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Hydrogen Peroxide Oxidation of Benzylic Alcohols to Benzaldehydes and Benzoic Acids Under Halide-Free Conditions

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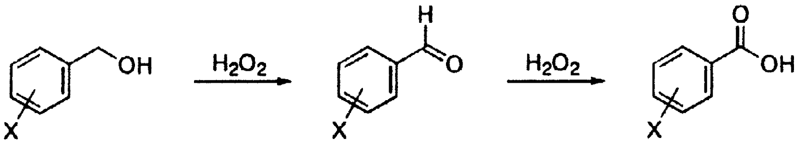
Abstract: A series of benzaldehyde and benzoic acid derivatives can be obtained from benzylic alcohols by tungsten-catalyzed oxidation with aqueous hydrogen peroxide under halide-free, aqueous/organic biphasic conditions. © 1998 Elsevier Science Ltd. All rights reserved.

Selective oxidation of benzylic alcohols to benzaldehydes or benzoic acids is not easy, particularly on a preparative scale.[1] The efficiency is highly dependent on substituents of the aromatic ring. Here we report that a system consisting of Na_2WO_4 and a quaternary ammonium hydrogensulfate as a phase-transfer catalyst (PTC)[2,3] allows for the selective oxidation of various substituted benzyl alcohols using aqueous H_2O_2 under halide-free, biphasic conditions.[4,5] This method is practical because of the low cost, safety, and with less harm to the environment. The scope and limitations are described below.



A benzylic alcohol is oxidized at 90 °C with 30% H_2O_2 in the presence of Na_2WO_4 and $[CH_3(n\text{-}C_8H_{17})_3N]HSO_4$ to give the corresponding benzaldehyde in a good yield. Some examples of the 100 g-scale reaction (alcohol:catalyst molar ratio = 50–330:1) are given in Table 1. Since unproductive decomposition of H_2O_2 is negligible with the tungsten catalyst system, the oxidation is accomplished with <1.5 equiv of the oxidizing agent per equiv of the alcohol.[6] This catalyst system is more reactive than Venturello's $[CH_3(n\text{-}C_8H_{17})_3N]_3PO_4[W(O)(O_2)_2]_4$ which has been used for solvent-free oxidation of benzyl alcohol and its *p*-methyl derivative.[4b] Furthermore, unlike oxidation with quaternary ammonium chloride[4a] that requires 70% H_2O_2 and 1,2-dichloroethane as solvent, this reaction is achieved under milder and chloride-free conditions.

In the oxidation of ring-substituted benzyl alcohols, water, H_2O_2, alcohols, and other nucleophiles present may react with the resulting aldehydes. The stability and reactivity of the tetrahedral intermediates are significantly affected by the electronic properties of the substituents as well as the reaction conditions. In fact, with the earlier catalytic systems,[4] the presence of certain polar substituents caused considerable side reactions. We can now obtain a series of aromatic aldehydes by selecting proper reaction parameters (Table 1). The oxidation of an oily or low-melting alcohol is accomplished without organic solvent. Toluene can be used as

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Table 1. Oxidation of benzylic alcohols to benzaldehydes[a]

$XC_6H_4CH_2OH$		H_2O_2,	Na_2WO_4 and PTC,		% yield of
X	mmol	mmol (equiv)	mmol (S/C)[b]	time, h	XC_6H_4CHO[c]
p-CH_3O	724	1086 (1.5)	14.5 (50)	5	90[d,e]
p-CH_3	819	983 (1.2)	4.1 (200)	4.5	91
o-CH_3	819	983 (1.2)	4.1 (200)	4.5	88
H	925	1018 (1.1)	2.8 (330)	3	87
p-Br	535	696 (1.3)	2.7 (200)	4.5	81
p-Cl	701	841 (1.2)	3.5 (200)	4.5	82
p-NO_2	5	10 (2)	0.1 and 0.05 (50 and 100)	17	59[f,g,h]
3,4-Benzo[i]	632	759 (1.2)	3.2 (200)	4.5	82[j,k]

[a] Unless otherwise stated, a 0.1 molar ratio of 5% H_2O_2 to an alcohol was used for activation of the W catalyst, and 30% H_2O_2 was added dropwise to a mixture of the catalysts and alcoholic substrate with stirring at 1000 rpm at 90 °C. See footnote 8. PTC = $[CH_3(n\text{-}C_8H_{17})_3N]HSO_4$. [b] Substrate/catalysts molar ratio. [c] Isolated by distillation. [d] Toluene (150 mL) was used as solvent. [e] Reaction at 70 °C. [f] Determined by HPLC analysis. [g] Toluene (8 mL) and ethyl acetate (2 mL) were used as solvent. [h] Conversion was 80%. *p*-Nitrobenzoic acid was formed in 15% yield. [i] 2-Naphthylmethanol. [j] Reaction was run using 5% H_2O_2 with stirring at 1000 rpm at 90 °C. [k] Yield of 2-naphthalenecarbaldehyde.

solvent, if necessary, as, for example, the oxidation of substrates such as *p*-methoxybenzyl alcohol which have low log *P* values[7] are conducted better in toluene. Even *p*-methoxybenzyl alcohol, regarded as the most difficult substrate,[4b] gave the aldehyde in 90% yield.[8] The high efficiency of this new procedure[9] is consistent with our recent finding that 3–5% aqueous H_2O_2 oxidizes alcohols more rapidly than 30% H_2O_2.[3] Oxidation of *p*-nitrobenzyl alcohol is still difficult, the highest yield obtained so far is 59%.

A range of benzyl alcohols are directly convertible to the corresponding benzoic acid derivatives using 2.5–5 equiv of H_2O_2 (theory, 2 equiv) and a 0.01 molar amount of Na_2WO_4 and PTC. Table 2 lists some examples of the 100-g scale oxidation. Mechanistically, hydration of benzaldehyde derivatives followed by tungsten-catalyzed dehydrogenation with H_2O_2 is expected to yield benzoic acids. However, addition of H_2O_2 or peracids[10] to the aldehydes competes with hydration. The resulting peroxy intermediates are transformed to either the desired benzoic acids (H migration) or aryl formates (aryl migration) by a Baeyer–Villiger mechanism. The latter undesired pathway becomes significant with electron-donating substituents, since the resulting phenols are further oxidized to give complex mixtures. Thus, *p*-methoxybenzoic acid cannot be obtained by this method. Electron-withdrawing substituents tend to efficiently give the carboxylic acids. Thus, *p*-nitrobenzyl alcohol was converted to the benzoic acid in 91% yield (97% by HPLC analysis) by oxidation using 4 equiv of H_2O_2 followed by treatment with an aqueous solution of $Na_2S_2O_3$.[11] Separate experiments using 30% H_2O_2 with or without Na_2WO_4 revealed that carboxylic acids are derived via dual pathways, *viz.*, the tungsten-catalyzed dehydrogenation of aldehyde hydrates (minor) and the acid-catalyzed Baeyer–Villiger reaction involving aldehyde peroxy hydrates (major).[12] The extent of the latter route increases with electron-withdrawing substituents.[13]

Table 2. Oxidation of benzylic alcohols to benzoic acids[a]

$XC_6H_4CH_2OH$		H_2O_2,	Na_2WO_4 and PTC,		% yield of
X	mmol	mmol (equiv)	mmol (S/C)[b]	time, h	XC_6H_4COOH[c]
p-CH_3O	5	25 (5)	0.05 (100)	12	1[d,e,f]
p-CH_3	819	4092 (5)	8.2 (100)	12	80[d]
H	925	2313 (2.5)	9.2 (100)	5	81[d]
p-Br	535	2138 (4)	5.4 (100)	4	86
p-Cl	701	2806 (4)	7.0 (100)	4	87
p-NO_2	653	2612 (4)	6.5 (100)	4	91

[a] Unless otherwise stated, the reaction was run with 30% H_2O_2 with stirring at 1000 rpm at 90 °C. See footnote 11. PTC = $[CH_3(n\text{-}C_8H_{17})_3N]HSO_4$. [b] Substrate/catalysts molar ratio. [c] Isolated by recrystallization from a 4:1 methanol–water mixture. [d] A 0.1 molar ratio of 5% H_2O_2 to an alcohol was used for activation of the W catalyst, and 30% H_2O_2 was added dropwise to a mixture of the catalysts and an alcoholic substrate. [e] Reaction was run in 1 mL of toluene at 70 °C. [f] Determined by GC analysis. *p*-Methoxybenzoic acid was analyzed after conversion to the methyl ester with trimethylsilyldiazomethane.

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8. Oxidation of *p*-methoxybenzyl alcohol to *p*-methoxybenzaldehyde: A 500-mL, three-necked, round-bottomed flask equipped with a magnetic stirring bar, a reflux condenser, a thermometer, and a 100-mL dropping funnel was charged with $Na_2WO_4 \cdot 2H_2O$ (4.77 g, 14.5 mmol), [$CH_3(n\text{-}C_8H_{17})_3N$]$HSO_4$ (6.74 g, 14.5 mmol), and aqueous 5% H_2O_2 (49.2 g, 0.0724 mol), and the mixture was vigorously stirred at room temperature for 10 min. *p*-Methoxybenzyl alcohol (100 g, 0.724 mol) and 150 mL of toluene were then added and the mixture was heated at 70 °C for 10 min. With stirring at 1000 rpm, aqueous 30% H_2O_2 (114.4 g, 1.009 mol) was added dropwise via the dropping funnel over a period of 5 h, while maintaining the temperature of the reaction mixture below 75 °C. After cooling to room temperature, the organic phase was separated, washed with 50 mL of saturated aqueous $Na_2S_2O_3$, and distilled through a 15-cm Vigreux column to give *p*-methoxybenzaldehyde (88.8 g, 90% yield) as a colorless liquid, bp 137–138 °C/23 mmHg.

   This particular reaction used a 0.02 molar amount of the W catalyst and PTC and toluene as solvent. However, oxidation of many other substrates was conducted with only a 0.005 molar amount of the catalysts without solvent and at 90 °C under otherwise identical conditions.
9. The procedure was improved from that reported earlier.[3]
10. A peracid may be produced from the benzoic acid formed initially and H_2O_2 under the reaction conditions.
11. Oxidation of *p*-nitrobenzyl alcohol to *p*-nitrobenzoic acid: A mixture of $Na_2WO_4 \cdot 2H_2O$ (2.15 g, 6.53 mmol), [$CH_3(n\text{-}C_8H_{17})_3N$]$HSO_4$ (3.04 g, 6.53 mmol), and aqueous 30% H_2O_2 (296.2 g, 2.612 mol) was vigorously stirred at room temperature for 10 min. Then, *p*-nitrobenzyl alcohol (100 g, 0.653 mol) was added, and the mixture was heated at 90 °C for 4 h with stirring at 1000 rpm. After the reaction mixture was allowed to stand at 0 °C for 12 h, the resulting yellow precipitate was separated by filtration, washed with 20 mL of cold water, dissolved in 500 mL of ethyl acetate and washed with 100 mL of saturated aqueous $Na_2S_2O_3$. The organic phase was separated and concentrated under reduced pressure. The product was recrystallized from 4:1 methanol–water giving 99.6 g (91%) of *p*-nitrobenzoic acid as a white solid, mp 238.0–239.0 °C. The yield determined by HPLC (column, Develosil ODS-5, 4.6 mm x 25 cm, NOMURA CHEMICAL) was 97%. The solid product prior to the treatment with aqueous $Na_2S_2O_3$ was contaminated with 5% of the perbenzoic acid.
12. Reaction of benzaldehyde (5 mmol) and 30% H_2O_2 (12.5 mmol) in the presence of $Na_2WO_4 \cdot 2H_2O$ (0.05 mmol) and [$CH_3(n\text{-}C_8H_{17})_3N$]$HSO_4$ (0.05 mmol) at 90 °C for 3 h gave benzoic acid in 91% yield (GC analysis). In the absence of $Na_2WO_4 \cdot 2H_2O$, the acid was obtained in 85% yield under the identical conditions. Note, however, that the latter is not a pure "back-ground" reaction, because the acidity of the reaction system is significantly increased by the removal of the tungsten salt.
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