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A magnetically separable gold catalyst for chemoselective reduction of nitro compounds†

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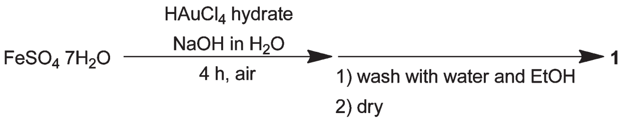
Magnetically separable gold-nanoparticle catalyst was prepared, and it showed excellent activity for chemoselective reduction of nitroarenes with hydrosilanes.

Recently, gold-nanoparticle (Au NP) catalysts have attracted the attention of many researchers due to their unique catalytic activities in a variety of reactions such as hydrogenation, epoxidation, oxidation of carbon monoxide, alcohols, amines or silanes, and formation of C–C or C–N bonds.[1] Frequently Au NPs are immobilized on metal oxide supports (*e.g.*, CeO_2, TiO_2, Fe_3O_4, Fe_2O_3, Al_2O_3, SiO_2) for enhancing activity, preventing agglomeration, and facilitating recovery. For easy recovery, magnetic supports have been applied for Au NP catalysts.[2,3] However, the preparation requires elaborate multistep processes (*e.g.*, preparation of iron oxide, surface modification, adsorption, and reduction of Au precursors) in general. Herein we report a reliable one-pot process to prepare a magnetically separable Au NP catalyst (**1**), which is highly active and selective for the reduction of functionalized nitroarenes with hydrosilanes.

The synthesis of catalyst **1** was carried out by treating $HAuCl_4$ in a $FeSO_4$ solution using a modified deposition precipitation method (Scheme 1). When a basified solution of $HAuCl_4$ was added to an aqueous solution containing an excess of $FeSO_4$ with vigorous stirring under air, a suspension containing black solid particles was generated. Transmission electron microscopy (TEM), high resolution TEM (HRTEM), and X-ray diffraction analysis (XRD) of the resulting solids revealed the formation of Au/Fe_3O_4 nanocomposites, in which multiple numbers of Au NPs averaging 10 (±3.6) nm in size are dispersively immobilized on the surface of Fe_3O_4 particles (Fig. 1a and 1b). This can be understood as a galvanic process in which $AuCl_4^-$ ions are reduced to Au(s), while oxidized Fe(III) species are co-precipitated together with Fe(II) ions into Fe_3O_4 crystallites.[4] The isolated powders of catalyst **1** could be re-dispersed in a polar solvent, such as ethanol, by shaking or sonication and they also could be easily attracted within several minutes simply by placing a small magnet on the side of the vessel (Fig. 1c). The magnetization measurement by using a superconducting quantum interference device (SQUID) showed that the powders of catalyst **1** have a saturation



Scheme 1 Preparation procedure of **1**.

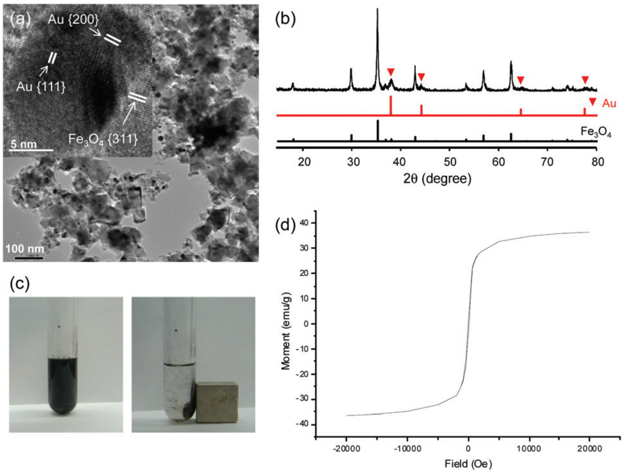


Fig. 1 (a) TEM and HRTEM (inset) images of catalyst **1**. (b) XRD pattern of catalyst **1**. The lines below show the position of the reflections corresponding to the fcc Au phase (JCPDS Card No. 04-0784) and the tetragonal Fe_3O_4 phase (JCPDS Card No. 88-0315). (c) Pictures of the EtOH suspension of catalyst **1** before (left) and 10 min after placing a magnet. (d) A field-dependent magnetization curve of catalyst **1** at 298 K, showing its weak ferromagnetic behavior.

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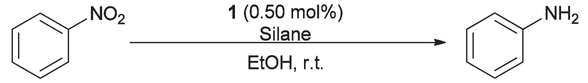
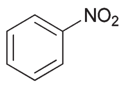
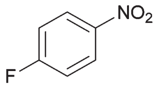
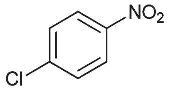
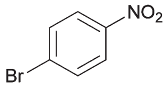
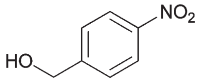
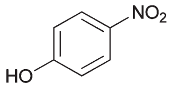
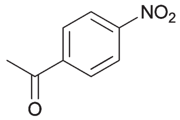
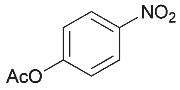
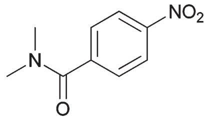
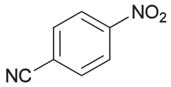
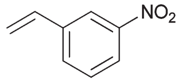
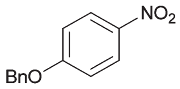
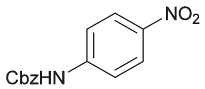
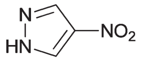
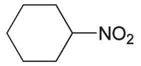
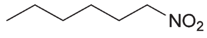
Table 1 Reduction of nitrobenzene with hydrosilanes[a]



Entry	Silane	Silane (equiv.)	Time (min)	Conv.[b] (%)	Yield[b] (%)
1	$MePh_2SiH$	4.5	5	>99	96
2	Me_2PhSiH	4.5	5	96	96
3	Et_3SiH	4.5	30	94	89
4	Ph_2SiH_2	2.25	60	82	66
5	$PhSiH_3$	1.5	60	82	65
6	$(Me_2SiH)_2O$	2.25	30	97	96
7	PMHS	4.7	360	38	30

[a] Nitrobenzene (0.30 mmol), **1** (0.50 mol%), EtOH (3.0 mL) and hydrosilane (4.5 equiv. based on Si–H) were employed at room temperature under Ar. [b] Determined by GC using *p*-cymene as an internal standard.

Table 2 Reduction of nitro compounds by **1**[a]

Entry	Substrate	TMDS (equiv. of Si–H)	Time	Yield[b] (%)
1		4.5	10 min	>99[c]
2		4.5	30 min	>99[c]
3		5.5	30 min	94
4[d]		5.5	1 h	95[c]
5		4.5	24 h	91
6		4.5	1.5 h	>99
7		4.5	15 min	>99
8		4.5	30 min	>99
9		5.5	45 min	>99
10		4.5	1 h	>99
11		5.5	1.5 h	90
12[e]		5.5	4 h	>99
13		5.5	1 h	93
14		6.5	24 h	>99
15		10	2 h	84[c]
16		10	2 h	85[c]

[a] Nitro compound (0.30 mmol), **1** (1.0 mol%), EtOH (3.0 mL) and TMDS were employed at room temperature under Ar. [b] Isolation yield. [c] Determined by GC using *p*-cymene as an internal standard. [d] Substrate (0.050 mmol), **1** (40 mol%) and EtOH (2.0 mL) were used. [e] EtOH (2.0 mL) and ethyl acetate (1.0 mL) were used as solvents.

magnetization of 37 emu g^{-1} and weak ferromagnetic behavior at 298 K (Fig. 1d).

Functionalized anilines are valuable building blocks for the synthesis of dyes, agrochemicals, pharmaceuticals, and polymers.[5] Generally, aniline derivatives are prepared by catalytic hydrogenation of nitroarenes. Although there are various catalyst systems for the hydrogenation,[6] developing a catalyst system that can selectively reduce the nitro group of nitroarenes in the presence of other reducible groups is a challenging research goal.[7,8] A noticeable example is the catalyst system of TiO_2-supported Au NPs using H_2 as the reductant. Highly chemoselective reduction of the nitro group in the presence of olefinic, cyano, or carbonyl groups was possible, but relatively high temperature and pressure were needed.[8a] A modified system using very small Au NPs on TiO_2 and CO/H_2O also needed high pressure for the reduction of functionalized nitroarenes.[8c] We tested the activity of **1** in the reduction of nitrobenzene with commercially available hydrosilanes (Table 1).[6,9–11] The reduction was completed within 5 min with 0.5 mol% of Au and $MePh_2SiH$ at room temperature (entry 1). The reaction with Me_2PhSiH was similarly efficient, while those with Et_3SiH, Ph_2SiH_2, and $PhSiH_3$ were slow (entries 2–5). Notably, cheap tetramethyldisiloxane (TMDS) was comparable to Me_2PhSiH;[12,13] aniline was obtained in 96% yield after 30 min (entry 6). The reduction with polymethylhydrosiloxane (PMHS) was the slowest among those tested (entry 7).

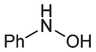
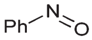
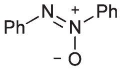
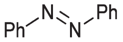
In order to investigate the scope of the reaction, various functionalized nitroarenes were subjected to the reduction with TMDS in the presence of **1** (Table 2). For the reduction of 4-fluoro- and 4-chloronitrobenzene 1 mol% of Au was enough to complete the reaction in 30 min (entries 2 and 3), while that of 4-bromonitrobenzene required 40 mol% of Au to give 4-bromoaniline in 95% yield with a 1 h reaction time (entry 4). However, 4-iodonitrobenzene was an inert substrate with our catalyst system. The hydroxyl groups in 4-nitrophenol and (4-nitrophenyl)methanol were compatible with the reaction conditions (entries 5 and 6).[14] Notably, the reducible moieties

Table 3 Recycling test for **1** in the reduction of nitrobenzene[a]

Run	1	2	3	4[c]	5[c]	6[c]
Yield (%)[b]	>99	91	84	98	90	81

[a] Nitrobenzene (0.30 mmol), **1** (0.50 mol%), EtOH (3.0 mL) and TMDS (0.83 mmol) were employed at room temperature under Ar for 30 min. [b] Determined by GC using *p*-cymene as an internal standard. [c] 0.98 mmol of TMDS was used.

Table 4 Hydrogenation of probable intermediates[a]

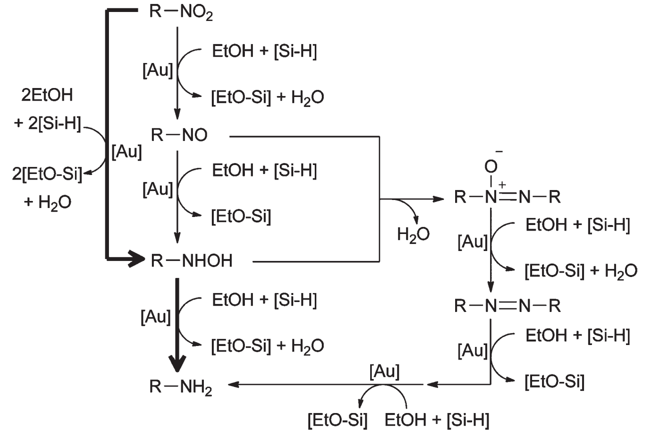
Entry	Substrate	Time	Yield of aniline[b] (%)
1		30 min	98
2		30 min	73
3[c]		2 h	20
4[c]		2 h	5

[a] Substrate (0.30 mmol), **1** (0.50 mol%), EtOH (3.0 mL) and TMDS (0.83 mmol) were employed at room temperature under Ar. [b] Determined by GC using *p*-cymene as an internal standard. [c] 0.15 mmol of substrate was used.

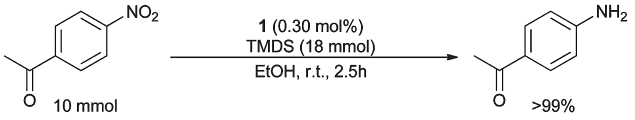
such as ketone, ester, amide, cyanide and alkene remained intact during the reduction of the nitro group (entries 7–11). The benzyloxy and carbobenzyloxy groups, which are labile to the hydrogenolysis reaction, survived during the reduction (entries 12 and 13). 4-Nitro-1*H*-pyrazole was successfully transformed to the corresponding amine, which is an important precursor for biologically active compounds (entry 14).[15] Our catalyst system was also effective for the reduction of nitroalkanes to aliphatic amines, although the reduction required a larger amount of TMDS than those of nitroarenes (entries 15 and 16).

The reusability of the catalyst was tested (Table 3). The activity of the recovered catalyst was somewhat lower than that of the original. However, increasing the amount of TMDS compensated the decrease; aniline was obtained in 90% yield in the 5th use by employing 0.98 mmol of TMDS for 0.30 mmol of nitrobenzene. TEM images of the recovered catalyst showed a slight increase of Au NPs on the Fe_3O_4 support after six reaction cycles (see ESI†). Inductively coupled plasma mass spectrometry (ICP-MS) analyses of the reaction solutions magnetically separated from the catalyst after the reaction also indicated no loss of Au NP or negligible Au leaching (<0.10 ppm) from the catalyst. On the other hand, continuously stirring the supernatant reaction solution of 60% conversion after removing the catalyst did not give any further conversion at all, confirming that heterogeneous catalysis by catalyst **1** is responsible for the observed performance.

To get clues for the mechanism of the reduction we carried out the reduction of nitrosobenzene, *N*-phenylhydroxylamine, azoxybenzene and azobenzene under the conditions for the reduction of nitrobenzene, which are suggested as the intermediates for the transformation of nitroarenes to the corresponding anilines (Table 4).[8d,16] Aniline was obtained in 98% yield in 30 min from *N*-phenylhydroxylamine, while in 73% yield from nitrosobenzene. However, the yield of aniline was much lower even after 2 h in the reduction of azoxybenzene and azobenzene. Based on these results, a plausible pathway for the reduction of nitro compounds with our catalyst system is outlined in Scheme 2. A hydroxylamine intermediate appears to be formed directly from nitro substrates without the accumulation of the nitroso intermediate,[16] while the side reaction between nitroso and hydroxylamine intermediates is not significant. The actual reducing species would be Au–H formed by the activation of the Si–H bond of hydrosilanes on the surface of Au nanoparticles.[8c,16,17] In fact, the reduction did not occur under a H_2 atmosphere (1 atm) instead of using hydrosilanes.



Scheme 2 Plausible reaction pathways for the reduction of nitro compounds with TMDS and the Au NP catalyst. The major pathway is highlighted with thick arrows.



Scheme 3 Reduction of 1-(4-nitrophenyl)ethanone in 10 mmol scale.

A large scale reaction was performed with 10 mmol of 1-(4-nitrophenyl)ethanone (Scheme 3). 1-(4-Aminophenyl)ethanone was obtained selectively in quantitative yield after 2.5 h using 0.30 mol% of Au (TON = 330, TOF = 130 h^{-1}).[18] Compared to the catalyst systems reported for the reduction of nitroarenes (see ESI†), ours showed the highest activity among those using hydrosilanes as the reductants.

Conclusions

We have developed a simple procedure for the preparation of a magnetically separable gold nanoparticle catalyst and an efficient catalyst system for the chemoselective reduction of nitroarenes into functionalized anilines. The combination of hydrosilanes and a heterogeneous gold catalyst is the first attempt applied for the reduction reaction, which is easily accessible to general chemists. Expanding utility of the gold catalyst and preparing other metal catalysts are now under progress.

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6 See ESI† for a tabular summary of various catalyst systems for the reduction of nitroarenes.

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12 J. Deng, *Synlett*, 2011, 2102–2103.

13 (*a*) Solvent screening was carried out using TMDS as the reducing agent; EtOH was chosen as the most proper solvent over MeOH due to the better reusability: see ESI†; (*b*) A significantly lower activity and selectivity were observed in the reduction when we used an Au NP catalyst prepared with commercial iron oxide by a conventional method: see ESI.†

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18 The conditions for the large scale reaction were not generally applicable for the reactions of other substrates under the conditions in Table 2. For instance, 4-nitrobenzonitrile was converted only in 62% yield even after 3 h when we employed 0.3 mol% of **1** and 1.8 equiv. of TMDS.