Development of a Titanium Dioxide-Supported Gold Nanoparticle Catalyst for the Selective *N*-Formylation of Functionalized Amines Using Carbon Dioxide

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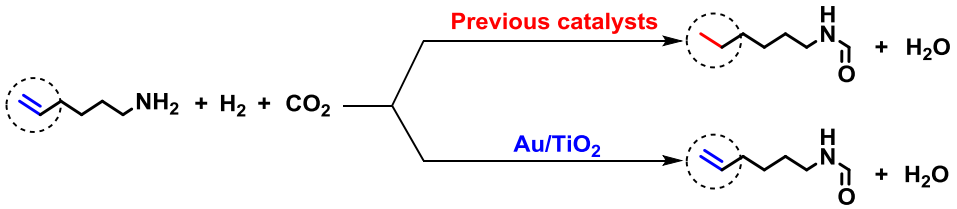
Abstract: A titanium dioxide-supported gold nanoparticle catalyst efficiently promoted the selective *N*-formylation of various amines using CO_2 as a carbonyl source under the pressured hydrogen conditions. The *N*-formylation of amines proceeded in high selectivity with reducible functional groups, such as olefin, carbonyl, cyano, halogen, amide and carbamate moieties, retaining intact. Furthermore, the catalyst after the reaction was easily recovered by filtration and reused without any loss of catalytic activity or selectivity.

Keywords: Gold nanoparticle, Formylation, Heterogeneous catalyst.

1. Introduction

Formamides are important intermediates for the production of pharmaceuticals, insecticidal agents, and fine chemicals. The formamides are currently synthesized by *N*-formylation of amines using toxic carbon monoxide as a carbonyl source or using hydrosilanes as reducing reagents and CO_2 as a carbonyl source with low atom efficiency. Recently, the green catalytic *N*-formylation of amines using CO_2 and molecular hydrogen (H_2) is attracting much attention. In this reaction, nontoxic CO_2 is used as a carbonyl source and water is produced as the sole byproduct. However, this method has crucial problems. The *N*-formylation of amines generally requires high pressure of H_2 at high temperature, which cause the hydrogenation of reducible functional groups, such as olefin, carbonyl, cyano, halogen, amide and carbamate moieties. Therefore, the selective *N*-formylation of amines with reducible functional groups is a challenging issue.

Herein, we report that the unique catalytic activity of titanium dioxide-supported gold nanoparticle catalyst (Au/TiO_2) for *N*-formylation of functionalized amines using CO_2 as a carbonyl source under H_2 atmosphere.[1] For example, Au/TiO_2 enables the selective *N*-formylation of 5-hexene-1-amine with retaining the carbon-carbon double bond while previous catalysts cause the hydrogenation (Scheme 1). The present Au/TiO_2 catalytic system is applicable to the *N*-formylation of various amines with other reducible functional groups, giving the corresponding products in excellent yields.



Scheme 1. Au/TiO_2-catalyzed selective *N*-formylation of 5-hexene-1-amine using CO_2 and H_2

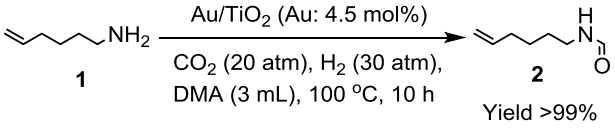
2. Experimental

Au/TiO_2 was synthesized as follows. TiO_2 was treated with aqueous $HAuCl_4$ solution at room temperature in the presence of aqueous NH_3. The resulting slurry was filtered, washed with deionized water and dried at room temperature in *vacuo* to afford TiO_2-supported Au^{III} species as a light yellow powder. Treatment of this powder with KBH_4 yielded Au/TiO_2 as a purple powder. A typical reaction procedure for *N*-formylation is as follows. Au/TiO_2 was placed in a stainless steel autoclave (with a Teflon inner cylinder) followed by

addition of amine and solvent. The reaction mixture was stirred under the pressured CO_2 with H_2. After the reaction, Au/TiO_2 was removed by filtered and the yield was determined by GC analysis.

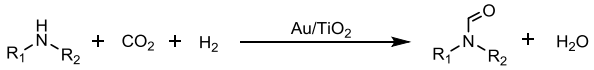
3. Results and discussion

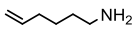
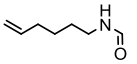
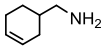
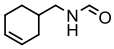
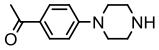
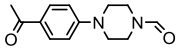
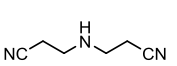
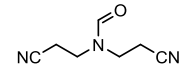
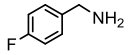
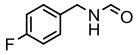
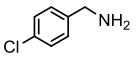
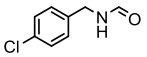
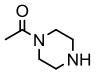
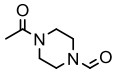
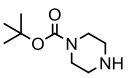
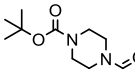
Au/TiO_2 showed high activity for the *N*-formylation of 5-hexen-1-amine (**1**) to afford the desired product (**2**) with retaining the olefinic moiety during the reaction under 20 atm of CO_2 and 30 atm of H_2 (Scheme 2). In sharp contrast, the TiO_2-supported other metal nanoparticles, such as Pd, Ru, Pt, Rh, Ag and Cu, did not afford **2** at all and the olefinic moiety of **1** was hydrogenated. Moreover, Au nanoparticles on the other supports, such as ZnO, CeO_2, Al_2O_3 and Nb_2O_5, catalyst were inactive for this reaction. From the above results, a combination of Au nanoparticles and TiO_2 specifically enable selective *N*-formylation of **1**.



Scheme 2. Selective *N*-formylation of **1** to **2** using Au/TiO_2 with CO_2 and H_2

Table. *N*-formylation of various amines catalyzed by Au/TiO_2[a]



Entry	Substrate	Product	Temp. [°C]	Time [h]	Yield [%][b]
1			100	10	>99 (91[c])
2[d]			100	10	>99
3			100	10	>99
4			140	10	98[c]
5			140	10	>99
6			120	5	>99 (96[c])
7			120	5	>99 (94[c])
8			140	5	>99 (98[c])
9			140	5	>99

[a]Reaction conditions: Au/TiO_2 (0.2 g, Au: 4.5 mol%), amine (0.5 mmol), DMA (3 mL), CO_2 (20 atm), H_2 (30 atm). [b]Determined by GC using internal standard technique. [c]Isolated yield. [d]5th reuse.

This Au/TiO_2 catalytic system is applicable to other amines with a wide range of reducible functional groups (Table). A series of reducible functional groups, such as olefin (entries 1 and 3), carbonyl (entry 4), cyano (entry 5), halogen (entries 6 and 7), amide (entry 8), and carbamate (entry 9) moieties, were completely retained during the *N*-formylation. In addition, the corresponding products were obtained in excellent yields without any by-products. From these results, Au/TiO_2 is completely inactive for diverse functionalities.

Au/TiO_2 is easily removed by filtration from the reaction mixture after the reaction. Inductively coupled plasma atomic emission spectra (ICP-AES) analysis of the resulting filtrate showed the absence of Au species in the filtrate (detection limit of 0.1 ppm), proving no leaching of Au species during the reaction. The recovered Au/TiO_2 catalyst is reused without any loss of activity or selectivity for the *N*-formylation of **1** even after the 5th recycling experiments (Table, entry 2).

4. Conclusions

A highly selective *N*-formylation of functionalized amines using CO_2 with H_2 was achieved by the Au/TiO_2 catalyst. Au/TiO_2 efficiently promoted for the first time the selective *N*-formylation of various amines to corresponding formamides in excellent yields without hydrogenation of reducible functional groups. This catalyst was reusable without any loss of catalytic activity or selectivity.

Reference

1. T. Mitsudome, T. Urayama, S. Fujita, Z. Maeno, T. Mizugaki, K. Jitsukawa, K. Kaneda, ChemCatChem. 9 (2017) 3632.