



<http://www.diva-portal.org>

Postprint

This is the accepted version of a paper published in *Chemistry - A European Journal*. This paper has been peer-reviewed but does not include the final publisher proof-corrections or journal pagination.

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

Bruneau, A., Gustafson, K P., Yuan, N., Tai, C-W., Persson, I. et al. (2017)
Synthesis of Benzofurans and Indoles from Terminal Alkynes and Iodoaromatics
Catalyzed by Recyclable Palladium Nanoparticles Immobilized on Siliceous
Mesocellular Foam
Chemistry - A European Journal, 23(52): 12886-12891
<https://doi.org/10.1002/chem.201702614>

Access to the published version may require subscription.

N.B. When citing this work, cite the original published paper.

Permanent link to this version:

<http://urn.kb.se/resolve?urn=urn:nbn:se:su:diva-148090>

Synthesis of Benzofurans and Indoles from Terminal Alkynes and Iodoaromatics Catalyzed by Recyclable Palladium Nanoparticles Immobilized on Siliceous Mesocellular Foam

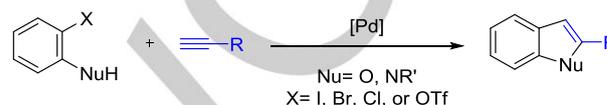
Alexandre Bruneau,^[a] Karl P. J. Gustafson,^[a] Ning Yuan,^[b,c] Cheuk-Wai Tai,^b Ingmar Persson,^[c] Xiaodong Zou,^[b] and Jan-E. Bäckvall*^[a]

Dedication ((optional))

Abstract: Herein, we report on the utilization of a heterogeneous catalyst, consisting of Pd nanoparticles supported on a siliceous mesocellular foam (Pd⁰-AmP-MCF), for the synthesis of heterocycles. Reaction of *o*-iodophenols and protected *o*-iodoanilines with acetylenes in the presence of a Pd nanocatalyst produced 2-substituted benzofurans and indoles, respectively. In general, the catalytic protocol afforded the desired products in good to excellent yields under mild reaction conditions without the addition of ligands. Moreover, the structure of the reported Pd nanocatalyst was further elucidated with Extended X-Ray Absorption Fine Structure spectroscopy and it was proven that the catalyst can be recycled multiple times without significant loss of activity.

Introduction

Indoles and benzofurans are common structural elements in natural and synthetic products. These heterocycles possess several unique properties, which explain their frequent occurrence in bioactive molecules as well as in materials.^[1] Because of their importance, numerous synthetic methods have been developed for the construction of these heterocycles during the past few decades.^[1f,2] Among these methods, palladium-catalyzed protocols have been frequently used for the formation of substituted benzofurans and indoles.^[1f,3] One of the most straightforward methods is based on the use of a terminal alkyne and an *ortho*-halogenated phenol/aniline (Scheme 1).



Scheme 1. Straightforward synthesis of heterocycles from *ortho* halogenated derivatives and terminal alkynes.

Many homogeneous systems have been reported for the transformation in Scheme 1 since the pioneering work described by Castro *et al.*,^[3a,3b,4] while less attention has been devoted to the corresponding heterogeneous processes.^[5] By utilizing a heterogeneous catalyst one can overcome the drawbacks of a homogeneous protocol, such as the removal of trace metal found in the product, purification, and recycling of the catalyst at the end of the reaction.^[6] Over the past few years, metal nanoparticles have found extensive use in the field of catalysis. Their large surface-to-volume ratio and the high density of unsaturated coordination sites have led to activities not seen for bulk metals.^[7]

The Bäckvall group has previously reported on the preparation and the application of a heterogeneous Pd catalyst, consisting of palladium nanoparticles supported on a siliceous mesocellular foam, Pd⁰-AmP-MCF.^[6] This catalyst has been found to effectively catalyze a wide range of transformations, exhibiting high recyclability and low metal leaching.^[9] The Pd^{II} pre-catalyst for the Pd⁰-AmP-MCF has also been shown to work well in several applications.^[10] Herein, we report our results on nanopalladium-catalyzed synthesis of benzofurans and indoles and provide further characterization of both the Pd^{II} pre-catalyst and the Pd⁰-AmP-MCF catalyst with the aid of EXAFS. The catalytic efficiency of Pd⁰-AmP-MCF was demonstrated by the synthesis of substituted heterocycles from terminal alkynes and iodoaromatics under mild conditions.

Results and Discussion

Characterization data of the catalysts

The Pd nanoparticle catalyst was prepared as previously reported (Figure 1).^[8b] Pristine MCF was functionalized with aminopropyl groups by refluxing it in toluene with 3-aminopropyltrimethoxysilane to give the AmP-MCF. The amino functionalized MCF was then impregnated with Li₂PdCl₄ in a pH

[a] Dr. A. Bruneau, K. P. J. Gustafson, Prof. J.-E. Bäckvall
Department of Organic Chemistry and
Berzelii Centre EXSELENT on Porous Materials
Arrhenius Laboratory, Stockholm University
SE-106 91 Stockholm (Sweden)
E-mail: jeb@organ.su.se

[b] N. Yuan, Prof. X. Zou
Berzelii Center EXSELENT on Porous Materials and
Department of Material and Environmental Chemistry (MMK)
Stockholm University, SE-106 91 Stockholm (Sweden)

[c] N. Yuan, Prof. I. Persson
Department of Molecular Sciences
Swedish University of Agricultural Sciences
P.O. Box 7015, SE-750 07 Uppsala (Sweden)

Supporting information for this article is given via a link at the end of the document.

9 LiOH solution to furnish the Pd^{II}-AmP-MCF precatalyst, which in the final step was reduced with NaBH₄ to yield the palladium nanoparticle catalyst Pd⁰-AmP-MCF.^[8b] The Pd^{II}-AmP-MCF and Pd⁰-AmP-MCF catalysts have previously been characterized by IR spectroscopy, elemental analysis (ICP-OES), scanning electron microscopy (SEM), high-angle annular dark-field scanning transmission electron spectroscopy (HAADF-STEM), X-ray photoelectron spectroscopy (XPS), N₂-absorption/desorption isotherms, high-resolution TEM and convergent-beam electron diffraction (CBED).^[8a,b,9] From the extensive analysis of the catalysts it was concluded that the Pd⁰-AmP-MCF consisted of predominantly crystalline palladium nanoparticles within a porous siliceous network in the size range 1.5-2.6 nm with an overwhelming amount residing in the oxidation state 0. Even though the Pd^{II}-AmP-MCF and Pd⁰-AmP-MCF have been thoroughly characterized, there is limited knowledge concerning coordination to the Pd atoms.^[9c]

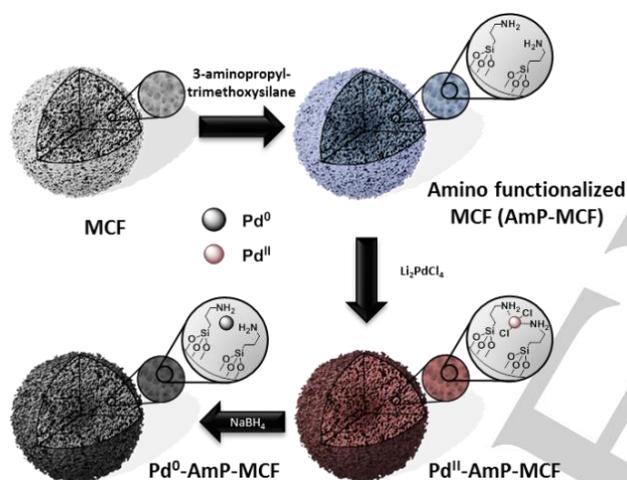


Figure 1. Preparation of the Pd nanoparticle catalyst Pd⁰-AmP-MCF.

We have now used extended X-Ray Absorption Fine Structure (EXAFS) spectroscopy to investigate the specific coordination environment of the Pd atoms in Pd^{II}-AmP-MCF precatalyst and Pd⁰-AmP-MCF (Figure 2).

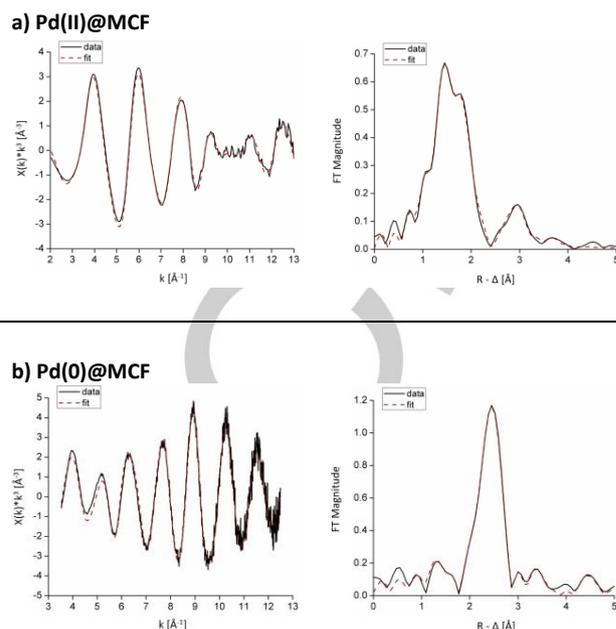


Figure 2. Pd K-edge EXAFS spectra (left) and Fourier transforms (right) for (a) Pd^{II}-AmP-MCF and (b) Pd⁰-AmP-MCF. Solid black lines show the experimental data and dashed red lines are the best fits. The Fourier transforms data are without phase correction.

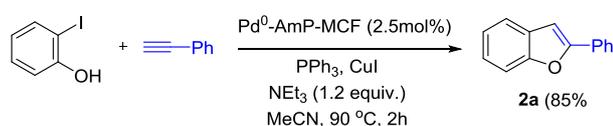
The Fourier transform data for the pre-catalyst Pd^{II}-AmP-MCF (Figure 2a) contains two major peaks corresponding to Pd–N and Pd–Cl bonds individually. The best fit revealed that each Pd atom in the pre-catalyst is bound to two nitrogen atoms with a Pd–N distance of 2.02 Å and to two chloride atoms with a Pd–Cl distance of 2.29 Å in a square planar geometry as a *trans* complex. This indicates that the Pd precursor was embedded on the amino groups in the framework in the form of a Pd(II) complex. Meanwhile, a noticeable peak at ca. 3.0 Å (without phase correction) with a shoulder is more likely attributed to single scatterings than a multiple scatterings (MS), which means that Pd(II) complex units were probably stacking together at distances of 3.07 Å and 3.42 Å.

Concerning the catalyst Pd⁰-AmP-MCF (Figure 2b), the EXAFS spectrum changed significantly compared to that of the pre-catalyst. In the Fourier transform, only one major peak corresponding to Pd–Pd bonds appeared. The best fit showed that on average each Pd atom is bound to approximately 6 Pd atoms in the first coordination shell with a bond distance of 2.78 Å. The true coordination number of Pd–Pd in the first coordination shell should be slightly higher than the value achieved from the refinement because there is a small fraction of Pd species other than nanoparticles. The peak for Pd–N bonds in Pd⁰-AmP-MCF became much less pronounced compared to the pre-catalyst and it appeared with a shoulder, which is due to the combination of the single scattering of Pd–N bonds and side peaks from the strong Pd–Pd contribution. The Pd–Cl bonds were not observed. The average number of Pd–N bonds per Pd was determined to be about 0.7 with a distance of 2.0 Å. It should be noted that the peak assigned to the Pd–N

bonds could in principle also be Pd–O bonds if the reduced Pd atoms are partially oxidized in air or the remaining small amount of Pd(II) species hydrolyzed into PdO. The significant decrease of the Pd–N (or possibly the Pd–O) bonds and the inflated signal for Pd–Pd bonds validates the efficient reduction of the pre-catalyst with NaBH₄ forming Pd nanoparticles. The detailed parameters of the fit can be found in the supporting information (Table S1). It should be noted that the number of Pd–N bonds per Pd and bond distances are average values.

Synthetic work

Starting from reaction conditions similar to those of the classical homogeneous Sonogashira reaction, the reaction of 2-iodophenol (**1a**) with phenylacetylene was studied in the presence of triphenylphosphine and copper(I) iodide (Scheme 2).



Scheme 2. Model reaction for the synthesis of benzofurans.

The catalytic system composed of 2.5 mol% of Pd⁰-AmP-MCF, 5 mol% of CuI, 5 mol% of PPh₃, 1.2 equiv. of NEt₃ in acetonitrile at 90 °C gave the expected benzofuran in high yield after 2h (85%, Scheme 2, Table 1, entry 1).

Table 1. Optimization of the reaction conditions^[a]

Entry	Alkyne equiv.	PPh ₃ (mol%)	CuI (mol%)	T (°C)	Time	NMR Yield ^[b]
1	1,5	5	5	90	2h	85
2	1,5	5	5	45	24h	63
3	1,5	5	5	rt	24h	48
4	1,5	-	5	90	5h	66
5	1,5	5	-	90	6h30	48
6	2	-	5	60	20h	75
7	2	-	5	70	20h	87 ^[c] (85)

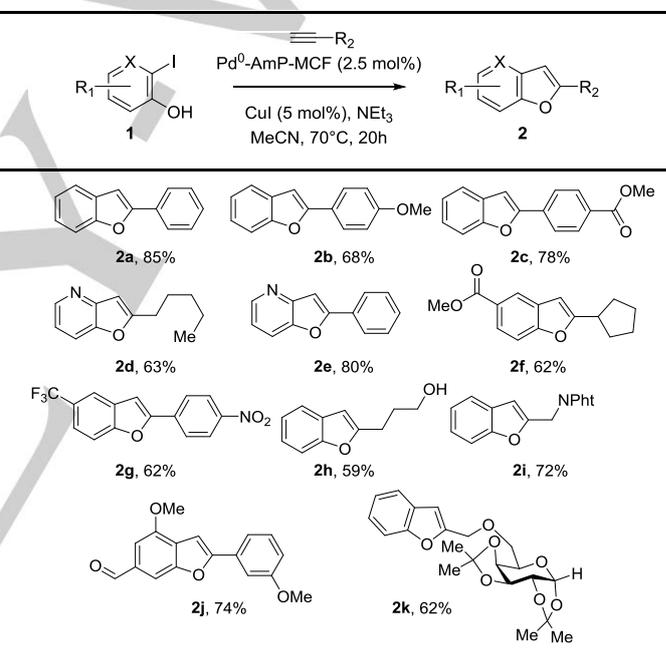
[a] The reaction was carried out in acetonitrile using 2.5 mol% of Pd⁰-AmP-MCF and 1.2 equiv. of Et₃N. [b] 1,3,5-trimethoxybenzene used as internal standard. [c] Average of 3 runs. Isolated yield in parenthesis.

Decreasing the temperature had a detrimental effect on the conversion but could be partially compensated by increasing the reaction time (entries 2 and 3). Omitting PPh₃ gave an acceptable yield within 5h (66%, entry 4), while the removal of CuI resulted in a considerable loss of the yield (48%, entry 5). Using 2 equiv. of alkyne at 60 °C in the absence of phosphine during 20h afforded the desired product in a good yield (75%, entry 6), and increasing the temperature to 70 °C afforded **2a** in 87% yield (entry 7).

With the optimal conditions in hand, we set out to evaluate the scope of the catalytic system (Table 2). To our delight, variously 2-substituted benzofurans could be obtained by using this catalytic system. Electron-rich or electron-deficient aryl-acetylenes can be used giving the corresponding benzofurans **2a-c** in good yields. No clear trend in the reaction rate of

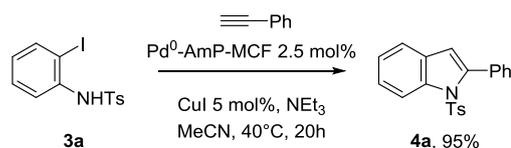
acetylenes with different electronic properties were observed. The slightly lower yield for the electron-rich acetylenes could be ascribed to their increased relative rate for the homocoupling to form diacetylenes. More sterically hindered acetylenes, such as (2-MeO-phenyl)acetylene, were not tolerated, and gave complicated mixtures. Alkynes bearing alkyl chains gave the desired products **2d** and **2f** in satisfactory yields (63% and 62%). It is worth noting that aza-benzofurans **2d** and **2e** were also obtained in good yields (63 and 80%, respectively) starting from 2-iodopyridin-3-ol. The synthesis of variously substituted benzofurans **2f-k**, with groups that can be functionalized (aldehyde, nitro, ester, phthalimide, alcohol, and sugar) was compatible with the catalytic system; benzofurans **2f-k** were obtained in good yields ranging from 59 to 74%. In most cases small amounts of starting material were observed together with dehalogenated and homocoupled arylidides.

Table 2. Synthesis of substituted benzofurans



Reaction conditions: 2-iodophenol (0.25 mmol), alkyne (0.5 mmol), Pd⁰-AmP-MCF (2.5 mol%), CuI (5 mol%), NEt₃ 1.2 equiv., acetonitrile (1 mL) at 70 °C under Ar for 20h.

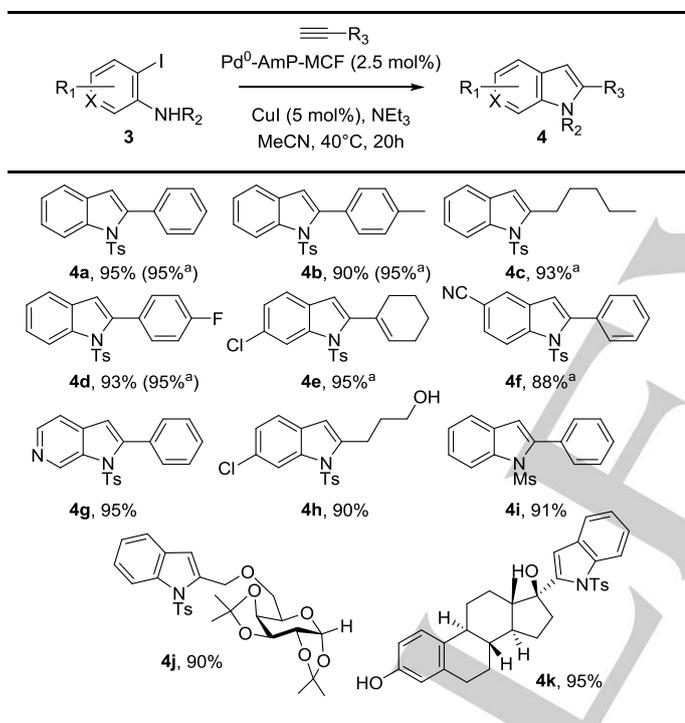
The catalytic system also proved to be compatible with aniline derivatives, and *N*-tosyl-2-iodoaniline **3a** afforded the corresponding indole **4a** in an excellent yield of 95% under slightly milder conditions (40 °C, Scheme 3).



Scheme 3. Indole synthesis using Pd⁰-AmP-MCF.

With the excellent results observed for *N*-tosyl-2-iodoaniline and phenylacetylene, we investigated the scope of the indole synthesis (Table 3). A wide range of aromatic and aliphatic alkynes (electron-rich and electron-deficient) were successfully coupled with *N*-tosylated *o*-iodoanilines to give indoles **4a-4f** in very good to excellent yields (88 to 95%). In the case of azaindoles, indole **4g** could be isolated in 95% yield. Gratifyingly, complete chemoselectivity toward the iodine was observed when using the 5-chloro-2-iodo derivative; only the expected products **4e** and **4h** were isolated in high yields (95% and 90% respectively). Free hydroxyl groups were tolerated (**4h**, 90%) as well as more complex structures such as a carbohydrate and steroid derivatives **4j** and **4k** (90 and 95% respectively). Mesyl protected iodoaniline proved also to be compatible with the reaction conditions and indole **4i** was isolated in 91% yield.

Table 3. Synthesis of substituted indoles



Reaction conditions: 2-iodoaniline (0.25 mmol), alkyne (0.5 mmol), $\text{Pd}^0\text{-AmP-MCF}$ (2.5 mol%), CuI (5 mol%), NEt_3 1.2 equiv., acetonitrile (1 mL) at 40°C under Ar for 20h. a. Reaction performed at 60°C .

The *N*-protecting group chosen for the iodoaniline was critical for the cyclization step, since acetyl, trifluoroacetyl, and Boc-protected iodoanilines as well as unprotected aniline did not lead to the desired indole product but rather gave the Sonogashira products **5a-d**, in 65-95% yields (Figure 3).

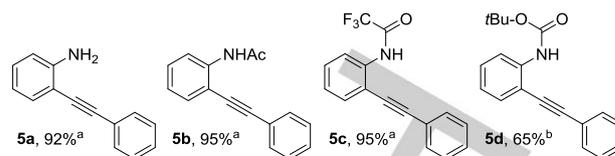


Figure 3. Uncyclized products a. NMR Yields given. b. Isolated yield).

Interestingly, water proved to influence the outcome of the reaction described above (Scheme 3), as shown in Figure 4. When examining the acetonitrile used it contained approximately one equivalent of water which also proved to be optimal for obtaining the maximum yield of the desired product **4a**. A probable explanation for the positive effect of small amounts of water is that the rate of hydrolysis of the vinylpalladium intermediate (*Int-A*, Scheme 5, see below), formed in the cyclization, is increased.

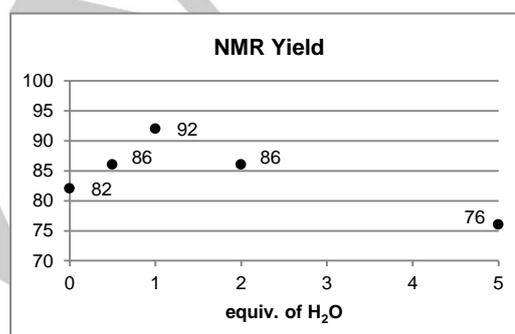
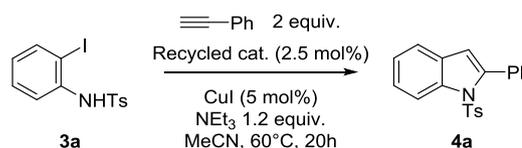


Figure 4. Influence of water on the formation of the indole **4a**. 1 equiv. is equal to approximately 5000 ppm.

When examining the reaction for leaching, it was found that a small but significant amount of palladium had leached, 25 ppm, which is a minor fraction of the total palladium used (3-4 % of the total palladium used). To gain further insight into the mechanism concerning if the reaction is catalyzed by homogenous or heterogeneous palladium, a hot filtration test was performed, which revealed that the reaction could be partially catalyzed by homogenous species (31 % NMR yield after 23 hours). Recycling of the catalyst is one of the most important advantages associated with heterogeneous catalysis compared to homogeneous. The recyclability of $\text{Pd}^0\text{-AmP-MCF}$ was therefore investigated in the synthesis of the indole **4a** from **3a** and phenylacetylene (Scheme 4).



Scheme 4. Conditions for investigation of the recyclability of the catalyst.

It was observed that the catalyst could be used for at least 5 cycles with good results (Figure 5). Due to issues with reproducing the results for the continued cycles, the recycling had to be performed at 60 °C. The catalyst was recovered simply by centrifugation and washing. TEM images of the recovered catalyst showed that the mesoporous siliceous structure was intact and that the palladium nanoparticles were still well dispersed, some slight agglomerations of the nanoparticle were observed (see Figure S1).

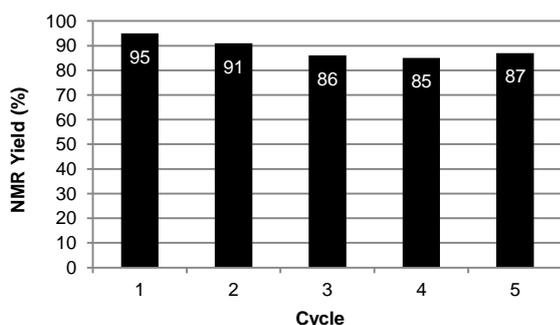
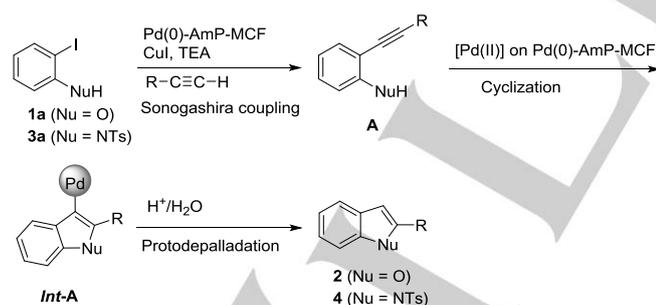


Figure 5. Representation of the recyclability of Pd⁰-AmP-MCF as catalyst in the synthesis of indole **4a**.

A likely mechanism for the formation of the benzofurans and indoles from the corresponding iodoaromatic compound and terminal acetylenes is shown in Scheme 5. Sonogashira coupling of the iodoaromatic compound (**1a** or **3a**) and terminal acetylene gives the acetylene compound **A**. A palladium-catalyzed oxy- or amino-palladation gives the vinylpalladium intermediate **Int-A**, which is hydrolyzed by water affording the product **2** or **4**.



Scheme 5. Mechanism of Pd-catalyzed transformation of iodoaromatics to benzofurans and indoles.

Conclusions

We have developed a phosphine-free catalytic system using a heterogeneous catalyst of Pd nanoparticles supported on mesocellular foam (Pd⁰-AmP-MCF) which allowed us to

synthesize a range of benzofuran and indole derivatives. The catalyst proved to be tolerant toward a wide range of functional groups giving diversely substituted heterocycles under mild reaction conditions in good to excellent yields. Interestingly, a significant water effect was observed, having an optimum around 1 equivalent of water. Furthermore, this Pd nanocatalyst showed an excellent recyclability as it could be reused several times with a constant activity.

Experimental Section

Standard procedure for the heterogeneous Pd-catalysed synthesis of benzofurans

Into a sealable microwave tube were added Pd⁰-AmP-MCF (2.5 mol%, 8.3 mg), CuI (5 mol%, 2.4 mg), and the *o*-iodophenol **1a** (0.25 mmol, 55 mg), and the reaction mixture was flushed with argon. Acetonitrile (1 mL, containing 1 equiv. water or 4.5 μL/mL), NEt₃ (1.2 equiv., 42 μL) and alkyne phenylacetylene (2 equiv., 55 μL) were successively added. The tube was capped and the reaction was heated at 70°C temperature during 20h. The reaction vessel was cooled down and the reaction mixture was diluted with ethyl acetate, concentrated in vacuo, and purified by silica gel chromatography using pentane to give 41 mg (85% yield) of benzofuran **2a** as a colorless solid. ¹H NMR (400 MHz, CDCl₃) δ 7.93 – 7.85 (m, 2H), 7.61 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.58 – 7.53 (m, 1H), 7.48 (dd, *J* = 8.5, 6.9 Hz, 2H), 7.41 – 7.35 (m, 1H), 7.31 (td, *J* = 7.7, 1.5 Hz, 1H), 7.28 – 7.22 (m, 1H), 7.06 (d, *J* = 1.0 Hz, 1H). ¹³C NMR (101 MHz, CDCl₃) δ 156.4, 155.4, 131.0, 129.7, 129.2, 129.0, 125.4, 124.7, 123.4, 121.4, 111.6, 101.8.

See table 2 for deviating parameters.

Standard procedure for the heterogeneous Pd-catalysed synthesis of indoles

Into a sealable microwave tube were added Pd⁰-AmP-MCF (2.5 mol%, 8.3 mg), CuI (5 mol%, 2.4 mg), and the *N*-tosyl protected *o*-iodoaniline **3a** (0.25 mmol, 93 mg), and the reaction mixture was flushed with argon. Acetonitrile (1 mL, containing 1 equiv. water or 4.5 μL/mL), NEt₃ (1.2 equiv., 42 μL) and alkyne phenylacetylene (2 equiv., 55 μL) were successively added. The tube was capped and the reaction was heated at 40°C temperature during 20h. The reaction vessel was cooled down and the reaction mixture was diluted with ethyl acetate, concentrated in vacuo, and purified by silica gel chromatography using a EtOAc: pentane (gradient 0-10%) to give 83 mg (95% yield) of indole **4a** as a colorless solid. ¹H NMR (400 MHz, CDCl₃) δ 8.33 (d, *J* = 8.4 Hz, 1H), 7.52 (dd, *J* = 7.2, 2.5 Hz, 2H), 7.49 – 7.42 (m, 4H), 7.38 (ddd, *J* = 8.4, 7.2, 1.3 Hz, 1H), 7.32 – 7.26 (m, 3H), 7.06 (d, *J* = 8.1 Hz, 2H), 6.56 (s, 1H), 2.30 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 144.6, 142.3, 138.4, 134.8, 132.6, 130.7, 130.5, 129.3, 128.8, 127.6, 126.9, 124.9, 124.4, 120.8, 116.8, 113.7, 21.7.

See table 3 for deviating parameters.

Standard procedure for the recycling of the heterogeneous Pd catalyst

Into a sealable microwave tube were added Pd⁰-AmP-MCF (2.5 mol%, 24.9 mg), CuI (5 mol%, 7.2 mg), and the *N*-tosyl protected *o*-iodoaniline **3a** (0.75 mmol, 279 mg), and the reaction mixture was flushed with argon.

Acetonitrile (3 mL, containing 1 equiv. water or 13.5 $\mu\text{L/mL}$), NEt_3 (1.2 equiv., 126 μL) and phenylacetylene (2 equiv., 165 μL) were successively added. The tube was capped and the reaction was heated at 60°C during 20h. After completion of the reaction, the reaction vessel was cooled down and the crude material was transferred to a Falcon tube. The tube was subsequently centrifuged for 10 min (4000 rpm). The supernatant liquid was removed and the catalyst was washed with acetone (2x2 mL) then water (2 mL) and acetone again (2 mL). The washing procedure was as follows; addition of acetone or water (2 mL) and centrifugation for 10 min followed by removal of supernatant liquid. The washed and dried catalyst was reused for the next reaction and NMR yields were measured between each cycle from the supernatant liquid.

Extended X-Ray Absorption Fine Structure parameters

EXAFS measurements on solid Pd^{II} -AmP-MCF and Pd^{0} -AmP-MCF were performed at the Pd K X-ray absorption edge. Data on Pd^{II} -AmP-MCF were collected at the wiggler beam line 4-1 at the Stanford Synchrotron Radiation Lightsource (SSRL), Stanford, USA, operating at 3.0 GeV and 297-300 mA (top-up mode), and on Pd^{0} -AmP-MCF at beamline BM01B at the ESRF, Grenoble, France. The EXAFS stations were equipped with Si[220] double crystal monochromators. Higher order harmonics were reduced by detuning the second monochromator crystal to reflect 60 % of maximum intensity at the end of the scans. Internal energy calibration was made with a palladium metal foil assigned to 24350 eV (Pd K edge).^[11]

All measurements were performed in transmission mode. Four scans were averaged for each sample after energy calibration by means of the EXAFSPAK program package.^[12] The data treatment, including pre-edge subtraction, spline removal, normalization and Fourier transformation, was performed with the EXAFSPAK package. The experimental k^3 -weighted EXAFS oscillations were analyzed by non-linear least-squares fits of the data to the EXAFS equation, refining the model parameters, number of backscattering atoms (N), mean interatomic distances (R), Debye-Waller factor coefficients (σ^2), and threshold energy (E_0). The theoretical phases and amplitudes used in the refinements were calculated using the FEFF7 program.^[13] The standard deviations reported for the refined parameters were obtained from k^3 weighted least-squares refinements of the EXAFS function $\chi(k)$, and without including systematic errors. These statistical error values allow reasonable comparisons, e.g. of the significance of comparing relative shifts in the distances. However, the variations in the refined parameters, including the shift in the E_0 value (with $k = 0$), using different models and data ranges, indicate that the accuracy of the distances given for an individual complex is between ± 0.005 and ± 0.02 Å for well-defined interactions. The "standard deviations" have been increased accordingly to include estimated additional systematic errors.

Acknowledgements

Financial support from the Swedish Research Council (2016-03897 and 349-2013-580 through the Röntgen Ångström Cluster), the Berzelii Centre EXSELENT, the European Research Council (ERC AdG 247014), and the Knut and Alice Wallenberg Foundation is gratefully acknowledged. Use of the Stanford Synchrotron Radiation Lightsource, SLAC National Accelerator Laboratory, is supported by the U.S. Department of Energy, Office of Science, Office of Basic Energy Sciences under Contract No. DE-AC02-76SF00515. The SSRL Structural Molecular Biology Program is supported by the DOE Office of Biological and Environmental Research, and by the National

Institutes of Health, National Institute of General Medical Sciences (including P41GM103393). The contents of this publication are solely the responsibility of the authors and do not necessarily represent the official views of NIGMS or NIH. We acknowledge the European Synchrotron Radiation Facility for provision of synchrotron radiation facilities in using beamline BM01B.

Keywords: heterogeneous catalysis • palladium nanoparticles • benzofurans • indoles • Extended X-Ray Absorption Fine Structure

- [1] a) M. Lounasmaa, A. Tolvanen, *Nat. Prod. Rep.* **2000**, *17*, 175-191; b) V. Sharma, P. Kumar, D. Pathak, *J. Heterocycl. Chem.* **2010**, *47*, 491-502; c) M. Watanabe, W.-T. Su, Y. J. Chang, T.-H. Chao, Y.-S. Wen, T. J. Chow, *Chem. - Asian J.* **2013**, *8*, 60-64; d) H. Khanam, Shamsuzzaman, *Eur. J. Med. Chem.* **2015**, *97*, 483-504; e) P. Han, X. Gong, B. Lin, Z. Jia, S. Ye, Y. Sun, H. Yang, *RSC Adv.* **2015**, *5*, 50098-50104; f) G. W. Gribble, in *Indole Ring Synthesis*, John Wiley & Sons, Ltd, **2016**, pp. 1-38.
- [2] a) M. G. Kadieva, É. T. Oganessian, *Chem. Heterocycl. Compd. (N. Y., NY, U. S.)* **1997**, *33*, 1245-1258; b) G. R. Humphrey, J. T. Kuethe, *Chem. Rev.* **2006**, *106*, 2875-2911; c) A. A. Abu-Hashem, H. A. R. Hussein, A. S. Aly, M. A. Gouda, *Synth. Commun.* **2014**, *44*, 2285-2312. (d) For a recent metal free one-pot synthesis of benzofuranes see: R. Ghosh, E. Stridfeldt, B. Olofsson, *Chem. Eur. J.* **2014**, *20*, 8888-8892.
- [3] a) S. Cacchi, G. Fabrizi, *Chem. Rev.* **2011**, *111*, PR215-PR283; b) M. Platon, R. Amardeil, L. Djakovitch, J.-C. Hierso, *Chem. Soc. Rev.* **2012**, *41*, 3929-3968; c) X.-F. Wu, Y. Li, in *Transition Metal-Catalyzed Benzofuran Synthesis*, Elsevier, **2017**, pp. 3-27.
- [4] C. E. Castro, E. J. Gaughan, D. C. Owsley, *J. Org. Chem.* **1966**, *31*, 4071-4078.
- [5] a) M. Pal, V. Subramanian, K. R. Yeleswarapu, *Tetrahedron Lett.* **2003**, *44*, 8221-8225; b) I. P. Beletskaya, A. N. Kashin, A. E. Litvinov, V. S. Tyurin, P. M. Valetsky, G. van Koten, *Organometallics* **2006**, *25*, 154-158; c) L. Djakovitch, V. Dufaud, R. Zaidi, *Adv. Synth. Catal.* **2006**, *348*, 715-724; d) E. K. Yum, O.-K. Yang, J.-E. Kim, H. J. Park, *Bull. Korean Chem. Soc.* **2013**, *34*, 2645-2649; e) C. Rossy, E. Fouquet, F.-X. Felpin, *Beilstein J. Org. Chem.* **2013**, *9*, 1426-1431; f) P. K. Mandal, D. K. Chand, *Synthesis* **2015**, *47*, 1661-1668; g) J. Kwon, J. Chung, S. Byun, B. M. Kim, *Asian J. Org. Chem.* **2016**, *5*, 470-476.
- [6] a) Yin, J. Liebscher, *Chem. Rev.* **2007**, *107*, 133-173; b) M. Pagliaro, V. Pandarus, R. Ciriminna, F. Bèland, P. Demma Carà, *ChemCatChem* **2012**, *4*, 432-445; c) R. Schlögl, *Angew. Chem. Int. Ed.* **2015**, *54*, 3465-3520.
- [7] a) J. M. Campelo, D. Luna, R. Luque, J. M. Marinas, A. A. Romero, *ChemSusChem* **2009**, *2*, 18-45; b) K. Philippot, P. Serp, in *Nanomaterials in Catalysis*, Wiley-VCH Verlag GmbH & Co. KGaA, **2013**, pp. 1-54.
- [8] a) M. Shakeri, C.-W. Tai, E. Göthelid, S. Oscarsson, J.-E. Bäckvall, *Chem. Eur. J.* **2011**, *17*, 13269-13273; b) E. V. Johnston, O. Verho, M. D. Kärkäs, M. Shakeri, C.-W. Tai, P. Palmgren, K. Eriksson, S. Oscarsson, J.-E. Bäckvall, *Chem. Eur. J.* **2012**, *18*, 12202-12206. c) For a previous preparation of the silicious mesocellular foam (MCF) material see: Y. Han, S. S. Lee, J. Y. Ying, *Chem. Mater.* **2006**, *18*, 643-649;
- [9] a) J. Malmgren, A. Nagendiran, C.-W. Tai, J.-E. Bäckvall, B. Olofsson, *Chem. Eur. J.* **2014**, *20*, 13531-13535; b) K. P. J. Gustafson, R. Lihammar, O. Verho, K. Engström J.-E. Bäckvall, *J. Org. Chem.* **2014**, *79*, 3747- 3751; c) O. Verho, T. Åkermark, E. V. Johnston, K. P. J. Gustafson, C.-W. Tai, H. Svengren, M. D. Kärkäs, J.-E. Bäckvall, B. Åkermark, *Chem. Eur. J.* **2015**, *21*, 5909-5915; d) A. Nagendiran, H. Sorensen, M. J. Johansson, C.-W. Tai, J.-E. Backvall, *Green Chem.* **2016**, *18*, 2632-2637.

- [10] A. Nagendiran, O. Verho, C. Haller, E. V. Johnston, J.-E. Bäckvall, *J. Org. Chem.* **2014**, *79*, 1399-1405.
- [11] G. N. George, I. J. Pickering, EXAFSPAK – A Suite of Computer Programs for Analysis of X-ray Absorption Spectra, SSRL, Stanford, CA. **1993**.
- [12] A. Thompson, D. Attwood, E. Gullikson, M. Howells, K.-J. Kim, J. Kirz, J. Kortright, I. Lindau, P. Pianetta, A. Robinson,; J. Scofield,; J. Underwood,; D. Vaughan,; G. Williams,; H. Winick, *X-ray data booklet*, Lawrence Berkeley National Laboratory, Berkeley, 2nd Ed., **2001**.
- [13] S. I. Zabinsky, J. J. Rehr, A. Ankudinov, R. C. Albers, M. J. Eller, *Phys. Rev. B* **1995**, *52*, 2995–3009.

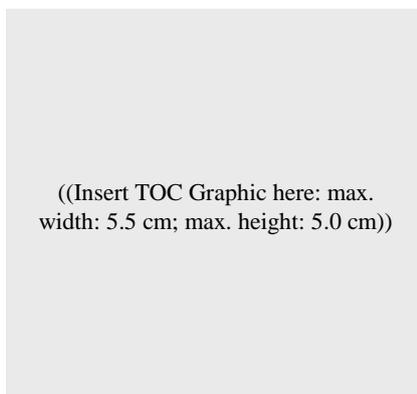
WILEY-VCH

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

Layout 1:

FULL PAPER

Text for Table of Contents



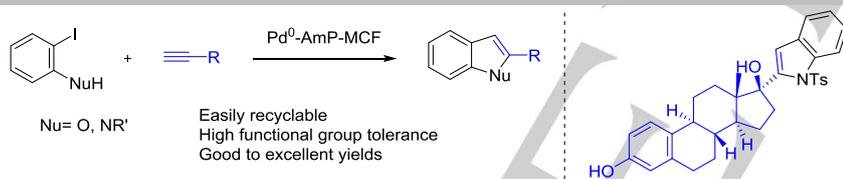
Author(s), Corresponding Author(s)*

Page No. – Page No.

Title

Layout 2:

FULL PAPER



Alexandre Bruneau, Karl P. J. Gustafson, Ning Yuan, Cheuk-Wai Tai, Ingmar Persson, Xiaodong Zou, and Jan-E. Bäckvall*

Page No. – Page No.

Synthesis of Benzofurans and Indoles from Terminal Alkynes and Iodoaromatics Catalyzed by Recyclable Palladium Nanoparticles Immobilized on Siliceous Mesocellular Foam

Pd nanoparticles supported on siliceous mesocellular foam (Pd⁰-AmP-MCF) were found to efficiently catalyze the reaction of *o*-iodophenols and protected *o*-iodoanilines with acetylenes to produce 2-substituted benzofurans and indoles, respectively. In general, the catalytic protocol afforded the desired products in good to excellent yields under mild reaction conditions without the addition of ligands.