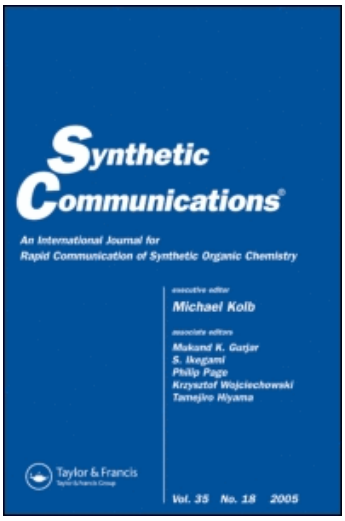

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Hydrogen Peroxide/Boric Acid: An Efficient System for Oxidation of Aromatic Aldehydes and Ketones to Phenols

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Abstract: Hydrogen peroxide activated by boric acid in the presence of sulfuric acid has been shown to be an efficient oxidizing system for direct conversion of aromatic aldehydes and ketones to phenols.

Hydrogen peroxide is one of the cheapest environmentally friendly and easy to handle oxidizing agents widely used for a range of oxidative transformations[1]. However it is a quite weak oxidizing agent and requires specific activation towards functional groups to be transformed for achieving higher efficiency and cleaner selectivity. Among the various transformations achieved by this reagent, conversion of benzaldehydes to phenols using alkaline hydrogen peroxide is generally known as Dakin oxidation. However, this reaction is limited in general to *o*-and *p*-hydroxybenzaldehydes[2,3]. A number of alkoxy substituted

benzaldehydes have also been examined under Baeyer-Villiger oxidation conditions using hydrogen peroxide in the presence of acidic methanol to afford the corresponding phenols in high yields[3]. Syper has utilized areneseleninic acid activated hydrogen peroxide[4] to oxidize a series of substituted and polycondensed benzaldehydes to afford the corresponding arylformates which were subsequently hydrolyzed to respective phenols in good yields. The oxidizing species in these reactions has been shown to be organoperoxyseleninic acid[4b] formed from seleninic acid and hydrogen peroxide. Sodium perborate (SPB) and sodium percarbonate (SPC) salts have also been shown to be versatile activating reagents of hydrogen peroxide for similar transformations[5]. Thus SPC in aqueous tetrahydrofuran under sonification[6] has been found to be useful reagent in Dakin oxidation of a range of salicylaldehydes and 2-hydroxy-4–methoxyacetophenones to the corresponding catechols. On the other hand, SPB/AcOH system has been shown to be an excellent reagent for the high yield oxidation of aromatic aldehydes[7] to the corresponding carboxylic acids. However, 2-and 4-methoxybenzaldehydes followed only Dakin oxidation under these reaction conditions to give 2- and 4-methoxyphenols in high yields. Shimizu and Ogata in a detailed mechanistic study, have suggested that SPB/AcOH system involves hydrogen peroxide activated by coordination with boric acid (generated *in situ* under the reaction conditions)[8] as the actual oxidizing species. We have now shown that 30% hydrogen peroxide in the presence of boric acid and sulfuric acid is an efficient oxidizing agent for the Dakin type oxidation of various benzaldehydes and acetophenones to phenols including those without any

activating group in *o*- and *p*-positions. We now report our results in this communication.

In a typical experiment, when a solution of benzaldehyde (1 eqv) in THF was added to a mixture of 30% hydrogen peroxide (2.2 eqv) and boric acid (5 eqv) in THF in the presence of trace of sulfuric acid, the reaction mixture after stirring (12 h) at room temperature followed by work up yielded phenol (Entry 1, Table 1) in 74% yield. Similarly the 2- and 4-hydroxy (Entry 2 and 3), 4-methoxy (Entry 4) and a number of di- and trimethoxybenzaldehydes (Entry 5 - 8) were smoothly converted to the corresponding phenols in 60-97% overall yields (Table 1). Oxidation of 2-allyloxybenzaldehyde (Entry 9) yielded the corresponding catechol monoallylether in 90% yield under identical reaction conditions. The allylic side chain remained unaffected under these conditions. On the other hand, vanillin (Entry 10) failed to undergo the observed oxidation even after prolonged (48 h) heating at 60–65°C, while its ethoxy analog (Entry 11) yielded only 30 % of phenol along with a trace of the corresponding benzoic acid.

The superiority of the present system was striking when it was applied to aromatic aldehydes with aryl group of lower migratory aptitude. Thus 4-methyl, 2-chloro, 4-chloro and 4-bromobenzaldehydes (Entry 12-15) yielded the corresponding phenols in moderate to good yields along with the respective acids. Interestingly, 4-nitrobenzaldehyde yielded a surprisingly high yield 70% (Entry-16) of 4-nitrophenol. These yields (Table 1, Entry 12-16) are highest for Dakin oxidation among all other oxidation systems so far reported. Thus the present system directs Dakin oxidation more selectively than the peracid oxidation and

Table 1. Oxidation of Aromatic Aldehydes with H_2O_2-H_3BO_3 in THF

Entry	Aldehydes	Reaction time (h)	Yield %[a] Phenol	Acid	Phenol mp/bp(°C)	Reported mp/bp(°C)	Acid mp/bp(°C)	Reported mp/bp(°C)
1.	Benzaldehyde	12	74	trace	44	43[11a]	123-124	122-123[12a]
2.	2-Hydroxybenzaldehyde	7	80	-	103-104	105[11b]	-	-
3.	4-Hydroxybenzaldehyde	24	90	-	170-171	170.5[11c]	-	-
4.	4-Methoxybenzaldehyde	24	97(90)[b]	-	56-57	58[4a]	-	-
5.	2,3-Dimethoxybenzaldehyde	24	77(30)[b]	-	oil	oil[4a]	-	-
6.	3,4-Dimethoxybenzaldehyde	18	80(60)[b]	-	79	81[4a]	-	-
7.	3,4-Methylenedioxy benzaldehyde	3.5	89(67)[b]	-	67-68	68[4a]	-	-
8.	3,4,5-Trimethoxybenzaldehyde	18	60	-	144-145	146-147[11d]	-	-
9.	2-Allyloxybenzaldehyde	15	90	-	oil	oil[11e]	-	-
10	4-Hydroxy-3-methoxy benzaldehyde	48[c]	-	-	-	-	-	-

[a] Yields of pure isolated products
[b] Yields in parenthesis are those reported by oxidation with H_2O_2/H^+ in MeOH[3].
[c] Heated at 60 °C .

Table 1.(contd.) Oxidation of Aromatic Aldehydes with H_2O_2-H_3BO_3 in THF

Entry	Aldehydes	Reaction time (h)	Yield %[a] Phenol	Acid	Phenol mp/bp(°C)	Reported mp/bp(°C)	Acid mp/bp(°C)	Reported mp/bp(°C)
11.	3-Ethoxy- 4-hydroxy-benzaldehyde	24[c]	30	trace	oil	oil[11]	166	164-165[12b]
12.	4-Methylbenzaldehyde	48[c]	50(28)[b]	40	37-38	36[11f]	180-181	180-182[12a]
13.	2-Chlorobenzaldehyde	19	58	20	oil	oil[11g]	136-137	138-140[12a]
14.	4-Chlorobenzaldehyde	48[c]	60	30	38-39	37[11g]	241-242	239-241[12a]
15.	4-Bromobenzaldehyde	48[c]	60	20	64-65	66[11h]	250-251	252-254[12a]
16.	4-Nitrobenzaldehyde	48[c]	70	28	112-113	114[11i]	242-243	239-241[12a]
17.	2-Nitrobenzaldehyde	50	trace	60	45-46	44.9[11i]	147-149	146-148[12a]
18.	1-Naphthaldehyde	24	52	_	94-95	94[4a]	_	_

[a] Yields of pure isolated products
[b] Yields in parenthesis are those reported by oxidation with H_2O_2/H^+ in MeOH[3].
[c] Heated at 60 °C .

the migratory aptitute of the aryl groups compared to hydrogen in these aldehydes are not similar to those reported in conventional Baeyer-Villiger oxidations[9].

Besides aromatic aldehydes, we have also examined the applicability of this method for the direct oxidation of acetophenones to phenols (Table 2). The *o*- and *p*-hydroxyacetophenones are known to be smoothly converted to the corresponding phenols under Dakin reaction conditions using alkaline hydrogen peroxide[2], while 4-hydroxyacetophenone fail to undergo the observed oxidation with SPC system even under sonification[6]. The other *p*-substituted acetophenones (i.e. 4-methoxy, 4-methyl, 4-chloro, 4-bromo and 4-phenyl) are reported to furnish *p*-substituted benzoic acid when oxidized with alkaline *t*-butylhydroperoxide[10]. On the other hand, oxidation of acetophenones to aryl formates under areneseleninic acid / H_2O_2 system[4a] involves drastic reaction conditions (90% H_2O_2) and requires at least two activating methoxy groups in the aryl ring. With our system, we have found that 2-hydroxy, 4-hydroxy, and 4-methoxyacetophenones are readily converted to the corresponding phenols in excellent yields (Entries 1-3, Table 2). Acetophenone and its 3-methoxy, 4-chloro, 4-nitro and 4-bromo derivatives (Entries 4-8) with aryl groups of lesser migratory aptitude could also be oxidized to the respective phenols in moderate to good yields along with the corresponding benzoic acid. Similarly 1-acetylnaphthalene (Entry 9) behave in identical manner to yield 1-naphthol, however, benzophenone (Entry 10) yielded the corresponding phenylbenzoate under similar conditions (Table 2).

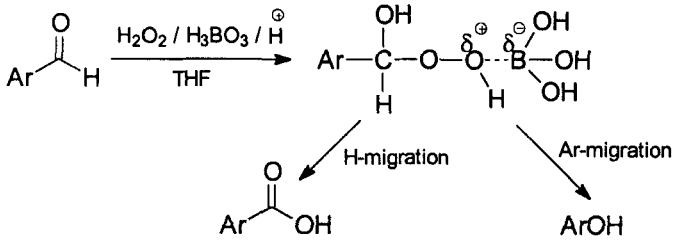
In summary we have demonstrated the feasibility of H_2O_2-H_3BO_3 oxidizing system for direct conversion of a variety of aromatic aldehydes and acetophenones

Table 2. Oxidation of Acetophenones to Phenols with H_2O_2-H_3BO_3

Entry	Ketones	Reaction time(h)	Yield %[a] Phenol	Acid	Phenol mp/bp°C	Reported mp/bp°C	Acid mp/bp°C	Reported mp/bp°C
1.	2-Hydroxyacetophenone	36	90	-	103-104	105[11b]	-	-
2.	4-Hydroxyacetophenone	36	86	-	170-171	170.5[11c]	-	-
3.	4-Methoxyacetophenone	24	71	-	56-57	58[4a]	-	-
4.	Acetophenone	24	63	15	41-42	43[11a]	123-124	122-123[12a]
5.	3-Methoxyacetophenone	48[b]	40	20	oil	oil[11j]	105-107	106-108[12a]
6.	4-Chloroacetophenone	48[b]	40	30	38-39	37[11g]	241-242	239-241[12a]
7.	4-Nitroacetophenone	48[b]	60	30	112-113	114[11l]	242-243	239-241[12a]
8.	4-Bromoacetophenone	48	63	23	64-65	66[11h]	250-251	252-254[12a]
9.	1-Acetylnaphthalene	24[b]	40	-	94-95	94[4a]	-	-
10.	Benzophenone	24	74[#]	-	66-67[#]	68[#11k]	-	-

[a] yields of the pure isolated products
[b] heated at 60° C
[#] Yield and mp of phenylbenzoate

to the corresponding phenols in higher yields compared to those reported earlier with various Dakin oxidation systems. Of particular importance is the oxidation of substrates having aryl ring with lower migratory aptitude which are incompatible with other oxidizing agents for which (i.e. *p*-nitrobenzaldehyde) to our knowledge, there are no precedence in the literature. The oxidation appears to proceed by intermediacy of highly polarized boric acid coordinated H_2O_2-aldehyde adduct which on facile heterolytic cleavage of borate ion and concerted migration of aryl group affords phenols (Scheme-1). The detailed mechanistic studies and synthetic scope of this valuable transformation is being investigated in our laboratory and will be published in due course.



Scheme 1

EXPERIMENTAL

General Procedure for Oxidation of Aromatic Aldehydes and Ketones to Phenols: To a stirring mixture of boric acid (3.1 g, 50 mmol) and 30% hydrogen peroxide (2.5 g, 22 mmol) in dry THF (30 mL), conc. H_2SO_4 (1 mL) was added and the reaction mixture was further stirred at room temperature for 0.5h. A solution of benzaldehyde or ketone (10 mmol) in dry THF (10 mL) was added and the reaction mixture was further stirred at room temperature (or 60°C, Tables 1

and 2) till the reaction was complete (monitored by TLC). The reaction mixture was filtered and washed with THF, the filtrate was neutralized with aqueous saturated sodium hydrogencarbonate solution (A) and extracted with $CHCl_3$ (3×25 mL). The combined organic extract was washed with water (50 mL), dried over Na_2SO_4 (anhydrous) and was evaporated to give the respective crude phenols which were purified by passing through silicagel column using hexane as eluent (Entries 2-9,11 Table 1, Entries 1-3,9 and 10 Table 2). The bicarbonate layer (A) obtained earlier afforded the corresponding acids on acidification with con. HCl (Entries 1, 12-17 Table 1, Entries 4-8 Table 2).

All the phenols and aromatic acids were identified by comparison of their physical and spectral (IR, NMR) data with that of authentic samples.

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