Aerobic Oxidation of Alcohols Catalysed by Cu(I)/NMI/TEMPO System and Its Mechanistic Insights

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Abstract

Homogeneous Cu(I)/NMI/TEMPO catalyst system (TEMPO = 2,2,6,6-tetramethylpiperidine-N-oxyl) has been investigated for its catalysis on the aerobic oxidation of 1-octanol and other alcohols into aldehydes under room temperature. The catalytic species was found to be a Cu(I) centre coordinated by two NMI molecules and other two weakly bound solvent molecules, $[Cu(NMI)_2(Sol)_2]^+$ (Sol = solvent). When CuI was used, this species could be $[Cu(NMI)I(Sol)_2]$. Not like being speculated previously, NMI in this system acts solely as a ligand and its role coordinated to the copper centre enhanced the electron density on the metal centre which promoted the O_2 binding in the catalysis. The labile solvent binding to the Cu(I) centre is essential to ensure both oxygen and substrate binding. The catalyst system is suitable for the oxidation of various alcohols using a simple reaction setup and workup. In particular, the system possesses strong oxidizing capability in quantitative conversion of benzylic alcohols regardless of the substituents on the phenyl ring and allylic alcohols into aldehydes. A plausible mechanism was also proposed for the catalysis.

Graphical Abstract

The aerobic oxidation of primary alcohols at room temperature to corresponding aldehydes was achieved by the catalyst composed by Cu(I) and methyl imidazole (NMI) mediated by TEMPO in acetonitrile. The catalytic species is proposed to

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be such a Cu(I) complex that two of its four coordinating sites are occupied by a strong ligand(s) and the rest two are weakly bound by solvent molecules.
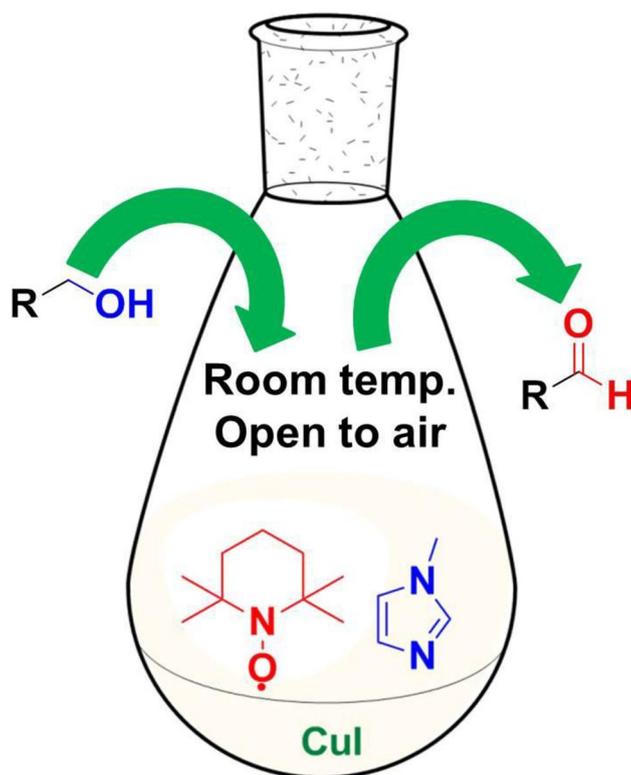
Keywords Aerobic oxidation · Alcohols · Copper · TEMPO · Catalytic mechanism

1 Introduction

The oxidation of alcohols has been one of the main industrious productions of aldehydes or ketones. Like other organic transformation reactions, mild and environmentally benign reaction conditions are desired. Thus, aerobic oxidation at ambient temperature is most preferred. For the catalysts of this oxidation, a number of metals such as, Ce(IV) [1, 2], V(IV, V) [3, 4], Fe(III) [5–7], Cu(I, II) [8–11] have been employed in the mediation of nitroxyl-radical, for example, 2,2,6,6-tetramethylpiperidinyl-1-oxyl (TEMPO) in the past decades. On the other hand, being inspired by the catalytic chemistry of copper-containing enzyme, galactose oxidasae (GOase), copper complexes have attracted particular attentions as the catalysts in the alcohol oxidations [12–14]. GOase possesses a copper centre coordinated with two histidine residues (imidazolyl group) and two tyrosinyl phenol groups [15]. It employs air as the oxidant to convert alcohols into aldehydes at physiological conditions. The oxidation state of the metal operates between I and II and a phenol radical is involved [16]. In addition to tremendous efforts put into structurally mimicking the copper centre [12–14,

17–23], functionally mimicking this catalytic system, essentially being consisted of the metal salt, a radical such as TEMPO and N-containing ligand(s), have also been under intensive investigations in the past decades [5–7, 24–31]. Among them, Cu(I)/nitroxyl catalyst systems have been proven the most efficient catalysts for aerobic oxidations of alcohols with high efficiency and versatility. It has been reported that the Cu(I)/nitroxyl catalyst systems can catalyse the aerobic oxidations of a variety of substrates, including aromatic alcohols, secondary and sterically hindered alcohols as well as even more complex substrates such as polysaccharides [26–31].

The Cu/nitroxyl catalyst system was first reported by Semmelhack and co-workers in 1980s [25]. They demonstrated the oxidations of benzylic and allylic alcohols with CuCl/TEMPO in DMF by pure oxygen and that aliphatic alcohols were substantially less reactive. Afterwards, intensive research has been carried out by using the combinatory system of Cu(I)/nitroxyl radical/ligands. In the reported systems [28, 30, 32–34], bidentate ligands such as 2,2′-bipyridine (bpy) alongside with excessive N-methylimidazole (NMI) have been proved to be the most common systems

for investigations. In the early stage, NMI might be simply regarded as an organic base to replace an inorganic one. Until recently, it has been found out by Stahl and co-workers [29, 35] that NMI acts both as a base and as a ligand during the catalysis. As an additive, it was found that a certain molar ratio of NMI/Cu alongside with another bidentate ligand, for example, 2,2′-bypyridine (bpy), gave the best catalytic performance. They postulated that "(bpy)Cu(II)(NMI)" was an intermediate in the catalytic cycle. Very recently, Brückner and co-workers restudied this well-defined catalytic system and found that the second NMI molecule most probably coordinates weakly to the metal centre forming a species, "(bpy)Cu(NMI)$_a$(NMI)$_b$", in which the Cu-N distances and/or angles for the two NMI molecules (NMI)$_a$ and (NMI)$_b$ are different [36]. The coordination of the second NMI molecule boosts the oxidation of Cu(I) to Cu(II) and thus facilitates the activation of O$_2$ by electron transfer from Cu(I) to O$_2$.

By looking further into catalyst optimization reported by Stahl and co-workers, the Cu/nitroxyl catalyst system using NMI as the sole ligand could also lead to moderate product yield (68%) [28, 37]. In this catalytic system, it is certain that NMI participated in the coordination with the metal centre, which may be analogous to Cu/nitroxyl/bpy/NMI catalyst system. However, questions remaining unanswered are what the catalytic species is and how the ligand NMI plays a role in the catalysis. Herein, we report our findings to attempt to understand the catalytic chemistry of this seemingly simple system. In our studies, both CuI and [Cu(CH$_3$CN)$_4$]PF$_6$ were employed as the Cu(I) sources for comparison. To establish the correlation between the ligands and the catalysis, other imidazole derivatives were also investigated. Techniques of electrochemistry, NMR titration, mass spectrometry and so on have been employed for the investigations. All the results suggest that a copper species with two relatively strongly bound ligands, either two NMI ligands or one NMI and one iodide and the other two labile coordinating sites such as solvent molecules, is the key component for the catalysis. Increasing the electron density on the metal centre enhances the catalysis, which implies strongly that the activation of oxygen may be one of the essential steps involved in the oxidation.

# 2 Experimental

2.1 General Procedures

Chemicals were purchased from J&K Scientific and Aladdin and used without further purification unless otherwise stated. Elemental analyses were performed on Elementar Vario EL III. Crystallographic data of complexes were collected on a Gemini diffractometer with graphite-monochromated Cu–Kα radiation ($\lambda = 1.54184$ Å). The crystal structures were solved using direct methods in SHELXS program and refined by full-matrix least-squares routines, based on F^2, using the SHELXL package [38].

The aerobic oxidation of 1-octanol to 1-octanal at room temperature in CH$_3$CN with ambient air as the oxidant was monitored and quantitatively analyzed by gas chromatography (Agilent 7890) with a packed column of Restek capillary SE-54. The temperature of the GC column was set at 60 °C for 1 min and then was programmed to 170 °C at the rate of 15 °C min^{-1}. Electrochemistry was performed in a gas-tighten three-electrode system in which a vitreous carbon disk ($\varphi = 1$ mm) was used as a working electrode, a carbon strip as counter electrode, and Ag/AgCl (inner reference solution: 0.45 mol L^{-1} [N^{n}Bu$_4$]BF$_4$ + 0.05 mol L^{-1} [N^{n}Bu$_4$]Cl in dichloromethane) against which the potential of ferrocenium/ferrocene couple is 0.55 V in 0.5 mol L^{-1} [N^{n}Bu$_4$]BF$_4$ in dichloromethane as described elsewhere [39, 40]. Ferrocene was added as an internal standard, and all potentials are quoted against ferrocenium/ferrocene couple (Fc$^+$/Fc). All electrochemical studies were performed at room temperature in dried CH$_3$CN under an nitrogen atmosphere with 0.5 mol L^{-1} [N^{n}Bu$_4$]BF$_4$. The initial measurement was performed with 0.02 mmol of CuI dissolved in the electrolyte. Subsequently, NMI in various ratios ranging from 0.5 to 4.0 equivalent were added. After each addition, CV scans were recorded.

2.2 Procedure for the Aerobic Oxidation

Catalytic oxidation of 1-octanol to 1-octanal in acetonitrile was conducted at room temperature in following way. A typical procedure is as follows. In a vessel of 50 mL, to a solution of CuI (0.25 mmol, 47.2 mg) in 5 mL of CH$_3$CN were added 0.5–8 equivalents of NMI (0.125–2 mmol), 1.0 equivalent of TEMPO (0.25 mmol, 39.1 mg) and 1-octanol (5 mmol, 651.0 mg) in open air atmosphere. Then the reaction was carried out at 25 °C for 24 h under vigorously stirring. The products were analyzed by gas chromatography using the internal standard method. Quantitative analysis of 1-octanal was achieved by establishing their calibration curves with linear equations under optimized conditions, $y = 0.0049 x + 0.0327$ (R$^2 = 0.9968$) for 1-octanal (Fig. S1), where y is the ratio of the peak areas of the analyte (1-octanal) and the internal standard biphenyl, x (mg) is the mass of the analytes. The yield of 1-octanal was calculated as follows: 1-octanal (mmol)/1-octanol initially used (mmol) × 100%. For other substrates, the oxidation reaction was analogously preformed. The reaction was analyzed by GC-MS.
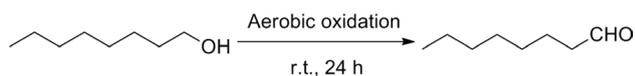
Scheme 1 Aerobic oxidation of 1-octanol into octanal at room temperature

Table 1 The optimal ratio of CuI/NMI/TEMPO for aerobic oxidation of 1-octanol

Entry	CuI/NMI/TEMPO	Yield (%)[a]
1	1:1:0	Trace
2	1:1:0.1	40
3	1:1:0.2	57
4	1:1:1	83
5	1:1:2	82
6	1:1:4	81
7	1:0:1	Trace
8	1:0.5:1	59
9	**1:2:1**	**89**
10	1:3:1	76
11	1:4:1	66
12	1:5:1	47
13	1:6:1	39
14	1:7:1	32
15	1:8:1	30
16	0:2:1	Trace
17[b]	1:2:1	Trace

Best catalytic performance under optimal reaction condition are highlighted in bold

Reaction conditions: 1-octanol (5 mmol, 651.0 mg), CuI (0.25 mmol, 47.2 mg), CH$_3$CN (5 mL), air, 25 °C, 24 h

[a]Yields calculated by GC analysis using biphenyl as the internal standard

[b]Controlled anaerobic reaction

3 Results and Discussion

3.1 Optimization of the Reaction Conditions of Alcohol Oxidation

To examine the optimal reaction conditions for the oxidation, 1-octanol was employed to be aerobically oxidised into octanal in acetonitrile, Scheme 1. By varying the ratios of both NMI and TEMPO over CuI, it was found that the co-presence of both NMI and TEMPO is of vital importance for the catalysis, Table 1. Furthermore, lacking any of the three components makes the reaction hardly proceed (entries 1, 7 and 16, respectively, Table 1). For TEMPO, one equivalent is sufficient to reach the best catalytic performance (entries 1–6, Table 1). The ratios of NMI over CuI at both 1:1 and 1:2 gave roughly the same reaction yields (entries 4 and 9, Table 1). Such ratios may

Table 2 The effect of solvents on the oxidation

Entry	Solvent (5 mL)	Yield (%)[a]
1	CH$_3$CN	89
2	DCM	79
3	DMSO	73
4	DMF	51
5	THF	27
6	Toluene	Trace

Reaction conditions: 1-octanol (5 mmol, 651.0 mg), CuI (0.25 mmol, 47.2 mg), NMI (0.5 mmol, 41.1 mg), TEMPO (0.25 mmol, 39.1 mg), solvent (5 mL), air, 25 °C, 24 h

[a]Yields calculated by GC analysis using biphenyl as the internal standard

Table 3 The effect of a base on the oxidation catalysed by CuI

Entry	Base	Yield (%)[a]
1	–	89
2	K$_2$CO$_3$ (5%)	68
3	K$_2$CO$_3$ (10%)	63
4	K$_2$CO$_3$ (20%)	55
5	K$_2$CO$_3$ (80%)	45
6	K$_2$CO$_3$ (120%)	28
7	NEt$_3$ (5%)	12
8	NaOH (5%)	43

Reaction conditions: 1-octanol (5 mmol), base (molar percentage of the substrate), NMI (0.5 mmol, 41.1 mg), CuI (0.25 mmol, 47.2 mg), TEMPO (0.25 mmol, 39.1 mg), CH$_3$CN (5 mL), air, 25 °C, 24 h

[a]Yields calculated by GC analysis using biphenyl as the internal standard

give up some clues to pinning down the catalytic species (*vide infra*). With the ratio of CuI:NMI:TEMPO = 1:2:1, it turned out that 24 h reaction gave the best yield (Table S1). Throughout the investigation, this ratio and reaction time were adopted. The oxidation is highly solvent-dependent as shown in Table 2. Among the common solvents, acetonitrile is the most suitable solvent. It does not seem that a straightforward correlation between the reaction and both the polarity and coordinating capability of a solvent can be established. In this study, acetonitrile was employed as the reaction medium throughout.

Since the oxidation of alcohols involves deprotonation, the presence of a base may facilitate the reaction. Indeed, there have been reports on the employment of a base in the catalytic oxidation [23, 26, 27, 29, 41]. Very often, NMI was used as an additive alongside with other bidentate ligands [28, 30, 32, 42, 43]. It was believed that NMI acts as a base [29, 35]. However, in the CuI/NMI/TEMPO system, any base deteriorated the oxidation reaction, Table 3. Triethylamine is the most efficient base in killing the reaction probably due to its good solubility in acetonitrile (Entry

6, Table 3) whereas inorganic bases are poorly soluble in organic solvents. The presence of a base may cause a loss of the copper species by forming Cu(II)-hydroxides [27, 35]. Certainly, it is also possible that the presence of a base may alter reaction pathway with low yield. The observation suggests that either deprotonation is a fast step in the oxidation or there is other pathway to deprotonate the substrate and therefore, no external base is needed in this system.

In addition to CuI, a number of other Cu(I) salts were also examined, Table 4. As shown in Table 4, both tetraacetonitrilecopper (I) (entry 4) and cuprous triflate (entry 5) possess comparable catalytic efficiencies to CuI (entry 1). However, for the cuprous halides (entries 1, 2 and 3), their activity decreases steadily from I^- to Cl^-. It is well known that the cuprous halides are polymeric with four-coordinated metal centre. As our experimental observation suggested, CuI is practically soluble in acetonitrile whereas the other two are much less soluble in the same solvent. Furthermore, the formation enthalpies of the three cuprous halide bonds are -67.8 (I^-), -104.6 (Br^-) and -137.2 kJ mol^{-1} (Cl^-), respectively. Thus, breaking the Cu$-$X (X$=$I, Br, Cl) bond to form a complex with NMI becomes more difficult from I^- to Cl^-. This behaviour suggests strongly that Cu(I) species coordinated by NMI should be the active component in the catalysis. The speculation is further supported by that varying the ligands changes significantly the catalytic efficiency as shown in Table 5.

In the catalysis, the activation of O_2 is generally believed an important step and is achieved by its binding to the copper(I) centre. Thus, the electron density on the metal is vital to the catalysis. Intrinsically, a coordination reaction between a metal ion and a ligand is an acid-base reaction. In general, a ligand with strong basicity can increase the electron density of the metal centre. Therefore, we intended to examine the correlation between the pK_a and the catalytic activity. Since not all the pK_a values of the ligands are available, their pH values at a fixed concentration (C$=$10 mmol L^{-1}) were taken. The correlation between the catalytic
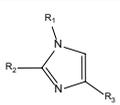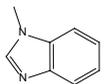
Table 4 The catalytic efficiency of various Cu(I) salts on the aerobic oxidation

Entry	Cu salt (5%)	Yield (%)[a]
1	CuI	89
2	CuBr	62
3	CuCl	37
4	Cu(CH$_3$CN)$_4$PF$_6$	83
5	Cu(OTf)	79

Reaction conditions: 1-octanol (5 mmol, 651.0 mg), NMI (0.5 mmol, 41.1 mg), TEMPO (0.25 mmol, 39.1 mg), CH$_3$CN (5 mL), air, 25 °C, 24 h

[a]Yields calculated by GC analysis using biphenyl as the internal standard

**Table 5** The catalytic efficiency of Cu(I) imidazole derivative systems

Entry	Ligand	pH	Yield (%)[a]
1	(imidazole structure) R$_1$ $=$ CH$=$CH$_2$[b]	8.17/9.03[c]	91
2	R$_1$ $=$ C$_6$H$_5$	8.17	87
3	R$_1$ $=$ C(CH$_3$)$_3$	9.36/9.06	87
4	R$_1$ $=$ CH(CH$_3$)$_2$	9.28/7.09	89
5	R$_1$ $=$ CH$_3$	9.22/8.23	89
6	(benzimidazole structure)	7.99	70
7	R$_1$ $=$ (CH$_2$)$_2$OH	9.03/8.61	62
8	R$_1$ $=$ R$_2$ $=$ H	9.17	36
9	R$_1$ $=$ COCH$_3$	5.89/7.85	22
10	R$_1$ $=$ COCF$_3$	4.72/5.25	12
11	R$_1$ $=$ R$_2$ $=$ CH$_3$	9.83	79
12	R$_1$ $=$ CH$_3$ R$_2$ $=$ CO$_2$CH$_2$CH$_3$	7.64	42
13	R$_1$ $=$ CH$_3$ R$_3$ $=$ CO$_2$CH$_2$CH$_3$	7.09	37

Reaction conditions: 1-octanol (5 mmol, 651.0 mg), CuI (0.25 mmol, 47.2 mg), L (0.5 mmol), TEMPO (0.25 mmol, 39.1 mg), CH$_3$CN (5 mL), air, 25 °C, 24 h. When the pH was measured in aqueous solution, the concentration of the ligand is 10 mmol L^{-1}

[a]Yields calculated by GC analysis using biphenyl as the internal standard

[b]For R$_2$ and R$_3$, they are all H atom unless otherwise stated

[c]Measured in acetonitrile after the forward slash
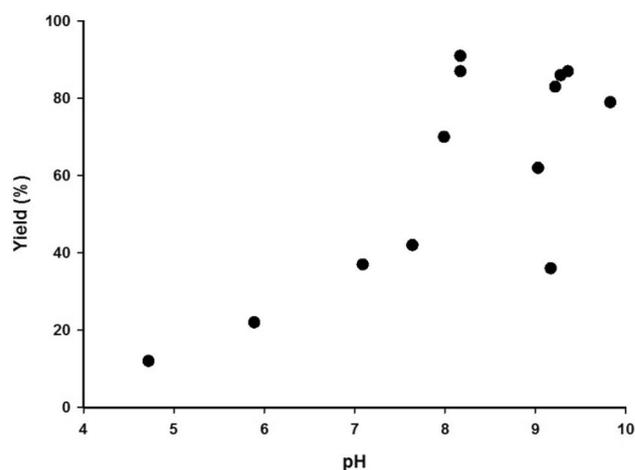

Fig. 1 The correlation of reaction yield to the basicity of imidazole derivative (pH of the ligands in water at the concentration of 10 mmol L^{-1})

activity (yield) and the pH values are depicted in Fig. 1. As shown in the plot, the boundary between the two groups is crystal-clear. The only exception is the ligand imidazole. This is probably due to the presence of HN group in the ring which would involve H-bonding with the substrate or other imidazole. Such interactions may cause hindrance in the catalysis [36]. It is obvious that electron-donating substituent(s) enhance the catalytic activity of CuI.

3.2 Probing the Catalytic Species and Possible Mechanism

As discussed above, when the ratio of CuI/NMI is both 1/1 and 1/2, the catalyst gave the best performance (entries 4 and 9, respectively, Table 1). Similar trend was also observed when $[Cu(CH_3CN)_4]PF_6$ was employed, Fig. 2. But one significant difference lies at the ratio of 1/1. Unlike CuI, when the ratio of 1/1 was used in the case of $[Cu(CH_3CN)_4]PF_6$, the activity dropped dramatically, Fig. 2. The observation
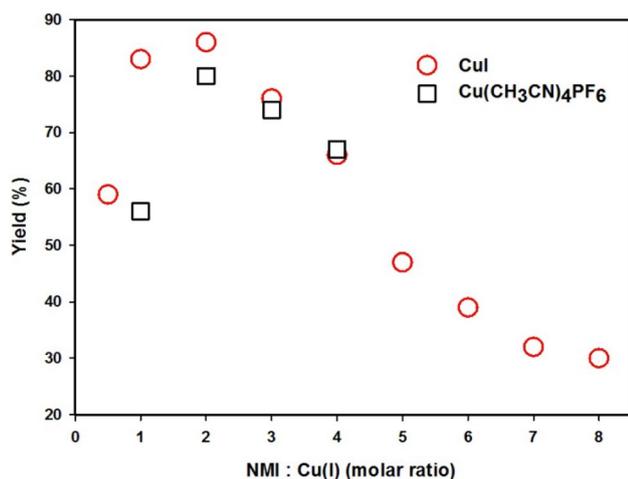
may strongly suggest that the active species is a Cu(I) complex with two sites relatively strongly bound by two ligands and the other two weakly bound by the solvent molecules. This explains reasonably why 1/1 ratio for CuI gave still comparable activity since I^- can bind to Cu(I) more strongly than CH_3CN. Therefore, the possible active species may be $[Cu(NMI)_2(CH_3CN)_2]^+$ (ratio 1/2) and $[Cu(NMI)I(CH_3CN)_2]$ (ratio 1/1). In other words, when ratio 1/1 was employed for CuI, the iodide could be one of the relatively strongly bound ligands to meet the required coordinating sphere around the Cu(I) centre.

In an attempt of isolating the proposed active species, synthetic reactions were performed by using various ratios of CuI over NMI. Except for the reaction at ratio 1/1 from which no solid product was isolated, solid products were isolated from reaction at ratio 1:2, 1:3 and 1:4, respectively. As microanalysis results revealed, these solids fit nicely to the compositions of the proposed structures shown in Fig. 3. All the solids possess the metal centre Cu(I). Their conductivity in acetonitrile, 54, 68, 80 μs cm^{-1} for **1**, **2** and **3**, respectively (Table S2), suggests also that the solutions of **1** and **2** less ionic than **3**. The same synthesis was also carried out using $[Cu(CH_3CN)_4]PF_6$ and solids **1′**, **2′** and **3′** were isolated. Microanalysis suggests that the three solids were complexes of Cu(II) and possible compositions were shown in Fig. S2 derived from the microanalysis results. The attempts of crystallising these solids were not quite successful. Only in the cases of **1** and **1′** did the crystallization produce crystals suitable for X-ray diffraction analysis. But unfortunately, the crystals growing from solid **1** turned out to be a cation, $[Cu(NMI)_4]^{2+}$, in which not only did the coordination change, but also did the oxidation of the copper centre from Cu(I) to Cu(II), Fig. S3. For solid **1′**, it ended up also with the same cation, Figs. S2 and S3.

The three solids **1**, **2** and **3** were examined for their catalysis on the aerobic oxidation of 1-octanol. But none of the solids exhibits efficient catalysis (yield: < 60%) under the optimized reaction conditions as described above. This is

Fig. 2 Plot of the yield of the oxidation of 1-octanol against the ratio of Cu(I)/NMI
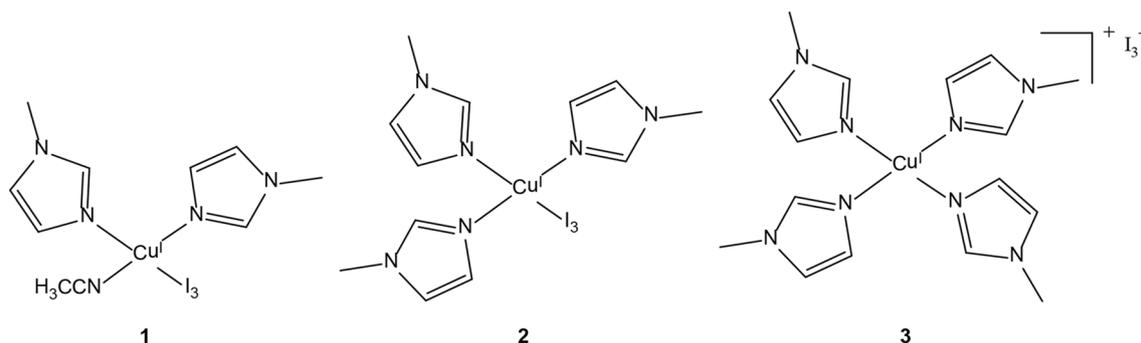
Fig. 3 Possible structures of the solids isolated from the reaction between CuI and NMI at the ratios 1:2, 1:3 and 1:4, respectively (from left to right)

surprising for solid **1** since at this ratio, a yield over 80% was achieved as suggested by the results in the optimization of the reaction conditions (Table 1). Examining the electrochemistry of both the solids (**1, 2** and **3**, Fig. 3) and Cu(I)/NMI systems revealed such huge differences in the electrochemical behaviours, Table 6 and Fig. S4. For all the complexes and systems examined, the reduction Cu(I) → Cu(0) occurred at a potential between − 1.10 and − 1.25 V. For the mixed Cu(I)/NMI systems, the reduction potential shift steadily with the addition of NMI. This complies simply with that increasing the number of NMI coordinated to the metal enhances its electron density. However, no such trend was observed for the three solids (**1, 2** and **3**, Fig. 3). Such discrepancies were also found in the oxidation processes, Table 6 and Fig. S4. This suggests that active species could be anything but the complex of the composition proposed in Fig. 3.

As discussed above, the active species ought to be $[Cu(NMI)_2(CH_3CN)_2]^+$ in which the solvent binding is labile and ready to dissociate for O_2 binding. Indeed, in the mass spectrum of the CuI/NMI (1:2) in both CH_3OH and CH_3CN, the signal of the fragment, $[Cu(NMI)_2]^+$ (227.0219), is the strongest (Fig. S5). To further confirm this, solid **3** (Fig. 3) was mixed with one equivalent of CuI to allow forming $[Cu(NMI)_2(CH_3CN)_2]^+$ and the mixture was then employed to catalyze the oxidation under the optimal reaction conditions. Prior to the catalytic reaction, the mixture was stirred for 0, 2 and 4 h, respectively, which led to the oxidation yield of 73, 75 and 80%, respectively. Without mixing with one equivalent CuI, the oxidation yield for the cation **3** was only 62% which is comparable to the yield 66% (entry 11,

Table 6 The redox potentials (E_p or $E_{1/2}$) of the CuI systems at various ratios of CuI:NMI and the solids **1, 2** and **3** in acetonitrile

CuI:NMI	1:1	1:2	1:3	1:4
^{a}Cu(I) → Cu(0)	− 1.162	− 1.191	− 1.193	− 1.198
^{a}Cu(I) → Cu(II)	− 0.248^c	− 0.338^c	− 0.357^c	− 0.366^c
^{a}Oxidation of I$^-$	− 0.005	− 0.014	− 0.012	0.008
^{a}Cu(II) → Cu(III)	0.363	0.382	0.385	0.399
^{b}Cu(I) → Cu(0)	–	− 1.248	− 1.137	− 1.160
^{b}Cu(I) → Cu(II)	–	0.259^c	0.259^c	0.264^c
^{b}Oxidation of I$_3^-$	–	− 0.037	− 0.055	− 0.032

^{a}CuI/NMI systems at various ratios. As shown in Fig. S4, for CuI, the oxidation of I$^-$ occurs at 0.034 V and that of Cu(I) → Cu(II) at 0.259 V ($E_{1/2}$)
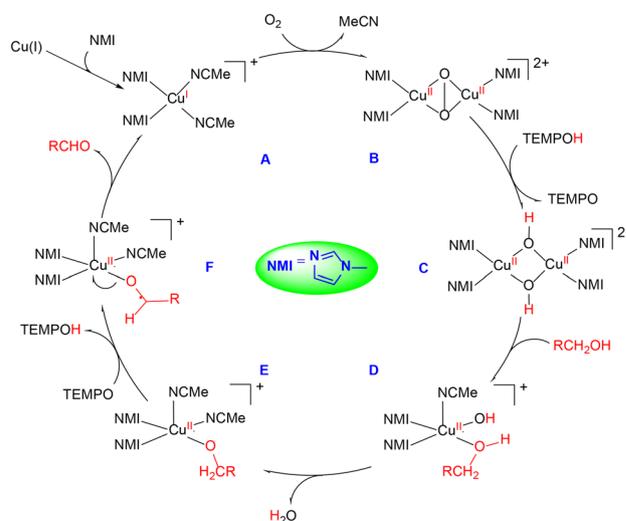
^{b}The isolated solids **1, 2** and **3** (Fig. 3)

^{c}$E_{1/2}$

Scheme 2 A plausible catalytic mechanism for the aerobic oxidation of alcohols in MeCN

Fig. 4 The NMR of $Cu(CH_3CN)_4PF_6$ in CD_3CN (C = 15 mmol L^{-1}) with the presence of a variety of amount of NMI (Right: zoomed-in signal changes of the methyl group proton). **a** NMI; **b** NMI:Cu(CH$_3$CN)$_4$PF$_6$ = 1:1; **c** NMI:[Cu(CH$_3$CN)$_4$]PF$_6$ = 2:1; **d** NMI:[Cu(CH$_3$CN)$_4$]PF$_6$ = 3:1; **e** NMI:[Cu(CH$_3$CN)$_4$]PF$_6$ = 4:1; **f** added one Eq. [Cu(CH$_3$CN)$_4$]PF$_6$ into **e** to afford a system analogous to **c**

Table 7 Substrates expansion for the catalytic system

Entry	Substrate	Product	Yield (%)[a]	TON	TOF (h^{-1})
1	(octanol) OH	(CHO chain)	89	17.8	0.74
2	OH	CHO	84	16.8	0.70
3	OH (ethanol)	acetaldehyde	34	6.8	0.28
4	cinnamyl alcohol OH	cinnamaldehyde CHO	99	19.8	0.83
5	crotyl OH	crotonaldehyde CHO	99	19.8	0.83
6	H$_3$CO—Ph—CH$_2$OH	H$_3$CO—Ph—CHO	99	19.8	0.83
7	O$_2$N—Ph—CH$_2$OH	O$_2$N—Ph—CHO	99	19.8	0.83
8	F$_3$C—Ph—CH$_2$OH	F$_3$C—Ph—CHO	99	19.8	0.83
9	Ph—CH$_2$OH	Ph—CHO	99	19.8	0.83
10	furfuryl alcohol OH	furfural CHO	99	19.8	0.83
11	1-phenylethanol OH	acetophenone O	44	8.8	0.36
12	cyclohexanol OH	cyclohexanone O	11	2.2	0.09
13	2-octanol OH	2-octanone O	2	0.4	0.02
14	phenethyl alcohol OH	phenylacetaldehyde CHO	3	0.6	0.03
15	adamantyl methanol OH	adamantyl CHO	1	0.2	0.01

Table 1). Using the methyl group on NMI as an indicator, we were able to titrate the system. Despite of the disappearance of the signals of the imidazole ring protons upon binding to the Cu(I) ion, the signal of the methyl proton was not affected much and can be employed to trace the change in coordination environment with the various ratios of NMI, Fig. 4. It is clearly demonstrated that the dissociation/association occurred between the ligand NMI and Cu(I). The coordinating environment at 1:4 (Cu(I)/NMI) restored steadily to 1:2 when one equivalent of Cu(I) was added (Fig. 4f).

Therefore, there is no doubt that depending on the Cu(I) salts, the catalytic specie can be either [Cu(NMI)(I)(CH$_3$CN)$_2$] or [Cu(NMI)$_2$(CH$_3$CN)$_2$]$^+$ (**A**). As suggested by others' investigations, the Cu(I) system turned to form a Cu(II)-dinuclear species upon O$_2$ binding and to form probably peroxo-bridged dinuclear intermediate (**B**) [44–47]. Once the catalytic cycle initiates, the peroxo-bridged species is reduced to dihydroxyl-bridged form (**C**) by a reduced form of TEMPO, that is, TEMPOH. Such an analogous dimeric species have been reported previously [35, 42]. It is at this stage, the metal centre is acidic enough to bind the substrate to form a mononuclear complex. Indeed, when benzyl alcohol was used as the substrate, a signal corresponding to the species [**D** + MeOH + H$^+$] was detected (426.2175) (Fig. S6). Sequentially, the hydroxyl group deprotonated readily the proton of the bound substrate to form alkoxide-bound adduct **E**. This explains also why this system does not need an external base at all for the catalysis. Being deprotonated, one of the hydrogen atoms of the ethylene group of the substrate can be abstracted by TEMPO to form the complex **F** as a radical. Through internal electron transfer, the Cu(II) was reduced to Cu(I) by releasing the aldehyde product and brought the catalyst back to the initial form **A**. Based on the above discussions and literature reports on mechanistic investigations [29, 36, 48–50], a plausible mechanism for the Cu(I)/NMI/TEMPO system was proposed in Scheme 2.

3.3 Substrates expansion for the catalytic system

Substrates expansion was performed for the system, Table 7. The results showed that the system presented excellent applicability. It catalyses quantitatively the aerobic oxidation benzylic type of alcohols with no influence of the substituent on the phenyl ring, either electron-withdrawing or donating groups. It showed also very good activity toward the oxidation of primary aliphatic alcohols. Some activity was observed for secondary alcohols of type of 2-phenylethanol. But it showed hardly any activity to other secondary alcohols. It is noteworthy that the yield for the oxidation of ethanol was not high. This may be attributed to the volatile nature rather than poor catalytic efficiency.

4 Conclusions

In summary, a Cu (I)-based catalytic system for the aerobic oxidation of alcohols into aldehydes at room temperature in acetonitrile was described. In the catalytic system, NMI acts solely as an essential ligand. Its role as a base can be neglected in our case. Its coordination to the Cu(I) centre helps maintain necessary electron density for oxygen activation. The positive correlation between imidazole derivatives with electron-donating group(s) and the catalytic efficiencies supports well this argument. To allow O$_2$ and substrate binding, fully coordinated Cu(I) centre is not beneficial to the catalysis. Our results suggest that the catalytic species contains two NMI ligands plus the weak binding of two solvent molecules such as CH$_3$CN. If CuI was used as the catalyst precursor, I$^-$ could act as one of the essential ligands to replace one of the two NMI ligands. By using TEMPO as the radical, the catalytic system of Cu (I) and NMI possesses excellent selectivity and strong oxidising capability towards the oxidation of benzylic, allylic and heterocyclic alcohols as well as partial aliphatic alcohols.

The results shown in this piece of work suggest that a simple system can achieve the desired functionality without involving delicate ligands design and synthesis providing that appropriate electron density on the metal centre maintains and labile binding sites exist. Currently, catalytic systems of this type for aerobically oxidising secondary alcohols into ketones have actively been pursued in our laboratory.

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