Clean preparation of methyl esters in one-step oxidative esterification of primary alcohols catalyzed by supported gold nanoparticles

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Methyl esters were prepared by the clean, one-step catalytic esterification of primary alcohols using molecular oxygen as a green oxidant and a newly developed SiO_2-supported gold nanoparticle catalyst. The catalyst was highly active and selective in a broad range of pressure and temperature. At 3 atm O_2 and 130 °C benzyl alcohol was converted to methyl benzoate with 100% conversion and 100% selectivity in 4 h of reaction. This catalytic process is much "greener" than the conventional reaction routes because it avoids the use of stoichiometric environmentally unfriendly oxidants, usually required for alcohol oxidation, and the use of strong acids or excess of reactants or constant removal of products required to shift the equilibrium to the desired esterification product.

Introduction

Methyl esters are important products in the chemical industry, for example, within the fragrance industry, as flavoring agents, solvent extractants, diluents and intermediates. They are present as odoriferous components in flowers and fruits.[1] Methyl esters are traditionally prepared by the reaction of carboxylic acid and methanol using acid catalysts such as sulfuric, sulfonic, phosphoric, hydrochloric and p-toluenesulfonic acid.[2] Alkoxides, such as sodium and potassium alkoxides, have also been used to prepare methyl esters from carboxylic acid precursors.[3] However, the direct oxidative esterification of alcohols, avoiding the use of the corresponding carboxylic acid, is very attractive. This reaction typically takes place in a two-step procedure, first the oxidation of the alcohol with manganese dioxide or sodium dichromate, and the subsequent conversion of the carboxylic acid intermediate to methyl ester.[4] The general requirement for the use of stoichiometric amounts (or excess) of toxic and expensive reagents render the process environmentally and economically unsuitable. The present ecological standards increase the pressure to the development of environmentally benign methods. The use of molecular oxygen or hydrogen peroxide in catalyzed oxidation reactions has attracted attention.[5] In this scenario, a more elegant and environmentally benign method for the preparation of methyl esters is based on the one-step direct oxidative esterification of primary alcohols. Examples include the use of hypervalent iodine(III) reagents,[6] N-heterocyclic carbene catalysts in the presence of stoichiometric oxidants,[7] and the greener gold-catalyzed reactions in the presence of O_2.[8]

Gold nanoparticle-catalysts have been applied to many oxidation reaction, such as CO,[9] alcohol,[10] glycerol,[11] glucose,[12] and olefin oxidations,[13] as well as esterification of aldehydes.[14] The direct oxidative esterification of alcohols using molecular oxygen

as oxidant is relatively rare.[8] In the oxidative esterification proposed reaction pathway, the alcohol is first oxidized to an aldehyde and after the aldehyde forms a hemiacetal with methanol, which is further oxidized leading to the corresponding ester.[8] The rate-determining step is the aerobic oxidation of alcohols to the corresponding aldehyde. The formation of hemiacetal and further methyl ester proceeds very fast, in fact with a reasonable rate even below −70 °C.[14a]

Gold catalysis has a strong dependence on the acidic nature of the supports and substrates, and exhibited unique reactivity when basic conditions are used. In general, carbonates (e.g. K_2CO_3, Na_2CO_3) are used as weak bases in many organic syntheses, particularly in reactions involving proton extraction. In most of these syntheses, a stoichiometric excess of carbonate is necessary to promote a high reagent conversion. However, in gold catalysis the ratio of carbonate/alcohol required is much lower.[15]

Here we report the synthesis of a gold catalyst for the esterification of primary alcohols in the presence of methanol under mild conditions. Pre-synthesized gold nanoparticles were used as precursor for the preparation of an oxide supported gold catalyst. In general, the preparation of supported gold nanoparticles using traditional methods, such as co-precipitation, deposition–precipitation, ion-exchange, impregnation, and successive reduction and calcination, has been widely reported.[16] However, these methodologies have some disadvantages, such as lack of control over size, morphology, and limited stability of the nanoparticles formed. It is especially difficult to process the nanoparticles once produced. Therefore, the immobilization of pre-synthesized nanoparticles has gained attention;[17] since it can lead to controllable size, shape and surface properties (more or less coordinating groups) of nanoparticles. By choosing the nanoparticles preparation method, such properties can be tuned as well as the catalytic activities.[18]
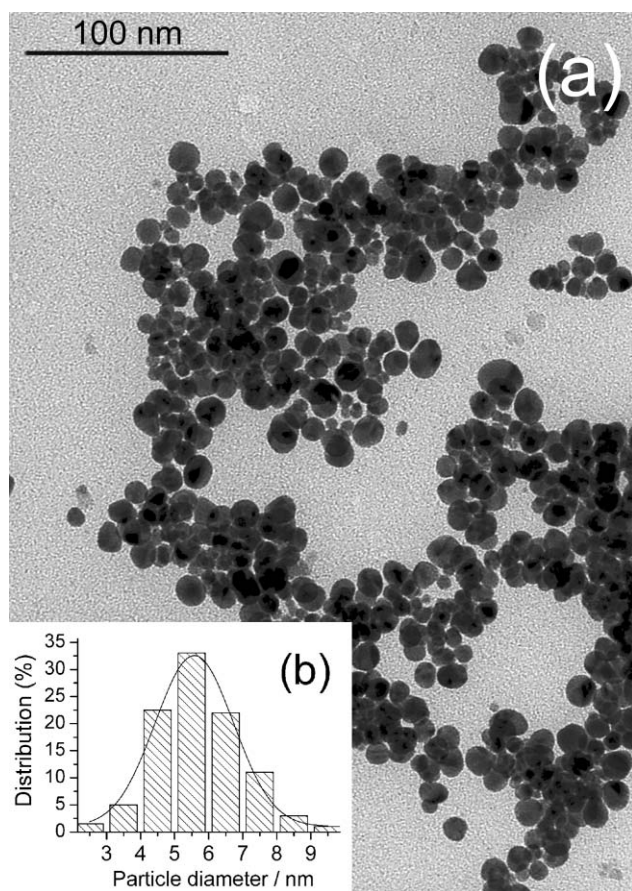
Results and discussion

Gold nanoparticles were synthesized by the modified Brust two-phase method.[19] This method consists of adjusting the pH of $HAuCl_4$ to 6.5, and transferring $[AuCl_x(OH)_y]$ from aqueous

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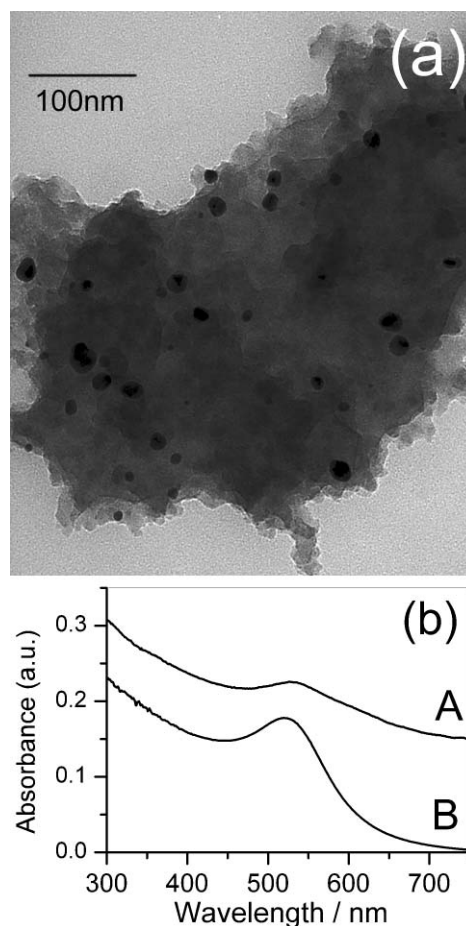*[b]Institute of Physics, USP, São Paulo, SP 05508-090, Brazil*

solution to toluene using tetraoctylammonium bromide (TOAB) as the phase transfer reagent, while the metal is reduced with aqueous $NaBH_4$. TOAB was chosen because of its interesting binding properties to metal surfaces. This capping ligand binds strong enough to stabilize narrow size gold nanoparticles, but "weak" enough to provide reactant access to the metal surface.[18]

The Au nanoparticles solution was impregnated on silica (Fumed silica WACKER HDK T40, BET surface area 360–440 $m^2.g^{-1}$) modified with 3-(aminopropyl)-triethoxysilane (APTES) in dry toluene under nitrogen. The surface area estimated by BET was reduced to 128 $m^2.g^{-1}$ after metal immobilization. The final gold content was 2.0 wt%, as determined by ICP-OES. The Au nanoparticles, before and after immobilization in silica, were observed by TEM. Fig. 1(a) shows a representative image of the pre-synthesized Au nanoparticles with a relatively narrow particle size distribution in the range of 2.5–9.5 nm. Fig. 1(b) shows the histogram of Au nanoparticle size distribution fitted to a Gaussian function with mean diameter of 5.7 ± 1.1 nm.

Fig. 2 (a) TEM of gold nanoparticles supported on silica and (b) UV-vis spectra of the gold nanoparticles supported on silica (A) and gold nanoparticles in solution (B).

Fig. 1 (a) TEM image of gold nanoparticles and (b) histogram showing particle size distribution.

The immobilization of the pre-synthesized Au nanoparticles in silica was confirmed by TEM (Fig. 2(a)) and by the characteristic SPR band of Au nanoparticles at 520 nm (Fig. 2(b)). No significant change was observed in the SPR band position before (curve A) and after Au-nanoparticle immobilization in the silica matrix (curve B), indicating no change of particle size during the immobilization process or particle agglomeration.

The first attempt to catalyze the oxidation of benzyl alcohol by the Au-supported catalyst under atmospheric pressure of O_2 failed, and no conversion of the substrate was observed after 4 h of reaction at 70 °C (Table 1, entry 1). Then, the system was submitted to pressure of oxygen (4 atm), which enhanced the conversion to 43% (Table 1, entry 4). The product obtained was the methyl benzoate with 100% selectivity, as determined by GC-MS. In absence of base, the catalyst was not efficient to catalyze the reaction (Table 1, entry 3). However, the addition of a small amount (55 mg, 0.4 mmol) of K_2CO_3 increased the conversion from 4 to 43% under similar reaction conditions (Table 1, entries 3 and 4). A control experiment in the absence of catalyst (only amino-modified silica present) under similar conditions (3atm of O_2, 130 °C and K_2CO_3) showed no conversion of benzyl alcohol.

An increase in the temperature of the reaction to 130 °C, resulted in 100% of conversion (Table 1, entry 6), while maintaining the selectivity. In all cases, methyl benzoate was obtained as the major product and benzaldehyde as the only by-product (Table 1, entry 5). Studies performed in different reaction conditions revealed that the catalytic activity of the Au-supported catalyst was strongly dependent on the reaction temperature and oxygen pressure (Fig. 3 and Fig. 4). The oxidation of some allylic alcohols, much more resistant to oxidation than

Table 1 Oxidative esterification of primary alcohols by Au-supported catalyst

Entry	Alcohol	T (°C)	Au/substrate (molar ratio)	P O$_2$ (atm)	Conversion (%)^d	Selectivity to methyl ester (%)	By-products (%)		
							aldehyde	ester (homo-coupling)	carboxylic acid
1^a	Benzyl alcohol	70	1/1026	—	0	0	0	0	0
2^a	Benzyl alcohol	70	1/1026	3	0^c	0	0	0	0
3^a	Benzyl alcohol	70	1/1026	4	4.0^c	100	0	0	0
4^a	Benzyl alcohol	70	1/1026	4	42.8	100	0	0	0
5^a	Benzyl alcohol	110	1/1026	3	96.1	97.0	3.0	0	0
6^a	Benzyl alcohol	130	1/1026	3	100	100	0	0	0
7^b	Allyl alcohol	130	1/410	3	15.8	83.0	0	0	17.0
8^b	Allyl alcohol	130	1/410	6	64.1	80.0	0	0	20.0
9^b	1-propanol	130	1/410	3	3.1	100	0	0	0
10^b	1-propanol	130	1/410	6	15.3	96.0	0	4.0	0
11^b	1-butanol	130	1/410	3	4.3	97.0	0	3.0	0
12^b	1-butanol	130	1/410	6	20.6	97.0	0	3.0	0
13^b	1-pentanol	130	1/410	3	4.3	96.0	0	0.1	3.9
14^b	1-pentanol	130	1/410	6	61.3	96.0	0	0	4.0

Conditions: ^{a} 2.5 mmol alcohol in methanol (2 mL); 55 mg of K$_2$CO$_3$, 24 mg of Au-supported catalyst (2.44. μmol Au), reaction time: 4 h; or ^{b} 1mmol alcohol in methanol (2 mL); 55 mg of K$_2$CO$_3$, 24 mg of Au-supported catalyst (2.44. μmol Au) reaction time: 7 h ^{c} without K$_2$CO$_3$ ^{d} conversion and selectivity were determined by GC-MS.
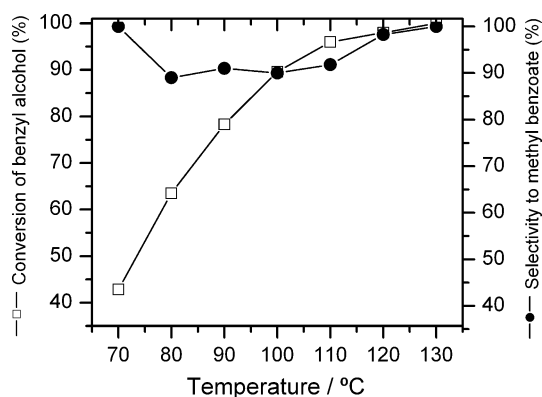
Fig. 3 Temperature dependence on the catalytic esterification of benzyl alcohol. Conditions: 20 mg Au-catalyst, 2.5 mmol benzyl alcohol, 2 mL methanol, 55 mg K$_2$CO$_3$, 3 atm O$_2$, 4 h.
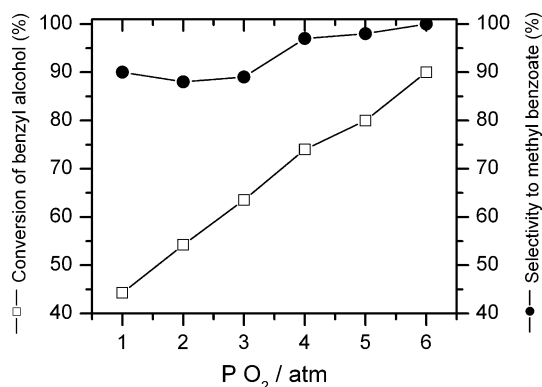
Fig. 4 Pressure dependence on the catalytic esterification of benzyl alcohol. Conditions: 20 mg Au-catalyst, 2.5 mmol benzyl alcohol, 2 mL methanol, 55 mg K$_2$CO$_3$, 80 °C, 4 h.

benzyl alcohol, was also catalyzed by our Au-supported catalyst (Table 1, entry 7 to 14). As expected, the conversion was lower when compared with benzyl alcohol oxidation. In all reactions, methyl ester was obtained as the major product (selectivity from 80 to 100%) and the corresponding carboxylic acids or esters (homo-coupling reaction) were found as by-products (Table 1, entry 7–14). Additionally, we do not expect the occurrence of methanol oxidation as a side reaction during the esterification reaction, since the GC chromatograms did not show any by-product of methanol oxidation, such as formic acid, methyl formate and formaldehyde.

The standard experimental condition used in all reactions reported in Table 1 was fixed to 1/20 benzyl alcohol to methanol molar ratio. We explored two conditions with higher and lower alcohol/methanol molar ratios using the esterification of benzyl alcohol as a model reaction. The reaction under standard conditions (1/20) was stopped in 3 h (one hour before 100% conversion and 100% selectivity was reached) and resulted in 76% conversion and 90% selectivity. In larger excesses of methanol (1/30) the reaction rates decreased (69% conversion and 84% selectivity), and in less excesses of methanol (1/5) 84% conversion and 94% selectivity was reached. It is interesting to show that the reaction can proceed with high conversion and selectivity using lower excesses of methanol.

Especially in liquid-phase oxidation reactions using supported catalysts, a major challenge is to prevent leaching of metal into the solution, because of the possible dissolution of metals by the reactants and particularly the carboxylic acid-type (by)products. The isolated product, methyl benzoate, obtained after filtering off the solid catalyst was analyzed by ICP OES and contains less than 2.5 ppb of Au (limit of quantification). Therefore, metal leaching was negligible in our very stable catalytic system. A control experiment was made in order to detect any catalytic activity of leached species. The reactor was loaded with the reaction supernatant obtained after centrifugation (14500 rpm, 15 minutes) and a new portion of benzyl alcohol (2.5 mmol) was added. The reaction mixture was submitted to similar conditions (3atm of O$_2$, 130 °C and K$_2$CO$_3$) and no conversion of benzyl alcohol was observed. However, the recovered solid could be reused in successive oxidations of benzyl alcohol under 3 atm of O$_2$ and 130 °C. It is worth mentioning that the Au-supported

catalyst maintained its high catalytic activity, affording 97% of benzyl alcohol conversion, after seven recycling and reuses of the same catalyst portion. This is a strong evidence of the high stability of our Au-supported catalyst.

Experimental

Synthesis of gold nanoparticles

Gold nanoparticles were synthesized by the modified Brust two-phase method.[19] An aqueous solution of hydrogen tetra-chloroaurate (30 mL, 30 mmol.L^{-1}, pH 6.5) was added to a toluene solution of tetra-n-octylammonium bromide (80 mL, 50 mmol.L^{-1}). The two-phase mixture was vigorously stirred until all the tetrachloroaurate was transferred into the organic layer. Then, a freshly prepared aqueous solution of sodium boronhydride (25 mL, 0.4 mol.L^{-1}) was added dropwise under vigorous stirring. After 30 minutes, the aqueous phase was separated and disposed. The organic phase was treated with an aqueous solution of H_2SO_4 (1 mol.L^{-1}) until pH 7 was reached. The organic phase was further washed with distilled water (2 × 50 mL) to obtain the final gold nanoparticles toluene solution.

Functionalization of silica surface with amino group

Amino-modified silica was prepared following the procedure described by Jacinto et al.[20] Typically, 750 µL of 3-(aminopropyl)-triethoxysilane (APTES), dissolved in 75mL of dried toluene, was added to 500 mg of commercial SiO_2 (Fumed silica WACKER HDK T40). The suspension was stirred for 2h at room temperature. The amino-functionalized solid SiO_2-NH_2 was washed with toluene, separated by filtration and dried at 100 °C for 20 h.

Impregnation of gold nanoparticles on silica

The solution containing pre-synthesized gold nanoparticles was diluted 1:2 in toluene and added to 660 mg of amino-modified silica. The suspension was stirred for 4h at room temperature. The purple solid was collected by filtration and dried in vacuum. The solid contains 2.0 wt% of gold, as determined by ICP OES.

Oxidation experiments

In a typical experiment, gold nanoparticles-supported on silica (24 mg of solid, 2.44. µmol Au), K_2CO_3 (55 mg, 0.4 mmol), and 2 mL of a methanol solution containing the desired quantity of substrate (2.5 mmol or 1 mmol) were added to a Fischer–Porter glass reactor. The reactor was evacuated and loaded with oxygen to the desired pressure (1 to 6 atm). The reaction was conducted under magnetic stirring (700 rpm) and the temperature was maintained by a hot-stirring plate connected to a digital controller (ETS-D4 IKA). After the desired time, the catalyst was recovered by centrifugation and the liquid phase was collected and analyzed by gas chromatography (GC) and GC-MS. The isolated catalyst was washed with a mixture of ethanol/water 1:1, and this solid could be reused when new amounts of substrate and base were added.

Materials and methods

TEM analysis. The morphology of the gold nanoparticles was obtained on a Philips CM 200 microscope operating at an accelerating voltage of 200 kV. The samples for TEM were prepared by collecting a small portion of nanoparticles dispersed in an aqueous solution on a carbon-coated copper grid. The histogram of nanoparticle size distribution was obtained from the measurement of about 250 particles found in an arbitrarily chosen area of enlarged micrographs.

GC-MS analysis. Gas chromatography analyses were performed on a Shimadzu GCMS-QP5050A, equipped with a 30 m capillary column with 5% phenyl- 95% dimethylpoloysiloxane stationary phases (AT5), using the following parameters: initial temperature: 40 °C, temperature ramp: 5 °C min^{-1} (from 40 °C to 150 °C), and 40 °C min^{-1} (from 150 °C to 250 °C), final temperature: 250 °C, injection volume: 1 µL. The products were quantified using external calibration.

ICP-OES analysis. The gold content in the solid catalyst and in the oxidation products was measured using an inductively coupled plasma optical emission spectrometer Genisis SOP (Spectro). Reference solutions of Au (1000 mg L^{-1}) with a high degree of analytical purity (ICP Standard, SpecSol) were used to obtain the calibration curves. Deionized water (MILLI-Q) was used to prepare all solutions. The sample digestion was carried out at 100 °C for 3 h with 5 mL aqua regia. For liquid samples, the organic phase was previously evaporated. The volume of the samples was then adjusted to 25 mL using DI water. The gold content was quantified in duplicate for each sample.

Conclusions

In summary, we have successfully demonstrated that pre-synthesized gold nanoparticles can be combined with silica for the favorable preparation of a new supported gold catalyst with excellent stability. The Au-catalyst was highly active, selective and recyclable for the one-step oxidative esterification of primary alcohols to methyl ester using the environmentally friendly oxidant, O_2, and sub-stoichiometric amounts of carbonates. This process is much superior to the traditional synthetic routes involving the use of carboxylic acids and requiring excesses of strong acids or bases. The methodology described here is a cost-effective and very attractive route for the clean synthesis of methyl esters.

Acknowledgements

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