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Solid supported Pd(0): an efficient recyclable heterogeneous catalyst for chemoselective reduction of nitroarenes ☆

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ABSTRACT

Solid supported palladium(0) (SS-Pd) catalyzed highly chemoselective reduction of nitroarenes to the corresponding anilines was accomplished under a milder reaction condition. This catalyst showed high compatibility with various reducing agents ($NaBH_4$, Et_3SiH, and $NH_2NH_2{\cdot}H_2O$) and a large number of reducible functional groups such as sulfonamide, amides, carboxylic acid, ester, alcohol, halide, hetero cycle, nitrile, alkene, carbonyl, *O*-benzyl, and *N*-benzyl were tolerated. Most of the reactions were clean and high yielding. The SS-Pd catalyst could be recycled up to seven runs without significant loss of activity.

Amino compounds are the main precursor or intermediate for a number of valuable molecules such as dyes, pesticides, herbicides, and agrochemicals.[1] Reduction of nitroarenes in a selective manner is the best route to obtain industrially important aryl amines. Palladium is an active transition metal of choice, which has been used in different catalytic forms to reduce organo nitro derivatives. $Pd(OAc)_2$/polymer supported formate,[2] Pd-carbon nanofiber (CNF)/H_2,[3] $Pd(OAc)_2$/silicon hydride,[4] and Pd-PEG/H_2[5] have been reported for the transformation of nitroarenes to corresponding anilines. It is well known that sodium borohydride has less potentiality to reduce nitro compounds to corresponding amines in the absence of additives.[6] In addition, usually reduction of nitroarenes with $NaBH_4$ stops at intermediate stage of azo, azoxy, and hydrazo derivatives.[7] Besides this problem, recyclability of catalyst, high loading of reducing agent, metal contamination, cost of the reagent, and high pressure apparatus for hydrogenation make the processes economically unfavorable as well as hazardous. Hence, an alternative fast, cost effective, milder, and chemoselective reduction of nitroarenes with negligible metal contamination is of high demand.

Recently our group described the synthesis of solid supported palladium(0) (SS-Pd) nano/microparticles as heterogeneous catalyst and their applications in cross coupling[8a] and oxidation[8b] reactions.

Herein, we report convenient methodologies for nitroarene reduction in the presence of SS-Pd as a ligand-free recyclable heterogeneous catalyst under milder reducing agents.

The SS-Pd catalyst was prepared following our previous report[8] and SEM analysis was performed to see nano/microparticles deposition over the solid surface (Fig. 1). In our previous studies, we realized that nanoparticles of palladium deposited inside the solid matrix were difficult to analyze by transmission electron microscopy (TEM). Here, for the first time we prepared the powdered form of borohydride exchanged amberlite resin for *in situ* conversion of Pd(II) to Pd(0) and their simultaneous deposition over solid matrix. The water suspension of the dispersed solid supported Pd(0) (SS-Pd́) was further characterized by TEM for nanoparticles analysis of Pd(0) (Fig. 2). Further, both the catalysts SS-Pd and SS-Pd́ were tested for different nitroarene reduction and no significant effect on product yields was observed. Due to easy handling, purification, reusability, and same reactivity, SS-Pd was further explored for reduction of nitroarenes.

Initially to search for the optimum reaction condition, reducing agent, best catalytic system, catalyst concentration, solvent, and temperature, 4-nitrotoluene was considered as test substrate. The combination of SS-Pd (2 mol % Pd) and $MeOH:H_2O$ (3:7) was found to be very effective for both $NaBH_4$ and $NH_2NH_2.H_2O$ reducing agents which gave 97 and 98% yields respectively of the corresponding amine **1**. Interestingly, Et_3SiH was also found to be effective with SS-Pd (3 mol % Pd) in THF solvent for the same reduction and ended with 82% yield at room temperature. The SS-Pd and $NaBH_4$ combination was also employed on the same

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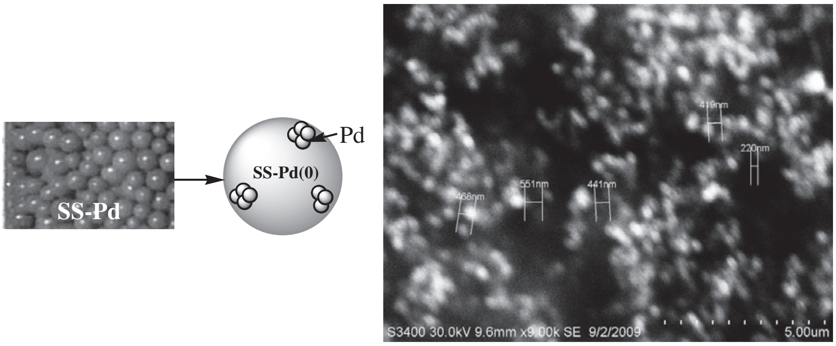


Figure 1. Scanning Electron Micrograph (SEM) image of SS-Pd.

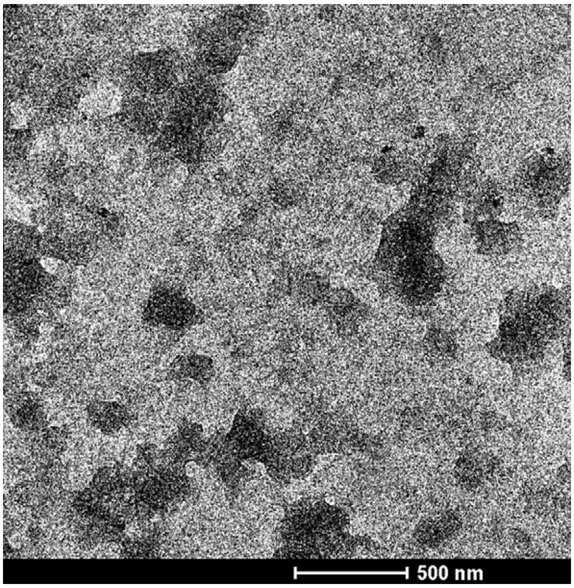


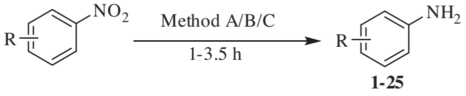
Figure 2. Transmission electron microscope (TEM) image of SS-Pd.

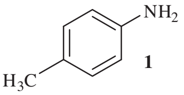
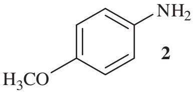
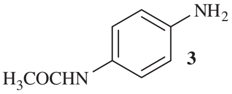
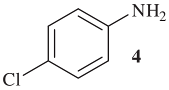
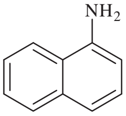
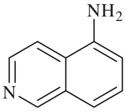
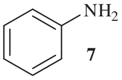
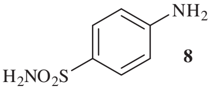
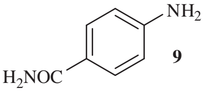
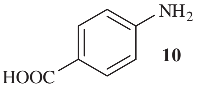
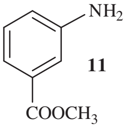
substrate up to 5 gm scale and gave **1** in 95% yield (GC-MS). Furthermore, hydrogenation with the ex situ produced molecular hydrogen that resulted in poor conversion of **1** (23%) (Table 1, entry 1).

To see the scope, the SS-Pd catalyst was further explored with the three reducing sources ($NaBH_4$/Et_3SiH/$NH_2NH_2.H_2O$) for different representative nitroarenes (Table 1; **2–6**). Due to comparative results in foremost reactions, further importance for the selection of reducing agents was given on chemoselective nitroarenes reduction through easy accessible, non-hazardous, trouble-free product separation, and cost effective process. Considering these issues, the reducing agents in combination with SS-Pd were further determined based on the functional groups with nitroarenes. Unsubstituted nitroarene under the standard SS-Pd and $NaBH_4$ condition afforded high yield of aniline **7**. Further this combination was found to be highly chemoselective in the presence of several reducible functional groups such as sulfonamide, amides, carboxylic acid, ester, alcohol, halides, and nitrile (**8-15)**. Polycyclic and heterocyclic nitroarenes also gave good to excellent yield of corresponding amines (**16** and **17**). 4-nitroaniline under similar condition gave 1,4-diamino benzene **18** in 91% yield. Similarly, in our typical method (Method A) 1,3-dinitrobenzene resulted in the corresponding diamino derivative **19** in an excellent yield.

As per our knowledge $NH_2NH_2.H_2O$ with palladium catalyst as a reducing agent for nitroarene reduction has not yet been reported in the literature. Regioselective reduction of dinitro compound is

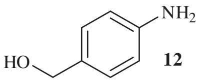
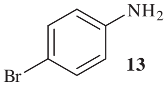
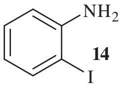
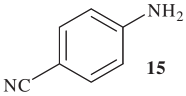
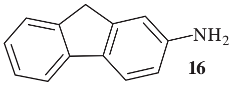
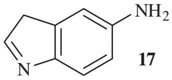
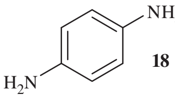
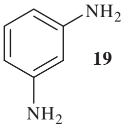
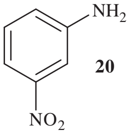
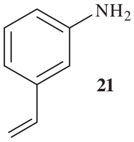
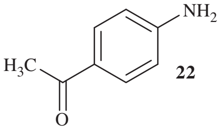
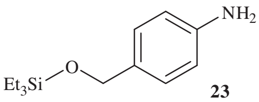
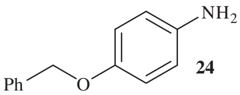
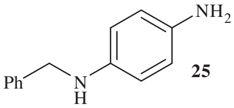
Table 1
Reduction of nitroarenes using milder reducing sources



Entry	Product	Time(h)/Yield[a](%)		
		A	B	C
1	 **1**	1.5/97	3/98	1/82, (23[b])
2	 **2**	1.5/99	1/92	2.5/96
3	 **3**	1.5/96	1.5/90	3/95
4	 **4**	1/93	1/90	1.5/82
5	 **5**	1.5/90	1/85	3/50
6	 **6**	2.5/80	1/72	3.5/76
7	 **7**	1/98		
8	 **8**	2/90		
9	 **9**	2/92		
10	 **10**	2.5/70		
11	 **11**	2.5/93		

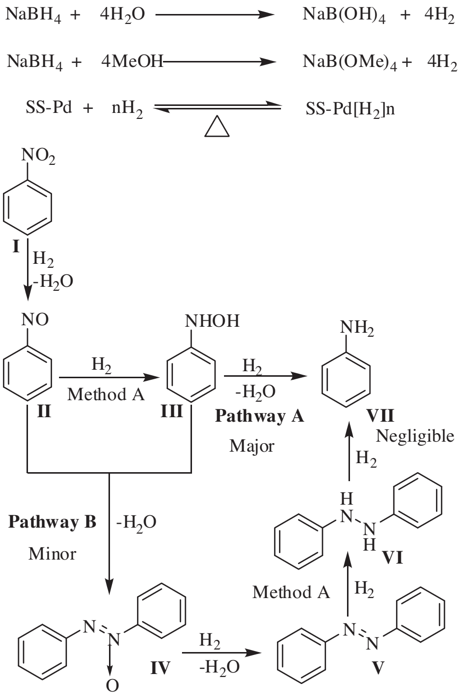
(*continued on next page*)

Table 1 (*continued*)

Entry	Product	Time(h)/Yield[a](%)		
		A	B	C
12	 **12**	0.66/75		
13	 **13**	1/95		
14	 **14**	1/80		
15	 **15**	1.5/97		
16	 **16**	2/99		
17	 **17**	2/94		
18	 **18**	1.4/91		
19	 **19**	3/90		
20	 **20**		2/75	3/80
21	 **21**			0.66/63
22	 **22**			1/75
23	 **23**		1.5/72	
24	 **24**	1.5/86		
25	 **25**	2/90		

[a] Otherwise stated all yields are isolated yields in three methods (A, B and C); Method A:SS-Pd (2 mol % Pd), $NaBH_4$ (3 equiv), MeOH:H_2O (3:7), 50 °C; Method B: SS-Pd (3 mol % Pd), Et_3SiH (4 equiv), THF, RT; Method C: SS-Pd (2 mol% Pd), $NH_2NH_2.H_2O$ (3 equiv), MeOH:H_2O (3:7), 80 °C;

[b] GC–MS yield, H_2 balloon, 2 mol% Pd, time 2 h.



Scheme 1. Possible mechanistic pathways of nitroarene reduction using SS-Pd and $NaBH_4$

an important feature of nitroarene reduction. Longer reaction time was the limitation of the previous method.[2] However, regioselective product **20** was observed in the presence of Et_3SiH (Method B) and $NH_2NH_2.H_2O$ (Method C). High chemoselective reduction of 3-nitrostyrene to corresponding amine **21** was observed under SS-Pd and $NH_2NH_2.H_2O$ condition. Chemoselective reduction of 4-nitro acetophenone was observed under SS-Pd and $NH_2NH_2.H_2O$ condition to produce **22** in 75% yield. The reduction of 4-nitrobenzaldehyde was reported to provide 4-toluedine as major byproduct using $PdCl_2$/ Et_3SiH system.[9] Using triethylsilane (Method B) unfortunately led to 4-aminobenzyltriethylsillylether **23** as the product in 72% yield. In the presence of $NaBH_4$ (Method-A) *O*-benzyl and *N*-benzyl functional groups attached to nitroarenes were well tolerated to give the desired products **24** and **25**.

Mechanistically the reduction of nitroarenes may go through the formation of hydroxylamine as well as azobenzene.[10] To understand the mechanistic pathway, two parallel reductionreactions of nitrosobenzene **II** and azobenzene **V** were conducted following the standard method[11] (Method A). Under this condition, nitrosobenzene gave aniline as major product with azobenzene as by-product (Scheme 1), whereas, azobenzene **V** under same conditions gave 1,2-diphenylhydrazine as major product and aniline as minor product. Therefore, the reaction might follow pathway A than pathway B for the nitroarene reduction to the corresponding aniline in Method A (Scheme 1). Similar observations were also found in Method B and Method C.

The recyclability experiment of the catalyst was evaluated on 4-nitrobenzonitrile (Supplementary data information). After completion, the reaction mixture was filtered off through a cotton bed, washed with methanol, dried under reduced pressure, and reused for further reaction. Up to seven runs with no significant loss of catalytic activities were observed.

In conclusion, we have developed solid supported nano and microparticles of Pd(0) (SS-Pd) as heterogeneous catalysts and their successful application for reduction of nitroarenes to corresponding amines. TEM study was performed to analyze the nanoparticles of Pd (0) deposition in the solid matrix. Easy hydrogen transfer capability of SS-Pd has been well documented at low reaction temperature with a larger substrate scope and compatible among different reducing sources. On completion, the air and moisture stable SS-Pd catalyst was easily separated from the reaction media and recycled up to nine times with reproducible results. Overall, SS-Pd was found to be a very efficient and versatile catalyst for the reduction of nitroarenes to anilines in small and large scale processes.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2012.06.132.

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11. Typical experimental procedure (Method A): A mixture of 4-nitrotoluene (150 mg, 1.1 mmol), SS-Pd (492 mg, 2 mol% Pd) and NaBH$_4$ (124.77 mg, 3.3 mmol) were taken in a 25 ml round bottomed flask. 3 ml of methanol:water (3:7) was added to the mixture by a syringe at room temperature under stirring condition. After 10 min the reaction mixture was heated at 50 °C for 1.5 h. The progress of the reaction was monitored by TLC. On completion, the reaction mixture was extracted with ethyl acetate (3 × 3 ml) and dried over anhydrous Na$_2$SO$_4$. Evaporation of the combined organic layer followed by silica gel (60–120 mesh) column chromatography (Hexane:EtOAc = 80:20) over silica gel afforded 4-methylaniline 1 as a white solid (113.7 mg, 97%); mp 40-41 °C; ^{1}H NMR (300 MHz, CDCl3) δ 2.25 (s, 3H), 3.54 (br, N–H), 6.62 (d, J = 8.1 Hz, 2H), 6.98 (d, J = 8.1 Hz, 2H); ^{13}C NMR (75 MHz, CDCl3) δ 20.34, 115.13 (2C), 127.66, 129.63 (2C), 143.69.