Excellent Catalytic Performances of a Au/C–CuO Binary System in the Selective Oxidation of Benzylamines to Imines under Atmospheric Oxygen

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ABSTRACT: A green method of the oxidation of benzylamines to imines was developed using a novel binary system of Au/C–CuO. This system was evaluated under atmospheric oxygen, and the corresponding imines were obtained in up to 100% yields by loading 0.006 mol % of Au/C and 1.25 mol % of CuO under mild conditions. This system was also successfully applied to the syntheses of N-containing functional molecules, as well as that of imines on the scale of several grams. Furthermore, the turnover number of the system (more than 8000 times on a gold basis) as well as its ability to be reused more than 10 times for benzylamine oxidation demonstrates the excellent durability and recyclability of the developed system.

INTRODUCTION

In recent years, environmental-friendly manufacturing has been in huge demand, and in many synthetic reactions, efforts have been made to reduce or eliminate their negative environmental impact and reduce the load on catalysts.1,2 Oxidation reactions are fundamental reactions involved in approximately 30% of industrial processes and have supported the development of modern science, including the synthesis of pharmaceuticals, agrochemicals, and functional dyes, and the production of chemical products on an industrial scale.3−5 However, most conventional oxidation methods use stoichiometric or excessive amounts of explosive peroxides and toxic heavy metal oxidants, and the reaction conditions are harsh, making the process environmentally hazardous. The lack of evolution toward environmentally friendly alternatives in oxidation reactions is attributed to the fact that oxidation reactions are exothermic and difficult to control. To make oxidation reactions environmentally friendly, it is necessary to develop new, powerful, catalytic systems that use atmospheric oxygen, an inexhaustible resource, and in which the catalyst can be recovered and reused.6−9 Herein, in this work, we have designed a new redox catalyst system using gold as a key catalyst, which has a high redox potential \(E^\circ = 1.52 \text{ V (Au}^{3+} + 3e^- \rightarrow \text{Au})\),10 and a combination of other metal(s) to develop an environmentally friendly oxidation method that enables the reuse of the gold catalyst under mild conditions. In conventional oxidation methods using gold catalysts, controlling the size of gold nanoparticles and their affinity to the catalytic supports is one of the important factors for efficient oxidation processes, and efforts have been made to focus on the improvement of the catalytic activities of gold nanoparticles for oxidation;11 however, some of these systems require the use of pressurized oxygen and high temperatures. Owing to catalyst deactivation caused by such harsh reaction conditions, the number of catalyst turns was about 100 times, and recycling the catalyst was somewhat difficult for the oxidation of amines. During the past few decades, various methods have been developed that could be carried out at around 100 °C under atmospheric oxygen; nevertheless, their application to the synthesis of N-containing functional molecules is still limited. Therefore, the development of novel practical oxidation processes of amines under ambient conditions is strongly desired.

In this paper, we have succeeded in achieving highly efficient gold reoxidation with atmospheric oxygen by constructing a
new redox system that combines a gold catalyst with a copper catalyst. In this system, the copper catalyst assists the regeneration of the active catalytic species from the gold catalyst, and the copper catalyst would be reactivated with atmospheric oxygen. By developing this new redox system in which the gold and copper catalysts act in concert, the loading of the gold catalyst could be dramatically reduced (0.006 mol %) compared to conventional methods, and the reaction could be conducted under mild conditions. Such a combination of multiple metal reagents in a gold-catalyzed system is very rare, and this method is the first demonstration of the practical and extremely efficient amine oxidation that can be achieved by combining gold catalysts and other metal catalysts. Furthermore, the novel catalyst system for highly selective oxidation of amines to imines has an extremely high catalytic activity.12 This method can also be performed in air, although the yield of benzylamines were successfully converted to the corresponding imines in moderate to excellent yields.13−15 Methoxy, chloro, bromo, and trifluoromethyl groups are well even in the presence of sterically bulky o-methoxy and p-t-butyl groups. Moreover, this system was also applicable to 1-naphthylmethanamine (1j) and 2-thiophenemethanamine (1k), and the corresponding imines (2j and 2k) were obtained in nearly quantitative yields.

**RESULTS AND DISCUSSION**

First, we investigated the oxidation of benzylamine 1a (0.79 mmol) using Au/Ag/Cu mixed catalysts but could not reduce the catalyst loading (see Table S1 in the Supporting Information). Interestingly, however, changing the Au catalyst from AuO2 to Au on activated carbon (Au/C), the loading of Au/C could be reduced to just 0.05 mol % (Table 1, entry 1). With these loadings, at a reaction temperature of 90 °C and a reaction time of 24 h, 2a was obtained in 86% yield (entry 2). Surprisingly, the reaction proceeded smoothly even in the absence of Ag2O and 2a was obtained in 99% yield (entry 3). A further reduction of the catalyst loading still yielded 2a in an excellent yield (entry 4), and the use of Au/C (0.02 mol %) or CuO (5.0 mol %) alone yielded trace amounts of 2a (entries 5 and 6). These results suggest that both the gold and copper catalysts work in concert to promote the oxidation of amines.

This method can also be performed in air, although the yield of 2a was slightly lowered (entry 7) than that provided by a similar reaction conducted under O2 (0.1 MPa) (entry 4). Notably, when the amount of 1a was increased to 8.0 mmol, imine 2a was obtained in an 80% yield in the absence of solvent (entry 8). When the reaction was carried out under all of the same conditions except for the addition of 0.75 mL of toluene, the yield of 2a was slightly improved (entry 9). However, heating at 110 °C or reducing the reaction time to 18 h did not have much effect on the oxidation of 1a (entries 10 and 11).

| Table 1. Optimization of Reaction Conditions for the Oxidation of Benzylamine\(\mathrm{a,b}\) |
| --- |
| **Reaction Conditions** | **Entry** | **Catalyst Loading** | **Yield (%)** |
|  | 1a (mmol) | Au/C (mol %) | CuO (mol %) | temp (°C) | yield (%) |
| 1 | 0.79 | 0.05 | 27.9 | 60 | 52 |
| 2 | 0.79 | 0.05 | 27.9 | 90 | 86 |
| 3 | 0.79 | 0.05 | 27.9 | 90 | 98 |
| 4 | 2.0 | 0.02 | 5.0 | 90 | 98 |
| 5 | 2.0 | 0.02 | 0 | 90 | 14 |
| 6 | 2.0 | 0.02 | 0 | 90 | 5 |
| 7 | 2.0 | 0.02 | 0.75 | 90 | 82 |
| 8 | 2.0 | 0.02 | 0.05 | 125 | 90 | 80 |
| 9 | 2.0 | 0.02 | 0.05 | 125 | 87 | 83 |
| 10 | 2.0 | 0.02 | 0.05 | 125 | 110 | 86 |
| 11 | 2.0 | 0.02 | 0.05 | 125 | 90 | 78 |

Yields were determined by 1H NMR spectroscopy (isolated yield). \(\mathrm{a}\)Au/C: 0.93 wt % Au on activated carbon. \(\mathrm{b}\)Ag2O (13.9 mol %) was added. \(\mathrm{c}\)In air. \(\mathrm{d}\)Neat condition. \(\mathrm{e}\)Reaction time: 18 h.

This Au/C−CuO-catalyzed oxidation was monitored by 1H NMR spectroscopy, and the results are summarized in Figure 2. As shown in Figure 2, the transformation of 1a to 2a slowly proceeded before the initial 5 h, and then, the yield of 2a was gradually increased. It was noted that benzylamine 1a was completely consumed in 24 h without any byproducts. Using the optimal conditions (Table 1, entry 9), we then evaluated the substrate scope of the Au/C−CuO-catalyzed oxidation with a series of primary amines (Table 2). A variety of benzylamines were successfully converted to the corresponding imines 2a−2i in moderate to excellent yields. Methoxy, chloro, bromo, and trifluoromethyl groups are tolerant in the reaction. Furthermore, the reaction proceeded well even in the presence of sterically bulky o-methoxy and p-t-butyl groups. Moreover, this system was also applicable to 1-naphthylmethanamine (1j) and 2-thiophenemethanamine (1k), and the corresponding imines (2j and 2k) were obtained in nearly quantitative yields.

As shown in eq 1, dibenzylamine 3 (2.0 mmol) was successfully oxidized to the corresponding imine 2a in 44% yield in the presence of Au/C (0.02 mol %) and CuO (5 mol %) at 130 °C under atmospheric oxygen.

To gain insight into the mechanism of catalytic amine oxidation, several control experiments were conducted. When benzylamine 1a (2.0 mmol) was oxidized in the presence of only 0.02 mol % Au/C, imine 2a was obtained in 14% yield (entry 5 in Table 1). In contrast, when 100 mol % of CuO was used under the same condition, 1.0 mmol of 1a was oxidized into imine 2a in a 19% yield. It is noteworthy that the turnover number (TON) of the Au/C catalyst (0.93 wt % gold on activated carbon) was 350, whereas that of CuO was only 0.095. These results strongly suggest that the gold catalyst primarily acts as an active catalyst for the oxidation of...
benzylamines. Regarding the role of CuO, it is suggested that the regeneration of the active species derived from the gold catalyst is facilitated by oxidation by CuO, and the resulting Cu\(^{+}\) species can be oxidized to Cu\(^{2+}\) by atmospheric oxygen.

Since Au/C and CuO are insoluble in organic solvents, the catalytic oxidation of benzylamine may proceed on the surface of these catalysts. To gain insight into whether this system is homogeneous or heterogeneous, an additional experiment was conducted. After the oxidation of 1a using the Au/C−CuO catalyst, the catalyst was separated from the reaction mixture by filtration. The filtrate was then concentrated under reduced pressure, and \(p\)-methoxybenzylamine (1d; 2.0 mmol) and toluene (0.75 mL) were added to the residue. The mixture was heated at 90 °C for 24 h under atmospheric oxygen to give 2a, 2d', and 2d in 60, 16, and 9% yields, respectively (eq 2). Imine 2a was formed in the first-step reaction, and 2d was expected.

![Figure 2. Time-dependent reaction profiles with consumption of benzylamine 1a and the yield of imine 2a monitored by \(^1\)H NMR spectroscopy.](image_url)

| Table 2. Au/C−CuO-Catalyzed Oxidation of Amines\(^{ac,b}\) |
|-----------------------------------------------|
| \(\text{R'NH}_2\) | \(\text{R'-N'}\text{R'}\) |
| 1 (8.0 mmol) | 2 |
| 2a, 83% | 2b, 56% |
| 2c, 80% | 2d', 95% |
| 2e, 54% | 2f, 62% |
| 2g, 83% | 2h, 77% |
| 2i, 98% | 2j, 96% |
| 2k, 100% | |

\(^{ac}\)Isolated yields. \(^{b}\)Au/C: 0.93 wt % Au on activated carbon.
to be formed from the second-step reaction using the filtrate of the first step. However, the yield of 2d was 9%, indicating that there were almost no active catalyst species left in the filtrate.

When hexylamine 1l was used as the substrate, the corresponding aliphatic imine could not be obtained in the presence of the Au/C−CuO mixed catalyst under the optimal conditions for oxidation of benzylamines. In other words, the Au/C−CuO catalyst indicated excellent selectivity, preferentially oxidizing benzylamines over aliphatic amines. This allowed us to investigate the oxidative cross-coupling of benzylamines with aliphatic amines. Fortunately, unsymmetrical imine 4 was successfully obtained in 42% yield with an excellent product selectivity from benzylamine 1a (1.0 mmol) and hexylamine 1l (4.0 mmol) in the presence of Au/C (0.05 mol %) and CuO (10 mol %) at 110 °C (eq 3).

Moreover, the present imine synthesis method was applied to the Ugi reaction, one of the typical multicomponent coupling reactions (eq 5). After the imine synthesis, the Au/C−CuO catalyst was easily removed by filtration, followed by the addition of benzoic acid (7; 1.0 mmol) and cyclohexyl isocyanide (8; 1.0 mmol) to the resulting imine 2a solution. The desired dipeptide (9) was successfully obtained in a 58% yield, omitting the purification step of 2a. These examples clearly demonstrate that this catalytic system using an Au/C−CuO mixed catalyst has the potential to be a powerful synthetic method for functional materials and pharmaceuticals.

Furthermore, this oxidation system can be implemented for the multigram-scale synthesis of imines. As shown in eq 6, benzylamine 1a (30 mmol, 3.2 g) was successfully oxidized to the corresponding imine 2a in an 81% yield (isolated yield: 69%, 2.0 g) over 48 h using atmospheric oxygen in the presence of Au/C (0.05 mol %) and CuO (10 mol %).

To further clarify the durability of the catalyst, catalyst-recycling experiments were conducted for the oxidation of benzylamine (Table 3). In these experiments, the catalyst was filtered and washed with AcOMe. The dried catalyst was then added directly to the reaction vessel for the next run. Surprisingly, the Au/C−CuO mixed catalyst could be successfully reused for the oxidation of benzylamine 10 more times to yield 2a in excellent yield in each run. It is noteworthy that the catalytic activity did not decrease at all even when the catalyst was recovered and reused more than 10 times.

**Table 3. Recycling Experiments Using the Au/C−CuO Mixed Catalyst**

| run | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|-----|---|---|---|---|---|---|---|---|---|----|
| yield (%) | 94 | 92 | 91 | 90 | 91 | 99 | 97 | 89 | 90 | 98 |

*Yields were determined by 1H NMR spectroscopy (isolated yield). ^b Au/C: 0.93 wt % Au on activated carbon.*

**CONCLUSIONS**

A green method for the oxidation of benzylamines to imines was developed using a new co-catalytic system employing Au/C and CuO catalysts. This system was conducted under atmospheric oxygen to oxidize the corresponding benzylamines with Au/C and CuO loadings of 0.006 and 1.25 mol %, respectively, to yield imines in excellent yields by oxidizing. It is noteworthy that this catalytic oxidation system exhibits an
excellent TON (max: 8333) over gold catalyst. Furthermore, the Au/C-CuO mixed catalyst could be recycled while maintaining its excellent catalytic performance. In conventional methods for amine to imine oxidation using gold catalysts, only a limited number of catalyst systems can be recycled. On the other hand, in this catalyst system, the catalytic activity does not decrease at all even if the catalyst is recovered and reused more than 10 times. This is quite remarkable, and this method would be a new basis for the development of sustainable amine oxidation methods. In addition, this system was also successfully applied to the syntheses of N-containing functional molecules, as well as that of imines on the scale of several grams. We believe that this novel catalytic system provides a foundation for further advances in not only environmentally friendly oxidation reactions but also in green chemistry as a whole.

**EXPERIMENTAL SECTION**

**General Remarks.** Unless otherwise stated, all starting materials and catalysts were purchased from commercial sources and used without further purification. Au (0.93 wt %) on activated carbon was purchased from Haruta Gold Inc. CuO was purchased from Nacalai Tesque, Inc. All solvents were distilled and degassed with nitrogen before use. 1H NMR spectra were recorded on a JEOL JNM-ECS400 (400 MHz) FT NMR system or a JEOL JNM-ECS400 (100 MHz) FT NMR system in CDCl₃. 13C{1H} NMR spectra were recorded on a JEOL JNM-ECS400 (400 MHz) FT NMR system or a JEOL JNM-ECS400 (100 MHz) FT NMR system in CDCl₃.

**General Procedure for the Oxidation of Amines Using Au/C-CuO Mixed Catalysts (Table 2).** Amine 1 (8.0 mmol), hexylamine (1.0 mmol), hexylamine/CuO mixed catalysts (Table 2). Using Au/C−CuO mixed catalysts (Table 2).

**N-(2-Methoxybenzyl)-1-(4-methoxyphenyl)methanimine (2d).** Yellow oil, 984.2 mg, 95%; 1H NMR (400 MHz, CDCl₃): δ 8.29 (s, 1H), 7.71 (dd, J = 8.7, 2.7 Hz, 2H), 7.24 (dd, J = 8.2, 2.3 Hz, 2H), 6.93-6.68 (m, 4H), 4.72 (s, 2H), 3.83 (s, 3H), 3.79 (s, 3H); 13C{1H} NMR (100 MHz, CDCl₃): δ 161.7, 161.0, 158.7, 131.7, 129.9, 129.3, 114.0, 64.5, 55.4, 55.3.

**N-(4-Methylbenzyl)-1-(4-methylphenyl)methanimine (2e).** Yellow solid, 466.1 mg, 54%; 1H NMR (400 MHz, CDCl₃): δ 8.32 (s, 1H), 7.66 (d, J = 7.7 Hz, 2H), 7.21 (dd, J = 7.9, 4.8 Hz, 4H), 7.14 (d, J = 8.2 Hz, 2H), 4.76 (s, 2H), 2.37 (s, 3H). 13C{1H} NMR (100 MHz, CDCl₃): δ 161.8, 141.1, 136.6, 136.5, 133.7, 129.4, 128.1, 127.5, 125.6, 64.9, 35.0, 34.5, 31.5, 31.3.

**N-(4-(tert-Butyl)phenyl)-1-(4-(tert-butyl)phenyl)methanimine (2f).** Yellow solid, 781.0 mg, 62%; 1H NMR (400 MHz, CDCl₃): δ 8.37 (s, 1H), 7.90 (d, J = 7.8 Hz, 2H), 7.43 (d, J = 8.2 Hz, 2H), 7.36 (d, J = 7.3 Hz, 2H), 7.26 (d, J = 8.6 Hz, 2H), 4.78 (s, 2H), 1.33 (s, 9H), 1.31 (s, 9H); 13C{1H} NMR (100 MHz, CDCl₃): δ 161.8, 143.8, 139.7, 133.2 (q, J = 32.6 Hz), 130.0 (q, J = 31.6 Hz), 129.2, 128.8, 126.4-126.3 (m), 126.2-126.1 (m), 123.4 (d, J = 33.6 Hz), 120.7 (d, J = 34.5 Hz), 65.1.

**N-(Chlorobenzyl)-1-(4-chlorophenyl)methanimine (2g).** Yellow oil, 819.4 mg, 77%; 1H NMR (400 MHz, CDCl₃): δ 8.30 (s, 1H), 7.69 (d, J = 8.6 Hz, 2H), 7.37 (d, J = 8.2 Hz, 2H), 7.30-7.23 (m, 4H), 4.71-4.77 (2H); 13C{1H} NMR (100 MHz, CDCl₃): δ 161.0, 137.7, 130.7, 134.5, 132.9, 129.6, 129.0, 128.7, 64.3.

**N-(2-Bromobenzyl)-1-(2-bromophenyl)methanimine (2h).** Brown oil, 1356.4 mg, 98%; 1H NMR (400 MHz, CDCl₃): δ 8.80 (s, 1H), 8.10 (dd, J = 7.7, 1.8 Hz, 1H), 7.56 (d, J = 6.3 Hz, 2H), 7.41 (d, J = 6.3 Hz, 1H), 7.35-7.73 (m, 4H), 7.15-7.11 (m, 1H), 4.91 (s, 2H); 13C{1H} NMR (100 MHz, CDCl₃): δ 162.1, 138.6, 134.6, 133.2, 132.7, 132.1, 129.9, 129.0, 128.7, 127.8, 127.7, 125.4, 123.7, 64.5.

**1-(Naphthalen-1-yl)-N-(naphthalen-1-ylmethyl)methanimine (2j).** Brown oil, 1140.4 mg, 96%; 1H NMR (400 MHz, CDCl₃): δ 9.09 (s, 1H), 8.33 (d, J = 8.2 Hz, 1H), 8.01-7.90 (m, 5H), 7.68-7.55 (m, 7H), 5.45 (s, 2H); 13C{1H} NMR (100 MHz, CDCl₃): δ 162.3, 153.8, 134.1, 134.0, 131.9, 131.8, 131.6, 131.4, 129.5, 129.0, 128.9, 128.7, 127.5, 127.4, 126.3, 126.0, 126.0 (overlapped), 125.9, 125.5, 124.8, 124.2, 63.5.

**1-(Thiophen-2-yl)-N-(thiophen-2-ylmethyl)methanimine (2k).** Yellow oil, 863.7 mg, 100%; 1H NMR (400 MHz, CDCl₃): δ 8.40 (s, 1H), 7.40 (d, J = 5.0 Hz, 1H), 7.31 (d, J = 3.7 Hz, 1H), 7.22 (dd, J = 5.0, 1.4 Hz, 1H), 7.07-7.05 (m, 1H), 6.99-6.97 (m, 2H), 4.93 (s, 2H) 13C{1H} NMR (100 MHz, CDCl₃): δ 155.6, 142.2, 141.7, 131.1, 129.5, 127.5, 127.0, 125.4, 125.0, 58.7.

**Experimental Procedure for the Oxidative Cross-Coupling of Benzylamine and Hexylamine (eq 3).** Benzylamine 1a (1.0 mmol), hexylamine 11 (4.0 mmol), Au/C (0.93 wt % Au) on activated carbon, 10 mg, 0.05 mol % based
on Au), CuO (0.10 mmol, 10 mol%), and p-xylene (0.35 mL) were added to a 10 mL two-neck flask equipped with an O2 balloon at 25 °C then stirred at 110 °C under an O2 atmosphere for 24 h. After this time, the resulting mixture was filtered using AcOMe, and the filtrate was concentrated under reduced pressure. The yields of unsymmetrical imine 4 and imine 2a were determined by 1H NMR spectroscopy using 1,3,5-trioxane as the internal standard.

**Experimental Procedure for the Au/C–CuO-Catalyzed Oxidative Synthesis of 2-Phenylbenzothiazole (eq 4).** Benzylamine 1a (2.0 mmol), 2-aminobenzenethiol 5 (2.0 mmol, 1.0 equiv), Au/C (0.93 wt % Au on activated carbon, 10 mg, 0.02 mol % based on Au), CuO (8.0 mg, 5.0 mol %), and p-xylene (0.75 mL) were added to a 10 mL two-neck flask equipped with an O2 balloon at 25 °C then stirred at 130 °C under an O2 atmosphere for 24 h. After the reaction was completed, the resulting mixture was filtered using AcOMe, and the filtrate was concentrated under reduced pressure. Then, the residue was dissolved in a combined solvent (AcOMe/isoo-hexane = 1:3; 20 mL) and filtered with a long length Sep-Pak. The filtrate was removed under reduced pressure, and the crude mixture was purified by distillation to obtain pure imine 2a in a 69% isolated yield (2.0 g).

**Experimental Procedure for the Catalyst-Recycling Tests for the Oxidation of Benzylamine (Table 3, First Run).** Benzylamine 1a (2.0 mmol), Au/C (0.93 wt % Au on activated carbon, 10 mg, 0.02 mol % based on Au), CuO (8.0 mg, 5.0 mol %), and toluene (0.75 mL) were added to a 10 mL two-neck flask equipped with an O2 balloon at 25 °C then stirred at 90 °C under an O2 atmosphere for 24 h. After this time, the resulting mixture was filtered using AcOMe, and the filtrate was concentrated under reduced pressure. The yield of imine 2a was determined by 1H NMR spectroscopy using 1,3,5-trioxane as the internal standard. After the filtration, the residue was washed with AcOMe (10 mL × 2) and dried under reduced pressure. This recovered catalyst was dried under reduced pressure for 3 h and directly used for the second run without any further purification.

![Experimental Procedure for the Au/C–CuO-Catalyzed Oxidative Synthesis of 2-Phenylbenzothiazole (eq 4).](https://pubs.acs.org/doi/10.1021/acsomega.1c04046)

**ASSOCIATED CONTENT**

**Supporting Information**

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.1c04046.

Optimization of reaction conditions, control experiments, and 1H NMR and 13C{1H} NMR spectra (PDF)

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**Experimental Procedure for Multigram-Scale Synthesis of Imine 2a via the Au/C–CuO-Catalyzed Oxidation of Benzylamine 1a (eq 6).** Benzylamine 1a (30 mmol, 3.2 g), Au/C (0.93 wt % Au on activated carbon, 317.7 mg, 0.05 mol % based on Au), CuO (238.6 mg, 10 mol %), and toluene (6 mL) were added to a 20 mL two-neck flask equipped with an O2 balloon at 25 °C then stirred at 90 °C under an O2 atmosphere for 48 h. After this time, the resulting mixture was filtered using AcOMe, and the filtrate was concentrated under reduced pressure. Then, the residue was dissolved in a combined solvent (AcOMe/isoo-hexane = 1:3 with 5% Et3N, 20 mL) and filtered with a long length Sep-Pak. The filtrate was removed under reduced pressure, and the crude mixture was purified by distillation to obtain pure imine 2a in a 69% isolated yield (2.0 g).

**Experimental Procedure for the Oxidative Ugi Reaction via Catalytic Oxidation of Benzylamine (eq 5).** Benzylamine 1a (2.0 mmol), Au/C (0.93 wt % Au on activated carbon, 10 mg, 0.02 mol % based on Au), CuO (8.0 mg, 5.0 mol %), and toluene (0.75 mL) were added to a 10 mL two-neck flask equipped with an O2 balloon at 25 °C then stirred at 90 °C under an O2 atmosphere for 24 h. After the reaction was completed, the resulting mixture was filtered using AcOMe and the filtrate was transferred to a 30 mL flask then concentrated under reduced pressure. Benzoic acid 7 (1.0 mmol), cyclohexyl isocyanide 8 (1.0 mmol), and EtOH (2.0 mL) were added to the flask and stirred at 25 °C for 24 h under open-air. The resulting solution was concentrated under reduced pressure, then the residue was washed with cold Et2O (5 mL). The resulting precipitate and the organic solvent were separated by decantation, and the precipitate was corrected. The solvent was also concentrated under reduced pressure and cold Et2O (5 mL) was added to form the precipitate. This procedure was repeated twice, and the combining precipitate was dried under reduced pressure to obtain pure dipeptide 9 in 58% isolated yield.

**N-Benzyl-N-(2-(tert-butylamino)-2-oxo-1-phenylethyl)benzamide (9).**21 White solid, 247.8 mg, 58%; 1H NMR (400 MHz, CDCl3): δ 7.48 (d, J = 6.9 Hz, 2H), 7.35–7.30 (m, 8H), 7.19–7.15 (m, 3H), 7.10 (d, J = 6.0 Hz, 2H), 5.68 (s, 1H), 5.47 (s, 1H), 4.68 (s, 1H), 4.47 (s, 1H), 3.81 (s, 1H), 1.93–1.83 (m, 2H), 1.65–1.55 (m, 3H), 1.38–1.28 (m, 2H), 1.11–1.05 (m, 3H); 13C{1H} NMR (100 MHz, CDCl3): δ 173.3, 168.4, 136.3, 135.2, 129.9, 129.7, 128.9, 128.7, 128.5, 128.4, 127.1, 126.8, 64.7, 53.0, 48.7, 32.8, 25.6, 24.9, 24.8.
Amines to Imines.

Synth. Catal.

Imines under Neat Conditions with Low Catalyst Loading.

Adimurthy, S. Copper-Catalyzed Aerobic Oxidation of Amines to via atmospheric oxidation in the presence of VO(Hhpic)2 catalyst. 2334.

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(13) In addition, the reaction system using a catalytic amount of Au\(_2\)O\(_3\) indicated similar results to the system using the Au/C catalyst. (see Table S2 in the Supporting Information).

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