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Tetrahedron Letters 49 (2008) 1083–1086

Tetrahedron Letters

CuCl catalyzed oxidation of aldehydes to carboxylic acids with aqueous *tert*-butyl hydroperoxide under mild conditions

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Received 15 October 2007; revised 21 November 2007; accepted 29 November 2007
Available online 4 December 2007

Abstract

Oxidation of aldehydes to the corresponding carboxylic acids can be performed highly efficiently at room temperature with 70% *tert*-butyl hydroperoxide (in water) in the presence of a catalytic amount of easily available ligand free CuCl in acetonitrile as solvent under very mild conditions. This oxidation protocol works well for various aldehydes including aliphatic aldehydes and aliphatic dialdehydes.

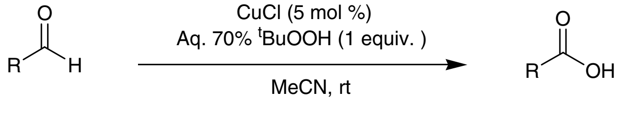
Keywords: Copper catalyst; Oxidation; Aromatic aldehydes; Carboxylic acids; Selective oxidation

Oxidation is one of the most fundamental reactions in synthetic organic chemistry and a variety of oxidants have been developed. The oxidation of aldehydes to carboxylic acids is an important synthetic transformation. A variety of conventional oxidants notably Mn and Cr based[1–3] reagents, which produce copious amounts of undesirable wastes are reported in the literature to accomplish this transformation. In recent years, various improved methods using 2-hydroperoxyhexafluoro-2-propanol (HPHI),[4] calcium hypochlorite,[5] Oxone[6] or hydrogen peroxide as oxidants under severe basic conditions,[7] or in combination with other reagents such as formic acid,[8] sodium chlorite,[9] benzeneselinic acid,[10] magnesium monoperoxyphthalate (MMPP)[11] and other transition metals have been reported in the literature.[12–17] However, all these methods have some limitations such as the requirement of strong acidic conditions, and stoichiometric or super stoichiometric amounts of costly or hazardous oxidizing agents or elevated temperatures. Therefore, mild, catalytic, economic and efficient alternative methods are required.

Very recently, we developed an efficient method for the selective oxidation of benzylic and allylic alcohols to the corresponding aldehydes and ketones using a DABCO–Cu complex as catalyst.[18] Similarly, we also showed that CuCl can be used as an efficient catalyst without using any ligand for the direct and selective oxidation of benzylic and allylic primary alcohols to the corresponding acids using anhydrous ^{t}BuOOH (5 M in decane) in acetonitrile at room temperature.[19]

As a part of our ongoing research towards copper catalyzed oxidation chemistry, herein, for the first time, we report the CuCl catalyzed oxidation of aldehydes to the corresponding carboxylic acids using aqueous *tert*-butyl hydroperoxide in acetonitrile at room temperature (Scheme 1). This procedure is very simple, mild, clean and works efficiently without any additives.

In preliminary studies, we used DABCO–CuCl complex/O_2/TEMPO for the oxidation of *p*-methoxybenzaldehyde in nitromethane. However, the reaction did not provide even a trace amount of the corresponding carboxylic acid (Table 1, entry 1). When we replaced the



Scheme 1. CuCl catalyzed oxidation of aldehydes to acids.

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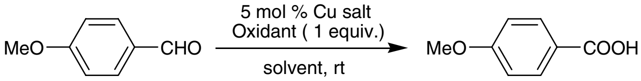
doi:10.1016/j.tetlet.2007.11.198

Table 1
Optimizing the conditions for oxidation of *p*-methoxybenzaldehyde to *p*-methoxybenzoic acid



Entry	Catalyst	Additive	Oxidant	Solvent	Time (h)	Isolated yield (%)	
						Recovered aldehyde	Acid
1	DABCO–CuCl	TEMPO	O_2	CH_3NO_2	20	Quantitative	0
2	DABCO–CuCl	—	30% H_2O_2 (in water)	CH_3NO_2	24	53	38
3	DABCO–CuCl	—	5 M ^{t}BuOOH (in decane)	CH_3NO_2	6	—	91
4	CuCl	—	5 M ^{t}BuOOH (in decane)	CH_3NO_2	6	—	91
5	CuCl	—	70% ^{t}BuOOH (in water)	CH_3NO_2	7	Trace	90
6	**CuCl**	—	**70% ^{t}BuOOH (in water)**	**CH_3CN**	**2**	—	**93**
7	—	—	**70% ^{t}BuOOH (in water)**	**CH_3CN**	**5**	—	**Trace**
8	CuCl	—	70% ^{t}BuOOH (in water)	THF	20	49	34
9	CuCl	—	70% ^{t}BuOOH (in water)	DCM	16	27	55
10	CuCl	—	70% ^{t}BuOOH (in water)	EtOAc	5	—	85
11	CuCl	—	70% ^{t}BuOOH (in water)	DMSO	24	34	63
12	CuCl	—	70% ^{t}BuOOH (in water)	DMF	24	37	53
13	CuCl	—	70% ^{t}BuOOH (in water)	Toluene	24	23	67
14	CuBr	—	70% ^{t}BuOOH (in water)	CH_3CN	1	—	87
15	CuI	—	70% ^{t}BuOOH (in water)	CH_3CN	24	31	62
16	$CuNO_2·3H_2O$	—	70% ^{t}BuOOH (in water)	CH_3CN	3	—	90
17	$CuCl_2·2H_2O$	—	70% ^{t}BuOOH (in water)	CH_3CN	5	—	90
18	$Cu(OAc)_2·H_2O$	—	70% ^{t}BuOOH (in water)	CH_3CN	9	—	86
19	$Cu(OTf)_2$	—	70% ^{t}BuOOH (in water)	CH_3CN	5	—	92
20	$CuCO_3Cu(OH)_2·H_2O$	—	70% ^{t}BuOOH (in water)	CH_3CN	9	—	88

Table 2
CuCl catalyzed aldehyde oxidation with aq 70% *tert*-butyl hydroperoxide in acetonitrile at room temperature[a]

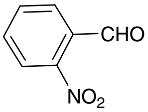
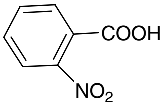
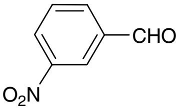
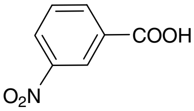
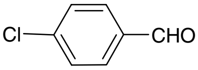
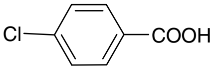
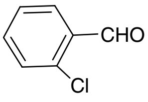
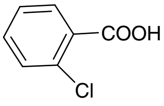
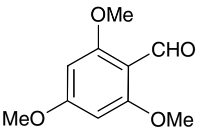
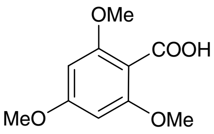
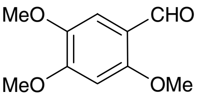
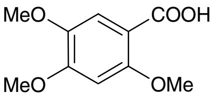
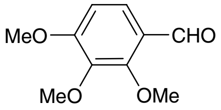
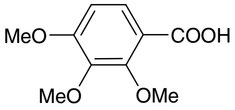
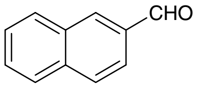
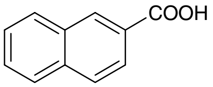
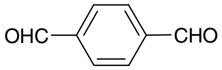
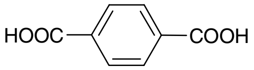
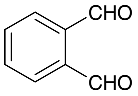
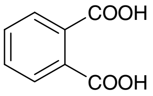
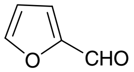
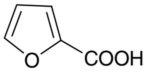
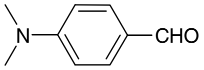
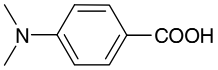
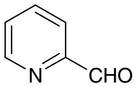
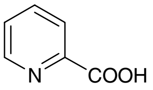
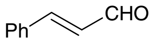
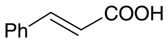
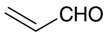
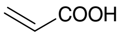
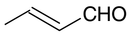
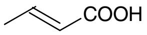
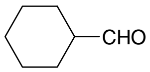
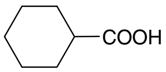
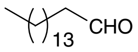
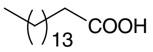
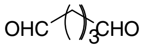
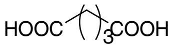
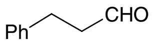
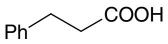
Entry	Alcohol	Product	Time (h)	Isolated yield (%)
1	Ph-CHO	Ph-COOH	1	90
2			7	89
3			9	90
4			4	92
5			4	93
6			1.5	93
7			2	70

Table 2 (*continued*)

Entry	Alcohol	Product	Time (h)	Isolated yield (%)
8			2	91
9			5	91
10			3	87[b]
11			2.5	84[b]
12			3	91
13			4	73
14			4	85[b]
15			5	93
16			2.5	80
17			2	81
18			3	83
19			2.5	80
20			3.5	78[b]
21			2	93

[a] All reactions were carried out with 5 mol % of CuCl and 1 equiv of 70% ^{t}BuOOH (in water) in MeCN at room temperature unless otherwise mentioned.[20]

[b] 2 equiv of 70% ^{t}BuOOH (in water) was used.

oxidant molecular oxygen and TEMPO with 30% H_2O_2, the reaction produced a 38% isolated yield of carboxylic acid in 24 h at room temperature (entry 2). When 30% H_2O_2 was replaced by anhydrous ^{t}BuOOH (5 M in decane) all the starting material was consumed in just 6 h at room temperature and the reaction provided a 91% isolated yield of acid (entry 3). To our surprise, the real catalyst in this reaction is the ligand free CuCl. CuCl alone without DABCO gave an identical result (entry 4). Replacement of anhydrous ^{t}BuOOH (5 M in decane) by 70% ^{t}BuOOH (in water) also provided almost the same results at room temperature. The cheaper cost of aqueous ^{t}BuOOH compared with anhydrous ^{t}BuOOH encouraged us to carry out the oxidation reaction with 70% ^{t}BuOOH (in water). Reaction without CuCl provided only a trace amount of acid (entry 7). This clearly indicates that CuCl is the catalyst.

We then screened the reaction with several solvents and acetonitrile turned out to be the best solvent providing the highest yield of acid in the shortest time (entry 6). Similarly CuCl became the choice of Cu salt in view of the yield and reaction rate.

To determine the scope of this new catalytic system, a wide range of aldehydes were oxidized under the optimized conditions (5 mol % CuCl, 1 equiv of 70% *tert*-butyl hydroperoxide (in water) in acetonitrile at room temperature) and the results are summarized in Table 2. It is clear that all the aromatic, vinylic and aliphatic aldehydes were easily oxidized to the corresponding acids in short times (1–9 h) with almost quantitative conversion and excellent isolated yields. Heteroatom-containing aldehydes such as furan-2-carbaldehyde and picolinaldehyde produced the corresponding acids, furan-2-carboxylic acid and picolinic acid in good yields, respectively (entries 12 and 14). Aromatic dialdehydes such as phthaldehyde and terephthaldehyde were also oxidized to the corresponding diacids, phthalic acid and terephthalic acid at room temperature in just 2.5 and 3 h, respectively, with excellent yields (entries 10 and 11). Allylic aldehydes such as cinnamaldehyde, crotonaldehyde and acrylaldehyde were also oxidized to the corresponding acids in short times and in good to excellent yields (entries 15–17). To our surprise, aliphatic aldehydes such as cyclohexanecarbaldehyde, palmitaldehyde and the aliphatic dialdehyde glutaraldehyde were also oxidized to the corresponding acids and diacids (entries 18–21). A detailed mechanistic study of this CuCl catalyzed oxidation and its application in the field of total synthesis of biologically active natural products is under progress.

In conclusion, we have developed a new procedure for the oxidation of aldehydes to acids using a catalytic amount of CuCl and 1 equiv of 70% ^{t}BuOOH (in water) in acetonitrile under very mild conditions. This procedure is very simple, and works efficiently at room temperature without any additives or ligands.

Acknowledgements

We thank DST (SERC Fast Track Research Project No.: SR/FTP/CS-19/2004) New Delhi, for the financial support. S.M. thanks CSIR, for a Junior Research Fellowship.

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20. *Typical experimental procedure:* To a solution of CuCl (4.95 mg, 0.05 mmol) in 2 mL of CH_3CN and aldehyde (1 mmol) was slowly added dropwise aqueous ^{t}BuOOH (0.142 mL, 1 mmol, 70% in water) over 5 min. The resulting reaction mixture was stirred at room temperature until the disappearance of starting material (TLC). After completion of the reaction, the solvent was evaporated and to the resulting crude reaction mixture water was added. The pH was adjusted to 8.0–8.5 with saturated $NaHCO_3$ and then the reaction mixture was extracted with ethyl acetate. The aqueous layer was acidified to pH 2.0 using 2 N HCl and extracted with ethyl acetate. The organic layer was concentrated and purified by silica gel column chromatography to give the carboxylic acid. All the products gave satisfactory spectral data.