



## Silver nitrate-catalyzed oxidation of aldehydes to carboxylic acids by H<sub>2</sub>O<sub>2</sub>

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### ABSTRACT

A variety of aromatic, aliphatic and conjugated aldehydes were converted to the corresponding carboxylic acid derivatives with 30% H<sub>2</sub>O<sub>2</sub> as the oxidant in the presence of catalytic amounts of AgNO<sub>3</sub>. The method described has wide range of applicabilities, does not involve cumbersome work-up, exhibits chemoselectivity and proceeds under mild reaction conditions, and the resulting products are obtained in good yields within reasonable time.

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### 1. Introduction

The oxidation of aldehydes to carboxylic acids has been a long standing interest in synthetic organic chemistry.<sup>1</sup> The popular conventional method is the use of Jones reagent.<sup>2</sup> This is a stoichiometric reaction using highly acidic conditions which may not be tolerated by acid sensitive functionalities in the substrate. Moreover, the generation of Cr-based side products may be viewed as a potential environmental hazard. Other efficient reagents that have been reported in the literature to achieve such transformation include Oxone,<sup>3</sup> calcium hypochlorite<sup>4</sup> and 2-hydroperoxyhexafluoro-2-propanol.<sup>5</sup> Some interesting methodologies involving metal-mediated transformation of the aldehyde functionality to carboxylic acid have been reported recently.<sup>6</sup> The use of H<sub>2</sub>O<sub>2</sub> for such an oxidation has been as early as 1941 where Späth reported the transformation of dodecanal to dodecanoic acid.<sup>7</sup> Based on this report, H<sub>2</sub>O<sub>2</sub> was considered as a weak oxidizer in bringing about the transformation of aldehydes to carboxylic acids. The above-mentioned methods have one or more limitations which include the use of superstoichiometric amounts of expensive reagents, employment of highly basic or acidic reaction conditions and high temperature. The search for catalytic processes involving environmentally benign reagents shall always remain an attractive avenue in this area. The use of Ag<sub>2</sub>O along with NaOH has been an established protocol for the conversion of aldehyde to acid functionality for the preparation of vanillic acid<sup>8</sup> and 3-theonic acid.<sup>9</sup> However, these reactions are stoichiometric in nature. Another popular

example is the Tollens reagent<sup>10</sup> test for aldehydes. These results suggest the possible capability of Ag(I) as a catalyst for oxidation. As a result, we were inspired to access the scope of employing Ag(I) as a catalyst in the presence of an oxidant. To the best of our knowledge, catalytic silver-based processes for oxidative transformation of aldehydes to carboxylic acids are unknown. Given the different forms of Ag(I) compounds, we decided to explore the possibility of using AgNO<sub>3</sub> as a catalyst in the presence of 30% H<sub>2</sub>O<sub>2</sub><sup>11</sup> since these are common synthetic table top reagents, AgNO<sub>3</sub> is stable under ambient conditions and 30% H<sub>2</sub>O<sub>2</sub> is an inexpensive and readily available oxidizer which produces only water as the co-product. The versatility of using H<sub>2</sub>O<sub>2</sub> as an efficient oxidizer in the transformation of aldehydes to carboxylic acids was realized in this study.

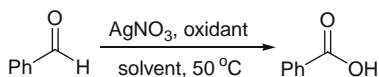
### 2. Result and discussion

Initial attempts to optimize the reaction conditions for the oxidation of aldehydes to the corresponding carboxylic acid were performed with benzaldehyde as a substrate, in the presence of different solvents, oxidants and silver salts (Table 1). The strength of the H<sub>2</sub>O<sub>2</sub> solution was determined prior to use. The conversion of benzaldehyde to benzoic acid was extremely facile in the presence of 10 mol % AgNO<sub>3</sub> and 5 equiv of 30% H<sub>2</sub>O<sub>2</sub> in acetonitrile at 50 °C (Table 1, entry 3). No reaction was found to occur under ambient conditions when the reaction mixture was stirred for 24 h. The oxidizing capability of 30% H<sub>2</sub>O<sub>2</sub> alone in the absence of catalytic amounts of AgNO<sub>3</sub> was found negligible and <5% isolated yield of the product was realized. With 5 mol % AgNO<sub>3</sub>, the completion of the reaction took 6 h with 72% isolated yield of

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**Table 1**

Optimization of the reaction conditions for the conversion of benzaldehyde to benzoic acid with 10 mol % AgNO<sub>3</sub> at 50 °C and various conditions



Entry	Oxidant	Solvent	Time <sup>a</sup> (h)	Yield <sup>b</sup> (%)
1	1 equiv of 30% H <sub>2</sub> O <sub>2</sub>	MeCN	9.0	78
2	2 equiv of 30% H <sub>2</sub> O <sub>2</sub>	MeCN	7.5	81
3	<b>5 equiv of 30% H<sub>2</sub>O<sub>2</sub></b>	<b>MeCN</b>	<b>3.5</b>	<b>88<sup>c,d</sup></b>
4	10 equiv of 30% H <sub>2</sub> O <sub>2</sub>	MeCN	3.4	82
5	20 equiv of 30% H <sub>2</sub> O <sub>2</sub> at rt	MeCN	3.4	80
6	5 equiv of 70% <sup>t</sup> BuOOH (water)	MeCN	7.5	91
7	5 equiv of 70% <sup>t</sup> BuOOH (decane)	MeCN	12.5	92
8	5 equiv of 30% H <sub>2</sub> O <sub>2</sub>	THF	10.0	83
9	5 equiv of 30% H <sub>2</sub> O <sub>2</sub>	CH <sub>2</sub> Cl <sub>2</sub>	24.0	81
10	5 equiv of 30% H <sub>2</sub> O <sub>2</sub>	EtOAc	11.3	83
11	5 equiv of 30% H <sub>2</sub> O <sub>2</sub>	DMF	3.8	80
12	5 equiv of 30% H <sub>2</sub> O <sub>2</sub>	DMSO	6.3	80
13	5 equiv of 30% H <sub>2</sub> O <sub>2</sub>	MeNO <sub>2</sub>	6.8	79
14	5 equiv of 30% H <sub>2</sub> O <sub>2</sub>	Toluene	10.5	82

<sup>a</sup> Monitored using TLC until all the aldehyde was found consumed.

<sup>b</sup> Isolated yield after column chromatography of the crude product.

<sup>c</sup> Use of AgCl, AgI and Ag(OTf) as catalysts under identical conditions required 8 h, 7 h and 6.5 h to give 56%, 52% and 61% of the product as isolated yield, respectively.

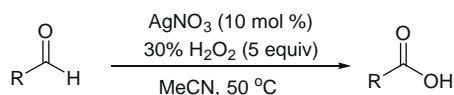
<sup>d</sup> With 5 mol % AgNO<sub>3</sub> at 50 °C, the reaction took 6 h for completion with 72% isolated yield of the product.

benzoic acid. With 5 equiv of 30% H<sub>2</sub>O<sub>2</sub>, the reaction proceeded to completion within a reasonable time frame as compared to lower amounts of H<sub>2</sub>O<sub>2</sub> (Table 1, entry 3 vs entries 1 and 2). Addition of higher equivalents of H<sub>2</sub>O<sub>2</sub> does not help anymore (Table 1, entry 3 vs entries 4–5). Other oxidants such as *t*-butyl hydroperoxide take longer periods for completion (Table 1, entries 6 and 7). MeCN was found to be a superior solvent as compared to others (Table 1, entries 8–14) in terms of time required for completion of the reaction and isolated yields.

Having understood the correct conditions for oxidation, we proceeded with a variety of aromatic and aliphatic substrates (Table 2). The scope of our catalytic system is applicable for a wide range of aromatic, conjugated and aliphatic substrates. These aldehydes were converted to the corresponding carboxylic acids in good isolated yields in reasonable time. Analysis reveals that aromatic aldehydes with electron-donating groups on the phenyl ring (Table 2, entries 1–9) are more reactive than those with electron-withdrawing substituents (Table 2, entries 10–12). Aldehydes with combination of electron-donating groups at 2- and 4-position of the ring reacts faster (Table 2, entries 1,2 and entries 3,4). It is pertinent to mention here that mild halogenic oxidants such as hypochlorites,<sup>4,12</sup> chlorites<sup>13</sup> and NBS<sup>14</sup> are not suitable for substrates with electron-rich aromatic rings, olefinic bonds and secondary hydroxyl groups. A -NO<sub>2</sub> substituent at the 3-position (Table 2, entry 12) retards the reactivity considerably. Substitutions at different

**Table 2**

AgNO<sub>3</sub>-catalyzed oxidation of aldehydes to carboxylic acids<sup>a</sup>



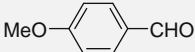
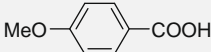
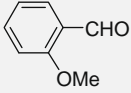
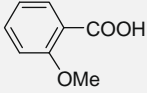
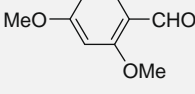
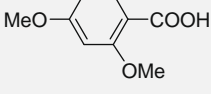
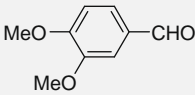
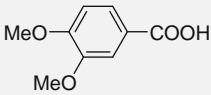
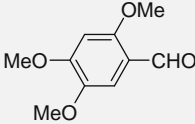
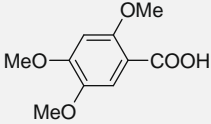
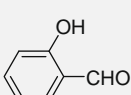
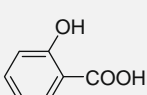
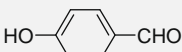
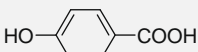
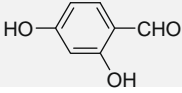
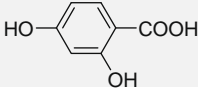
Entry	Aldehyde	Acid	Time <sup>b</sup> (h)	Yield <sup>c</sup> (%)
1			2.2	90
2			2.3	91 <sup>d</sup>
3			1.5	89
4			2.1	87
5			0.5	93
6			2.3	83
7			1.7	82
8			1.0	90

Table 2 (continued)

Entry	Aldehyde	Acid	Time <sup>b</sup> (h)	Yield <sup>c</sup> (%)
9			2.7	86 <sup>d</sup>
10			17.3	95
11			23.6	97
12			30.0	98
13			5.8	87
14			3.7	85 <sup>d</sup>
15			5.0	88 <sup>d</sup>
16			1.8	84
17			2.5	88
18			2.4	90

<sup>a</sup> Reactions performed in acetonitrile with 10 mol % AgNO<sub>3</sub> and 5 equiv of 30% H<sub>2</sub>O<sub>2</sub> at 50 °C unless stated otherwise.

<sup>b</sup> Monitored using TLC until all the aldehyde was found consumed.

<sup>c</sup> Isolated yield after column chromatography of the crude.

<sup>d</sup> Reactions performed with 10 mol % AgNO<sub>3</sub> and 2 equiv of 30% H<sub>2</sub>O<sub>2</sub> in acetonitrile at 50 °C.

positions on the phenyl ring do not hinder the reaction, although the reaction time is affected. Our catalytic system is mild and shows sufficient selectivity in carrying out the expected oxidation without affecting other functionalities such as phenol and amine (Table 2, entries 6–9). Oxidation of  $\alpha,\beta$  unsaturated derivatives (Table 2, entries 14 and 15) resulted in the formation of the expected acid in good yield. It must be mentioned that for salicylaldehyde (Table 2, entry 6), 4-(dimethylamino)benzaldehyde (Table 2, entry 9), crotonaldehyde (Table 2, entry 14) and cinnamaldehyde (Table 2, entry 15), 2 equiv of 30% H<sub>2</sub>O<sub>2</sub> is sufficient to give optimum yield.

The kinetic studies of this oxidation using 4-methoxybenzaldehyde, 3,4-dichlorobenzaldehyde, furan-2-carboxaldehyde and cyclohexanecarboxaldehyde were explored next. High-pressure liquid chromatography (HPLC) was used to determine the distribution of the aldehyde starting material and acid product present as a function of time. The concentration of reactant and product versus time for 3,4-dichlorobenzaldehyde is shown in Figure 1. The conversion of 4-methoxybenzaldehyde and cyclohexanecarboxaldehyde is more facile than the others. This conclusion is corroborated by much shorter reaction times for these aldehydes as compared to others (Table 2, entries 1 and 18 vs entries 11 and 13). We have attempted to calculate the rate of such conversions

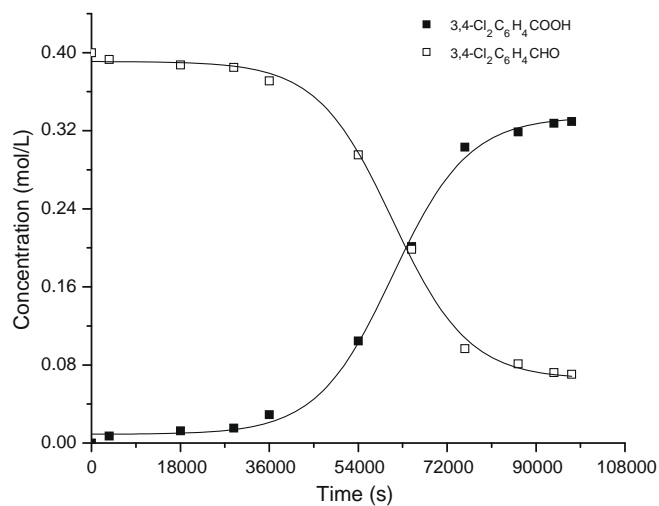
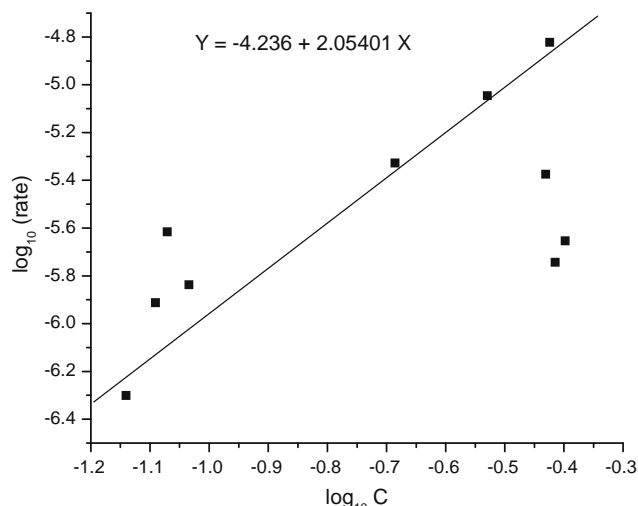


Figure 1. Concentration versus time in the oxidation of 3,4-dichlorobenzaldehyde with 10 mol % AgNO<sub>3</sub> and 5 equiv of 30% H<sub>2</sub>O<sub>2</sub> in MeCN at 50 °C.

from Figure 1. As an example, let us consider the transformation of 3,4-dichlorobenzaldehyde to 3,4-dichlorobenzoic acid. Van't



**Figure 2.** Van't Hoff differential plot for the oxidation of 3,4-dichlorobenzaldehyde with 10 mol %  $\text{AgNO}_3$  and 5 equiv of 30%  $\text{H}_2\text{O}_2$  in MeCN at 50 °C.

Hoff differential method was used to determine the order ( $n$ ) and rate constant ( $k$ ) (Fig. 2). From Figure 1, the rate of the reaction at different concentrations can be estimated by evaluating the slope of the tangent for each point on the curve corresponding to that of 3,4-dichlorobenzaldehyde. With these data,  $\log_{10}(\text{rate})$  vs  $\log_{10}(\text{concentration})$  is plotted. The order ( $n$ ) and the rate constant ( $k$ ) are given by the slope of the line and its intercept on the  $\log_{10}(\text{rate})$  axis. From Figure 2, it is clear that this reaction proceeds with second-order kinetics ( $n=2.05$ ) and the rate constant  $k = 5.81 \times 10^{-5} \text{ L mol}^{-1} \text{ s}^{-1}$ . For the other aldehydes namely furan-2-carboxaldehyde, cyclohexanecarboxaldehyde and 4-methoxybenzaldehyde, the order of the reactions  $n \approx 2$  with rate constants ( $k$ ) was  $5.64 \times 10^{-4} \text{ L mol}^{-1} \text{ s}^{-1}$ ,  $1.29 \times 10^{-3} \text{ L mol}^{-1} \text{ s}^{-1}$  and  $5.74 \times 10^{-1} \text{ L mol}^{-1} \text{ s}^{-1}$ , respectively.

### 3. Conclusions

In summary, we have developed a simple, efficient, chemoselective and inexpensive catalytic method for the oxidation of aldehydes to carboxylic acids using a table top reagent such as  $\text{AgNO}_3$ .<sup>15</sup> It is noteworthy that this methodology does not rely upon ligands and other additives.

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### Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tetlet.2009.09.044.

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- Typical experimental procedure:** To a stirred solution of  $\text{AgNO}_3$  (16.99 mg, 0.1 mmol) and aldehyde (1 mmol) in 2 mL MeCN was added 30%  $\text{H}_2\text{O}_2$  (0.57 mL, 5 mmol). The reaction mixture was slowly heated to 50 °C. The progress of the reaction was monitored using TLC until all aldehyde was found consumed. The reaction was quenched with cold 10%  $\text{Na}_2\text{S}_2\text{O}_3$  solution and extracted with dichloromethane. All the volatiles were removed to yield the crude product. The crude product was treated with saturated  $\text{NaHCO}_3$  solution. This was extracted with dichloromethane. Finally, the aqueous layer was acidified using 2 N HCl and extracted with dichloromethane. The organic layer was concentrated and subjected to column chromatography. Comparable yields and purity of the products were obtained employing ethyl acetate as an alternative solvent for work-up. The spectral data of the various carboxylic acids were found to be satisfactory in accord with the literature.