



Mild aerobic oxidation of benzyl alcohols to benzaldehydes in water catalyzed by aqua-soluble multicopper(II) triethanolamine compounds[☆]

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ABSTRACT

The aqua-soluble multinuclear copper(II) compounds $[\text{Cu}_2(\mu\text{-H}_2\text{tea})_2\{\mu_3\text{-Na}_2(\text{H}_2\text{O})_4\}(\mu_6\text{-pma})]_n \cdot 10n\text{H}_2\text{O}$ (**1**) and $[\text{O} \subset \text{Cu}_4(\text{tea})_4(\text{BOH})_4][\text{BF}_4]_2$ (**2**) (H_3tea = triethanolamine, H_4pma = pyromellitic acid) have been applied as efficient catalysts for the mild, selective and clean oxidation of benzyl alcohols to benzaldehydes, which proceeds in sole water as solvent at 50 °C, under atmospheric pressure of air (or O_2) as oxidant, and is mediated by TEMPO radical. Molar yields of benzaldehydes (based on alcohol) up to 99% have been achieved (with a high selectivity). Attractive features of these catalytic systems include the use of organic-solvent-free reaction medium, air or dioxygen as oxidant, and aqua-soluble copper catalysts that are readily available by self-assembly.

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1. Introduction

Water is the ideal green solvent for many mild catalytic transformations from both economical and environmental perspectives [1–4]. However, the performance of catalytic reactions in aqueous medium typically requires the use of aqua-soluble catalysts, which often mimic the functions of enzymes. Although a great variety of bioinspired metal complexes has been reported and tested in diverse catalytic processes, most of those catalysts are not soluble in water. During the last years we have been interested in the design and synthesis of new water-soluble multinuclear Cu(II) compounds [5–8], which possess a *N,O*-environment and mimic the particulate methane monooxygenase (pMMO) [9,10], an enzyme that can catalyze the oxidation of different substrates including inert alkanes. Within the series of synthesized multinuclear Cu(II) complexes and coordination polymers with various *N,O*-ligands [11–15], two compounds have sparked our particular attention. These are the 2D coordination polymer $[\text{Cu}_2(\mu\text{-H}_2\text{tea})_2\{\mu_3\text{-Na}_2(\text{H}_2\text{O})_4\}(\mu_6\text{-pma})]_n \cdot 10n\text{H}_2\text{O}$ (**1**) (H_3tea = triethanolamine, H_4pma = pyromellitic acid) and the tetramer $[\text{O} \subset \text{Cu}_4(\text{tea})_4(\text{BOH})_4][\text{BF}_4]_2$ (**2**) (Scheme 1) [5,6], which possess not only high solubility and stability in aqueous solution, but also act as remarkably efficient and recyclable homo-

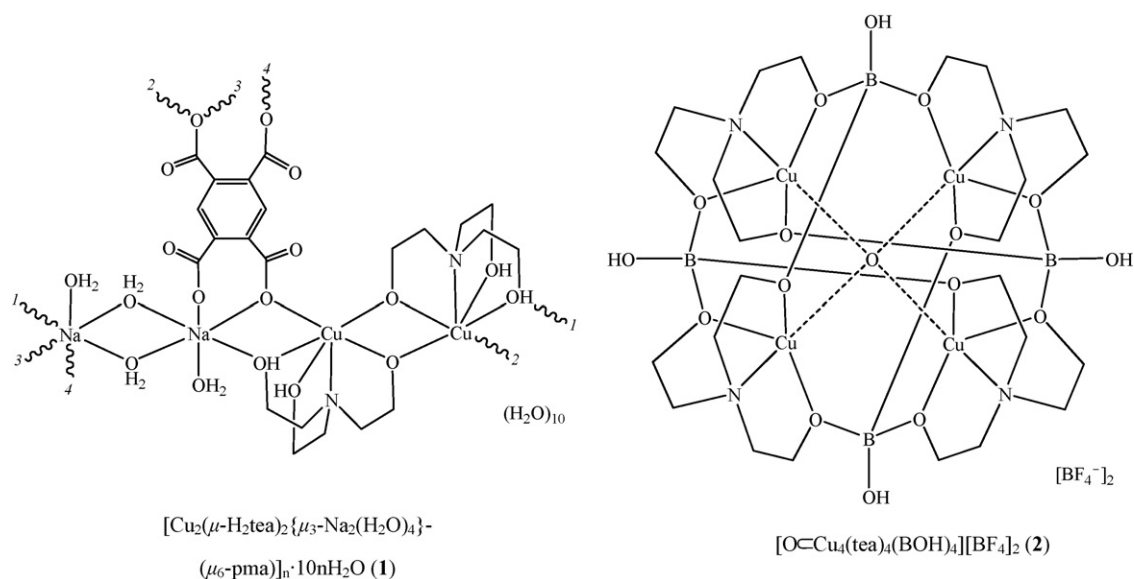
geneous catalysts towards mild peroxidative (by H_2O_2) oxidation of cyclohexane and other alkanes [5,6,12,15].

As a continuation of these studies, the present work aims to broaden the scope of catalytic transformations catalyzed by **1** and **2**, by evaluating their potential for another catalytic reaction, namely the selective aqueous oxidation of benzyl alcohols to benzaldehydes by the TEMPO/ O_2 system (TEMPO = 2,2,6,6-tetramethylpiperidine-1-oxyl). The choice of this model reaction was justified by the possibility of occurrence in aqueous medium (although typically requiring the presence of a second organic solvent [16–19]) and by its importance in organic synthesis and chemical industry. In fact, aromatic aldehydes are not only key intermediates in numerous transformations, but are also frequently used as (or in the production of) plastic additives, perfume and flavoring compounds, and in the textile industry [20]. However, in spite of being rather efficient, many of the conventional and even recently developed processes for the oxidation of aromatic alcohols to their corresponding aldehydes are still characterized by one or several of the following drawbacks: (i) need for stoichiometric (e.g. KMnO_4 , CrO_3) or other relatively expensive (H_2O_2 , OCl^-) oxidants, (ii) application of catalysts containing expensive metals (e.g. Pd, Ru, Au), (iii) use of organic solvents or rather costly ionic liquids, and (iv) generation of considerable amount of toxic waste [16–19,21–32]. Hence, for both environmental and economical demands, the development of alternative oxidation protocols using e.g. Cu compounds, dioxygen (or air) and water as inexpensive metal catalyst, oxidant and sole solvent, respectively, constitutes an important aim, that is possible to fulfill in the presence of the TEMPO radical as a mediator [33].

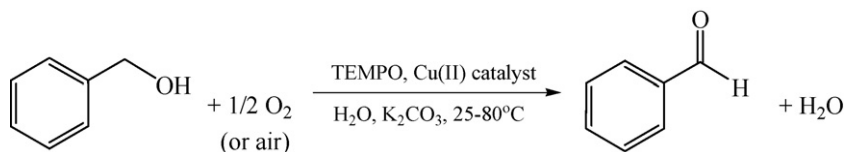
[☆] Dedicated to the memory of Professor Eric G. Derouane as a recognition for his relevant scientific achievements.

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Scheme 1. Schematic representations of compounds **1** and **2**. In **1**, numbers indicate the corresponding extensions of polymeric chains.



Scheme 2. Selective oxidation of benzyl alcohol to benzaldehyde in water.

2. Experimental

2.1. Materials and methods

All chemicals were purchased from commercial sources (Aldrich, Fluka) and used without purification. Water used in the catalytic studies was doubly distilled and deionized. Multicopper(II) compounds **1** and **2** were obtained according to published procedures [5,6]. Chromatographic analyses were undertaken by

using a Fisons Instruments GC 8000 series gas chromatograph with a DB-624 (J&W) capillary column (FID detector) and the Jasco-Borwin v.1.50 software.

2.2. Oxidation of alcohols

Oxidation reactions under atmospheric pressure were typically carried out in 100 mL two-necked round-bottom flasks equipped with a condenser and connected to a balloon filled with O_2 . Before

Table 1
Selective oxidation of benzyl alcohol to benzaldehyde by the Cu catalyst/TEMPO/ O_2 system.^a

Entry	Catalyst	Oxidant	Time (h)	Temperature ($^\circ\text{C}$)	Yield ^b (%)
1	1	O_2	2	25	21
2	1	O_2	2	50	25
3 ^c	1	O_2	2	50	17
4 ^d	1	O_2	2	50	1
5	1	O_2	2	80	12
6	1	O_2 (10 atm)	2	80	39
7	1	O_2	17	50	49
8	2	O_2	2	50	26
9	2	O_2	2	80	28
10	2	O_2	17	50	74
11	$\text{Cu}(\text{NO}_3)_2 \cdot 2.5\text{H}_2\text{O}^e$	O_2	2	50	15
12	1	Air (1 atm)	17	50	47
13	1	Air (1 atm)	48	50	99
14	2	Air (1 atm)	48	50	99
15	1	$\text{H}_2\text{O}_2^{e,f}$	2	50	25

^a Reaction conditions (unless stated otherwise): benzyl alcohol (3.06 mmol), catalyst (1 mol%), 5 mol% TEMPO, 33 mol% K_2CO_3 , water (10 mL), O_2 (1 atm); mol% are vs. substrate.

^b Moles of benzaldehyde/100 mol of benzyl alcohol (GC yield); in all cases, selectivity was >99%; TON values (moles of product/mol of catalyst) are equal to the total % yields.

^c Reaction without K_2CO_3 .

^d Reaction without TEMPO.

^e Tested for comparative purposes.

^f 12.0 mmol of H_2O_2 (30% in H_2O).

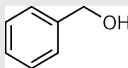
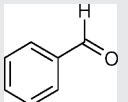
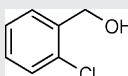
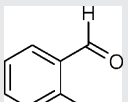
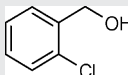
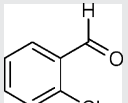
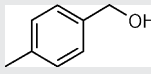
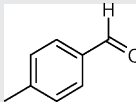
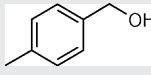
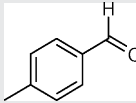
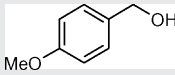
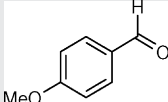
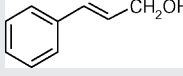
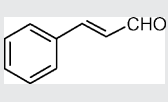
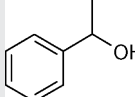
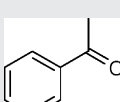
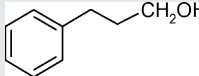
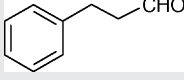
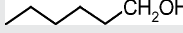

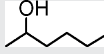
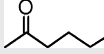
the experiment, the apparatus was vacuumed and flushed with O₂ (three times). The experiments with air as oxidant were performed in a similar way, but allowing the atmospheric air uptake through the upper part of the reflux condenser. Under typical conditions the reaction mixtures were prepared as follows: to 10 mL of water were added 3.06 mmol (320 μL) of benzyl alcohol (or another alcohol), 1 mol% catalyst (compound **1** or **2**), 5 mol% TEMPO, and 1.00 mmol (33 mol%) of K₂CO₃ (as a base). All the above mol% are versus the substrate. For the reactions under elevated pressure, a stainless steel reactor (13.0 mL) was used. In this case, the reactor was loaded with reagents and solvent (5.0 mL of water) and then pressurized with 10 bar of O₂ from a dioxygen cylinder. The reaction solutions in all cases were vigorously stirred using magnetic stirrers. The desired reaction temperature (in the 25–80 °C range) was achieved using an oil bath. The reaction mixtures after the oxidations were neutralized by appropriate amounts (typically ca. 1.0 mL) of 1 M HCl, and then 10.0 mL of ethyl acetate was added for the extraction. The

organic phase was analyzed by gas chromatography in the presence of acetophenone (150 μL) as an internal standard. Blank tests were performed under typical reaction conditions in the absence of the Cu catalyst and shown the formation of only minor amounts (<5%) of benzaldehydes.

3. Results and discussion

The oxidation of benzyl alcohol (Scheme 2) was chosen as a model reaction to test the catalytic potential of the water-soluble compounds **1** and **2** for aerobic oxidations of alcohols in aqueous medium, free from any organic solvent. It has been shown previously [16,17,19,33] that the use of basic media leads to more efficient oxidation reactions of alcohols in various Cu/TEMPO systems. The possible role of base consists in easing the deprotonation of benzyl alcohol [19]. Hence, our experiments were typically performed in basic (K₂CO₃) aqueous solutions under atmospheric pressure of O₂

Table 2
Aerobic oxidation of selected alcohols by the **2**/TEMPO/air system.^a

Entry	Substrate	Main product	Time (h)	Yield ^b (%)	Selectivity (%)
1 ^c			22	77	100
2			22	68	93
3			44	94	94
4			22	70	97
5			44	96	96
6			22	85	96
7			22	34	88
8			22	2	100
9			22	0	0
10			22	0	0
11			22	0	0

^a Reaction conditions: alcohol (3.0 mmol), catalyst **2** (1 mol%), 5 mol% TEMPO, 33 mol% K₂CO₃, water (10 mL), air (1 atm); mol% are vs. substrate.

^b Moles of aldehyde product/100 mol of alcohol substrate (GC yield); TON values (moles of product/mol of catalyst) are equal to the total % yields.

^c Given for comparative purposes.

(or air) and in the presence of TEMPO mediator, using as starting conditions the previously optimized reaction parameters [33]. The obtained results are summarized in Table 1.

Hence, both Cu(II) compounds **1** and **2** catalyze the selective oxidation of benzyl alcohol, leading to yields of benzaldehyde of 49% and 74%, respectively, observed at 50 °C after 17 h reaction time under atmospheric pressure of dioxygen (Table 1, entries 7 and 10). Reasonable conversions are achieved at the shorter reaction time of 2 h with yields of ca. 25% for both catalysts (entries 2 and 8). An increase of reaction temperature up to 80 °C leads to a yield drop for **1** (entries 2 and 5), while for **2** the yield remains almost unchanged (entries 8 and 9). In the reaction of **1** at 80 °C, the increase of dioxygen pressure from 1 to 10 atm results in the improvement of yield from 12% to 39% (entries 5 and 6). Nevertheless, the elevated concentration of dioxygen does not appear to be very important, since even 1 atm of air is enough to achieve a considerable product yield of 47% (vs. 49% with 1 atm of O₂) after 17 h reaction time (entry 12). Furthermore, the quantitative aerobic conversion of benzyl alcohol to benzaldehyde (i.e. 99% yield) can be obtained using any of the catalysts **1** or **2**, with atmospheric pressure of air at a prolonged reaction time (48 h, entries 13 and 14). The suitability of air as oxidant is of particular importance from the economical point of view.

It should be stressed that the presence of TEMPO is essential for the observed catalysis, since only 1% of benzaldehyde is obtained in the absence of this mediator (Table 1, entry 4). Besides, the beneficial use of base is evident from the lower yield of benzaldehyde in the absence of K₂CO₃ (entry 3 vs. 2). For comparative purposes, we have tested copper(II) nitrate as a reference catalyst, which leads to a lower yield of 15% (entry 11), thus underlining the importance of the *N,O*-environments around the copper centres in compounds **1** and **2**. In spite of being more reactive than O₂, hydrogen peroxide oxidizes benzyl alcohol to benzaldehyde with 25% yield (entry 15), similarly to that observed when using an atmospheric pressure of dioxygen (entry 2).

On the basis of these results (Table 1) we selected catalyst **2** for further studies aiming to test the substrate versatility of this system using air as oxidant. Hence, following the behaviour of benzyl alcohol itself, substituted derivatives i.e. 2-chlorobenzyl alcohol, 4-methylbenzyl alcohol and 4-methoxybenzyl alcohol, can be efficiently and selectively converted into the corresponding aldehydes (Table 2). The yields of the latter vary in the 68–78% range upon 22 h reaction time (Table 2, entries 2, 4 and 6) and approach the quantitative value after prolonging to 44 h (94–96%, entries 3 and 5). Cinnamyl alcohol can also be oxidized to cinnamaldehyde with a moderate yield of 34% and selectivity of 88% after 22 h reaction time (entry 7). However, a typical secondary aromatic alcohol, 1-phenylethanol, is only barely reactive under our reaction conditions (Table 2, entry 8), conceivably due to the steric hindrance associated to this substrate and to the copper centres as proposed by Sheldon et al. [18,23], while unactivated aliphatic alcohols are unreactive under the applied conditions (Table 2, entries 9–11).

Although various efficient copper containing TEMPO/O₂ systems for the oxidation of benzyl alcohol to benzaldehyde have already been reported, a main limitation from environmental and/or economical points of view consists in the need for an organic solvent (i.e. DMF [27], CH₂Cl₂ [28], CH₃COOH [29], CH₃CN [19]) or an ionic liquid [30–32]. Some improved systems can use a CH₃CN/H₂O medium [16–19], but the shift towards greener organic-solvent-free oxidations in water is of particular importance [33]. In this context, the application of our aqua-soluble catalysts **1** and **2** is specially significant, allowing the performance of the oxidation reactions in sole water, with high yields that are comparable to those of the above systems [16–19,27–33]. Further advantages of our systems consist in the use of an inorganic base (e.g. K₂CO₃ vs. *t*-BuOK [17–19]) and Cu(II) catalysts readily obtained by self-

assembly from commercially available chemicals. Nevertheless, in our study, the use of water as the only solvent, milder temperature and atmospheric pressure of air (vs. e.g. 4–10 atm of dioxygen [28,33]) are factors that determine a longer reaction time necessary to achieve a quantitative conversion of benzyl alcohols.

We suppose the present catalysts can function similarly to previously proposed [17,18,24,33] mechanisms for other Cu/TEMPO/O₂ systems, of the galactose oxidase type. They involve coordination of TEMPO and benzyl alcohol to Cu centres, metal-centred dehydrogenation and oxidation of the alcohol via hydrogen abstraction or one-electron oxidation processes.

4. Conclusions

In summary, we have extended the application in catalysis of aqua-soluble multicopper(II) triethanolamine compounds (recognized [5,6,12,15] catalysts for the oxidation of alkanes by hydrogen peroxide) to another reaction, i.e. the selective oxidation of benzyl alcohols into the corresponding benzaldehydes. This proceeds with air (or O₂) as oxidant in sole water with a high efficiency (up to 99% yield of benzaldehyde with >99% selectivity) and without the need of any organic solvent, or of an ionic liquid, thus providing both environmental and economical benefits in comparison with previously reported systems for benzyl alcohols oxidation.

Future research will focus on optimizing the reaction conditions, establishing reaction kinetics and the detailed mechanism and testing other aqua-soluble catalysts.

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