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VIP **Heterogeneous Catalysis**

Aerobic Oxidation of Alcohols at Room Temperature and Atmospheric Conditions Catalyzed by Reusable Gold Nanoclusters Stabilized by the Benzene Rings of Polystyrene Derivatives**

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The selective oxidation of alcohols is one of the most important transformations in organic synthesis.[1] Whilst several metal-based oxidizing reagents have been developed, these reagents usually require stoichiometric amounts of metal oxidants, and thus a large amount of waste is formed. In this respect, the oxidation of alcohols using molecular oxygen catalyzed by reusable heterogeneous catalysts is ideal from an environmental and atom-economical point of view.[2] Although the hydroxyapatite (HAP) bound RuHAP[3] and PdHAP,[4] as well as Ru/Al_2O_3,[5] Au/CeO_2,[6] and Au–Pd/TiO_2[7] are excellent catalysts for the aerobic oxidation of alcohols, they work only at high temperatures or under solvent-free conditions in most cases. Oxidation reactions at room temperature in appropriate solvents are necessary for alcohols such as those with high melting points or low stability at high temperatures, but examples of these room-temperature reactions are very limited.[8] Moreover, satisfactory results were obtained in only limited cases when catalysts were reused.[8a] Therefore, the development of reusable catalysts for the liquid-phase aerobic oxidation of alcohols under mild conditions, especially at room temperature, is an attractive and challenging subject in both organic synthesis and green chemistry.

In 1989 Haruta et al. reported the low-temperature oxidation of CO by molecular oxygen using gold nanoclusters,[9] in which a crucial charge transfer from gold nanoclusters to molecular oxygen results in the concomitant activation of the O–O bond to form a superoxo-like state.[10] Although some alcohol oxidations catalyzed by gold nanoclusters have been reported, they usually can be applied only to a very limited range of substrates.[11] Conversely, it is known that aromatic molecules such as benzene can interact weakly with gold surfaces or gold nanoclusters through the π electrons of benzene rings.[12] Therefore, we reasoned that if the gold nanoclusters could be stabilized by weak interactions with the aromatic sections of polymers, these gold nanoclusters might be versatile catalysts that could be used for liquid-phase organic synthesis with a wide range of substrates. Herein we demonstrate a new method for the formation of a size-controllable gold nanocluster catalyst, polymer-incarcerated gold (PI Au), which used multiple interactions with the benzene rings of polymer **1**. The selective aerobic oxidation of alcohols catalyzed by PI Au under air or oxygen atmosphere at room temperature is also reported.

First, we tested whether gold nanoclusters could be stabilized by the π electrons from benzene rings, and chose chlorotriphenylphosphine gold ([$AuClPPh_3$]) as the gold source.[13] This complex was reduced by sodium borohydride ($NaBH_4$) in THF, and the solution immediately turned from colorless to wine red, which implied the formation of gold(0) species. However, after the reaction mixture had been stirred for five minutes, aggregation of the clusters occurred to afford a black precipitate. Aggregation of the clusters also occurred in the presence of toluene. We then added polystyrene as a stabilizing reagent. It was revealed that the solution retained its wine-red color even after it was stirred for 12 h without aggregation of the clusters. Hexane was slowly added to this solution to afford wine-red microencapsulated[14] gold nanoclusters (PSMC Au). TEM analysis showed that PSMC Au contains stabilized gold nanoclusters (1 nm).[13]

On the basis of the results that showed that the gold nanoclusters could be stabilized by the benzene rings of polystyrene, we next decided to use polymer **1**, which contained alcohol and epoxide moieties for cross-linking. The polymer-incarcerated gold nanocluster catalysts (PI Au) were first prepared as shown in Scheme 1.[15] The solution of [$AuClPPh_3$] in a small amount of THF was slowly added to a mixture of polymer **1** and $NaBH_4$ in THF at room temperature. The color of the solution immediately turned wine red. Hexane was then added to form microcapsules, which were filtered, washed, and dried under vacuum. The microcapsules were next heated at 150 °C for 5 hours to cross-link the side chains and then washed with THF and water to afford PI Au (**2**) as a deep-purple solid. Small gold nanoclusters (around 1 nm) were observed by TEM analysis (Figure 1), and elemental analysis showed no contamination from phosphorus.

PI Au nanoclusters **2a** thus prepared were used for the aerobic oxidation of (±)-1-phenylethanol. The reaction proceeded in a dichloromethane/water solvent mixture at room temperature and under oxygen at atmospheric conditions in the presence of **2a** (3 mol %) and potassium carbonate to afford acetophenone quantitatively (Table 1, entry 1). The reaction also proceeded smoothly in toluene/

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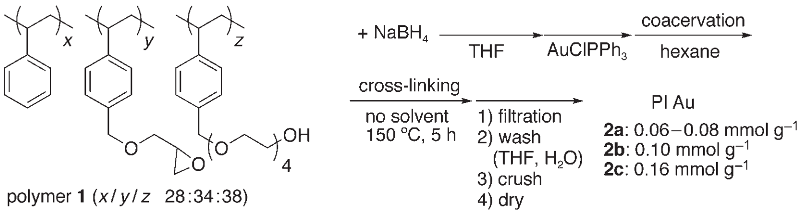


Scheme 1. Synthesis of PI Au **2**.

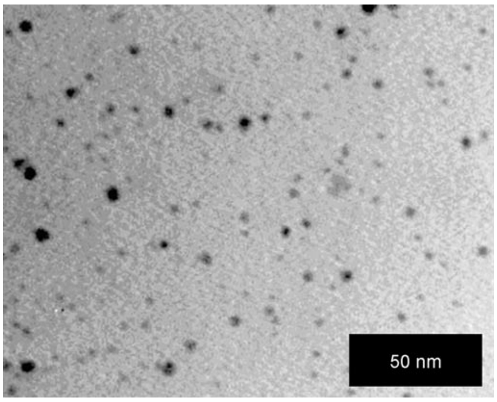
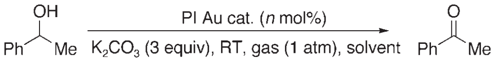


Figure 1. TEM image of the PI Au nanoclusters **2a**.

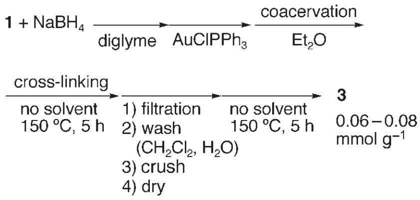
Table 1: Oxidation of (±)-1-phenylethanol using the PI Au nanoclusters.[a]



Entry	PI Au	n	Solvent	t [h]	Gas	Yield[b] [%]
1	**2a**	3	CH_2Cl_2/H_2O 1:1	24	O_2	> 99
2	**2a**	3	toluene/H_2O 1:1	24	O_2	98
3	**2a**	3	BTF/H_2O 1:1	24	O_2	99
4	**2b**	3	BTF/H_2O 1:1	24	O_2	72
5	**2c**	3	BTF/H_2O 1:1	24	O_2	58
6	**2a**	1	BTF/H_2O 1:1	3	O_2	74
7	**3**	1	BTF/H_2O 1:1	3	O_2	96
8	**3**	1	BTF/H_2O 1:1	3	O_2	18 [c]
9	**3**	1	BTF/H_2O 1:1	5	O_2	> 99
10	**3**	1	BTF/H_2O 1:1	5	air	88

[a] Reaction conditions: substrate (0.5 mmol), solvent (6 mL), RT, 1 atm; BTF = benzotrifluoride. [b] Determined by GC analysis. [c] Base-free conditions.

water and benzotrifluoride/water solvent mixtures (entries 2 and 3). It is notable that in all cases no metal leaching was detected by inductively coupled plasma (ICP) analysis (< 0.04 %). Examination of the relationship between the reactivities and the loadings of the gold catalysts revealed that use of a lower loading gave higher activity, which could be rationalized by the fact that a lower catalyst loading contained smaller clusters (compare entries 3–5).[13] Furthermore, it was found that a slight modification of the preparation method of the PI Au nanoclusters (Scheme 2) greatly increased their catalytic activity (entries 6 and 7). It was proved that the reaction was promoted by a base, and the reaction did not proceed at all in the absence of water or base (entry 8). The nanoclusters **3** thus prepared were highly active, and the oxidation reaction reached completion when a catalyst loading of only 1 mol % was used (entry 9). The nanoclusters **3** showed high reactivity even when the reaction was carried out in air rather than under oxygen (entry 10).



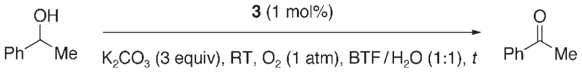
Scheme 2. Synthesis of the PI Au **3**.

The catalyst was recovered by simple filtration and reused without significant loss of activity (Table 2). The recovered catalyst could be heated at 150 °C for 5 hours to facilitate its reuse.

Several alcohols were then oxidized in an oxygen or air atmosphere in the presence of 1–3 mol % of **3**. Aromatic secondary alcohols were oxidized smoothly to afford the corresponding ketones quantitatively (Table 3, entries 1–4). Although aliphatic ketones have relatively low reactivity, the desired ketones were also obtained in high yields by increasing the reaction times or in the presence of a stronger base (entries 5 and 6). Aromatic and allylic primary alcohols were oxidized smoothly in the presence of a weak base to afford the corresponding aldehydes in good yields, although the products were accompanied by small amounts of carboxylic acids or esters (entries 7–9). Moreover, alcohols that contained heteroatoms such as S and N, which are well known to coordinate strongly to gold nanoparticles, could be oxidized smoothly to give the desired ketones in high yields without leaching of the metal (entries 10 and 11).

The PI Au catalyst **3** could also be used for the aerobic oxidation of alcohols under solvent- and base-free conditions. The catalyst showed a very high turnover frequency (TOF) of an average $2.0 \times 10^4\ h^{-1}$ at 160 °C after the initial 30 minutes (Scheme 3), which exceeded that achieved by the Au/CeO_2 catalyst.[6]

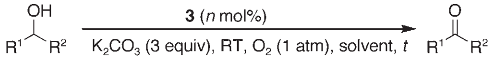
Table 2: Recovery and reuse of PI Au **3**.

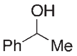
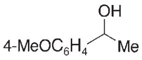
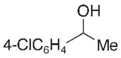
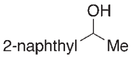
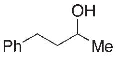
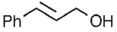
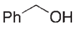
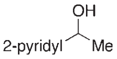
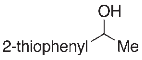


Entry	t [h]	Use						
		1st [%]	2nd [%]	3rd [%]	4th [%]	5th [%]	6th [%]	7th [%]
1	24	> 99	> 99	94	98[a]	> 99	92	> 99[a]
2	12	> 99	> 99[a]	> 99[a]	> 99[a]	> 99[a]	99[a]	> 99[a,b]

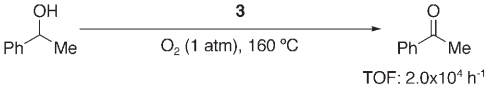
[a] The recovered catalyst was heated at 150 °C for 5 h without solvent in air before use. [b] 8th: > 99 %, 9th: 99 %, 10th: > 99 %.

Table 3: Oxidation of various alcohols catalyzed by **3**.



Entry	Substrate	*n*	Base	Solvent	*t* [h]	Yield[a] [%]
1		1	K_2CO_3	BTF/H_2O 1:1	5	> 99
2		1	K_2CO_3	BTF/H_2O 1:1	5	> 99
3		1	K_2CO_3	BTF/H_2O 1:1	5	91
4		1	K_2CO_3	BTF/H_2O 1:1	5	> 99
5		1	K_2CO_3	BTF/H_2O 1:1	30	95
6	cyclopentanol	1	KOH	BTF/H_2O 1:1	30	> 99
7		1	K_2CO_3	BTF/H_2O 1:1	12	64
8		1	Cs_2CO_3	diglyme	15	79
9		2	K_2CO_3	BTF/H_2O 1:1	5	78
10		3	K_2CO_3	BTF/H_2O 1:1	24	> 99
11		1	K_2CO_3	BTF/H_2O 1:1	24	94

[a] Determined by GC analysis.



Scheme 3. Average TOF for the oxidation of (±)-1-phenylethanol for the initial 0.5 h of reaction (ratio of moles of acetophenone per mole of Au per hour). Reaction conditions: (±)-1-phenylethanol (29.3 mmol), 6.1×10^{-4} mol% (substrate to catalyst ratio). Yield after 0.5 h was 6.1%.

The uptake of oxygen was measured under the reaction conditions with of (±)-1-phenylethanol (15.6 mmol), **2a** (0.0048 mol%), anisole (1.0 mL), and KOH (10 mol%). It was found that almost 0.5 moles of oxygen was used compared to the formation of 1 mole of the oxidation product in the course of the reaction.[13] From these results, it was concluded that water was formed as a coproduct in the presence of PI Au, although hydrogen peroxide might have been formed, which then decomposed to water and oxygen.[16]

In summary, we have developed gold nanoclusters that are stabilized by multiple interactions with the benzene rings of polystyrene. This is the first successful example of a stabilization of gold nanoclusters using such interactions. These nanoclusters catalyzed the aerobic oxidation of several alcohols efficiently at room temperature under atmospheric conditions, in which only oxygen was consumed and water produced as a sole coproduct. Moreover, the catalyst was easily recoverable and could be reused several times without leaching of metals or loss of activity. Further investigations of the application of this catalyst to other oxidation processes as well as to clarify the precise mechanism of this oxidation process are currently in progress.

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