

# Heterogeneous Catalysis by Covalent Organic Frameworks (COF): Pd(OAc)<sub>2</sub>@COF-300 in Cross-Coupling Reactions

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COF-300, an imine-linked, crystalline, and microporous covalent organic framework, modified by coordination of Pd(OAc)<sub>2</sub> to its walls, afforded a hybrid material, Pd(OAc)<sub>2</sub>@COF-300, which was used as an efficient heterogeneous catalyst for cross-coupling reactions. This material showed excellent catalytic activity for the phosphine-free Suzuki–Miyaura, Heck, and Sonogashira cross-coupling reactions with low palladium loadings (0.1 mol% Pd). X-ray photoelectron spectroscopy analysis of the catalyst after the reaction showed that Pd<sup>II</sup> is converted to Pd<sup>0</sup>, which is trapped within the COFs nanopores. This was confirmed by high-resolution transmission electron microscopy. Moreover, promising results were obtained using Pd(OAc)<sub>2</sub>@COF-300 under continuous-flow conditions for a Suzuki–Miyaura cross-coupling reaction.

### Introduction

Covalent organic frameworks (COFs) are all organic micro/mesoporous materials built from covalent-bonding of organic prepared by small, appropriately functionalized, organic compounds. These materials are structurally related to zeolites but have the advantage that their properties and the presence of functional groups can be tailor made.<sup>[11]</sup> Differently from metalorganic frameworks (MOFs) or their inorganic counterparts (zeolites, SBA-15, MCM-41, etc.), COFs do not contain metallic ions or heavy elements as part of their structure. COF-300 is one of these interesting nanoporous materials that is crystalline and has a high surface area (1400–1500 m<sup>2</sup> g<sup>-1</sup>).<sup>[2]</sup> It is prepared from the condensation of tetrakis-(4-aminobenzyl)methane with terephthalaldehyde and has both porous and interpenetrated structure. The pore apertures are of approximately

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Supporting Information for this article is available on the WWW under http://dx.doi.org/10.1002/cctc.201500926. 8 Å (interpenetrated structure) and potentially approximately 28–30 Å in the case of the noninterpenetrated structure (Figure 1). The building blocks are held together by imine functional groups, thus the structure can be classified as an imine-based COF. Inspired by the reactions within zeolites, one could imagine the use of this material as host for catalysts such as those used in cross-coupling reactions.<sup>[1b,3]</sup>



**Figure 1.** Synthesis and structure of COF-300, illustrating A) its diamond-like symmetry, B) its interpenetrated structure, and C, D) its pore aperture.

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In recent years, some examples of palladium supported on porous materials have been described as catalyst for cross-coupling reactions.<sup>[4]</sup> Zhang et al. reported the use of palladium nanoparticles supported on nanocrystals of MOF based on scandium.<sup>[4e]</sup> They found interesting catalytic activities for Suzuki-Miyaura cross couplings, but their catalyst seems to lack robustness and was only synthesized on a small scale in a microwave reactor vial. Xamena and co-workers displayed a Pd-containing MOF as a catalyst for Suzuki cross-coupling reaction between *p*-bromoanisole and phenylboronic acid.<sup>[4f]</sup> A conversion of 85% was observed after 5 h in o-xylene, at 150°C, employing 2.5 mol % Pd. Milder conditions (ethanol, 25 °C) led to a conversion of 87%, but a longer reaction time was required (48 h). The best results for Pd@MOF in Suzuki reactions were obtained with MIL-101 and its analogs.<sup>[4g-j]</sup> For example, Pascanu and co-workers displayed the synthesis of more than 40 biaryls, including highly functionalized substrates, employing Pd@MIL-101(Cr)-NH<sub>2</sub> as catalyst, with a Pd loading of 1 mol%, under mild conditions.<sup>[4]]</sup>

Ding and co-workers demonstrated Pd/COF-LZU1, a Pd-containing COF, as a catalyst for Suzuki cross-coupling reactions.<sup>[4b]</sup> Eight examples were described, with excellent yields. However, harsh conditions (*p*-xylene at 150 °C) and long reaction times (2-3 h) were employed. In addition, after the first reaction cycle the intensity of the powder XRD signals decreased, which was attributed to the exposure to harsh conditions, decreasing the structural regularity of the material. An excellent compilation about Suzuki–Miyaura palladium catalysis for several materials can be found in the Supporting Information of ref. [4j].

Other cross-coupling reactions using this kind of material have also been reported.<sup>[5e]</sup> Mullangi et al. reported  $Pd^0@$ -trzn-COF as catalyst for multifold Heck reactions, C–C couplings and CO oxidation.<sup>[5e]</sup>

As there are relatively few examples for the use of COF in catalysis,<sup>[4a-c,5]</sup> we decided to explore the COF-300 topology for palladium-catalyzed cross-coupling reactions.<sup>[1b,3]</sup> It was envisaged that the imine groups of the COF-300 structure would afford a coordination site or a stable complex for a palladium salt in the nanostructured material.

In the present study we describe the use of a palladium-salt-modified COF-300,  $Pd(OAc)_2@COF-300$ , as a catalyst for cross-coupling reactions.

### **Results and Discussion**

#### Synthesis and characterization of COF-300

The host COF-300 was prepared based on the procedure previously reported,<sup>[2]</sup> with modifications, which made the procedure simpler and allowed a gram-scale synthesis (for details see the Supporting Information).

#### Synthesis and characterization of Pd(OAc)<sub>2</sub>@COF-300

 $Pd(OAc)_2$  was dissolved in  $CH_2CI_2$  and this solution was kept in contact with COF-300 for 1 h at reflux (Scheme 1, for details

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**Scheme 1.** Preparation of Pd(OAc)<sub>2</sub>@COF-300 through impregnation of Pd(OAc)<sub>2</sub> into COF-300 pores.

see Supporting Information). The resulting yellowish solid was filtered and thoroughly washed with  $CH_2Cl_2$  in a Soxhlet extractor for 3 days.

Powder XRD and FTIR analysis for  $Pd(OAc)_2@COF-300$ showed no qualitative difference in relation to the parent COF-300, demonstrating that introduction of the palladium salt into COF-300 structure occurred without loss of crystallinity or substantial changes in the chemical environment, indicating that the host framework integrity was maintained (Figure 2a,b). However, the signals of the powder XRD analysis of Pd(OAc)<sub>2</sub>@COF-300 are slightly displaced towards smaller angles in comparison to those of the PXRD of COF-300, indicating an increase in the lattice parameter of the former, compatible with the idea that the presence of the guest Pd(OAc)<sub>2</sub> in the COF-300 cage led to unit cell expansion.

The BET surface area obtained for  $Pd(OAc)_2@COF-300$  (270 m<sup>2</sup>g<sup>-1</sup>) decreased in relation to the parent COF-300 (1373 m<sup>2</sup>g<sup>-1</sup>), in agreement with the literature for other COF structures.<sup>[5]</sup> This result also suggests that the  $Pd(OAc)_2$  occupied the pores of the COF-300. The observed adsorption isotherms for both materials are typical of microporous materials (type I).

XPS measurements with  $Pd(OAc)_2@COF-300$  showed characteristic peaks at 337.7 eV and 342.9 eV (Figure 3a), which can be assigned to the  $3d_{5/2}$  and  $3d_{3/2}$  states of  $Pd^{II}$ . A peak with a positive shift of the binding energy by 1.2 eV for the N1s region and an intensity ratio of 1:1 with  $Pd^{II}$  peak can be attributed to imine N atoms bonded to  $Pd^{II}$  species (Figure 3b). It is known that a strong Pd–N interaction can lead to differences in the binding energy of nitrogen.<sup>[6]</sup> Thus, this indicates that the palladium is coordinatively bonded to the imine nitrogen atoms of the COF-300.

The morphology of  $Pd(OAc)_2@COF-300$  was studied by SEM and a ricelike morphology of COF-300 was observed (Figure 4). Finally, the amount of Pd in the organic framework host was determined by atomic absorption and a concentration of 1.74% w/w was found. Detailed data on characterization of



**Figure 2.** Characterization of Pd(OAc)<sub>2</sub>@COF-300. a) Comparison of the PXRD profile of Pd(OAc)<sub>2</sub>@COF-300 and COF-300. b) Comparison of the FTIR spectra of Pd(OAc)<sub>2</sub>@COF-300 and COF-300.

the parent COF-300 and  $Pd(OAc)_2@COF-300$  can be found in the Supporting Information.

## Evaluation of $Pd(OAc)_2@COF-300$ as a catalyst in the Suzuki-Miyaura coupling

To evaluate the catalytic activity of Pd(OAc)<sub>2</sub>@COF-300, the Suzuki-Miyaura coupling was chosen as model reaction, as this reaction is considered to be a valuable synthetic tool. Preliminary experiments were carried out using the reaction between phenylboronic acid (0.44 mmol) and bromobenzene (0.40 mmol), in methanol (3 mL), with  $K_2CO_3$  (0.80 mmol) as base and 5 mg of Pd(OAc)<sub>2</sub>@COF-300 (0.2 mol% Pd), under reflux. These conditions lead to a 99% yield after 20 min of reaction. Aiming to optimize the reaction conditions, a series of experiments were performed varying the nature of the base (K<sub>2</sub>CO<sub>3</sub>; Cs<sub>2</sub>CO<sub>3</sub>; tetraethylammonium, TEA) and different combinations of methanol/water (for details see the Supporting Information). The best results were obtained employing K<sub>2</sub>CO<sub>3</sub> as base and methanol/water (4:1) as solvent, at 70 °C. Under these conditions, a yield of 99% was obtained in the same 20 min, but with half the amount of  $Pd(OAc)_2@COF-300$  (2 mg, 0.08 mol % Pd). It is known that Suzuki-Miyaura cross-couplings are improved by the addition of water,<sup>[7]</sup> and a probable explanation is the greater solubility of the inorganic base in



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**Figure 3.** a) XPS spectrum of  $Pd(OAc)_2@COF-300$  in the 3d region showing characteristic peaks at 337.7 eV and 342.9 eV, corresponding to the  $3d_{5/2}$  and  $3d_{3/2}$  states of  $Pd^{II}$ . b) XPS spectrum of  $Pd(OAc)_2@COF-300$  in the 1s region showing characteristic peaks at 398.6 eV (free imine nitrogen) and 399.8 eV (imine nitrogen bounded to  $Pd^{II}$ ).



Figure 4. SEM images of Pd(OAc)<sub>2</sub>@COF-300. Scale bars = 2  $\mu$ m.

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the reaction medium. In this sense, it is interesting to highlight the compatibility of  $Pd(OAc)_2@COF-300$  with the aqueous medium and this could allow for further development of environmentally friendly methodologies employing this palladium catalyst.

In a subsequent step, the reaction conditions were fixed and a number of varying substrates with different reactivity were evaluated. The compilation of the results is shown in Table 1. The results clearly demonstrate the efficiency and versatility of the new catalyst.

Palladium loadings as low as 0.1 mol% were found to efficiently catalyze the reaction. In general, nearly quantitatively yields were observed for X = Br or I, and Ar = phenyl or naphthyl. The turnover numbers (TON) and frequencies (TOF) were determined and range from very good to excellent (entries 1–12, 31–41). Heteroaromatic boronic acids and aryl halides gave moderated to good yields, which could also be enhanced by an increased reaction time (entries 13–30). These are interesting results as heterocyclic moieties are presented in a range of natural products, drugs, and new drug candidates. Crude products are obtained in relatively high purity, as shown by GC–MS analysis (see the Supporting Information).

Pd/C for the same reaction was reported to afford 55% yield of products using the double of catalyst loading (0.2 mol % Pd) in 10 h of reaction.<sup>[9]</sup> Comparison with other heterogeneous catalysts<sup>[4,5]</sup> reveals very good performance of the Pd(OAc)<sub>2</sub>@COF300.

Aryl chlorides also react under catalysis by Pd(OAc)<sub>2</sub>@COF300, but with low conversions (approximately 20%), smaller than those for the corresponding aryl bromides and iodides (Supporting Information, Table S3). This result is related to the low reactivity of aryl chlorides in Suzuki–Miyaura cross-coupling reactions. However, improvements were obtained by increasing the reaction time.

To confirm the heterogeneous nature of the catalyst, a typical test for catalyst leaching was carried out. Briefly, Pd(OAc)<sub>2</sub>@COF-300 and K<sub>2</sub>CO<sub>3</sub> were mixed in methanol and H<sub>2</sub>O. The solution was heated to 70 °C, with magnetic stirring, for 60 min. After that, it was hot-filtered into another roundbottom flask. The substrates (Table 1, entry 1) were added to the filtrate and the reaction was heated to 70 °C, with magnetic stirring, for 60 min. GC/MS analysis revealed the absence of the product, suggesting that, if Pd is present in solution, the amounts are insufficient to promote a significant level of catalysis. In another test, using *p*-bromoacetophenone and phenylboronic acid as substrates, under the optimized reactions conditions, the catalyst was filtered off from the hot reaction mixture after 2 min. However, analysis of the filtered solution indicated a 100% conversion of p-bromoacetophenone in the cross-coupled product. To stop the reaction before it is completed, 3-bromophenol, which is a less reactive substrate, was used. The catalyst was filtered off from the hot reaction mixture after one minute and the analysis of the filtered solution indicated 80% conversion. The filtered solution was left stirring at 70 °C and after one hour no extra conversion was observed.

The concentration of metals in drug products is a great concern for the pharmaceutical industry if metal catalysis is used in drug synthesis. Therefore, we decided to verify the concentration of palladium in the crude isolated product of a model reaction using a substrate with  $NH_2$  group to potentially increase the possibility of coordination to the Pd in the product (Table 1, entry 10). Analysis by inductively coupled plasma mass spectrometry (ICP–MS) gave a value of 85 ppb, much smaller than the maximum of 10000 ppb fixed for orally administered drugs.<sup>[8]</sup> This result is in line with the findings of the previous test where leaching was not observed.

To evaluate the recyclability of Pd(OAc)<sub>2</sub>@COF300, the reaction between bromobenzene and phenylboronic acid was used as a model. Deactivation was not observed until the fifth cycle, demonstrating the robustness of the catalyst (for details see the Supporting Information). X-ray photoelectron spectroscopy (XPS) analysis of the catalyst after the first cycle revealed that Pd<sup>0</sup> is the predominant catalytic species (Figure 5 a), demonstrating that reduction of Pd<sup>II</sup> occurs in the reaction medium. Powder XRD analysis for the same sample indicates that crystallinity is maintained. Additionally, the lack of peaks of metallic palladium indicates that Pd<sup>0</sup> is present either as small crystallites or are not aggregated at all (Figure 5 b).



**Figure 5.** Characterization of Pd(OAc)<sub>2</sub>@COF-300 after the first cycle. a) XPS spectrum of Pd(OAc)<sub>2</sub>@COF-300 in the 3d region showing characteristic peaks at 337.1 eV (3d<sub>5/2</sub>) and 342.3 eV (3d<sub>3/2</sub>), relative to Pd<sup>III</sup>, and 334.9 eV (3d<sub>5/2</sub>) and 340.2 eV (3d<sub>3/2</sub>), relative to Pd<sup>0</sup>. b) Powder XRD profile of Pd(OAc)<sub>2</sub>@COF-300 after the first cycle and powder XRD profile of Pd<sup>0</sup>. The absence of peaks, for (111) and (200) planes of Pd nanoparticles at 40.0° and 46.5° respectively, in the PXRD profile of Pd(OAc)<sub>2</sub>@COF-300 after the first cycle, indicates that, besides formation of Pd<sup>0</sup>, it could not be detected by XRD analysis, because the size of the formed nanoparticles would be close to the XRD detection limit (5–15 nm range, depending on the instrument and acquisition conditions).<sup>[10]</sup>



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Table 1. Suzuki–Miyaura cross-coupling employing Pd(OAc)2@COF-300 as catalyst. <sup>[a]</sup>										
		B(OH) <sub>2</sub> X Pd(OAc) <sub>2</sub> @COF-300 solvent P <sup>2</sup>								
	l	$R^1$ $R^2$	base/additive							
Entry	ArB(OH) <sub>2</sub> or R <sup>1</sup>	ArX or R <sup>2</sup>	Х	Time [min]	Yield <sup>(b)</sup> [%]	TON	TOF			
1	 Н	н	Br	20	100 (80)	1000	3000			
2	Н	н	I	20	100 (00)	1000	3000			
3	Н	p-CHO	Br	20	99 (92)	990	2973			
4	Н	p-COCH₃	Br	20	100 (80)	1000	3000			
5	Н	p-CH <sub>3</sub>	Br	20	96 (70)	960	2883			
6	Н	p-OCH <sub>3</sub>	Br	20	99 (88)	990	2973			
7	Н	m-OH	Br	20	91 (75)	910	2733			
8a	Н	p-OH	Br	20	100 (92)	1000	3000			
8b	Н	<i>p</i> -OH	1	20	92 (86)	920	2763			
9	Н	p-OH	1	120	97	970	485			
10	п		1	20	05 05 (70)	050	1952			
12	н	$\rho$ -NO	1	20	95 (70) 100	1000	3000			
12				20	100	1000	5000			
13	Н	N Br		20	41	410	1231			
14				<u>()</u>	41	410	410			
14	н	N Br		60	41	410	410			
15	Н	SBr		20	26	260	781			
16	Н	SBr		120	47	470	235			
17	Н	SBr		960	77	770	48			
18	<i>p</i> -CHO	Н	Br	20	65	650	1952			
19	<i>p</i> -CHO	Н	Br	60	68	680	680			
20	o-OCH₃	Н	Br	20	100 (88)	1000	3000			
21	o-OCH <sub>3</sub>	Н	I	20	100	1000	3000			
22	o-OCH₃	p-NO <sub>2</sub>	I	20	100	1000	3000			
23	o-OCH₃	p-CH <sub>3</sub>	Br	20	100	1000	3000			
24	0-UCH₃	p-OCH <sub>3</sub>	Br	20	92 (84)	920	2763			
25	0-0CH	<i>р</i> -СПО <i>р</i> -СОСН	Br	20	99 (91)	990	2073			
20	0-0CH3	<i>p</i> -coch <sub>3</sub> <i>m</i> -OH	Br	20	83	830	2973			
28	0-OCH2	o-NH <sub>2</sub>	1	20	49	490	1471			
	∠O <sub>N</sub> B(OH)₂	2								
29		Н	Br	20	42	420	1261			
30	B(OH) <sub>2</sub>	Н	Br	60	48	480	480			
	B(OH) <sub>2</sub>									
31		Н	Br	20	96 (76)	960	2883			
	B(OH) <sub>2</sub>									
32		Н	I	20	100	1000	3000			
22	B(OH) <sub>2</sub>	011	I	20	80	800	2402			
33		<i>р</i> -ОН	Br	20	100 (95)	1000	3000			
34	B(OH) <sub>2</sub>	o-NH <sub>2</sub>	I	20	76	760	2282			
	B(OH) <sub>2</sub>									
35		p-NO-	I	20	100	1000	3000			
			·	20			5000			

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Table 1. (Continued)									
Entry	$ArB(OH)_2 \text{ or } R^1$	ArX or R <sup>2</sup>	Х	Time [min]	Yield <sup>(b)</sup> [%]	TON	TOF [h <sup>-1</sup> ]		
36	B(OH) <sub>2</sub>	p-CH₃	Br	20	74	740	2222		
37	B(OH) <sub>2</sub>	p-OCH <sub>3</sub>	Br	20	100 (97)	1000	3000		
38	B(OH) <sub>2</sub>	p-CHO	Br	20	100 (80)	1000	3000		
39	B(OH) <sub>2</sub>	p-COCH <sub>3</sub>	Br	20	100 (94)	1000	3000		
40	B(OH) <sub>2</sub>	<i>m</i> -OH	Br	20	100 (88)	760	2282		
41	B(OH) <sub>2</sub>	p-OCH <sub>3</sub>	Br	20	100	1000	3000		
[a] Conditions: base = $K_5CO_{3}$ ; solvent: MeOH/H <sub>2</sub> O 4:1, 70°C, 0.1 mol% Pd. [b] Yield of the coupled product determined by GC on the basis of the aryl									

halide. In parenthesis, isolated yield after flash chromatography purification.

Transmission electron microscopy (TEM) has also been performed to evaluate the morphological and structural characterization of the Pd(OAc)<sub>2</sub>@COF-300 after the reaction. To determine the Pd nature, high-resolution (HR) TEM was performed. TEM images (Figure 6a) reveal uniformly distributed nanoparti-



**Figure 6.** a) TEM and b,c) HRTEM images of the catalyst, showing the presence of Pd<sup>0</sup> nanoparticles into the COF-300 cages. EDS of a single nanoparticle showing the presence of Pd without oxygen.

cles in the matrix, with spherical morphology and average diameter of  $5 \pm 1$  nm. HRTEM images (Figure 6b) show interplanar distances (0.22 nm) compatible with (111) atomic planes of Pd<sup>0</sup> on the [110] direction. Spectroscopic characterization using energy-dispersive spectroscopy (EDS) performed in a single nanoparticle confirms the presence of Pd (Figure 6c). Therefore Pd<sup>0</sup> nanoparticles are formed within the COF pores during the reaction and the Pd<sup>0</sup> agglomerates are stabilized into the pores of the organic framework.

#### Catalytic evaluation of Pd(OAc)2@COF-300 for continuousflow Suzuki-Miyaura cross-coupling reaction

To take full advantage of the heterogeneous nature of  $Pd(OAc)_2@COF-300$  and its high catalytic activity, we decided to conduct proof-of-concept experiments using this catalyst in continuous-flow Suzuki cross-coupling reactions.

The experiment was performed by using a glass column (Omnifit column; volume: 6.3 mL) that was filled with glass beads (2 mm) and then a 100 mg sample of Pd(OAc)<sub>2</sub>@COF-300 was dispersed through the column volume. Bromobenzene (1 equiv.) and phenylboronic acid (1.2 equiv.) were dissolved in a 2 M solution of sodium methoxide in methanol. The resulting solution was passed through the column with a residence time of 20 min, during 200 min at 60°C. Aliquots were collected each 20 min and analyzed by GC-MS. In Figure 7, the conversion of bromobenzene is displayed as well as the selectivity in biphenyl formation as a function of the operation time. The catalyst remained active during the course of the experiment and only a small drop in conversion from 56% at the beginning of the reaction to 44% for the last aliquot were observed. On the other hand, 100% selectivity was observed during the reaction. It is important to highlight that unconverted bromobenzene remained intact after passage though the column and it could be converted in a second passage.

# Evaluation of $Pd(OAc)_2@COF-300$ on other coupling reactions

Encouraged by the results presented above we decided to investigate the ability of  $Pd(OAc)_2@COF-300$  to catalyze other

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**Figure 7.** Continuous-flow Suzuki–Miyaura cross-coupling reaction employing Pd(OAc)<sub>2</sub>@COF-300 as heterogeneous catalyst. Bromobenzene conversion (squares) and selectivity in biphenyl formation (circles) as a function of time on stream.



cross-coupling reactions. The catalyst was used for Heck, Sonogashira, and Heck–Matsuda reactions (Table 2). Very interesting results were found for the Heck coupling between aryl bromides and styrene (entries 1 a - 1 e) and in the Sonogashira coupling between aryl iodides and phenylacetylene (entries 2 aand 2 b, see the Supporting Information for reaction conditions optimization). Isolated yields between 40 and 90% were observed in both cases, by employing small catalyst loading (0.1 mol% in Pd for Heck cross-coupling and 0.5 mol% for Sonogashira cross-coupling). On the other hand, formation of the desired product in Heck–Matsuda reaction was not observed. Aiming to find a reason for this, we performed the reaction under the same conditions, however, employing Pd(OAc)<sub>2</sub> as catalyst. To our surprise, a conversion of 20% was observed in the reaction between phenyldiazonium tetrafluoroborate and styrene. This may indicate that the highly polar diazonium salt substrate has difficulties in accessing the (hypothetically) hydrophobic pore channel system of the organic framework or the solvated structure of the salt has too large volume for diffusing into the pores.

### Conclusions

Pd(OAc)<sub>2</sub> coordinated on the walls of the nanoporous covalent organic framework COF-300, by post-synthetic modification of the support, has been shown to be an interesting heterogeneous catalyst for cross-coupling reactions such as Suzuki, Heck, and Sonogashira, and is a good alternative as a heterogeneous catalyst for such reactions. The COF-300 pore structure probably has some effects in the preorganization of the reactants, entropically favoring the reaction, which is commonly called a "confinement effect". Analysis through XPS showed that the Pd(OAc)<sub>2</sub> is bound to the COF-300 surface by coordination with the imine functional group. Furthermore, no leaching has been observed during the reaction, which demonstrates coordination of the palladium into the pores. This is an important advantage, as the product is essentially palladium-free, and therefore may be of interest for the pharmaceutical industry. We have shown that palladium nanoparticles are formed within the COF-300 pores.

### **Experimental Section**

For experimental details, see the Supporting Information.

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