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Copper(II) catalyzed selective oxidation of primary alcohols to aldehydes with atmospheric oxygen

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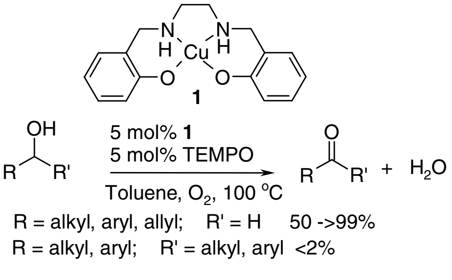
Abstract—Copper(II) complex **1** selectively catalyzes the oxidation of primary alcohols to aldehydes in high yields by atmospheric oxygen in the presence of TEMPO. This procedure does not require an additive and the catalyst **1** is recyclable without loss of activity.

The oxidation of alcohols to carbonyl compounds is one of the most important and fundamental reactions in synthetic chemistry.[1] Numerous oxidizing reagents have been developed for this purpose. Most of these reagents are, however, required in stoichiometric quantities which are sometimes expensive and toxic. From an environmental and economic standpoint, catalytic oxidation processes are thus valuable and those employing molecular oxygen as a primary oxidant are particularly attractive, aerial oxygen is convenient and generates water as the only by-product.[2] Accordingly, several studies have been recently reported for the oxidation of alcohols with molecular oxygen using transition metal salts as catalysts (V,[3] Co,[4] Cu,[5] Mo,[6] Ru,[7] Rh,[8] Pd[9] and polyoxometalates[10]).

Most of these systems catalyze the oxidation of primary as well as secondary alcohols to give the corresponding aldehydes and ketones. Alternatively, the selective oxidation of primary alcohols to aldehydes is crucial for the synthesis of fine chemicals such as fragrances or food additives.[11] Presently, only a few studies with molecular oxygen are known for such transformations[5a–e,7a–c] and await the further discovery of suitable catalytic systems, especially without sacrificial reducing agents. Recently, we have found that copper(II) complex **1** catalyzes the oxidation of organic compounds with 30% H_2O_2 in high yields.[12] Since the catalyst **1** is readily accessible, is recyclable and less expensive and is soluble in common organic solvents, we have further studied its application in other oxidation reactions. Herein, we report the selective oxidation of primary alcohols to aldehydes using copper(II) complex **1** in the presence of TEMPO with atmospheric oxygen (Scheme 1). Aliphatic as well as aromatic alcohols can be oxidized to the corresponding aldehydes in high yields.

The oxidation of benzyl alcohol, as a standard substrate, was first investigated. We were pleased to find that the oxidation occurred to provide benzaldehyde in quantitative yield when the reaction was allowed to stir in the presence of a catalytic amount of **1** and TEMPO in toluene at 100 °C (Table 1, entry 1).[13] No over-oxidation to benzoic acid was observed. A control experiment without either copper(II) complex **1** or TEMPO showed no reaction. To evaluate the scope of this procedure, the oxidation of other alcohols was next studied (entries 2–14). Aromatic alcohols possessing both electron-withdrawing and -donating groups on the benzene ring, that



Scheme 1.

Keywords: Oxidation; Alcohol; Selective; Catalyst; Copper(II) complex.

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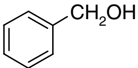
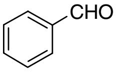
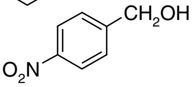
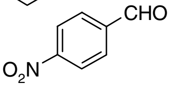
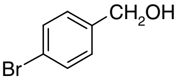
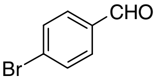
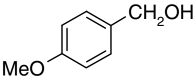
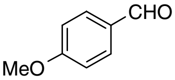
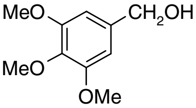
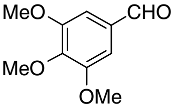
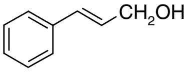
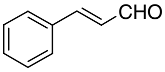
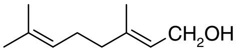
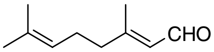
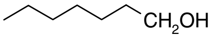
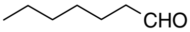
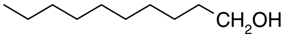
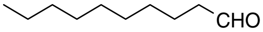
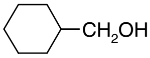
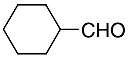
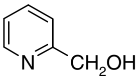
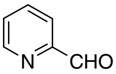
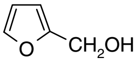
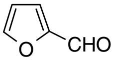
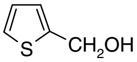
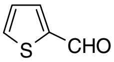
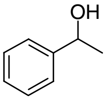
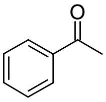
Table 1. Copper(II) complex **1** and TEMPO catalyzed oxidation of alcohols with molecular oxygen[a]

Entry	Substrate	Product	Time (h)	Yield (%)[b]
1			10	99[c]
2			14	98
3			19	70
4			9	98
5			13	97
6			11	98
7			23	79
8			21	90[d]
9			25	84[d]
10			22	75[d]
11			26	92[d]
12			19	98
13			21	94
14			12	2

[a] Alcohol (5 mmol), copper(II) complex **1** (5 mol %) and TEMPO (5 mol %) were stirred in toluene (10 mL) at 100 °C under atmospheric oxygen.

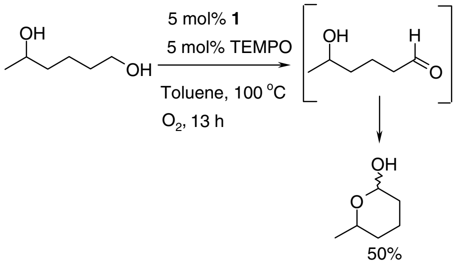
[b] Isolated yield.

[c] GC yield.

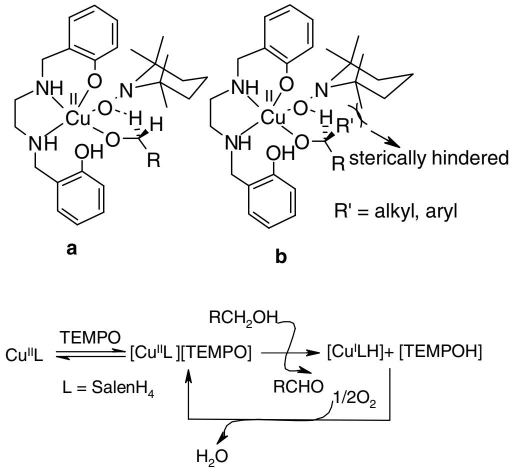
[d] 7 mol % of **1** and TEMPO used.

is, 4-nitro-, 4-bromo-, 4-methoxy- and 3,4,5-trimethoxybenzyl alcohols, were oxidized to give the corresponding aldehydes in high yields. Similarly, the allylic alcohols, cinnamyl alcohol and geraniol, underwent oxidation without affecting the carbon–carbon double bonds. Oxidation of the aliphatic alcohols, heptanol, decanol and cyclohexyl methanol, required slightly longer reaction times compared to aromatic and allylic alcohols. The heterocyclic alcohols, pyridine-2-methanol, 2-furfurol and thiophene-2-methanol, could be transformed to the respective aldehydes without affecting the N and S atoms. The secondary alcohol, 1-phenylethanol, was less reactive, affording the corresponding ketone in 2% yield.

To study the selectivity, the oxidation of a 1:1 mixture of benzyl alcohol and 1-phenylethanol was investigated. As above, the reaction occurred affording benzaldehyde and acetophenone in 98% and 1% yields. A similar result was obtained with a 1:1 mixture of heptanol and cyclohexanol providing heptanal and cyclohexanone in 70% and 1% yields, respectively. Under these conditions, 1,5-hexanediol was oxidized to provide 6-methyl-δ-lactol as a mixture of diastereomers in 50% yield (Scheme 2). These studies clearly reveal that primary alcohols could be oxidized selectively by this method in the presence of secondary hydroxyl groups. This may be due to less steric hindrance between the methyl groups of TEMPO and the β-hydrogen of primary alcohols thereby enhancing the formation of the active species **a** compared to **b** that would arise from a secondary alcohol.[14a,b] Intramolecular transfer of the β-hydrogen followed by oxidative elimination of **a** would lead to a copper(I) complex, TEMPOH and the carbonyl com-



Scheme 2.

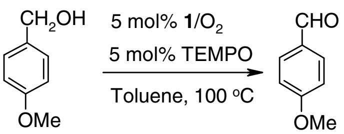


Scheme 3.

pound (Scheme 3).[14c] Oxidation of TEMPOH to TEMPO by the copper(I) complex with molecular oxygen completes the catalytic cycle.[5a–d,14c]

For the recyclability of **1**, after completion of the oxidation of 4-methoxybenzyl alcohol, the reaction mixture was treated with water (3 mL), and the organic layer, after drying (Na_2SO_4) and GC analysis, was passed through a short pad of silica gel using ethyl acetate and hexane as eluent to afford analytically pure 4-methoxybenzaldehyde in quantitative yield. Evaporation of the aqueous layer afforded a copper complex that was reused for the oxidation of 4-methoxybenzyl alcohol up to three runs in the presence of fresh TEMPO and no loss of activity was observed (Table 2).

Table 2. Recycling of catalyst **1**



Run	Recovery (%)[a]	Product (%)
1	>99	97
2	>98	96
3	>96	95

[a] Alcohol (1 mmol), TEMPO (5 mol %) and recovered copper complex were stirred in toluene (3 mL) at 100 °C for 9 h under atmospheric oxygen.

In conclusion, a novel procedure has been described for the oxidation of primary alcohols to aldehydes. This method can be used for the selective oxidation of primary alcohols in the presence of secondary alcoholic groups and the catalyst **1** is recyclable without loss of activity over three cycles.

Acknowledgements

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13. Alcohol (5 mmol) and catalyst **1** (5 mol %, 84 mg) and TEMPO (5 mol %, 39 mg) were stirred at ca. 100 °C in toluene (10 ml) under atmospheric oxygen for the appropriate time (Table 1). After completion, the reaction mixture was treated with water (3 mL) and the organic layer, after drying (Na_2SO_4) and GC analysis, was passed through a short pad of silica gel using ethyl acetate (or diethyl ether) and hexane as eluent to provide the analytically pure aldehyde or ketone which was characterized by NMR (^1H and ^{13}C), IR and mass analysis.
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