# Efficient Synthesis of Amides and Esters from Alcohols under Aerobic Ambient Conditions Catalyzed by a Au/ Mesoporous Al<sub>2</sub>O<sub>3</sub> Nanocatalyst

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An efficient heterogeneous Au/mesoporous alumina nanocatalyst has been successfully developed for the synthesis of amides and esters from simple building blocks of readily available alcohols and amines. The processes were simple and were performed at room temperature and atmospheric pressure of  $O_2$  to form the desired products with up to 97% isolated yield. The ability of Au/mesoporous alumina to catalyze these reactions under ambient conditions further enhances the sustaina-

#### Introduction

Amides and esters are important functional groups found extensively in fine chemicals, pharmaceuticals, natural products, and materials.<sup>[1]</sup> For example, the amide bond is crucial in the formation of proteins as well as critical drugs such as antibiotics (e.g., penicillin), antiviral drugs (e.g., Tamiflu), statins (e.g., Lipitor), and anesthetics (e.g., bupivacaine). Ester bonds are found widely in the production of biodegradable polymers (e.g., polylactic acid), thermoplastics (e.g., polyethylene terephthalate), and analgesics (e.g., aspirin). Amides and esters are usually produced by the reaction of carboxylic acids (after conversion to activated derivatives, such as acid chlorides or anhydrides) with amines and alcohols, respectively.<sup>[2]</sup> These traditional synthetic methods involve the use of stoichiometric quantities of toxic and reactive coupling reagents, which thus results in a high cost and excessive chemical waste generation.

The development of more sustainable and environmentally friendly methodologies for amide<sup>[3–5]</sup> and ester<sup>[6–8]</sup> bond formation has been reported by different research groups in recent years. These include the direct amidation of aldehydes,<sup>[4a]</sup> hydration of nitriles,<sup>[4f]</sup> and oxidative coupling of alcohols and amines<sup>[5]</sup> for amide bond formation, and the esterification of aldehydes<sup>[6]</sup> and oxidative esterification of alcohols<sup>[6a,7,8]</sup> for ester bond formation. Of these reported methods, the oxidative coupling of alcohols and amines to produce amides and the oxidative esterification of alcohols to produce esters are of particular interest as these systems use readily available alcohols and amines as the starting materials, oxygen as the inexpensive and environmentally friendly oxidant, and heterogeneous

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bility of these chemical processes. Furthermore, the nanocatalyst was stable to air and water and could be recovered and reused easily. The enhanced catalytic activity of Au/mesoporous alumina might be attributed to the presence of negatively charged Au nanoparticles that could promote oxidation processes as well as the stability of the mesoporous alumina support calcined at a high temperature of 800 °C.

catalysts, which offer several advantages, such as high reactivity, ease of handling, air- and water-stability, and reusability.<sup>[9]</sup>

For the oxidative amidation of alcohols with amines, Aubased nanomaterials have been developed to produce the desired amides in good to excellent yields.<sup>[5]</sup> However, these reported systems still present certain drawbacks, such as the use of a high Au loading (3.8 mol% Au),<sup>[5e]</sup> the application of heat (40–65 °C) for reaction completion,<sup>[5]</sup> the use of organic solvents,<sup>[5a-c]</sup> and additional heat activation (170 °C for 4–5 h) for the reuse of the recycled catalyst.<sup>[5b,c]</sup> To improve the sustainability of this chemical process, the catalytic reaction should be performed under ambient conditions using a low catalyst loading. The recovery and reuse of the catalyst should also be achieved without an additional heat activation procedure.

For the reported Au-based catalytic systems involved in the oxidative esterification of alcohols, some shortcomings include the use of high temperatures (70–130 °C) and O<sub>2</sub> pressures (3–10 bar)<sup>[8b–d]</sup> and a long reaction time (24 h) for a room-temperature, atmospheric O<sub>2</sub> pressure system.<sup>[8a]</sup>

We are interested in the engineering of nanocatalysts that can perform multiple catalytic reactions with high atom efficiencies, yields, and selectivities within a one-pot system, which could lead to green and sustainable chemical processes.<sup>[10]</sup> Herein we report the development of Au nanoparticles supported on mesoporous alumina for the efficient synthesis of amides and esters from simple building blocks of alcohols and amines under aerobic ambient conditions using a low Au catalyst loading.

#### **Results and Discussion**

The support material, mesoporous alumina,<sup>[11]</sup> was synthesized by evaporation-induced self-assembly between the inorganic aluminum isopropoxide precursor and the organic surfactant,

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163 to 172, 48, and  $114 \text{ m}^2\text{g}^{-1}$ . Al<sub>2</sub>O<sub>3</sub>-3-700 has the lowest BET surface area, possibly because of the incomplete pyrolysis of organics that results in the formation of a coating on the alumina, as seen from the inhomogeneous grayish-black solid obtained after calcination at 700 °C (Fig-

Pluronic P123, as a soft template, with 1,3,5-triisopropylbenzene (TIPB) as the swelling agent. After the vigorous mixing of the reaction mixture in ethanol under acidic conditions at room temperature (RT) for 12 h, the mixture was kept under static conditions at 45 and 60 °C for one and two days, respectively. The resulting white solid was calcined in air for 4 h to yield the desired product. Six different samples of mesoporous alumina (Table 1) were prepared by varying the weight ratio of TIPB/P123 (1, 2, and 3) and the calcination temperature (500, 600, 700, and 800 °C). sponding increase in the BET surface area of the mesoporous alumina samples ( $Al_2O_3$ -3-800: 114 m<sup>2</sup>g<sup>-1</sup>,  $Al_2O_3$ -2-800: 165 m<sup>2</sup>g<sup>-1</sup>, and  $Al_2O_3$ -1-800: 187 m<sup>2</sup>g<sup>-1</sup>). Conversely, the average pore width decreased from 21.7 to 19.8 and 14.5 nm with a decrease in the weight ratio of TIPB/P123 from 3 to 2 and 1 after calcination at 800 °C. At a fixed TIPB/P123 weight ratio of 3, there was a slight increase in the average pore width (from 16.9 to 21.7 nm) if the calcination temperature was increased from 500 to 800 °C. Correspondingly, as the calcination temperature increased from 500 to 600, 700, and 800 °C, the BET surface area changed from

Table 1. Characteristics of mesoporous $Al_2O_3$ materials as analyzed by $N_2$ adsorption-desorption isotherms.							
Sample	Weight ratio TIPB/P123	Calcination temperature [°C]	Average pore width [nm]	Cumulative pore volume [cm <sup>3</sup> g <sup>-1</sup> ]	BET surface area [m <sup>2</sup> g <sup>-1</sup> ]		
Al <sub>2</sub> O <sub>3</sub> -3-500	3	500	16.9	0.64	163		
Al <sub>2</sub> O <sub>3</sub> -3-600	3	600	17.6	0.72	172		
Al <sub>2</sub> O <sub>3</sub> -3-700	3	700	18.5	0.24	48		
Al <sub>2</sub> O <sub>3</sub> -3-800	3	800	21.7	0.61	114		
Al <sub>2</sub> O <sub>3</sub> -2-800	2	800	19.8	0.83	165		
Al <sub>2</sub> O <sub>3</sub> -1-800	1	800	14.5	0.74	187		

Large mesopores were observed in the TEM images of the mesoporous alumina samples synthesized with a TIPB/P123 weight ratio of 3 (Figure 1a–d), independent of the calcination temperature. At the same calcination temperature of 800 °C, if the weight ratio of TIPB/P123 was decreased from 3 to 2 or 1, the large porous structure was no longer observed in the TEM images (cf. Figure 1 d with Figure 1e–f). The TEM energy dispersive X-ray (EDX) spectra of the six mesoporous alumina samples (Figure S1a–f) showed strong signals for Al and O, which verifies the elemental composition of the alumina samples.

No XRD peaks were observed in the XRD patterns of the mesoporous alumina calcined at 500 and 600 °C (Al<sub>2</sub>O<sub>3</sub>-3-500 and Al<sub>2</sub>O<sub>3</sub>-3-600, respectively; Figure 2 a and b), which confirms their amorphous structure. Three very weak diffraction peaks (indexed to the 311, 400, and 440 reflections of  $\gamma$ -Al<sub>2</sub>O<sub>3</sub>, JCPDS 10-0425) were seen in the XRD pattern of the sample calcined at 700 °C (Al<sub>2</sub>O<sub>3</sub>-3-700; Figure 2 c). With an increase of the calcination temperature to 800 °C, crystalline peaks (indexed to the 311, 222, 400, 511, 440, and 444 reflections of  $\gamma$ -Al<sub>2</sub>O<sub>3</sub>, JCPDS 10-0425) were clearly observed in the XRD patterns of Al<sub>2</sub>O<sub>3</sub>-3-800, Al<sub>2</sub>O<sub>3</sub>-2-800, and Al<sub>2</sub>O<sub>3</sub>-1-800 (Figure 2 d-f). The low-angle XRD patterns of the six mesoporous alumina samples displayed a single broad peak at  $2\theta < 2^{\circ}$  (Figure S2), which suggests the presence of a mesostructure that was disordered.<sup>[12]</sup>

The N<sub>2</sub> adsorption-desorption isotherms of Al<sub>2</sub>O<sub>3</sub>-3-500, Al<sub>2</sub>O<sub>3</sub>-3-600, Al<sub>2</sub>O<sub>3</sub>-3-800, Al<sub>2</sub>O<sub>3</sub>-2-800, and Al<sub>2</sub>O<sub>3</sub>-1-800 displayed typical type IV curves with H1 hysteresis (Figure 3 a, b, d-f).<sup>[13]</sup> For the sample calcined at 700 °C (Al<sub>2</sub>O<sub>3</sub>-3-700), the N<sub>2</sub> adsorption-desorption isotherm exhibited an H3 hysteresis loop (Figure 3 c). The adsorption parameters of the mesoporous alumina samples shown in Figure 3 are summarized in Table 1. At a fixed calcination temperature of 800 °C, if the weight ratio of TIPB/P123 was decreased, there was a corre-



**Figure 1.** TEM images of mesoporous alumina with different TIPB/P123 weight ratios and calcination temperatures: a)  $Al_2O_3$ -3-500, b)  $Al_2O_3$ -3-600, c)  $Al_2O_3$ -3-700, d)  $Al_2O_3$ -3-800, e)  $Al_2O_3$ -2-800, and f)  $Al_2O_3$ -1-800. Scale bar = 40 nm.



Figure 2. XRD patterns of various mesoporous alumina samples: a)  $Al_2O_3$ -3-500, b)  $Al_2O_3$ -3-600, c)  $Al_2O_3$ -3-700, d)  $Al_2O_3$ -3-800, e)  $Al_2O_3$ -2-800, and f)  $Al_2O_3$ -1-800.



Figure 3. N<sub>2</sub> adsorption–desorption isotherms of various mesoporous alumina samples: a) Al<sub>2</sub>O<sub>3</sub>-3-500, b) Al<sub>2</sub>O<sub>3</sub>-3-600, c) Al<sub>2</sub>O<sub>3</sub>-3-700, d) Al<sub>2</sub>O<sub>3</sub>-3-800, e) Al<sub>2</sub>O<sub>3</sub>-2-800, and f) Al<sub>2</sub>O<sub>3</sub>-1-800.

Thermogravimetric analysis (TGA) and derivative thermogram (DTG) curves of the as-synthesized alumina sample prepared with a TIPB/P123 weight ratio of 3 exhibited four weight loss steps (Figure S4). A small weight loss of 4.5 wt% between 50 and 100 °C could be ascribed to the desorption of adsorbed water and volatile organic molecules. The decomposition of Pluronic P123 and other organic compounds at ~170 and ~300 °C led to substantial weight losses of 8.3 and 30.3 wt%, respectively. The 17.2 wt% loss at ~470 °C could be caused by dehydroxylation upon the conversion of aluminum oxide hydroxide into alumina.<sup>[14]</sup>

The six mesoporous alumina samples were employed as supports for Au catalysts. Au/mesoporous  $Al_2O_3$  nanocatalysts were prepared by the reduction of  $HAuCI_4$  in water with  $NaBH_4$  in the presence of L-lysine and mesoporous alumina. The Au loadings on the Au/mesoporous  $Al_2O_3$  nanocatalysts were de-

termined by inductively coupled plasma mass spectrometry (ICP-MS) and ranged from 0.7 wt% to 1.0 wt%. The presence of Au in these nanocatalysts was further confirmed by TEM-EDX analysis (Figure S5). Depending on the mesoporous alumina support used, the Au nanoparticles were 2–11 nm in diameter (Figure 4), and the average particle sizes of Au were 5.5–6.1 nm (Figure S6).



Figure 4. TEM images of a) Au/Al<sub>2</sub>O<sub>3</sub>-3-500, b) Au/Al<sub>2</sub>O<sub>3</sub>-3-600, c) Au/Al<sub>2</sub>O<sub>3</sub>-3-700, d) Au/Al<sub>2</sub>O<sub>3</sub>-3-800, e) Au/Al<sub>2</sub>O<sub>3</sub>-2-800, and f) Au/Al<sub>2</sub>O<sub>3</sub>-1-800 nanocatalysts. Scale bar = a-c, e-f) 40 and d) 20 nm.

The XRD patterns of the six Au/mesoporous Al<sub>2</sub>O<sub>3</sub> nanocatalysts are shown in Figure 5. For Au/Al<sub>2</sub>O<sub>3</sub>-3-500, Au/Al<sub>2</sub>O<sub>3</sub>-3-600, and Au/Al<sub>2</sub>O<sub>3</sub>-3-700 (Figure 5 a–c), the alumina support was amorphous, but crystalline peaks were observed for Au at  $2\theta = 38.1^{\circ}$  (indexed to the 111 reflection of Au (JCPDS 4-0784)). The XRD patterns of Au/Al<sub>2</sub>O<sub>3</sub>-3-800, Au/Al<sub>2</sub>O<sub>3</sub>-2-800, and Au/Al<sub>2</sub>O<sub>3</sub>-1-800 nanocatalysts consisted of peaks associated with  $\gamma$ -Al<sub>2</sub>O<sub>3</sub> nanocrystals and Au nanocrystals (Figure 5 d–f).

X-ray photoelectron spectroscopy (XPS) was used to determine the surface chemistry of the Au nanocrystals in the six Au/mesoporous  $Al_2O_3$  nanocatalysts. The Au4f XPS spectra (Figure 6) for all the nanocatalysts could be curve-fitted to one set of doublets. The Au4f<sub>7/2</sub> peak of the six Au/mesoporous



Figure 5. XRD patterns of a) Au/Al\_2O\_3-3-500, b) Au/Al\_2O\_3-3-600, c) Au/Al\_2O\_3-3-700, d) Au/Al\_2O\_3-3-800, e) Au/Al\_2O\_3-2-800, and f) Au/Al\_2O\_3-1-800 nanocatalysts.



Figure 6. XPS patterns of a) Au/Al\_2O\_3-3-500, b) Au/Al\_2O\_3-3-600, c) Au/Al\_2O\_3-3-700, d) Au/Al\_2O\_3-3-800, e) Au/Al\_2O\_3-2-800, and f) Au/Al\_2O\_3-1-800.

alumina nanocatalysts (binding energy (BE) = 83.5-83.7 eV) was lower than the BE = 84.0 eV value for bulk metallic gold (Au<sup>0</sup>). A negative shift to lower BE could be because of the nanocrystal size effect (which results from an increase in the number of low-coordinated Au surface atoms) or an electron transfer from the metal oxide support to the Au nanoparticles.[15-16] Lower Au4f<sub>7/2</sub> BEs than that of bulk Au have been reported for Au nanocrystals on  $\gamma$ -Al<sub>2</sub>O<sub>3</sub> (BE = 83.7 eV),<sup>[15b]</sup> Au nanocrystals on  $MoO_x$  (BE = 82.9 eV),<sup>[16a]</sup> Au clusters stabilized by poly(Nvinyl-2-pyrrolidinone) (BE = 82.7 eV),<sup>[16b]</sup> and poly(N-vinyl-2-pyrrolidinone)-capped micrometer-sized Au plates (BE =83.6 eV).<sup>[15d]</sup> The lower Au4f<sub>7/2</sub> BEs in these reports were attributed to the negative charge states of Au. Hence, for our Au/ mesoporous alumina nanocatalysts, the negative shift of the Au  $4f_{7/2}$  peak likely arose from an electron transfer from the alumina support to the Au nanocrystals.

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$\square$	`ОН <sub>+</sub>	<u>).5 or 1 mol% Au ca</u> LiOH, H <sub>2</sub> O O <sub>2</sub> , RT, 14 h		
1a	2a		3a	
Entry	Catalyst	Au [mol%]	Au loading [wt%] <sup>[b]</sup>	Yield <sup>[c]</sup> [%]
1	Au/Al <sub>2</sub> O <sub>3</sub> -3-500	0.5	0.7	85
2	Au/Al <sub>2</sub> O <sub>3</sub> -3-500	1.0	0.7	88
3	Au/Al <sub>2</sub> O <sub>3</sub> -3-600	0.5	0.7	83
4	Au/Al <sub>2</sub> O <sub>3</sub> -3-600	1.0	0.7	84
5	Au/Al <sub>2</sub> O <sub>3</sub> -3-700	0.5	0.9	76
6	Au/Al <sub>2</sub> O <sub>3</sub> -3-700	1.0	0.9	76
7	Au/Al <sub>2</sub> O <sub>3</sub> -3-800	0.5	1.0	96
8	Au/Al <sub>2</sub> O <sub>3</sub> -3-800	1.0	1.0	98
9	Au/Al <sub>2</sub> O <sub>3</sub> -2-800	0.5	0.8	95
10	Au/Al <sub>2</sub> O <sub>3</sub> -2-800	1.0	0.8	97
11	Au/Al <sub>2</sub> O <sub>3</sub> -1-800	0.5	0.9	94
12	Au/Al <sub>2</sub> O <sub>3</sub> -1-800	1.0	0.9	96
13	Al <sub>2</sub> O <sub>3</sub> -3-500	-	-	0
14	Al <sub>2</sub> O <sub>3</sub> -3-600	-	-	0
15	Al <sub>2</sub> O <sub>3</sub> -3-700	-	-	0
16	Al <sub>2</sub> O <sub>3</sub> -3-800	-	-	0
17	Al <sub>2</sub> O <sub>3</sub> -2-800	-	-	0
18	Al <sub>2</sub> O <sub>3</sub> -1-800	-	-	0
19	HAuCl <sub>4</sub> ·3 H <sub>2</sub> O	1.0	-	0
20	no catalyst	-	-	0
[a] Reaction benzyl alco with O <sub>2</sub> for	n conditions: Au catal bhol (0.1 mmol), LiOF	yst (0.5 or 1 m I (0.1 mmol), a	iol%), aniline (0.05 and H <sub>2</sub> O (0.2 mL, mined by ICP-MS	o mmol), purged analysis

Table 2. Amidation of benzyl alcohol with aniline over Au/mesoporous

The six Au/mesoporous alumina nanocatalysts were investigated for their activities in the direct oxidative amidation of alcohols with amines using the model substrates benzyl alcohol and aniline under ambient conditions (Table 2). The initial screening experiments showed that with a catalyst loading of 0.5 mol% Au, LiOH as the base, water as the solvent, and a reaction time of 14 h at RT under an O<sub>2</sub> atmosphere, three of the six nanocatalysts, that is,  $Au/Al_2O_3$ -3-800,  $Au/Al_2O_3$ -2-800, and Au/Al<sub>2</sub>O<sub>3</sub>-1-800, provided excellent yields of 94–96% (Table 2, entries 7, 9, and 11). An increase of the catalyst loading to 1.0 mol% Au resulted in a slightly improved yield of the desired product (96-98%; Table 2, entries 8, 10, and 12). The amidation reaction did not proceed in the absence of the Au/mesoporous alumina nanocatalyst (Table 2, entry 20) or in the presence of the mesoporous alumina support alone (Table 2, entries 13-18). If the homogeneous Au salt (HAuCl<sub>4</sub>) was used as a catalyst (Table 2, entry 19), no amide was detected in the GC-MS analysis of the reaction mixture.

[c] GC-MS yield based on aniline using n-dodecane as an internal stan-

The reactivity of the six Au/mesoporous alumina nanocatalysts could be correlated to the stability of these materials in the solvent (water). The physical state of the three most active nanocatalysts, Au/Al<sub>2</sub>O<sub>3</sub>-3-800, Au/Al<sub>2</sub>O<sub>3</sub>-2-800, and Au/Al<sub>2</sub>O<sub>3</sub>-1-800, remained unchanged if the materials were left suspended in water for 24 h (Figure S7). These three nanocatalysts were prepared with supports that crystallized as  $\gamma$ -Al<sub>2</sub>O<sub>3</sub> after calcination at 800 °C. In contrast, the less active nanocatalysts, Au/

dard.



Al<sub>2</sub>O<sub>3</sub>-3-500, Au/Al<sub>2</sub>O<sub>3</sub>-3-600, and Au/Al<sub>2</sub>O<sub>3</sub>-3-700 (prepared with amorphous alumina supports calcined at 500, 600, and 700 °C), started to aggregate if they were left in contact with water for one day (Figure S7). Similar results were attained if the six Au/mesoporous alumina nanocatalysts were suspended in 0.5  $\kappa$  LiOH aqueous solution for 14 h (Figure S8). This aggregation could reflect a less stable dispersion of the nanocatalysts in water, which led to lower catalytic activities.

The stability of the six mesoporous alumina supports in aqueous LiOH solution was also investigated by stirring the support materials in 0.5 M LiOH. Very small quantities of Al (1–3%) were leached into the aqueous solution after 14 h at RT (Table S1). Similarly, minor amounts of Al (2–4%) were detected in the aqueous reaction media after the amidation reaction with the six Au/mesoporous alumina nanocatalysts (Table S2).

The recyclability of the three most active nanocatalysts, Au/ Al<sub>2</sub>O<sub>3</sub>-3-800, Au/Al<sub>2</sub>O<sub>3</sub>-2-800, and Au/Al<sub>2</sub>O<sub>3</sub>-1-800, was investigated by the recovery of the materials by centrifugation after the addition of ethyl acetate followed by washing with ethyl acetate three times. The nanocatalysts recovered by centrifugation were dried by using a rotary evaporator before use in a subsequent run. Although there was a gradual decrease in the activities of the three nanocatalysts upon recycling, 85– 91% yield was still achieved in the sixth run (Table 3). There was no change in the size of the Au nanocrystals after six runs

of the amidation reaction, as confirmed by TEM (Figure S9a). There was also no significant change in the position of the Au 4f XPS peaks after the reaction (Figure S10b). Hence, the gradual decrease in the product yield might be attributed to some loss of the nanocatalysts in the recovery process.

Optimization of the reaction conditions for the direct amidation reaction was performed using the most active nanocatalyst, Au/Al<sub>2</sub>O<sub>3</sub>-3-800. Different reaction conditions such as solvent, base, reaction temperature, and amount of reactants used were investigated (Table 4). Among the 10 solvents tested (Table 4, entries 1–10), water was found to be the best solvent for this reaction (94%, Table 4, entry 1). The use of the stronger base NaOH or KOH resulted in lower yields of the product (42-78%; Table 4, entries 11-12), and very little or no product was obtained if weak bases such as K<sub>2</sub>CO<sub>3</sub> and Cs<sub>2</sub>CO<sub>3</sub> were employed (0–1%; Table 4, entries 13-14). Lower yields of the

Table 3. Recycling of Au/Al\_2O\_3-3-800, Au/Al\_2O\_3-2-800, and Au/Al\_2O\_3-1-800 in the amidation of benzyl alcohol with aniline  $^{\rm [a]}$ 

Nanocatalyst	Yield of product on successive runs [%] <sup>[b]</sup>					
	1	2	3	4	5	6
Au/Al <sub>2</sub> O <sub>3</sub> -3-800	98	96	93	92	92	91
Au/Al <sub>2</sub> O <sub>3</sub> -2-800	97	95	92	91	85	85
Au/Al <sub>2</sub> O <sub>3</sub> -1-800	96	93	89	87	87	86

[a] Reaction conditions: Au catalyst (1 mol%), aniline (0.05 mmol), benzyl alcohol (0.1 mmol), LiOH (0.1 mmol), and  $H_2O$  (0.2 mL, purged with  $O_2$  for 5 min), RT, 14 h, under  $O_2$ . [b] GC–MS yield based on aniline using *n*-do-decane as an internal standard.

product were attained if the reaction was performed in the presence of air or Ar (83 and 11%, respectively; Table 4, entries 17–18) instead of O<sub>2</sub>. A decrease of the Au catalyst loading to 0.2 mol% led to a significant decrease in the product yield (69%; Table 4, entry 21), which did not improve substantially if the reaction temperature was increased to 40 °C (72%; Table 4, entry 22). After detailed investigation, we found the best reaction conditions to be 1 mol% Au, 2 equivalents of LiOH, 2 equivalents of benzyl alcohol, water as the solvent, and a reaction time of 14 h at RT under an O<sub>2</sub> atmosphere (Table 4, entry 23), which led to 98% yield.

Table 4	. Optimizat	ion of the	e amida	ition of benz	yl alcohol with anilin	e over Au/Al <sub>2</sub> O <sub>3</sub> -3-	800. <sup>[a]</sup>	
		ſ	$\sim$	он , 🏹	NH2 Au/Al2O3-3-800			
		Ľ			Base, Solvent	H H		
			1a	2a		3a		
Entry	Au [mol%]	<i>T</i> [°C]	t [h]	Solvent	Base	Benzyl alcohol [equiv.]	Atmosphere	Yield <sup>[b]</sup> [%]
1	0.5	RT	14	H <sub>2</sub> O	LiOH (2 equiv.)	2	O <sub>2</sub>	94
2	0.5	RT	14	THF	LiOH (2 equiv.)	2	O <sub>2</sub>	0
3	0.5	RT	14	DMF	LiOH (2 equiv.)	2	O <sub>2</sub>	0
4	0.5	RT	14	CH₃CN	LiOH (2 equiv.)	2	O <sub>2</sub>	0
5	0.5	RT	14	DMSO	LiOH (2 equiv.)	2	O <sub>2</sub>	0
6	0.5	RT	14	$CH_2CI_2$	LiOH (2 equiv.)	2	O <sub>2</sub>	12
7	0.5	RT	14	hexanes	LiOH (2 equiv.)	2	O <sub>2</sub>	87
8	0.5	RT	14	MeOH	LiOH (2 equiv.)	2	O <sub>2</sub>	0
9	0.5	RT	14	toluene	LiOH (2 equiv.)	2	O <sub>2</sub>	12
10	0.5	RT	14	CHCl₃	LiOH (2 equiv.)	2	O <sub>2</sub>	0
11	0.5	RT	14	H <sub>2</sub> O	NaOH (2 equiv.)	2	O <sub>2</sub>	78
12	0.5	RT	14	H <sub>2</sub> O	KOH (2 equiv.)	2	O <sub>2</sub>	42
13	0.5	RT	14	H <sub>2</sub> O	K <sub>2</sub> CO <sub>3</sub> (2 equiv.)	2	O <sub>2</sub>	0
14	0.5	RT	14	H <sub>2</sub> O	Cs <sub>2</sub> CO <sub>3</sub> (2 equiv.)	2	O <sub>2</sub>	1
15	0.5	RT	14	H <sub>2</sub> O	LiOH (1.1 equiv.)	2	O <sub>2</sub>	85
16	0.5	RT	14	H <sub>2</sub> O	LiOH (2 equiv.)	1.5	O <sub>2</sub>	91
17 <sup>[c]</sup>	0.5	RT	14	H <sub>2</sub> O	LiOH (2 equiv.)	2	Air	83
18 <sup>[d]</sup>	0.5	RT	14	H <sub>2</sub> O	LiOH (2 equiv.)	2	Ar	11
19	0.5	RT	24	H <sub>2</sub> O	LiOH (2 equiv.)	2	O <sub>2</sub>	96
20	0.5	40 °C	14	H <sub>2</sub> O	LiOH (2 equiv.)	2	O <sub>2</sub>	96
21	0.2	RT	14	H <sub>2</sub> O	LiOH (2 equiv.)	2	O <sub>2</sub>	69
22	0.2	40 °C	14	H <sub>2</sub> O	LiOH (2 equiv.)	2	O <sub>2</sub>	72
23	1	RT	14	H <sub>2</sub> O	LiOH (2 equiv.)	2	02	98

[a] Reaction conditions: Au/Al<sub>2</sub>O<sub>3</sub>-3-800 catalyst, aniline (0.05 mmol), benzyl alcohol, LiOH, and H<sub>2</sub>O (0.2 mL, purged with O<sub>2</sub> for 5 min). [b] GC–MS yield based on aniline using *n*-dodecane as an internal standard. [c] Solvent was purged with air for 5 min. [d] Three freeze–pump–thaw cycles were performed on the reaction mixture before the introduction of Ar gas into the glass vial.

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used.



After the optimized conditions for this amidation reaction were established, we investigated the scope of the direct amidation reaction with Au/Al<sub>2</sub>O<sub>3</sub>-3-800 using a variety of substituted benzyl alcohols and aryl and alkyl amines (Table 5). For the substituted benzyl alcohol substrates, electron-withdrawing (-F, -Cl, -Br) and weakly electron-donating (-CH<sub>3</sub>) functional groups at the para position gave good yields of the desired products (75-95%; Table 5, 3b, 3d-f). However, the presence of a stronger electron-donating group such as -OCH<sub>3</sub> at the para position resulted in a lower yield of the expected product (56%; Table 5, 3c). Electron-withdrawing halogen groups (-F, -Cl, -Br) at the meta position of the benzyl alcohol moiety also gave excellent yields of the amides (90-94%; Table 5, 3 g-i).

Different types of substituted aromatic primary amines and dialkyl secondary amine substrates were studied with Au/ Al<sub>2</sub>O<sub>3</sub>-3-800 (Table 5, 3 j-z). Aromatic amines with the weakly electron-donating --CH3 group at the ortho, meta, or para posi-

# halogen groups (--F, --Cl, --Br) at either the meta or para position of the aniline moiety also furnished good to excellent yields

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tion gave good yields of the de-

sired amides (85-89%; Table 5,

3 j, 3 n, 3 r). Electron-withdrawing

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of the product (72-94%; Table 5, 3k-m, 3o-q). However, low yields of 30-47% were attained if the halogen groups (--F, --Cl, -Br) were at the ortho position of the aniline moiety (Table 5, 3 s-u). For dialkyl secondary amine substrates, such as dimethyl and cyclic secondary amines (four-, five-, or six-membered rings), good yields of the required amides were achieved (80–91%; Table 5, 3v–z).

To investigate the amidation reaction mechanism, we performed a number of control experiments. No amide product was obtained if benzoic acid was reacted with aniline under the optimized reaction conditions (Scheme S1). This result indicated that benzoic acid was not an intermediate for this reaction. The reaction of benzaldehyde with aniline gave 50% of the amide product and 43% of the byproduct (Table S3, imine entry 1). The amide yield could be improved to 90% if the benzaldehyde substrate was added in small portions at regular intervals of 30 min over a period of

10 h (Table S3, entry 3). This finding suggested that benzaldehyde was an intermediate, and a low concentration was required to achieve high selectivity. The reaction of the imine compound over Au/Al<sub>2</sub>O<sub>3</sub>-3-800 under the optimized reaction conditions yielded no amide product (Scheme S2). This result suggested that the imine byproduct could not be hydrated back to the hemiaminal intermediate, and its formation led to a decrease in the amide product yield.

Based on the above findings, a tentative mechanism for the direct amidation reaction from benzyl alcohol and amine catalyzed by Au/mesoporous alumina is proposed (Scheme 1). Au/ Al<sub>2</sub>O<sub>3</sub>-3-800 catalyzed the oxidation of aryl alcohol I to aldehyde II. Amine III reacted with II to produce the hemiaminal intermediate IV. The hemiaminal intermediate IV can either be oxidized to the product VI or dehydrated to form the imine byproduct V. Under the current oxidative reaction conditions, Au/Al<sub>2</sub>O<sub>3</sub>-3-800 was able promote the oxidation of IV to form the amide product VI, and thus compete successfully against



 $\label{eq:scheme 1. Proposed mechanism of amidation of benzyl alcohol over Au/mesoporous alumina nanocatalyst. R^1 = aryl, alkyl; R^2 = H, alkyl.$ 

the dehydration reaction that led to the formation of the unwanted byproduct **V**. The reactivity of the Au/Al<sub>2</sub>O<sub>3</sub>-3-800 nanocatalyst to promote the oxidation of **IV** to **VI** might arise from the presence of negatively charged Au nanocrystals as observed by XPS analysis (vide supra). Negatively charged Au nanoparticles have been reported to be highly active catalysts for the selective aerobic oxidation of alcohols.<sup>[16]</sup> In our case, the negatively charged Au nanocrystals could promote not only the selective aerobic oxidation of aryl alcohol I to aldehyde II but also the oxidation of the hemiaminal intermediate **IV** to the amide product **VI**.

In addition to the direct amidation reaction, the six Au/Al<sub>2</sub>O<sub>3</sub> nanomaterials were also examined for the oxidative esterification of alcohols using the model substrates benzyl alcohol and methanol under ambient conditions (Table 6). The initial screening results showed that with a catalyst loading of 0.5 mol% Au, K<sub>2</sub>CO<sub>3</sub> as the base, MeOH/hexanes (1:4) as the solvent, and 14 h at RT under an O<sub>2</sub> atmosphere, Au/Al<sub>2</sub>O<sub>3</sub>-3-800, Au/Al<sub>2</sub>O<sub>3</sub>-2-800, and Au/Al<sub>2</sub>O<sub>3</sub>-1-800 displayed the highest activities (94–96% yields; Table 6, entries 7, 9, and 11). If the catalyst loading was increased to 1.0 mol% Au, the yields improved to 99% (Table 6, entries 8, 10, and 12). No product was obtained if the esterification reaction was performed in the absence of Au/mesoporous alumina nanocatalysts (Table 6, entry 19) or in the presence of the mesoporous alumina support alone (Table 6, entries 13–18).

The recyclability of the three most active nanocatalysts, Au/ Al<sub>2</sub>O<sub>3</sub>-3-800, Au/Al<sub>2</sub>O<sub>3</sub>-2-800, and Au/Al<sub>2</sub>O<sub>3</sub>-1-800, was examined by recovering the nanocatalysts by centrifugation after the addition of ethyl acetate, followed by three more ethyl acetate washes. The nanocatalysts were recovered by centrifugation and dried by using a rotary evaporator before use in the next run. All three Au/mesoporous alumina nanocatalysts displayed good recyclability and achieved 91–97% yields even after six runs (Table 7). The size of the Au nanocrystals remained unchanged after the sixth run, as confirmed by the TEM image (Figure S9b). No significant change in the position of the Au4f XPS peaks was observed after six runs of the reaction (Figure S10 c).

The reaction conditions for the direct oxidative esterification reaction were examined systematically using  $Au/Al_2O_3$ -3-800, which showed excellent activity and the best recyclability (Table 8). Various solvents and solvent mixtures were investi-

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gated (Table 8, entries 1–15), and a MeOH/hexanes solvent mixture of 1:4 furnished the highest yield (94%; Table 8, entry 13). Much lower product yields were achieved if stronger hydroxide bases, LiOH, NaOH, and KOH, were used (0–22%; Table 8, entries 16–18). Na<sub>2</sub>CO<sub>3</sub> gave a low product yield (31%; Table 8, entry 19), whereas Cs<sub>2</sub>CO<sub>3</sub> and K<sub>3</sub>PO<sub>4</sub> provided good yields (85– 90%; Table 8, entries 20–21). O<sub>2</sub>

	$\bigcup  \bigcup  \bigcup  \bigcup  \bigcup  \bigcup  \bigcup  \bigcup  \bigcup  \bigcup $	r 1 mol% Au catalys CH <sub>3</sub> OH/Hexanes ( O <sub>2</sub> , RT, 14 h	st 0 1/4)	
	1a		4a	
Entry	Catalyst	Au [mol %]	Au loading <sup>(b)</sup> [wt %]	Yield <sup>[c]</sup> [%]
1	Au/Al <sub>2</sub> O <sub>3</sub> -3-500	0.5	0.7	80
2	Au/Al <sub>2</sub> O <sub>3</sub> -3-500	1.0	0.7	87
3	Au/Al <sub>2</sub> O <sub>3</sub> -3-600	0.5	0.7	82
4	Au/Al <sub>2</sub> O <sub>3</sub> -3-600	1.0	0.7	88
5	Au/Al <sub>2</sub> O <sub>3</sub> -3-700	0.5	0.9	86
6	Au/Al <sub>2</sub> O <sub>3</sub> -3-700	1.0	0.9	93
7	Au/Al <sub>2</sub> O <sub>3</sub> -3-800	0.5	1.0	94
8	Au/Al <sub>2</sub> O <sub>3</sub> -3-800	1.0	1.0	99
9	Au/Al <sub>2</sub> O <sub>3</sub> -2-800	0.5	0.8	96
10	Au/Al <sub>2</sub> O <sub>3</sub> -2-800	1.0	0.8	99
11	Au/Al <sub>2</sub> O <sub>3</sub> -1-800	0.5	0.9	95
12	Au/Al <sub>2</sub> O <sub>3</sub> -1-800	1.0	0.9	99
13	Al <sub>2</sub> O <sub>3</sub> -3-500	-	-	0
14	Al <sub>2</sub> O <sub>3</sub> -3-600	-	-	0
15	Al <sub>2</sub> O <sub>3</sub> -3-700	-	-	0
16	Al <sub>2</sub> O <sub>3</sub> -3-800	-	-	0
17	Al <sub>2</sub> O <sub>3</sub> -2-800	-	-	0
18	Al <sub>2</sub> O <sub>3</sub> -1-800	-	-	0
19	No catalyst	-	-	0

(0.05 mmol), K<sub>2</sub>CO<sub>3</sub> (0.05 mmol), and MeOH/hexanes (1:4, 0.2 mL, purged with O<sub>2</sub> for 5 min), RT, 14 h, under O<sub>2</sub>. [b] Determined from ICP-MS analysis. [c] GC-MS yield based on benzyl alcohol using *n*-dodecane as an internal standard.

Table 7.Recyclinin the oxidative e	g of Au	/Al <sub>2</sub> O <sub>3</sub> -3-80 tion of be	00, Au/Al <sub>2</sub> 0 nzyl alcoh	O <sub>3</sub> -2-800, ol with m	and Au/Al ethanol. <sup>[a]</sup>	<sub>2</sub> O <sub>3</sub> -1-800
Nanocatalyst		Yield of p	product or	n successiv	ve runs <sup>[b]</sup> [	%]
	1	2	3	4	5	6
Au/Al <sub>2</sub> O <sub>3</sub> -3-800	99	99	99	98	97	97
Au/Al <sub>2</sub> O <sub>3</sub> -2-800	99	99	99	98	98	95
Au/Al <sub>2</sub> O <sub>3</sub> -1-800	99	99	99	98	97	91
[a] Reaction cond $K_2CO_3$ (0.05 mmo 5 min), RT, 14 h, u	litions: A bl), and I under O <sub>2</sub>	u catalyst NeOH/hex . [b] GC–N	: (1 mol %) anes (1:4, 15 yield ba	, benzyl a 0.2 mL, p ased on b	lcohol (0.0 ourged wi enzyl alco	05  mmol), th O <sub>2</sub> for hol using



		OH <u>Au/Al</u> Base RT	03-3-800 , Solvent , 14 h	/	
		1a	4a		
Entry	Au [mol%]	Solvent	Base	Atmosphere	Yield <sup>[b]</sup> [%]
1	0.5	MeOH	K <sub>2</sub> CO <sub>3</sub> (1 equiv.)	0,	83
2	0.5	MeOH/hexanes (1:1)	K <sub>2</sub> CO <sub>3</sub> (1 equiv.)	O <sub>2</sub>	90
3	0.5	MeOH/H <sub>2</sub> O (1:1)	K <sub>2</sub> CO <sub>3</sub> (1 equiv.)	O <sub>2</sub>	54
4	0.5	MeOH/THF (1:1)	K <sub>2</sub> CO <sub>3</sub> (1 equiv.)	O <sub>2</sub>	60
5	0.5	MeOH/toluene (1:1)	K <sub>2</sub> CO <sub>3</sub> (1 equiv.)	O <sub>2</sub>	73
6	0.5	MeOH/CHCl <sub>3</sub> (1:1)	K <sub>2</sub> CO <sub>3</sub> (1 equiv.)	O <sub>2</sub>	67
7	0.5	MeOH/CH <sub>2</sub> Cl <sub>2</sub> (1:1)	K₂CO₃ (1 equiv.)	O <sub>2</sub>	89
8	0.5	MeOH/DMF (1:1)	K <sub>2</sub> CO <sub>3</sub> (1 equiv.)	O <sub>2</sub>	44
9	0.5	MeOH/DMSO (1:1)	K <sub>2</sub> CO <sub>3</sub> (1 equiv.)	O <sub>2</sub>	4
10	0.5	MeOH/CH <sub>3</sub> CN (1:1)	K <sub>2</sub> CO <sub>3</sub> (1 equiv.)	O <sub>2</sub>	43
11	0.5	MeOH/EtOAc (1:1)	K <sub>2</sub> CO <sub>3</sub> (1 equiv.)	O <sub>2</sub>	12
12	0.5	MeOH/hexanes (1:9)	K₂CO₃ (1 equiv.)	O <sub>2</sub>	83
13	0.5	MeOH/hexanes (1:4)	K <sub>2</sub> CO <sub>3</sub> (1 equiv.)	O <sub>2</sub>	94
14	0.5	MeOH/CH <sub>2</sub> Cl <sub>2</sub> (1:9)	K <sub>2</sub> CO <sub>3</sub> (1 equiv.)	O <sub>2</sub>	38
15	0.5	MeOH/CH <sub>2</sub> Cl <sub>2</sub> (1:4)	K <sub>2</sub> CO <sub>3</sub> (1 equiv.)	O <sub>2</sub>	45
16	0.5	MeOH/hexanes (1:4)	LiOH (1 equiv.)	O <sub>2</sub>	9
17	0.5	MeOH/hexanes (1:4)	NaOH (1 equiv.)	O <sub>2</sub>	0
18	0.5	MeOH/hexanes (1:4)	KOH (1 equiv.)	O <sub>2</sub>	22
19	0.5	MeOH/hexanes (1:4)	Na <sub>2</sub> CO <sub>3</sub> (1 equiv.)	O <sub>2</sub>	31
20	0.5	MeOH/hexanes (1:4)	Cs <sub>2</sub> CO <sub>3</sub> (1 equiv.)	O <sub>2</sub>	90
21	0.5	MeOH/hexanes (1:4)	K <sub>3</sub> PO <sub>4</sub> (1 equiv.)	O <sub>2</sub>	85
22	0.5	MeOH/hexanes (1:4)	K <sub>2</sub> CO <sub>3</sub> (0.5 equiv.)	O <sub>2</sub>	90
23 <sup>[c]</sup>	0.5	MeOH/hexanes (1:4)	K <sub>2</sub> CO <sub>3</sub> (1 equiv.)	air	61
24 <sup>[d]</sup>	0.5	MeOH/hexanes (1:4)	K <sub>2</sub> CO <sub>3</sub> (1 equiv.)	Ar	< 1
25	1.0	MeOH/hexanes (1:4)	K <sub>2</sub> CO <sub>3</sub> (1 equiv.)	<b>O</b> <sub>2</sub>	99

(0.2 mL, purged with  $O_2$  for 5 min), RT, 14 h. [b] GC-MS yield based on benzyl alcohol using *n*-dodecane as an internal standard. [c] Solvent was purged with air for 5 min. [d] Three freeze-pump-thaw cycles were performed on the reaction mixture before the introduction of Ar gas into the glass vial.

halogen groups (-F, -CI, -Br) at the *meta* position of the benzyl alcohol moiety also furnished good yields of the product (75–90%; Table 9, **4h–k**). Allylic alcohol could be esterified in this reaction (70%; Table 9, **4l**), and diesters were obtained easily (72–85%; Table 9, **4m–n**).

Control experiments were conducted to study the reaction mechanism for this esterification reaction. Under the optimized reaction conditions, no ester product was achieved if benzoic acid was reacted with methanol (Scheme S3), which confirms that benzoic acid was not an intermediate for this reaction. The reaction of benzaldehyde with methanol furnished 97% of the ester product (Scheme S4). This finding suggested that benzaldehyde was an intermediate in the esterification reaction. A tentative mechanism for the oxidative esterification of benzyl alcohol with methanol over Au/Al<sub>2</sub>O<sub>3</sub>-3-800 is proposed (Scheme 2). The oxidation of the aryl alcohol I to the aldehyde II was catalyzed by the Au/mesoporous alumina nanocatalyst. Aldehyde II then reacted with methanol to form the hemiacetal intermediate VII. The oxidation of VII catalyzed by Au/Al<sub>2</sub>O<sub>3</sub>-3-800 would result in the formation of the ester product VIII.

### Conclusions

An efficient heterogeneous Au/mesoporous alumina nanocatalyst was developed successfully for the direct amidation of benzyl alcohols with amines in water and the oxidative esterification of alcohols with methanol under aerobic conditions. The reac-

gas was critical in this esterification reaction as no product was formed if the reaction was performed under Ar (Table 8, entry 24), and a lower yield of 61% was achieved if air was used instead of O<sub>2</sub> (Table 8, entry 23). From these systematic



Scheme 2. Proposed mechanism of oxidative esterification of benzyl alcohol catalyzed by Au/mesoporous alumina.

investigations, we found the optimized reaction conditions to be 1 mol% Au, 1 equivalent of  $K_2CO_3$ , a MeOH/hexanes solvent mixture (1:4), and a reaction time of 14 h at RT under an  $O_2$  atmosphere (Table 8, entry 25).

Next, the scope of the oxidative esterification reaction for a variety of substituted benzyl alcohols was examined with Au/Al<sub>2</sub>O<sub>3</sub>-3-800 (Table 9). We found that electron-donating (-CH<sub>3</sub>, -OCH<sub>3</sub>) and halogen functional groups (-F, -Cl, -Br) at the *para* position provided good to excellent yields of the desired esters (84–97%; Table 9, **4b**–**f**). The presence of an electron-withdrawing -NO<sub>2</sub> group at the *para* position resulted in a low yield of the expected product (50%; Table 9, **4g**). The electron-donating -CH<sub>3</sub> substituent and electron-withdrawing tions were performed easily under ambient conditions without the need for heating or high  $O_2$  pressure. Moreover, the nanocatalyst was stable to air and water and could be recovered and reused easily.

# **Experimental Section**

#### Materials

Difunctional block copolymer surfactant based on ethylene oxide and propylene oxide Pluronic P123 ( $M_{av} = 5750 \text{ gmol}^{-1}$ ) was purchased from BASF. All other reagents were purchased from Aldrich, Fluka, and Merck, and used as received. Silica gel 60 (230–400 mesh, Merck) was used for column chromatography.





#### Synthesis of mesoporous alumina

Mesoporous alumina materials were synthesized by the evaporation-induced self-assembly method using an established procedure<sup>[11b]</sup> with some modifications. Aluminum isopropoxide, Pluronic P123, and TIPB were used as the precursor, template, and swelling agent, respectively. Three different TIPB/ P123 weight ratios (1, 2, and 3) were used in the synthesis of mesoporous alumina. In general, TIPB (6.0 g) was added to a solution of Pluronic P123 (2.0 g) in ethanol (40 mL) and stirred vigorously at RT under air for 1 h. Aluminum isopropoxide (4.08 g), concentrated HCI (3.2 mL), and citric acid (0.9 g) were added, and the resulting mixture was stirred vigorously at RT under air for 12 h. The reaction mixture was transferred to a Petri dish and evaporated in an oven at 45 °C for 24 h and at 60 °C for 48 h. The white solid was calcined at 500, 600, 700, or 800 °C under air for 4 h with a heating rate of  $1\,^\circ C\,min^{-1}.$  The mesoporous alumina materials were labeled as Al<sub>2</sub>O<sub>3</sub>-

#### Characterization

TEM was performed by using a FEI Tecnai G<sup>2</sup> F20 electron microscope operated at 200 kV with the software package for automated electron tomography. For TEM studies, a drop of the nanomaterial solution was dispensed onto a 3 mm carbon-coated copper grid. Excess solution was removed by an absorbent paper, and the sample was dried under air in an oven at 80 °C. EDX analysis of the nanomaterials was performed by using the FEI Tecnai G<sup>2</sup> F20 electron microscope equipped with an EDX detector. XPS analysis was conducted by using a VG ESCALAB MKII spectrometer. The powder XRD patterns were collected by using PANalytical X'Pert PRO and Bruker D8 ADVANCE X-ray diffractometers using CuK<sub>a</sub> irradiation  $(\lambda = 1.5406 \text{ Å})$ . <sup>1</sup>H and <sup>13</sup>C NMR spectra were collected in CDCl<sub>3</sub> by using a Bruker AV-400 spectrometer at 25 °C. Chemical shifts were reported in ppm from tetramethylsilane with the solvent resonance as the internal standard. GC-MS analysis was performed by using a Shimadzu GCMS-QP2010 spectrometer. ICP-MS analyses were performed by using a PerkinElmer Elan DRC II. N<sub>2</sub> adsorptiondesorption isotherms were measured at 77 K by using a Micromeritics Tristar system, and the sample was degassed at 180°C for 12 h before analysis. The surface area was calculated using the BET method using adsorption data in a relative pressure range of 0.06-0.3. The pore size and total pore volume were derived from the adsorption isotherm using the Barrett-Joyner-Halenda (BJH) model. TGA was conducted by using a PerkinElmer Pyris 1 thermogravimetric analyzer, and the samples were heated at  $10\,^\circ\text{C\,min}^{-1}$  from 25– 900 °C in flowing air.

*a-b*, in which *a* and *b* represent the TIPB/P123 weight ratio and the calcination temperature, respectively. The six mesoporous alumina materials (Al<sub>2</sub>O<sub>3</sub>-3-500, Al<sub>2</sub>O<sub>3</sub>-3-600, Al<sub>2</sub>O<sub>3</sub>-3-700, Al<sub>2</sub>O<sub>3</sub>-3-800, Al<sub>2</sub>O<sub>3</sub>-2-800, and Al<sub>2</sub>O<sub>3</sub>-1-800) were characterized by TEM, TEM-EDX, XRD, and N<sub>2</sub> adsorption–desorption isotherms.

#### Synthesis of Au/mesoporous alumina nanocatalysts

Mesoporous alumina (0.200 g) in water (4.4 mL) was sonicated for 30 s to disperse the solids. HAuCl<sub>4</sub> aqueous solution (0.0186 mL, 0.58 m) was added with vigorous stirring, followed by the addition of L-lysine (0.5 mL, 0.53 m). The suspension was stirred vigorously at RT under air for 30 min. NaBH<sub>4</sub> aqueous solution (0.25 mL, 0.35 m) was added dropwise, followed by HCI aqueous solution (0.25 mL, 0.35 m). The resulting reddish suspension was stirred at RT under air for 18 h. The Au/mesoporous alumina was collected by centrifugation (10000 rpm for 20 min), washed twice with deionized water (10 mL) and once with acetone (10 mL), and dried at RT under vacuum overnight. The material was characterized by TEM, TEM-EDX, XRD, and ICP-MS.

#### Synthesis of amides

The general procedure for the direct amidation of substituted benzyl alcohol with amine was as follows. A mixture of the Au/ Al<sub>2</sub>O<sub>3</sub>-3-800 nanocatalyst (1 mol% Au), amine (0.2 mmol), substituted benzyl alcohol (0.4 mmol), lithium hydroxide (0.4 mmol), and deionized water (0.8 mL, purged with O<sub>2</sub> for 5 min) were added to a 10 mL glass vial equipped with a rubber septum. The headspace in the glass vial was purged with O<sub>2</sub>, and the reaction mixture was subjected to sonication to disperse the catalyst. The reaction mix-

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ture was stirred at RT under an  $O_2$  balloon for 14 h. EtOAc (3 mL) was added, and the biphasic mixture was stirred at RT for 30 min. The mixture was centrifuged at 4500 rpm for 5 min. The upper organic layer that contained the product was recovered, and the lower layer that contained the catalyst was extracted with EtOAc (3×3 mL). The solvent was removed from the combined organic layers by rotary evaporation, and the product was purified by column chromatography.

#### Synthesis of esters

The general procedure for the oxidative esterification of substituted benzyl alcohol with methanol was as follows. A mixture of the Au/Al<sub>2</sub>O<sub>3</sub>-3-800 nanocatalyst (1 mol% Au), benzyl alcohol (0.2 mmol), potassium carbonate (0.2 mmol), and MeOH/hexanes (1:4, 0.8 mL, purged with O<sub>2</sub> for 5 min) was added to a 20 mL glass vial equipped with a silicon cap. The headspace in the glass vial was purged with O<sub>2</sub>, and the reaction mixture was subjected to sonication to disperse the catalyst. The reaction mixture was stirred at RT under O<sub>2</sub> for 14 h. EtOAc (3 mL) was added, and the mixture was stirred at 4500 rpm for 5 min. The organic layer that contained the product was recovered, and the catalyst was extracted with EtOAc (3 × 3 mL). The solvent was removed from the combined organic layers by rotary evaporation, and the product was purified by column chromatography.

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