Copper(II)-Catalyzed Oxidation of Alcohols to Carbonyl Compounds with Hydrogen Peroxide

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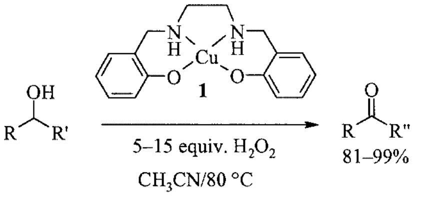
Copper(II) complex **1** efficiently catalyses the oxidation of alcohols to the corresponding carboxylic acid analogues and ketones in the presence of H_2O_2 in high yields.

Introduction

The selective oxidation of alcohols to the corresponding carbonyl compounds is a frequently used functional transformation in organic synthesis and numerous methods have been developed.[1] However, most of these traditional oxidations usually require stoichiometric amounts of the reagents and the purification of the reaction products is often demanding. To circumvent these problems, a number of catalytic oxidation processes based upon the combination of metal salts and atom-efficient oxidants, such as molecular oxygen[2–4] or H_2O_2,[5] have been recently devised. Copper(I) salts have been shown to catalyze the oxidation of alcohols to aldehydes and ketones with molecular oxygen.[3] Attention has also been focused on the development of functional models of galactose oxidase (GO) and their application for the aerobic oxidation of alcohols to aldehydes.[4] We now report the first example of copper-catalyzed oxidation of alcohols to the corresponding carboxylic acid analogues and ketones with H_2O_2 as the source of oxygen (Scheme 1). This protocol is simple, clean and functions in the absence of additives.

Results and Discussion

Reaction of ethylenediamine with 2 equiv. of salicylaldehyde followed by $NaBH_4$ reduction provided salen-H_4 that was further treated with $Cu(OAc)_2$ to afford the complex **1** as a green powder. In the presence of a catalytic amount of **1**, the oxidation of 4-chlorobenzyl alcohol (**2b**) was first examined with H_2O_2 under ambient conditions in acetonitrile. We were pleased to find that **2b** was oxidized to a 2:1 mixture of 4-chlorobenzaldehyde and 4-chlorobenzoic acid (**3b)** in 30% yield in the presence of 1 mol % of **1** and 10 equiv. of H_2O_2. Alternatively, the reaction could be driven to completion with 92% yield of **3b** by heating at 80 °C for 4.5 h (Table 1, Entry 2). Control experiments without complex **1** under the same reaction conditions showed no oxidation. Similarly, no significant oxidation was observed with molecular oxygen as a terminal oxidant. $Cu(OAc)_2$ and Cu^{II}(salen) were also examined as catalysts for the oxidation of **2b** under the same reaction conditions. The reaction of the latter afforded 65% of **3b**, while the process of the former was less effective and provided a 1:5 mixture of **3b** and 4-chlorobenzaldehyde in 30% yield.



Scheme 1

To evaluate the scope of this protocol, the oxidation of other aromatic and aliphatic alcohols **2a** and **2c−n** was further examined with complex **1** (Table 1). As above, primary alcohols **2a** and **2c−h** were consistently oxidized to give the corresponding carboxylic acids **3a** and **3c−j** in the presence of 10−15 equiv. of H_2O_2. Secondary alcohols **2k−n** were oxidized faster and could be converted into the corresponding ketones with 5 equiv. of H_2O_2. Substrates **2b−h** having both electron-donating as well as electron-withdrawing substituents were compatible with this system. The oxidations of cinnamyl alcohol and benzoin were also examined, however, those reactions mainly afforded benzoic acid due to cleavage of the carbon−carbon bonds.

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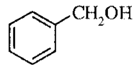
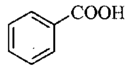
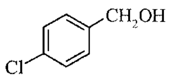
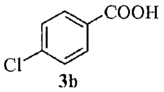
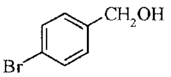
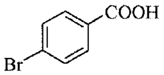
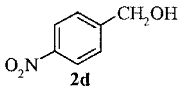
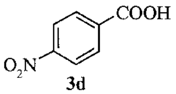
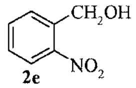
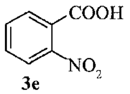
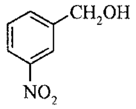
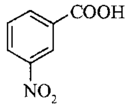
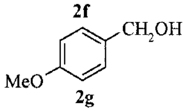
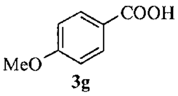
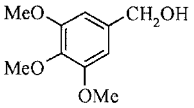
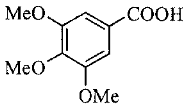
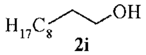
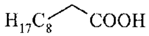
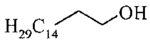
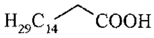
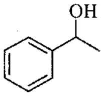
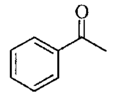
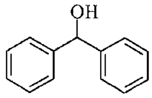
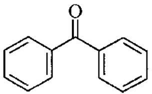
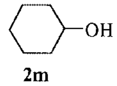
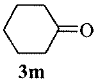
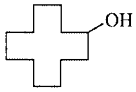
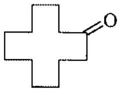
Table 1. Oxidation of alcohols with complex **1** in the presence of H_2O_2

Entry	Substrate	H_2O_2 [equiv.]	Time [h]	Product	Yield (%)[a,b]
1	 **2a**	10	5	 **3a**	92
2	 **2b**	10	4.5	 **3b**	95
3	 **2c**	10	4	 **3c**	94
4	 **2d**	10	8	 **3d**	82
5	 **2e**	10	8	 **3e**	83
6	 **2f**	10	7	 **3f**	89
7	 **2g**	10	3	 **3g**	93
8	 **2h**	10	2	 **3h**	93
9	 **2i**	15	8	 **3i**	93
10	 **2j**	15	9	 **3j**	90
11	 **2k**	5	0.5	 **3k**	99[c]
12	 **2l**	5	0.5	 **3l**	98
13	 **2m**	5	4	 **3m**	99[c]
14	 **2n**	5	4	 **3n**	81

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[a] Catalyst **1** (1 mol %), alcohol (2 mmol), 30% H_2O_2 (10−30 mmol) and acetonitrile (2 mL) were stirred at ca. 80 °C. [b] Isolated yield. [c] GC yield.

Conclusion

An efficient catalytic oxidation procedure that allows the transformation of simple alcohols into carboxylic acids and ketones has been described.

Experimental Section

Preparation of Complex 1: The reaction of salicylaldehyde (122 mg, 1 mmol) with ethylenediamine (30 mg, 0.5 mmol) in methanol (5 mL) afforded salen-H_2 as a lemon-yellow powder in 81% (217 mg), which was further treated with $NaBH_4$ (1 mmol, 37.83 mg) in methanol (5 mL) at ambient temperature for 2 h. Removal of the solvent in a rotary evaporator followed by treatment with water afforded salen-H_4 as a colorless powder in 72% (162 mg) yield. ^1H NMR ($CDCl_3$, 90 MHz): $\delta = 6.7-7.2$ (m, 8 H), 3.9 (s, 4 H), 2.85 (s, 4 H) ppm. IR (KBr): $\tilde{\nu} = 3288$, 2909, 2868, 2827, 1608, 1565, 1398, 1260, 999 cm^{-1}. $C_{16}H_{20}N_2O_2$ (272.3): calcd. C 70.56, H 7.40, N 10.29; found C 70.59, H 7.38, N 10.25. The salen-H_4 (150 mg, 0.55 mmol) was then treated with $Cu(OAc)_2$ (200 mg, 1 mmol) in methanol (10 mL) at 50 °C for 2.5 h under nitrogen. Evaporation of the solvent in a rotary evaporator gave a powder which was purified on silica gel (60−120 mesh) column chromatography using EtOAc and MeOH (15:5) as a eluent to afford complex **1** as a green powder in 70% yield. UV/Vis (CH_3CN): $\lambda_{max} = 328$, 584 nm. FAB-MS: $m/z = 334$ [M^+]. $C_{16}H_{18}CuN_2O_2$ (333.9): calcd. C 57.55, H 5.43, Cu 19.03, N 8.39; found C 57.51, H 5.42, Cu 19.00, N 8.40.

Typical Procedure for the Oxidaiton: Alcohol (2 mmol), complex **1** (1 mol %) and 30% H_2O_2 (10 mmol, 2.26 mL) were dissolved in acetonitrile (2 mL) and the homogeneous solution was heated at ca. 80 °C under atmospheric oxygen for the appropriate time. After completion of the reaction, the reaction mixture was treated with dimethyl sulfide (ca. 50 µL) at room temperature and the aqueous acetonitrile was removed in a rotary evaporator under reduced pressure. The residue was treated with ethyl acetate and the insoluble copper salt was separated. The organic solution was concentrated and passed through a short pad of silica gel (60−120 mesh) using ethyl acetate and hexane to afford the analytically pure compound whose identity was ascertained by IR, NMR (^1H and ^{13}C) and melting point (solid) and by comparison with authentic sample.

Acknowledgments

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