Nanopalladium on Amino-functionalized Mesocellular Foam as an Efficient and Recyclable Catalyst for the Selective Transfer Hydrogenation of Nitroarenes to Anilines

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Abstract

Herein, we report on the use of nanopalladium on amino-functionalized siliceous mesocellular foam as an efficient heterogeneous catalyst for the transfer hydrogenation of nitroarenes to anilines. In all cases, the protocol proved to be highly selective favoring the formation of the desired aniline as the single product in high yields with short reaction times, when employing the naturally-occurring and renewable γ-terpinene as hydrogen donor. Furthermore, the catalyst displayed excellent recyclability over five cycles and negligible leaching of metal into solution, making it an eco-friendly and economic alternative for carrying out this transformation. The scalability of the protocol was demonstrated with the reduction of 4-nitroanisole on a 2 g scale, where *p*-anisidine was isolated in 98% yield.

Introduction

The selective reduction of nitroarenes to anilines is an important transformation in both academic and industrial-scale organic chemistry given that anilines constitute key intermediates or targets in the synthesis of agrochemicals, dyes, pharmaceuticals, pigments and polymers.[1] This transformation has traditionally been performed with stoichiometric amounts of metallic Fe-[2] or Zn-based[3] reagents in the presence of a proton source, by various Raney Ni-based protocols,[4] or by other catalytic systems employing toxic reductants such as $NaBH_4$,[5] H_2S,[6] or N_2H_4.[7]

Consequently, a substantial amount of research has been dedicated into developing new and efficient catalytic protocols that use environmentally-friendly reductants. Many catalytic systems for transition metal-catalyzed hydrogenation of nitroarenes to anilines have shown excellent efficiency and synthetic utility,[8] but the handling of hydrogen gas on an industrial-scale is associated with safety issues. Therefore, recent attention has been directed towards transfer hydrogenation methods that avoid the use of hydrogen gas, by applying safer and more convenient hydrogen donors. The latter studies have resulted in a range of catalytic methods for reduction of nitroarenes based on both homogeneous[9] and heterogeneous[10] transition metal catalysts that employ green hydrogen donors, such as formic acid, formate salts, and isopropanol. Heterogeneous compared to homogeneous catalysis hold greater promise for use in large-scale industrial applications, due to the simple separation and recycling of the catalyst, as well as the minimization of metal contaminations in the final product.

Recently, we reported the preparation of Pd nanoparticles on aminopropyl-functionalized siliceous mesocellular foam (AmP-MCF).[11] This powerful catalyst has thus far been successfully employed as an efficient and recyclable catalyst for the aerobic oxidation of alcohols,[11a] racemization of amines,[11b] Suzuki cross-couplings,[11c] and for the transfer hydrogenation of alkenes using 1-methyl-1,4-cyclohexadiene as the hydrogen donor.[11c]

This mesoporous silica material possesses many desirable properties, which are reflected by its frequent use as a support for both bio- and chemical catalysts.[11, 12] The material has an adjustable three-dimensional network of pores which confers a high surface area and shields the catalytic species from mechanical grinding, thus reducing catalyst leaching. Furthermore, the material has a high surface concentration of silanol groups that can serve as handles for immobilization of various catalytic species, such as enzymes, nanoparticles and defined transition metal complexes.

Considering our successful results in the transfer hydrogenation of alkenes with the nanopalladium catalyst on AmP-MCF, we envisioned that it would be possible to extend this methodology to also include the selective reduction of nitro compounds to the corresponding amines. The protocol reported herein can be applied to the reduction of a broad range of nitro compounds to amines in an economical and practical fashion.

Results and Discussion

Screening of Reaction Conditions

4-Nitroanisole (**1a**) was chosen as a model substrate for reaction optimizations, in which the effects of hydrogen donor, solvent and reaction temperature were investigated. From previous studies in our laboratory on related hydrogen transfer reactions the best solvent was found to be EtOH, which worked well at 90 ^{o}C.[11c] We therefore used this starting point and screened the most commonly used hydrogen donors. These experiments were carried out with 0.40 mmol substrate **1a** and 1 mol% Pd nanocatalyst, in 1 mL EtOH at 90 °C. All experiments were performed under identical conditions in pressure-sealed microwave vessels under air atmosphere and were probed by ^{1}H NMR.

Initial experiments performed with our Pd nanocatalyst and formate salts showed promising results, where sodium formate (**2**), potassium formate (**3**) and cesium formate (**4**) gave 73%, 91% and >99% conversion to **1b**, respectively (Table 1, Entries 1-3). The observed cation effect for these hydrogen donors was expected, since an increase in cation size increases the solubility of the formate salt in EtOH and allows for a more efficient reaction. Unfortunately, the use of formate salts (**2-4**) as hydrogen donors resulted in substantial amounts of precipitated ethoxide salts during the course of the reaction. Not only did the ethoxide salt formation hinder the stirring of the reaction, but it also significantly increased the pH of the reaction, which had a negative effect on the silica-based support. As a consequence, the recyclability of the catalyst for these entries proved to be poor, where TEM-images of the collected catalyst indicated agglomeration of the Pd nanoparticles, a marker for support degradation. Moreover, we cannot rule out the possibility that the ethoxide salt blocks the pores of the support, thereby restricting access to the nanoparticles on the inside. Attempts to improve the recyclability of the catalyst by decreasing the extent of ethoxide salt precipitation were performed by diluting the reaction or by addition of a phosphate buffer; however, neither method proved to be successful.

In contrast to the formate salts, the use of formic acid (**5**) as the hydrogen donor proved to be significantly less efficient, with only a low conversion to 4-methoxyaniline (**1b**) observed, when a 1:1 mixture of formic acid:ethanol was used (Table 1, Entry 4). Running the reaction in neat formic acid (Table 1, Entry 5) resulted in only formation of traces of product with significant

byproduct formation as observed by ^{1}H-NMR. Addition of triethylamine (NEt_3) to the reactions employing **5** as hydrogen donor greatly enhanced the rate and selectivity, resulting in 85% conversion with 1.2 equiv of NEt_3 (Table 1, Entry 6) and 92% conversion with 3 equiv. of NEt_3 (Table 1, Entry 7). Unfortunately, a slight loss in catalyst activity was observed over multiple cycles under the employed reaction conditions, most likely due to the basic nature of NEt_3, and therefore this donor system was not investigated any further in this study.

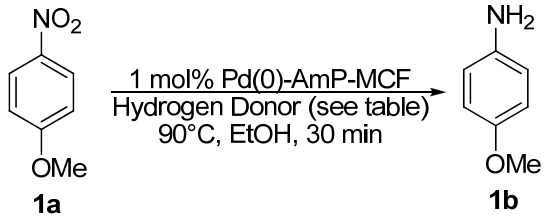
We next turned our attention towards 1-methyl-1,4-cyclohexadiene (**6**), which was used as the hydrogen donor in our previous study.[11c] The smooth transfer of two hydrogens with such dienes makes the overall reaction pH stay neutral, and under these conditions no catalyst degradation occurs. Diene **6** turned out to be rather slow as hydrogen donor and only 29% yield of aniline **1b** was obtained from **1a** after 30 min of reaction (Table 1, entry 8). Attempts to increase the rate by the use of the corresponding unsubstituted 1,4-cyclohexadiene (**7**) were unsuccessful and lead to a lower rate with a 23% yield after 30 min (Table 1, Entry 9). We therefore decided to try the more substituted diene γ-terpinene (**8**). Diene **8** is a readily available and inexpensive natural product extracted from plants and trees;[13] its cost is comparable to the formate salts **2** and **3**. The side product from **8**, *p*-cymene is not to be considered only as waste since it is used in chemical industry for the production of *p*-cresol, fragrances, pharmaceuticals, herbicides, and other fine chemicals.[14] There are rather few reports on the successful use of **8** in the literature.[15]

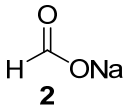
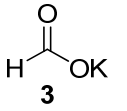
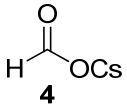
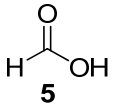
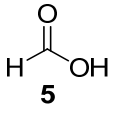
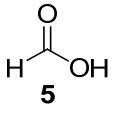
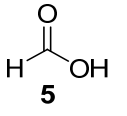
Interestingly, diene **8** (Table 1, Entry 10) proved to be a significantly more efficient hydrogen donor than 1-methyl-1,4-cyclohexadiene (**6**) and 1,4-cyclohexadiene (**7**) giving a conversion of 73% after 30 min. Increasing the amount of **8** to 4 and 5 equiv., enhanced the conversion to 91% and >99%, respectively after 30 min (Table 1, Entries 11 and 12). Switching to the related natural product (*R*)-limonene (**9**) resulted in no formation of product (Table 1, Entries 13), suggesting that higher reaction temperatures is most likely required for this donor to efficiently aromatize through hydrogen transfer.

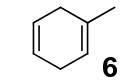
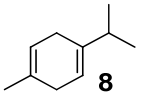
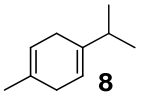
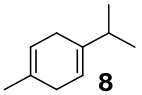
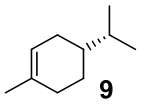
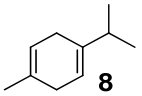
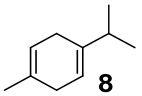
The reduction of **1a** was also tested in neat isopropanol, with or without base (1 equiv. Cs_2CO_3), but no formation of **1b** could be observed in either case (Table 1, Entries 14 and 15). At this stage, control experiments were performed to compare the efficiency of the Pd nanocatalyst to the commercially available and standard Pd/C (10 wt%). Only a conversion of 32% was obtained

with Pd/C, demonstrating that our Pd nanocatalyst is indeed more efficient for this transformation (Table 1, Entry 16). Control experiments were carried out in the absence of either the Pd nanocatalyst or the hydrogen donor **6**, and none of these experiments gave any detectable amounts of **1b** (Table 1, Entries 17 and 18).

Table 1: Hydrogen donor screening of the Pd(0)-AmP-MCF-catalyzed transfer hydrogenation of 4-nitroanisole (**1a**).[a]



Entry	H-donor	Equiv.	Conv.[b] (%)
1	 **2**	3.0	73
2	 **3**	3.0	91
3	 **4**	3.0	>99
4	 **5**	11.0	14
5	 **5**	neat	0
6[c]	 **5**	3.0	85
7[d]	 **5**	3.0	92

8	 **6**	3.0	29
9	 **7**	3.0	23
10	 **8**	3.0	73
11	 **8**	4.0	91
12	 **8**	5.0	>99
13	 **9**	3.0	0
14	*i*PrOH	neat	0
15[e]	*i*PrOH	neat	0
16[f]	 **8**	3.0	32
17[g]	 **8**	3.0	0
18[h]	-	-	0

[a] Unless otherwise noted reaction conditions were: 1 mol% of Pd, 0.40 mmol of 4-nitroanisole, hydrogen donor (see table), in 1 mL of EtOH, at 90 °C, for 30 min in an 8 mL microwave vial. [b] Conversion by ^{1}H NMR. [c] Carried out with 1.2 equiv. of NEt_3 (Commerical formic acid: NEt_3 complex 5:2 was used). [d] Carried out with 3.0 equiv.of NEt_3. [e] Carried out with 1 equiv. of Cs_2CO_3. [f] Carried out with 1 mol% of Pd/C. [g] Performed in the absence of Pd(0)-AmP-MCF. [h] Performed in the absence of hydrogen donor.

We next studied the solvent effect on the reaction with the use of 4 equiv. of hydrogen donor **8**. In order to clearly visualize the outcome of the reaction, product formation was measured by ^{1}H-NMR after only 10 min since the reaction reaches >90% conversion after 30 min. Acetone, EtOH, and MeOH were shown to be the best solvents, giving conversions around 70% after 10 min (Table 2, Entries 1-3), while EtOAc and THF were found to be poor solvents for this reaction (Table 2, Entries 4 and 5), giving 32% and 26% conversion, respectively. DMSO and

toluene were incompatible with this protocol, resulting in no formation of product after 30 min (Table 2, Entry 6 and 7). Subsequent experiments were continuously run using EtOH as the solvent, since it is a greener alternative than MeOH and acetone.

It was also investigated whether it was possible to run the reaction at a lower temperature and retain acceptable yields and reaction times. Unfortunately, initial experiments in sealed microwave vessels at 80°C proved to be quite disappointing giving only 82% after 2h (Table 2, Entries 8-10). A prolonged reaction time only marginally improved the yield, suggesting that it was not possible to obtain complete conversion within reasonable times under these reaction conditions. These results cannot be explained by the decrease in temperature alone, and we suspected that the pressure of the reaction was also important for the outcome of the reaction. To evaluate this hypothesis we decided to change from a microwave vial (8 mL total volume) to a smaller capped vial (4 mL). By doing so, the free volume of gas in the reaction was substantially decreased, allowing for an increased concentration of *in situ* formed H_2 in the solution. Gratifyingly, this had a significant positive influence on the rate of the reaction, allowing for 95% conversion at 80 °C (Table 2, Entry 11), after only 30 min.

Table 2: Solvent and temperature screening of the Pd(0)-AmP-MCF-catalyzed transfer hydrogenation of 4-nitroanisole (**1a**).[a]

Entry	Solvent	Temp(°C)	Time (min)	Conv.[b] (%)
1	EtOH	90	10	68
2	MeOH	90	10	73
3	Acetone	90	10	69
4	EtOAc	90	10	32
5	THF	90	10	26
6	DMSO	90	10	0
7	Toluene	90	10	0
8	EtOH	80	30	49
9	EtOH	80	60	63
10	EtOH	80	120	82
11[c]	EtOH	80	30	95

[a] Reaction conditions: 1 mol% Pd, 0.40 mmol 4-nitroanisole, 4 equiv. γ-terpinene (**8**), in 1 mL total volume (hydrogen donor + EtOH), at the temperature and time given in the table, in an 8 mL microwave vial. [b] Conversion by ^{1}H-NMR. [c] 1 mol% Pd, 1.20 mmol γ-terpinene (4 equiv.), in 3 mL total volume hydrogen donor + EtOH), at the temperature and time given in the table, in a 4 mL capped vial.

Substrate Scope

A major strength of this reaction protocol is its ability to tolerate substrates containing a wide range of functional groups. General reaction trends related to the electronic properties of the substrate were difficult to establish, and we speculate that this is the result of several parameters governing the overall rate of the reaction. One could argue that electron-withdrawing groups should facilitate the reaction, since it would decrease the electron-density of the nitro-group and make it more prone to undergo reduction. On the other hand, efficient substrate coordination to the metal surface is a prerequisite for the reaction to occur and this process would be favored for substrates containing electron-rich π-systems. An electron-rich π-system could also impede the reaction, since the resulting aniline could compete for the free coordination sites on the Pd. The introduction of a strongly electron-donating substituent on the substrate could therefore result in an increased coordination ability of the amine group of the product, which could prevent access of the substrate and hydrogen donor to the catalyst surface. Steric properties of the substrate are also expected to play an important role in the coordination ability of the substrate.

Variation of substrate substitution was observed to affect the extent of the non-productive Pd-catalyzed dehydrogenation of **8** to produce *p*-cymene and H_2. In order to account for this decomposition, we found it necessary to optimize the amount of hydrogen donor in reactions of certain substrates.

As shown in Table 3, 4-nitroanisole (**1a)** (Entry 1) reacted rapidly under the optimized standard conditions (1 mol% Pd, 4 equiv. γ-terpinene, 80°C), affording **1b** in 95% yield after 30 min. The less electron-rich substrates 4-nitrotoluene (**10a**) and 1-tert-butyl-4-nitrobenzene (**11a**) required longer reaction times than **1a** to reach completion (Table 3, Entries 2 and 3). Reduction of **10a** afforded the corresponding aniline (**10b**) in quantitative yield after 1 h under the standard conditions (Entry 2), while substrate **11a** required 5 equiv. of **8** and a reaction time of 45 min to give comparable results (Entry 3). Interestingly, nitrobenzene (**12a**) reacted significantly slower than substrate **1a**, **10a**, and **11a**, requiring 6 equiv. of **8** and a reaction time of 3 h, to give aniline **(12b**) in 97% yield (Table 3, Entry 4). 1-Fluoro-4-nitrobenzene (**13a**) displayed a similar reactivity as that of nitrobenzene, and required 6 equiv. of **8** and a longer reaction time to give a quantitative yield of **13b** (Table 3, Entry 5). Gratifyingly, the reaction protocol showed to be

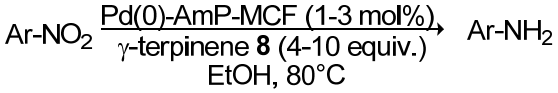
compatible with substrates containing trifluoromethyl, cyano, ester, ketone and hydroxyl groups, affording the corresponding anilines **14b**-**21b** in high to excellent yields in short reaction times (Table 3, Entries 6-14). Of particular interest is that the nitro group can be selectively reduced in the presence of a keto group as shown by the reduction of nitroacetophenones **17a**-**19a**. This selective reduction has been considered to be particularly challenging.[9b,16]

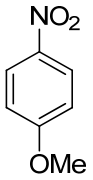
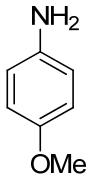
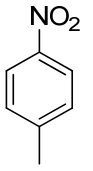
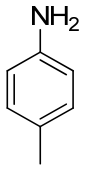
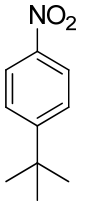
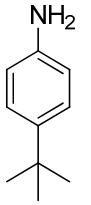
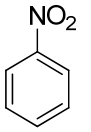
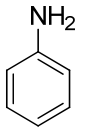
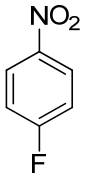
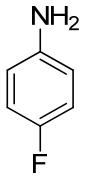
Furthermore, in the reduction of the **17a**-**19a**, a reactivity trend was observed where the *para* isomer reacted significantly faster than the *ortho* isomer, which in turn reacted faster than the *meta* isomer under the standard conditions. The higher reactivity of the *para* and *ortho* isomers can be attributed to an electronic resonance effect, which withdraws electrons from the nitro group and makes it more prone to undergo reduction. This effect does not exist in the *meta* isomers, and consequently it reacts significantly slower. The difference in reactivity between the *para* and *ortho* isomers can be ascribed to sterics, where the rather bulky keto group in the *ortho* position prevents access to the nitro-group in **18a**. Interestingly, when doing the same comparison for the three isomers of nitrophenol, we observed the following trend; *ortho* > *meta* > *para*. Since the hydroxyl-group is electron-donating, we predicted a reactivity trend of *meta* > *ortho* > *para*, based on electronic effects. We believe the reason for the high reactivity of the *ortho* isomer **20a** is due to a directing coordinative effect of the hydroxyl, which steers the nitro group towards the Pd surface and facilitates the reaction.

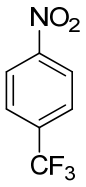
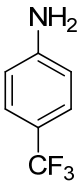
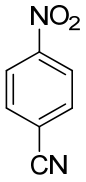
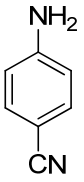
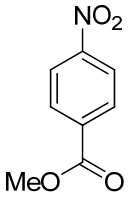
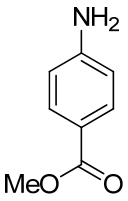
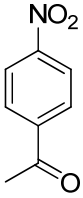
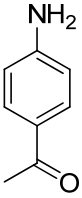
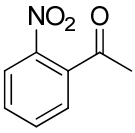
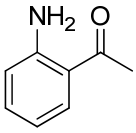
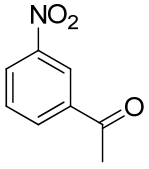
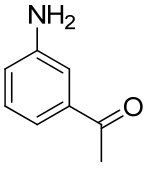
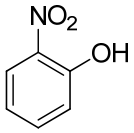
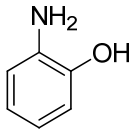
We also demonstrated that the protocol could be optimized to work for 2-methyl-5-nitroaniline (**23a**) and the bulky 2-nitrobiphenyl (**24a**), giving the corresponding anilines **23b** and **24b** in 89% and 97%, respectively (Table 3, Entries 15 and 16). Moreover, it was possible to achieve quantitative yields of the bulky 1-nitronaphthalene (**25a**) and the heteroaromatic 3-nitropyridine (**26a**), but in both cases elevated catalyst loadings and 10 equiv. of **8** were required (Table 3, Entries 17 and 18) The protocol also showed to be successful for the reduction of an aliphatic substrate, where 1-hexylamine (**27b**) was obtained in 92% yield from 1-nitrohexane (**27a**) (Table 3, Entry 19). It is also important to point out that in all reaction described in Table 3, the desired aniline was formed as the exclusive product and the remaining material was identified as unreacted starting material by quantification against internal standard. This further confirms that the formation of other reduction products, such as for instance hydroxylamines, oximes, nitrones and azo-compounds can only occur to negligible extent. Moreover, a great portion of the aniline

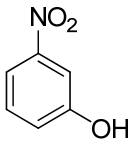
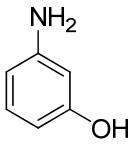
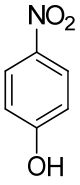
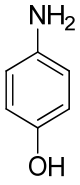
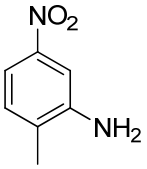
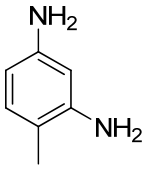
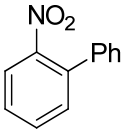
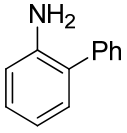
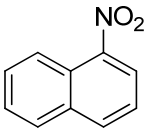
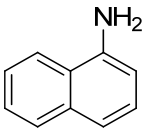
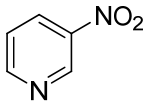
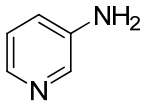
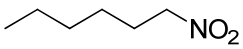
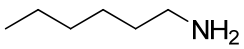
products where isolated by either extraction or column chromatography to affirm that the isolated yields were in line with the NMR-yields.

Table 3: Transfer hydrogenation of various nitroarenes catalyzed by Pd(0)-AmP-MCF.[a]



Entry	Substrate	Product	Catalyst (mol%)	Donor (Equiv.)	Time (min)	Yield (%)[b]
1	 **1a**	 **1b**	1.0 (0.25[c])	4.0 (6.0 [c])	30 (300[c])	95 (98[c])
2	 **10a**	 **10b**	1.0	4.0	60	>99
3	 **11a**	 **11b**	1.0	5.0	45	>99 (96)
4	 **12a**	 **12b**	1.0	6.0	180	97 (93)
5	 **13a**	 **13b**	1.0	6.0	150	>99

6	 **14a**	 **14b**	1.0	5.0	60	90 (87)
7	 **15a**	 **15b**	2.0	4.0	60	91 (88)
8	 **16a**	 **16b**	1.0	4.0	60	96 (93)
9	 **17a**	 **17b**	1.0	4.0	30	97 (95)
10	 **18a**	 **18b**	1.0 1.0	6.0 4.0	60 60	90 61
11	 **19a**	 **19b**	1.5 1.0	6.0 4.0	120 60	96 33
12	 **20a**	 **20b**	1.0	5.0	90	>99 (99)

13	 **21a**	 **21b**	1.0	5.0	90	85
14	 **22a**	 **22b**	2.0 1.0	6.0 5.0	150 90	>99 39
15	 **23a**	 **23b**	2.0	5.0	150	89
16	 **24a**	 **24b**	1.0	5.0	120	97 (96)
17	 **25a**	 **25b**	2.0	10.0	120	>99 (95)
18[d]	 **26a**	 **26b**	3.0	10.0	120	>99
19	 **27a**	 **27b**	2.0	6.0	120	92

[a] Unless otherwise noted the reactions were performed in a 4 mL capped vial, with nitroarenes (1.20 mmol), γ-terpinene **8** (see Table), and Pd nanocatalyst (see Table) in EtOH at 80°C for the time given in the Table. The total volume of all the reactions (EtOH + γ-terpinene) was always kept at 3 mL. [b] NMR-yield, against the internal standard 1,3,5-trimethoxybenzene. Isolated yield in parenthesis. [c] Large scale experiment (13 mmol). For experimental details see the Supporting Information [d] 0.60 mmol nitroarene in 2.2 mL EtOH and 0.8 mL γ-terpinene (10 equiv.).

Unfortunately, the protocol gave poor results in the reduction of nitroarenes containing olefin, acetylene and halogen (Cl, Br, I) substituents. In the case of 4-nitrophenylacetylene and 3-nitrostyrene, no reaction took place and only starting material was recovered after 1 h at 80°C,

which suggest that the acetylene and olefin moieties exhibited a poisoning effect on the catalyst. Most likely the hydrogen donor cannot compete with these substrates for access to the Pd surface, and no Pd hydrides are formed that can perform the reduction. Also, in contrast to our previous study of the transfer hydrogenation of alkenes,[11c] no reduction of the C=C bond could be observed under these reaction conditions, which was attributed to the lower reaction temperature of the current protocol.

A similar effect was observed for the reactions involving halogenated substrates, where no signs of products arising from nitro-group reduction were observed. It is suspected that the cause for the poor conversion of these substrates can also be ascribed to a poisoning effect, where we propose that the aryl-halide undergoes an oxidative addition to the Pd and prevents it to take part in further reactions. This theory was supported by ^{1}H-NMR analysis of the traces of reaction products from the reactions of 1-chloro-4-nitrobenzene, 1-bromo-4-nitrobenzene and 1-iodo-4-nitrobenzene, where peaks belonging to nitrobenzene could be observed, arising from a reductive dehalogenation reaction. However, this process was slow under the reaction conditions employed, with less than 5% of the dehalogenated products observed in all cases. The remaining >95% was also in this case identified as unreacted starting material by ^{1}H-NMR analysis.

Recycling and Large-scale Experiments

The recyclability of heterogeneous catalysts is of fundamental importance and an important advantage over homogeneous counterparts. Consequently, we carried out a recycling study, in which the activity and selectivity of the Pd(0)-AmP-MCF were investigated for the reaction of 4-nitroacetophenone over 5 cycles. Gratifyingly, the catalyst exhibited excellent recyclability with sequential conversions of 97%, 97%, 97%, 95%, 95%, with a selectivity of >99% towards the 4-aminoacetophenone over all cycles. In conformity with previous studies where the recyclability of this catalyst was exhibited, a sample of the catalyst was recovered from the last cycle of this transformation and analyzed by STEM to evaluate the nanoparticle size and distribution.[11] As can be seen from the TEM images (Figure 1 and Figure S1), no significant change in either particle size or distribution occurred after use in multiple cycles, confirming the recyclability and robustness of the catalyst. The high recyclability can also be ascribed to the low leaching of Pd from the catalyst, which was found to be <0.1 ppm by ICP-OES analysis.[17]

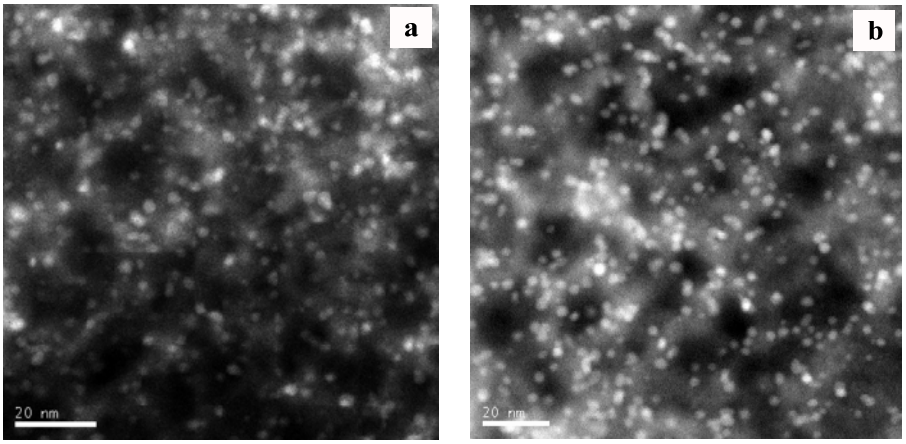
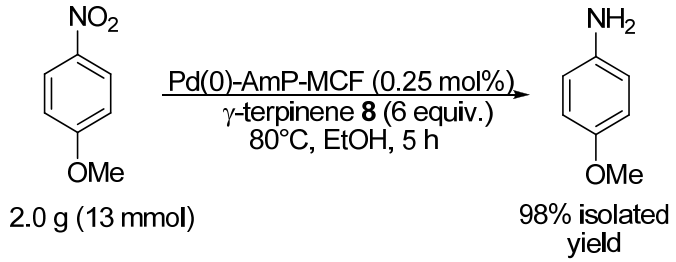


Figure 1. Images taken of the Pd(0)-AmP-MCF by Scanning Transmission Electron Microscopy (STEM) with a 20 nm scale bar, showing well-dispersed Pd nanoparticles in the size range of 1-2 nm. a) unused Pd nanocatalyst b) Pd nanocatalyst recovered after the fifth cycle.

As a measurement to test the practical utility of this protocol, the reduction of **1a** was performed on a larger scale (Scheme 1). At a 2.0 g scale (13 mmol) using 0.25 mol% Pd(0)-AmP-MCF and 6 equiv. of **8**, we were able to isolate **1b** in 98% yield after a reaction time of 5 h (at 80°C) and a simple extraction procedure (Scheme 1).



Scheme 1. Large-scale reduction of 4-nitroanisole (**1a**)

Comparison with other systems for transfer hydrogenation of nitroarenes

The present system compares very well with previously published systems for transfer hydrogenation of nitroarenes.[7a,10a-f] It has the advantage that it works under neutral conditions, whereas some of the previous systems require the presence of base.[10a,b,f] Another advantage of

the present method is that the catalyst allows for simple separation and can be recycled several times without any significant loss of activity. This has not been possible with some of the previous systems where catalyst deactivation and difficulties in separation of the catalyst from the reaction mixture have resulted in decreased reaction efficiencies over multiple cycles.[10c,e]

Conclusion

We have demonstrated that Pd(0)-AmP-MCF is a highly efficient catalyst for the selective transfer hydrogenation of a wide variety of nitroarenes, furnishing the corresponding anilines in good to excellent yields after short reaction times, when using γ-terpinene as the hydrogen donor. With this hydrogen donor the overall reaction pH stays neutral and this feature makes γ-terpinene (**8**) suitable for transfer hydrogenation of substrates that are either acid or base sensitive. The Pd nanocatalyst proved to be highly recyclable and displayed low leaching (<0.1 ppm) in the reaction of 4-nitroacetophenone. Moreover, the protocol proved to be scalable, which was demonstrated by performing the reduction of 4-nitroanisole on a 2 g scale, to give *p*-anisidine in 98% isolated yield. Future work will be dedicated towards discovering new synthetic applications of the Pd(0)-AmP-MCF to enable for the construction of tandem reactions sequences that make use of the many reactivity modes of this nanocatalyst. This would offer a more eco-friendly and waste-reducing approach to produce chemicals for both academic and industrial use.

Acknowledgements

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(17) A leaching test was performed on the reduction of 4-nitroacetophenone. Upon completion of the reaction, the reaction vessel was centrifuged and an aliquot was withdrawn from the liquid phase. The aliquot was passed through a pad of celite to remove smaller Pd nanocatalyst particles that did not sediment during the centrifugation. The filtered aliquot was analyzed by elemental analysis (ICP-OES by MedacLtd, UK) and the Pd content was determined to be <0.1 ppm, which is below the limit of quantification for this technique.

Table of contents graphics (TOC)

Expanding the repertoire: Nano-palladium immobilized on amino-functionalized mesocellular foam was found to be an efficient catalyst for the selective transfer hydrogenation of nitroarenes to anilines in high yields, when using γ-terpinene as hydrogen donor. The catalyst displayed excellent recyclability without any significant loss of activity over five cycles and the leaching of metal into solution was found to be very low (<0.1 ppm), making it an economic and eco-friendly alternative.