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Efficient method for the oxidation of aldehydes and diols with *tert*-butylhydroperoxide under transition metal-free conditions

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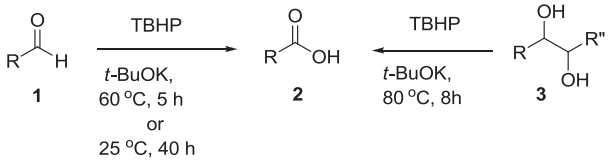
ABSTRACT

An efficient, mild, and simple protocol is presented for the oxidation of aldehydes and diols to carboxylic acids utilizing 70% aq TBHP as oxidant and *t*-BuOK as additive. The oxidation of aldehydes could be achieved by two methods under aqueous medium. Excellent yields of products were obtained in short reaction times. Notably, the products were isolated by simple filtration technique and do not involve chromatographic separation. These reactions may prove to be valuable alternatives to traditional metal-mediated oxidations. Oxidation does not require any transition metals or organic solvents in reaction, making this protocol green.

1. Introduction

Carboxylic acids are ubiquitous and important key functional groups that are present in natural products, agricultural and bio-active molecules, pharmaceuticals and polymers. Thus, synthesis of carboxylic acids by oxidation of a variety of substrates is one of the fundamental transformations in organic synthesis, which has extensively used both in academia and industry.[1] As a result a variety of oxidizing methods to the direct oxidations of aldehydes or diols to carboxylic acids or carbonyl compounds had been developed, which led to the discovery of several new oxidizing various reagents.[2] Conventionally, oxidation of aldehydes to carboxylic acids has been achieved employing Jones reagent (CrO_3/H_2SO_4/acetone) or manganese salts.[3] However, Mn- and Cr-based side products may be considered as a potentially environmental hazard.[4] Moreover, metal-free reagents, oxone,[5] porphyrin sensitizer,[6] NHC,[7] biomimetic-flavin,[8] are reported in literature to accomplish this transformation. Several attempts had been made by different groups finding alternatives to such oxidation procedures. For example, metal-mediated oxidations were reported employing Ca,[9] Ni,[10] Se,[11] Mg,[12] W,[13] Co,[14] Pd,[15] V,[16] Mo,[17] and Au.[18] Sedelmeier, Ley, and Baumann together disclosed to achieve oxidation of aldehydes to carboxylic acids employing stoichiometric amount of oxidant $KMnO_4/NaH_2PO_4$.[19] The combination of metal catalyst CuCl,[20] $AgNO_3$,[21] Bi_2O_3,[22] with stoichiometric oxidants TBHP or H_2O_2 were also described in literature. Despite considerable progress in such transformations, the search for new and more efficient methods is still under actively pursuing that involves implication of cheap and eco-friendly reagents.

Modern organic synthesis requires using oxidants, which are highly selective, efficient, and environmental friendly. Aqueous *tertiary*-butyl hydroperoxide (TBHP) is an effective oxidant,[23] for numerous transformations and its utility has also grown rapidly. This is due in part to TBHP's stability, non-toxic nature, non-polluting by products, and cost effectiveness. Also, environmentally friendly oxidizing agents allow to get rid of harmful compounds in manufacturing processes. Herein, we report efficient transition metal-free, operationally convenient protocols for the direct oxidation of aldehydes and diols to the corresponding carboxylic acids in aqueous medium using combination of aq 70% TBHP/potassium *tert*-butoxide (*t*-BuOK) (Scheme 1).



Scheme 1.

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2. Results and discussion

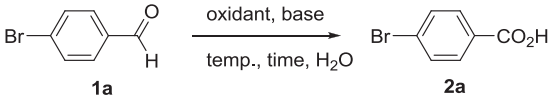
2.1. Oxidation of aldehydes

According to the literature reports, several methodologies have been utilized TBHP as oxidant in combination with metal-catalyzed[20–22] oxidation of aldehydes to carboxylic acids. Amongst them the usage of transition metals, such as copper, silver, and bismuth have been recently reported.[20–22] Therefore, it is important and useful to develop new metal-free methods to oxidize aldehydes to carboxylic acids by user-friendly protocols.

We chose to focus our initial attention on determining whether aq 70% TBHP alone promoted oxidation of aldehydes. In preliminary studies, we used stable, 4-bromobenzaldehyde (**1a**) for the oxidation reaction in aqueous medium and the results are presented in Table 1. When 4-bromobenzaldehyde was reacted with stoichiometric amount of aq 70% TBHP and 0.5 equiv *t*-BuOK in water at 25 °C, the corresponding 4-bromobenzoic acid (**2a**) was obtained in 10% yield (Table 1, entry 1). Under similar reaction conditions, **2a** was obtained in 45% yield at 60 °C (entry 1). While variation in concentration of base and temperature provided the oxidized product upto 32% yields (entries 2–3). When we increased the oxidant aq 70% TBHP to 2 equiv, the reaction produced a 40% isolated yield of 4-bromobenzoic acid and unreacted 4-bromobenzaldehyde was recovered (entry 4). Interestingly, the combination of aq 70% TBHP and NaOH gave competently conversions within short reaction time of 5 h (entries 5–6). To evaluate the effect of additives, the blank oxidation was carried out with aq 70% TBHP alone under similar reaction conditions without employing NaOH. However, the oxidation was found to be very slow and gave very poor yield of the oxidized product (entry 7). Changing the source of base from NaOH to K_3PO_4, $NaHCO_3$, pyridine, and triethylamine did not showed any improvement in oxidation reaction. Replacement of aq 70% TBHP by other oxidants, such as, NMO, TEMPO, and O_2 were ineffective or resulted in low yield of carboxylic acids (entries 10–12). Furthermore, the oxidation of **1a**, in the presence of aq 70% TBHP and KOH resulted in the formation of carboxylic acid **2a**, in 89% yields (entry 13). Good results were obtained employing *t*-BuOK produced **2a**, in excellent yield of 92% (entry 14). Additionally, we were interested to perform this oxidation process at room temperature. Thus, we subjected aldehyde **1a**, to the oxidation reaction at 25 °C and monitored very carefully. Surprisingly, the 4-bromobenzoic acid was excellently obtained in 90% within 40 h (entry 15). These results lead to the assumption that the oxidation of aldehydes (**1**), to the corresponding carboxylic acid (**2**), could be achieved by two methods (i) Method-A: aq 70% TBHP, *t*-BuOK, H_2O, 60 °C, 5 h (ii) Method-B: aq 70% TBHP, *t*-BuOK, H_2O, 25 °C, 40 h.

With the optimized oxidation conditions in hand, the substrate scope with various aromatic and aliphatic aldehydes using method-A [aq 70% TBHP, *t*-BuOK, H_2O, 60 °C, 5 h] was investigated. These results are presented in Table 2. All the aldehydes were selectively and smoothly converted to the corresponding carboxylic acids as sole product in excellent yields without any evidence for the formation of Dakin (phenols)[24a] and other over-oxidized products.[24b] The oxidation of benzaldehyde (**2b**) proceeds smoothly under the standard reaction conditions to give the benzoic acid in 94% following acidic work-up (Table 1, entry 1). Aldehydes having *para*-, *meta*- and *ortho*-substituted halides afforded the corresponding carboxylic acids **2a**, **2c**, **2d**, and **2d** in excellent yields (92, 93, 90, and 90%, respectively, entries 2–5, Table 2). Both electron-rich and electron-deficient aldehydes were smoothly oxidized to the

Table 1
Optimization of oxidation of aldehydes[a]

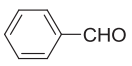
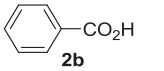
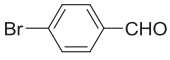
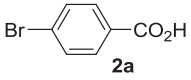
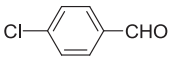
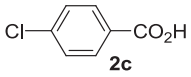
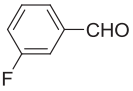
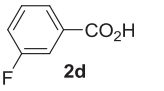
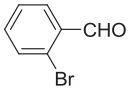
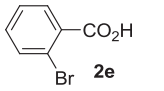
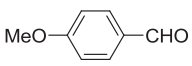
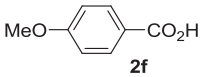
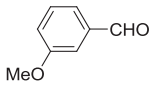
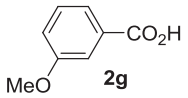
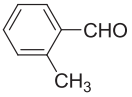
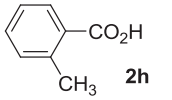
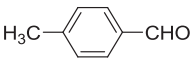
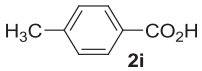
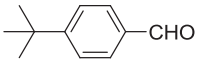
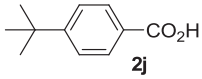
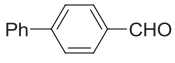
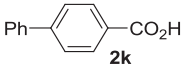


1a **2a**

Entry	Oxidant (equiv)	Additive (equiv)	Temp °C	Time h	Yield (%)
1	TBHP (1)	K_2CO_3 (0.5)	25	15	10(45)[b]
2	TBHP (1)	K_2CO_3 (1)	25	12	20
3	TBHP (1)	K_2CO_3 (1)	50	12	32
4	TBHP (2)	K_2CO_3 (1)	50	8	40
5	TBHP (2)	NaOH (1)	50	8	72
6	TBHP (2)	NaOH (1)	60	5	86
7	TBHP (2)	None	60	20	Trace
8	TBHP (2)	K_3PO_4 (1)	60	5	42
9	TBHP (2)	Pyridine (1)	60	5	Trace
10	NMO (2)	NaOH (1)	60	5	nr
11	TEMPO (1)	NaOH (1)	60	5	nr
12	O_2	NaOH (1)	60	5	nr
13	TBHP (2)	KOH (1)	60	5	89
14	TBHP (2)	*t*-BuOK (1)	60	5	92 (93%)[c]
15	TBHP (2)	*t*-BuOK (1)	25	40	90

[a] Reaction conditions: aldehyde (0.5 mmol), oxidant, additive, water; acidic work-up.
[b] Reaction was carried out 60 °C.
[c] The reaction was conducted in acetonitrile.

Table 2
Oxidation of aldehydes to carboxylic acids[a]

Entry	Aldehyde	Product[b]	Yield (%)[c]
1		 **2b**	94, 96[d]
2		 **2a**	92, 90[d]
3		 **2c**	93
4		 **2d**	90
5		 **2e**	90
6		 **2f**	88
7		 **2g**	85
8		 **2h**	93
9		 **2i**	95
10		 **2j**	96
11		 **2k**	82