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Citation for the original published paper (version of record):

Carson, F., Pascanu, V., Bermejo Gómez, A., Zhang, Y., Platero-Prats, A E. et al. (2015)
Influence of the Base on Pd@MIL-101-NH₂(Cr) as Catalyst for the Suzuki-Miyaura
Cross-Coupling Reaction
Chemistry - A European Journal, 21(30): 10896-10902
<https://doi.org/10.1002/chem.201500843>

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Influence of the Base on Pd@MIL-101-NH₂(Cr) as a Catalyst for the Suzuki–Miyaura Cross-Coupling Reaction

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Abstract: The chemical stability of metal–organic frameworks (MOFs) is a major factor preventing their use in industrial processes. Here we show that judicious choice of the base for the Suzuki–Miyaura cross-coupling reaction can avoid decomposition of the MOF catalyst, Pd@MIL-101-NH₂(Cr). Four different bases were compared for the reaction: K₂CO₃, KF, Cs₂CO₃ and CsF. The carbonates were the most active, achieving excellent yields in shorter reaction times compared to the fluorides. However, X-ray powder diffraction (XRPD) and N₂ sorption measurements showed that the MOF catalyst degraded when carbonates were used, but remained crystalline and porous with the use of fluorides. X-ray absorption near-edge structure (XANES) measurements revealed that the trimeric chromium cluster in Pd@MIL-101-NH₂(Cr) is present in the degraded MOF. In addition, the different counteranions of the base significantly affected the catalytic activity of the material. Transmission electron microscopy (TEM) revealed that after several catalytic runs many of the Pd nanoparticles (NPs) had migrated to the external surface of the MOF particles and formed larger aggregates. The Pd NPs were larger after catalysis with caesium bases compared to potassium bases.

Introduction

Supported metal nanoparticles (NPs) are important as catalysts in research and industrial processes.^{1–5} The support hinders aggregation of the NPs and facilitates separation from the reaction media and recycling of the catalyst. Typical supports include carbons, polymers, metal oxides and aluminosilicates.^{6–9} However, tailoring the properties of the support for catalysis remains a challenge. Metal–organic frameworks (MOFs) have several advantages as supports for catalysis: high surface areas, controllable pore sizes and tuneable pore environments.^{10–13} Small, finely dispersed particles with high catalytic activity can

be synthesised inside the MOF because the intrinsic framework pore shape and size restrict the NP growth.^{14–26}

The palladium-catalysed Suzuki–Miyaura cross-coupling reaction is one of the most important and effective methods for C–C bond formation.^{27–29} It is used in industry to prepare a wide range of pharmaceuticals and fine chemicals.^{30–34} Many different forms of palladium can be used to catalyse the reaction, including molecular complexes,³⁵ supported NPs³⁶ and ligand-free palladium.³⁷ In many cases for Suzuki–Miyaura reactions, the catalyst is a “precatalyst” that converts to the active form under the reaction conditions.³⁸ There has been much debate about the nature of the actual catalytic species and mechanism involved for reactions catalysed by Pd nanoparticles.^{38–41} For example, Rothenberg and co-workers found that leached Pd species (from Pd NPs) are the active catalytic species for Suzuki–Miyaura cross-coupling reactions at high temperatures in DMF.^{8,42,43} Similarly, Köhler and co-workers showed that dissolved molecular Pd is the catalytically active species when Pd/C is used as the catalyst at 120 °C in *N*-methyl-2-pyrrolidone (NMP); palladium then redeposits onto the support at the end of the reaction.⁴⁴ Pd dissolution and redeposition often occur during Suzuki–Miyaura and Heck reactions with Pd/C catalysts, resulting in eggshell catalysts with lower catalytic activity.^{44–48} In contrast, Lee and co-workers used *in situ* X-ray absorption spectroscopy (XAS) to confirm that Pd NPs do not leach during catalysis at low temperatures in moderate polarity solvents.^{49,50} The mechanism therefore depends on several factors, such as the temperature, solvent, base, stabilising agent and support, among others, and different pathways may even operate simultaneously.

While there have been reports on the role of the base in Suzuki–Miyaura reactions under homogeneous conditions, too little is understood about the effect of the base on the solid support in heterogeneous catalysis.^{51,52} The base (e.g., hydroxide or fluoride) plays several roles in the catalytic cycle, such as formation of the key complex that undergoes transmetalation with the boronic acid, [ArPd(Y)L₂] (Ar = aryl, L = ligand, e.g., PPh₃; Y = OH[−], F[−]) from [ArPd(X)L₂] (X = I[−], Br[−], Cl[−]), and formation of unreactive aryl boronates. The base can also interact with the solid support in a heterogeneous system. Because MOFs are constructed from metal ions or clusters and organic linkers connected by coordination bonds, they are often sensitive to certain reaction conditions. While there has been an abundance of studies on the water stability of MOFs,^{53–56} similar systematic investigations regarding their stability with different bases (i.e., conditions relevant for Suzuki–Miyaura coupling reactions) are missing. The behaviour of the support in catalysis is important to reduce metal leaching, which is essential for the synthesis of pharmaceuticals.⁵⁷ Whereas most attention is generally given to the activity of the catalyst, recyclability and stability of the support are also important. In many cases, MOF stability is a major factor preventing their use in industry.^{58–61}

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There have been several studies on the synthesis of palladium NPs supported on MOFs and their application in the Suzuki–Miyaura cross-coupling reaction.^{22,24,62–68} MIL-101(Cr)^{69–73} has been an attractive support for metal NPs due to its excellent chemical stability, high surface area, wide pore apertures and mesoporous cavities. Yuan *et al.* used Pd@MIL-101(Cr) as a catalyst, with NaOMe in H₂O, for Suzuki–Miyaura cross-couplings—although the catalyst reusability was only shown for the Ullmann coupling reaction.⁶³ Huang *et al.* supported Pd onto the surface of MIL-53–NH₂(Al) and demonstrated its recyclability for the coupling of *p*-bromobenzene with phenylboronic acid.⁶⁴ The amine groups can stabilise the Pd NPs and prevent their aggregation. Interestingly, they observed that MIL-53–NH₂(Al) decomposed when NaOMe was used as the base. Gascon and co-workers also observed decomposition of Pd@MIL-101(Cr) during Suzuki–Miyaura reactions when potassium carbonate was used in the presence of water or alcohols.⁶⁵ We found that Pd@MIL-101–NH₂(Cr) is a good and versatile catalyst for the Suzuki–Miyaura cross-coupling of (hetero)aryl boronic acids with (hetero)aryl halides using K₂CO₃ as the base in aqueous solvent at room

temperature.^{22,24} We also used Pd@MIL-101–NH₂(Cr) in a continuous flow setup to synthesise a wide range of biaryl compounds.²⁴ Although the material retained a high catalytic activity for 10 cycles and palladium leaching was minimal—MIL-101–NH₂(Cr) acts as an efficient scavenger of Pd—the MOF structure had decomposed after catalysis. Avoiding collapse of the MOF can increase the potential catalytic activity of the material, particularly for use in a continuous flow setup.

Herein, we report insightful results regarding the influence of the base on the stability of 8 wt% Pd@MIL-101–NH₂(Cr) when used for Suzuki–Miyaura cross-coupling reactions. We have compared the different anions (carbonates and fluorides) and cations (potassium and caesium) of the base and determined their effect on the catalytic activity, crystallinity, porosity and Pd distribution of Pd@MIL-101–NH₂(Cr). We have used a combination of X-ray powder diffraction (XRPD), X-ray absorption spectroscopy (XAS), N₂ sorption and transmission electron microscopy (TEM) to study the material before and after catalysis.

Table 1. Suzuki–Miyaura cross-coupling reaction of aryl bromides **1a–c** with boronic acids **2a–c** catalysed by Pd@MIL-101–NH₂(Cr).^[a]

Entry	R ¹	R ²	Run	Base	<i>t</i> [h]	Yield [%] ^[b]	Cr leaching [ppm] ^[c]	Pd leaching [ppm] ^[c]
1	CO ₂ Et	CH ₃	1	K ₂ CO ₃	0.5	>99	0.8	2.0
2	CO ₂ Et	CH ₃	2	K ₂ CO ₃	0.5	98	0.3	0.5
3	CO ₂ Et	CH ₃	3	K ₂ CO ₃	0.5	99	0.1	0.2
4	CO ₂ Et	CH ₃	1	KF	0.5	38	n.d. ^[d]	n.d. ^[d]
5	CO ₂ Et	CH ₃	1	KF	2.0	66	<0.1	0.4
6	CO ₂ Et	CH ₃	2	KF	2.0	60	<0.1	0.7
7	CO ₂ Et	CH ₃	3	KF	2.0	47	<0.1	0.1
8	CO ₂ Et	CH ₃	1	Cs ₂ CO ₃	0.5	>99	<0.1	0.1
9	CO ₂ Et	CH ₃	2	Cs ₂ CO ₃	0.5	>99	<0.1	<0.1
10	CO ₂ Et	CH ₃	3	Cs ₂ CO ₃	0.5	>99	<0.1	<0.1
11	CO ₂ Et	CH ₃	1	CsF	0.5	37	n.d. ^[d]	n.d. ^[d]
12	CO ₂ Et	CH ₃	1	CsF	2.0	>99	0.1	0.3
13	CO ₂ Et	CH ₃	2	CsF	2.0	>99	0.1	0.2
14	CO ₂ Et	CH ₃	3	CsF	2.0	>99	0.1	<0.1
15	CH ₃	CH ₃	1	CsF	2.0	93	n.d. ^[d]	n.d. ^[d]
16	OCH ₃	CH ₃	1	CsF	2.0	78	n.d. ^[d]	n.d. ^[d]
17 ^[e]	CO ₂ Et	CO ₂ Me	1	CsF	2.0	>99%	n.d. ^[d]	n.d. ^[d]
18 ^[e]	CO ₂ Et	CHO	1	CsF	2.0	58%	n.d. ^[d]	n.d. ^[d]

[a] Aryl bromide **1a–c** (0.6 mmol), boronic acid **2a–c** (0.9 mmol), base (1.2 mmol) and 8 wt% Pd@MIL-101–NH₂(Cr) (24 mg, 0.024 mmol, 3 mol% Pd) were suspended in a mixture of deionised H₂O (6 mL) and EtOH (6 mL) and stirred vigorously at 25 °C for 0.5 h or 2 h. [b] Yields of **3a–c** were determined by ¹H NMR spectroscopy from the crude reaction mixture using 1,2,4,5-tetrachloro-3-nitrobenzene as an internal standard. [c] For leaching evaluation, the reactions were repeated in a 0.1 mmol scale with respect to the aryl bromide **1a–c**. The reaction mixture was filtrated and analysed by ICP-OES. [d] n.d. = not determined. [e] Reaction temperature 40 °C.

Results and Discussion

The coupling of ethyl 4-bromobenzoate (**1a**) with *p*-tolylboronic acid (**2a**) in the solvent mixture EtOH / H₂O (v/v = 1:1) was chosen as a model reaction (Table 1). We initially used 2 equiv. of K₂CO₃ as the base due to the excellent results we previously reported (high conversions are achieved in short reaction times with the catalyst being recycled up to 10 times without significant loss of catalytic activity).^{22,24} Using the chosen model system, excellent yields of the coupling product **3a** were obtained in short reaction times for 3 runs of 0.5 h each (Table 1, entries 1–3). Despite retaining a high catalytic activity, the MOF was significantly less crystalline after the third run as confirmed by XRPD (Figure 1a). This partial decomposition could be attributed to the effect of the base used, K₂CO₃. Cation and linker exchange can occur in some MOFs even under mild conditions.^{76,77} Carbonates could coordinate to the metal component (chromium cluster) in the MOF and displace the ligand, resulting in framework decomposition.^{65,78} In addition, carbonates form hydroxides in aqueous media⁷⁹ that can destroy the MOF structure; tests with NaOH as the base for the catalytic reaction result in MOF decomposition,²² and aqueous NaOH has been used to digest MIL-101-NH₂(Cr).⁷⁵ We previously found that organic nitrogen-containing bases show significant Pd

leaching and reduction in the catalytic activity of this material, presumably due to the high affinity of Pd for nitrogen ligands.²²

With those results in mind, we decided to test the cross-coupling reaction of **1a** and **2a** using KF as the base (Table 1, entries 4–7). Fluoride salts are common bases for Suzuki–Miyaura cross-coupling reactions and they have also been used to wash and activate MIL-101(Cr).⁷¹ The reaction with KF only reached 38% of yield of **3a** after 0.5 h (Table 1, entry 4). Increasing the reaction time, the yield was 66% after 2 h for the first run and decreased to 60% and 47% for the second and third runs, respectively (Table 1, entries 5–7). The XRPD patterns of Pd@MIL-101-NH₂(Cr) after catalysis using KF confirmed that the MOF remained crystalline after three cycles (Figure 1b). We then performed the coupling of **1a** and **2a** with Pd@MIL-101-NH₂(Cr) using Cs₂CO₃ to determine the influence of the Cs⁺ cation in the carbonate salt. Reactions with Cs₂CO₃ gave comparably high yields of **3a** to those obtained with K₂CO₃ in the same reaction time (0.5 h) (Table 1, entries 8–10 vs 1–3). The XRPD patterns of Pd@MIL-101-NH₂(Cr) after catalysis using Cs₂CO₃ as the base confirmed that the MOF lost crystallinity even faster when Cs₂CO₃ was used instead of K₂CO₃ (Figure 1c vs 1a), which may be due to its stronger basicity, leading to a higher concentration of hydroxide ions in the reaction media.

Next, we studied the effect of the counter-cation in the fluoride salt. The use of CsF instead of KF showed better activity, increasing the yield of **3a** to >99% after 2 h during the three

Figure 1. XRPD patterns of Pd@MIL-101-NH₂(Cr) a) before and after catalysis with K₂CO₃ as the base, b) after catalysis with KF as the base, c) after catalysis with Cs₂CO₃ as the base and d) after catalysis with CsF as the base.

Figure 2. Cr *K*-edge XANES spectra of Pd@MIL-101-NH₂(Cr) before and after catalysis with Cs₂CO₃ and CsF as the base.

cycles without any loss of activity (Table 1, entries 12–14). The ions of caesium salts generally have a lower degree of solvation and ion-pairing compared to other alkali salts, which may explain the higher activity of CsF than KF. As shown in the XRPD data, the MOF retained its crystallinity after three runs with CsF (Figure 1d).

All these data suggest that the structure of the MOF partially collapsed in the presence of carbonates (K₂CO₃ or Cs₂CO₃), but the material remained crystalline when fluorides (KF or CsF) were used. While the cation did not affect the MOF

structure, it did have an impact on the catalytic activity. Caesium carbonate resulted in less metal leaching (Cr and Pd) than potassium carbonate (Table 1). CsF gave higher yields compared to KF, similar to the higher catalytic activity of Cs₂CO₃ than K₂CO₃ previously reported.²² To further test the versatility of CsF as the base, we also used less reactive, electron-rich bromoarenes **1b** (*p*-Me) and **1c** (*p*-OMe), which were coupled with **2a** in a mixture of H₂O / EtOH (1:1) as the solvent for 2 h at room temperature, giving **3b** and **3c** in very good yields (93% and 78% respectively, Table 1, entries 15 and 16). Even electron deficient boronic acids **2b** and **2c** (R² = *p*-CO₂Me and *p*-CHO respectively), known to be less reactive, could be successfully used to obtain the desired biphenyls **3d** and **3e** in moderate to excellent yields (Table 1, entries 17 and 18).

While the XRPD results imply loss of long-range order in the MOFs after catalysis with carbonate bases, the local coordination environment of chromium in the MOFs is unknown. Therefore, we carried out Cr *K*-edge XAS on the MOFs before and after catalysis and the X-ray absorption near-edge structure (XANES) spectra are shown in Figure 2. The XANES spectra of Pd@MIL-101-NH₂(Cr) before and after catalysis with Cs₂CO₃ and CsF as bases are remarkably similar, which indicates that the trinuclear, trigonal {Cr₃OX(H₂O)₂(CO₂)₆} (X = OH[−], F[−]) secondary building units (SBUs) of the MOF are still present in the poorly crystalline material.

Figure 3. N₂ adsorption (●) and desorption (○) isotherms of Pd@MIL-101-NH₂(Cr) a) before and after catalysis with K₂CO₃, b) after catalysis with KF as the base, c) after catalysis with Cs₂CO₃ as the base and d) after catalysis with CsF as the base. Before catalysis is shown in green, after 1 run in dark blue, after 2 runs in blue and after 3 runs in cyan.

Table 2. Specific surface areas and pore volumes of Pd@MIL-101-NH₂(Cr) before and after catalysis.

Entry	Material after run #	Base ^[a]	BET Surface Area (m ² g ⁻¹)	Pore Volume (cm ³ g ⁻¹)
1	0 ^[b]	-	2660	1.43
2	1	K ₂ CO ₃	1040	0.57
3	2	K ₂ CO ₃	360	0.22
4	3	K ₂ CO ₃	30	0.05
5	1	Cs ₂ CO ₃	880	0.47
6	2	Cs ₂ CO ₃	680	0.36
7	3	Cs ₂ CO ₃	60	0.09
8	1	KF	2200	1.12
9	2	KF	2080	1.09
10	3	KF	1950	0.98
11	1	CsF	2340	1.20
12	2	CsF	1990	1.01
13	3	CsF	1820	0.94

[a] The base used for catalysis. [b] Run 0 denotes Pd@MIL-101-NH₂(Cr) before catalysis.

In order to validate the structural stability of the MOF under the different reaction conditions, the porosity of the materials was examined by N₂ sorption after the recycling studies with different bases (Figure 3). The surface areas and pore volumes were measured and are reported in Table 2. The BET surface area and pore volume of Pd@MIL-101-NH₂(Cr) were 2660 m² g⁻¹ and 1.43 cm³ g⁻¹, respectively, before catalysis (Table 2, entry 1).

When carbonates were used as the base for the catalysis, the surface area decreased drastically to 30 and 60 m² g⁻¹ after three runs with K₂CO₃ (Figure 3a and Table 2, entry 4) and Cs₂CO₃ (Figure 3c and Table 2, entry 7), respectively. The pore volume also decreased to 0.05 cm³ g⁻¹ for K₂CO₃ (Table 2, entry 4) and 0.09 cm³ g⁻¹ for Cs₂CO₃ after three runs (Table 2, entry 7).

On the other hand, when fluorides were used as the base for catalysis, the surface area only decreased to 1950 and 1820 m² g⁻¹ and the pore volume to 0.98 and 0.94 cm³ g⁻¹ after three runs with KF (Figure 3b; and Table 2, entry 10) and CsF (Figure 3d; and Table 2, entry 13) respectively. The textural analysis supports the results from the XRPD analysis: Pd@MIL-101-NH₂(Cr) collapses when carbonates are used in aqueous media for the catalytic reaction, but remains porous when fluorides are used.

We then used TEM to investigate the effect of the base on the Pd NP dispersion and size distribution in the MOF. TEM images of the MOFs before and after catalysis are shown in Figure 4. TEM analysis revealed that the Pd NPs before catalysis were highly dispersed with an average particle size of 1 nm or less (Figures 4a and 4b). In all cases, there was an increase in the size of the Pd NPs and aggregation of Pd NPs on the MOF after three runs of catalysis (Figures 4c–4j). Interestingly, many of the Pd NPs were significantly larger after catalysis with caesium bases compared to potassium bases.

Electron tomography revealed that the larger Pd NPs were located on the external surface of the MOF (See video, Supplementary Information). Although dissolution and

redeposition of Pd NPs during Suzuki–Miyaura reactions has been observed with other solid supports, the influence of different bases on the Pd NP distribution has not been reported.

Figure 4. TEM images of Pd@MIL-101-NH₂(Cr) before catalysis (a,b) and after three runs of catalysis with K₂CO₃ (c,d), KF (e,f), Cs₂CO₃ (g,h) and CsF (i,j) as the base.

The larger Pd NP size when caesium bases were used implies that more Pd migration took place. This can be related to the higher activity observed with caesium bases compared to potassium bases, and suggests that homogeneous Pd species contribute significantly to the catalytic activity of Pd@MIL-101-

$\text{NH}_2(\text{Cr})$ (*vide infra*). Amatore *et al.* found that under homogeneous conditions, the counter-cation (when associated to OH^- and in DMF) affects the transmetalation step of the Suzuki–Miyaura reaction and the reactivity decreases in the order: $n\text{Bu}_4\text{N}^+ > \text{K}^+ > \text{Cs}^+ > \text{Na}^+$.⁸⁰ Under our catalytic conditions, the effect of the counter-cation on the Pd distribution in the MOF is more important than its role in the catalytic cycle.

After catalysis with carbonate bases, Pd NPs that remain encapsulated in the MOF are inaccessible to reactants for further catalysis because these supports have lost their porosity. Therefore, catalysis will only take place on the MOF surface (or in solution). Despite this, the catalyst is still efficient for numerous substrates for a short-to-medium time period (*i.e.*, when used in a continuous flow process).⁸¹ Even though the MOF does not collapse with fluoride salts, some Pd migrates to the surface during catalysis and forms larger aggregates. This partial relocation of the active species opens the way for new catalytic pathways, but the substrates can still access the pores of the MOF where catalysis can take place in a homogeneous or heterogeneous manner.^{38,42,43} As previously mentioned,²² leached Pd species can be responsible for the catalysis in Suzuki–Miyaura cross-coupling reactions. In Pd@MIL-101- $\text{NH}_2(\text{Cr})$, the small Pd NPs in the MOF can act as a reservoir of Pd atoms or ions, which subsequently reform larger Pd NPs on the MOF surface.⁴⁵ In this case, Pd@MIL-101- $\text{NH}_2(\text{Cr})$ effectively acts as a palladium scavenger after the coupling reaction is complete. Alternatively, catalysis can continue to function heterogeneously on the surface of the Pd NPs if the porosity of the framework is maintained. Nevertheless, the stability and lifetime of the catalyst are particularly important for use in continuous flow processes.²⁴

Conclusions

The choice of base for the Suzuki–Miyaura cross-coupling reaction has an impact on the catalyst structure when using palladium NPs encapsulated in MIL-101- $\text{NH}_2(\text{Cr})$. Not only does it influence the catalytic activity, but also the stability of the framework. The use of carbonates (K_2CO_3 and Cs_2CO_3) as the base for the catalytic reaction leads to high yields in short reaction times, but also results in decomposition of the MOF. Importantly, by using fluorides as the base instead of carbonates, the crystallinity and porosity of the MOF are preserved during the reaction conditions tested here. Although the cross-coupling reaction requires longer times with the use of fluorides, the activity can be increased and controlled by using different counter-cations (Cs^+ instead of K^+) for the fluoride base. TEM analysis of the materials after catalysis indicates aggregation of Pd NPs on the surface of the MOF. Interestingly, the best results in catalysis are obtained with caesium bases, even though larger Pd NPs are formed. This is due to more palladium migration and redeposition occurring, which indicates that homogeneous Pd species contribute significantly to the catalytic activity. In the Pd@MIL-101- $\text{NH}_2(\text{Cr})$ system, the anions have a large effect on the MOF structure, and they also influence the catalysis. On the

other hand, the cations have a larger impact on the catalysis outcome and the Pd NP's distribution.

Stability is an important aspect if MOFs are to be used for large-scale catalytic setups, particularly for the industrial synthesis of pharmaceuticals that require catalysts with high activity and long half-life in order to avoid metal contamination and reduce waste and cost. Although the crystallinity and porosity of the MOF do not seem to influence the catalytic activity of the material, in catalytic processes where the framework structure is crucial, such as size-selective catalysis, maintaining MOF crystallinity could be important. In addition, prolonging the lifetime of the catalyst may be a valuable approach in continuous flow processes.

Experimental Section

Materials and equipment

All chemicals and reagents were used as received without further purification. XRPD data were collected on a PANalytical X'Pert PRO diffractometer using $\text{Cu K}\alpha_1$ radiation in Bragg–Brentano geometry, recorded on a Pixel detector with a speed of $0.1^\circ (2\theta) \text{ min}^{-1}$. The samples were dispersed on zero-background Si plates with ethanol. N_2 sorption isotherms were measured at 77 K on a Micromeritics ASAP 2020 system. The samples were degassed under dynamic vacuum at 150°C for 12 h prior to measurements. TEM observations were performed on a JEOL JEM-2100LaB₆ microscope operating at 200 kV. A tilt series of bright field images were acquired over an angular range of $\pm 70^\circ$ with increments of 1.0° . The 3D reconstructions were carried out using the weighted back-projection algorithm. Inductively coupled plasma-optical emission spectrometry (ICP-OES) was used for chromium and palladium determination with a Varian Vista MPX ICP-OES instrument. Medac Ltd in the UK carried out the elemental analysis. ^1H NMR spectra were recorded at 400 MHz on a Bruker Advance spectrometer. Cr K-edge XAS was conducted at beamline B18, Diamond Light Source, UK, using a Si(111) double-crystal monochromator and a 9-element Ge detector. The current of the storage ring was approximately 300 mA. Spectra were energy-calibrated to chromium foil (absorption edge taken at 5988.8 eV). MOF samples were ground with cellulose and pressed as pellets. XAS data processing was performed using the Athena software package.⁷⁰

General procedure for the Suzuki–Miyaura cross-coupling reaction

8 wt% Pd@MIL-101- $\text{NH}_2(\text{Cr})$ was prepared according to the literature procedures.^{22,65,71} Aryl bromide (**1a-c**, 0.6 mmol), boronic acid (**2a-c**, 0.9 mmol), base (1.2 mmol) and 8 wt% Pd@MIL-101- $\text{NH}_2(\text{Cr})$ (24 mg, 0.024 mmol, 3 mol% Pd) were suspended in a mixture of deionised H_2O (6 mL) and EtOH (6 mL) in a sealed 20 mL vial and stirred vigorously at 25°C for 0.5 h or 2 h. The solid was centrifuged and washed with EtOH (10 mL), EtOAc ($2 \times 10 \text{ mL}$) and H_2O ($2 \times 10 \text{ mL}$). The combined phases were separated and the aqueous phase was washed with EtOAc ($2 \times 10 \text{ mL}$). The combined organic phases were dried over MgSO_4 and filtered. The volatiles were removed under reduced pressure. Yields were determined by ^1H NMR spectroscopy from the crude reaction mixture against 1,2,4,5-tetrachloro-3-nitrobenzene as an internal standard.

Acknowledgements

This project was supported by the Swedish Research Council (VR) and the Swedish Governmental Agency for Innovation Systems (VINNOVA) through the Berzelii Center EXSELENT, the Knut and Alice Wallenberg Foundation through the project grants 3DEM-NATUR and Catalysis in Selective Organic Synthesis, and by the MATsynCELL project through the Röntgen Ångström Cluster. B.M.-M. also thanks VINNOVA for a VINNMER grant. We are grateful to Dr Andrew Dent for XAS measurements at beamline B18, Diamond Light Source, UK, under the Rapid Access Proposal SP12120.

Keywords: metal–organic framework • heterogeneous catalysis • palladium • nanoparticles • cross-coupling

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- [81] In a continuous flow setup using similar conditions, after a period of relative stability and high activity (48 to 66 h), the catalyst was deactivated leading to high levels of metal leaching and the amorphisation of the MOF. The deactivation of the catalyst occurred even more rapidly when more functionalised substrates were used.

Entry for the Table of Contents (Please choose one layout)

Layout 1:

FULL PAPER

The heterogeneous metal–organic framework catalyst Pd@MIL-101-NH₂(Cr) is highly affected by the base during the Suzuki–Miyaura cross-coupling reaction. The base influences the catalytic activity, crystallinity, porosity and palladium distribution of the material. Use of carbonates as the base leads to MOF degradation, whereas use of fluorides preserves the MOF structure.

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Page No. – Page No.

Influence of the Base on Pd@MIL-101-NH₂(Cr) as a Catalyst for the Suzuki–Miyaura Cross-Coupling Reaction