PAPER

Facile and efficient gold-catalyzed aerobic oxidative esterification of activated alcohols†

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A facile and efficient methodology is presented for the direct oxidative esterification of alcohols with alcohols catalyzed by NaAuCl₄. Just in the presence of a low catalytic amount of base additive, the newly developed catalytic system proceeds with high selectivity and broad substrate scope under mild conditions with dioxygen or air as the environmentally benign terminal oxidant. Various alcohols including benzylic and allylic alcohols were smoothly reacted with methanol and even with long-chain aliphatic alcohols, affording the desired products in good to excellent yields (up to 95% yield). The present system showed high catalytic activity with a TOF up to 219 h^{-1}. Kinetic studies of the reaction process provide fundamental insights into the catalytic pathway, and a possible reaction pathway was proposed based on the results of the control experiments. XPS, TEM, and UV-vis were carried out to characterize the chemical state of the Au catalyst in the present catalytic system. The results indicate that the Au nanoparticles were generated *in situ* and supported on K_2CO_3, forming a simple, recyclable and selective catalyst system for the direct oxidative esterification of alcohols.

Introduction

Esters are some of the most important compounds in organic synthesis and are used in production of bulk and fine chemicals, natural and pharmacological compounds.[1] Therefore, a tremendous number of approaches for ester synthesis have been developed. Traditionally, methodologies for the synthesis of esters have involved the Fischer esterification reaction of activated acid derivatives with alcohols or transesterification reactions.[2] In those methods, strong acidic or basic conditions limit the reaction scope and large amounts of unwanted byproducts are produced. The third useful approach for the synthesis of esters is the Baeyer–Villiger oxidation reaction, which normally suffers from low regioselectivity.[3]

With the developments in transition-metal-catalyzed oxidation reactions, oxidative esterification has received more and more attention and has become an economical alternative to traditional ester synthesis.[4] In recent years, considerable effort has been devoted to developing the direct synthesis of esters from the oxidative esterification of aldehydes with alcohols.[5]

However, these protocols usually require stoichiometric amounts of reagents such as oxone, MnO_2, sodium dichromate and peroxides, and thus a large amount of unwanted waste is produced.[6] In addition, the required aldehydes are usually obtained from alcohols by selective oxidation. Therefore, the development of a single-step instead of a multi-step process for the direct catalytic oxidative esterification of alcohols with alcohols is highly desirable from both economic and environmental points of view, as alcohols are more readily available as bulk chemicals, more stable than the carbonyl compounds, cheaper, less toxic, and easier to handle.[7] Although several reported methods with stoichiometric amounts of oxidants such as molecular iodine, hypochlorite, MnO_2 or $PhI(OAc)_2$ can achieve this transformation, large amounts of toxic waste are formed.[8]

From the viewpoints of green and sustainable chemistry, the use of green oxidants, such as molecular oxygen as a terminal oxidant, is the focus of great attention because dioxygen is inexpensive and water is produced as the only by-product. In this respect, direct oxidative esterification reactions from alcohols using molecular oxygen as the terminal oxidant catalyzed by transition metal catalysts are an attractive and challenging subject for both organic synthesis and green chemistry. However, so far only a few catalysts reported can promote the oxidative esterification of alcohols with molecular oxygen as the terminal oxidant, and in most cases gold nanoparticles were employed to achieve this transformation.[9] In this process, preparation of complex materials is required. In addition, the catalyst is easily deactivated in the recycling process. Moreover,

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these reported supported Au-NP catalysts usually require large amounts (stoichiometric or excess) of base additives, relatively high temperature and high operating oxygen pressure (3–20 atm) to obtain high yields of esters.[9b–f,h,i,k–n,p] Only Au/K$_2$Ti$_6$O$_{13}$, Au/Mg$_5$Al-HT and polymer-incarcerated gold catalyst (PI-Au) were reported to be effective under 1 atm O$_2$.[9g,j,o] Quite recently, Beller and Lei reported a synthetically interesting palladium-catalyzed oxidative cross-esterification of benzylic and aliphatic alcohols by using oxygen as the terminal oxidant, respectively.[10] In their methods, although various esters were prepared in good yields, high loading of Pd catalyst (2–5 mol %) and the need for large amounts of ligands, additives and bases make them less attractive for practical purposes. Therefore, it is still desirable to develop a facile and green, efficient and practical method for the aerobic oxidative direct esterification of alcohols.

Herein, we wish to disclose a facile and atom-economical methodology for the direct oxidative esterification of alcohols with alcohols catalyzed by NaAuCl$_4$. In the presence of only a low catalytic amount of base additive, the newly developed catalytic system proceeds with high selectivity and broad substrate scope under mild conditions with dioxygen or air as the environmentally benign terminal oxidant. It was found that the present catalyst system was effective for the oxidative esterification of benzylic and allylic alcohols with methanol and various long-chain aliphatic alcohols. It was worth noting that the oxidative self-esterification of the benzylic alcohols and even the unreactive aliphatic primary alcohols can proceed under solvent-free conditions to give the desired esters in good yields with quite good selectivity. To the best of our knowledge, no similar Au-catalyzed oxidative esterification reactions from alcohols using air as an oxidant are known to date.

Experimental

General methods

All chemicals used in this study were analytical grade, commercially available and used without further purification unless otherwise noted. All experiments were carried out in a Teflon-lined 316 L stainless steel autoclave (inner volume 100 mL) equipped with a magnetic stirrer. Prior to the experiment, the air in the autoclave was exchanged three times with oxygen. GC calculations of yields were performed on an Agilent 7890A with a flame ionization detector. All products were confirmed by GC-MS with an Agilent 6890N GC/5973 MS detector, SE-54 capillary column, 30 m × 350 μm × 0.5 μm; FID detector, 300 °C; injection: 250 °C; carrier gas: nitrogen; carrier gas rate: 20 mL min^{-1}. All substrates and their corresponding products unless otherwise noted were detected under the following conditions: column temperature: 100 °C for 7 minutes, raised to 250 °C at a rate of 15 °C min^{-1}. Methallyl alcohol and its corresponding product were detected under the following conditions: column temperature: 35 °C for 7 minutes, raised to 250 °C at a rate of 15 °C min^{-1}. ^{1}H NMR and ^{13}C NMR spectra were recorded on a 400 MHz NMR

spectrometer using CDCl$_3$ as the solvent with TMS as an internal reference. [1]H and ^{13}C positive chemical shifts (δ) in ppm are downfield from tetramethylsilane (CDCl$_3$: δC = 77.1 ppm; residual CHCl$_3$ in CDCl$_3$: δH = 7.26 ppm). Transmission electron microscopy (TEM) images were obtained on a FEI Tecnai G2 Spirit electron microscope at an accelerating voltage of 120 kV. UV-vis diffuse reflectance spectra were recorded on a Shimadzu-2550 spectrometer with a wavelength range from 900–190 nm with an integrating sphere accessory, and BaSO$_4$ high reflectance white optical paint was used as a reference material. X-ray photoelectron spectroscopy (XPS) measurements were performed on a VG ESCALAB MK2 spectrometer equipped with Al Kα radiation ($h\nu$ = 1486.6 eV, tube voltage = 12.5 kV, power = 250 W).

General procedure for the oxidation of benzyl alcohol to esters

A mixture of NaAuCl$_4$·2H$_2$O (1.97 mg, 0.005 mmol) and K$_2$CO$_3$ (13.8 mg, 0.1 mmol) in methanol (4 mL) was stirred for 1 min at room temperature in a 25 mL flask. Then, benzyl alcohol (108 mg, 1 mmol) was added to the mixture. After stirring for 2 min, the resulting mixture was transferred to an autoclave. After the autoclave was closed, dioxygen was charged to 0.1 MPa. After reaction was complete, the reactor was quickly cooled to room temperature. The excess oxygen was depressurized slowly. GC analysis of the reaction mixtures using biphenyl as an internal standard gave a 96% yield of methyl benzoate. The solvent was removed under reduced pressure and the product was isolated by column chromatography (200–400 mesh silica gel, petroleum ether–ethyl acetate = 10/1) in 91% yield (123 mg).

Methyl benzoate.[10b] Table 2 entry 1, colorless liquid: ^{1}H NMR (400 MHz, CDCl$_3$) δ ppm: 3.91 (s, 3H), 7.43 (t, J = 7.6 Hz, 2H), 7.55 (t, J = 8.0 Hz, 1H), 8.04 (d, J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ ppm: 167.1, 132.9, 130.2, 129.6, 128.3, 52.0.

Methyl 4-methylbenzoate.[10b] Table 2 entry 2, light yellow liquid: ^{1}H NMR (400 MHz, CDCl$_3$) δ ppm: 2.38 (s, 3H), 3.89 (s, 3H), 7.28–7.35 (m, 2H), 7.82–7.85 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ ppm: 167.1, 143.5, 129.6, 129.0, 127.4, 51.8, 21.6.

Methyl 3-methylbenzoate.[10b] Table 2 entry 3, colorless liquid: ^{1}H NMR (400 MHz, CDCl$_3$) δ ppm: 2.38 (s, 3H), 3.89 (s, 3H), 7.28–7.35 (m, 2H), 7.82–7.85 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ ppm: 167.2, 138.1, 133.6, 130.1, 128.2, 126.7, 52.0, 21.2.

Methyl 2-methylbenzoate.[11] Table 2 entry 4, colorless liquid: ^{1}H NMR (400 MHz, CDCl$_3$) δ ppm: 2.60 (s, 3H), 3.88 (s, 3H), 7.21–7.24 (m, 2H), 7.36–7.40 (m, 1H), 7.89–7.91(m, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ ppm: 168.1, 140.2, 132.0, 131.7, 130.6, 129.6, 125.7, 51.8, 21.7.

Methyl 3,4-dimethylbenzoate.[12] Table 2 entry 5, colorless liquid: ^{1}H NMR (400 MHz, CDCl$_3$) δ ppm: 2.27 (s, 6H), 3.87 (s, 3H), 7.16 (d, J = 8.0 Hz, 1H), 7.75 (d, J = 8.8 Hz, 1H), 7.80 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ ppm: 167.9, 142.7, 137.2, 131.2, 130.2, 128.3, 127.7, 52.4, 20.5, 20.2.

Methyl 4-chlorobenzoate.[13] Table 2 entry 6, white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ ppm: 3.86 (s, 3H), 7.35 (d, J = 8.4 Hz,

2H), 7.91 (d, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ ppm: 166.1, 139.3, 130.9, 128.6, 128.5, 52.2.

Methyl 2-chlorobenzoate.[14] Table 2 entry 7, light yellow liquid: ^{1}H NMR (400 MHz, CDCl$_3$) δ ppm: 3.91 (s, 3H), 7.29–7.31 (m, 1H), 7.37–7.44 (m, 2H), 7.79–7.81 (m, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ ppm: 166.1, 133.7, 132.6, 131.4, 131.1, 130.1, 126.6, 52.4.

Methyl 3-chlorobenzoate.[15] Table 2 entry 8, light yellow liquid: ^{1}H NMR (400 MHz, CDCl$_3$) δ ppm: 3.92 (s, 3H), 7.37 (t, J = 8.0 Hz, 1H), 7.52 (d, J = 8.0 Hz, 1H), 7.92 (d, J = 7.6 Hz, 1H), 8.02 (s, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ ppm: 165.9, 134.6, 133.0, 131.9, 129.7, 127.8, 122.0, 52.5.

Methyl 4-methoxybenzoate.[10b] Table 2 entry 9, white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ ppm: 3.85 (s, 3H), 3.88 (s, 3H), 6.91 (d, J = 8.8 Hz, 2H), 7.99 (d, J = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ ppm: 166.9, 163.4, 131.6, 122.6, 113.6, 55.4, 51.9.

Methyl 3-methoxybenzoate.[10b] Table 2 entry 10, light yellow liquid: ^{1}H NMR (400 MHz, DMSO) δ ppm: 3.77 (s, 3H), 3.81 (s, 3H), 7.17–7.20 (m, 1H), 7.37–7.41 (m, 2H), 7.51 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, DMSO) δ ppm: 166.1, 159.3, 131.0, 129.9, 121.4, 119.3, 113.8, 55.3, 52.2.

Methyl 3,4-dimethoxybenzoate.[16] Table 2 entry 11, white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ ppm: 3.88 (s, 3H), 3.92 (s, 6H), 6.88 (d, J = 8.4 Hz, 1H), 7.53 (d, J = 1.6 Hz, 1H), 7.67 (dd, J_1 = J_2 = 1.6 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ ppm: 167.4, 153.5, 149.2, 124.1, 123.2, 112.5, 110.8, 56.6, 52.6.

Methyl 3,4,5-triemthoxybenzoate.[17] Table 2 entry 12, white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ ppm: 3.89 (s, 12H), 7.29 (s, 2 H); ^{13}C NMR (100 MHz, CDCl$_3$) δ ppm: 166.8, 153.0, 142.2, 125.2, 106.8, 103.1, 61.0, 56.3, 52.3.

Methyl 1-naphthoate.[15] Table 2 entry 13, colorless liquid: ^{1}H NMR (400 MHz, CDCl$_3$) δ ppm: 4.01 (s, 1H), 7.48–7.56 (m, 1H), 7.60–7.64 (m, 1H), 7.89 (d, J = 8.4 Hz, 1H), 8.02 (d, J = 8.4 Hz, 1H), 8.20 (d, J = 7.2 Hz, 1H), 8.92 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ ppm: 168.1, 133.9, 133.4, 131.4, 130.3, 128.6, 127.8, 127.2, 126.3, 125.9, 124.6, 52.2.

Methyl 4-bromobenzoate.[15] Scheme 1, white solid: ^{1}H NMR (400 MHz, DMSO) δ ppm: 3.83 (s, 3H), 7.71 (d, J = 8.8 Hz, 2H), 7.85 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, DMSO) δ ppm: 166.6, 133.0, 132.1, 129.8, 128.4, 51.4.

Methyl 4-nitrobenzoate.[10b] Scheme 1, white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ ppm: 2.38 (s, 3H), 3.89 (s, 3H), 7.28–7.35 (m, 2H), 7.82–7.85 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ ppm: 167.1, 143.5, 129.6, 129.0, 127.4, 51.8, 21.6.

Methyl cinnamate.[10b] Scheme 1, light yellow solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ ppm: 3.81 (s, 3H), 6.45(d, J = 16 Hz, 1H), 7.39 (s, 3H), 7.52 (s, 2H), 7.70 (d, J = 16 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ ppm: 167.5, 145.0, 134.4, 130.4, 129.0, 128.1, 117.9, 51.8.

Propyl benzoate.[10a] Table 3 entry 2, colorless liquid: ^{1}H NMR (400 MHz, CDCl$_3$) δ ppm: 1.04 (t, J = 7.2 Hz, 3H), 1.77–1.83 (m, 2H), 4.28 (t, J = 6.4 Hz, 2H), 7.44 (t, J = 7.6 Hz, 1H), 7.55 (t, J = 7.2 Hz, 1H), 8.04–8.06 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ ppm: 166.8, 132.9, 130.2, 129.6, 128.4, 66.6, 22.2, 10.6.

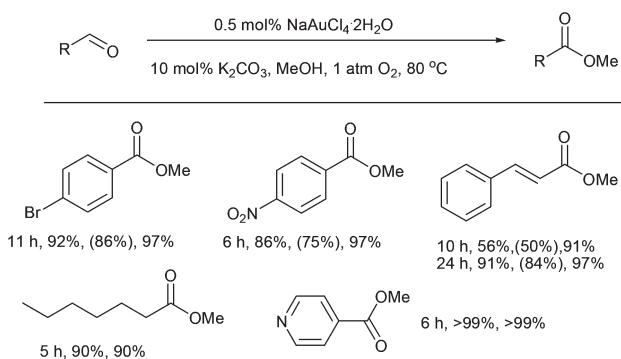**Butyl benzoate.**[10a] Table 3 entry 3, colorless liquid: ^{1}H NMR (400 MHz, CDCl$_3$) δ ppm: 0.98 (t, J = 7.6 Hz, 3H), 1.44–1.53 (m, 2H), 1.72–1.79 (m, 2H), 4.33 (t, J = 6.8 Hz, 2H), 7.43 (t, J = 7.6 Hz, 1H), 7.55 (t, J = 7.2 Hz, 1H), 8.05 (d, J = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ ppm: 166.8, 132.9, 130.6, 129.6, 128.4, 64.9, 30.9, 19.4, 13.8.

Pentyl benzoate.[10a] Table 3 entry 5, colorless liquid: ^{1}H NMR (400 MHz, CDCl$_3$) δ ppm: 0.93 (t, J = 7.2 Hz, 3H), 1.34–1.47 (m, 4H), 1.74–1.81 (m, 2H), 4.32 (t, J = 6.8 Hz, 2H), 7.43 (t, J = 7.2 Hz, 1H), 7.55 (t, J = 7.6 Hz, 1H), 8.04–8.06 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ ppm: 166.7, 132.8, 130.6, 129.6, 128.4, 65.2, 28.5, 28.3, 22.4, 14.0.

Propyl 4-chlorobenzoate.[16] Table 3 entry 7, colorless liquid: ^{1}H NMR (400 MHz, CDCl$_3$) δ ppm: 1.02 (t, J = 7.2 Hz, 3H), 1.74–1.83 (m, 2H), 4.27 (t, J = 608 Hz, 1H), 7.40–7.42 (m, 2H), 7.96–7.99 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ ppm: 165.9, 139.3, 131.0, 129.0, 128.7, 66.9, 22.2, 10.6.

Scheme 1 Au-catalyzed oxidative esterification of aldehydes with methanol [reaction time, GC yield, (isolated yield), and GC selectivity].

Results and discussion

Benzyl alcohol was reacted with methanol as a probe reaction to optimize the reaction conditions. Initially, the reaction of benzyl alcohol with methanol in the presence of 1.5 mol% NaAuCl$_4$ and 3 mol% K$_2$CO$_3$ at 80 °C under 1 atm of oxygen atmosphere for 3.5 h afforded methyl benzoate in 30% yield (Table 1, entry 1). When the amount of K$_2$CO$_3$ was increased to 5 mol%, a yield of 69% for methyl benzoate was obtained (Table 1, entry 2). The results prompted us to further adjust the amount of base (Table 1, entries 3, 4). Much to our delight, a good yield of methyl benzoate was obtained with the amount of K$_2$CO$_3$ increasing to 10 mol%, and up to 97% yield could be achieved by prolonging the reaction time (Table 1, entry 4). Next, the amount of NaAuCl$_4$ was examined (Table 1, entries 5–8). When the amount of NaAuCl$_4$ was reduced to only 0.5 mol%, excellent yield can also be obtained (Table 1, entry 8). This oxidative esterification was markedly influenced by the base used (Table 1, entries 9–16). The addition of a base was essential for achieving the reaction, and no desired product

Table 1 Optimization of the Au-catalyzed cross-esterification of benzyl alcohol and methanol[a]

Entry	$NaAuCl_4 \cdot 2H_2O$ (mol%)	Base (mol%)	Time (h)	Yield[b] (%)	Selectivity[b] (%)
1	1.5	K_2CO_3 (3)	3.5	30	83
2	1.5	K_2CO_3 (5)	3.5	69	91
3	1.5	K_2CO_3 (10)	3.5	81	90
4	1.5	K_2CO_3 (10)	5	97	99
5	1	K_2CO_3 (10)	3.5	86	95
6	1	K_2CO_3 (10)	5	97	>99
7	0.5	K_2CO_3 (10)	3.5	84	93
8	0.5	K_2CO_3 (10)	5	96	99
9	0.5	—	5	n.r.	—
10	0.5	Na_2CO_3 (10)	5	95	98
11	0.5	Li_2CO_3 (10)	5	68	93
12	0.5	Cs_2CO_3 (10)	5	50	83
13	0.5	$KHCO_3$ (10)	5	62	85
14	0.5	K_3PO_4 (10)	5	6	65
15	0.5	NaOAc (10)	5	3	11
16	0.5	KOAc (10)	5	1	6
17[c]	1.5	K_2CO_3 (10)	3.5	62	91
18[d]	1	K_2CO_3 (10)	12	38	84
19[e]	0.5	K_2CO_3 (10)	5.5	84	90
20[f]	0.5	K_2CO_3 (10)	5	4	20
21[g]	0.5	K_2CO_3 (20)	12	92	98
22[h]	—	K_2CO_3 (10)	5	90	97
23[i]	—	K_2CO_3 (10)	5	68	90

[a] Reaction conditions: benzyl alcohol (1 mmol), 4 mL MeOH, 80 °C, 1 atm O_2. n.r. = no reaction. [b] Determined by GC using internal standard. [c] 60 °C. [d] 25 °C [e] Under air. [f] Under N_2. [g] Benzyl alcohol (10 mmol). [h] $HAuCl_4 \cdot 4H_2O$ (0.5 mol%). [i] AuCl (0.5 mol%).

was produced in the absence of a base (Table 1, entry 9). Among the screened bases, K_2CO_3 and Na_2CO_3 were found to be effective bases (Table 1, entries 8, 10). Li_2CO_3, Cs_2CO_3 and $KHCO_3$ had moderate activity, giving the desired product in 68%, 50% and 62% yields, respectively (Table 1, entries 11–13). Other employed bases including K_3PO_4, NaOAc, and KOAc were less effective, giving methyl benzoate in only 6%, 3%, and 1% yields, respectively (Table 1, entries 14–16). The reaction temperature was also investigated (Table 1, entries 8, 17, 18). The best result was obtained at 80 °C. An important advantage of this simple catalytic system is that an air atmosphere in place of a pure dioxygen also affords good yields (Table 1, entry 19). The blank experiment shows that only a 4% yield of methyl benzoate was obtained under N_2 atmosphere (Table 1, entry 20). Next, the practical utility of this catalytic system was evaluated, and up to 92% yield was obtained on a scale of 10 mmol (Table 1, entry 21). Other chemical states of gold catalysts, such as $HAuCl_4$, and AuCl, were also examined resulting in the desired product in 90% and 68% yields, respectively (Table 1, entries 22, 23).

Having identified the optimized reaction conditions, we turned our attention to the examination of substrate scope and limitation of this catalytic oxidation system. The results are summarized in Table 2. In order to get a high yield of the product, the reaction time is not a priority consideration. Benzylic alcohols with electron-donating and electron-withdrawing groups gave excellent yields of products (Table 2, entries 1–13). Like *para*-and *meta*-substituted substrates, the

sterically more hindered *ortho*-substituted alcohols also gave excellent results under the same reaction conditions. It was worth noting that lignin model compounds could be successfully oxidized into the desired products in excellent yields (Table 2, entries 11, 12). Naphthyl ester was also produced in good yield from the corresponding alcohol (Table 2, entry 13). Even for allylic alcohols, the desired esters were also obtained with moderate yields (Table 2, entries 14–16). Improvement of the yield was observed for allylic alcohol oxidation by increasing the loading of $NaAuCl_4$ to 1 mol% (Table 2, entry 15). Methyl methacrylate, a very important raw material in organic chemical engineering, was synthesized from methallyl alcohol by the present aerobic oxidation protocol with 72% yield determined by GC-MS (Table 2, entry 16). However, 4-nitrobenzyl alcohol and 4-bromobenzyl alcohol showed low reactivity (Table 2, entries 17, 18). The yields of the desired products obtained were 28% and 8%, respectively. Unfortunately, the catalytic system was not suitable for the oxidation of heteroatom alcohols such as pyridine-4-methyl alcohol, giving the desired product in very low yield (Table 2, entry 19). In order to obtain the desired esters, the corresponding aldehydes served as substrates and much to our delight, the desired esters were obtained with good yields (Scheme 1). The cinnamaldehyde, heterocyclic, and also aliphatic aldehyde proceeded well and gave the corresponding esters in good to excellent yields.

Using air instead of pure oxygen as the oxygen source has obvious advantages. For example, security and low cost. We next examined the ability of the $NaAuCl_4$–K_2CO_3 catalytic system to catalyze the oxidative esterification of alcohols using air instead of pure oxygen as the terminal oxidant. Three different electronic properties of alcohol are employed and all were converted to the corresponding esters in excellent yields (Scheme 2). To the best of our knowledge, no Au-catalyzed aerobic oxidative esterification reactions using air as an oxidant have been reported.

To further expand the application of this catalytic system, benzylic alcohols were tested in the oxidative esterification reactions with long-chain aliphatic alcohols. Based on the above optimized reaction conditions, *n*-propanol was the first selected in the oxidative esterification reaction and the reaction was performed under air atmosphere (Table 3). The desired product **3a** was obtained in 54% yield (Table 3, entry 1). The improvement of the yield was observed in 76% in the case of increasing the loading of $NaAuCl_4$ to 1 mol% (Table 3, entry 2). Then, the catalytic experiments were carried out in the presence of 1 mol% $NaAuCl_4$ and 10 mol% K_2CO_3 at 80 °C under 1 atm of air atmosphere. Benzyl alcohol reacts smoothly with *n*-butanol, *i*-butanol, *n*-pentanol, and *n*-octyl alcohol; these reactions give the desired products in good yields (Table 3, entries 3–6). Similarly, substituted benzyl alcohols also gave the corresponding esters in good yields (Table 3, entries 7, 8). Next, the oxidative self-esterification of different benzyl alcohols was examined under solvent-free conditions and the corresponding benzoate esters were obtained in good yields (Table 3, entries 9–11). Only a few catalytic systems have been reported for the direct self-esterification of aliphatic

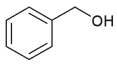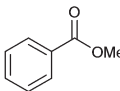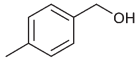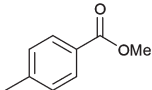**Table 2** Au-catalyzed oxidative esterification of benzylic alcohols with methanol[a]
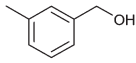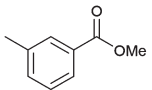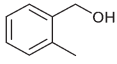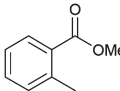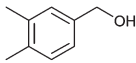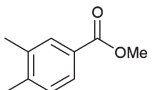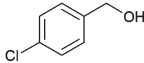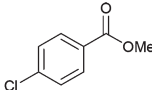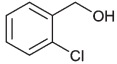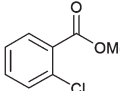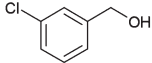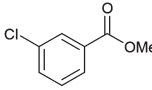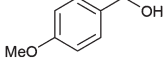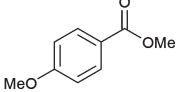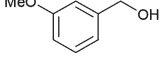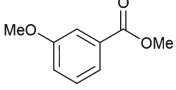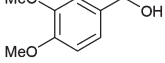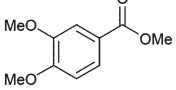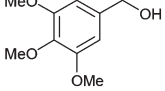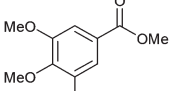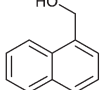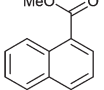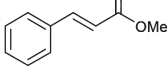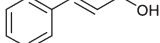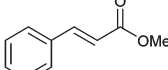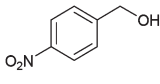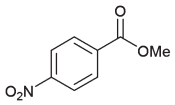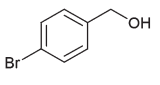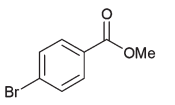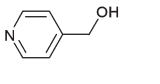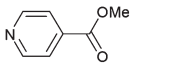
Entry	Substrate	Product	Yield[b] (%)	Selectivity[b] (%)
1			98 (91)	99
2			>99 (91)	99
3			98 (86)	98
4			98 (94)	98
5			>99 (94)	99
6			97 (95)	99
7			92 (90)	96
8			98 (90)	97
9			96 (85)	97
10			94 (88)	96
11			>99 (92)	99
12			81 (75)	85
13			82 (77)	83
14[c]			36	44
15[d]			69	72
16[d]			72	72

Table 2 (Contd.)

Entry	Substrate	Product	Yield[b] (%)	Selectivity[b] (%)
17			28	30
18			8	25
19			2	4

[a] Reaction conditions: alcohols (1 mmol), NaAuCl$_4$·2H$_2$O (0.5 mol%), K$_2$CO$_3$ (10 mol%), 4 mL MeOH, 80 °C, 1 atm O$_2$, 5–24 h. [b] Determined by GC; values in parenthesis are the yields of the isolated products. [c] 31% of cinnamaldehyde was obtained. [d] NaAuCl$_4$·2H$_2$O (1 mol%).
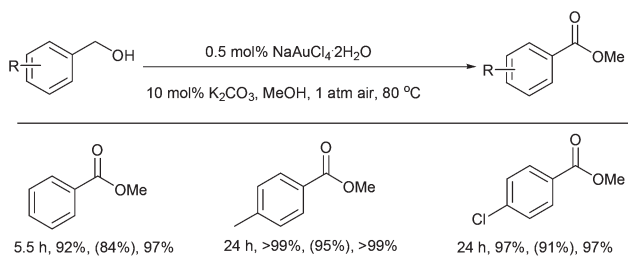
Scheme 2 Au-catalyzed oxidative esterification of alcohols with methanol under 1 atm of air atmosphere [reaction time, GC yield, (isolated yield), and GC selectivity].

alcohols.[10a,18] It was worth noting that the oxidative self-esterification of the unreactive aliphatic primary alcohols could also give the desired esters in good yields with quite good selectivity (Table 3, entries 12, 13).

In order to shed light on the chemical state of Au in the catalytic reaction process, firstly, we study the catalyst evolution from the observed experimental phenomena. After reaction, a pink colored solid was observed at the bottom of the bottle, which was similar to the previously reported NaAuCl$_4$–Cs$_2$CO$_3$ system for aerobic alcohol oxidation.[19] In this system, Cs$_2$CO$_3$ was found to be effective for achieving the reaction which is different to the present catalytic system. We speculate that Au nanoparticles were generated *in situ* and stabilized by K$_2$CO$_3$, which was acting as a heterogeneous support. The recovered catalyst was subjected to X-ray photoelectron spectroscopy (XPS) to probe the chemical state of the Au catalyst. Fig. 1 shows the XPS spectra of Au 4f in the recovered catalyst. The two peaks at the binding energies of 84.0 and 87.7 eV can be assigned to the spin–orbit splitting components of the Au^0 4f$_{7/2}$ and Au^0 4f$_{5/2}$, respectively.[20] No Au–O peaks were present in the spectra. These results indicated that NaAuCl$_4$ was converted to Au^0 in the catalytic reaction process. The peaks located around 292.9 eV were assigned to the K 2p.[21]
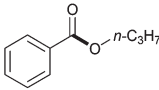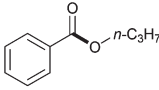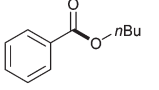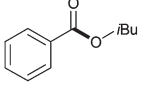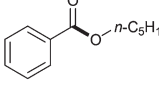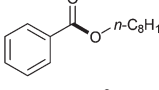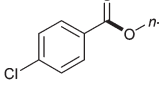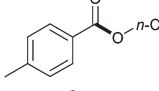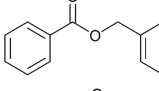
In an attempt to further confirm the presence of Au^0, UV-visible spectroscopy and transmission electron microscopy (TEM) were conducted to investigate the catalyst. Fig. S1 (ESI†) and Fig. 2 show the evidence for the formation of Au^0 by UV-

visible spectroscopy. As shown in Fig. S1,† the UV-visible spectrum of NaAuCl$_4$ + MeOH has the maximum at 320 nm; after reaction, the reaction mixture (liquid) was examined using UV-visible spectroscopy (Fig. S1†). Neither the typical absorption peak of [AuCl$_4$]$^-$ ion precursor (λ = 320 nm) nor the surface-plasmon peak typical for Au nanoparticles ($\lambda \approx 535$ nm) was observed. Fig. 2 shows the UV-visible spectrum of the recovered catalyst (pink colored solid). The maximum absorption peak appears at 535 nm, which is a surface-plasmon of Au nanoparticles, suggesting the formation of Au nanoparticles. These results indicate the evolution of [AuCl$_4$]$^-$ to Au^0.[22] TEM images of the recovered catalyst further confirmed the formation of Au nanoparticles with a size distribution of *ca.* 10 nm in diameter over the K$_2$CO$_3$ surface (ESI, Fig. S2†).

The reaction process was studied in more detail with benzyl alcohol as a substrate in order to get a better understanding of the reaction mechanism. After reaction, a trace amount of benzyl benzoate and benzaldehyde was detected from GC-MS, which clearly exhibited that one or both of them was most likely to be the reaction intermediate. A kinetic study of the oxidation of benzyl alcohol was also carried out, and it was observed that benzaldehyde and benzyl benzoate were detected from GC-MS along with the consumption of the starting benzyl alcohol (Fig. 3). It should be noted that the hemiacetal was not observed by GC-MS. The control experiments were carried out for the reaction pathway exploration (Scheme 3). When benzaldehyde was subjected as the substrate under the standard conditions, methyl benzoate was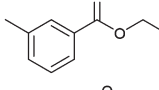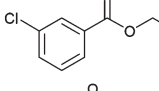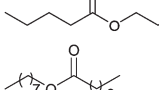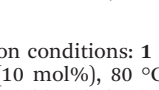 obtained in 85% yield within only 1.5 h. Similarly, for the benzyl benzoate, 81% yield of methyl benzoate was obtained with 5 h. The oxidative self-esterification of benzyl alcohol was performed under solvent-free conditions. The desired benzyl benzoate was obtained in 70% yield. These results clearly indicate that both of benzaldehyde and benzyl benzoate were the reaction intermediates.
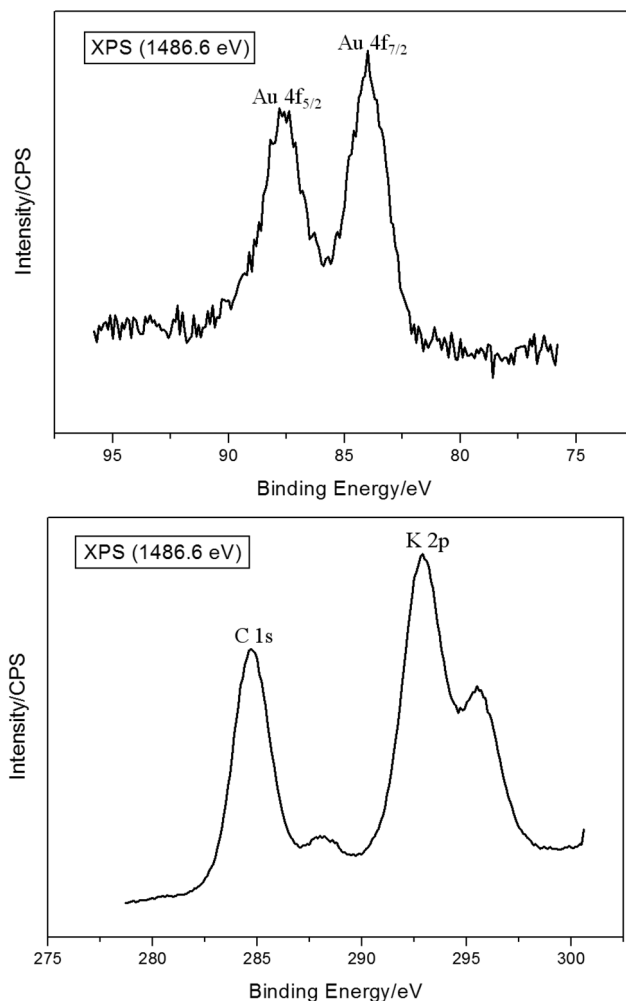
On the basis of the catalyst characterization, kinetic study, control experiments and pertinent literature,[9] the following pathway was proposed, which was similar to the reaction reported previously (Scheme 4). The alcohol was firstly oxidized to benzaldehyde and then formed the hemiacetal. The

Table 3 Au-catalyzed oxidative esterification of benzylic alcohols with long-chain aliphatic alcohols and self-esterification of alcohols[a]

$$R\text{—}OH \;+\; HO\text{—}R' \;\xrightarrow[\text{10 mol\% K}_2\text{CO}_3,\ 80\ °\text{C, air}]{\text{1 mol\% NaAuCl}_4\cdot 2\text{H}_2\text{O}}\; R\text{—}C(=O)\text{—}O\text{—}R'$$

Entry	Product	3	Yield[b] (%)	Selectivity[b] (%)
1[c]	(benzoate, O-n-C₃H₇)	3a	64 (54)	80
2	(benzoate, O-n-C₃H₇)	3a	81 (76)	82
3	(benzoate, O-nBu)	3b	72 (64)	74
4	(benzoate, O-iBu)	3c	56	56
5	(benzoate, O-n-C₅H₁₁)	3d	82 (75)	82
6	(benzoate, O-n-C₈H₁₇)	3e	67	67
7	(4-Cl benzoate, O-n-C₃H₇)	3f	79 (70)	89
8	(4-Me benzoate, O-n-C₃H₇)	3g	66	66
9[d]	(benzyl benzoate)	3h	70	80
10[d,e]	(3-methyl benzoate)	3i	68	72
11[d,e]	(3-Cl benzoate)	3j	73	85
12[d,e]	(pentyl pentanoate)	3k	62	92
13[d,e]	(ester)	3l	54	92

[a] Reaction conditions: **1** (1 mmol), **2** (1 mL), NaAuCl₄·2H₂O (1 mol%), K₂CO₃ (10 mol%), 80 °C. [b] Determined by GC; values in parenthesis are the yields of the isolated products. [c] NaAuCl₄·2H₂O (0.5 mol%). [d] Substrate (2 mmol), under solvent-free conditions. The major byproducts were aldehydes. [e] K₂CO₃ (50 mol%).

Fig. 1 XPS spectra of the recovered catalyst (Au–K₂CO₃).
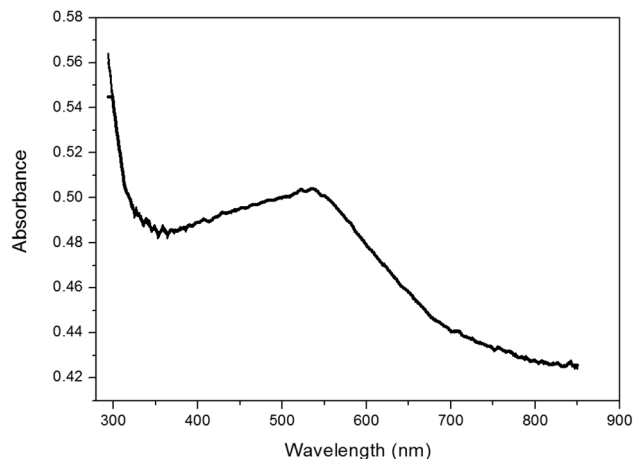
Fig. 2 UV-vis spectrum of the recovered catalyst (Au–K₂CO₃).

hemiacetal was subsequently oxidized to the ester. In this process, the oxidative homocoupling reaction occurs catalyzed by NaAuCl₄ to form the benzyl benzoate, which readily undergoes transesterification with methanol to give the methyl benzoate. Meanwhile, based on the kinetic data and control experiments, the oxidation of alcohols to aldehydes might be the key rate-determining step in the course of the reaction.

Fig. 3 A kinetic study for the oxidation of benzyl alcohol. Yields determined by GC using biphenyl as an internal standard.
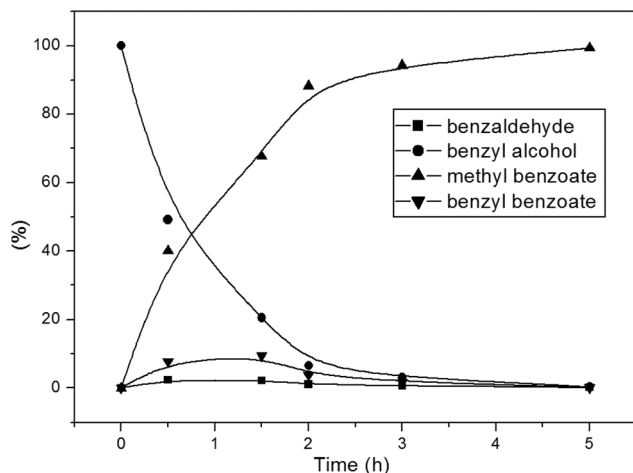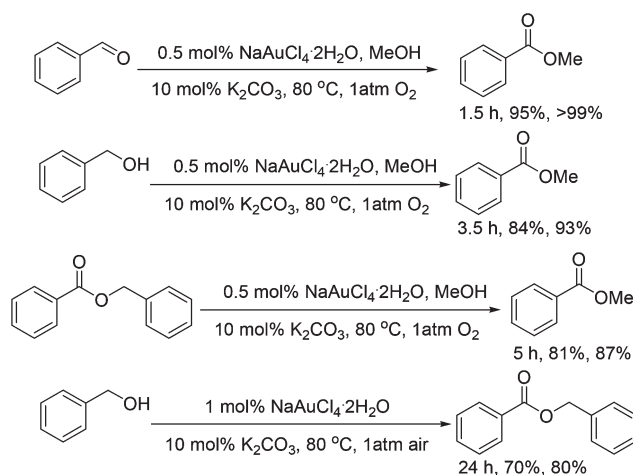

Scheme 3 Control experiments.

Based on the results of the UV-visible spectrum analysis, the pink colored solid observed at the bottom of the bottle containing the Au nanoparticles was Au–K_2CO_3. The reusability of the recovered catalyst (Au–K_2CO_3) was investigated using benzyl alcohol as a model substrate. After fresh reaction, the reaction mixtures were readily washed with MeOH without further reactivation. Then, benzyl alcohol and K_2CO_3 were added. The recycling results showed that the Au–K_2CO_3 can be

reused 8 times without appreciable loss of catalytic activity (ESI, Fig. S3†). The consistent catalytic activity also suggests that the Au *in situ* supported on simple inorganic salt K_2CO_3 shows high stability for the aerobic oxidative esterification of benzyl alcohol.

The turnover frequency (TOF) usually represents the catalytic activity of the catalyst. To further evaluate the catalytic activity of the present catalytic system, benzyl alcohol was used as a representative substrate and the reaction was performed on a gram scale. Reducing the catalyst loading from 0.5 mol% to 0.15 mol%, a 10 mmol (1.08 g) reaction of benzyl alcohol was performed in the presence of 10 mol% K_2CO_3 under 3 atm O_2 at 100 °C. After reaction 1 h, the initial turnover frequency (TOF) based on Au was obtained up to 219 h^{-1} with 43% of conversion (with 39% of conversion, TOF = 197 h^{-1}, 3 atm O_2, 80 °C). The TOF value obtained herein is comparable to the best results reported for Au catalysts.[90] Based on the comparison, it is clear that the present system showed high catalytic activity for the tandem synthesis of esters from alcohols.

Conclusions

In conclusion, we have developed a facile gold-catalyzed method for the aerobic oxidation of alcohols to the corresponding esters in the presence of a low catalytic amount of base under air or dioxygen atmosphere. The gold catalyst showed high catalytic activity for the direct oxidative esterification reaction in the absence of any oxide or polymer supports. Various benzylic alcohols and allylic alcohols were smoothly reacted with methanol and even with long-chain aliphatic alcohols, affording the desired products in good to excellent yields. The oxidative homocoupling of benzylic alcohols and even aliphatic primary alcohols proceeded well under solvent-free conditions to give the corresponding esters in good yields. Characterizations by XPS, TEM, and UV-vis proved that the catalytic system involved gold nanoparticles, which were generated *in situ* and supported on K_2CO_3, and which were the true catalytically active species. The gold catalyst generated *in situ* from gold salts and the support in the reaction process did not include any purification step, and the residue from the gold precursor did not prevent high catalytic activity. The present catalytic protocol was performed on a 10 mmol scale, resulting in an excellent TOF of 219 h^{-1}. Very importantly, the catalytic system is very easy to handle, which makes the catalyst
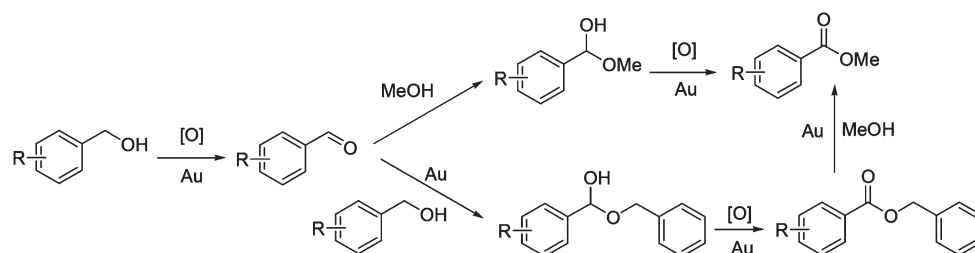
Scheme 4 Possible reaction pathway for the Au-catalyzed oxidative esterification of alcohols.

especially useful for practical applications in organic synthesis. Further work on other applications of the present catalytic system is currently ongoing in our laboratory.

Acknowledgements

Notes and references

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