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Zn(0)-Catalysed mild and selective hydrogenation of nitroarenes

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The hydrogenation of nitroarenes is one of the most important strategies for preparation of anilines. However, it is still a great challenge to develop mild and efficient synthetic routes toward aniline synthesis, particularly those employing both non-precious metal catalysts and low-pressure H₂. Herein, we report a highly efficient protocol for the selective hydrogenation of nitroarenes in neutral H₂O using H₂ (1atm) over a heterogeneous Zn (0) catalyst under mild conditions. The nitro groups of an array of nitroarenes can be converted to -NH₂ in up to 99% conversions with selectivity of >99%, even when functionalized with easily reducible substituents, or in presence of aromatic ketones or styrene. This study might open an avenue for the selective hydrogenation of nitroarenes over a zinc catalyst using H₂ of 1atm.

1. Introduction

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Anilines are important building blocks for the production of agrochemicals, pigments, dyes, pharmaceuticals and polymers. Hitherto, extensive efforts have been made to develop various catalytic systems for efficient converting nitroarenes into anilines, nevertheless, most of them rely on noble metal catalysts mediated hydrogenation using pressurized molecular hydrogen¹ (Entry 1-3, Table 1) or stoichiometric amounts of sodium hydrosulfite,^{2a} iron,^{2b} tin,^{2c} or zinc/ammonia^{2d} as reductants to get a preferential selectivity to the nitro group, leading to increased expense on preparation or large wasted stream of metal salts/muds which might cause seriously environmental concerns. Some others focused on developing nonnoble metal catalysts for efficient and selective transformation of nitroarenes into anilines, however, the majority of the procedures are found with low selectivity but requiring pressurized H₂ or/and elevated temperatures (Entry 4-6, Table 1).³ Currently, the environmentally benign commercial production of anilines functionalized with other easily reducible groups, such as unsaturated bonds, or carbonyl groups, remains as an important challenge, particularly those over non-precious metal catalysts and using low pressurized H₂, and processing under mild conditions, are highly desirable. As has been illustrated in our previous work that compared with homogeneous catalysts, catalytic hydrogenation over easier recyclable heterogeneous ones are preferable, particularly for industrial purposes. The efficient and chemoselective hydrogenation ofnitroarenes using normal atmospheric hydrogen (1atm) over heterogeneous non-precious metal catalysts under mild conditions has been less studied.

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 Table 1. Some recently developed metal catalyst promoted chemoselective hydrogenations

		Metal Catalyst			
	R		H ₂	R	
Entry	Metal	Pressure of H ₂ (bar)	Sel.(%)	T (°C)	Ref.
1	Pt	6-40	95–100	60	[1a,1c]
2	Pd	6-20	21->99	40–210	[1b,1f]
3	Ru	6-40	86–100	100–275	[1d,1e]
4	Ni	3-20	85–96	40–60	[3d]
5	Со	3-50	5–96	110–150	[3a,3b]
6	Fe	50	20–80	120	[3c]

Our laboratory recently reported a complementary mild approaches for the hydrogenation of nitroarenes, ketones, aldehydes, and nitriles with heterogeneous palladium-based nanoparticles using normal atmospheric H_2 ,⁴ we wonder if similar reaction conditions can be extended to the selectively reductive hydrogenation of nitroarenes using non-precious metal catalysts. Herein, we detail how our envisagement was translated in experimental reality, leading to the development of a novel nonprecious metal Zn(0)-catalyzed chemoselective hydrogenation of nitroarenes in base- or acid- free H_2O under mild conditions using low-pressure H_2 at 1atm, representing an alternation to currently developed ones for environmentally benign preparation of anilines.

2. Results and discussion

In order to find suitable catalyst(s) and conditions, nitrobenzene was selected as the model substrate. Four different metal salts and ligands were tested to prepare a list of metal-ligands (**Table 2**). It was found through experiments that

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the catalysts prepared by the four metal salts and the corresponding three ligands L_1 , L_2 , and L_3 did not play a role in during the hydrogenation reduction of nitrobenzene. With which, reactions were initially carried out at 25°C, and Zn-L₄ was found the best as the yield of the desired product aniline was 35% and the selectivity was >99% (Entry 2, **Table 2**). Elevated temperatures and pHs were as well investigated, results indicated the best yield was 99% when proceeded at 35°C (Entry 5, **Table 2**), a higher temperature at 40°C or a lower one at 30°C would lead to poorer yields (Entries 4,6, **Table 2**).

Table 2. Optimization studies for hydrogenation of nitrobenzene.^a



Entry	M-L	T (°C)	Yield/Selectivity (%/%)
1	Cu-L ₄	25	12/99
2	Zn-L ₄	25	35/99
3	Ni-L ₄	25	5/99
4	Zn-L ₄	30	60/99
5	Zn-L ₄	35	99/>99
6	Zn-L ₄	40	73/99
7	Zn-L ₄	45	30/99

^aConditions: Reactions were carried out in 10mL H_2O stirred with a magnetic bar; pH, 7.0; H_2 was filled in a balloon; Metal-ligands, 2.5mg; Nitrobenzene, 20mM; Reaction time, 20h; Yields and selectivities were determined by HPLC analysis.

2.1 Characterization of Zn-NPs (Zn-L₄)

To better understand the zinc-bound 1,8diaminonaphthalene ($Zn-L_4$), transmission electron microscopy images indicated that they were not well dispersed nanoparticles (**Fig.1**), with an average distribution of particle diameter of 4.18 nm, which can thus be classified as nanoparticles (NPs).

The Zn-NPs were further characterized by X-ray diffraction (XRD), elemental analysis (EA), inductively coupled plasmaoptical emission spectrometer, X-ray photoelectron spectroscopy (XPS), ¹H NMR, ¹³C NMR and HH-COSY. The XRD pattern of Zn-NPs shows that the peaks at $31.7^{\circ}_{V,24}$ $A^{\circ}_{Ucl} 36_{n} A^{\circ}_{e}$ 47.5°, 56.5°, 62.7°, 67.8° exhibit diffiatibition (MRF) corresponding to the crystal planes at (100), (002), (101), (102), (110), (103), and (112), respectively, indicating the existence of the metal Zn in Zn-NPs (**Fig. 2**).



Fig. 1 TEM image of the Zn-L₄

To further characterize the chemical state of catalyst, XPS analyses were performed (**Fig.3**), which proved the presence of zinc, hydrogen and carbon in Zn-NPs. The peak of Zn $2p_{1/2}$ and $2p_{3/2}$ at 1046.08 and 1022.98eV correlated well with the peak of Zn (0), Nitrogen affected Zn (0), causing its binding energy to change, thereby confirming the presence of Zn (0).^{5, 6}



Fig. 2 XRD pattern of heterogeneous catalyst Zn-NPs

EA showed that an average of one zinc atom were found for each ligand 1,8-diaminonaphthalene (**Table S1**). NMR spectroscopic studies on 1,8-diaminonaphthalene functionalized Zn-NPs dispersed in alkaline D_2O to demonstrate that 1,8-diaminonaphthalene was successfully bound to the particle surface.

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In order to demonstrate that these signals originate from Znbound 1,8-diaminonaphthalene while not from desorbed ligand molecules, a certain amount of 1,8-diaminonaphthalene was mixed at an unequal equivalent (Figure S2). the ¹H signals of -NH₂ at 4.46ppm in free 1,8-diaminonaphthalene was chemically shifted to 4.52 after bound to Zn and the fact that $^{\rm 13}{\rm C}$ signals of Zn-bound 1,8- diaminonaphthalene were chemically shifted confirmed the chemically binding state of Zn-bound 1,8diaminonaphthalene as well (Figure S4).



Fig. 4 The proposed catalytic mechanism for Zn(0)-catalysed selective hydrogenation of nitroarenes.

Several control reactions (Figure S7) were performed to explore the possible mechanism of the Zn(0)-catalyzed hydrogenation. Based on reaction facts and some references,⁴ the catalytic cycle of our proposed mechanism is outlined in Fig. 4. The catalyst B was incubated with H₂, and activated to form C, which later reacted with nitroarene to form A, and simultaneously, H₂O was released, accompanied with which

 Table 3. Catalytic hydrogenation of nitroarenes over Zn-NPs
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Ent	Nitroare	Time	.	Conv.	Dehal.	Sel.ª
ry	ne	(h)	Product	(%)	(%)	(%)
1	NO ₂	15	NH ₂	>99		>99
2	NO2	15	NH ₂	99		>99
3	H ₂ N NO ₂	15	H ₂ N NH ₂	99		>99
4	H ₃ C NO ₂	20	H ₃ C NH ₂	98		>99
5		20	CI NH2	99	13	>99
6	Br NO2	25	Br NH2	99	39	>99
7	H ₃ CO NO	20	H ₃ CO NH	98		>99
8	F NO2	32	F NH2	98	0	>99
9	NO ₂ Br	35	Br NH2	98	55	>99
10		32		99	19	>99
11	H ₃ C	20	H ₃ C	99		>99
12	HOOC	25	HOOC	99		>99
13	O2N NO2	20	H ₂ N	99		>99
14	NO ₂	15	NH2 NH2	99		>99
15	NO ₂	28	NH ₂	98		>99

Conditions: Reactions were carried out in H2O of 10 mL as the solvent stirred with a magnetic bar; pH, 7.0; H2 was filled in a balloon; Metalligands, 2.5mg; Nitrobenzene, 20mM; Reaction time, 20h; Temperature, 35oC; Conversions were determined by HPLC analysis; a Selectivity was calculated by comparing the proposed anilines (including the halogenated and dehalogenated) with nitroarenes.

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 $\label{eq:table_table_table} \ensuremath{\textbf{Table}}\xspace 4. Selective hydrogenation of nitroarene in the presence of carbonyl compounds.$



Entr Y	Nitroarene	Aryl ketone	Product	Conv. (%)	Sel. (%)
1		CH ₃		99	>99
2	NO ₂	H ₃ C	NH ₂	99	>99
3		CI CH3		99	>99
4		CH ₃		99	>99
5	C ₂ H ₅ NO ₂	H ₉ C CH ₃	C2H5 NH2	99	>99
6		CI CH3		99	>99
7		CH3		98	>99
8	H ₃ C NO ₂	H ₃ C CH ₃	H _a C NH ₂	98	>99
9		CI CH3		98	>99
10		CH ₃		99	>99
11		H ₃ C CH ₃	$R_2 = CI (86\%) + H (13\%)$	99	>99
12		CI CH3		99	>99
13		CH ₃		99	>99
14	Br NO2	H ₃ C	$R_2 = Br (60\%) + H (39\%)$	99	>99
15		CI CH3		99	>99

Conditions are identical with which described in the footnote of Table 3.

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were nitrosoarene (**D**) and **B**, which was activated again into **C** after absorbing H₂, followed is the combination of the method of the second se

With the optimized conditions described in Table 2, the scope of substrates was investigated (Table 3). All reactions were proceeded well with excellent conversions of up to >99% (Entry 1, Table3). Several nitroarenes bearing halogen substituents were tested as well, results indicated that when the substituent is fluorine, dehalogenation reaction did not occur (Entry 8, Table 3), nevertheless, when it was chlorine or bromine, dehalogenation took place, leading to reduced product yields though conversions kept excellent. It seems that progress degree of dehalogenation depended on its position on the aryl ring, an example is when the bromine is at the para position, about 39% of products are the dehalogenated ones (Entry 6, Table 3), however when it is at the meta position, about 55% of substrates would undergo dehalogenation process (Entry 9, Table 3). It seems that when the halogen atom is closer to the carbon where nitro group connects, more products are the dehalogenated ones (Entries 6, 9, Table 3), and it is the same rule to chloride substituent (Entries 5, 10, Table 3). Interestingly, when nitroarenes functionalized with easily reducible groups, for example, carbonyl- or unsaturated C=C groups, the hydrogenation reaction occurs specifically toward the nitro group, resulting in excellent selectivity of substrates or products (Entries 11, 15, Table 3), this promotes us to further explore whether the chemoselective reactions occur and how the selectivity will be when nitroarenes are mixed with reducible aryl ketones or aryl olefins.

 Table 5. Selective hydrogenation of nitroarene mixed with aryl ethylene.



Conditions were described in the footnote of Table 3.

An array of mixtures ($\frac{1}{2}$ nitroarene + $\frac{1}{2}$ aryl ketone) were then subjected, and all reactions could afford satisfied conversions and excellent selectivity (**Table 4**). Results showed there were basically

no aryl alcohols deriving from the hydrogenation of aryl ketones were formed, proving the excellent performance of Zn-NPs in catalytic hydrogenation of nitroarenes even in the presence of easily reducible carbonyl compounds. Later, several different mixtures consisting of equal equivalents of nitroarene and aryl ethylene were evaluated as well (**Table 5**). Similarly, Zn-NPs showed excellent selectivity in hydrogenating nitroanilines and specific activity toward nitro groups, the result agreed well with which the reaction employing 4-nitrosyene, whose unsaturated C=C bonds remained unchanged (Entry 15, **Table 3**).

3. Conclusions

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In conclusion, we have, for the first time, under normal atmospheric pressure and over a heterogeneous non-precious Zn-based catalyst, achieved the highly chemoselective hydrogenation of nitroarenes using H_2 in H_2O under mild conditions. The Zn-NPs are proved to possess excellent selectivity and stability in high-efficiency and selective hydrogenation of nitroarenes, making the hydrogenation extremely easy and environmentally benign. The corresponding product anilines functionalized with easily reducible unsaturated C=C bonds or carbonyl groups were provided in excellent yields of up to > 99% with selectivity of >99%. Besides, when mixed with carbonyl compounds or olefins, the selectivity can still make us satisfied though dehalogenation occur when substrates bearing halogen (F is excluded) atoms on aromatic ring. The Zn-NPs and its developed methodologies are applicable for a wide range of nitroarenes. In addition, due to chemically binding state of ligands to the surface of Zn atoms, the stable heterogeneous Zn-NPs could be easily recycled and reused for many times without losing its major activity and selectivity.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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