# Hydrogen peroxide oxidation of aldehydes to carboxylic acids: an organic solvent-, halide- and metal-free procedure

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## Abstract

Aqueous hydrogen peroxide oxidizes aldehydes to carboxylic acids under aqueous/organic biphasic conditions without affecting olefinic or alcoholic functions © 2000 Elsevier Science Ltd. All rights reserved.
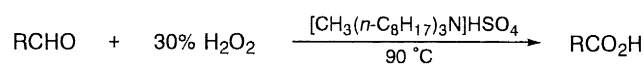
*Keywords:* aldehydes; Baeyer–Villiger reaction; carboxylic acids; hydrogen peroxide; oxidation; quaternary ammonium salts.

Despite the growing awareness of the need for 'green chemistry', many chemists still use environmentally unacceptable reagents or unnecessarily sophisticated conditions for the oxidation of aldehydes.[1–3] Certain aldehydes can be oxidized to carboxylic acids with 3–60% aqueous $H_2O_2$ *without organic solvents or metallic catalysts.* Here we propose a very simple procedure which is suitable for medium and large scale reactions.

Ignoring the ability of aqueous $H_2O_2$ to oxidize aldehydes, tremendous efforts have been made to develop metal-based catalysts[4] and inorganic[5] or organic promoters[6] for the oxidation of aldehydes. In 1941, Späth found that $H_2O_2$ reacts with dodecanal to form a perhydrate, which decomposes slowly at 120°C to give dodecanoic acid.[7] Since then aqueous $H_2O_2$ has been considered to have a weak ability to oxidize aldehydes. Some benzaldehyde derivatives can be converted to methyl benzoates with 31% $H_2O_2$ in methanol containing 38 mol% $H_2SO_4$,[8] and a patent claimed that 35% $H_2O_2$ in dioxane containing HBr oxidizes aldehydes to carboxylic acids.[9] However, the general capability of $H_2O_2$ to oxidize aldehydes to carboxylic acids has not yet been reported explicitly in academic literature. During our recent study of the alcohol dehydrogenation reaction,[10] we found that the oxidation of some aliphatic and aromatic aldehydes with $H_2O_2$ proceeds under aqueous/organic biphasic conditions without organic solvents, halides, or metal catalysts (Scheme 1). The reaction is catalyzed simply by an acid. Thus, when a mixture of octanal, 30% $H_2O_2$, and $[CH_3(n\text{-}C_8H_{17})_3N]HSO_4$ ($QHSO_4$) in a 200:220:1 molar ratio was heated at 90°C for 2 h with magnetic stirring at 1000 rpm, octanoic acid was obtained with a yield of 82%. Without stirring under otherwise identical conditions, the yield was lowered to 73%. The reaction at 70°C gave the carboxylic acid with a yield of only 4%. When a biphasic mixture of octanal and 30% $H_2O_2$ was stirred at 1000 rpm at 90°C without the acidic quaternary ammonium salt, octanoic acid was produced in a yield
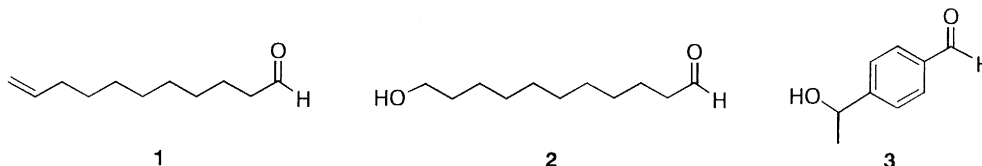
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of only 30%.[11] Decreased lipophilicity of the catalysts tends to lower the reaction rate. The reaction of octanal and 30% $H_2O_2$ at 90°C for 2 h in the presence of other acids (aldehyde:$H_2O_2$:acid=200:220:1) gave yields of 47% with [($n$-$C_4H_9$)$_4$N]HSO$_4$, 36% with $H_2SO_4$, 55% with HBr, 39% with HCl, 41% with $n$-$C_{12}H_{25}SO_3H$, and 34% with Nafion-H. Thus, the use of a lipophilic, acidic Q salt as catalyst[12] is the key to efficient biphasic oxidation. As oxidant, 3% $H_2O_2$ can also be used. Reaction with 60% $H_2O_2$ at 90°C takes place faster, but such conditions are not recommended because of the production of some peroxy acids.

$$RCHO \quad + \quad 30\% \ H_2O_2 \quad \xrightarrow[\text{90 °C}]{[CH_3(n\text{-}C_8H_{17})_3N]HSO_4} \quad RCO_2H$$

Scheme 1.

Examples of the simple oxidation are given in Table 1. Although the reaction was performed normally in a 5–75 mmol range with substrate/catalyst ratios of 100 to 1000, no technical problems in scaling-up are foreseen. The reaction of 100 g of octanal (aldehyde:$H_2O_2$:QHSO$_4$=200:300:1, 90°C, 2 h, 1000 rpm) gave octanoic acid in a yield of 81% after distillation (85% by $^1$H NMR).[13] $\alpha$-Branched aldehydes were converted to acids with lower yields. Benzaldehyde derivatives with an electron-withdrawing group produced the benzoic acids in reasonable yields. The reaction of melted $p$-nitrobenzaldehyde (m.p. 105°C) under the standard conditions gave $p$-nitrobenzoic acid with a yield of 93%. If necessary, toluene can be employed as a solvent. Unfortunately, $p$-methoxybenzaldehyde afforded the carboxylic acid with a yield of only 9%.
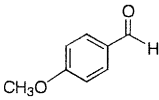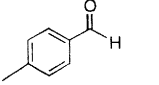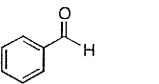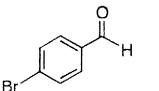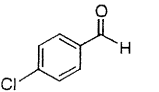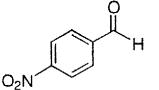
Because of the absence of metallic catalysts, olefinic and alcoholic (primary and secondary) functions survive the oxidation conditions (Table 1). 10-Undecenal (**1**) was converted to 10-undecenoic acid with a yield of 85% with 30% $H_2O_2$ and QHSO$_4$ (substrate:$H_2O_2$:Q salt=200:220:1, 90°C, 2 h, 1000 rpm).[14] Under the same conditions, 11-hydroxyundecanal (**2**) selectively gave 11-hydroxyundecanoic acid with a yield of 75%. Even $p$-(1-hydroxyethyl)benzaldehyde (**3**) which has a highly reactive alcoholic moiety was oxidized solely at the aldehyde group to give the hydroxy carboxylic acid with a yield of 79%.
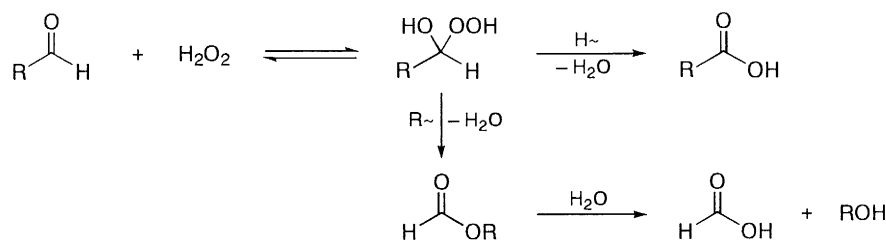


We consider that the oxidations proceed via perhydrate intermediates. The acidic Q salt facilitates the addition of $H_2O_2$ to aldehydes in the organic layer and, more importantly, the elimination of water from the tetrahedral intermediate via a Baeyer–Villiger type fragmentation. This view is consistent with the structure-dependent efficiency of the reaction. Straight-chain aliphatic aldehydes are cleanly converted to carboxylic acids, because the perhydrates eliminate water by selective hydride migration. Whereas, secondary and tertiary $R$ groups tend to migrate competitively with hydride, resulting in the formation of formate products (Scheme 2). In fact, oxidation of 2-ethylhexanal with 30% $H_2O_2$ and QHSO$_4$ under the standard conditions gave 3-heptanol and 3-heptanone with a total yield of 11% together with the desired 2-ethylhexanoic acid with a yield of 65%. The efficiency observed with $para$-substituted benzaldehydes also agrees with this mechanism.

Aqueous $H_2O_2$ is a cheap, safe oxidant which produces only water as a coproduct. Although its ability to oxidize aldehydes has been ignored, it is very useful for this purpose. Changing current practices to a process using this environmentally friendly oxidant is highly desirable.

Table 1
Hydrogen peroxide oxidation of aldehydes to carboxylic acids[a]

| aldehyde | | $H_2O_2$ | $[CH_3(n\text{-}C_8H_{17})_3N]HSO_4$ | time | % yield of |
|---|---|---|---|---|---|
| structure | mmol | mmol (equiv) | mmol $(S/C)^b$ | h | carboxylic acid[c] |
| $C_6H_5(CH_2)_2CHO$ | 745 | 820 (1.1) | 3.7 (200) | 2 | $73^d$ |
| | 74.5 | 82 (1.1) | 0.37 (200) | 2 | $78^d$ |
| | 74.5 | 82 (1.1) | 0.075 (1000) | 4 | $77^d$ |
| $n\text{-}C_7H_{15}CHO$ | 780 | 1170 (1.5) | 3.9 (200) | 2 | $81,^d 85^e$ |
| | 10 | 11 (1.1) | 0.05 (200) | 2 | $82^e$ |
| | 10 | $11 (1.1)^f$ | 0.05 (200) | 1 | $73^{e,g}$ |
| $n\text{-}C_4H_9CH(C_2H_5)CHO$ | 10 | 11 (1.1) | 0.05 (200) | 2 | 65 |
| $(CH_3)_3CCHO$ | 10 | 11 (1.1) | 0.05 (200) | 2 | $40^e$ |
| $C_6H_5CH(CH_3)CHO$ | 10 | 11 (1.1) | 0.05 (200) | 2 | 17 |
| (4-methoxybenzaldehyde, $CH_3O$) | 5 | 12.5 (2.5) | 0.05 (100) | 3 | 9 |
| (4-methylbenzaldehyde) | 5 | 12.5 (2.5) | 0.05 (100) | 3 | 41 |
| (benzaldehyde) | 5 | 12.5 (2.5) | 0.05 (100) | 3 | 85 |
| (4-bromobenzaldehyde, Br) | 5 | 12.5 (2.5) | 0.05 (100) | 3 | 78 |
| (4-chlorobenzaldehyde, Cl) | 5 | 12.5 (2.5) | 0.05 (100) | 3 | 76 |
| (4-nitrobenzaldehyde, $O_2N$) | 5 | 12.5 (2.5) | 0.05 (100) | 3 | $93^h$ |
| | 5 | 12.5 (2.5) | 0.05 (100) | 3 | $88^{i,j}$ |
| $CH_2=CH(CH_2)_8CHO$ (1) | 10 | 11 (1.1) | 0.05 (200) | 2 | $85^e$ |
| $HO(CH_2)_{10}CHO$ (2) | 5 | 5.5 (1.1) | 0.025 (200) | 2 | $75^e$ |
| $p\text{-}[CH_3CH(OH)]C_6H_4CHO$ (3) | 5 | 12.5 (2.5) | 0.05 (100) | 3 | $79^k$ |

[a] Unless otherwise stated, reactions were run using 30% $H_2O_2$ at 90 °C. [b] Substrate/catalyst molar ratio. [c] Determined by GC analysis. Carboxylic acids were analyzed after conversion to their methyl esters with trimethylsilyldiazomethane. Conversion of aldehydes was >90%. [d] Isolated by distillation. [e] Determined by ^{1}H NMR. [f] Reaction with 60% $H_2O_2$. [g] Contaminated with 6% of the peroxy acid. [h] Determined by HPLC analysis. [i] Toluene (2 mL) was used as solvent. [j] Isolated by recrystallization from ethanol. [k] Isolated by silica-gel column chromatography.

Scheme 2.

## Acknowledgements

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11. Venturello reported that heating a mixture of octanal and 40% H$_2$O$_2$ (1:1.2 mol ratio) at 90°C for 1 h gave octanoic acid with a yield of 34%, while the presence of 0.5% [CH$_3$(*n*-C$_8$H$_{17}$)$_3$N]$_3$PO$_4$[W(O)(O$_2$)$_2$]$_4$ increased the yield to 87%.[4a]
12. When a mixture of [CH$_3$(*n*-C$_8$H$_{17}$)$_3$N]HSO$_4$ (0.3 mmol), toluene (10 mL), and water (10 mL) in a 20 mm diameter test tube was mechanically stirred at 1000 rpm for 2 h at room temperature and then allowed to stand for 1 h, the acid was partitioned in toluene and water in a ratio of about 7:3. No concentration gradient was seen in both organic and aqueous phases. $^1$H NMR analysis showed that 1 mL of D$_2$O dissolves 0.068 mmol of [CH$_3$(*n*-C$_8$H$_{17}$)$_3$N]HSO$_4$ at 25°C.
13. Typical procedure: A 500 mL, round-bottomed flask equipped with a magnetic stirring bar and a reflux condenser was charged with 1.82 g (3.90 mmol) of [CH$_3$(*n*-C$_8$H$_{17}$)$_3$N]HSO$_4$ and 133 g (1.17 mol) of aqueous 30% H$_2$O$_2$. The mixture was vigorously stirred at room temperature for 10 min, and then 100 g (780 mmol) of octanal was added. The biphasic mixture was heated at 90°C with stirring at 1000 rpm for 2 h and then cooled to room temperature. The organic phase was separated, washed with 100 mL of saturated aqueous Na$_2$S$_2$O$_3$, and distilled through a short column to give 91.5 g (81%) of octanoic acid as a colorless liquid, b.p. 114.0–116.0°C/3 mmHg.
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