

# Aqueous Room-Temperature Gold-Catalyzed Chemoselective Transfer Hydrogenation of Aldehydes

Lin He, Ji Ni, Lu-Cun Wang, Feng-Jiao Yu, Yong Cao,\* He-Yong He, and Kang-Nian Fan<sup>[a]</sup>

Reduction of aldehydes to the corresponding alcohols is one of the most fundamental and useful reactions that are important in the pharmaceutical and chemical industry.<sup>[1]</sup> Among the various available reduction protocols for the synthesis of valuable hydroxy compounds,<sup>[2]</sup> catalytic transfer hydrogenation (TH)<sup>[3]</sup> has emerged as the most viable, mainly due to the non-involvement of highly flammable and explosive molecular hydrogen or highly expensive metal hydride donors. Moreover, TH processes generally involve easy handling and recovery of products, recycling of catalyst and minimization of undesired toxic wastes. One of the recent highlights in this field is the use of cheap and easily accessible formic acid<sup>[4]</sup> or its salts<sup>[5]</sup> as possible in situ hydrogen sources, which has attracted special attention owing to their ease of hydrogen donation as compared to most other transfer reduction agents. In this context, TH of aldehydes in the presence of formate salts is an area of growing interest.<sup>[6]</sup> Although many transition-metal-based TH catalysts have been developed,<sup>[6b,c]</sup> the focus has been largely on homogeneous rather than heterogeneous catalysis. To the best of our knowledge, few heterogeneous catalysts have been reported that enable fast, chemoselective, and productive TH of aldehydes with inexpensive, eco-friendly formates, and that can tolerate the presence of synthetically useful functional groups.

Supported gold nanoclusters have attracted increased interest in the past few years as new generation of advanced catalysts for a number of organic transformations<sup>[7]</sup> including chemoselective reduction of unsaturated carbonyl or nitro

compounds by molecular hydrogen.<sup>[8]</sup> One critical limitation associated with the present Au-catalyzed hydrogenation process, however, is the unfavorably low hydrogen-delivery rates compared to other noble metals.<sup>[8b]</sup> Very recently, we have described the use of a facile gold-catalyzed, 2-propanol-mediated TH strategy that bypasses the inconvenient H<sub>2</sub> activation thus enabling fast and chemoselective reduction of a range of aromatic ketone and nitro groups.<sup>[9]</sup> From an environmental and an economic viewpoint, efficient functional transformations under milder conditions would be most desirable. Herein, we report a highly efficient, aqueous, room temperature, formate-mediated TH of aldehydes catalyzed by supported gold nanoclusters. Our results have shown that the reaction is general and can proceed at temperatures as low as 25 °C. Moreover, an inert atmosphere is not required.

Initially, various heterogeneous catalysts were applied to the transformation of benzaldehyde to benzyl alcohol in aqueous HCOOK without inert gas protection at 80 °C (Table 1). The benefit of using redox CeO<sub>2</sub> as a support,

Table 1. Catalytic results of transfer hydrogenation of benzaldehyde under various conditions.<sup>[a]</sup>

Entry	Catalyst	% Metal [mol]	T [°C]	Time [h]	Yield [%] <sup>[e]</sup>
1 <sup>[b]</sup>	Au/ <i>meso</i> -CeO <sub>2</sub>	1	80	3	>99 (97)
2 <sup>[c]</sup>	Au/CeO <sub>2</sub> (Adnano 90)	1	80	3	21
3	Au/TiO <sub>2</sub> (WGC)	1	80	3	13
4	Au/Fe <sub>2</sub> O <sub>3</sub> (WGC)	1	80	3	8
5	Au/C (WGC)	1	80	3	1
6	Au/Al <sub>2</sub> O <sub>3</sub> (Mintek)	1	80	3	12
7	Pd/C (Alfa Aesar)	1	80	3	20
8	Pt/C (Alfa Aesar)	1	80	3	17
9	<i>meso</i> -CeO <sub>2</sub>	1	80	3	–
10	Au/ <i>meso</i> -CeO <sub>2</sub>	3	25	6	>99
11 <sup>[d]</sup>	Au/ <i>meso</i> -CeO <sub>2</sub>	3	25	6	94

[a] Reaction conditions: 1 mmol substrate, HCOOK (5 equiv), water (15 mL), in air. [b] BET surface area of *meso*-CeO<sub>2</sub> is 263 m<sup>2</sup> g<sup>-1</sup>. [c] BET surface area of CeO<sub>2</sub> (Adnano 90) is 90 m<sup>2</sup> g<sup>-1</sup>. [d] Fifth run. [e] Yield was determined by GC. Numbers in parenthesis refer to yields of isolated products.

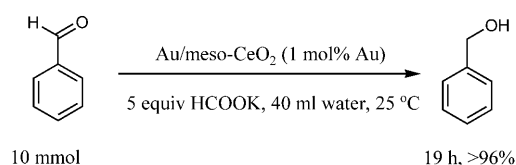
[a] L. He, J. Ni, L.-C. Wang, F.-J. Yu, Prof. Dr. Y. Cao, Prof. Dr. H.-Y. He, Prof. K.-N. Fan  
Shanghai Key Laboratory of Molecular Catalysis and Innovative Materials  
Department of Chemistry, Fudan University  
Shanghai 200433 (P.R. China)  
Fax: (+86) 21-6564-3774  
E-mail: yongcao@fudan.edu.cn

Supporting information for this article is available on the WWW under <http://dx.doi.org/10.1002/chem.200901261>.

especially mesoporous CeO<sub>2</sub> (*meso*-CeO<sub>2</sub>) with very high specific surface area (263 m<sup>2</sup>g<sup>-1</sup>), became obvious when comparing the activity of Au/*meso*-CeO<sub>2</sub> with the activities of Au supported on conventional ceria (Au/CeO<sub>2</sub> Adnano 90), Au/TiO<sub>2</sub>, Au/Fe<sub>2</sub>O<sub>3</sub>, Au/C supplied by the World Gold Council (WGC) and Au/Al<sub>2</sub>O<sub>3</sub> provided by Mintek (Table 1, entries 1–6). A clear advantage of the Au/*meso*-CeO<sub>2</sub> catalyst over other noble metals was also noticed when benzaldehyde was reduced by using Pd/C or Pt/C under otherwise identical conditions (Table 1, entries 7–8). Note that this behavior is in stark contrast to recent liquid phase direct hydrogenation studies,<sup>[8b,10]</sup> where Au was found to be much inferior to Pd or Pt in terms of the hydrogenation rate. Most remarkably, at room temperature, transfer hydrogenation of benzaldehyde still could proceed smoothly in the presence of Au/*meso*-CeO<sub>2</sub> (Table 1, entry 10). No conversion was found in the absence of catalysts or in the presence of Au-free *meso*-CeO<sub>2</sub> catalyst under identical conditions (Table 1, entry 9), illustrating that the presence of gold was indispensable for high catalytic activity.

Au/*meso*-CeO<sub>2</sub> was filtered from the reaction mixture at 50% conversion of benzaldehyde under the conditions in entry 10 of Table 1. Continued stirring of the filtrate under similar conditions did not give any products. Inductively coupled plasma atomic emission spectroscopy (ICP-AES) analysis of the filtrate showed that no Au was present (<0.10 ppm). Furthermore, the recovered Au/*meso*-CeO<sub>2</sub> catalyst could be reused at least five runs without appreciable loss of the original catalytic activity (Table 1, entry 11). These results rule out any possible contribution of homogeneous catalysis by leached gold species.

The Au/*meso*-CeO<sub>2</sub>-catalyzed protocol is equally effective on a larger scale. For example, the transfer reduction of benzaldehyde (10 mmol) in the presence of Au/*meso*-CeO<sub>2</sub> (1 mol% Au) and 5 equivalents (with respect to benzaldehyde) of HCOOK in aqueous media gave the corresponding benzyl alcohol in 96% isolated yield (Scheme 1).



Scheme 1. Larger-scale TH of benzaldehyde.

With these findings in hand, we then extended our studies to various kinds of aldehydes to establish the scope of the aqueous TH of aldehydes with Au/*meso*-CeO<sub>2</sub>. Table 2 showed that the catalyst system was surprisingly versatile. Various structurally diverse aldehydes, including aromatic, aliphatic, unsaturated, and heterocyclic aldehydes, could be transformed into the corresponding alcohols in high to excellent yields. The transformation of substituted benzaldehydes, which contain electron-donating as well as electron-withdrawing substituents, proceeded efficiently to give the

Table 2. The TH reaction of various aldehydes with HCOOK.<sup>[a]</sup>

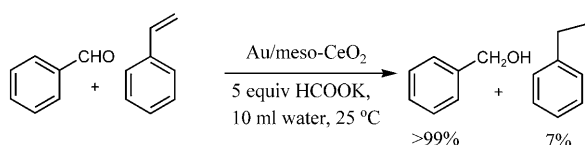
Entry	Aldehyde	Product	Time [h]	Yield [%] <sup>[d]</sup>
1			6	99 (97)
2			12	99
3			5	99 (96)
4			4	99
5			6	98
6			12	99 (97)
7			8	99
8			6	99
9 <sup>[b]</sup>			14	84 (82)
10 <sup>[b]</sup>			7	80
11			10	96
12			18	92 (88)
13 <sup>[c]</sup>			21	90

[a] Reaction conditions: 1 mmol substrate, Au/*meso*-CeO<sub>2</sub> (3 mol% Au), HCOOK (5 equiv), water (15 mL), 25 °C, in air. [b] 1 mmol substrate, Au/*meso*-CeO<sub>2</sub> (3 mol% Au), HCOOK (5 equiv), water (15 mL), 80 °C, in air. [c] 0.4 mmol substrate, Au/*meso*-CeO<sub>2</sub> (7.5 mol% Au), HCOOK (5 equiv), water (15 mL), 25 °C, in air. [d] Yield was determined by GC. Numbers in parenthesis refer to yields of isolated products.

corresponding benzyl alcohols at ambient conditions (Table 2, entries 1–8). In the transformations of chlorobenzaldehydes, the lower reaction rate of *o*-chlorobenzaldehyde relative to *m*- and *p*-analogues indicated a steric effect (entries 2–4). Moreover, high selectivity could also be attained for the reduction of halogen substituted benzaldehydes (Table 2, entries 2–5), with no observation of dehalogenation or ring reduction. Hetero-aromatic aldehydes could be reduced in almost quantitative yield in a short time (Table 2, entry 11). The less reactive aliphatic ones could also be hydrogenated to the corresponding aliphatic alcohols with longer reaction time (Table 2, entries 12 and 13) at room temperature.  $\alpha,\beta$ -unsaturated aldehydes were more challenging as substrates because thermodynamics favors hydrogenation of C=C over C=O,<sup>[10,11]</sup> yet the present system under mild TH condition still led to promising results

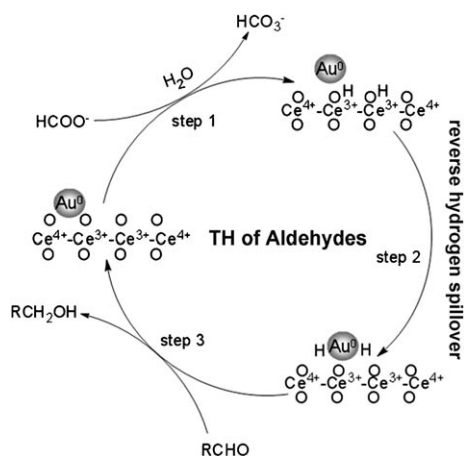
(Table 2, entries 9 and 10), in marked contrast to the unfavorably poor selectivity (<30%) as previously achieved for direct liquid phase crotonaldehyde hydrogenation by gold supported on CeO<sub>2</sub>.<sup>[11]</sup>

In an intermolecular competitive reaction between benzaldehyde and acetophenone, benzyl alcohol was the only reduction product without formation of 1-phenylethanol from acetophenone. The high selectivity for the specific reduction of the C=O moiety in  $\alpha,\beta$ -unsaturated aldehydes was also confirmed by the competitive reaction of benzaldehyde and styrene. When the yield of benzyl alcohol was >99%, the conversion of styrene did not exceed 7% (Scheme 2). Therefore, the intrinsic higher rate for the reduction of the aldehydes group on the gold catalyst is responsible for the high chemoselectivity observed.



Scheme 2. Competitive reaction of benzaldehyde and styrene.

To obtain an insight into the origin of the enhanced Au-mediated TH activity achieved by using *meso*-CeO<sub>2</sub> as support, we examined a series of Au/CeO<sub>2</sub> samples in which the surface area of CeO<sub>2</sub> was varied by calcination at elevated temperatures. Interestingly, a good linear correlation for the rate as a function of CeO<sub>2</sub> surface area was observed (Figure S4). We speculate that the dehydrogenation of formate salts occurs mainly on the surface of ceria, particularly on considering that the ceria surface acts as a sink for the reactive formate in the case with water gas shift (WGS) reaction (Scheme 3).<sup>[12]</sup> This hypothesis is corroborated by the fact that the kinetic studies revealed a first-order dependence on the amount of Au/*meso*-CeO<sub>2</sub> catalysts, a zero-order de-



Scheme 3. A tentative mechanism for aqueous formate-mediated TH of aldehydes over Au/*meso*-CeO<sub>2</sub>

pendence on the concentration of aldehydes and a first-order dependence on the concentration of HCOOK (Figures S6, S7 and S8). This scenario, in conjunction with the significantly retarded conversion identified for using other formate sources as the hydrogen donors (Figure S5),<sup>[13]</sup> further confirms the CeO<sub>2</sub>-mediated formate dehydrogenation is the rate-determining step.

A reaction mechanism based on the mechanistic and kinetic experiments for the aqueous formate-mediated TH of aldehydes by Au/*meso*-CeO<sub>2</sub> was depicted in (Scheme 3). Ceria sites (Ce<sup>3+</sup> and Ce<sup>4+</sup> were detectable by XPS, Figure S2) facilitated by H<sub>2</sub>O were involved in the rate-determining dehydrogenation of formate to bicarbonate species (step 1). The hydrogen species thus formed could transfer to vicinal Au<sup>0</sup> clusters (Figure S2 and S3, data for XPS and CO adsorption coupled with DRIFTS) via reverse hydrogen spillover to form Au<sup>0</sup>-H complexes,<sup>[14]</sup> which is believed to be the key active intermediate for transfer hydrogenation (step 2). Au<sup>0</sup>-H complexes were rapidly consumed together with a final formation of the alcohol product (step 3).<sup>[15]</sup>

In summary, we have shown that gold nanoclusters supported on a mesoporous ceria matrix are highly active and chemoselective catalysts for the aqueous-phase TH of aldehydes at room temperature. Of significant practical importance is that the catalyst tolerates a wide variety of synthetically useful functional groups including halogens, ketones, and olefins. To the best of our knowledge, this aqueous Au-mediated catalysis represents the most efficient, simple, and eco-friendly catalytic system for the selective reduction of aldehydes to date.

## Experimental Section

**General procedure for the TH reaction of aldehydes:** A mixture of aldehyde (1 mmol), metal catalysts (3 mol% metal), and formate salts (5 equiv), water (15 mL) was put into a flask (50 mL) fitted with a magnetic stirring bar and a reflux condenser. After the mixture was stirred at 25°C (80°C for  $\alpha, \beta$ -unsaturated aldehydes) for a given reaction time, the product mixtures were extracted with Et<sub>2</sub>O for 3 times and analyzed (the water phase was also analyzed) by using a Shimadzu GC-17 A gas chromatograph equipped with a HP-FFAP column (30 m  $\times$  0.25 mm) and a flame ionization detector (FID). The identification of the products was performed by using a GC-MS spectrometer comparing with commercially pure products. For isolation, the combined organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, concentrated, and purified by silica gel column chromatography to give the product.

## Acknowledgements

This work was supported by the National Natural Science Foundation of China (20633030, 20721063, and 20873026), the National Basic Research Program of China (2009CB623506), Science & Technology Commission of Shanghai Municipality (08DZ2270500, 07QH14003) and the Committee of the Shanghai Education (06SG03).

**Keywords:** aldehydes • chemoselectivity • gold • room temperature • transfer hydrogenation

- [1] a) S. Nishimura, *Handbook of Heterogeneous Catalytic Hydrogenation for Organic Synthesis*, Wiley, New York, **2001**, pp. 170–185; b) B. Chen, U. Dingerdissen, J. G. E. Krauter, H. G. J. Lansink Rotgerink, K. Möbus, D. J. Ostgard, P. Panster, T. H. Riermeier, S. Seebald, T. Tacke, H. Trauthwein, *Appl. Catal. A* **2005**, *280*, 17–46; c) J. W. Yang, M. T. Hechavarria Fonseca, N. Viganola, B. List, *Angew. Chem.* **2004**, *116*, 6829–6832; *Angew. Chem. Int. Ed.* **2004**, *43*, 6660–6662.
- [2] a) R. C. Larock, *Comprehensive Organic Transformations: A Guide to Functional Group Preparation*, Wiley-VCH, Weinheim, **1999**, pp. 823–840; b) K. Everaere, A. Mortrex, J.-F. Carpentier, *Adv. Synth. Catal.* **2003**, *345*, 67–77.
- [3] a) R. Johnstone, A. H. Wilby, I. D. Entwistle, *Chem. Rev.* **1985**, *85*, 129–170; b) T. Ikariya, A. J. Blacker, *Acc. Chem. Res.* **2007**, *40*, 1300–1308; c) R. Noyori, S. Hashiguchi, *Acc. Chem. Res.* **1997**, *30*, 97–102; d) S. K. Mohapatra, S. U. Sonavane, R. V. Jayaram, P. Selvam, *Org. Lett.* **2002**, *4*, 4297–4300.
- [4] a) J. Zhang, P. G. Blazicka, M. M. Bruendl, Y. Huang, *J. Org. Chem.* **2009**, *74*, 1411–1414; b) J. Yu, H. Wu, C. Ramarao, J. B. Spencer, S. V. Ley, *Chem. Commun.* **2003**, 678–679; c) T. Koike, K. Murata, T. Ikariya, *Org. Lett.* **2000**, *2*, 3833–3836.
- [5] a) N. A. Cortez, G. Aguirre, M. Parra-Hake, R. Somanathan, *Tetrahedron Lett.* **2009**, *50*, 2228–2231; b) K. Prasad, X. Jiang, J. S. Slade, J. Clemens, O. Repic, T. J. Blacklock, *Adv. Synth. Catal.* **2005**, *347*, 1769–1773; c) H. Wiener, J. Blum, Y. Sasson, *J. Org. Chem.* **1991**, *56*, 4481–4486; d) S. Rajagopal, A. F. Spatola, *J. Org. Chem.* **1995**, *60*, 1347–1355.
- [6] a) M. Baidossi, A. V. Joshi, S. Mukhopadhyay, Y. Sasson, *Synth. Commun.* **2004**, *34*, 643–650; b) X. F. Wu, J. K. Liu, X. H. Li, A. Zannotti-Gerosa, F. Hancock, D. Vinci, J. W. Ruan, J. L. Xiao, *Angew. Chem.* **2006**, *118*, 6870–6874; *Angew. Chem. Int. Ed.* **2006**, *45*, 6718–6722; c) J. Li, Y. M. Zhang, D. F. Han, J. B. Gao, L. Zhong, C. Li, *Green Chem.* **2008**, *10*, 608–611; d) R. Bar, L. K. Bar, Y. Sasson, J. Blum, *J. Mol. Catal.* **1985**, *33*, 161–177.
- [7] a) F. Z. Su, Y. M. Liu, L. C. Wang, Y. Cao, H. Y. He, K. N. Fan, *Angew. Chem.* **2008**, *120*, 340–343; *Angew. Chem. Int. Ed.* **2008**, *47*, 334–337; b) H. Sun, F. Z. Su, J. Ni, Y. Cao, H. Y. He, K. N. Fan, *Angew. Chem.* **2009**, *121*, 4454–4457; *Angew. Chem. Int. Ed.* **2009**, *48*, 4390–4393; c) H. Tsunoyama, H. Sakurai, Y. Negishi, T. Tsukuda, *J. Am. Chem. Soc.* **2005**, *127*, 9374–9375; d) G. J. Rodriguez-Rivera, W. B. Kim, S. T. Evans, T. Voitl, J. A. Dumesic, *J. Am. Chem. Soc.* **2005**, *127*, 10790–10791.
- [8] a) P. Claus, A. Brueckner, C. Mohr, H. Hofmeister, *J. Am. Chem. Soc.* **2000**, *122*, 11430–11439; b) C. Mohr, H. Hofmeister, J. Radnik, P. Claus, *J. Am. Chem. Soc.* **2003**, *125*, 1905–1911; c) A. Corma, P. Serna, *Science* **2006**, *313*, 332–334; d) A. Corma, P. Serna, H. Garcia, *J. Am. Chem. Soc.* **2007**, *129*, 6358–6359.
- [9] F. Z. Su, L. He, J. Ni, Y. Cao, H. Y. He, K. N. Fan, *Chem. Commun.* **2008**, 3531–3533.
- [10] C. Milone, M. L. Tropeano, P. Gulino, R. Ingaglia, G. Neri, S. Galvagno, *Chem. Commun.* **2002**, 868–869.
- [11] a) B. Campo, C. Petit, M. Volpe, S. Ivanova, R. Touroude, *J. Catal.* **2006**, *242*, 162–171; b) B. Campo, C. Petit, M. Volpe, *J. Catal.* **2008**, *254*, 71–78; c) B. Campo, G. Santori, C. Petit, M. Volpe, *Appl. Catal. A* **2009**, *359*, 79–83.
- [12] a) G. Jacobs, S. Ricote, U. M. Graham, P. M. Patterson, B. H. Davis, *Catal. Today* **2005**, *106*, 259–264; b) A. Karpenko, R. Leppelt, V. Plzak, J. Cai, A. Chuvilin, B. Schumacher, U. Kaiser, R. J. Behm, *Top. Catal.* **2007**, *44*, 183–198.
- [13] The transfer reduction rate was found to depend critically on the counterion of the formates, the ionic size of which determines the hydrogen-donating ability thus the dehydrogenation efficiency of the formate salts (see Table S1 and Ref. [4d]). On the other hand, the addition of a base such as potassium acetate to HCOOH accelerated the aldehyde reduction rate (see Figure S9) further confirms that HCOO<sup>-</sup> ion is essential for the reaction to proceed.
- [14] a) A. Abad, C. Almela, A. Corma, H. Garcia, *Chem. Commun.* **2006**, 3178–3180; b) M. Conte, H. Miyamura, S. Kobayashi, V. Chechik, *J. Am. Chem. Soc.* **2009**, *131*, 7189–7196.
- [15] Based on the GC-MS analysis, no hydrogen was generated during the process of the Au/meso-CeO<sub>2</sub>-catalyzed TH of aldehydes, which indicates that the encountered reduction was a true hydrogen transfer rather than a consecutive dehydrogenation-hydrogenation reaction.

Received: May 12, 2009  
Published online: October 1, 2009