

Non-nanogold catalyzed aerobic oxidation of secondary amines to imines†

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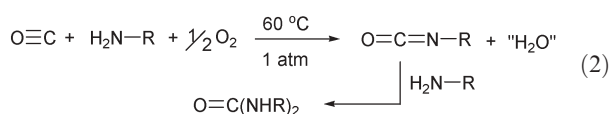
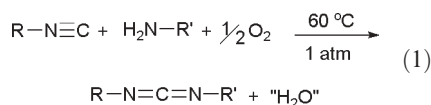
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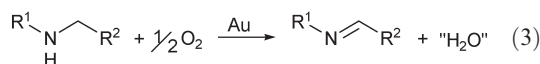
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Bulk gold powder (~10³ nm particle size) is a highly active catalyst for the oxidative dehydrogenation of secondary amines to imines under the mild conditions of 1 atm O₂ and 60–100 °C.

Considering its well-established reputation for poor catalytic activity, gold metal has recently attracted a great deal of interest because of its high activity when created in nano-sized forms (<5 nm) when supported on metal oxides.^{1–3} A common test of nanogold catalytic activity is in the reaction of CO and O₂ to form CO₂. In contrast, bulk gold metal, especially gold metal powder, has a very low catalytic activity in this reaction.^{1–4} Very recently, we reported that bulk gold powder, which consists of particles (~1000 nm) much larger than nanoparticles, can catalyze under mild conditions reactions of isocyanides (eqn (1))⁵ or carbon monoxide (eqn (2))⁶ with primary amines and oxygen to produce the



corresponding carbodiimides or ureas. These results were especially notable because of the high activity of the non-nanogold catalyst. During the course of our investigations of catalysis by gold powder, we found that it also catalyzes the aerobic oxidation of secondary amines to imines. These reactions, which are described herein, involve a key step (eqn (3)), the oxidative



dehydrogenation of an amine. This type of gold powder-catalyzed reaction is fundamentally different than those (eqn (1) and (2)) reported previously and represents a significant new finding in non-nanogold catalysis.

The reactions were performed by stirring (magnetic bar) 1.00 g of gold powder with 5 mL of a solution containing 0.20 mmol of the secondary amine in a glass tube. A syringe needle attached to a

balloon containing approximately 1.0 L of O₂ (~1 atm, a stoichiometric excess) was inserted into the septum covering the opening of the tube. These oxidations of secondary amines (eqn. (3)) gave products (Table 1) that were identified by their GC-mass spectra, and yields were determined by GC using authentic samples of the products as calibrants. After each catalytic reaction, the gold powder was cleaned with "piranha" solution (30% H₂O₂, concentrated H₂SO₄) as described previously;⁵ the gold retained the same activity even after more than 20 piranha solution treatments. The reactions were usually conducted in both acetonitrile (at 60 °C for 40 h) and toluene (at 100 °C for 24 h). As seen in Table 1, yields are generally much higher in toluene than acetonitrile. Also, benzylic amines (entries 2 and 3) give higher yields than diisopropylamine (entry 1). To ensure that the reactions required both the gold catalyst and oxygen, the reactions of dibenzylamine and 1,2,3,4-tetrahydroisoquinoline were performed in the absence of the Au and O₂ (in Ar). The amine did not react in either reaction. Water is a presumed product in all of these

Table 1 Gold-catalyzed aerobic oxidation of secondary amines to imines according to eqn. (3)^a

Entry	Substrate	Product	Yield [%]
1			15 ^b
2			35 ^b ; 64 ^c
3			40 ^b ; 87 ^c
4			46 ^b ; 93 ^c
5			41 ^b ; 75 ^c
6			22 ^b

^a Reaction conditions: amine (0.20 mmol), 5 mL of solvent, gold powder (1.0 g), O₂ (~1.0 L at ~1 atm). ^b At 60 °C for 40 h in acetonitrile. ^c At 100 °C for 24 h in toluene.

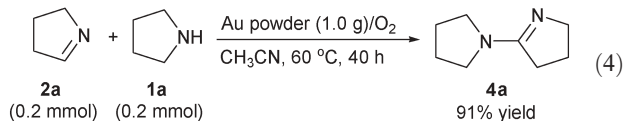
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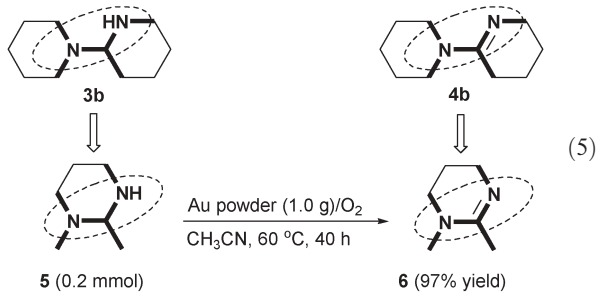
reactions (eqn. (3)), but it was not specifically identified. Dibenzylamine has also been reported to be oxidized with O₂ to the imine over the more common catalyst Ru/Al₂O₃ under similar condition (100 °C, 1 atm O₂).⁷

In contrast to the amines in entries 1, 2, and 3, the 5-, 6-, and 7-membered cyclic amines (**1a–c**) gave imine products (**4a–c**) that consist of two molecules of the amines (Scheme 1). Yields of the imine products decreased significantly as the size of the ring increased from 5 to 6 to 7. In the absence of the gold catalyst or O₂, piperidine (**1b**) did not react. It has been reported previously that palladium black catalyzes the reaction of **1a** to give the same product under an Ar atmosphere at 80 °C.⁸

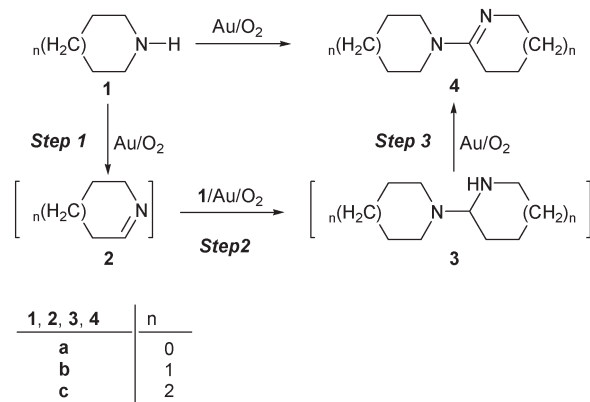
In Scheme 1 is a possible mechanism for the conversion of the cyclic amines (**1a–c**) to their imines (**4a–c**). *Step 1* involves the oxidative dehydrogenation of the amine (**1**) to the monomolecular imine (**2**), a reaction that stops at this stage for the more sterically bulky amines in Table 1 (entries 1, 2, and 3). For the less hindered cyclic amines, intermediate **2** reacts with amine **1** in *step 2*. That this step could occur under the conditions of the reactions is established by the reaction of Δ^1 -pyrroline (**2a**), prepared according to the literature method,⁹ with amine **1a** which gives **4a** directly in 91% yield (eqn (4)). This reaction appears to be faster than *step 1* because it is nearly complete after only 20 h. This reaction is also catalyzed by the Au as no reaction occurs in



the absence of the Au. Especially surprising is the observation that no reaction occurs in the absence of O₂, which suggests that *step 3* provides the driving force for *step 2* (and/or O₂ is required to activate the gold catalyst for *step 2*). As compounds **3a–c** are not known and **3a** was not obtained in the reaction of **2a** (eqn (4)), we chose **5** (eqn (5)) as a model for **3b**.¹⁰ Compound **5** contains amine



groups in the same positions as in **3b**. When the Au-catalyzed oxidation of **5** was carried out under the standard conditions, the expected imine **6**¹¹ was produced in almost quantitative yield. This reaction is almost complete within only 10 h, which is much faster than the aerobic oxidation of the amines in Table 1. Thus, the gold-catalyzed aerobic oxidation of an amine with the unit R₂N–CH–NHR' to give the R₂N–C=NR' imine is faster than the oxidative dehydrogenation of a normal RCH₂–NHR' amine to give a RCH=NR' imine. It has been noted previously that the dehydrogenation (H₂) of nitrogen-containing hydrocarbons is thermodynamically more favourable than simple hydrocarbons when catalyzed by heterogeneous catalysts like Pd/C and Rh/C at 110 °C.¹² Results of the above studies (eqn (4) and (5)) support the



Scheme 1 Proposed pathway for the gold-catalyzed formation of imines (**4a–c**) from cyclic secondary amines (**1a–c**).

mechanism in Scheme 1 for the reactions of cyclic amines and also suggest that *step 1* in this mechanism is slower than *steps 2* and *3*.

To check for possible *colloidal* or *soluble* catalytic gold species in these reactions, piperidine (0.20 mmol) was reacted with O₂ in the presence of 1.0 g of Au powder under the standard conditions (60 °C in acetonitrile). The reaction was stopped after 6 h when the imine (**4b**) yield was 9%. The reaction solution was decanted from the Au powder and put under the standard O₂ atmosphere. Reheating the solution to 60 °C and stirring the solution for 15 h gave no additional product (beyond the 9% produced in the presence of the Au powder). This result indicates that soluble species (ligated nanogold particles or Au complexes) are not the catalytically active species in the reactions of secondary amines.

Considering the high catalytic activity of bulk gold, we explored the possibility that its less expensive congeners would also be catalysts in eqn (3). However, when 1.0 g of commercial Ag (2–3.5 μm) or Cu (1–5 μm) powder was stirred with piperidine (0.20 mmol) and O₂ in acetonitrile (at 60 °C for 40 h), the piperidine did not react and no imine product was detected.

In summary, bulk gold powder is a highly active catalyst for the aerobic oxidation of secondary amines to imines under the mild conditions of 1 atm O₂ and 60 °C or 100 °C. Considering the previously reported gold powder-catalyzed reactions of isocyanides (eqn (1)) and carbon monoxide (eqn (2)), it appears that non-nanogold is capable of catalyzing several types of reactions. None of these reactions requires nano-sized gold particles or supported gold. Although the primary purpose of this communication is to highlight the catalytic activity of bulk gold in a new type of reaction, the application of these results to the practical conversion of amines to imines requires making more efficient use of the gold metal by supporting it on a high surface area material; such studies are in progress.

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Notes and references

‡ Acetonitrile and the amines (pyrrolidine, piperidine, hexamethyleneimine, and diisopropylamine) were dried and purified according to a literature procedure,¹³ Toluene, dibenzylamine, 1,2,3,4-tetrahydroisoquinoline, and *N*-benzylidenebenzylamine were purchased from Sigma Aldrich or Fisher and used as received. Authentic samples of 2-isopropyliminopropane¹⁴ and

3,4-dihydroisoquinoline¹⁵ were prepared as described previously. The gold powder was prepared from HAuCl₄ by reduction with hydroquinone according to a published procedure.¹⁶ It was washed with methanol in a Soxhlet extractor for 24 h and then dried in air in an oven at 110 °C for 1 h. Regeneration of used gold powder was previously reported.^{5,6} Electron micrographs of the gold powder showing large (~10³ nm) particle sizes were reported previously.¹⁷ O₂ (99.5%) was used as received. The oxidation of amines was typically carried out as follows: A mixture of amine (0.20 mmol) and gold powder (1.0 g) in solvent (5 mL) was prepared in a glass tube (2.5 × 18 cm, ~85 mL volume). The O₂ gas (about 1.0 L) was introduced into a rubber balloon that was attached to a syringe needle, which was inserted into the septum covering the tube opening. The mixture was stirred vigorously (magnetic stir bar) at 60 or 100 °C and then worked up by filtration to remove the gold powder. Products of these reactions were identified by comparison of their mass spectra and GC retention times with those of authentic samples. Yields were determined by GC using authentic samples of the products as calibrants. (When the reactions were run using Ar gas instead of O₂, no product was formed; occasionally a trace of product is detected, presumably due to adventitious O₂.)

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