

Copper Catalyzed Selective Oxidation of Benzyl Alcohol to Benzaldehyde

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INTRODUCTION

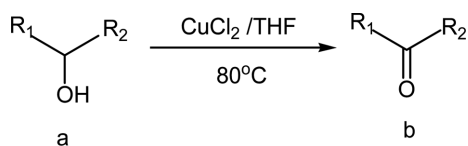
The oxidation of alcohols to the corresponding carbonyl compounds is one of the most fundamental and important transformations in synthetic organic chemistry. To date, many excellent catalytic methods have been developed for alcohol oxidations.¹⁻⁸ However, there is a strong need for more efficient, chemoselective, and greener methods that do not require heavy metallic species for such transformations, particularly in the pharmaceutical industry.^{9,10} The oxidation of alcohols is traditionally carried out with stoichiometric amounts of oxidants such as chromium reagents,¹¹⁻¹⁵ permanganates,^{16,17} ruthenium (VIII) oxide,^{18,19} TPAP/NMO (tetra-N-propylammonium perruthenate/N-methyl-morpholine-N-oxide),^{20,21} activated dimethyl sulfoxide (DMSO) reagents,²² or Dess-Martin periodinane reagent.²³ Unfortunately, these methods often require one or more equivalents of these relatively expensive oxidizing agents. Some of these processes also generate equal amounts of metal waste. Furthermore, oxidation reactions are usually carried out in halogenated organic solvents, typically chlorinated hydrocarbons, which are environmentally undesirable. Therefore, developing green, selective and efficient catalysts for the oxidation of alcohols is of paramount importance for both economic and environmental reasons.

During our investigation on selective oxidation reactions we recently developed economical method for the oxidation of acetophenone to benzoic acid by using copper chloride in DMSO.²⁴ Previously this reagent system was used for oxidative cyclization of 2'-hydroxychalcones to 3-chloroflavones and o-hydroxycarbonyl derivative to chlorochromones²⁵⁻²⁷ and oxidative chlorination of flavones to 3-chloroflavones.²⁸⁻³⁰ The catalytic system composed of CuCl₂ and 2, 2'-biquiniline 4-4' dicarboxylic acid dipotassium salt (BQC) was found to use for selective oxida-

tion of alcohols under phase transfer conditions.³¹

RESULT AND DISCUSSION

Here we report that environment friendly oxidation of benzyl alcohol by using CuCl₂ in THF at 80 °C it was observed that both primary and secondary alcohols oxidized by CuCl₂ in THF on heating at 80 °C. Several salient features of the oxidation are recently observed. The use of 2 moles of CuCl₂·2H₂O was required in THF solvent for oxidation. The conditions are usually appreciable and tolerant many functional groups. Oxidation of both primary and secondary alcohols occurs in good to excellent yields. The reaction of primary benzylic alcohols was very clean using 2 moles of copper chloride in THF for 2 hrs at 80 °C. The only product identified was benzaldehydes. An interesting electronic effect seems to exist for benzylic systems (entry 1-11). We observed that the reaction times for electron releasing arenes were significantly shorter. The reaction time for o-hydroxybenzaldehydes required longer reaction time which might be attributed to co-ordination of the phenolic OH group with copper chlorides. The substrates with electron withdrawing group also required longer reaction times and gave lower yields. Increasing the temperature and adding the base to these reactions did not improve the yields. Secondary benzylic alcohols (entry 18-21) gave very clean and high yield of ketones for example the oxidation benzoin required only half an hour to reach completion with 100% yield. The electronic effect for the oxidation of secondary benzylic alcohols is similar to that of primary alcohols. Very few aliphatic alcohols has been studied for the oxidation reaction as they required a longer time and gave a lower yield when compared to primary and secondary alcohols containing one of the aromatic substituents. Allylic alcohols like cinnamyl alcohols smoothly undergo oxidation reaction to gave cinnamyl

**Scheme 1.****Table 1.** Conversion of alcohol to carbonyl compound using CuCl_2/THF

Entry	Substrate A	Product B	Time(hr)	Yield in %
1.			2	85
2.			1.5	72
3.			1.5	90
4.			1.5	82
5.			3	68
6.			3	61
7.			1.5	67
8.			1.5	68
9.			3	70
10.			2	62
11.			1.5	85
12.			1.5	82
13.			1.5	84
14.			2	76
15.			2	77

Table 1. Conversion of alcohol to carbonyl compound using CuCl_2/THF —Continued

Entry	Substrate A	Product B	Time(hr)	Yield in %
16.			2	79
17.			1.5	78
18.			1	78
19.			0.5	100
20.			1	82
21.			1.5	75

aldehyde without any change like isomerisation or addition to alkenes bond. Similarly 2'-allyloxybenzyl alcohols undergo oxidation reaction to gave high yields of 2'-allyloxybenzaldehyde without any change in allyl group like deallylation, isomerisation and addition to alkene bond. Under present condition of oxidation reaction no over oxidation was observed to benzoic acids. The reaction is general for benzyl alcohol and the reaction conditions are compatible with functional group like phenolic -OH, -NO₂, -Cl, -C=C-, -OCH₃ and -CH₃.

CONCLUSION

Our method is fast, mild, simple to perform and can be applied to system with a variety of functional groups. Selective oxidation of benzyl alcohols was observed in presence of allyl, -CH₃ and phenolic-OH group. It can tolerate moisture and oxygen from the reaction system. Thus the present work provides an efficient and inexpensive oxidation of alcohols. The ease of handling, short reaction time, and availability of the reagent added the advantages to this procedure.

Experimental Section

All oxidation products were known compounds and were identified by comparison of their physical and spectral data with those of authentic samples.³² Alcohols, DMSO and CuCl_2 were purchased from Fluka and Merck. The purity of the products and reaction monitoring were

accomplished by TLC on silica gel PolyGram SILG/UV 254 plates.

General Procedure for the Preparation of B (1-21)

To the stirred solution of THF (3 ml) Compound A (1 mmol) and copper chloride (2 mmol) was added reaction mixture was heated at 80 °C, completion of reaction was followed by monitoring TLC. After completion of reaction mixture was diluted with water, acidified with HCl and then extracted with ether.

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