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Efficient and Selective Aerobic Alcohol Oxidation Catalyzed by Copper(II)/2,2,6,6,-Tetramethylpiperidine-1-oxyl at Room Temperature

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Abstract: A simple and efficient copper(II)/2,2,6,6,-tetramethylpiperidine-1-oxyl (TEMPO)-catalyzed aerobic oxidation of both primary and secondary benzylic, allylic, and aliphatic alcohols to their corresponding aldehydes and ketones at room temperature using the copper(II) complex $[Cu(\mu\text{-}Cl)(Cl)(phen)]_2$ as the Cu(II) source is reported. The conversion of both electron-rich and electron-neutral benzyl alcohols is smooth and faster than those of electron-deficient ones. The chemoselectivity of a primary benzyl alcohol over the secondary alcohol is also observed. Alcohols regarded as difficult substrates for oxidation due to their coordinating ability with transition metal catalyst such as 4-(methylthio)-benzyl alcohol and 3-pyridinemethanol are also oxidized easily. In addition, a lignin model alcohol is oxidized to the corresponding aldehyde in excellent yield. Conversions of benzylic and allylic alcohols are faster as compared to those of aliphatic alcohols in accordance with their C_α–H bond strengths. A plausible mechanism of the TEMPO-based catalytic cycle is proposed.

Keywords: aerobic oxidation; alcohols; catalysis; copper; 2,2,6,6,-tetramethylpiperidine-1-oxyl (TEMPO)

Introduction

Selective alcohol oxidation to the corresponding carbonyl compounds is widely recognized as one of the fundamental transformations in organic synthesis.[1] The catalytic conversion of primary alcohols to aldehydes is important for the preparation of fine chemicals.[2] There are numerous diverse methods that accomplish this fundamental selective oxidation. Traditional stoichiometric oxidants (i.e., $KMnO_4$, MnO_2, CrO_3, SeO_2, Br_2, etc.) are reported for this transformation with considerable drawbacks such as high cost, toxicity, and production of large amounts of waste. Moreover, the reactions are often performed in environmentally undesirable solvents; typically chlorinated hydrocarbons.[3] Thus interest in developing an economic and environmental-friendly protocol is increased. In this regard, catalytic aerobic alcohol oxidation in non-halide solvent is a highly desirable system.

For catalytic aerobic alcohol oxidation, transition metals such as V,[4] Co,[5] Mn,[6] Fe,[7] Cu,[8] Mo,[9] Ru,[10] Pd,[11] Os,[7] Au[7] have been used as catalysts. Of particular interest are the catalytic systems involving inexpensive transition metal compounds with less hazardous metals such as copper. In nature, copper enzymes are ubiquitous, and a few of them have been involved in the binding of molecular oxygen for aerobic oxidation transformations of natural products in a mild and highly selective way.[12] Copper complexes are thus expected to be an efficient and selective catalysts for oxidative transformations.

Recently the nitroxyl radical, 2,2,6,6, tetramethylpiperidine-1-oxyl (TEMPO), has been extensively studied as a catalyst or catalyst component for alcohol transformations with[8,13] and without[14] transition metals. The combination of TEMPO and copper ions (i.e., a copper-TEMPO catalytic system) is expected to be an efficient and selective catalytic system for the aerobic oxidation of alcohols.[13a,c–r] Generally, copper salts or *in situ*-generated copper complexes with nitrogen-containing ligands are used for alcohol oxidation to the corresponding carbonyl compounds.[8,13a,c–r] The alcohol oxidation reactions using well-defined copper complexes are less reported.[8b,c,f,i,13n,p,r] Herein, we report the selective aerobic alcohol oxidation

using the isolated copper complex $[Cu(\mu\text{-}Cl)(Cl)(phen)]_2$ with TEMPO as the catalyst system at room temperature and an easy and simple method for the preparation of the complex in high yield. A possible reaction mechanism is also highlighted.

Results and Discussion

The synthesis and structure of dimer $[Cu(\mu\text{-}Cl)(Cl)(phen)]_2$ were reported in the recent past.[15] A complex with same composition $[Cu(\mu\text{-}Cl)(Cl)(phen)]_2$ but of different structure was also synthesized under non-hydrothermal conditions, and its DNA binding behavior was studied.[16] Although the biological and non-linear optical activities of the complexes with the composition $[Cu(\mu\text{-}Cl)(Cl)(phen)]_2$ were investigated, their catalytic behavior was not examined.

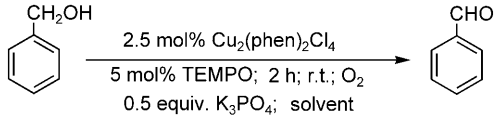
The reported yields of the complexes using the hydrothermal technique are low and difficult for further study. In order to evaluate the catalytic activity of $[Cu(\mu\text{-}Cl)(Cl)(phen)]_2$, a direct reaction between copper(II) chloride and phenanthroline was carried out. Room temperature stirring of a dichloromethane solution of equimolar amounts of $CuCl_2{\cdot}2H_2O$ and phenanthroline overnight gave a green complex. Both elemental analysis and single-crystal X-ray diffraction study identified the green complex to be $[Cu(\mu\text{-}Cl)(Cl)(phen)]_2$ (**1**). The yield of the reaction is high (91%).

The stability and solubility of **1** in water qualify this complex to potentially be a good catalyst under aqueous conditions. We have optimized the conditions of catalytic aerobic alcohol oxidations in different solvent systems using **1** and TEMPO as the catalyst system and benzyl alcohol as the model substrate. The results are summarized in Table 1.

Both neat acetonitrile and the 1:1 mixture of acetonitrile and water are effective solvents in the benzyl alcohol oxidation. Water alone was found to be unsuitable. This may be due to the poor solubility of benzyl alcohol in water. Both TEMPO and base are essential for a successful conversion because the Cu complex alone is ineffective. Air can be used instead of oxygen with a slightly longer reaction time because of the lower partial pressure of oxygen in air. Subsequently, the catalytic system was then applied to various alcohols in acetonitrile as summarized in Table 2.

Various primary and secondary alcohols of benzylic, allylic, and aliphatic types were successfully oxidized to their corresponding carbonyl derivatives. Benzyl alcohol is almost quantitatively and selectively converted to benzaldehyde (entry 1) in high yield. In general, the conversions of benzylic and allylic alcohols to the corresponding carbonyl compounds were faster and more efficient (entries 1–12), whereas the aliphatic alcohols reacted more slowly (entries 13 and 14). This

Table 1. Optimization of the reaction conditions for aerobic oxidation of benzyl alcohol.

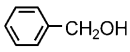
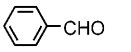
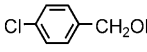
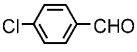
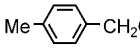
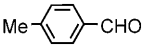
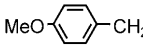
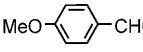
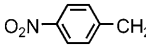
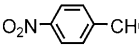
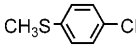
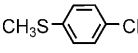
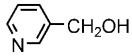
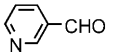
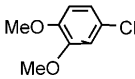
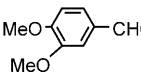
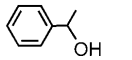
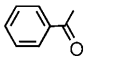
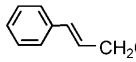
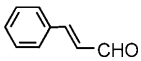
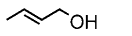
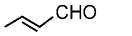
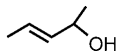
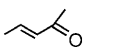
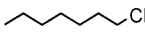
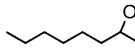
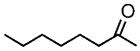
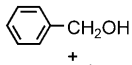
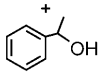
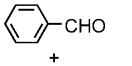
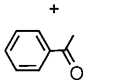


Solvents	Base	TEMPO	Yield[a] [%]
acetonitrile	yes	no	trace
	no	yes	trace
	yes	yes	99[b,c]
	no	no	no reaction
acetonitrile + water (1:1)	yes	no	trace
	no	yes	trace
	yes	yes	99[b,c]
	no	no	no reaction
water	yes	no	trace
	no	yes	trace
	yes	yes	25
	no	no	no reaction

[a] GC yields using 1,4-di-*tert*-butylbenzene as an internal standard.
[b] When air is used instead of O_2, the conversion was 95%.
[c] Same results were obtained using K_2CO_3 as a base.

selectivity towards oxidation of benzylic and allylic alcohols is consistent with their weaker C_α–H bond strengths in comparison with those in aliphatic alcohols (<7 kcal mol^{-1}).[13q] Moreover, the conversions of primary alcohols (entries 1–8, 10, and 11) were faster than those of the secondary alcohols (entries 9, 12, and 14) of the benzylic, allylic, and aliphatic systems. This may be attributed to the steric hindrance of the α-substituents in secondary alcohols. The initial conversion of aliphatic 1-octanol was satisfactory but the reaction slows down dramatically after 3 h, giving a final conversion of 57% (entry 13). Longer reaction time, up to 22 h, did not improve the conversion yield. The instability of the oxoammonium ion in the presence of an aliphatic aldehyde and oxygen may decrease the catalytic activity as reported.[13a] Furthermore, the conversions of electron-rich and electron-neutral benzyl alcohols are faster and more efficient than those of electron-deficient ones (entries 1–5). Surprisingly, 4-(methylthio)benzyl alcohol and 3-pyridinemethanol, which are usually regarded as difficult substrates in most aerobic oxidations involving transition metals due to their strong coordinating ability, were also very smoothly converted into their corresponding aldehydes with high yields (entries 6 and 7). In addition, the lignin model compound could be selectively oxidized into its corresponding aldehyde with excellent conversion yield (entry 8). The conversion yields of both primary and secondary allylic alcohols are excellent (entries 10–12). A typical reaction involving a mixture of benzyl alcohol and 1-phenylethanol shows specificity of the copper(II)-TEMPO

Table 2. Aerobic oxidation of alcohols into aldehydes and ketones.

Entry	Alcohols	Products	Time in hour[f]	Conversion[a]	GC yield[a]	Yield[b] [%]	(Conversion/GC yield)[f]
1			2 (3)	100	99	83	(100/99)
2			1.5 (2)	100	98	95	(100/98)
3			2 (3)	92	91	89	(100/97)
4			2 (3)	95	93	91	(100/96)
5			2 (4)	75	71[c]	65	(78/75)
6			2 (3)	94	91	87	(99/95)
7			2 (3)	98	95	85	(100/97)
8			2 (4)	89	87	83	(100/97)
9			5 (7)	99	97	91	(100/98)
10			2 (3)	93	91	84	(98/96)
11			2 (3)	97	95[c,e]	_[d]	(100/98)
12			5 (6)	99	97	71	(100/53)
13			3 (3)	57	53	47	(59/53)
14			10 (15)	86	83	78	(99/96)
15	 + 	 + 	2 (3)	92	91	73	(100/98)
				8	7	2	(14/11)

[a] The conversion and GC yield were measured by GC with an internal standard (1,4-*tert*-butylbenzene).
[b] Isolated yield.
[c] K_2CO_3 used as a base.
[d] Unable to isolate pure poduct.
[e] Decane as a GC internal standard.
[f] Time, conversion, and GC yield included in the parentheses are from the alcohols oxidation reactions with less solvent and base.

catalytic system towards primary alcohol because 92% of benzyl alcohol was converted into aldehyde, whereas only 8% of the 1-phenylethanol was oxidized within 2 h (entry 15). This chemoselectivity, a characteristic of the natural copper protein galactose oxidase,[8b,c,17] may be useful for selective oxidations of alcohol in synthetic organic chemistry when there are different alcoholic functions in the substrate. It was also noted that, after the end of the oxidation reaction, the copper catalyst is still active because addition of more equivalents of benzyl alcohol to the reaction mixture led the conversion to completion in 4 h. In general, side products including formation of acids from further oxidation of aldehydes and ketones were not observed. The possibility of over-oxidation may be inhibited by TEMPO.[6b,c,13b,14i] The catalytic reaction conditions were further optimized using minimum solvent and base (see Supporting Information), and then alcohol oxidation reactions were repeated and we tried to reach high conversion yield (~100%) by increasing the reaction time over that of the initial runs. The results are summarized in Table 2.

Mechanism

In an investigation towards the mechanism for the copper(II)-TEMPO-catalyzed oxidation of alcohol to aldehyde, Semmelhack[13a,18] first proposed that the formation of an oxoammonium ion, generated by the oxidation of TEMPO, involves the abstraction of a β-hydrogen forming an ionic transition state **A** (Figure 1). Later on, Sheldon et al.[13g] proposed a mechanism based on copper-centred radical-mediated

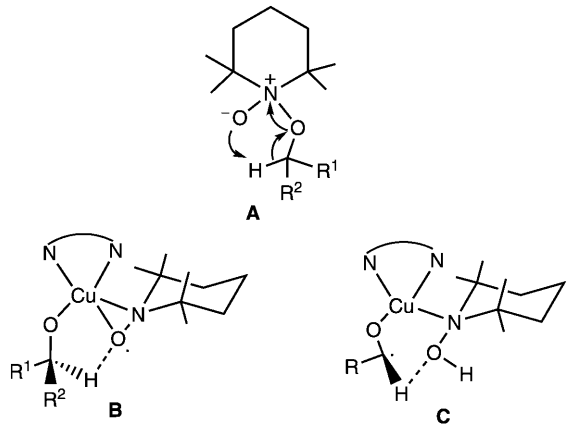
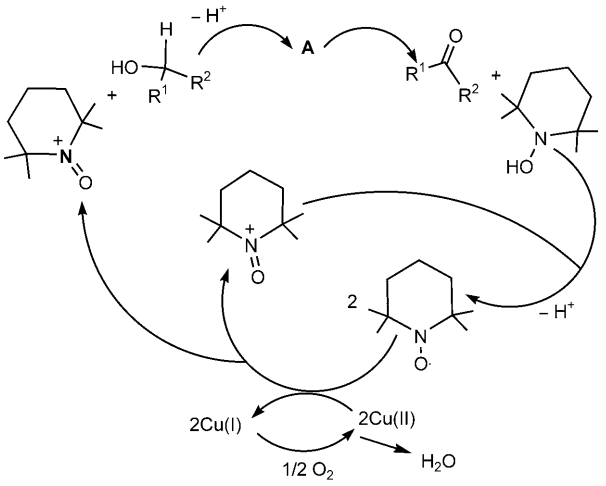


Figure 1.



Scheme 1. Proposed catalytic cycle.

β-hydrogen abstraction *via* a transition state **B** (Figure 1) during aerobic alcohol oxidation by the $CuBr_2$(Bipy)-TEMPO catalytic system. These authors explained the failure of the secondary alcohol 1-phenylethanol to undergo oxidation in the $CuBr_2$(Bipy)-TEMPO catalytic system by the steric effect of the methyl substituent on the α-carbon atom, which hindered the formation of **B**, and that is crucial for the C–H abstraction from the alcohol by the coordinated TEMPO molecule. Moreover, in the case of primary alcohols, the second β-hydrogen atom can be bonded to the oxygen atom of TEMPOH and stabilizes the radical intermediate **C** (Figue 1), which is not possible in secondary alcohols.[13g] Sheldon et al.[13h] also applied the Semmelhack procedure[13a] (CuCl-TEMPO) to the aerobic oxidation of a wider range of alcohol substrates and found out that benzylic and allylic alcohols were smoothly oxidized, and simple aliphatic alcohols were inactive.[13h] This trend is inconsistent with the well known oxoammonium ion mechanism because oxoammonium ion can catalyze a wider range of alcohols, including the facile oxidation of simple aliphatic alcohols.[14c,e] The results obtained in our experiments favour the oxoammonium ion-mediated mechanism (which was also proposed for oxidation of alcohols by other oxidants and TEMPO[14c,e]) because the catalytic system involves smooth oxidation of different kinds of alcohols including aliphatic ones (Table 2). The observation of a peak at 1630 cm^{-1} in the IR spectrum (see Supporting Information) of the catalytic reaction mixture indicates the formation of the oxoammmonium ion[14c] and further supports the above proposed mechanism.

The catalytic cycle is shown in Scheme 1. Initially, the nitroxyl radical is oxidized to the oxoammonium ion by the Cu(II) complex; then the oxoammonium ion serves as the catalytic oxidant and oxidizes the alcohol substrates *via* a possible ionic transition state **A** (Figure 1) to the corresponding carbonyl compounds. During oxidation of alcohols, the oxoammonium ion itself is reduced to hydroxylamine; successive oxidation of hydroxylamine regenerates the oxoammonium ion. The oxidation of hydroxylamine with oxoammonium ion gives two nitroxyl radicals, which are again oxidized by Cu(II) to two oxoammonium ions. Here, Cu(II) is regenerated by the oxidation of Cu(I) with primary oxidant oxygen producing water as a by-product and thus completes the catalytic cycle.

As the isolation of reaction intermediates cannot be achieved, it is difficult to ascertain the fate of the catalyst **1** during alcohol oxidation reactions in accetonitrile. Recently, electrospray ionization-mass spectrometry (ESI-MS) has been used as an effective method for the characterization of reaction intermediates.[13o,u,19] We have performed the ESI-MS in the following manner. Complex **1** is immersed in the acetonitrile solution and stirred for 10 min under oxygen bubbled conditions. The ESI-MS measurements in the positive-ion mode were then performed. Besides the dominating peak at $m/z = 458$, two moderate peaks at $m/z = 773$ and $m/z = 319$ and two weak peaks at $m/z = 423$ and $m/z = 593$ were obseved in the ESI-mass spectrum. According to the isotope distributions, these can be assigned as $[C_{24}H_{16}N_4ClCu]^+$ ($m/z = 458$), $[C_{36}H_{24}N_6Cl_3Cu_2]^+$ ($m/z = 773$), $[C_{14}H_{11}N_3ClCu]^+$ ($m/z = 319$), $[C_{24}H_{16}N_4Cu]^+$ ($m/z = 423$) and $[C_{24}H_{16}N_4Cl_3Cu_2]^+$ ($m/z = 593$), respectively (see Supporting Information). After addition of K_3PO_4 and TEMPO, the peak intensities at $m/z = 593$ and $m/z = 319$ are significantly reduced and the dominant peak at $m/z = 458$ prevailed as before along with the moderate peaks at $m/z = 773$ and $m/z = 423$. After adding benzyl alcohol into the system for an hour, the peak at $m/z = 423$ with high intesitiy was observed. Thus, although a dimeric copper complex was used initially, monomeric copper species were formed during the alcohol oxidation in the basic acetonitrile solution. However, the peaks corresponding to the

formation of the complexes [Cu(Phen)(TEMPO)], [Cu(phen)(benzyl alcohol)], and [Cu(phen)-(TEMPO)(benzyl alcohol)] were not observed.[13o]

The present catalytic system is different with respect to its catalytic behaviour, in particular with reagrd to secondary alcohol oxidation, from that of the previously reported Cu(diimine) catalytic systems.[13g–i,n,k,o,u] This may be due to the difference in their oxidation paths as in the present case where oxoammonium ion mechanism has been favoured. To justify this pathway, we need to consider two points: (i) feasibility of oxoammonium ion formation *via* oxidation of TEMPO by Cu(II) and (ii) stability of this ion in the catalytic conditions of the alcohol oxidation reactions. Electrochemical studies suggest that Cu(II) can oxidize the nitroxyl into the corresponding nitosonium species since a required potential (+0.4 V) for that oxidation is much below the one reported for the Cu(I)/Cu(II) couple (+0.7 V) in acetonitrile solvent[13a,20] and such a type of oxidation by Cu(II) is also reported.[20] With regards to stability in aquous solutions, it has been observed that the oxoammonium ions orignating from various nitroxyl radicals including TEMPO are rather unstable in water, especially at alkaline pH.[13k,14e]

It is also well known that solvent as a reaction medium has an important impact not only on reactivity and selectivity but also on sustainability.[13u,21] The most commonly used solvent for nitrosonium ion oxidations has been acetonitrile.[14c] Other solvents, such as nitromethane, acetic anhydride, and *tert*-butyl alcohol have also been used.[14c] We carried out the alcohol oxidation in acetonitrile solvent with a weak base. For the Cu(diimine)-TEMPO catalytic system, oxidation reactions were performed in aqueous solution[13o,u] or acetonitrile/water (2/1, v/v) mixed solvent[13g–i,n,k,14c] with a strong base. The oxoammium ion may not be stable under such reaction conditions,[13k,14c] and no alcohol oxidation was observed in neat acetonitrile.[13g–i] These findings indicate that both catalytic systems differ in their catalytic pathway, and that for our system involves an oxoamminium ion which is stable under the reaction conditions as supported by the IR spectra and its broad reaction scope including the facile oxidation of aliphatic alcohols.[14c,e]

Conclusions

The copper(II)-TEMPO catalytic system reported here is simple to prepare and easy to use for the efficient aerobic oxidation of primary and secondary benzylic, allylic, and aliphatic alcohols to their corresponding aldehydes and ketones at room temperature. The catalytic system is also unique as it succeeds to oxidize different kinds of alcohols and possesses chemoselectivity of primary over secondary alcohols. To the best of our knowledge, there is no such report on a Cu catalytic system that alone can oxidize different types of alcohols leading to the diverse aspects of alcohol oxidation.

Experimental Section

General Information

All chemicals were obtained from commercial sources and used without further purification. Decane, 4-chlorobenzyl alcohol, 4-methylbenzyl alcohol, 4-methoxybenzyl alcohol, 4-nitrobenzyl alcohol, 3,4-dimethoxybenzyl alcohol, 1-phenyl ethyl alcohol, 4-(methylthio)benzyl alcohol, *trans*-cinnamyl alcohol, 3-penten-2-ol, phenanthroline, 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO), and cuppric chloride dihydride were purchased from Acros. 3-Pyridinemethanol was obtained from TCI, and benzyl alcohol, 1-octanol, 2-octanol, 2-buten-1-ol were purchased from Alfa Aesar. Flash chromatography was performed using silica gel (MN 60, 230–400 mesh). The reactions were carried out under air or oxygen. Gas chromatographic analyses were performed on an Agilent 6890 instrument with an FID detector and an Aglient 30 m × 0.53 mm × 3.0 μm HP-1 capillary column. Infrared spectra were recorded on a Perkin–Elmer 100 infrared spectrometer. NMR spectra were measured in $CDCl_3$ on a Bruker AV 400 MHz. High resulation ESI-MS were measured using a Waters LCT Premier XE with a dual ionization ESCi® in the Mass Spectrometry Facility in the Institute of Chemistry, Academia Sinica. Leucine-enkephalin $[M+H]^+$ $m/z = 556.277$ was used as a reference standard.

Synthesis of Complex $[(phen)Cu(\mu\text{-}Cl)(Cl)]_2$

Room temperature stirring of a dichloromethane solution (75 mL) of $CuCl_2 \cdot 2H_2O$ (852 mg, 5.0 mmol) and phenanthroline (991 mg, 5.0 mmol) overnight under air afforded the green crystalline complex $[(phen)Cu(\mu\text{-}Cl)(Cl)]_2$; yield: 1431 mg (91%). The complex was characterized by single-crystal X-ray diffraction and elemental analyses (anal. calcd. for $C_{24}H_{16}N_4Cl_4Cu_2$: C 45.80, H 2.56, N 8.90; found: C 45.70, H 2.52, N 8.67).

Typical Procedure for the Oxidation

To a solid mixture of $[(phen)Cu(\mu\text{-}Cl)(Cl)]_2$ (141 mg, 0.225 mmol), TEMPO (70 mg, 0.45 mmol), internal standard 1,4-di-*tert*-butylbenzene (190 mg, 1.0 mmol) or decane 142 mg, 1.0 mmol), and K_3PO_4 (955 mg, 4.5 mmol) or K_2CO_3 (622 mg, 4.5 mmol), 30 mL acetonitrile were added and the mixture was stirred for 10 min at room temperature. Alcohol (9.0 mmol) was then added and stirring was continued with oxygen bubbling. The color of the reaction mixture turned from green to reddish orange. The products were analyzed by GC. The reaction mixture was then portioned between diethyl ether (50 mL) and water (50 mL). The aqueous phase was extracted with diethyl ether (2 × 20 mL). The combined organic extracts (90 mL) were washed successively with water (50 mL), 1 M HCl (50 mL), and 50 mL of saturated aqueous NaCl solution, dried over $MgSO_4$, and then

concentrated under vacuum for purification. In the case of 3-pyridinecarboxaldehyde, the combined ether extracts (90 mL) were washed only with water (50 mL) and dried over $MgSO_4$, and then concentrated under vacuum for purification.

For alcohol oxidation, reactions with less solvent and base were carried out in a similar procedure as that of stated above. Alcohol (9.0 mmol) and 477.5 mg, 2.25 mmol base in 20 mL accetonitrile were used in the reaction. The reaction time, conversion, and GC yields are given in the parentheses in the Table 2.

Benzaldehyde: Silica gel column chromatography (hexane/dichloromethane = 4:1) gave benzaldehyde as a colorless liquid; yield: 792 mg (83%). ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 9.99$ (s, 1H), 7.86–7.48 (m, 5H); ^{13}C NMR ($CDCl_3$, 400 MHz): $\delta = 192.11$, 136.17, 134.21, 129.48, 128.76.

4-Chlorobenzaldehyde: Silica gel column chromatography (hexane/dichloromethane = 1:1) gave 4-chlorbenzaldehyde as a white solid; yield: 1202 mg (95%). ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 9.92$ (s, 1H), 7.76 (d, $J = 8.4$ Hz, 2H), 7.74 (d, $J = 8.4$ Hz, 2H); ^{13}C NMR ($CDCl_3$, 400 MHz): $\delta = 190.86$, 140.89, 134.78, 130.93, 129.46.

Methylbenzaldehyde: Silica gel column chromatography (hexane/dichloromethane = 1:4) gave 4-methylbenzaldehyde as a colorless liquid; yield: 961 mg (89%). ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 9.91$ (s, 1H), 7.72 (d, $J = 8.0$ Hz, 2H), 7.27 (d, $J = 7.6$ Hz, 2H), 2.38 (s, 3H); ^{13}C NMR ($CDCl_3$, 400 MHz): $\delta = 192.06$, 145.63, 134.31, 129.92, 129.80, 21.94.

4-Methoxybenzaldehyde: Silica gel column chromatography (hexane/dichloromethane = 1:1) gave 4-methoxybenzaldehyde as a colorless liquid; yield: 1115 mg (91%). ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 9.91$ (s, 1H), 7.86 (d, $J = 8.0$ Hz, 2H), 7.03 (d, $J = 8.0$ Hz, 2H), 3.91 (s, 3H); ^{13}C NMR ($CDCl_3$, 400 MHz): $\delta = 189.15$, 162.91, 130.31, 128.25, 112.68, 54.07.

4-Nitrobenzaldehyde: Potassium carbonate was used as the base in the reaction. Silica gel column chromatography (hexane/dichloromethane = 1:4) gave 4-nitrobenzaldehyde as a white solid; yield: 884 mg (65%). ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 10.12$ (s, 1H), 8.34 (d, $J = 8.8$ Hz, 2H), 8.04 (d, $J = 8.8$ Hz, 2H); ^{13}C NMR ($CDCl_3$, 400 MHz): $\delta = 190.52$, 151.23, 140.20, 130.62, 124.42.

4-(Methylthio)benzaldehyde: Silica gel column chromatography (hexane/dichloromethane = 1:4) gave 4-(methylthio)benzaldehyde as a colorless liquid; yield: 1192 mg (87%). ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 9.81$ (s, 1H), 7.65 (d, $J = 8.4$ Hz, 2H), 7.20 (d, $J = 8.0$ Hz, 2H), 2.41 (s, 3H); ^{13}C NMR ($CDCl_3$, 400 MHz): $\delta = 191.07$, 147.83, 132.83, 129.85, 125.06, 14.53.

3-Pyridinecarboxaldehyde: Silica gel column chromatography (dichloromethane) gave 3-pyridinecarboxaldehyde as a colorless liquid; yield: 814 mg (85%). ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 10.01$ (s, 1H), 8.97 (s, 1H), 8.73 (d, $J = 4.8$ Hz, 1H), 8.06 (d, $J = 8.0$ Hz, 1H), 7.40–7.37 (m, 1H); ^{13}C NMR ($CDCl_3$, 400 MHz): $\delta = 189.91$, 153.54, 150.75, 134.77, 130.27, 123.03.

3,4-Dimethoxybenzaldehyde: Silica gel column chromatography (hexane/dichloromethane = 0.5:9.5) gave 3,4-dimethoxybenzaldehyde as a white solid; yield: 1243 mg (83%). ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 9.70$ (s, 1H), 7.32–7.24 (m, 2H), 6.84 (d, $J = 8.0$ Hz, 1H), 3.81 (d, 6H); ^{13}C NMR ($CDCl_3$, 400 MHz): $\delta = 190.71$, 154.36, 149.49, 130.02, 126.66, 110.34, 108.86, 56.03, 55.84.

Acetophenone: Silica gel column chromatography (dichloromethane) gave acetophenone as a colorless liquid; yield: 984 mg (83%). ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 7.88$ (d, $J = 7.6$ Hz 2H), 7.50–7.46 (m, 1H), 7.40–7.36 (m, 2H), 2.51 (s, 3H); ^{13}C NMR ($CDCl_3$, 400 MHz): $\delta = 198.11$, 137.10, 133.10, 128.57, 128.29, 26.56.

***trans*-Cinnamaldehyde:** Silica gel column chromatography (ether/pentane = 1:4) gave *trans*-cinnamaldehyde as a colorless liquid; yield: 998 mg (84%). ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 9.62$ (d, $J = 8.0$ Hz, 1H), 7.47–7.33 (m, 6H), 6.61 (m, 1H); ^{13}C NMR ($CDCl_3$, 400 MHz): $\delta = 193.46$, 152.56, 133.84, 131.10, 128.93, 128.35.

3-Penten-2-one: Silica gel column chromatography (ether/pentane = 1:4) gave 3-penten-2-one as a colorless liquid; yield: 538 mg (71%). ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 6.69$–6.60 (m, 1H), 5.89 (d, $J = 15.6$ 1H), 2.03 (s, 3H), 1.71 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 400 MHz): $\delta = 198.29$, 143.55, 132.74, 26.48, 18.03

Octanal: Silica gel column chromatography (dichloromethane) gave octanal as a colorless liquid; yield: 542 mg (47%). ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 9.67$ (s, 1H), 2.33 (t, $J = 7.2$ Hz, 2H), 1.57–1.51 (m, 2H), 1.22–1.19 (m, 8H), 0.79 (t, $J = 6.8$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 400 MHz): $\delta = 202.76$, 43.95, 31.69, 29.18, 29.08, 22.64, 22.14, 14.06.

2-Octanone: Silica gel column chromatography (dichloromethane) afforded 2-octanone as a colorless liquid; yield: 542 mg (78%). ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 2.30$ (t, $J = 7.2$ Hz, 2H), 2.07 (s, 3H), 1.46–1.16 (m, 8H), 0.76 (t, $J = 6.0$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 400 MHz): $\delta = 209.10$, 43.74, 31.59, 29.75, 28.84, 23.81, 22.48, 13.97.

Oxidation of Benzaldehyde and *sec*-Phenylethyl Alcohol

In a typical reaction, to a solid mixture of $[(phen)Cu(\mu\text{-}Cl)(Cl)]_2$ (142 mg, 0.225 mmol), TEMPO (70 mg, 0.45 mmol), internal standard 1,4-di-*tert*-butylbenzene (190 mg, 1.0 mmol) and K_3PO_4 (955 mg, 4.5 mmol), 30 mL acetonitrile were added and the mixture was stirred for 10 min at room temperature. Benzyl alcohol (487 mg, 4.5 mmol) and *sec*-phenylethyl alcohol (550 mg, 4.5 mmol) were then added and stirring was continued with oxygen bubbling. The extraction of the reaction mixture was done as above. The silica gel column chromatography (ether/pentane = 0.5:9.5) afforded benzaldehyde and acetophenone as colorless liquid in yields of 73% (349 mg) and 2% (11 mg), respectively. ^{1}H NMR and ^{13}C NMR of isolated benzaldehyde and acetophenone are similar to those reported above.

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