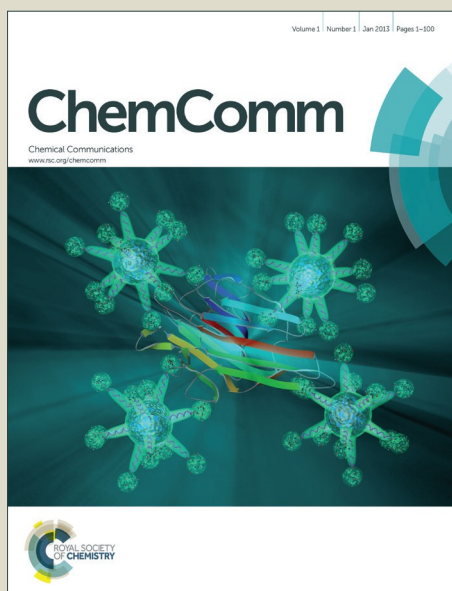


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## Pd-supported on N-doped carbon: Improved heterogeneous catalyst for base-free alkoxy carbonylation of aryl iodides

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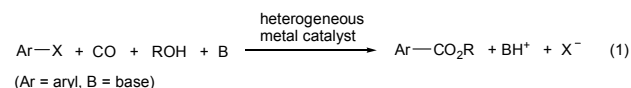
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**Novel Pd-based heterogeneous catalysts were prepared through immobilization of Pd(OAc)<sub>2</sub>/phenanthroline on carbon and subsequent pyrolysis. The most active catalyst was characterized by TEM, XPS and XRD techniques and was successfully used for the base-free methoxy carbonylation of aryl iodides. Notably, no metal contamination (detection limit <0.5 ppm) in the final products was observed.**

The development of heterogeneous catalysts for advanced organic transformation is of increasing interest for organic and material chemists.<sup>1</sup> In general, such catalysts present several advantages over the classical homogeneous systems, due to their easy recovery (by simple filtration or centrifugation procedures) and the possibility to recycle it.<sup>2</sup> This is of particular importance when the catalyst is based on less abundant and expensive noble metals. On the other hand, heterogeneous catalysts often display lower reactivity and selectivity with respect to their homogeneous counter parts. Among the various catalytic transformations applied for the synthesis of bio-active compounds, palladium-catalyzed coupling reactions are of exceptional importance. We have a long standing interest in this area, especially in Pd-catalyzed carbonylation of aryl halides and related substrates.<sup>3</sup> In addition to molecular-defined palladium-phosphine complexes, recently also several heterogeneous catalysts have been developed for the alkoxy carbonylation of aryl halides to afford benzoate esters (Equation 1).<sup>4</sup>

Although in most cases the catalytic system could be easily recovered and reused for several additional runs, the possible contamination of the organic product by the metal catalyst was not systematically investigated. However, such

contamination is of primary importance for applications in the life science area, particularly for pharmaceuticals.<sup>5</sup> In fact, the removal of metal impurities for late stage pharmaceutical intermediates can be cost determining for the process.



Moreover, the amount of metal impurities allowed in drugs is currently critically debated. Therefore, there is an increasing demand for stable, non-leaching catalysts. In this respect, here we report a new heterogeneous palladium-based catalyst (Pd/PdO@NGr-C), able to promote the alkoxy carbonylation of aryl iodides in the absence of any added external base.<sup>6</sup> Our system can be easily recovered and recycled for several times and no metal contamination could be detected in the final product.

In the past, palladium has been mainly supported on "classic" inorganic oxides as well as carbon. Recently, the incorporation of dopants into the matrix of the parent support has become a highly active and interesting area in material sciences. More specifically, N-doped carbon materials generated major interest.<sup>7</sup> We thought that such doping could result in improved binding properties of the support and therefore minimizes the leaching of palladium atoms (small clusters).

Initially, palladium supported on N-doped carbon (Pd/PdO@NGr-C) was prepared using palladium acetate (as palladium precursor) and 1,10-phenanthroline as a nitrogen-rich ligand. The resulting complex [Pd-Phen]<sup>2+</sup> was adsorbed on carbon and then subjected to pyrolysis under vacuum at 800°C for 2 h (Scheme 1). The amount of palladium, determined by elemental analysis, was 5.63 wt%, while the nitrogen and carbon contents were 2.2 wt% and 85.93 wt%, respectively.

In order to investigate the structure of the catalyst in more detail, several characterization methods were carried out.<sup>8</sup> The nature of the palladium and nitrogen species on the surface of the catalyst were analyzed by X-ray photoelectron

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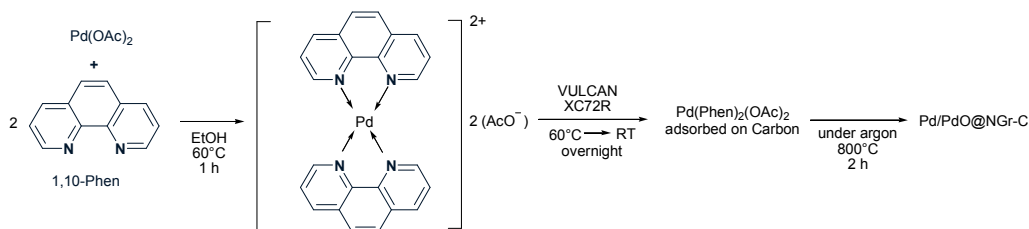
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spectroscopy (Figure 1A). The Pd3d XPS data (Figure 1B) reveal the presence of two Pd species. The first one has a binding energy of approximately 334.9 eV and is attributed to Pd(0) (19.7%). The second Pd species has a binding energy of approximately 337.3 eV and is attributed to Pd(II) in the form of palladium oxide (80.3%).<sup>9</sup> Three distinct peaks are observed in the N1s spectra with an electron-binding energy of 398.2 eV,

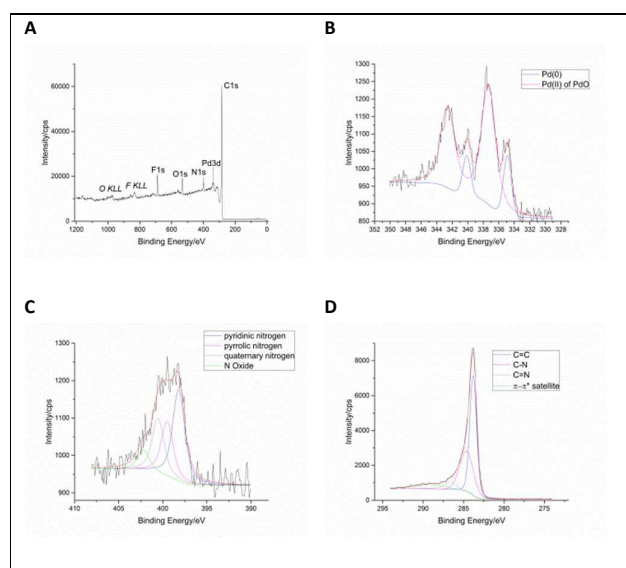
399.5 eV and 400.5 eV (Figure 1C). The lowest binding-energy peak can be attributed to pyridine-type nitrogen (sp<sup>2</sup> hybridized, 41.4%). The electron-binding energy of 399.5 eV is characteristic of a pyrrole-type nitrogen (sp<sup>3</sup> hybridized, 24.8%). The peak at 400.5 eV is typical of quaternary N (sp<sup>2</sup> hybridized, 24.6%). Apart from these three nitrogen types, N oxide of pyridinic N (small peak at 402.2 eV, 9.3%) was also



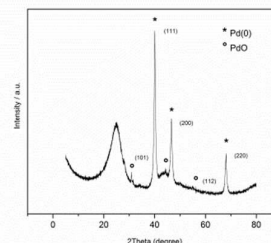
**Scheme 1.** Preparation of palladium supported on N-doped carbon (Pd/PdO@NGR-C).

observed, the oxygen atoms probably arising from the acetate counter ions. Also, the C1s spectra showed 3 peaks (Figure 1D): the sharp peak at 283.8 eV corresponds to the sp<sup>2</sup> carbon with C=C, meanwhile the smaller peaks at 284.6 eV and 286.6 eV are assigned to C=N and C-N respectively.<sup>10</sup> The peak observed at 289.1 eV is ascribed to the π-π\* transition typical for aromatic rings.<sup>11</sup> As shown in Figure 2 the X-ray diffraction (XRD) studies confirmed the presence of palladium dispersed into the carbon powder. Comparing XRD patterns of the new material with the XRD patterns of Pd/C, it is possible to identify the characteristic broad peak of the amorphous carbon support (around 2θ = 25°) and also the three peaks belong to palladium (0), at 2θ = 40°, 46° and 68°. On the other hand, the peaks at 2θ = 31°, 44° and 55° demonstrate the existence of PdO.

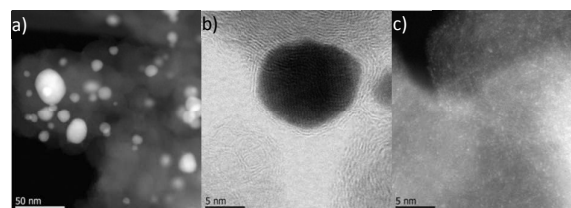
TEM analysis confirmed the presence of well-defined and spherical-like Pd nanoparticles with a very broad range of sizes (Figure 3a). On some particles layers of several graphenes were formed through the carbonization of the nitrogen ligand. These layers cover or partially cover some of the Pd particles (Figure 3b). Additionally palladium atoms could be found in a carbon phase on the Vulcan particles (Figure 3c). Due to HAADF image contrast and EDXS data showing the presence of Pd in an area without Pd particles, these finely distributed atoms and clusters are likely Pd atoms.



**Figure 1.** A: XPS spectra for palladium supported on N-doped carbon (Pd/PdO@NGR-C); B: Pd3d XPS spectrum; C: N1s XPS spectrum; D: C1s XPS spectrum.



**Figure 2.** XRD pattern of palladium supported on N-doped carbon (Pd/PdO@NGR-C).

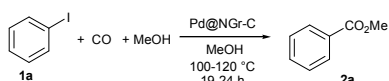


**Figure 3.** a) HAADF-STEM image of palladium supported on N-doped carbon (Pd@NGR-C) showing the broad range of different particle sizes, b) ABF-STEM image of a Pd particle showing several graphene layers covering a Pd particle, c) HAADF-STEM images of finely distributed heavy atoms or clusters of heavy atoms, probably Pd, in a carbon phase on Vulcan particles.

In order to examine the activity of the prepared catalyst for the alkoxy carbonylation of aryl halides, we tested Pd/PdO@NGr-C with iodobenzene as the model substrate. The reaction was initially carried out in anhydrous MeOH in the presence of a catalytic amount of Pd/PdO@NGr-C (0.01 mol%, Pd=5.63 wt%) and hexadecane as internal standard under 20 bar CO pressure at 100°C for 19h. The reaction mixture was filtered through a silica plug and analyzed by GLC and GC-MS, which showed the formation of the desired methyl benzoate in 53% yield. This result confirmed the general activity of the newly developed catalyst. It is worth noting that this procedure occurred successfully without the need for an external base. Under the same conditions, other similar heterogeneous catalysts, based on iron (Fe<sub>2</sub>O<sub>x</sub>@NGr-C),<sup>12</sup> cobalt (Co<sub>3</sub>O<sub>4</sub>@NGr-C),<sup>13</sup> or copper, (CuO<sub>x</sub>@NGr-C) were not active.

Increasing the reaction temperature and the palladium content (Table 1), the product yield was improved to 79%. A "hot filtration experiment" showed that no significant palladium leaking occurred from the catalyst, thus avoiding the removal of metal impurities from the product.

**Table 1.** Methoxycarbonylation of iodobenzene catalyzed by heterogeneous Pd/PdO@NGr-C: optimization of reaction conditions.<sup>a</sup>



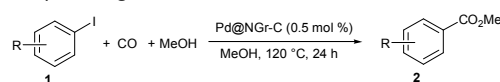
Entry	Pd@NGr-C (mol %)	Conc. of <b>1a</b> <sup>b</sup>	T (°C)	t (h)	Conv. of <b>1a</b> (%) <sup>c</sup>	Yield of <b>2a</b> (%) <sup>d</sup>
1	0.01	0.25	100	19	64	53
2	0.1	0.25	100	19	79	71
3	0.1	1.0	100	19	59	57
4	0.1	0.5	100	19	78	78
5	0.1	0.5	120	19	74	55
6	0.5	0.5	120	19	86	77
7	0.5	0.5	120	24	90	79

<sup>a</sup> Reaction conditions: 0.5 mmol iodobenzene, 20 bar CO. <sup>b</sup> Mmol of **1a** per mL of MeOH. <sup>c</sup> Determined by GLC. <sup>d</sup> GLC yield.

To generalize the process, the best reaction conditions found on the model substrate were applied to different aryl iodides; the results obtained are shown in Table 2. Different halo-substituted aryl iodides including bromides were selectively alkoxy carbonylated and produced the corresponding esters in moderate to good yields (Table 2, entries 2-6). The reaction also worked nicely with substrates substituted both with electron-withdrawing groups such as the methoxycarbonyl (Table 2, entry 7), and with electron-donating groups such as amino, methoxy and alkyl (Table 2, entries 8-10). Notably, 4-iodostyrene gave the corresponding ester in 53% yield (Table 2, entry 11) without any carbonylation at the double bond. Finally, vinyl 2-iodonaphthalene **11** afforded an excellent yield of methyl 2-naphthoate **21** (90%; Table 2, entry 12). To demonstrate the stability and utility of this novel heterogeneous catalyst for life science applications ICP analysis on representative products **2a**, **2b**,

**2g** and **2i** was performed. Gratifyingly, no trace of palladium was observed in all the products (ICP Instrument Sensitivity= 0.5 ppm).

**Table 2.** Substrate scope for the methoxycarbonylation of aryl iodides catalyzed by heterogeneous Pd/PdO@NGr-C.<sup>a</sup>



Entry	<b>1</b>	Conv. of <b>1</b> (%) <sup>b</sup>	<b>2</b>	Yield of <b>2</b> (%) <sup>c</sup>
1		98		69 (79)
2		98		84
3		99		74
4		100		82
5		99		74
6		98		52
7		96		55
8 <sup>d</sup>		98		70
9		99		84
10		98		57
11		100		53
12		99		90

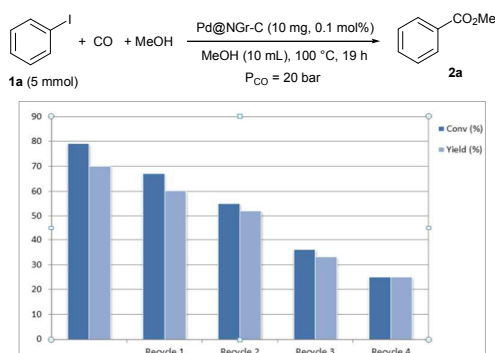
<sup>a</sup> Reaction conditions: 0.5 mmol of **1**, 20 bar CO. Substrate concentration was 0.5 mmol per mL of MeOH. <sup>b</sup> Determined by isolation of unreacted **1**. <sup>c</sup> Isolated yield (GLC yield). <sup>d</sup> The reaction was carried out in presence of Et<sub>3</sub>N (1.5 equiv) to obtain free methyl 3-aminobenzoate.

To test the recyclability of the catalyst, the model reaction was performed under the optimized reaction conditions. The catalyst was easily separated from the reaction mixture by centrifugation at 8000 RPM for 10 min, and then reused for an additional four runs. As shown in Figure 4, we observed a

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decline of the conversion, but not of selectivity which remained around 90%. This loss of catalytic is explained by some agglomeration of the smaller active particles and the mechanical abrasion of the catalytic material during the reaction and the work-up procedure.



**Figure 4.** Recycle study of Pd/PdO@NGR-C for alkoxy carbonylation of aryl iodide.

In conclusion, we have developed a heterogeneous palladium catalyst via adsorption of a defined palladium–phenanthroline complex onto commercially available carbon support and subsequent pyrolysis. This new material was fully characterized by several techniques and allows for the alkoxy carbonylation of aryl iodides to give the corresponding benzoates in good yields. Notably, these coupling reactions occurred without the need for an external base. No metal contamination in the alkoxy carbonylation products makes Pd/PdO@NGR-C a promising catalyst for the synthesis of intermediates required for material of life science applications, where high product purity is required.

## Notes and references

- Selected recent examples: (a) D.T.D. Tang, K. D. Collins and F. Glorius, *J. Am. Chem. Soc.*, 2013, **135**, 7450; (b) S. Vázquez-Céspedes, A. Ferry, L. Candish and F. Glorius, *Angew. Chem. Int. Ed. Engl.*, 2015, **54**, 5772; (c) E. Bratt, O. Verho, M.J. Johansson and J.-E. Bäckvall, *J. Org. Chem.* 2014, **79**, 3946; (d) A. Volkov, K.P.J. Gustafson, C.-W. Tai, O. Verho and J.-E. Bäckvall, *Angew. Chem. Int. Ed. Engl.*, 2015, **54**, 5122; (e) L. He, K. Natte, J. Rabeah, C. Taeschler, H. Neumann, A. Brückner and M. Beller, *Angew. Chem. Int. Ed. Engl.*, 2015, **54**, 4320; (f) F. Zhu, Y. Li, Z. Wang, X.-F. Wu, *Catal. Sci. Technol.*, 2016, **6**, 2905; (g) K. Natte, H. Neumann, X.-F. Wu, *Catal. Sci. Technol.*, 2015, **5**, 4474; (h) C.-L. Li, X. Qi, X.-F. Wu, *J. Mol. Catal. A-Chem.*, 2015, **406**, 94.
- (a) *Heterogeneous Catalysis and Solid Catalysts*. Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, 2009; (b) Charles N. Satterfield. *Heterogeneous Catalysis in Industrial Practice*. Krieger Pub Co., 2<sup>o</sup> edition, 1996; (c) X. Fan, G. Zhanga and F. Zhanga, *Chem. Soc. Rev.*, 2015, **44**, 3023; (d) R. Schlögl, *Angew. Chem. Int. Ed.*, 2015, **54**, 3465; (e) M. Opanasenko, P. Stepnicka and J. Cejka, *RSC Adv.*, 2014, **4**, 65137; (f) Y. Monguchi and H. Sajiki, *J. Synth. Org. Chem. Jpn.*, 2012, **70**, 711; (g) C. Lucarelli and A. Vaccari, *Green Chem.*, 2011, **13**, 1941; (h) M. J. Climent, A. Corma and S. Iborra, *Chem. Rev.*, 2011, **111**, 1072; (i) A. Molnàr, *Chem. Rev.*, 2011, **111**, 2251; (j) L. Yin and J. Liebscher, *Chem. Rev.*, 2007, **107**, 133.
- (a) A. Brennführer, H. Neumann and M. Beller, *Angew. Chem. Int. Ed.*, 2009, **48**, 4114; (b) X.-F. Wu, H. Neumann and M. Beller, *ChemSusChem*, 2006, **6**, 229; (c) X.-F. Wu, H. Neumann and M. Beller, *Chem. Rev.*, 2013, **113**, 1.
- (a) Y. Lei, L. Wu, X. Zhang, H. Mei, Y. Gu and G. Li, *J. Mol. Catal. A-Chem.*, 2015, **398**, 164; (b) R. S. Mane, T. Sasaki and B. M. Bhanage, *RSC Adv.*, 2015, **5**, 94776; (c) S. M. Islam, K. Ghosh, A. S. Roy and R. A. Molla, *RSC Adv.*, 2014, **4**, 38986; (d) H. Mei, S. Xiao, T. Zhu, Y. Lei and G. Li, *Transition Met Chem*, 2014, **39**, 443; (e) Z. Zhang, Y. Chen, S. He, J. Zhang, X. Xu, Y. Yang, F. Nosheen, F. Saleem, W. He and X. Wang, *Angew. Chem. Int. Ed.*, 2014, **53**, 12517; (f) T.T. Dang, Y. Zhu, J.S.Y. Ngiam, S.C. Ghosh, A. Chen and A.M. Seayad, *ACS Catal.*, 2013, **3**, 1406; (g) A. S. Prasada and B. Satyanarayana, *J. Mol. Catal. A-Chem.*, 2013, **370**, 205; (h) E. Ullah, J. McNulty, M. Sliwinski and A. Robertson, *Tetrahedron Lett.*, 2012, **53**, 3990; (i) J. Salvadori, E. Balducci, S. Zaza, E. Petricci and M. Taddei, *J. Org. Chem.*, 2010, **75**, 1841; (j) J. Liu, J. Chen and C. Xia, *J. Catal.*, 2008, **253**, 50; (k) A. Gniewek, A.M. Trzeciak, J.J. Ziółkowski, L. Kepinski, J. Wrzyszc and W. Tylus, *J. Catal.*, 2005, **229**, 332; (l) C. Ramesh, R. Nakamura, Y. Kubota, M. Miwa and Y. Sugi, *Synthesis*, 2003, **4**, 501; (m) M.Z. Cai, C.S. Song and X. Huang, *J. Chem. Soc., Perkin T. 1*, 1997, 2273.
- (a) C. E. Garrett and K. Prasad, *Adv. Synth. Catal.*, 2004, **346**, 889; (b) C. J. Welch, J. Albanese-Walker, W. R. Leonard, M. Biba, J. DaSilva, D. Henderson, B. Laing, D. J. Mathre, S. Spencer, X. Bu and T. Wang, *Org. Process Res. Dev.*, 2005, **9**, 198; (c) K. Kçhler, R. G. Heidenreich, S. S. Soomro and S. S. Prçckla, *Adv. Synth. Catal.* 2008, **350**, 2930.
- The reaction works under base free conditions, since the formed hydrogen iodine is not fixed on the Pd-particles. We believe the basic nitrogen sides on the support also reversibly bind the acid and release it into the protic solution.
- L. He, F. Weniger, H. Neumann and M. Beller, *Angew. Chem. Int. Ed. Engl.* 2016 accepted.
- J. M. Thomas and W. J. Thomas, *Principles and Practice of Heterogeneous Catalysis*, Wiley-VCH, 1st edition, 1996.
- P. Zhang, Y. Gong, H. Li, Z. Chen and Y. Wang, *Nat. Commun.*, 2013, **4**, 159.
- H. Wang, T. Maiyalagan and X. Wang, *ACS Catal.*, 2012, **2**, 781.
- T.I.T. Okpalugo, P. Papakonstantinou, H. Murphy, J. McLaughlin and N.M.D. Brown, *Carbon*, 2005, **43**, 153.
- R.V. Jagadeesh, T. Stemmler, A.E. Surkus, H. Junge, K. Junge and M. Beller, *Nature Protocols*, 2015, **10**, 548.
- F. A. Westerhaus, R.V. Jagadeesh, G. Wienhöfer, M.M. Pohl, J. Radnik, A.E. Surkus, J. Rabeah, K. Junge, H. Junge, M. Nielsen, A. Brückner and M. Beller, *Nature Chem.*, 2013, **5**, 537.