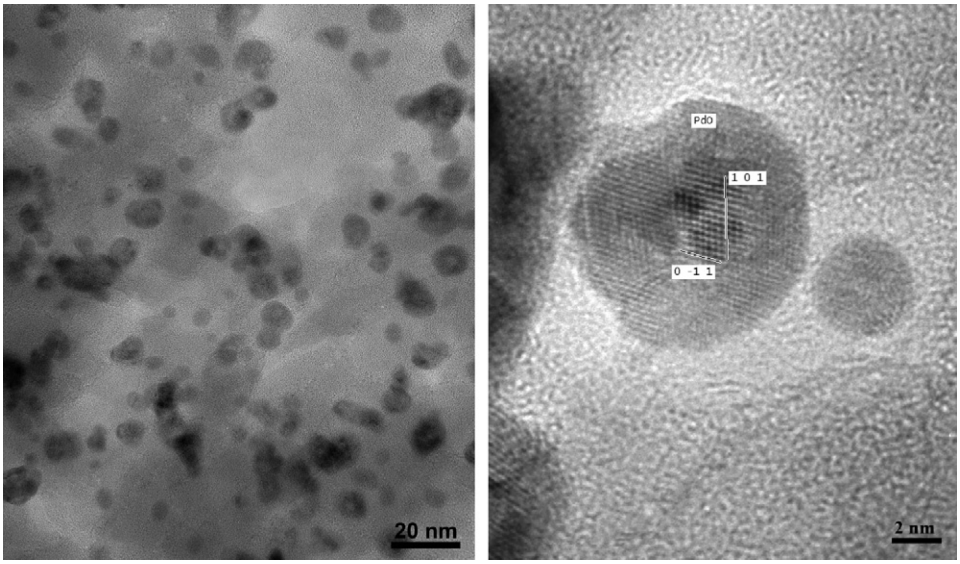


Fig. 6. TEM of the fresh Pd/SiO_2 catalyst at two magnifications.

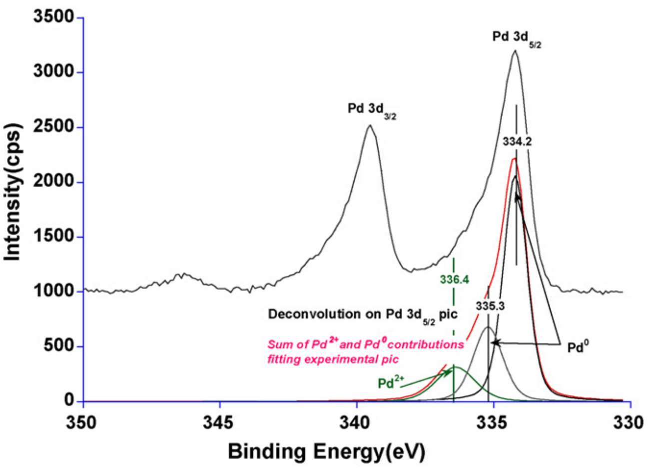


Fig. 7. XPS of the Pd/SiO$_2$ catalyst used in the coupling reaction of iodobenzene with diethyl vinylphosphonate. Deconvolution of the Pd3d$_{5/2}$ exhibits value at 334.2 eV (63%) and 335.3 eV (26%) corresponding to Pd(0)-species. The peak at 336.4 corresponds to residual Pd(II)-species.

firmed by XPS that indicate the presence of palladium species at oxidation state (II) with values at 336.8 eV and 335.9 eV (Fig. 9, Table 4). Accordingly, TEM recording showed numerous small particles those diffractograms correlate with palladium oxide (Fig. 10).

In summary, analytical data indicate that in the reaction of 2-bromonaphtalene with diethyl vinylphosphonate, the absence of efficient reaction is clearly related to the absence of pre-catalyst reduction, a situation that strongly contrasts with the reaction of iodobenzene with diethyl vinylphosphonate. This interpretation was further supported by performing the coupling reaction in the presence of a previously reduced Pd/SiO$_2$ material: under those conditions, 35% conversion of 2-bromonaphtalene toward the expected *trans*-2-naphtylvinylphosphonate was achieved. This modest activity could be attributed to the poor palladium dispersion on the support [38].

3.6. Scopes and limitations

Having the optimised conditions in hands (1.3 mol% [Pd] as [Pd]/NaY, DMF, K$_2$CO$_3$, 110–140 °C) we next applied them to a large range of aryl and heteroaryl halides focusing on bromide derivatives (Scheme 1).

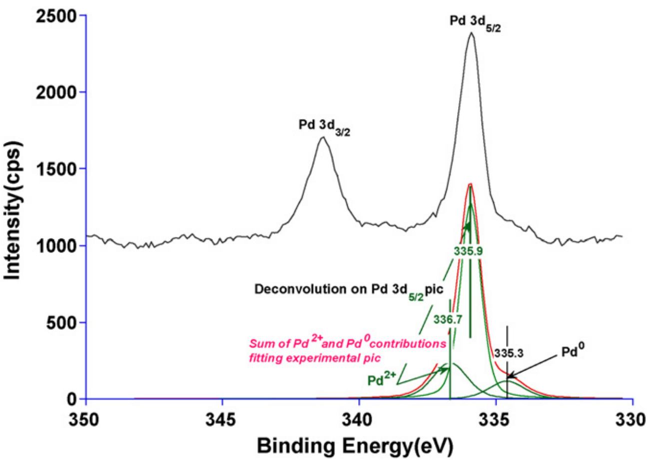
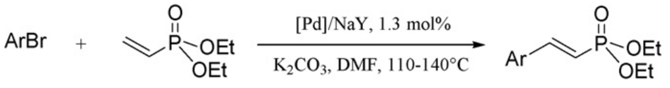


Fig. 9. XPS of the Pd/SiO$_2$ catalyst used in the coupling reaction of iodobenzene with diethyl vinylphosphonate. Deconvolution of the Pd3d$_{5/2}$ exhibits value at 336.8 eV (21%) and 335.9 eV (68%) corresponding to Pd(II)-species. The peak at 334.6 corresponds to Pd(0)-species probably produced under electron beam.



Scheme 1. Heterogeneous Heck arylation of the diethyl vinylphosphonate by various aryl and heteroaryl bromides.

Initially, we engaged condensed aryl and heteroaryl bromides (Table 5). The results reported in Table 5 showed that all evaluated condensed aryl and heteroaryl bromides led to full conversion in short reaction time when working at 140 °C, giving in almost all case good isolated yields in the target compounds. In some cases, reaction temperature could be decreased down to 110 °C (entries 2 and 8); however despite longer reaction time (24 h). Remarkably, the 3-bromobenzothiophene gave high conversion, leading to useful isolated yield of 64% in only 7 h.

Next we evaluated variously substituted aryl bromides (Table 6). In all cases, high yields were achieved whatever the nature of the substituent (i.e. electro-donating or withdrawing) except for the 2- and 3-chlorobromobenzene and 2- and 4-bromotoluene that led to low conversions. These results were already observed while using homogeneous catalysts, a situation for which the palladium

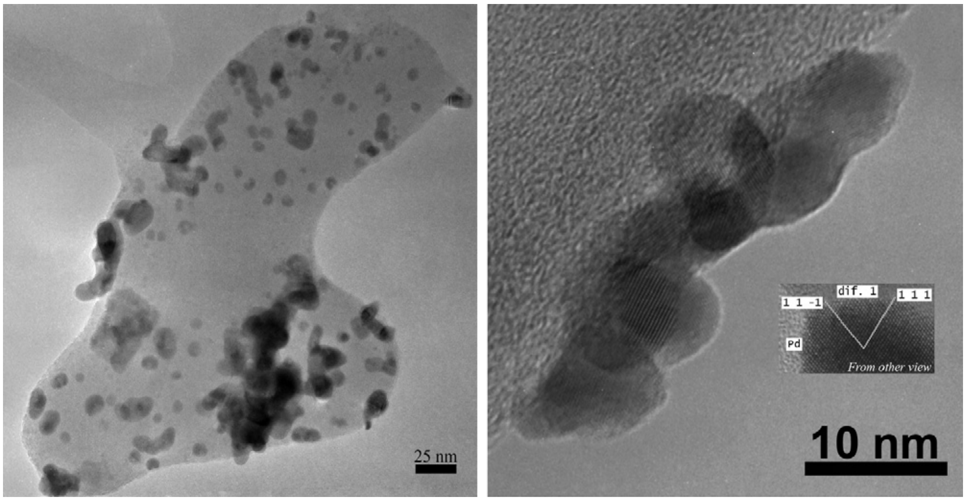
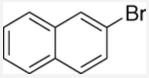
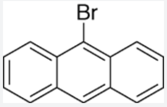
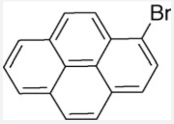
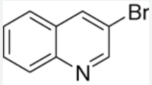
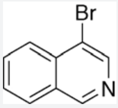
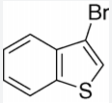


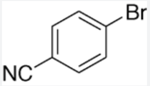
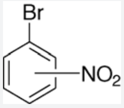
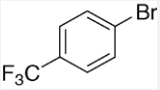
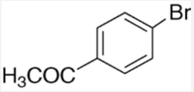
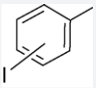
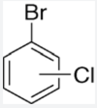
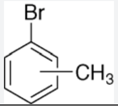
Fig. 8. TEM of the Pd/SiO$_2$ catalyst used in the coupling of iodobenzene with diethyl vinylphosphonate at two magnifications.

Table 5
Heck arylation of the diethyl vinylphosphonate by various condensed aryl and heteroaryl bromides (Scheme 1).

Entry	ArBr	T (°C)	Time (h)	Conv. (%)	Yield (%)[a]
1		140	6	100	100
2		120	4	100	100 [74]
3		110	24	83	80
4		140	24	100	100 [55]
5		140	4	100	85
6		120	20	100	95 [72]
7		140	2	100	100 [70]
8		110	24	100	96
9		140	6	90	87 [65]
10		120	20	100	100 [64]
11		140	7	100	90 [64]

[a] Yields were determined by GC with an internal standard (biphenyl) (Δrel = ±5%). [Isolated yields] are reported in brackets.

Table 6
Heck arylation of the diethyl vinylphosphonate by various aryl bromides (Scheme 1).[a]

Entry	ArX	Substituent position	T (°C)	Conv. (%)	Yield (%)[b]
1			120	100	100 [54]
2		*o-*	120	88	85 [55]
3		*m-*	120	90	80 [50]
4		*p-*	120	100	100 [70]
5			120	100	100 [70]
6			120	100	95 [65]
7		*o-*	110	90	80 [50][c]
8		*p-*	110	100	95 [80]
9		*o-*	140	45	44 [40]
10		*p-*	140	80	80 [57]
11		*o-*	140	10	–
12		*p-*	140	37	37 [32]

[a] All reactions were carried out in 24 h.

[b] Yields were determined by GC with an internal standard (biphenyl) (Δrel = ±5%). [Isolated yields] are reported in brackets.

[c] The corresponding (*E*)-diethyl 2-iodostyrylphosphonate resulting from the bromine reaction was observed in 10% GC-yield.

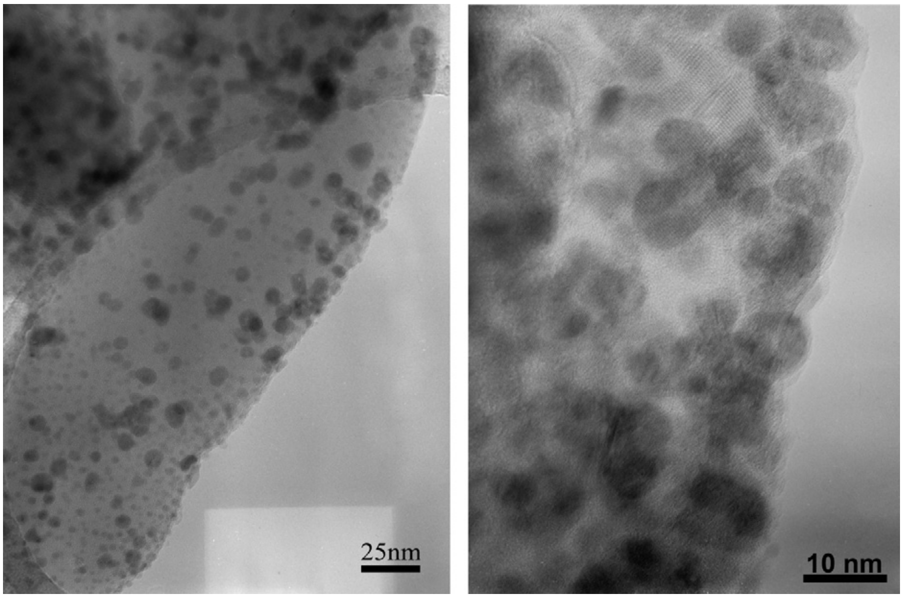


Fig. 10. TEM of the Pd/SiO$_2$ catalyst used in the coupling of 2-bromonaphtalene with diethyl vinylphosphonate at two magnifications.

N-heterocyclic carbene complexes have led to useful isolated yields [44].

In all cases, the results achieved here using the heterogeneous [Pd]/NaY catalyst are competitive to those previously described with the Herrmann palladacycle [44]; however, with the easier removal of the catalytic material and *possible* recycling.

4. Conclusions

We reported in this contribution an alternative route to the synthesis of diethyl 2-(aryl)vinylphosphonate by direct Heck coupling reaction of the diethyl vinylphosphonate with various aryl or heteroaryl halides in the presence of solid catalysts. Several heterogeneous catalysts ([Pd]/NaY, Pd/C, Pd/SiO$_2$) were evaluated for this purpose; both optimisation of the reaction conditions and kinetic studies revealed that the [Pd]/NaY catalyst represents the best alternative to the use of homogeneous palladium complexes like the Herrmann palladacycle.

In more details, this catalyst when correctly activated – that can be achieved by working at least at 120 °C – is almost as efficient as the homogeneous one.

Generally high conversions and selectivities were achieved whatever the homogeneous or the heterogeneous catalyst used under optimised reaction conditions (1.3 mol% [Pd(NH$_3$)$_4$]/NaY, DMF, K$_2$CO$_3$, 110–140 °C). However, for some aryl halides, like the 2- and 4-bromotoluene, limitations were observed as with the Herrmann palladacycle. Therefore, this simple heterogeneous catalyst offers viable alternative to the use of homogeneous catalysts precursors offering easier separation procedure of the catalytic material and possible recycling. Moreover, it was shown that in the case of aryl iodides or activated aryl bromides, the palladium loading could be decreased up to 0.25 mol%.

In addition, we performed a detailed study concerning the Pd/SiO$_2$ catalyst precursor. While being highly active as only 0.15 mol% palladium was necessary to achieve full conversions is 24 h, it was found to be limited to the coupling reaction of aryl iodides with diethyl vinylphosphonate despite the available literature. Careful analyses (XPS, TEM, XRD) of the fresh and used materials revealed that when engaging aryl bromides in the reaction, for any reasons, *in situ* reduction of Pd(II) to active Pd(0)-species is prevented, limiting therefore cross-coupling reaction.

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