A green and efficient oxidation of alcohols by supported gold catalysts using aqueous H_2O_2 under organic solvent-free conditions†

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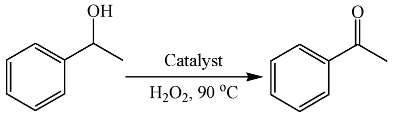
The use of supported gold nanoparticles as an efficient, green and reusable catalyst for the oxidation of various alcohols to the corresponding carbonyl compounds using aqueous hydrogen peroxide as an environmentally benign oxidant is presented. The reaction proceeds with good to excellent yields in particular for nonactivated alcohols under base-free conditions.

Oxidation of alcohols to their corresponding carbonyl compounds is one of the most important processes for production of fine and specialty chemicals.[1] Traditional methods involve use of toxic and expensive stoichiometric metal oxidants, such as chromate and permanganate,[2] or harmful organic solvents,[3] or require vigorous reaction conditions.[4] From both the environmental and economic points of view, there is a strong incentive to develop a green, economic and efficient alcohol oxidation process.[5] In this context, much recent attention has been directed toward the aerobic oxidation of alcohols with reusable heterogeneous solid catalysts in aqueous media under mild conditions,[6] which is particularly suitable for industrial practices. However, very few catalysts are sufficiently active for nonactivated alcohols, like aliphatic and alicyclic alcohols.[7] In particular, bases such as KOH or K_2CO_3 are frequently needed for oxidation of primary aliphatic alcohols (*e.g.* 1-octanol) in water,[8] which is clearly not green and presents notorious problems such as corrosion and waste base treatment. In this respect, the development of a novel catalytic system that exhibits a wide range of substrate tolerance under mild and base-free aqueous conditions still remains a major challenge.

Supported gold catalysts have attracted tremendous recent attention owing to their unique catalytic properties for a broad array of organic transformations,[9] especially for aerobic oxidation of alcohols under mild conditions.[6c,d,9a,10–12] Over the last few years, our group,[11] Kobayashi *et al.*[6c] and Corma *et al.*[12] reported that Au nanoclusters deposited on metal oxides or polymers are highly effective for aerobic oxidation of various alcohols. In general, organic solvents and/or bases are necessary to achieve high yield and selectivity.[11] The oxidation of alcohols under solvent- and base-free conditions was reported,[12,13] the yield of target product was, however, much lower than that obtained with organic solvent and/or base conditions. Herein, we report the development of a new efficient H_2O_2–Au system exhibiting significantly enhanced activity for the oxidation of alcohols under base-free aqueous conditions. Hydrogen peroxide (H_2O_2), previously established to be an ideal oxidant for the green oxidation of alcohols with homogeneous metal peroxo complexes,[14] has shown to be particularly effective for gold catalyzed selective oxidation of nonactivated alcohols. To the best of our knowledge, this study also forms the first hectogram-scale clean synthesis of aliphatic acids using gold catalysts.

First of all, 1-phenylethanol was used as a model substrate to study the catalytic activity of the different supported gold catalysts. The results of these studies (Table 1) show that gold supported on carbon leads to very low conversion (*ca.* 12%). The Au/Fe_2O_3 and Au/Al_2O_3 catalysts show moderate activity (*ca.* 34–37%), while Au/TiO_2 supplied by the World Gold Council and Au/CeO_2 give a higher conversion value (*ca.* 58–62%), gold supported on TiO_2 supplied by Mintek afford the highest conversion (*ca.* 99%), with yields of isolated product of between 98 and 100%.‡ No conversion was found in the absence of catalyst or the use of Au-free TiO_2 catalysts under similar reaction conditions. Additional examination of the relationship between the alcohol oxidation activities and a series of Mintek Au/TiO_2 catalysts calcined at elevated temperatures (Fig. S1–4 in ESI)† revealed that use of smaller Au nanoparticles gave higher activity, as shown in Fig. 1. This result, together with the fact that the small Au NPs can substantially facilitate the crucial H_2O_2 decomposition,[15] strongly suggests that the high dispersion of Au NPs in combination with a beneficial synergetic interaction with the TiO_2 support is the key factor

Table 1 Oxidation of 1-phenylethanol by aqueous H_2O_2 [a]



Entry	Catalyst	Conversion (%)
1[b]	0.8% Au-C (WGC)	12
2	4.5% Au-Fe_2O_3 (WGC)	34
3	1.5% Au-TiO_2 (WGC)	62
4	0.9% Au-Al_2O_3 (Mintek)	37
5	1% Au-TiO_2 (Mintek)	99
6	1% Au-CeO_2	58

[a] Reaction conditions: 10 mmol 1-phenylethanol, 10 mL H_2O, 90 °C, 5% H_2O_2 added dropwise, substrate:H_2O_2:Au = 100:150:1. [b] This sample catalyst was used as-received. According to the characterizations of the Au/C sample provided by the World Gold Council, the water content of the Au/C reference catalyst was equal to 40%.

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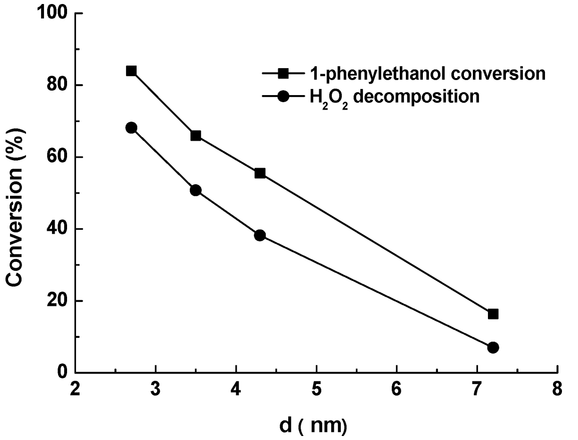


Fig. 1 1-Phenylethanol conversion and H_2O_2 decomposition *versus* gold particle dimension; oxidation of 1-phenylethanol: 10 mmol 1-phenylethanol, Au/TiO_2 (Mintek), 10 mL H_2O, 90 °C, 5% H_2O_2 added dropwise, substrate:H_2O_2:Au = 100:110:1; H_2O_2 decomposition: 1.5 wt% H_2O_2 aqueous solution 10 mL, Au/TiO_2 (Mintek) 80 mg, 25 °C for 80 min in open air. The rate of decomposition was calculated based on the amount of H_2O_2 remaining, which was measured by the titration of 0.1 M $Ce(SO_4)_2$ with 1.5 w/v% ferroin solution as an indicator.

for achieving high activity in the H_2O_2-mediated oxidation of alcohols.

The Mintek Au/TiO_2 catalyst was stable and can be easily reused in the oxidation of 1-phenylethanol. After the first alcohol oxidation, the catalyst was separated from the reaction mixture by filtration, thoroughly washed with water, and then reused as catalyst for the next run under the same conditions. As shown in Fig. 2, the acetophenone yields remained essentially constant for the five successive cycles, reflecting the high stability and reusability of the catalyst. This was consistent with the characterization results for this catalyst. TEM and XPS results (Fig. S5 and S7 in ESI)† showed essentially no changes in the mean diameters of the Au nanoparticles and in the metallic state of Au, respectively, after the five successive runs. Moreover, it was confirmed by induced coupled plasma (ICP) techniques that the Au content of the used Au/TiO_2 catalyst was the same as that of the fresh catalyst and that no Au was in the filtrate.

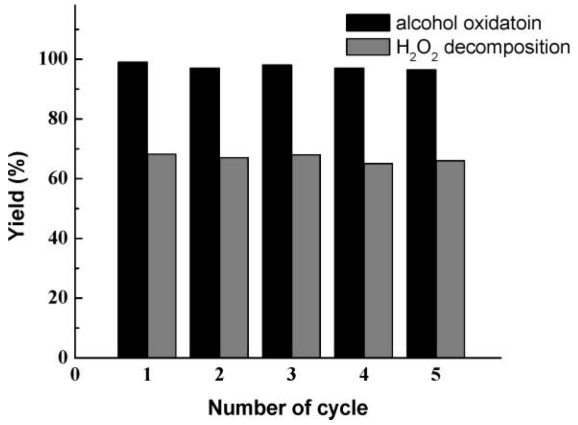
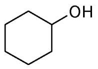
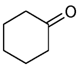
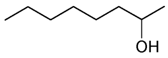
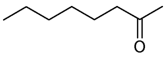
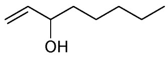
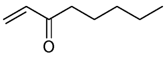
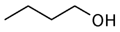
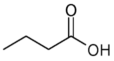
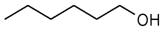
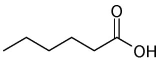
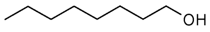
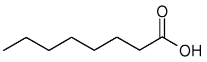


Fig. 2 Recycling of the Mintek Au/TiO_2 catalyst for the oxidation of 1-phenylethanol: 10 mmol substrate, 10 mL H_2O, 90 °C, 5% H_2O_2 added dropwise. Substrate:H_2O_2:Au = 100:150:1. For comparison, the corresponding H_2O_2 decomposition rates are also included.

Table 2 Oxidation of non-activated alcohols by aqueous H_2O_2[a]

Entry	Substrate	Product	Conv. (%)	Sel. (%)
1			87	100
2			98	100
3			>99	100
4[b]			>99	100
5[b]			>99	>99
6[b]			>99	90[c]

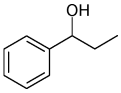
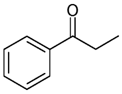
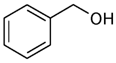
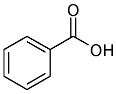
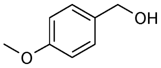
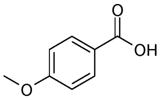
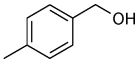
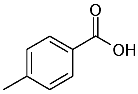
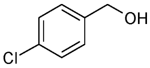
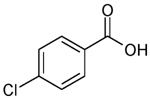
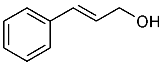
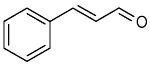
[a] Reaction conditions: 10 mmol Substrate, 10 mL H_2O, 90 °C, 5% H_2O_2 added dropwise, substrate:H_2O_2:Au = 100:150:1. [b] Substrate:H_2O_2:Au = 100:250:1. [c] Octyl octanate was found as by-product.

To examine the scope of the alcohol reaction with the H_2O_2–Au/TiO_2 system, we extended our studies to various structurally different alcohols. The results are summarized in Table 2. It was found that primary and secondary alcohols were oxidized to the corresponding carboxylic acids and ketones, respectively. Notably, H_2O_2–Au/TiO_2 was capable of catalyzing the oxidation of various nonactivated alcohols. For alicyclic alcohols and secondary aliphatic alcohols, *i.e.* 2-octanol, they gave ketones in excellent yields of 87–98% (Table 2, entries 1–2). Moreover, it was found that the chemoselective oxidation of allylic alcohols having a terminal double bond, such as 1-hexene-3-ol, also proceeded efficiently (Table 2, entry 3). Contrastingly, a previously reported H_2O_2–Pt black system is found to be totally inactive for this substrate, owing to a strong coordination of the –C=CH_2 group to the Pt^0 complex.[16] It is especially noteworthy that H_2O_2–Au/TiO_2 was highly active for the oxidation of primary aliphatic alcohols, the most inactive alcohols, in the absence of any bases (Table 2, entries 4–6). For example, the yield of 1-hexanoic acid in 1-hexanol oxidation was as high as 99% at a 100% conversion.

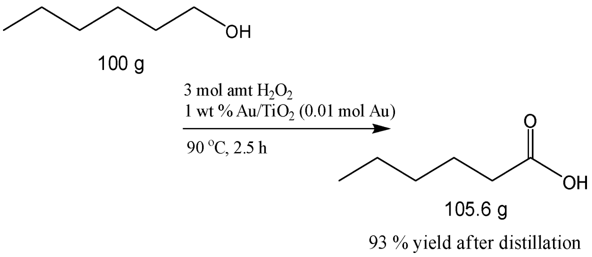
Furthermore, it was found that the H_2O_2-mediated oxidations also proceeded smoothly in a hectogram-scale synthesis to give a high yield of formation of the corresponding carboxylic acids. As shown in Scheme 1, by stirring a mixture of 1-hexanol (100 g) in the presence of a 0.01 molar amount of Au catalyst and 3.0 molar amount of aqueous H_2O_2 (5%) for 2.5 h, 1-hexanoic acid could be obtained in a 93% yield (105.6 g). Notably, this is the first example of a hectogram-scale clean oxidation of alcohols under base-free conditions in neat water using a heterogeneous gold catalysts.

Activated alcohols, such as benzylic alcohols, were also oxidized at 90 °C with H_2O_2 in the presence of Au/TiO_2 to give the corresponding carbonyl compounds in good to excellent yields (Table 3). Like most of the catalysts reported

Table 3 Oxidation of activated alcohols by aqueous H_2O_2[a]

Entry	Substrate	Product	Conv. (%)	Sel. (%)
1[b]			>99	100
2			>99	85[c]
3			>99	44[c]
4			>99	61[c]
5			>99	37.5[c]
6[b]			>99	100

[a] Reaction conditions: 10 mmol substrate, 10 ml H_2O, 90 °C, 5% H_2O_2 added dropwise, substrate:H_2O_2:Au = 100:250:1. [b] Substrate:H_2O_2:Au = 100:150:1. [c] Aldehyde was found as by-product.



Scheme 1 Hectogram-scale oxidation of 1-hexanol.

previously,[6–12] Au/TiO_2 efficiently catalyzed the oxidation of secondary aromatic alcohol, such as 1-phenylpropanol (Table 3, entry 1), almost quantitatively to their target products (~99% yields). Benzyl alcohol was oxidized to benzoic acid at a 100% conversion, although with a selectivity of only 85% (Table 3, entry 2; the other product was mainly benzaldehyde). Benzyl alcohols with electron-donating groups were also successfully oxidized, in which a shift in selectivity from acids to benzaldehydes was observed (Table 3, entries 3–5). It is worth noting that chemoselective oxidation of cinnamyl alcohol with the sole formation of cinnamaldehyde could be accomplished (Table 3, entry 6). Interestingly, an epoxidized compound of cinnamyl alcohol was not observed. All these results clearly showed the efficiency of the H_2O_2–Au/TiO_2 system in the oxidation of both activated and nonactivated alcohols in water.

Attempting to gain insight into the origin of the enhanced activity achieved by using aqueous H_2O_2 as oxidant is important. Although an extensive mechanistic study has not yet been conducted, it is known that the α-hydrogen abstraction of an alcohol may be involved in the rate determining step based on the isotope kinetic study (k_H/k_D = 1.7–2.0).[17] In addition, H_2O_2 was found to be indispensable for the reaction progress as inferred by the data in Fig. 1, which prompted us to propose a possible mechanism of the present H_2O_2–Au-mediated alcohol oxidation, as illustrated in Fig. S8 (ESI).† The key aspect of H_2O_2 is to facilitate the abstraction of the α-hydrogen as a hydrogen scavenger, leading to the formation of a meta-alcoholate species during the initial step of the reaction. The Au-alcoholate complex may be further attacked by H_2O_2 or the Au-hydridoperoxide complex generated from the reaction of Au^0 with H_2O_2, to form the final carbonyl compound *via* a β-elimination pathway. The overall effect is that a dramatically boosted activity for alcohol oxidation is achieved in contrast to the normal aerobic process in which dioxygen or air was used as the oxidant.

In summary, we have demonstrated that the Au/TiO_2 catalyst has great potential for the environmentally benign oxidation of alcohols with aqueous hydrogen peroxide under mild and organic solvent-free conditions. The H_2O_2–Au/TiO_2 protocol has been proven to be particularly efficient in the oxidative transformation of nonactivated alcohols in aqueous media. The stability of the catalyst has also been demonstrated convincingly by conducting five successive runs without a significant drop in the reaction rate. Further extension of the present H_2O_2–Au catalytic system to many other key oxidative transformations is currently being explored.

Acknowledgements

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Notes and references

‡ Without the use of H_2O_2 (under an air atmosphere), acetophenone was obtained in only <10% yield over the Mintek Au/TiO_2 catalyst.

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