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$CuBr_2$-$LiOBu^t$ as a New Reagent for Oxidation of Alcohols

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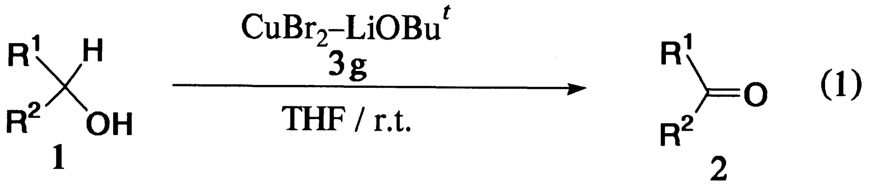
The reagent of the title was found to promote the oxidation of alcohols to give the corresponding carbonyl compounds in good yields. The copper(II) oxidizing agent was easily prepared by the reaction of copper(II) bromide with lithium *t*-butoxide in THF.

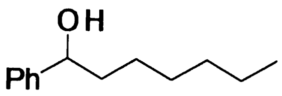
A variety of metal salts, such as derivatives of Cr(VI) and Mn(VII), have been well studied as oxidizing agents for the transformation of alcohols to carbonyl compounds. These metal salts have advantages of inexpensiveness and easiness of handling. However, they are highly toxic in general, and the overoxidation sometimes becomes a serious side reaction in the oxidation using these metal salts. Consequently, the less toxic and mild oxidizing agent for such a transformation is still required.

Recently, we showed that alkoxystannanes are easily oxidized to the corresponding carbonyl compounds by the treatment with copper(II) bromide in the presence of lithium bromide and *t*-butoxytributylstannane.[1) Although copper(II) acetate and copper(II) sulfate pentahydrate are employed for the oxidation of α-hydroxy ketones (acyloins) into α-diketones,[2) the oxidation of simple alcohol using copper(II) salt has not yet been reported.[3) On the basis of the above results, we expected that copper(II) salts would be powerful enough to oxidize alcohols to ketones or aldehydes. In this communication, we summarize the preliminary results of the oxidation of alcohols using the copper(II) reagent prepared from copper(II) bromide and lithium *t*-butoxide (**3g**) as a mild and less toxic oxidizing agent (Eq. 1).



First we examined the oxidation of 1-phenyl-1-heptanol (**1a**) with several copper(II) reagents (**3**) including the copper(II) species prepared by the reaction of copper(II) salts with lithium *t*-butoxide. The results listed in Table 1 show that the efficiency of copper(II) reagent as an oxidizing agent apparently depends on its legands. The corresponding ketone was obtained only when the copper(II) reagents prepared from copper(II) halides and an equimolar amount of lithium *t*-butoxide (**3e** and **3g**) were employed (runs 5 and 7). On the contrary, no reaction was observed using simple copper(II) salts (**3a**, **b**, and **c**) or the reagent prepared from copper(II) triflate (**3d**) (runs 1, 2, 3, and 4). It was also found that the copper(II) species formed by the reaction of copper(II) bromide with two equivalents of lithium *t*-butoxide (**3f**) or the copper(I) reagent (**3h**) were ineffective for the present oxidation (runs 6 and 8).

Table 1. The oxidation of 1-phenyl-1-heptanol (**1a**) with the copper(II) reagents (**3**)a)

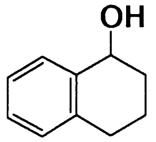
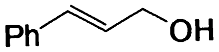
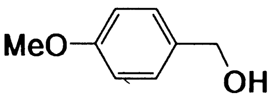
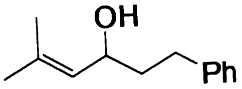
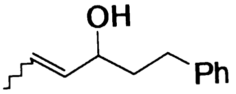
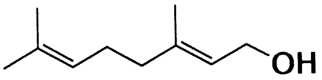
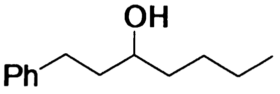
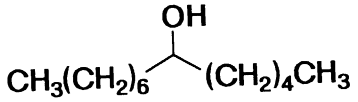
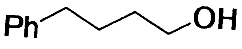
Run	1	Copper(II) reagent (3) (equiv.)	Time h	Yield %
1		$Cu(OAc)_2$ (2.2) (**3a**)	2	–
2		$CuSO_4$ (2.2) (**3b**)	2	-
3		$CuBr_2$ (2.2) (**3c**)	3	-
4		$Cu(OTf)_2$ (2.2)-$LiOBu^t$ (2.1) (**3d**)	overnight	-
5	 **1a**	$CuCl_2$ (2.2)-$LiOBu^t$ (2.1) (**3e**)	2.5	54b)
6		$CuBr_2$ (2.1)-$LiOBu^t$ (4.2) (**3f**)	53	-c)
7		$CuBr_2$ (2.1)-$LiOBu^t$ (2.1) (**3g**)	0.25	93
8		CuBr (2.2)-$LiOBu^t$ (2.2) (**3h**)	2	-

a) All reactions were performed with a similar procedure as described in the text, unless otherwise noted. b) The corresponding α-chloroketone was isolated in 15% yield, and 29% of **1a** was recovered. c) The corresponding α-bromoketone was isolated in 9% yield, and 52% of **1a** was recovered.

Since the copper(II) reagent (**3g**) gave the best result, the oxidation of various alcohols was performed using **3g** under the similar reaction conditions (Table 2). It was found that the oxidation of secondary, primary benzylic, and primary allylic alcohols were oxidized to give the corresponding carbonyl compounds in good to high yields. On the other hand, the reaction of primary aliphatic alcohol (**1j**) with **3g** was complicated and the formation of aldehyde was not observed (see run 9).

A typical experimental procedure is as follows: To a THF (3 ml) suspension of copper(II) bromide (246 mg, 1.1 mmol) was added a THF solution of lithium *t*-butoxide (1.9 ml, 1.1 mmol), which was prepared from butyllithium and *t*-butyl alcohol, at r.t. under argon. The insoluble copper salt gradually disappeared and the solution turned dark brown. After being stirred for 15 min, the THF solution of oxidizing agent was added to a THF (2 ml) solution of 4-methoxybenzyl alcohol (**1d**) (69 mg, 0.5 mmol) at r.t., and the mixture was stirred for 5 h. Then the reaction was quenched by addition of saturated NH_4Cl solution, and the organic materials were extracted with CH_2Cl_2. The extract was dried (Na_2SO_4) and condensed under reduced pressure. The residue was chromatographed on silica-gel (hexane : AcOEt = 4 : 1) to afford 4-methoxybenzaldehyde (**2d**) (66mg, 97%).

Table 2. The oxidation of alcohols (**1**) with CuBr$_2$-LiOBu^t (**3g**)$^{a)}$

Run	1		CuBr$_2$-LiOBu^t (**3g**) equiv.	Time h	Yield$^{b)}$ %
1		**1b**	3.0	0.17	94
2		**1c**	3.0	5	96
3		**1d**	2.2	5	97
4		**1e**	3.0	0.67	73
5		**1f**	3.0	0.5	80
6		**1g**	3.0	3	65
7		**1h**	3.0	4	87
8	 $CH_3(CH_2)_6CH(OH)(CH_2)_4CH_3$	**1i**	3.0	4	89
9$^{c)}$		**1j**	2.2	5	-$^{d)}$

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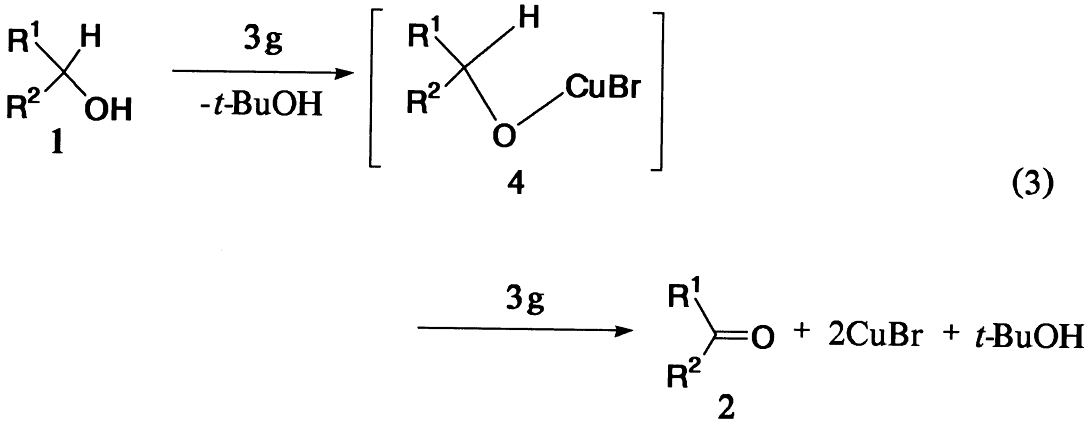
a) All the reactions were performed with a similar procedure as described in the text, unless otherwise noted.
b) The structures of these compounds were supported by IR and NMR spectra. c) The reaction was carried out at 40 °C. d) The starting material (**1j**) (28%) was recovered .

It was reported by Brubaker and Wicholas that copper(II) alkoxide is produced by the reaction of copper(II) halide with lithium alkoxide in alcohol.[4)] Therefore, it is reasonable to assume that bromo(*t*-butoxy)-copper(II) was produced by the reaction of copper(II) bromide with an equimolar amount of lithium *t*-butoxide (Eq. 2). Since Saegusa et al. reported that the methanolysis of copper(II) di-*t*-butoxide gave *t*-butyl alcohol quantitatively with concomitant formation of copper(II) dimethoxide,[5)] the first step of the present oxidation would be the formation of alkoxycopper(II) species (**4**), which in turn reacts with another equivalent of copper(II) reagent (**3g**) to give carbonyl compounds (**2**) along with copper(I) bromide as outlined in Eq. 3.

$$\mathrm{CuBr_2} \;+\; t\text{-}\mathrm{BuOLi} \xrightarrow[\mathrm{THF}]{} \underset{\mathbf{3g}}{\mathrm{BrCuOBu}^t} \;+\; \mathrm{LiBr} \qquad (2)$$



(3)

It should be noted that the present reaction provides a facile method for the oxidation of alcohols using the reagent with low toxicity. Further study including the application of copper(II) reagent (**3g**) to the oxidation of various organic compounds is now in progress.

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References

1) J. Yamaguchi and T. Takeda, *Chem. Lett.,* **1992**, 423.

2) For example: A. T. Blomquist and A. Goldstein, *Org. Synth.,* **Coll. Vol. 4**, 838 (1963); T. S. Gardner, E. Weins, and J. Lee, *J. Org. Chem.,* **23**, 823 (1958).

3) It was confirmed that **1a** was not oxidized under the same reaction conditions as those of the oxidation of acyloins with copper(II) sulfate[a)] or acetate[b)]; a) I. A. Pearl, *J. Am. Chem. Soc.*, **74**, 4260 (1952). b) A. T. Blomquist, L. H. Liu, and J. C. Bohrer, *ibid.*, **74**, 3643 (1952).

4) C. H. Brubaker, Jr. and M. Wicholas, *J. Inorg. Nucl. Chem.*, **27**, 59 (1965).

5) T. Tsuda, T. Hashimoto, and T. Saegusa, *J. Am. Chem. Soc.*, **94**, 658 (1972).

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