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Highly chemoselective reduction of imines using a AuNPore/$PhMe_2SiH$/water system and its application to reductive amination

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ABSTRACT

An unusually strong affinity of unsupported nanoporous gold (AuNPore) towards aldimines and ketimines has been demonstrated. By using $PhMe_2SiH$ and water as a hydrogen source and AuNPore as a catalyst, ketimines and aldimines can be reduced to the corresponding amines in high chemical yields under mild conditions. This system was also applied to the reductive amination of aldehydes and ketones.

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1. Introduction

Amines are considered to be important intermediates for synthesis of agrochemicals and pharmaceuticals.[1] One of the most common methods used for their preparation is the one-pot reductive amination of aldehydes and ketones with amines or ammonia in the presence of a reducing agent and hydrogenation catalysts, which proceeds through *N*,*O*-acetal and/or imine intermediates.[2] Various reducing reagents, especially inorganic hydrides, have been used for the reduction of in situ formed imines. However, some of them possess drawbacks such as toxicity, laborious work up procedures, and their hygroscopic nature.[3] In this context, many papers have appeared recently describing silanes in combination with metal catalysts as reducing source.[2e,4] Their use for reduction is advantageous, because these reagents and catalysts are easily available and they can be handled in open air. However, the one-pot reductive amination makes the situation more complicated, since it is accompanied often with the formation of side products. The isolation of imines followed by their reduction is other way to prepare amines, where the products are easy to handle. Hitherto, a number of chemical methods have been developed for the reduction of imines and majority of them use metal catalyst with hydrogen gas.[5] Nevertheless, the use of hydrogen gas is not chemoselective if the substrates contain more than one double bond.

Recently, remarkable catalytic activity of unsupported nanoporous gold (AuNPore) has been explored in diverse reactions.[6,7] As compared to gold nanoparticles (AuNPs), AuNPore doesn't need any oxide support.[8] Hence, the catalytic activity of AuNPore is only based on metallic gold, which can further help understanding the mechanism of heterogeneous gold catalyzed reactions. Accordingly, we have investigated more selective and efficient reducing method of aldimines. On the way of this research, we have discovered that imines can be reduced with very high selectivity in high yields in the coexistence of aldehydes, by the use of AuNPore catalyst together with $PhMe_2SiH$ (Scheme 1, previous work).[9] This unprecedented selectivity warranted further investigation in the reduction of ketimines. In this paper, we report a highly selective reduction of ketimines in the coexistence of the corresponding ketones and related aldehydes, together with full scope for reductive amination of aldehydes and ketones (Scheme 1, this work).

2. Results and discussion

The reaction of ketimine **1a** (R^1=Ph, R^2=CH_3, R=Ph) with 2 mol % AuNPore, 1.2 equiv of $PhMe_2SiH$, and 1.2 equiv of H_2O at 50 °C for 5 h gave the corresponding reduced amine **2a** in 94% yield (Table 1). The same conditions were applied to other ketimines, and

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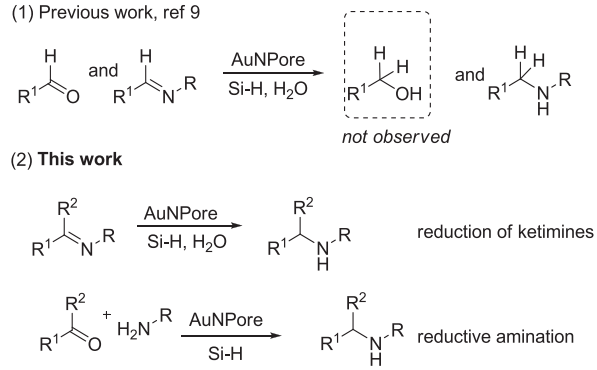
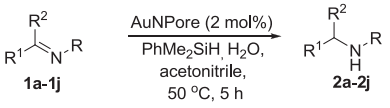
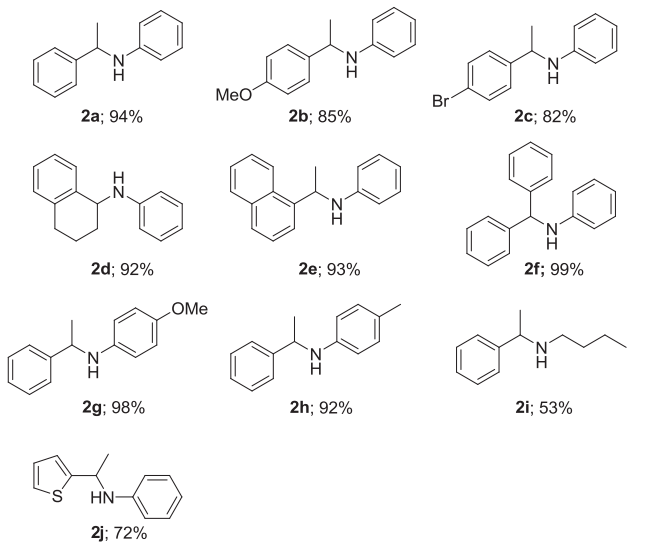


Scheme 1. Reduction of ketimines and reductive amination using AuNPore/Si–H system.

Table 1
Reduction of ketimines using AuNPore/silane[a]



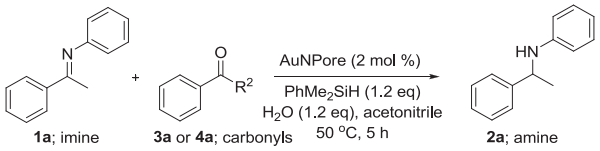


[a] Reaction conditions: a mixture of **1** (0.5 mmol), $PhMe_2SiH$ (0.6 mmol), H_2O (0.6 mmol) and acetonitrile (2 mL) was stirred in the presence of AuNPore (2 mol%) at 50 °C for 5 h; yields shown are isolated yields.

interestingly the electronic characteristics of *para*-substituent of aromatic ring of R^1 did not exert significant influence on the yield of the product (cf. electron rich imine **1b** vs electron deficient imine **1c**). Changing R^1 and R^2 to an alicyclic group also gave an excellent yield of the desired product **2d**. Additionally, sterically bulky imines **1e** and **1f** could be reduced without problem, giving the corresponding amines **2e** and **2f**, respectively, in excellent yields. Substitutions on phenyl group at R also gave the desired products **2g** and **2h** in excellent yields. However an aliphatic substituent at R resulted in a lower yield of the expected product **2i**. Interestingly, heteroaromatic substitution at R^1 could also furnish the desired product **2j** in 72% yield.

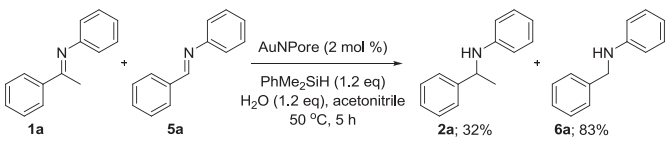
Since an exclusive chemoselectivity for reduction of aldimines in the co-existence of the corresponding aldehydes was obtained previously,[9] we were interested in chemoselectivity of a ketimine in the presence of the corresponding ketone or related aldehyde. The ketimine **1a** was reduced exclusively in the coexistence of the corresponding ketone **3a** (entry 1, Table 2). The reduction of a 1:1 mixture of **1a** and **4a** (benzaldehyde) gave 98% of **2a** and here again no reduction of **4a** was observed (entry 2, Table 2). These results suggest that the chemoselectivity of ketimines toward ketones and aldehydes is very high, as observed in the case of aldimines.[9] When a 1:1 mixture of the ketimine **1a** and aldimine **5a** (0.5 mmol each) was reduced, the aldimine was reduced with high selectivity in 83% yield (0.41 mmol of **6a**) while the ketimine was reduced in significantly lower yield (32%) (0.16 mmol of **2a**) (Scheme 2). Moreover, even a separate reaction of benzaldehyde or acetophenone under the standard conditions failed to provide the desired reduction product. This reveals that these substrates are inert towards AuNPore/silane/water system (Scheme 3) under the conditions noted.

Table 2
Chemoselective reduction of ketimine in the co-presence of carbonyls using AuNPore/silane[a]

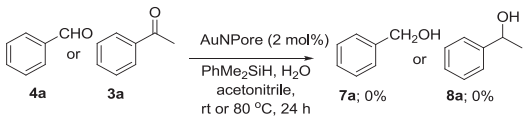


Entry	R^2	Yield of amine **2a** (%)[b]	Reduced alcohol of **3a** or **4a**
1	**3a**; CH_3 (acetophenone)	92	ND[c]
2	**4a**; H (benzaldehyde)	98	ND[c]

[a] Reaction conditions: a mixture of **1a** (0.5 mmol), **3a** or **4a** (0.5 mmol), $PhMe_2SiH$ (0.6 mmol), H_2O (0.6 mmol), and acetonitrile (2.0 mL) was stirred in the presence of AuNPore (2 mol %) at 50 °C for 5 h.
[b] Isolated yield.
[c] ND; not detected. The reduced alcohols were not obtained, and the starting carbonyls were recovered.



Scheme 2. Chemoselectivity in the reduction of ketimine versus aldimine using AuNPore/silane.



Scheme 3. No reduction of carbonyls using AuNPore/silane under the standard conditions.

The above selectivity studies led us to perform direct reductive amination of aldehydes using anilines and the results are summarized in Table 3. The reductive amination of benzaldehyde **4a** (0.5 mmol) was carried out using aniline **9a** (0.5 mmol) and 1.2 equiv $PhMe_2SiH$ in the presence of AuNPore (5 mol %) at 80 °C, and the desired amine **6a** could be isolated in 69% yield (entry 1). It should be noted that water was produced in situ at the time when the aldimines was formed, and therefore it was not necessary to add water at the beginning of the reaction. This protocol was applied to other substrates. In all the cases, moderate to good yields of the desired products (cf. **6a**–**j**) were obtained. Aliphatic aldehydes were also examined using this protocol and resulted in moderate yields of the desired products (cf. **6f**–**i**) being formed. Additionally, the heterocyclic aldehyde **4f** could undergo reductive amination in moderated yield (cf. **6j**). It should be mentioned that in all cases the reduction of aldehydes to alcohols was not observed.

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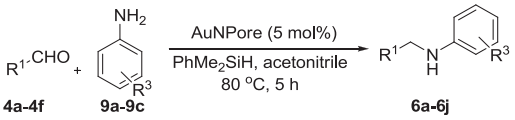
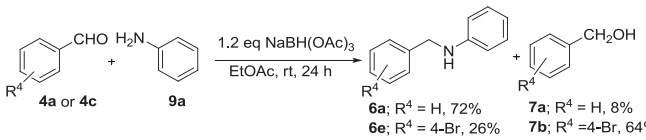
Table 3
Reductive amination of aldehydes using AuNPore[a]



Entry	Substrate **4**	Substrate **9**	Product **6**	Yield of **6** (%)[b]
1	**4a**; R^1=Ph	**9a**; R^3=H	**6a**	69
2	**4a**; R^1=Ph	**9b**; R^3=4-OMe	**6b**	85
3	**4a**; R^1=Ph	**9c**; R^3=4-Me	**6c**	79
4	**4b**; R^1=4-ClC_6H_4	**9a**; R^3=H	**6d**	65
5	**4c**; R^1=4-BrC_6H_4	**9a**; R^3=H	**6e**	88
6	**4d**; R^1=$(CH_2)_2$Ph	**9a**; R^3=H	**6f**	79
7	**4d**; R^1=$(CH_2)_2$Ph	**9c**; R^3=4-Me	**6g**	63
8	**4e**; R^1=*n*-Pr	**9a**; R^3=H	**6h**	69
9	**4e**; R^1=*n*-Pr	**9b**; R^3=4-OMe	**6i**	65
10	**4f**; R^1=furyl-2-	**9a**; R^3=H	**6j**	64

[a] Reaction conditions: a mixture of **4** (0.5 mmol), **9** (0.5 mmol), $PhMe_2SiH$ (0.6 mmol), and acetonitrile (2.0 mL) was stirred in the presence of AuNPore (5 mol %) at 80 °C for 5 h.
[b] Isolated yield.

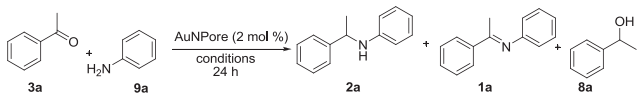
Even though the previously reported reagents[10] show high selectivity for reductive amination over reduction of aldehydes, the possibility of competitive reduction of aldehydes cannot be overlooked. For example, the reductive amination of benzaldehyde **4a** with aniline **9a** using $NaBH(OAc)_3$ gave **6a** in 72% yield, together with **7a** in 8% yield (Scheme 4). However, the reductive amination of 4-bromobenzaldehyde **4c** with **9a** under the reported conditions resulted in 26% yield of the desired product **6e** along with 4-bromobenzyl alcohol **7b** in 64% yield (Scheme 4). This suggests that the reductive amination of an aromatic aldehyde having an electron withdrawing group at the *para*-position does not proceed very well under the reported conditions.[10] However, as shown in entry 5, Table 3, the reductive amination through our new procedure using AuNPore catalyst proceeded very well without forming the alcohol side product.



Scheme 4. Reductive amination of aldehydes with aniline using $NaBH(OAc)_3$. Partial reduction of aldehydes.

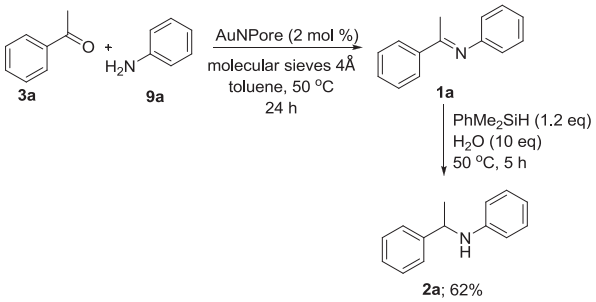
Since the reductive amination of aldehydes proceeded very well, we next examined the reductive amination of ketones. It is well-known that ketimine formation from ketones is much slower than aldimine formation from aldehydes. Accordingly, we thought that there would be difficulty in the reductive amination of ketones. When we tried the reductive amination of **3a** with **9a** under two different conditions, AuNPore/$NaBH_4$[11] and AuNPore/$PhMe_2SiH$, the reductive amination using $NaBH_4$ as the hydrogen source did not proceed well (Table 4, entries 1–4). The use of $PhMe_2SiH$ in the presence of 4 Å molecular sieves resulted in a low yield of desired amine (entry 5). The use of 4 Å molecular sieves in the absence of a water additive came from the idea that the presence of water might retard the formation of ketimine, but this attempt was not successful. The yield was further improved to 42% by using catalytic amount of Brønsted acid (CF_3COOH) (entry 6). A major reason for poor yield in this case is a lower rate of formation of ketimines; perhaps liberation of H_2 from Au surface is much quicker than the reduction of ketimines.[6c,g] To overcome this reactivity problem, it was necessary to perform reaction in two steps; the first step is generation of ketimine and the second step is addition of reductant ($PhMe_2SiH/H_2O$). After stirring for 24 h in the first step followed by 5 h in the second step, an overall 62% yield could be obtained (Scheme 5).

Table 4
Reductive amination of ketone using AuNPore[a]



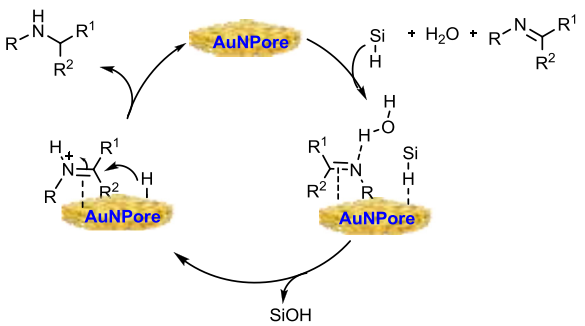
Entry	Conditions	Yield (%)[b]		
		2a	**1a**	**8a**
1	$NaBH_4$ (1 equiv) MeOH, rt	ND[c]	ND	76
2	$NaBH_4$ (1 equiv) MeOH, 50 °C	ND	ND	79
3	$NaBH_4$ (1 equiv) MS 4 Å (0.2 g), toluene, 110 °C	ND	15	ND
4	$NaBH_4$ (1 equiv), MS 4 Å (0.2 g), tetrahydrofuran, 50 °C	ND	ND	ND
5	$PhMe_2SiH$ (1.2 equiv), MS 4 Å (0.2 g), toluene, 110 °C	22	12	0
6	10 mol % CF_3COOH, MS 4 Å (0.2 g), $PhMe_2SiH$ (1.2 equiv), toluene, 110 °C	42	9	0

[a] Reaction conditions: a mixture of **3a** (0.5 mmol), **9a** (0.5 mmol), and AuNPore (2 mol %) was stirred at respective conditions for 24 h (MS: molecular sieves).
[b] Isolated yield.
[c] ND: not detected. In entries 3 and 4, unreacted **3a** was recovered. Also, in entries 5 and 6, significant amounts of **3a** were recovered.



Scheme 5. One pot reductive amination of a ketone using AuNPore/silane.

A plausible reaction pathway is shown in Scheme 6. Initially, $PhMe_2SiH$ ($PhMe_2SiH$ is represented as Si–H for clarity) and the imine co-ordinates on the nanoporous gold surface. The imine then abstracts a proton from water, resulting in the formation of protonated imine along with AuNPore–H species, and Si–OH is released. Finally, co-ordinated protonated imine is attacked by H^- to furnish the desired product and AuNPore is regenerated (Scheme 6).



Scheme 6. Plausible pathway for reduction of imines using AuNPore/silane.

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3. Conclusions

In conclusion, we have described highly chemoselective reduction of ketimines using AuNPore/$PhMe_2SiH$/H_2O system. The respective amines could be achieved in high chemical yields under mild conditions. Accordingly, this reducing system may provide a new and selective procedure for reductive amination of aldehydes and ketones.

4. Experimental section

4.1. Preparation of AuNPore catalyst

The AuNPore catalyst was prepared by minor change of the reported procedure.[6c] Gold (99.99%) and silver (99.99%) were melted at high temperature with the help of electric arc-melting furnace under Ar atmosphere. The resultant $Au_{30}Ag_{70}$ alloy (30:70, in at. %), was rolled down to thickness of 40–60 μm. Further, this foil was annealed at 850 °C for 20 h and cut into small pieces (5×2 mm square). Treatment of the resulting pieces (50 mg) with 70 wt % nitric acid (50 mL) at room temperature for 18 h led to the formation of the nanoporous skeleton through selective de-alloying of silver. The copper colored pieces were washed with a saturated aqueous solution of $NaHCO_3$, distilled water, and acetone, successively. Drying the resultant material under vacuum gave the nanoporous gold with composition $Au_{\sim 100}Ag_0$ as calculated from the weight loss of silver.

4.2. General methods and materials

^1H and ^{13}C NMR spectra were recorded on either a Varian Inova-400 spectrometer (400 MHz for ^1H, 100 MHz for ^{13}C) or a Bruker Avance II-400 spectrometer (400 MHz for ^1H, 100 MHz for ^{13}C); DMSO-d_6 and $CDCl_3$ were used as a solvent, while TMS was used as an internal standard, The chemical shifts are reported in parts per million downfield (δ) from TMS, the coupling constants J are given in Hertz. The peak patterns are indicated as follows: br s, broad singlet; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. IR spectra were recorded on an NEXUS FTIR spectrometer. TLC was carried out on SiO_2 (silica gel 60 F_{254}, Merck) plates. Solvents were obtained and used without previous purification. All of the other reactants were obtained and also used without any previous treatment.

4.3. General procedure for reduction ketimine (1a) using AuNPore catalyst

In acetonitrile solution (2 mL) were added AuNPore (2 mol %), imine **1a** (0.5 mmol), $PhMe_2SiH$ (0.6 mmol), H_2O (0.6 mmol) successively at 50 °C in a V-shaped reactor. The reaction mixture was stirred at 50 °C for 5 h and was monitored by thin layer chromatography (TLC). Later, the solution was taken out from the V-shaped reactor with the help of pipette and the reactor was washed three times with acetone. The combined organic solution was evaporated to give the crude product, which was purified by silica gel column chromatography using pet ether/ethyl acetate (20:1) as an eluent to obtain pure product; amine **2a** was obtained in 94% yield.

*4.3.1. N-(1-Phenylethyl)aniline (**2a**).*[12] ^1H NMR (400 MHz, $CDCl_3$) δ 7.38–7.29 (m, 4H), 7.24–7.20 (m, 1H), 7.10–7.06 (m, 2H), 6.63 (t, J=7.2 Hz, 1H), 6.57 (dd, J_1=8.4 Hz, J_2=1.2 Hz, 2H), 4.48 (q, J=6.8 Hz, 1H), 4.02 (br s, 1H), 1.51 (d, J=6.8 Hz, 3H).

*4.3.2. N-(1-(4-Methoxyphenyl)ethyl)aniline (**2b**).*[13] ^1H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, J=8.8 Hz, 2H), 7.09 (t, J=8.8 Hz, 2H), 6.85 (d, J=8.8 Hz, 2H), 6.63 (t, J=7.6 Hz, 1H), 6.51 (d, J=8.0 Hz, 2H), 4.44 (q, J=6.8 Hz, 1H), 3.98 (br s, 1H), 1.49 (d, J=6.8 Hz, 3H).

*4.3.3. N-(1-(4-Bromophenyl)ethyl)aniline (**2c**).*[12] ^1H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, J=8.0 Hz, 2H), 7.23 (d, J=8.8 Hz, 2H), 7.08 (t, J=8.0 Hz, 2H), 6.65 (t, J=7.6 Hz, 2H), 6.46 (d, J=8.4 Hz, 1H), 4.42 (q, J=6.8 Hz, 1H), 3.98 (br s, 1H), 1.47 (d, J=6.8 Hz, 3H).

*4.3.4. N-Phenyl-1,2,3,4-tetrahydronaphthalen-1-amine (**2d**).*[14] ^1H NMR (400 MHz, $CDCl_3$) δ 7.43–7.40 (m, 1H), 7.24–7.14 (m, 5H), 6.74–6.68 (m, 3H), 4.65 (q, J=4.8 Hz, 1H), 3.89 (br s, 1H), 2.88–2.78 (m, 2H), 2.02–1.81 (m, 4H).

*4.3.5. N-(1-(Naphthalen-1-yl)ethyl)aniline (**2e**).*[12] ^1H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J=8.4 Hz, 1H), 7.90 (d, J=8.4 Hz, 1H), 7.74 (d, J=8.4 Hz, 1H), 7.65 (d, J=7.2 Hz, 1H), 7.58–7.49 (m, 2H), 7.40 (t, J=7.6 Hz, 1H), 7.06 (t, J=8.0 Hz, 2H), 6.63 (t, J=7.6 Hz, 1H), 6.48 (dd, J_1=8.4 Hz, J_2=0.8 Hz, 2H), 5.28 (q, J=6.8 Hz, 1H), 4.16 (br s, 1H), 1.66 (d, J=6.8 Hz, 3H).

*4.3.6. N-Benzhydrylaniline (**2f**).*[15] ^1H NMR (400 MHz, $CDCl_3$) δ 7.34–7.19 (m, 10H), 7.07 (t, J=7.6 Hz, 2H), 6.66 (t, J=7.6 Hz, 1H), 6.50 (d, J=8.0 Hz, 2H), 5.47 (s, 1H), 4.18 (s, 1H).

*4.3.7. 4-Methoxy-N-(1-phenylethyl)aniline (**2g**).*[2c] ^1H NMR (400 MHz, $CDCl_3$) δ 7.37–7.21 (m, 5H), 6.68 (d, J=8.8 Hz, 2H), 6.46 (d, J=9.2 Hz, 2H), 4.41 (q, J=6.8 Hz, 1H), 3.78 (br s, 1H), 3.69 (s, 3H), 1.49 (d, J=6.8 Hz, 3H).

*4.3.8. 4-Methyl-N-(1-phenylethyl)aniline (**2h**).*[2c] ^1H NMR (400 MHz, $CDCl_3$) δ 7.37–7.19 (m, 5H), 6.89 (d, J=8.0 Hz, 2H), 6.43 (d, J=8.4 Hz, 2H), 4.44 (q, J=6.8 Hz, 1H), 3.92 (br s, 1H), 2.17 (s, 3H), 1.49 (d, J=6.4 Hz, 3H).

*4.3.9. N-(1-Phenylethyl)butan-1-amine (**2i**).*[16] ^1H NMR (400 MHz, $CDCl_3$) δ 7.31–7.20 (m, 5H), 3.74 (q, J=6.8 Hz, 1H), 2.42 (m, 2H), 1.44 (m, 2H), 1.34 (d, J=6.4 Hz, 3H), 1.29 (m, 2H); 0.87 (t, J=7.2 Hz, 3H).

*4.3.10. N-(1-(Thiophen-2-yl)ethyl)aniline (**2j**).*[17] ^1H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, J=8.0 Hz, 1H), 7.33–7.29 (m, 3H), 7.24–7.22 (m, 1H), 6.98 (d, J=8.0 Hz, 1H), 6.49 (t, J=7.6 Hz, 1H), 6.37 (d, J=8.0 Hz, 1H), 4.70 (br s, 1H), 4.52 (q, J=6.4 Hz, 1H), 1.57 (d, J=6.8 Hz, 3H).

4.4. Reductive amination using AuNPore catalyst

In acetonitrile solution (2 mL) were added AuNPore (5 mol %), benzaldehyde **4a** (R^1=Ph; 0.5 mmol) aniline **9a** (R^2=H; 0.5 mmol), $PhMe_2SiH$ (0.6 mmol) successively at room temperature in a V-shaped reactor. The reaction mixture was stirred at 80 °C for 5 h and was monitored by Thin Layer Chromatography (TLC). Later, the solution was taken out from the V-shaped reactor with the help of pipette and the reactor was washed three times with acetone. Collective organic solution was evaporated to give crude product, which was purified by silica gel column chromatography using pet ether/ethyl acetate (20:1) as an eluent to obtain pure product **6a** in 69% yield.

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*4.4.1. N-Benzylaniline (**6a**).*[12] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.27 (m, 5H), 7.19–7.15 (m, 2H), 6.73–6.69 (t, *J*=7.6 Hz, 1H), 6.64 (dd, J_1=8.0 Hz, J_2=0.8 Hz, 2H), 4.33 (s, 2H), 4.02 (br s, 1H).

*4.4.2. N-Benzyl-4-methoxyaniline (**6b**).*[2c] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.25 (m, 5H), 6.77 (d, *J*=8.8 Hz, 2H), 6.60 (d, *J*=8.2 Hz, 2H), 4.28 (s, 2H), 3.74 (s, 3H).

*4.4.3. N-Benzyl-4-methylaniline (**6c**).*[12] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.22 (m, 5H), 6.97 (d, *J*=8.0 Hz, 2H), 6.55 (d, *J*=8.4 Hz, 2H), 4.29 (s, 2H), 3.89 (br s, 1H), 2.23 (s, 3H).

*4.4.4. N-(4-Chlorobenzyl)aniline (**6d**).*[18] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.30 (m, 2H), 7.22–7.14 (m, 2H), 7.03–6.99 (m, 2H), 6.73–6.60 (m, 3H), 4.28 (s, 2H), 3.99 (br s, 1H).

*4.4.5. N-(4-Bromobenzyl)aniline (**6e**).*[12] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46–7.44 (m, 2H), 7.22–7.14 (m, 4H), 6.72 (t, *J*=7.6 Hz, 1H), 6.59 (dd, J_1=8.4, J_2=1.2 Hz, 2H) 4.29 (s, 2H), 4.04 (br s, 1H).

*4.4.6. N-(3-Phenylpropyl)aniline (**6f**).*[12] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31–7.27 (m, 3H), 7.21–7.14 (m, 5H), 6.69 (t, *J*=7.2 Hz, 1H), 6.57 (dd, J_1=8.4 Hz, J_2=0.8 Hz, 2H), 3.61 (br s, 1H), 3.14 (t, *J*=7.2 Hz, 2H), 2.73 (t, *J*=7.6 Hz, 2H), 1.94 (m, *J*=7.2 Hz, 2H).

*4.4.7. 4-Methyl-N-(3-phenylpropyl)aniline (**6g**).*[19] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28–7.24 (m, 2H), 7.20–7.18 (m, 3H), 7.01–6.96 (m, 2H), 6.51 (d, *J*=8.4 Hz, 2H), 3.70 (br s, 1H), 3.12 (t, *J*=7.2 Hz, 2H), 2.72 (t, *J*=7.6 Hz, 2H), 2.23 (s, 3H), 1.93 (m, *J*=7.2 Hz, 2H).

*4.4.8. N-Butylaniline (**6h**).*[20] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.17–7.13 (m, 2H), 6.67 (t, *J*=7.3 Hz, 1H), 6.58 (d, *J*=8.2 Hz, 2H), 3.56 (br s, 1H), 3.10 (t, *J*=7.0 Hz, 2H) 1.59 (m, 2H), 1.41 (m, 2H), 0.95 (t, *J*=7.4 Hz, 3H).

*4.4.9. 4-Methoxy-N-butylaniline (**6i**).*[16] ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.77 (d, *J*=8.8 Hz, 2H), 6.57 (d, *J*=8.8 Hz, 2H), 3.74 (s, 3H), 3.05 (t, *J*=7.2 Hz, 2H), 1.59 (m, 2H), 1.40 (m, 2H), 4.28 (s, 2H), 0.95 (t, *J*=7.2 Hz, 2H).

*4.4.10. N-(Furan-2-ylmethyl)aniline (**6j**).*[4a] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, *J*=1.6 Hz, 1H), 7.19 (t, *J*=7.8 Hz, 2H), 6.74 (t, *J*=7.2 Hz, 1H), 6.67 (d, *J*=7.6 Hz, 2H), 6.32 (m, 1H), 6.23 (d, *J*=3.2 Hz, 1H), 4.31 (s, 2H), 4.02 (br s, 1H).

4.5. Reductive amination using $NaBH(OAc)_3$

To an ethylacetate solution (5 mL) were added benzaldehyde **4a** (0.5 mmol), aniline **9a** (0.55 mmol), $NaBH(OAc)_3$ (0.6 mmol), successively at room temperature. The reaction mixture was stirred at room temperature for 24 h. Later, the solution was diluted with water (10 mL) and extracted with EtOAc (3×10 mL). Collective organic layers were evaporated to give crude product, which was purified by silica gel column chromatography using pet ether/ethyl acetate (20:1) as an eluent to obtain pure products; amine **6a** was obtained in 72% yield and alcohol **7a** was obtained in 8% yield.

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Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2014.11.023.

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