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Aerobic oxidative transformation of primary alcohols and amines to amides promoted by a hydroxyapatite-supported gold catalyst in water

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ABSTRACT

In the presence of an easily prepared hydroxyapatite-supported gold catalyst, namely Au/HAP, various kinds of structurally diverse primary alcohols including benzylic and aliphatic ones, and amines involving aromatic and secondary ones could be converted into the corresponding amides in water with up to 99% yield. Meanwhile, on the basis of experimental observations and literatures, a plausible reaction pathway was described to elucidate the reaction mechanism.

Introduction

Amide groups are among the highly important and abundant functional groups in chemistry and can be found in the pharmaceutical industry, natural products, and materials science.[1] The traditional synthesis of amides involves carboxylic acids and their derivatives, often using promoters, organic solvents, or coupling reagents and leading to much waste.[2] Great efforts have been made to update this old process.[3] In this context, the direct catalytic aerobic oxidative coupling of alcohols and amines to form amides in the presence of heterogeneous catalysts represents a step forward toward green, economic, and sustainable process.[4] Nevertheless there are few efficient examples despite offering significant advantages from an environmental standpoint. In 2011, Wang et al. demonstrated the first highly efficient amide synthesis from aromatic alcohols and amines by a water-soluble gold/DNA catalyst.[4b] Meanwhile, Kobayashi and co-workers introduced powerful PICB (polymer-incarcerated carbon black)-supported Au/Co bimetallic catalysts for the reaction to afford various amides with good to excellent yields.[4c] However, tedious procedure for the catalyst synthesis or organic solvent was involved in these cases. Furthermore, organic synthesis reactions using water as solvent have some significant advantages: low cost, abundance, safety, and easy separation because most of organic products are water-insoluble. Thus, searching for facile catalysts that could achieve high reactivity and selectivity in water and extending the substrate scope (especially for aliphatic alcohols) are highly desirable and challenging in this field.

On the other hand, heterogeneous catalysts based on supported gold nanoparticles have attracted considerable research interest because of their unique catalytic properties for a broad array of organic transformations.[5] Recently, we have been interested in unique catalytic activities and selectivities of supported gold nanoparticle catalysts and involved in their application for fine chemical synthesis.[4i,6] With our ongoing interest in this area, herein, we wish to demonstrate that gold nanoparticle supported on hydroxylapatite (HAP: $Ca_{10}(PO_4)_6(OH)_2$) can act as a highly efficient heterogeneous catalyst for the aerobic oxidative transformation of primary alcohols and amines to amides under aqueous conditions. Our Au/HAP is applicable to various alcohols and amines, particularly for aliphatic alcohols, which are notoriously difficult to oxidize, with up to 99% yield.

Preparation of the Au/HAP catalyst and optimization of the reaction conditions

Initially, we selected the oxidative coupling reaction of ethanol **1a** and aniline **2a** as the model reaction, which would readily give access to acetanilide **3a**, an important intermediate in pharmaceutical industry. Different gold catalysts were tested in water at a mild temperature of 40 °C with NaOH as the base under O_2 atmosphere. Table 1 summarizes some results obtained during the

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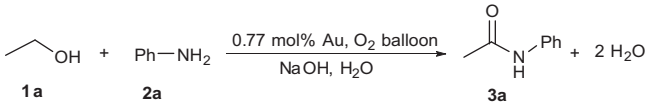
optimization of the reaction. Acetanilide **3a** was formed in a yield of 46% (Table 1, entry 1) with the catalyst Au/TiO_2 (average gold particle size ca. 3.5 nm, supplied by the World Gold Council). Prompted by this result, we examined a series of catalysts with Au on other inorganic supports, such as Fe_2O_3, hydrotalcite, HAP, CeO_2, and ZnO. Among them, Au/HAP showed the highest catalytic activity for the transformation with up to 99% yield (Table 1, entry 6 vs entries 1–5). Other reaction parameters were also screened including base and catalyst loading, and no further improvement could be achieved with this catalyst (Table 1, entries 7–9). The Au/HAP was prepared with homogeneous deposition precipitation (HDP)-$NaBH_4$ reduction method[7] and characterized by X-ray Powder Diffraction (XRD) and HAADF-STEM analysis. As shown in Figure 1, the XRD peak positions of the Au/HAP were similar to those of a parent HAP, and no diffraction peak of Au was observed, implying that Au nanoparticles were highly dispersed on HAP. HAADF-STEM images of the Au/HAP catalyst showed gold particles with an average size of 2.8 nm were uniformly dispersed on the support (Fig. 2). The loading of Au was determined to be 1.69 wt % by inductively coupled plasma-atomic emission spectrometry (ICP-AES). In addition, the use of Au(III)/HAP and HAP

Table 1
Reaction condition screening



Entry[a]	Catalysts	Temp (°C)	*T* (h)	Yield[b] (%)
1	Au/TiO_2 (1.5 wt %)	40	20	46
2	Au/Fe_2O_3 (4 wt %)	40	20	42
3	Au/CeO_2 (2 wt %)	40	24	29
4	Au/ZnO (1 wt %)	40	20	22
5	Au/HT (2 wt %)	40	24	45
6	Au/HAP (1.69 wt %)	40	24	99
7[c]	Au/HAP (1.69 wt %)	40	24	55
8[d]	Au/HAP (1.69 wt %)	40	24	20
9[e]	Au/HAP (1.69 wt %)	40	24	71
10[f]	Au(III)/HAP	40	24	N.R.
11[f]	HAP	40	24	N.R.
12[g]	Au/HAP (1.69 wt %)	40	24	Trace
13[h]	Au/HAP (1.69 wt %)	40	24	Trace

[a] Unless otherwise noted, reactions were carried out with **1a** (10 mmol), aniline **2a** (0.5 mmol), 0.77 mol % Au, and NaOH (0.5 mmol) in H_2O (0.5 mL) at 40 °C under oxygen balloon.
[b] Isolated yields.
[c] 0.3 equiv NaOH was used.
[d] 0.18 mol % Au was used.
[e] 5.0 mmol **1a** was used.
[f] N.R. = no reaction.
[g] Without NaOH.
[h] In the presence of N_2.

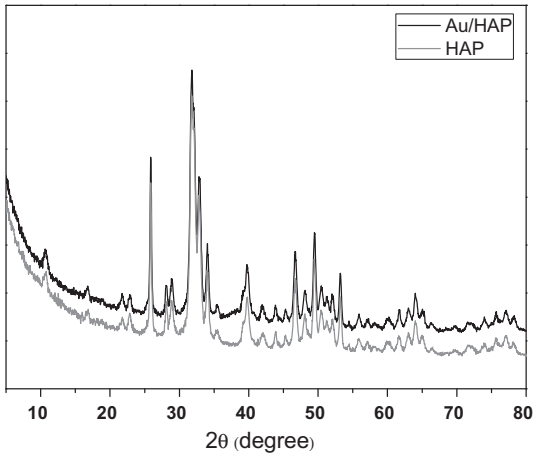


Figure 1. XRD patterns of HAP and Au/HAP.

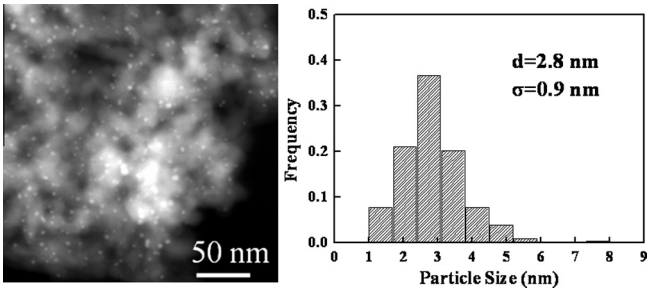
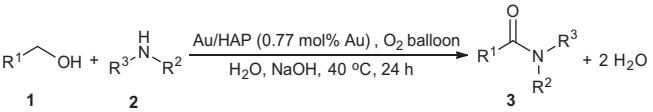


Figure 2. HAADF-STEM image of Au/HAP (Au: 1.69 wt %) and histogram of the Au particle size distribution.

Table 2
The substrate scope for the reaction[a]



Entry	R^1	R^2	R^3	Product	Yield[b] (%)
1	Me	Ph	H	**3a**	99
2	Et	Ph	H	**3b**	97
3	Pr	Ph	H	**3c**	98
4	Bu	Ph	H	**3d**	89
5	$CH_3(CH_2)_4$	Ph	H	**3e**	96
6	$CH_3(CH_2)_6$	Ph	H	**3f**	72
7	*i*-Pr	Ph	H	**3g**	91
8	Cy	Ph	H	**3h**	85
9	Me	3-$MeOC_6H_4$	H	**3i**	93
10	Me	2-$MeOC_6H_4$	H	**3j**	79
11	Me	3-MeC_6H_4	H	**3k**	88
12	Me	2-MeC_6H_4	H	**3l**	68
13	Me	Bn	H	**3m**	91
14	Ph	Ph	H	**3n**	94
15	4-MeC_6H_4	Ph	H	**3o**	93
16	3-MeC_6H_4	Ph	H	**3p**	70
17[c]	2-MeC_6H_4	Ph	H	**3q**	73
18	4-*i*-PrC_6H_4	Ph	H	**3r**	87
19	4-$MeOC_6H_4$	Ph	H	**3s**	99
20	3-$MeOC_6H_4$	Ph	H	**3t**	74
21	3,4-OCH_2O-C_6H_3	Ph	H	**3u**	65
22	4-FC_6H_4	Ph	H	**3v**	71
23	4-ClC_6H_4	Ph	H	**3w**	76
24	2-Furyl	Ph	H	**3x**	50
25	2-Pyridyl	Ph	H	**3y**	71
26	Ph	Bn	H	**3z**	89
27	Ph	4-MeC_6H_4	H	**3aa**	61
28	Ph	3-$MeOC_6H_4$	H	**3ab**	85
29[d]	Ph	Me	Me	**3ac**	90
30[d]	4-$MeOC_6H_4$	Me	Me	**3ad**	98
31[d,e]	2-Naphthyl	Me	Me	**3ae**	87
32[d]	4-BrC_6H_4	Me	Me	**3af**	96
33[d]	Ph	H	H	**3ag**	60
34[d]	4-$MeOC_6H_4$	H	H	**3ah**	67

[a] Unless otherwise noted, reactions were carried out with alcohol **1** (1–10 mmol), amine **2** (0.5 mmol), 0.77 mol % Au/HAP, and NaOH (0.5 mmol) in H_2O (0.5 mL) at 40 °C under oxygen balloon for 24 h.
[b] Isolated yields.
[c] 1.54 mol % Au/HAP.
[d] Reactions were carried out with alcohol **1** (0.5 mmol), amine **2** (10 mmol), 0.77 mol % Au/HAP, and NaOH (0.5 mmol) in H_2O (0.5 mL) at 25 °C under oxygen balloon for 24 h.
[e] *t*-BuOH (5.0 mmol) was added to improve the solubility of alcohol.