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Copper-free heterogeneous catalysts for the Sonogashira cross-coupling reaction: Preparation, characterisation, activity and applications for organic synthesis

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Abstract

Heterogeneous copper-free catalysts supported on microporous ($[Pd(NH_3)_4]^{2+}$/NaY) and mesoporous materials ([Pd]/SBA-15) have been prepared, characterised and evaluated in the Sonogashira coupling reaction of aryl halides with phenyl acetylene. Generally, these catalysts showed high activity and selectivity, somewhat comparable to that of homogeneous catalysts (i.e. $\{Pd[P(o\text{-}C_6H_4CH_3)_2(C_6H_4CH_2)[OCOCH_3]\}_2$ and $PdCl_2(PPh_3)_2$). In addition, it was found that the catalyst based on the SBA-15 material (i.e. [Pd]/SBA-15), was particularly active when using large aryl halides such as bromonaphtalene and bromoanthacene, whereas, the heterogeneous catalyst based on microporous support (i.e. $[Pd(NH_3)_4]^{2+}$/NaY) was inactive. The recycling of various catalyst and X-ray diffraction and ^{31}P CP-MAS NMR studies of fresh and recycled catalyst are also briefly discussed.

Keywords: Heterogeneous catalysts; Microporous support; Mesoporous support; Palladium; Sonogashira cross-coupling

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1. Introduction

The Sonogashira cross-coupling of aryl halides and terminal alkynes or arylenes is a useful tool for the synthesis of alkyl-aryl and diaryl-susbtituted acetylenes [1–8]. Functionalised alkynes are important building blocks for the synthesis of biologically active molecules and, surprisingly, have common structural features with natural products that have been isolated from plants and in the marine organisms, or synthetic drugs [2,4,9–12]. Therefore, the Sonogashira reaction is frequently used as a key step in the synthesis of pharmaceuticals, such as the enediyne antibiotics or oral contraceptives [13–21].

Generally the Sonogashira reaction is carried out in an organic solvent such as toluene, THF or DMF, using at least a stoichiometric amount of base, and a Pd(0)/Cu(I) catalytic system [22]. To extend the Sonogashira reaction for fine chemical applications, numerous studies have been reported in the literature over the last 10 years including the use of a phase transfer agent [23], reaction in aqueous media or without solvent [24–29], reaction in ionic-liquids [30], copper-free versions [31–42], and the use of promoters such as Zn, Mg, Sn and R_4NI [43–46].

Nickel catalysed Sonogashira reactions have been described by Beletskaya et al. for homogeneous Ni(II)-species [47] and Wang et al. for Ni(0)-particles [48]. However, these catalysts require the use of CuI as co-catalyst and PPh_3 in order to achieve high activities. Alternatively, Leadbeater et al. reported a transition-metal free procedure for the Sonogashira coupling reactions of aryl iodides and bromides with phenylacetylene under phase-transfer conditions and using microwave irradiation to efficiently

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activate the aryl halides [49]. Nevertheless, while interesting, these Pd-free methodologies remain limited by the narrow choice of the reactants and reaction conditions, which lead to high conversions.

The most important improvement concerned the elimination of CuI as co-catalyst, as CuI can induce homocoupling reactions of terminal alkynes to diynes in the presence of oxygen (Glaser-type reactions) [50]. This improvement is also of importance for industrial applications of the Sonogashira cross-coupling reactions, since copper is very tedious to recycle. As a solution, several efficient copper-free homogeneous catalytic systems have been reported since 1992 for the cross-coupling reaction of alkynes with aryl- or vinyl-halides [41,42,51–58]. While these examples contributed to the improvement of the Sonogashira reaction, the use of homogeneous Pd-catalysts makes the separation and the recovery of the catalysts difficult, if not impossible, and might result in unacceptable palladium contamination of the products.

As an answer to these problems Astruc and co-workers [59,60] recently reported the use of a dendritic material to support the homogeneous [Pd{t-Bu$_2$PCH$_2$N(CH$_2$Ph)CH$_2$Pt-Bu$_2$}(OAc)$_2$] complex [35], which they had previously applied to the Sonogashira reaction (79% yield for the reaction of iodobenzene with phenylacetylene under reflux in the presence of Et$_3$N using 1 mol% of the Pd-dendritic catalyst after 24 h). The authors claimed that the dendritic catalysts could be recovered by precipitation and reused without significant loss of activity. Although interesting, this method required the precipitation of the catalyst by a co-solvent (generally pentane), which increased the amount of effluent waste during the process.

Few reports describe the Sonogashira reaction heterogeneously catalysed by supported palladium catalysts, examples being generally limited to highly reactive aryl iodides and 2-halopyridines. Separately, Köhler et al. [61] and Kotschy et al. [62] have described the Pd/C catalysed Sonogashira reaction of aryl halides with acetylenes in presence of CuI. When optimised, using 5 mol% Pd/C, 10 mol% CuI as co-catalyst and diisopropylamine as the base, Kotschy and co-workers achieved the quantitative conversion of 2-bromopyridine with various acetylenes, such as 1-hexyne, after 24 h under reflux in DMAc/H$_2$O. However, the success of these examples remained linked to the use of CuI as co-catalyst. Kotschy and co-workers clearly demonstrated that the overall activity of the [Pd/C + CuI] catalytic system was related to the leaching of the active Pd-species in the solution during the reaction, thus contaminating the reaction mixture ($\leq$2% of Pd) [62].

The intensive application of the Sonogashira reaction in the chemical industry depends on the development of new, stable and recyclable heterogeneous copper-free palladium catalysts. With this aim, the use of palladium supported on metal-oxides appears to be the most appropriate heterogeneous catalyst to perform this cross-coupling reaction on a large scale.

Some of us have previously reported the first very efficient heterogeneous Pd-catalyst for the Sonogashira reaction using zeolites as supports [39,63]. In these studies, zeolite supports were found to be particularly effective in the stabilisation of active Pd-species during the reaction, leading to highly active, easily separable and recyclable heterogeneous palladium catalysts. However, for synthetic applications such as those encountered in the pharmaceutical and agrochemical industries, these catalysts remain limited, since the pore structure of the zeolite support restricted the size of the molecule that could be involved over the syntheses.

The present contribution describes the remarkable catalytic activity of a Pd-modified mesoporous catalyst ([Pd]/SBA-15) for the Sonogashira cross-coupling reaction of aryl-iodides and -bromides with phenylacetylene and the potential application of this system to the synthesis of relatively large molecules. Particular attention has been paid to the comparison of the activity and selectivity of this [Pd]/SBA-15 to other metal oxide supported Pd-catalysts and to homogenous palladium complexes.

2. Experimental

2.1. General

All manipulations were conducted under a strict inert atmosphere or vacuum conditions using Schlenk techniques including the transfer of the catalysts to the reaction vessel. All glassware was base- and acid-washed and oven dried.

The solvents were dried using standard methods and stored over activated 4 Å molecular sieves. The toluene used for the synthesis of the "palladacyle" catalyst {Pd[P(o-C$_6$H$_4$CH$_3$)$_2$-(o-C$_6$H$_4$CH$_2$)(CH$_3$CO$_2$)]}$_2$ was distilled under argon before use over sodium from purple benzophone ketyl.

Tetraethoxysilane (TEOS), poly(ethyleneoxide)-poly(propyleneoxide)-poly(ethyleneoxide) block copolymer (Pluronic 123, Mw: 5000) and diethoxymethylvinylsilane were purchased from Aldrich Chemical and used without further purification. PdCl$_2$ and PdCl$_2$(PPh$_3$)$_2$ were obtained, respectively, from Alfa and Strem Chemicals. Diphenylphosphine was supplied from Fluka. 2-(diphenylphosphino)ethyldiethoxymethylsilane, PPh$_2$-(CH$_2$)$_2$-SiCH$_3$(OCH$_2$CH$_3$)$_2$, was synthesized by adapting the procedure reported by Schmid et al. [64]. Equimolar quantities of HPPh$_2$ and diethoxymethylvinylsilane were irradiated for 4 days using a UV light (high pressure Hg lamp) and a water-cooled quartz reactor; the product was purified by distillation under vacuo (b.p. 170–180 °C/0.1 Torr, 85% yield). All the chemicals (organic reagents and solvents) were deaerated by an argon flow before they were used.

The supports (TiO$_2$ {P25}, SiO$_2$ {Aerosil 200}, Al$_2$O$_3$ {Aluminium oxide C}), were donated by Degussa AG. The NaY zeolite (LZ-Z-52) was purchased from Sigma–Aldrich Chemicals. Silica Aerosil 200 was agglomerated prior to use by treatment with water. After evaporation and drying at 120 °C for 3 days the resulting material was crushed and sieved to give a selected fraction with a particle size of 40–60 mesh. BET of a silica sample dehydroxylated at 500 °C under 10^{-5} mmHg for 6 h gave the following characteristics: specific surface = $240 \pm 4\ \mathrm{m^2/g}$. The support materials $\mathrm{AlF_3}$ and $\mathrm{MgF_2}$ were prepared by a modified procedure given in the literature [65,66] and calcined for 4 h at 200 °C. The resulting fluorides were characterized by X-ray powder diffraction and IR spectroscopy. The specific surface area of the materials (determined via $\mathrm{N_2}$ physisorption at 77 K; BET method) was $180\ \mathrm{m^2/g}$ ($\mathrm{AlF_3}$) and $250\ \mathrm{m^2/g}$ ($\mathrm{MgF_2}$). The Pd/C catalyst (5.1 wt.% on dry basis, 49% water) was purchased from Aldrich Chemicals.

2.2. *Catalyst preparation*

2.2.1. *Homogeneous catalysts*

$\mathrm{PdCl_2(PhCN)_2}$ was prepared according procedures previously described in the literature [67]. The homogeneous "palladacycle" $\{\mathrm{Pd[P(\mathit{o}\text{-}C_6H_4CH_3)_2(C_6H_4CH_2)[OCOCH_3]}\}_2$ catalyst was prepared from $\mathrm{Pd(OAc)_2}$ and Tri(*o*-tolyl)phosphine following the procedure reported by Herrmann and co-workers [68]. $\mathrm{PdCl_2\{PPh_2\text{-}(CH_2)_2\text{-}SiCH_3(OCH_2CH_3)_2\}_2}$ was synthesized by reacting two equivalents of $\mathrm{PPh_2\text{-}(CH_2)_2\text{-}SiCH_3(OCH_2CH_3)_2}$ with bis(benzonitrile)palladium dichloride at room temperature in methylene chloride by adapting a procedure reported elsewhere [69].

2.2.2. *Heterogeneous catalysts*

All catalyst supports were dried prior to use at 120 °C for 48 h under dynamic vacuum (5.10^{-2} mmHg). After the synthesis, the catalysts obtained were stored under argon.

2.2.2.1. Preparation of $[\mathrm{Pd(NH_3)_4}]^{2+}$*/NaY [70–73].* A 0.1 M ammonia solution of $\mathrm{[Pd(NH_3)_4]Cl_2}$ prepared from $\mathrm{PdCl_2}$ and a commercial ammonia solution was added dropwise (4 mL/g zeolite, corresponding to ca. 5 wt.% Pd in the final catalyst) to a suspension of the zeolite NaY in bidistilled water (100 mL/g zeolite). The mixture was stirred for 24 h at room temperature and the exchanged zeolite was filtered off and washed until no trace of chloride was detected in the filtrate ($\mathrm{AgNO_3}$ test). Then the zeolite was allowed to dry at room temperature to give the entrapped $[\mathrm{Pd(NH_3)_4}]^{2+}$/NaY catalyst as slightly yellow material. ICP-AES analysis: 5.4 wt.% Pd.

2.2.2.2. Preparation of [Pd(II)]/NaY [72]. The Pd(II) exchanged zeolite was obtained by calcination of the entrapped $[\mathrm{Pd(NH_3)_4}]^{2+}$ zeolite in a U-reactor under a pure oxygen flow (180 mL/min) using a heating rate of 2 °C/min from room temperature to 500 °C. The temperature was maintained at 500 °C for 30 min and the reactor was cooled to room temperature under a flow of argon to give the modified Pd(II) zeolite as a golden brown powder. The [Pd(II)]/NaY was then stored under argon to prevent hydration. ICP-AES analysis: 5.5 wt.% Pd.

2.2.2.3. Preparation of [Pd(0)]/NaY [72]. The Pd(0) exchanged zeolite was obtained by reduction of the [Pd(II)]/NaY in a U-reactor under a pure hydrogen flow (70 mL/min) using a heating rate of 8 °C/min from room temperature to 350 °C. The temperature was maintained at 350 °C for 15 min and the reactor was cooled to room temperature under a flow of argon to give the Pd(0) modified zeolite as a black powder. The [Pd(0)]/NaY was then stored under argon to prevent re-oxidation. ICP-AES analysis: 5.5 wt.% Pd.

2.2.2.4. Preparation of $\mathrm{[Pd(0)]/SiO_2}$ *[74].* A solution of $\mathrm{Pd(acac)_2}$ in benzene (made from 143.1 mg of $\mathrm{Pd(acac)_2}$ in 15 mL of benzene) was added to 1.0 g of $\mathrm{SiO_2}$. After stirring the mixture for 1 h at room temperature, the toluene was evaporated to give a slightly yellow material. This latter was reduced under $\mathrm{H_2}$ flow (150 mL/min) in a U-reactor at 70 °C for 2 h to give the desired $\mathrm{[Pd(0)]/SiO_2}$ catalyst as grey materials. ICP-AES analysis: 4.4 wt.% Pd.

2.2.2.5. Preparation of the $\mathrm{[Pd]/AlF_3}$*,* $\mathrm{[Pd]/MgF_2}$*,* $\mathrm{[Pd]/Al_2O_3}$ *catalysts: general procedure.* These catalysts were prepared according to a modified precipitation method of $\mathrm{Pd(OH)_2}$ on the fluorides or oxides supports from a $\mathrm{PdCl_2}$-HCl solution by controlled addition of a base like a procedure originally described by Pearlman [75]. ICP-AES analysis of the resulting catalysts gave: 1.0 wt.% Pd.

2.2.2.6. Preparation of $\mathrm{PdCl_2\{PPh_2\text{-}(CH_2)_2\text{-}SiCH_3(OCH_2CH_3)_2\}_2/SBA\text{-}15}$*.* Mesoporous SBA-15 type silica was used as support and was prepared by the acid catalyzed, non-ionic assembly pathway described by Margolese et al. [76]. The structure-directing agent (Pluronic 123) was removed by calcination under air at 500 °C and the surfactant-free mesoporous silica was rigorously dried under a flow of nitrogen at 200 °C prior to the grafting reaction. Typically, $\mathrm{PdCl_2\{PPh_2\text{-}(CH_2)_2\text{-}SiCH_3(OCH_2CH_3)_2\}_2}$ (∼500 mg) dissolved in dry toluene was added dropwise to a suspension of calcined SBA-15 (1 g) in toluene and stirred at 25 °C for 2 h to allow the diffusion of the molecular precursor into the channels of the pores. The reaction mixture was then heated at 85 °C overnight. After filtration of the solid, the unreacted palladium precursor was removed by a soxlhet extraction with $\mathrm{CH_2Cl_2}$ during 10 h. Finally, the resulting solid was dried in vacuo at 25 °C. The organometallic-inorganic hybrid material, denoted [Pd]/SBA-15, has been characterized by several analytical, physical and spectroscopic techniques including small-angle X-ray powder diffraction and nitrogen sorption isotherms. Solid-state ^{1}H, ^{13}C, ^{31}P and ^{29}Si NMR spectra as well as the TGA profile are given in Supporting information.

ICP-AES analysis: 2.1 wt.% Pd and 1.3 wt.% P. MAS ^{1}H NMR δ: 0.6 ($-\mathrm{SiC}\mathit{H}_3$, $-\mathrm{SiC}\mathit{H}_2\mathrm{CH_2P}$, $-\mathrm{OCH_2C}\mathit{H}_3$), 3.3 ($-\mathrm{SiCH_2C}\mathit{H}_2\mathrm{P}$, $-\mathrm{OC}\mathit{H}_2\mathrm{CH_3}$), 6.7 (phenyl ring). CP-MAS ^{13}C NMR δ: −4.6 ($-\mathrm{Si}\mathit{C}\mathrm{H_3}$), 10.5 ($-\mathrm{Si}\mathit{C}\mathrm{H_2CH_2P}$), 18.7–20.1 ($-\mathrm{OCH_2}\mathit{C}\mathrm{H_3}$ and $-\mathrm{SiCH_2}\mathit{C}\mathrm{H_2P}$, respectively), 58.2 ($-\mathrm{O}\mathit{C}\mathrm{H_2CH_3}$), 129.7–137.8 (phenyl ring). CP-MAS ^{29}Si NMR δ: −12.6 ($\mathrm{D^1}$ and $\mathrm{D^2}$ sites), −91.6 ($\mathrm{Q^2}$ sites),

−101.4 (Q^3 sites), −108.2 ppm (Q^4 sites). CP-MAS ^{31}P NMR δ: 20.7 (*trans*-isomer), 30.9 (*cis*-isomer).

2.3. Characterisation

All solid-state NMR spectra were recorded on a BRUKER DSX-300 or Avance-500 spectrometers equipped with a standard 4 mm probehead. The spinning rate was typically 10 kHz. ^{13}C, ^{29}Si and ^{31}P NMR spectra were obtained by use of cross-polarisation (contact time 5 ms). To achieve a good polarisation transfer, a ramp was used on the X channel. Recycle delays were typically 1 s (a study on the ^{1}H nucleus showed that it was sufficient to allow all protons to fully relax). ^{1}H, ^{13}C and ^{29}Si MAS spectra were referenced to tetramethylsilane. ^{31}P MAS spectra were referenced to 85% H_3PO_4.

X-ray powder diffraction (XRD) data were acquired on a Bruker D5005 diffractometer using Cu Kα radiation (λ = 1054184 Å). A TA instruments thermoanalyser 2950 HR V5.3. was used for simultaneous thermal analysis combining thermogravimetric (TGA) and differential thermoanalysis (DTA) at a heating rate of 5 °C/min in air. Nitrogen adsorption and desorption isotherms were measured at 77 K. The organometallic-inorganic hybrids were evacuated at 160 °C for 24 h before the measurements. Specific surface areas were calculated following the BET procedure. Pore size distribution was obtained by using the BJH pore analysis applied to the desorption branch of the nitrogen adsorption/desorption isotherm.

The palladium content determinations of the heterogeneous catalysts {$[Pd(NH_3)_4]^{2+}$/NaY, [Pd(II)]/NaY, [Pd(0)]/NaY, [Pd(0)]/SiO_2, [Pd]/AlF_3, [Pd]/MgF_2, [Pd]/Al_2O_3 and [Pd]/SBA-15} 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.

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: C_6D_6, δ 7.15 ppm for ^{1}H, 128 ppm for ^{13}C; CD_2Cl_2, δ 5.32 ppm for ^{1}H, 53.8 ppm for ^{13}C; $CDCl_3$, δ 7.25 ppm for ^{1}H, 77 ppm for ^{13}C. 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 is used as carrier gas. The mass spectra were obtained on a HP 6890 gas chromatograph equipped with a HP 5973 mass detector and a HP-5 MS column (cross-linked 5% phenyl-methylsiloxane, 30 m × 0.25 mm i.d. × 0.25 μm film thickness). Helium is used as carrier gas. The experimental error was estimated to be $\Delta_{rel} = \pm 5\%$.

2.4. Catalytic tests

The catalytic reactions were carried out in a three-necked flask, or alternatively in pressure sealed tubes, under argon. The qualitative and quantitative analysis of the reactants and the products was made by gas chromatography. Conversion and yields were determined by GC based on the relative area of GC-signals referred to an internal standard (diethylene glycol di-*n*-butyl ether) calibrated to the corresponding pure compound. All catalysts were handled and transferred under argon.

2.4.1. General procedure for the first runs of the catalysts

A total of 5 mmol of aryl halide, 8 mmol of phenylacetylene, 10 mmol of base and 1 mol% [Pd]-catalyst was introduced in a three-necked flask under argon. Then 10 mL of solvent (previously deaerated) was added and the mixture was further deaerated by an argon flow for 5 min. The reactor was placed in a preheated oil bath at 80 °C. The reaction was conducted under vigorous stirring for 6 h and then the reaction mixture was cooled to room temperature before GC analysis.

2.4.2. General procedure for the recycling of separated catalysts

For recycling experiments the catalyst used in a first run was separated by centrifugation, washed two times with 10 mL DMF/H_2O (4:1) and reused after drying at room temperature as described for the fresh catalyst.

2.4.3. General procedure for the evaluation of the catalytic activity of non-separated catalysts

A total of 10 mmol of *p*-iodotoluene (2.18 g), 15 mmol of phenylacetylene (1.53 g), 20 mmol of Et_3N (2.02 g) and 1 mol% [Pd]-catalyst was introduced in a three-necked flask under argon. Then 20 mL of DMF/H_2O (4:1) previously deaerated was added and the mixture was further deaerated by an argon flow for 5 min. The reactor was placed in a preheated oil bath at 80 °C. The reaction was conducted under vigorous stirring and followed by GC analysis until completion of the reaction. At completion of the first run (i.e. 2 h) new amounts of reagents (10 mmol of *p*-iodotoluene, 15 mmol of phenylacetylene, 20 mmol of Et_3N) were added, and the volume of solvent adjusted in order to restore the concentrations of reagents to that of the initial run. Immediately after addition, based on GC analysis, the concentration of the *p*-iodotoluene was considered as 100% and the concentration in 1-methyl-4-phenylethynyl-benzene to 0%. The reaction was followed by GC until 80% conversion and the procedure was repeated once.

2.4.4. General procedure for leaching studies by hot-filtration

A total of 10 mmol of *p*-iodotoluene, 15 mmol of phenylacetylene, 20 mmol of Et_3N and 1 mol% [Pd]-catalyst was introduced in a three-necked flask under argon. Then 20 mL of DMF/H_2O (4:1) previously deaerated was added and the mixture was further deaerated by an argon flow for 5 min. The reactor was placed in a preheated oil bath at 80 °C. The reaction was conducted under vigorous stirring for 10 min of reaction. The supernatant solution was filtered through a cannula with a microglass Whatman filter (in order to remove all fine particles) and then treated for further 5 h under the standard reaction conditions.

The reaction was monitored over the total period by GC and the results compared to a standard catalytic reaction.

2.4.5. GC analysis

A 3 mL sample of the reaction mixture was 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 analyzed by GC. GC-rate program: 2 min at 100 °C, heating 15 °C/min up to 170 °C, 2 min at 170 °C, heating 35 °C/min up to 240 °C, 10 min at 240 °C, heating 50 °C/min up to 270 °C and 2 min at 270 °C.

2.4.6. Purification of the products 3–11

The reaction mixture was diluted with 250 mL of water and the resulting mixture was extracted with 4 × 20 mL CH_2Cl_2. The combined organic layers were washed three times with 15 mL H_2O, one time with 15 mL brine, dried over $MgSO_4$ and evaporated. The residue was then purified by flash chromatography on silica gel.

Products 3–4, 6–9 gave ^{1}H and ^{13}C NMR data in accordance with the literatures [11,63,77–82].

3. Data for the compounds 5, 10, 11

3.1. Trimethyl(3-phenylprop-2-ynyloxy)silane 4

Eluant petroleum-ether (40–60)/CH_2Cl_2 = 70/30, R_f = 0.68, 57% as a colourless oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ ppm: 7.48 (m, 2H, *o*-C≡C-C_6H_5), 7.29 (m, 3H, *m*-C=C-C_6H_5; *p*-C=C-C_6H_5), 4.51 (s, 2H, CH_2OH), 0.09 (s, 9H, CH_3Si). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ (ppm): 131.69 (*o*-C≡C, C_6H_5), 128.48 (*p*-C≡C, C_6H_5), 128.32 (*m*-C≡C, C_6H_5), 122.71 (C_q-C≡C, C_6H_5), 87.29 (C≡*C*-CH_2OH), 85,62 (*C*≡C-CH_2OH), 51.50 (CH_2OH). C_9H_8O: mol. wt.: 204.34 g mol^{-1}. MS: *m/z* (%) [M^+] 204 (100), [M^+ –$Si(CH_3)_3$] 131 (85) [M^+ –$OSi(CH_3)_3$] 115 (22), [$C_6H_5^+$] 77 (32).

3.2. 2-(Phenylethynyl)naphthalene 10

Eluant petroleum-ether (40–60)/CH_2Cl_2 = 80/20, R_f = 0.58, 99% as a white solid. ^{1}H NMR (250 MHz, $CDCl_3$): δ (ppm): 7.99 (brs, 1 H, *CH*-$C_{10}H_7$), 7.76 (m, 2H, *CH*-$C_{10}H_7$), 7.73 (m, 1H, *CH*-$C_{10}H_7$), 7.51 (m, 3H, *CH*-$C_{10}H_7$ and *CH*-C_6H_5), 7.42 (m, 2H, *CH*-$C_{10}H_7$), 7.30 (m, 3 H, *CH*-C_6H_5). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ (ppm): 133.00 (C_q-$C_{10}H_7$), 132.78 (C_q-$C_{10}H_7$), 131.64 (*CH*-C_6H_5), 131.41 (*CH*-$C_{10}H_7$), 128.40 (*CH*-$C_{10}H_7$), 128.36 (*CH*-C_6H_5), 128.29 (*CH*-C_6H_5), 127.98 (*CH*-$C_{10}H_7$), 127.75 (*CH*-$C_{10}H_7$), 126.64 (*CH*-$C_{10}H_7$), 126.53 (*CH*-$C_{10}H_7$), 123.27 (C_q-C_6H_5), 120.56 (C_q-$C_{10}H_7$), 89.78 (C≡*C*), 89.72 (*C*≡C). C_9H_8O: mol. wt.: 228.09 g mol^{-1}. MS: *m/z* (%) [M^+] 228 (100).

3.3. 9-(Phenylethynyl)anthracene 11

Eluant petroleum-ether (40–60)/CH_2Cl_2 = 80/20, R_f = 0.58, 76% as a yellow solid. ^{1}H NMR (250 MHz, $CDCl_3$): δ (ppm): 8.63 (d, $^3J(HH)$ = 8.4 Hz, 2H, *CH*-$C_{14}H_9$), 8.39 (s, 1H, *CH*-$C_{14}H_9$), 7.98 (d, $^3J(HH)$ = 8.6 Hz, 2H, *CH*-C_6H_5), 7.75 (dd, $^3J(HH)$ = 8.1 Hz, $^4J(HH)$ = 1.9 Hz, 2H, *CH*-$C_{14}H_9$), 7.57 (td, $^3J(HH)$ = 7.9 Hz, $^4J(HH)$ = 1.3 Hz, 2H, *CH*-$C_{14}H_9$), 7.45 (td, $^3J(HH)$ = 7.9 Hz, $^4J(HH)$ = 1.49 Hz, 2H, *CH*-$C_{14}H_9$), 7.37 (m, 3H, *CH*-C_6H_5). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ (ppm): 132.61 (C_q-$C_{14}H_9$), 131.66 (*CH*-C_6H_5), 131.20 (C_q-$C_{14}H_9$), 128.69 (*CH*-$C_{14}H_9$), 128.53 (*CH*-C_6H_5), 128.49 (*CH*-C_6H_5), 127.72 (*CH*-$C_{14}H_9$), 126.78 (*CH*-$C_{14}H_9$), 126.61 (*CH*-$C_{14}H_9$), 125.69 (*CH*-$C_{14}H_9$), 123.64 (C_q-C_6H_5), 117.28 (C_q-$C_{14}H_9$), 100.75 (C≡*C*), 86.31 (*C*≡C). C_9H_8O: mol. wt.: 278.35 g mol^{-1}. MS: *m/z* (%) [M^+] 278 (100).

4. Results and discussion

4.1. Preparation and characterisation of $PdCl_2\{PPh_2\text{-}(CH_2)_2\text{-}SiCH_3(OCH_2CH_3)_2\}_2$/SBA-15

We chose to prepare catalyst on the base of ordered mesoporous materials, a class of oxides which, given their wide pore size range, have shown to be of great use as catalyst supports in chemical transformations involving bulky molecules. In addition to accurate control of pore shapes and dimensions, organic fonctionalisation of the internal surface of the support can produce precisely controlled active site microstructures [83–85]. In this study, we chose to support our catalysts on mesoporous SBA-15 type silicas, as these supports can be prepared with a pore size up to 80 Å and they tend to be thermally and mechanically very stable (due to their relatively thick walls). The transition metal complex integrated into this material, the $PdCl_2\{PPh_2\text{-}(CH_2)_2\text{-}SiCH_3(OCH_2CH_3)_2\}_2$ complex, was chosen on the basis of literature reports that analogous palladium trisarylphosphine complexes were active and efficient catalysts for the Sonogashira reaction [35,86].

The SBA-15 type silica was synthesized following a protocol adapted from Zhao's report [87–89] by acid catalyzed polycondensation of TEOS in the presence of the non-ionic tri-block copolymer, pluronic 123. The oxide support was calcined at 500 °C under flowing air to remove the template molecule and liberate the pores. The metal precursor,

$PdCl_2\{PPh_2\text{-}(CH_2)_2\text{-}SiCH_3(OCH_2CH_3)_2\}_2$, which contains four condensable siloxane groups per molecule was reacted with the oxide support in a toluene slurry at 85 °C overnight. The complex presumable reacted with the surface by condensation of surface silanol of the oxide support with the alkoxysilane groups of the metal precursor. After the reaction period, the solid was washed by soxhlet extraction with CH_2Cl_2 for 15 h, which assured the total removal of physisorbed metal precursor ([Pd]/SBA-15).

The catalyst was characterized by a variety of spectroscopic and quantitative methods, namely ^{1}H, ^{13}C, ^{29}Si, ^{31}P NMR, X-ray diffraction, nitrogen sorption, thermogravimetric analysis and elemental analysis. The small angle X-ray diffractogram of SBA-15 exhibits a series of three peaks between 1° and 2° (2θ, Fig. 1a) which corresponds to a hexagonal mesoporous structure with d(1 0 0) spacing of 9.0 nm. After the grafting reaction, the diffractogram of [Pd]/SBA-15 shows little change excepting a slight decrease in the intensity of the d(1 0 0) peak.

The results of the analysis of the nitrogen adsorption–desorption isotherms and the pore size distribution curves of the calcined SBA-15 and hybrid material [Pd]/SBA-15 are shown in Fig. 2. Both samples show a type IV isotherm characteristic of mesoporous solids. Relatively narrow pore diameter distributions were observed for both materials and the median pore diameter varies somewhat between the two samples (6.2 and 5.4 nm, respectively), undoubtedly due to the incorporation of the palladium complex in the cavity. Not surprisingly, the BET specific surface area also decreased significantly due to the grafting of the metal precursor, from 920 m^2/g for SBA-15 to 520 m^2/g for [Pd]/SBA-15.

On the molecular level, it is apparent from the NMR spectra and from the comparative elemental analyses that the transition metal precursor has been integrated into the material without significant change in its coordinative structure. The elemental analysis of [Pd]/SBA-15 showed a palladium loading of 2.1 wt.%. The phosphorous analysis (1.3 wt.%) corresponds to a molar ratio of P:Pd of 2.1 (expected 2.0). The ^{31}P CP-MAS NMR (see Supporting information) exhibits two peaks at δ 20.7 and δ 30.9, which can be attributed respectively to the *trans*- and *cis*-isomers of the grafted species (the solid state NMR spectrum of the molecular precursor showed two peaks at δ 20.6 and δ 26.6). This result clearly indicates that the phosphine ligands have survived the grafting reaction and are still coordinated by pairs to the palladium central atom. The ^{1}H MAS NMR and the ^{13}C CP-MAS NMR spectra also show no significant modification of the organic ligand of the metal complex after the grafting reaction. One should note the presence of signals in the ^{13}C spectrum of [Pd]/SBA-15 corresponding to unreacted alkoxysilane groups (δ 17, $-OCH_2\mathit{CH_3}$, and δ 58, $-O\mathit{CH_2}CH_3$). This observation is also indicated by the overbroad peak at δ −12.6 in the ^{29}Si CP-MAS NMR spectrum which would correspond to the presence of D^1 sites (containing the ligand grafted in the form $PPh_2\text{-}(CH_2)_2\text{-}SiCH_3(OCH_2CH_3)(OSi\equiv)$).

Several other types of catalysts were prepared and used for comparison with these new catalytic materials. Supported palladium catalysts used for this comparison have previously been described in the literature, including zeolite supported $[Pd(NH_3)_4]^{2+}$/NaY [73], silica supported palladium(0) ([Pd(0)]/SiO_2) [74], [Pd]/AlF_3, [Pd]/MgF_2 and [Pd]/Al_2O_3 [75] and a commercial catalyst, Pd/C (type Degussa E101 NE/W, 5.1 wt.% Pd – 49 wt.% water). Furthermore, two homogeneous catalysts were tested, the “palladacycle” $\{Pd[P(o\text{-}C_6H_4CH_3)_2(C_6H_4CH_2)[OCOCH_3]\}_2$ [68] and $PdCl_2(PPh_3)_2$ (Strem).

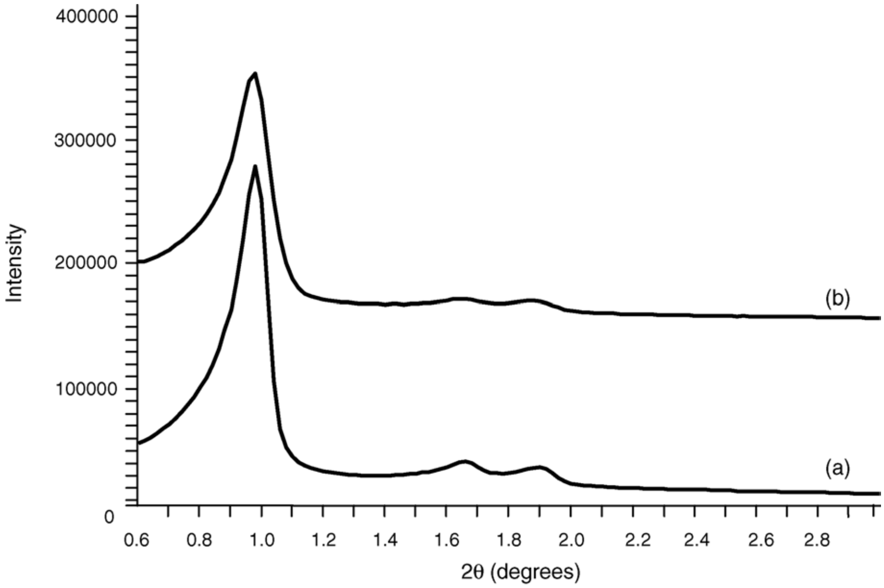


Fig. 1. XRD patterns of (a) calcined SBA-15; (b) (a) after the grafting of $PdCl_2\{PPh_2\text{-}(CH_2)_2\text{-}SiCH_3(OCH_2CH_3)_2\}_2$.

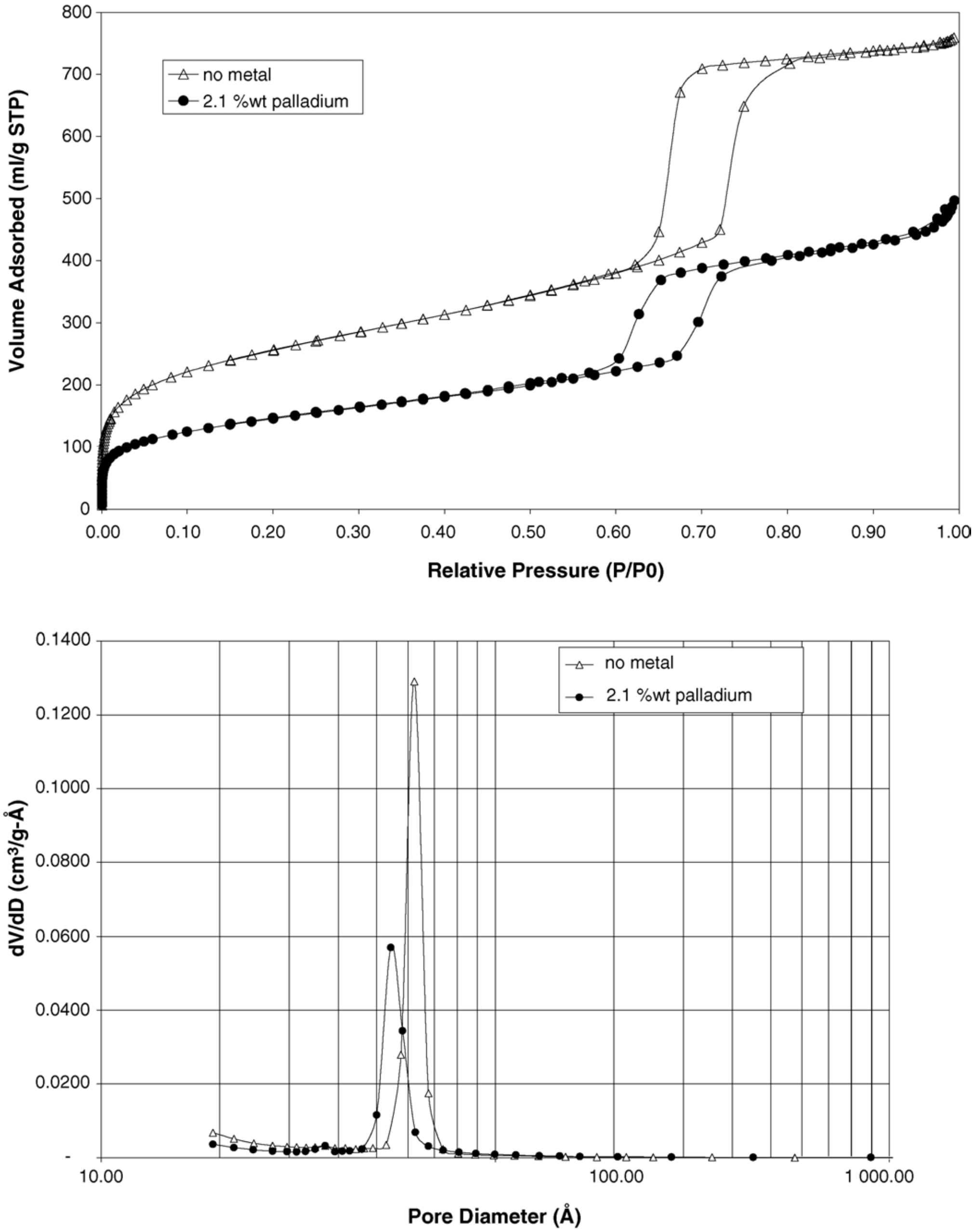


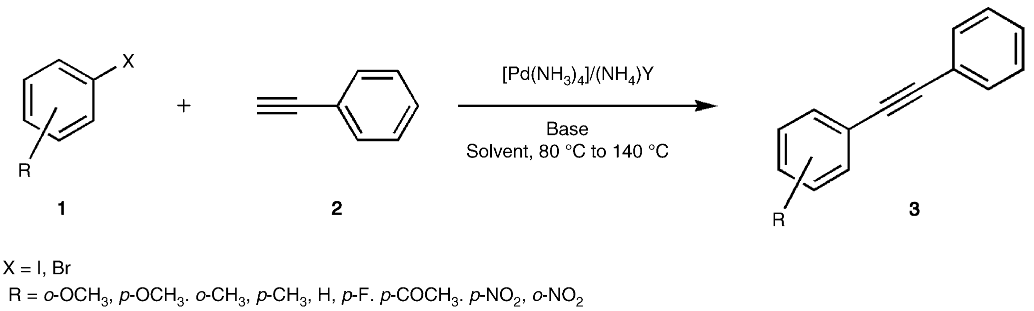
Fig. 2. Nitrogen adsorption/desorption isotherms and pore size distributions (from the BJH calculations) of calcined SBA-15 and palladium modified SBA-15 silica (2.1 wt.% Pd).

4.2. *Catalytic activity and kinetic studies*

In previous studies, the reactivity of $[Pd(NH_3)_4]^{2+}$/$(NH_4)Y$ towards the Sonogashira reactions of various aryl iodides and bromides with phenyl acetylene was evaluated. Remarkable catalytic activity was observed for this specific catalyst independently of the aryl halides used.

In the present contribution, we limited our experiments to the Sonogashira coupling reaction of bromobenzene with phenyl acetylene (Scheme 1: R = H, X = Br). In the literature, aryl bromides as substrates using homogeneous copper-free palladium catalysts led generally to low conversions (10–60%) under standard reaction conditions [22]. Generally, when using heterogeneous supported palladium species (particles, organometallic complexes), the use of CuI as co-catalyst is required in order to attain reasonable activities [62]. Therefore, the coupling reaction of bromobenzene with phenyl acetylene appears to be of interest for developing new heterogeneous copper-free palladium catalysts and to demonstrate effects related to the nature/structure of the Pd-species as well as related to the support.

Generally, all heterogeneous catalysts based on molecular palladium complexes ($[Pd(NH_3)_4]^{2+}$/NaY, [Pd(II)]/NaY, [Pd]/SBA-15) and homogeneous catalysts gave reasonable



Scheme 1. Sonogashira coupling reaction of aryl halides with phenyl acetylene catalysed by copper-free Pd-catalysts.

to high conversions in bromobenzene under our standard reaction conditions {5 mmol bromobenzene, 7 mmol phenylacetylene, 10 mmol Et_3N, 1 mol% [Pd]-catalyst, 80 °C, $DMF/H_2O = 4{:}1$, 6 h} (Table 1). On the contrary, the heterogeneous catalysts based on Pd-particles led to low product yields (≤10%) while giving, comparatively, at the same time high yield in benzene due to the relatively rapid dehalogenation of bromobenzene. Surprisingly, the catalysts prepared following the procedure described by Pearlman ([Pd]/AlF_3, [Pd]/MgF_2 and [Pd]/Al_2O_3) gave low conversions.

Clearer insight into the behavior of the different copper-free palladium catalysts was obtained by following the evolution of the reaction mixture for the coupling reaction of *p*-iodoanisole with phenylacetylene with the time (Fig. 3; Scheme 1: R = *p*-OCH_3, X = I). This reaction was chosen in order to achieve a complete conversion of the aryl halide over a relatively short reaction time. As expected, homogeneous catalysts and heterogeneous catalysts involving immobilised molecular Pd-species ($[Pd(NH_3)_4]^{2+}$/NaY and [Pd]/SBA-15) gave nearly complete conversion of iodoanisole within less than 2 h. On the contrary, the [Pd(II)]/NaY catalyst showed a lower activity, giving only 53% conversion after 6 h.

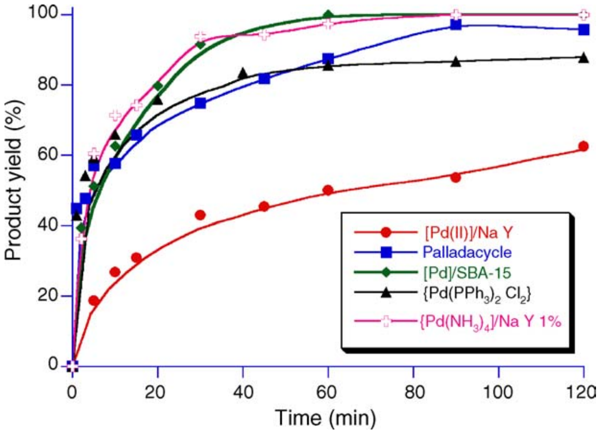


Fig. 3. Sonogashira coupling reaction of *p*-iodonanisole with phenyl acetylene.

The initial activities observed for the different heterogeneous catalysts further account for these observations (Table 2). As expected, the "palladacycle" $\{Pd[P(o\text{-}C_6H_4CH_3)_2(C_6H_4CH_2)[OCOCH_3]\}_2$ and the $PdCl_2(PPh_3)_2$

Table 1
Sonogashira coupling reaction of bromobenzene with phenyl acetylene

Catalyst	Conversion (%)[a]	GC-yield (%)[a]
$[Pd(PPh_3)_2Cl_2]$	86	85
"Palladacycle"	92	90
[Pd]/SBA-15	74	73
$[Pd(NH_3)_4]$/NaY	42	42
[Pd(II)]/NaY	22	20
[Pd(0)]/NaY	17	10[b]
[Pd(0)]/SiO_2	16	4[b]
[Pd]/Al_2O_3	10	5[b]
[Pd]/AlF_3	11	4[b]
[Pd]/MgF_2	12	7[b]
[Pd(0)]/C	17	3[b]

Reaction conditions: 5 mmol bromobenzene, 8 mmol phenylacetylene, 10 mmol Et_3N, 1 mol% [Pd]-catalyst, 80 °C, $DMF/H_2O = 4{:}1$, 6 h.

[a] Conversions based on unreacted bromobenzene and yields were determined by GC with an internal standard (diethylene glycol di-*n*-butyl ether) ($\Delta_{rel} = \pm 5\%$).

[b] The mass balance between conversions and yields is related to the relatively high formation of benzene.

Table 2
Sonogashira coupling reaction of *p*-iodonanisole with phenyl acetylene

Catalyst	Conversion (%)[a]	GC-yield (%)[a]	Initial rate[c] (mmol/gPd × min)
$[Pd(PPh_3)_2Cl_2]$	86	85	235
"Palladacycle"	89	87	272
[Pd]/SBA-15	100	100	127
$[Pd(NH_3)_4]$/NaY	92	91	125
[Pd(II)]/NaY	53	50	37
[Pd(0)]/NaY	35	27[b]	23
[Pd(0)]/SiO_2	27	13[b]	17
[Pd]/Al_2O_3	85	71[b]	171
[Pd]/AlF_3	64	57[b]	125
[Pd]/MgF_2	73	63[b]	106
[Pd(0)]/C	96	88[b]	94

Reaction conditions: 5 mmol *p*-iodoanidale, 8 mmol phenylacetylene, 10 mmol Et_3N, 1 mol% [Pd]-catalyst, 80 °C, $DMF/H_2O = 4{:}1$, 6 h.

[a] Conversions based on unreacted bromobenzene and yields were determined by GC with an internal standard (diethylene glycol di-*n*-butyl ether) after 1 h reaction time ($\Delta_{rel} = \pm 5\%$).

[b] The mass balance between conversions and yields is related to the relatively high formation of anisole.

[c] Initial rates were determined from the kinetic experiments by tracing the tangent at $t = 0$ (see Fig. 3) and account only for the formation of the coupling product.

catalysts showed the highest initial activity (>230 mmol/gPd × min) as expected for a homogeneous catalyst. The $[Pd(NH_3)_4]^{2+}$/NaY and [Pd]/SBA-15 heterogeneous catalysts led to high initial activity (>125 mmol/gPd × min) and gave quantitative conversions. As predictable from the lower palladium dispersion, the [Pd(II)]/NaY catalyst exhibited a lower initial activity, with only 37 mmol/gPd × min and the supported Pd(0) catalysts ([Pd(0)]/NaY and Pd(0)/SiO_2) showed the lowest initial activity. However, as was already observed for C–C coupling reactions, the related commercially available Pd(0)/C catalyst gave remarkably good conversions. Again, surprisingly, while showing a relatively high initial activity (>106 mmol/gPd × min), the [Pd]/AlF_3, [Pd]/MgF_2 and [Pd]/Al_2O_3 catalysts, did not give very high product yields, probably due to a lack of stability of the supported Pd-species.

After demonstrating the applicability of heterogeneous copper-free palladium catalysts for the Sonogashira reaction of bromobenzene with phenyl acetylene, the questions regarding the leaching of active Pd-species in solution and the recyclability of the heterogeneous catalysts were addressed.

Leaching was examined for the coupling reaction of *p*-iodoanisole with phenylacetylene under optimised reaction conditions (10 mmol *p*-iodoanisole, 15 mmol phenylacetylene, 20 mmol Et_3N, 1 mol% [Pd]-catalyst, 80 °C, 20 mL DMF/H_2O = 4:1) using the hot-filtration method: a catalytic run was started as for a standard reaction, and after 10 min of reaction, corresponding to ca. 55% yield, the reaction mixture was filtered through a celite pad to afford a clear filtrate. The composition of the clear filtrate was followed by GC and compared to that of a standard catalytic run. We particularly studied the behaviour of $[Pd(NH_3)_4]^{2+}$/NaY and [Pd]/SBA-15 for which a high initial activity was observed.

Some of us previously demonstrated the heterogeneity of a $[Pd(NH_3)_4]^{2+}$/(NH_4)Y catalyst in the Heck reaction [73] and, recently, in the Sonogashira reaction [63]. As expected, the $[Pd(NH_3)_4]^{2+}$/NaY catalyst used in the present experiments gave very similar results: after hot filtration, the filtrate exhibited further reactivity with a slow increase of conversion of ca. 5%, which is interpreted as evidence of leaching (Fig. 4). However, leaching cannot explain the overall activity of the $[Pd(NH_3)_4]^{2+}$/NaY catalyst for which a quantitative conversion was obtained after ca. 180 min of reaction under the same conditions.

Generally, Pd-phosphine complexes grafted onto metal oxide support are reputed to lead to high leaching. For these reasons, we studied in detail the leaching of the [Pd]/SBA-15 heterogeneous catalyst. As depicted in Fig. 5, no progression of the conversion was observed after the hot filtration of the catalyst indicating that no leaching of active Pd-species occurred. For all catalysts, including the Pd-supported zeolites, AAS analyses of the clear filtrates gave a palladium concentration <7 ppm.

These results are very different from those reported by Kotschy and co-workers where 80% of the overall activity of the Pd/C catalyst was linked to dissolved (leached) Pd-species. They seem to indicate that, in our case, pore confinement (the micro- and meso-environment) may participate to the stabilisation of the immobilised molecular Pd-complexes, i.e. the $\{[Pd(NH_3)_4]^{2+}\}$ and the $\{PdCl_2(PPh_2R)_2\}$ fragments, thus preventing leaching.

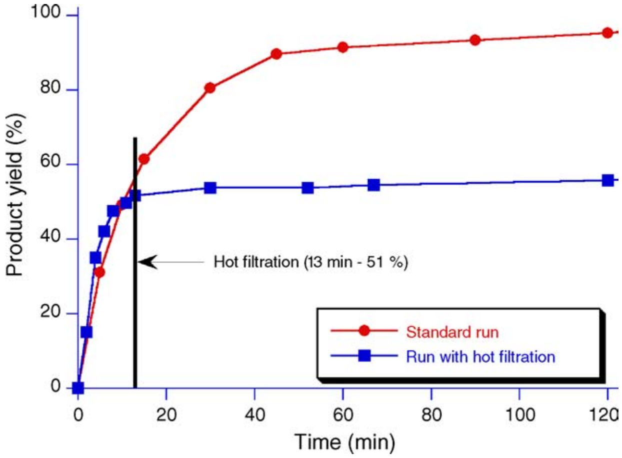


Fig. 4. Residual catalytic activity of $[Pd(NH_3)_4]^{2+}$/NaY after hot filtration (■) after 10 min reaction vs. standard catalytic (●) run. Reaction conditions: 10 mmol *p*-iodoanisole, 15 mmol phenylacetylene, 20 mmol Et_3N, 1 mol% $[Pd(NH_3)_4]^{2+}$/NaY, 80 °C, 20 mL DMF/H_2O (4:1).

The remarkable activity and stability toward leaching of the $[Pd(NH_3)_4]^{2+}$/NaY and [Pd]/SBA-15 catalysts make the study of their recycling particularly interesting. As both catalysts gave comparable results, the study on [Pd]/SBA-15 is described, here, in details (see Supporting information for the $[Pd(NH_3)_4]^{2+}$/NaY catalyst).

The recycling was first examined for the coupling reaction of bromobenzene with phenylacetylene under optimised reaction conditions (5 mmol bromobenzene, 7 mmol phenylacetylene, 10 mmol Et_3N, 1 mol% [Pd]/SBA-15, 80 °C, 6 h, 10 mL DMF/H_2O = 4:1). The method used corresponds to

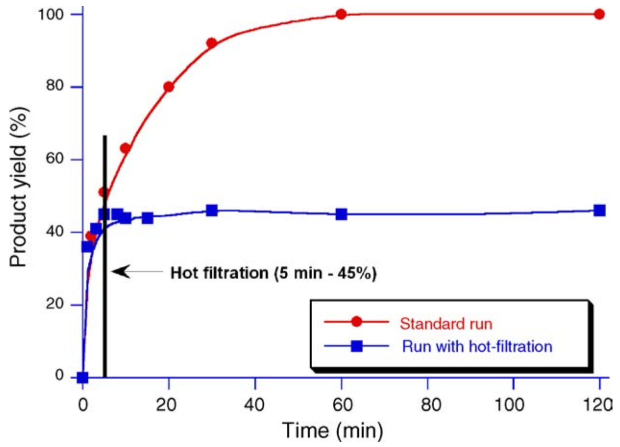


Fig. 5. Residual catalytic activity of [Pd]/SBA-15 after hot filtration (■) after 10 min reaction vs. standard catalytic (●) run. Reaction conditions: 10 mmol *p*-iodoanisole, 15 mmol phenylacetylene, 20 mmol Et_3N, 1 mol% [Pd]/SBA-15, 80 °C, 20 mL DMF/H_2O (4:1).

the following procedure: after the first run of the catalyst, the reaction mixture was allowed to cool to room temperature and the catalyst was separated by centrifugation and washed with DMF/H_2O (4:1). The recycled [Pd]/SBA-15 catalyst was then used without any regeneration as the fresh catalyst under the same reaction conditions giving 44, 18 and 17% conversion of bromobenzene for the first, second and third runs, respectively. These results showed that significant deactivation of the catalyst occurred during the first run, but not subsequently.

To confirm that the loss of activity was not due to the filtration and washing of the catalyst between runs, a second type of recycling study was performed. For this study, we chose to use the more reactive substrate, *p*-iodotoluene. At the completion of the first run (∼2 h), a fresh portion of substrates and solvent was added directly to the product/solvent/catalyst slurry, and the conversion of this fresh substrate into 1-methyl-4-phenylethynyl-benzene, 3, was followed by GC over a period of 5 h. This procedure was repeated once. The initial rate observed for the first run (126 mmol/gPd × min) falls to a stable much lower activity for the second and third runs (5.5 mmol/gPd × min, Fig. 6).

In order to explain the observed deactivation, we studied the fresh and the recycled catalyst by X-ray powder diffraction and by ^{31}P CP-MAS NMR (Fig. 7). The X-ray diffractogram of the used catalyst showed no significant change from the diffractogram of the fresh catalyst, that is it shows three clear peaks in the 0°–3° (2θ) range (see Supporting information), indicating that the structural order of the mesoporous material was not perturbed by the catalytic reaction. The ^{31}P NMR spectrum of the fresh catalyst (Fig. 7a) exhibited two principle peaks at δ 20.7 and 30.9, which indicates that the phosphine ligands are coordinated to palladium and can be attributed to the *cis*- and *trans*-isomers of the square planar grafted transition metal complex. The catalyst used in the second recycling test protocol (no separation of products between cycles) was isolated by filtration, washed with fresh solvent mixture and dried under vacuum prior to CP-MAS NMR characterisation (Fig. 7b). A dramatic decrease in the signal of the coordinated phosphine ligands, in particular the signal associated with the *cis*-isomer, was observed with the appearance of a new peak at δ 40, which would generally be associated with the formation of a phosphine oxide. The oxidation of phosphine in the presence of water leading to the very weakly coordinating phosphine oxide is often cited as a deactivation pathway for such complexes [90]. Thus, we wished to examine the activity and stability of the same catalyst under anhydrous conditions.

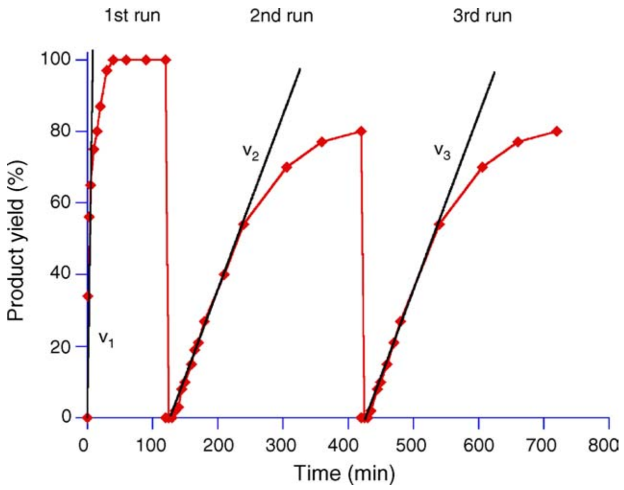


Fig. 6. Recyclability of [Pd]/SBA-15 for the Sonogashira coupling reaction of *p*-iodotoluene with phenylacetylene. Reaction conditions: 10 mmol *p*-iodotoluene, 15 mmol phenylacetylene, 20 mmol Et_3N, 1 mol% [Pd]/SBA-15, 80 °C, 20 mL DMF/H_2O (4:1).

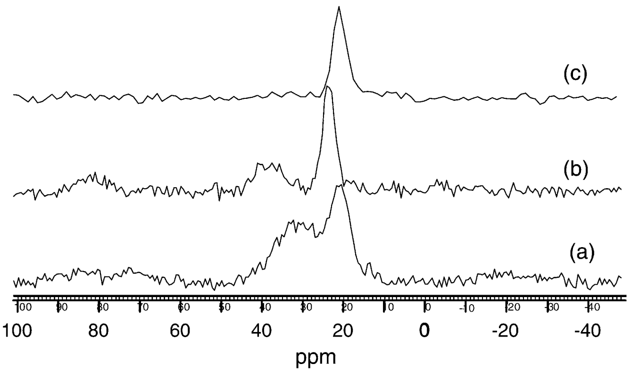


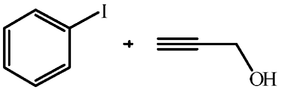
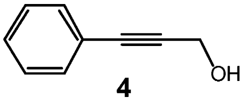
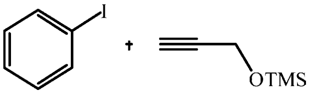
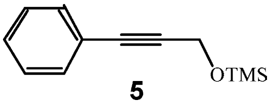
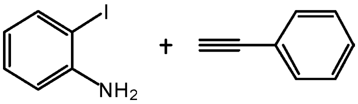
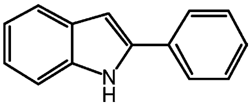
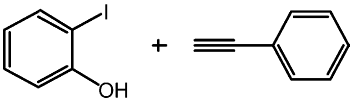
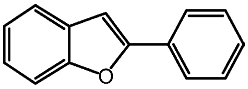
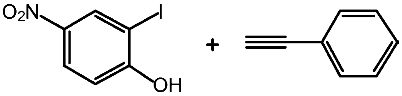
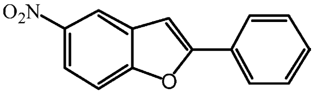
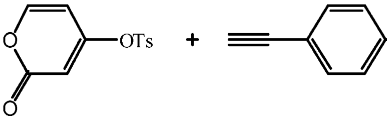
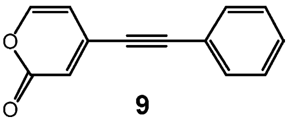
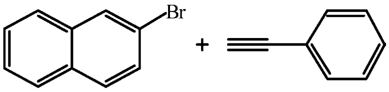
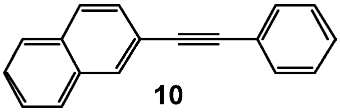
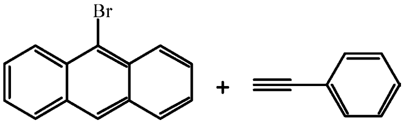
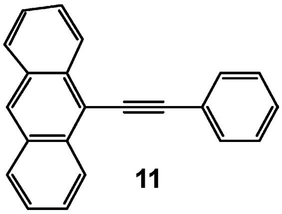
Fig. 7. CP-MAS ^{31}P NMR of (a) $PdCl_2\{PPh_2\text{-}(CH_2)_2\text{-}SiCH_3(OCH_2CH_3)_2\}_2$ grafted on SBA-15; (b) (a) after catalysis in the presence of water; (c) (a) after catalysis in the absence of water.

The Sonogashira reaction of *p*-iodotoluene with phenylacetylene was performed as above in dry DMF, but major catalyst deactivation was observed. The fresh catalyst showed an initial activity of 57 mmol/gPd × min, somewhat lower than that seen when using the H_2O/DMF solvent mixture. One should also note the inflection point in the product yield versus time curve at about 10 min (25% yield, see Supporting information) which may suggest that the active centers are encumbered by the build-up of the organic salt biproduct (at this conversion, 110 mg of salt have been formed, to be compared with the 48 mg of catalyst). In the second and third runs, the activity maintains relatively constant, much lower activities of 1.6 mmol/gPd × min and 1.2 mmol/gPd × min, respectively. The catalyst was then filtered, washed and dried prior to X-ray and NMR analysis (Fig. 7c). Again, the X-ray diffractogram showed no significant change due to the catalytic reaction (see Supporting information), indicating that the overall structural order material was maintained, and thus activity loss cannot be attributed to mesostructural degradation (which might lead to diffusional inhibition). The fresh catalyst peaks have totally disappeared and a new, sharper peak at δ 21 appeared. We cannot determine exactly what has occurred, but one might postulate the reduction of the chelated palladium to a tetrahedral, stable and catalytically less active species. We cannot exclude the effect of the precipitation of organic salt as a factor, which may prevent the diffusion of the reagents to the catalytic species. In any case, water induced phosphine oxidation is clearly not the only catalyst deactivation route available.

Regarding the high activity of the $[Pd(NH_3)_4]^{2+}$/NaY and the [Pd]/SBA-15 catalysts in the Sonogashira cross-coupling reaction, we were interested in evaluating and comparing their catalytic performances for the synthesis of important substructure, namely propargylic alcohols, indoles or furans, as those encountered in various natural or synthetic biologically active molecules.

As reported in Table 3, except for specific reagents like the propargylic alcohol, the [Pd]/SBA-15 catalyst is generally more active than the zeolite supported $[Pd(NH_3)_4]^{2+}$/NaY catalyst. This could be reasonably attributed to the larger aperture of the channels in the SBA-15 material, improving thus the diffusion of the reagents and products to and from the active centres. The lack of reactivity of

Table 3
Sonogashira coupling reaction catalysed by $[Pd(NH_3)_4]^{2+}$/NaY or [Pd]/SBA-15 applied to the synthesis of target organic molecules

Substrates	Product	$[Pd(NH_3)_4]^{2+}$/NaY		[Pd]/SBA-15	
		Time [h]	Conversion[a] [%]	Time [h]	Conversion[a] [%]
	 **4**	6	100 (73)	6	0
	 **5**	–	–	24	80 (57)
	 **6**	6	93	2	100 (72)
	 **7**	6	99	4	100 (78)
	 **8**	6	100 (69)	2	100
	 **9**	3	100 (95)	1	100
	 **10**	24	0	24	100 (99)
	 **11**	24	0	24	100 (76)

Reaction conditions: 5 mmol aryl- or vinyl-halide, 8 mmol alkyne, 10 mmol Et_3N, 1 mol% [Pd]-catalyst, 80 °C, DMF/H_20 (4:1).

[a] Conversion were determined by GC with an internal standard (diethylene glycol di-*n*-butyl ether) ($\Delta_{rel} = \pm 5\%$). Values in parentheses correspond to isolated product yields.

the propargylic alcohol using the [Pd]/SBA-15 catalyst, compared to the $[Pd(NH_3)_4]^{2+}$/NaY, could be related to a relatively strong adsorption of this reagent at the surface of the catalyst's support (specific surface = 520 ± 4 m^2/g), resulting to a deactivation of the catalytic centres, since the corresponding silated derivative lead to good conversion.

Probably, the most interesting results concern the differences observed in the catalytic activities when relatively large educts are engaged into the reaction. Whereas the 2-bromonaphtalene and the 9-bromoanthracene did not react when using the $[Pd(NH_3)_4]^{2+}$/NaY catalyst due to the relatively small apertures (ø = 7.4 Å), they did give a complete conversion using the [Pd]/SBA-15. These results are particularly stimulating for developing further these catalysts toward industrial applications for the fine chemical syntheses.

5. Conclusion

The Sonogashira coupling reaction of bromobenzene with phenylacetylene was found to be a suitable model reaction for the comparison of various heterogeneous and homogeneous catalyst systems. Generally, heterogeneous catalysts involving molecular palladium species (i.e. [Pd]/SBA-15 and $[Pd(NH_3)_4]^{2+}$/NaY) are more active than classical Pd(0)-based catalysts, probably due to higher dispersion and stability of the active species.

These heterogeneous [Pd]/SBA-15 and $[Pd(NH_3)_4]^{2+}$/NaY catalysts were found to be particularly active and selective in various Sonogashira coupling reaction of aryl halides with acetylenes giving generally complete conversion within few hours (3–6 h), the [Pd]/SBA-15 catalyst giving also excellent results when using relatively large aryl halides such as naphthalene or anthracene.

The stability towards leaching and the recyclability of these heterogeneous catalysts were also evaluated. While the [Pd]/SBA-15 and $[Pd(NH_3)_4]^{2+}$/NaY catalysts show excellent stability towards leaching, it was found that they were strongly deactivated during the first run but maintained their lower activity during a subsequent cycle. X-ray diffraction study of fresh and used catalyst showed that the deactivation was not due to structural degradation. However ^{31}P CP-MAS NMR seems to indicate transformation of the observed complexed phosphine ligand during reaction.

In summary, it was established that the heterogeneous [Pd]/SBA-15 and $[Pd(NH_3)_4]^{2+}$/NaY catalysts are efficient, stable with respect to leaching, and recyclable for the copper-free Sonogashira cross-coupling of aryl halides with terminal alkynes. Further work is in progress to develop more active and stable catalysts to improve further both the activity and the recyclability of the heterogeneous copper-free supported palladium catalysts by optimisation of the preparation and/or the reaction conditions for large-scale application in the fine chemical industry.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version at doi:10.1016/j.molcata.2005.05.046.

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