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Oxidant-dependent selective oxidation of alcohols utilizing multinuclear copper-triethanolamine complexes

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ABSTRACT

Multinuclear Cu(II)-triethanolamine complexes were employed as catalysts for the selective oxidation of primary and secondary alcohols using *tert*-butylhydroperoxide (TBHP) and O_2/2,2′,6,6′-tetramethylpiperidinyl-1-oxyl (TEMPO) system, respectively. The catalytic performances, especially in terms of selectivities, were oxidant-dependent in forming the corresponding carbonyl compounds as the major products. Excellent selectivities and moderate to good yields were obtained for the transformation of secondary alcohols to ketones in the case of TBHP and also for the conversion of benzylic primary alcohols to aldehydes in the case of O_2/TEMPO system.

1. Introduction

The transformation of an alcohol to the corresponding carbonyl product via catalytic selective oxidation has received considerable attention in organic synthesis. There are numerous diverse methods that accomplish this fundamental functional group manipulation.[1,2] Traditional stoichiometric oxidants are known for this transformation, such as chromates, hypochlorites, permanganates, and others.[3] But most of them are toxic and produce large amounts of waste. There has been an increased interest in developing clean and economic processes for the selective oxidation of alcohols to aldehydes or ketones. In this respect, the heterogeneous or homogeneous catalytic systems in combination with environmentally benign oxidants like O_2, H_2O_2, and *tert*-butylhydroperoxide (TBHP) are highly desirable systems.[4] The catalysts including complexes, heterogenized complexes, mixed oxides, and nanoparticles, containing transition metals such as V, Cr, Co, Cu, Ru, Pd, Pt, Au, etc., have been screened for more efficient processes.[2a,b,5] In recent years, nitroxyl radical TEMPO (2,2′,6,6′-tetramethylpiperidinyl-1-oxyl) has been extensively studied as a catalyst or catalyst component for the transformation, with or without transition metals.[2,6] For instance, Chou showed that CuCl–TEMPO was effective with benzylic and allylic alcohols whereas less effective with primary and secondary alcohols.[6a] Knochel[6b,c] followed by Gree[6d] developed CuCl–TEMPO catalytic systems for the oxidation of alcohols under dioxygen, at 363 K under fluorous biphasic conditions and at 338 K in an ionic liquid, respectively.

Recently, a family of copper-triethanolamine complexes, such as dimeric $[Cu_2(H_2tea)_2(C_6H_5COO)_2]\cdot 2H_2O$ **1**, trimeric $[Cu_3(H_2tea)_2(4\text{-}OC_6H_4COO)_2(H_2O)]\cdot 4H_2O$ **2**, tetrameric $[O\subset Cu_4(tea)_4(BOH)_4][BF_4]_2$ **3**, and polymeric $[Cu_2(H_2tea)_2\{\mu\text{-}C_6H_4(COO)_2\text{-}1,4\}]_n\cdot 2nH_2O$ **4**, have been employed as catalysts for the selective oxidation of cyclohexane and alkanes to the corresponding oxygenates using H_2O_2 by Pombeiro et al.[7] and the oxidation of alkylarenes to phenyl ketones using TBHP oxidant by us.[8] The reactions showed potentially higher yields. In an extension to the selective oxidation of alcohols using the copper-triethanolamine complexes as catalysts, we found that the selectivities were oxidant-dependent to form the corresponding carbonyl compounds. Excellent selectivities up to 100% and moderate to good yields were obtained for the transformation of secondary alcohols to ketones when TBHP was used as the oxidant, and also for the conversion of benzylic primary alcohols to aldehydes when O_2/TEMPO was used as the oxidative system.

2. Results and discussion

The geometries of the complexes **1**–**4** are shown in Figure 1. Clearly, the Cu(II) atoms in the complexes **1** and **4** are hexa-coordinated with triethanolamine ligand and carboxylate ligand (for **1**) or terephthalic acid ligand (for **4**), respectively, while the Cu(II)

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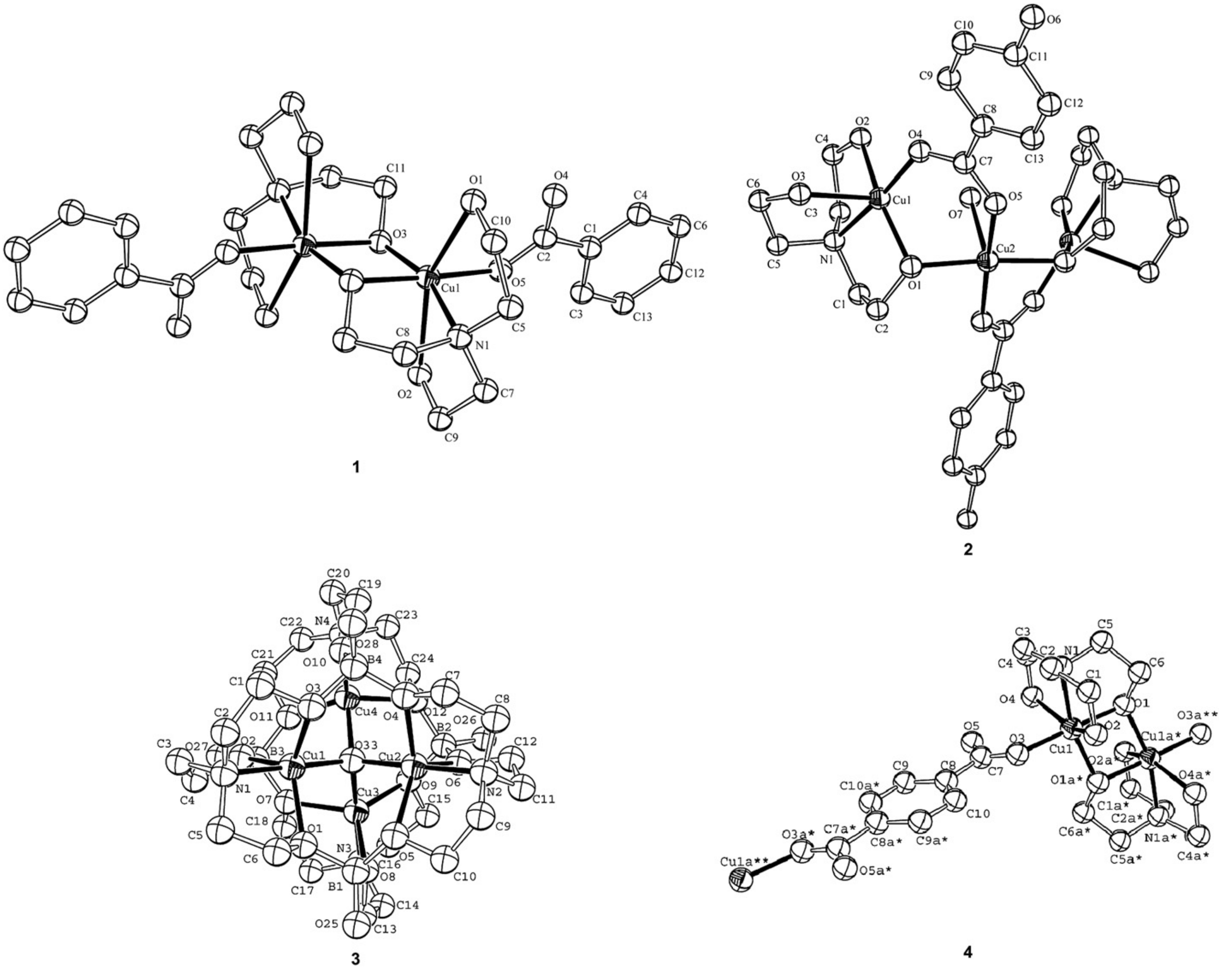


Figure 1. The ORTEP drawing of **1**–**4** (only one dinuclear repeating unit).

species in the complexes **2** and **3** are pentacoordinated with triethanolamine ligand. Complex **3** possesses a cage structure composed of centro-symmetric subunits $[\mathrm{O}\subset\mathrm{Cu_4(tea)_4(BOH)_4}]^{2+}$ and $\mathrm{BF_4^-}$ per unit, in which an oxygen atom is embedded into the center of four Cu atoms and each Cu atom coordinates with one tetradentate triethanolamine ligand and the central oxygen atom. Moreover, four B–OH groups connect three oxygen atoms of different triethanolamine ligands.[7,8]

Initially, we carried out the catalytic oxidation of benzyl alcohol using the copper complexes and $Cu(NO_3)_2$ as catalysts in the presence of TBHP. The results are listed in Table 1. In all cases, the major product was benzaldehyde with small amount of benzoic

Table 1
Selective oxidation of benzyl alcohol by several copper compounds using TBHP oxidant

Entry	Catalyst	TBHP/substrate (molar ratio)	Temperature (K)	Time (h)	Conversion[a] (%)	Selectivity[b] (%)	Yield[c] (%)
1	$Cu(NO_3)_2$	2	343	4	39.8	50.1	19.9
2	**1**	2	343	2	36.7	82.1	30.1
3	**2**	2	343	2	24.3	79.6	19.3
4	**3**	2	343	2	53.2	80.7	42.9 (38.5)
5	**4**	2	343	4	10.0	78.3	7.8
6	Blank	2	343	4	2.1	92.3	19.4
7	**3**	2	343	4	74.4	49.2	36.6 (33.7)
8	**3**	2	308	2	17.8	70.3	12.5
9	**3**	2	323	2	38.5	79.2	30.5
10	**3**	2	353	2	80.1	46.9	37.6 (33.4)
11	**3**	1	343	4	42.3	69.8	29.5
12	**3**	3	343	2	72.5	66.1	47.9 (44.8)

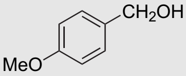
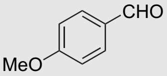
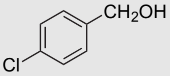
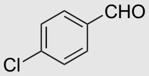
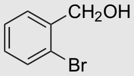
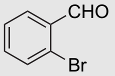
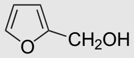
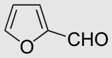
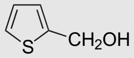
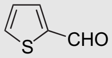
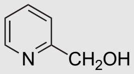
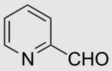
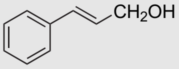
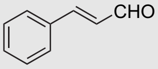
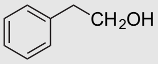
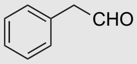
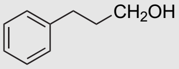
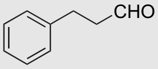
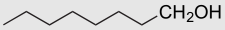
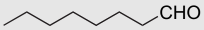
Reaction conditions: benzyl alcohol (6 mmol) and copper compound (0.015 mmol) in CH_3CN (5 mL).

[a] Average conversion of two runs based on GC results (DM-Wax 30 m×0.25 mm×1.0 μm).

[b] Selectivity to benzaldehyde.

[c] The data in parenthesis are the isolated yield of benzaldehyde.

Table 2
Selective oxidation of primary alcohols catalyzed by complex **3** using TBHP oxidant

Entry	Substrate	Major product	Time (h)	Conversion (%)	Selectivity (%)	Yield (%) [a]
13			6	74.6	74.3	55.4 (52.6)
14			4	72.3	82.3	59.5 (55.4)
15			6	81.2	78.3	63.6 (61.8)
16			6	66.6	75.1	50.1 (46.5)
17			5	57.0	84.2	48.0 (45.1)
18			6	26.1	80.5	21.0
19			16	12.5	61.2	7.7
20			19	17.3	36.2	6.3
21			21	22.3	16.9	3.8
22			12	6.2	42.8	2.7

The reaction conditions are the same as in Table 1.

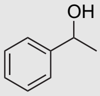
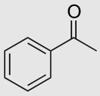
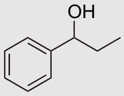
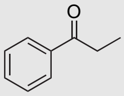
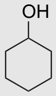
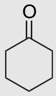
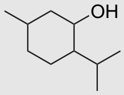
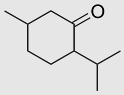
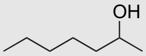
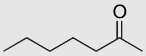
[a] The data in parenthesis are the isolated yields of the corresponding major products.

acid (entries 1–5). A controlled experiment without catalyst under identical conditions gave negligible conversion (entry 6). Among them, similar benzaldehyde selectivity of 78–82% was obtained using complexes **1**–**4** and the worst selectivity to benzaldehyde was obtained using $Cu(NO_3)_2$ only. On the other hand, the activity sequence as represented by conversion in a decreasing order was found as **3**>**1**>**2**>$Cu(NO_3)_2$>**4**. The influences of different parameters (the ratio of TBHP to benzyl alcohol, temperature, and reaction time) on the performance of **3** for the oxidation of benzyl alcohol are also incorporated in Table 1. A prolonged reaction time increased conversion but caused a quick decrease in the selectivity due to the conversion of benzaldehyde to benzoic acid. The ratio of TBHP to benzyl alcohol could also significantly affect the conversion and benzaldehyde selectivity. When the ratio of TBHP to benzyl alcohol was set at 3:1, higher conversion associated with lower selectivity was obtained. When the reaction temperature was increased from 308 to 343 K, the conversion of benzyl alcohol increased drastically from 17.8 to 53.2%, where the selectivity to benzaldehyde was also increased from 70.3 to 80.7%. However, when the reaction temperature was further increased to 353 K, the benzaldehyde selectivity dropped to 46.9% and a considerable amount of benzoic acid was formed.

We then conducted the selective oxidation of several alcohols by complex **3** using TBHP oxidant. The results are summarized in Tables 2 and 3. Similar to the oxidation of benzyl alcohol, moderate conversion and selectivity were obtained over the alcohols bearing electron-withdrawing and -donating groups in the aromatic ring, i.e., 4-chloro, 4-methoxyl, and 2-bromobenzyl alcohols. Heterocyclic alcohols like 2-furfurol and 2-thiophenemethanol were oxidized to the corresponding aldehydes in 26–66% conversion and 75–81% selectivity. No oxidation occurred on S and N heteroatoms. Some secondary alcohols, i.e., 1-phenylethanol, 1-phenylpropanol, 2-heptanol, and cyclohexanol, are oxidized to the corresponding ketones in high conversions with excellent selectivities up to 100%. However, menthol acquired a lower conversion compared to cyclohexanol probably due to the steric hindrance. The corresponding primary alcohols and allylic alcohol, i.e., 2-phenylethanol, 3-phenylpropanol, 1-octanol, and cinnamyl alcohol, were less reactive and provided a mixture of aldehydes and acids after a prolonged reaction time.

It is known that O_2/TEMPO proved to be one of the most effective oxidants for the oxidation of alcohols. In the copper catalyst system, the base promotes the deprotonation of alcohol and the coordination of the resulting alcohol species to the copper center. To obtain a higher selectivity in the transformation of primary alcohols to the corresponding aldehydes, we have further tested the reaction under O_2/TEMPO using the complex **3** (Tables 4 and 5) as catalyst and NaOH as a basic promoter. In all cases, benzylic primary alcohols were oxidized by O_2/TEMPO to the corresponding aldehydes in 100% selectivity with a reasonable conversion (Table 4). Negligible reactions were observed when the TEMPO or copper complex was not employed (entries 32 and 33). The *para*-chloro- or methoxyl-substituted benzylic alcohol exhibited a higher reactivity, whereas a lower conversion for *ortho*-bromo-substituted

Table 3
Selective oxidation of secondary alcohols catalyzed by complex **3** with TBHP oxidant

Entry	Substrate	Major product	Time (h)	Conversion (%)	Selectivity (%)	Yield[a] (%)
23			4	96.6	100	96.6 (93.4)
24			6	86.9	100	86.9 (80.3)
25			2	40.2	100	40.2 (37.8)
26			3	13.2	88.7	11.7
27			7	100	100	100 (100)

The reaction conditions are the same as in Table 1.

[a] The data in parenthesis are the isolated yields of the corresponding major products.

benzylic alcohol was obtained under identical conditions (Table 5, entries 37–39). The results implied that there existed a steric effect in the catalytic system. The allylic alcohol, cinnamyl alcohol, could also be converted to the corresponding aldehyde in 100% selectivity with good conversion (entry 41), which was much better than that using TBHP oxidant. However, such system in the oxidations of secondary and aliphatic primary alcohols (entries 42–46) afforded lower conversions under the identical conditions. Although the exact role of TEMPO was unclear, we assumed that, as reported in the literature,[6i,j] the TEMPO might act as a hydrogen acceptor during the catalytic cycle.

3. Conclusion

In summary, we have developed a selective oxidation of primary and secondary alcohols to the corresponding carbonyl compounds with multinuclear copper complexes **1**–**4** as catalysts using TBHP or O_2/TEMPO system, respectively. Among them, the copper complex **3** showed the best performance. The corresponding aldehydes and ketones were obtained with moderate to excellent yields. On the performance of the two classes of oxidants, the secondary alcohols were effectively oxidized to ketones in the case of TBHP, whereas the benzylic primary alcohols could be effectively oxidized to aldehydes in the case of O_2/TEMPO system. Both conditions exhibited the advantages of mild reaction conditions and efficiency, providing a simple method to synthesize aromatic aldehydes or ketones starting from alcohol substrates.

Table 4
Selective oxidation of benzyl alcohol by copper-triethanolamine complexes in the presence of O_2/TEMPO

Entry	Catalyst	Temperature (K)	Conversion[a] (%)	Selectivity[b] (%)	Yield[c] (%)
27	**1**	343	46.7	100	46.7
28	**2**	343	50.2	100	50.2
29	**3**	343	69.3	100	69.3 (65.2)
30	**4**	343	38.2	100	38.2
31[d]	**3**	343	60.1	100	60.1
32[e]	**3**	343	2.1	100	2.1
33[f]	**3**	Not detected	Not detected	—	0.0
34	**3**	303	10.6	100	10.6
35	**3**	323	42.3	100	42.3
36	**3**	353	72.8	100	72.8 (69.7)

Reaction conditions: substrate (6 mmol), NaOH (0.18 mmol), copper complex **3** (0.015 mmol), and TEMPO (0.18 mmol) in CH_3CN (6 mL) and H_2O (3 mL), temperature=343 K, O_2=0.1 MPa, time=20 h.

[a] Average results of two runs based on GC results (DM-Wax 30 m×0.25 mm×1.0 μm).

[b] Selectivity to benzaldehyde.

[c] The data in parenthesis are the isolated yields of the corresponding major products.

[d] 4-Acetamido-TEMPO was used.

[e] No TEMPO was added.

[f] No copper complex **3** was added.

4. Experimental

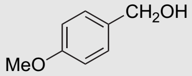
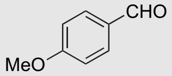
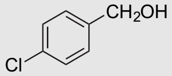
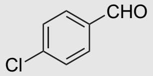
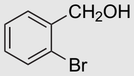
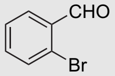
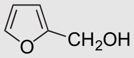
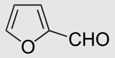
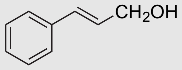
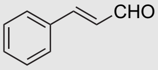
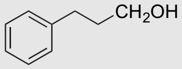
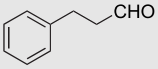
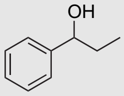
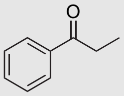
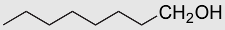
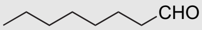
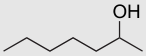
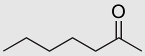
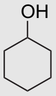
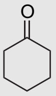
4.1. Preparation of catalysts

The syntheses of copper-triethanolamine complexes **1**–**4** have been reported elsewhere.[7,8] Typically, triethanolamine (2 mmol) was added dropwise to an aqueous solution (20 mL) of $Cu(NO_3)_2 \cdot 3H_2O$ (2 mmol) with HNO_3 (concentration 65–67%, 2 mmol) and then an aqueous solution of NaOH (6 mL, 1 mmol/mL) was added with continuous stirring at room temperature. Benzoic acid (2 mmol, for **1**) or 4-hydroxybenzoic acid (2 mmol, for **2**) or sodium tetrafluoroborate (18 mmol, for **3**) or terephthalic acid (1 mmol, for **4**) was dissolved in an aqueous solution of NaOH (2 mL for **1**, **2**, and **4**; 4 mL for **3**) and then was added to the mixture. This was stirred overnight, filtered, and then left to evaporate in a beaker at ambient temperature. Crystals of **1**–**4** were formed in a few days, and then collected and dried in air. The yields of **1**–**4** were 0.48 g (68%), 0.52 g (92%), 0.49 g (86%), and 0.56 g (90%), respectively. Their structures and compositions were measured by means of FTIR and elemental analyses. The IR spectra were recorded on Nicolet Advatar 360 instrument in KBr pellets. The elemental analyses were performed on a Perkin–Elmer series II CHNS/O analyzer 2400 with a combustion temperature at 1048 K. The Cu content was detected by AAS (atomic adsorption spectroscopy) on a WFX-1E2 instrument. All the structural data obtained were coincided with the results in the literature.[7,8]

4.2. Typical procedures for the oxidation

The primary and secondary alcohols were purchased from Sigma–Aldrich without further pretreatment unless otherwise notified. Typically, alcohol (6 mmol), catalyst (0.015 mmol), and (i) TBHP (12 mmol) were stirred at 343 K in acetonitrile (5 mL) or (ii)

Table 5
Oxidation of various alcohols catalyzed by complex **3** in the presence of O_2/TEMPO

Entry	Substrate	Product	Conversion (%)	Selectivity (%)	Yield[a] (%)
37			76.0	100	76.0 (74.1)
38			76.8	100	76.8 (72.4)
39			60.7	100	60.7 (57.0)
40			61.2	100	61.2 (54.4)
41			71.0	100	71.0 (66.7)
42			6.3	100	6.3
43			3.1	100	3.1
44			3.2	100	3.2
45			2.4	100	2.4
46			<0.1	100	—

The reaction conditions are the same as in Table 4.

[a] The data in parenthesis are the isolated yields of the corresponding major products.

TEMPO (0.18 mmol), NaOH (0.18 mmol), and O_2 (0.1 MPa) were stirred at 343 K in acetonitrile/water (6 mL/3 mL) for appropriate time. The products were characterized by comparison with authentic samples on a capillary gas chromatography (GC) equipped with a column of DM-Wax (30 m×0.25 mm×1.0 μm) and a Flame Ionization Detector (FID). The conversion and product selectivity were calculated using cyclohexanone as the internal standard. Purifications of the crude products by chromatography over silica gel (hexane/AcOEt=12/1 as eluent) gave analytically pure products.

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