

# Microwave-Assisted Oxidation of Alcohols Using Aqueous Hydrogen Peroxide

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Received 15 October 1999

**Abstract:** Primary and secondary alcohols were oxidised into equivalent carboxylic acids and ketones within 10-20 min using 30% aqueous hydrogen peroxide and commercially available catalysts under microwave irradiation.

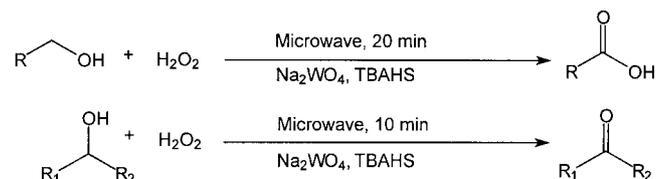
**Key words:** oxidation, hydrogen peroxide, biphasic system, alcohols, microwave irradiation

The oxidation of alcohols plays an important role in organic synthesis and since carbonyl compounds are widely used as intermediates both in manufacturing and laboratory,<sup>1</sup> the development of new oxidative protocols continues to receive attention in spite of the availability of several methods to achieve such objectives.<sup>2</sup> In oxidation processes, the use of a number of non-environmental oxidants (e.g., heavy metals, peracids) is very common, although other compounds are sought that are not detrimental to the environment. In this context, the application of hydrogen peroxide as an oxidant is appreciated because water is the sole expected side product.

Use of aqueous hydrogen peroxide as the oxidant under phase transfer catalytic conditions was described by Venturello et al.<sup>3</sup> who employed  $\text{Na}_2\text{WO}_4 \cdot \text{H}_3\text{PO}_4$ -quaternary ammonium salt combined catalyst and chlorinated hydrocarbons as solvents. Recently, a more effective solvent- and halide-free version of this process was published by Noyori et al.<sup>4</sup> They found that the substitution of ammonium chlorides with ammonium hydrogen sulfates under *solventless* organic/aqueous biphasic conditions led to the increase of the reaction yields as well as made the process clean, safe and operationally simple.

Since the reactions in solventless solid-liquid PTC systems and microwave activation of such reactions are the main interest of our laboratory,<sup>5</sup> we decided to explore Noyori's procedure for the oxidation of alcohols under microwave irradiation. Accelerations of organic reactions by microwaves have been largely exemplified<sup>6</sup> and gained popularity over the usual homogenous and heterogeneous reactions<sup>7</sup> as they can be conducted rapidly and in many cases provide pure products in quantitative yield without the use of solvents. Recently, using reactants adsorbed on inorganic supports and microwave activation, Varma et al.<sup>8</sup> have published several examples of oxidation reactions of alcohols to carbonyl compounds as well as sulfides to sulfoxides and sulfones. Under similar conditions ( $\text{KMnO}_4$  adsorbed on alumina), Loupy et al.<sup>9</sup> have converted aromatic hydrocarbons to aromatic ketones; whereas Palombi et al.<sup>10</sup> oxidised alcohols using *t*-butyl hydroperoxide supported on zeolites.

In the present paper we report a fast and facile microwave accelerated oxidation of primary alcohols to carboxylic acids and secondary alcohols to ketones (Scheme).



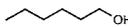
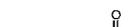
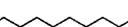
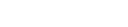
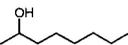
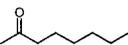
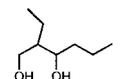
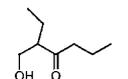
## Scheme

The reactions were carried out under organic/aqueous biphasic conditions using 30% aqueous  $\text{H}_2\text{O}_2$  in the presence of sodium tungstate and tetrabutylammonium hydrogen sulfate (TBAHS) as a phase-transfer catalyst. The experimental procedure involves a simple mixing of an alcohol,  $\text{Na}_2\text{WO}_4 \cdot 2\text{H}_2\text{O}$  and TBAHS followed by the addition of 30% aqueous  $\text{H}_2\text{O}_2$  in 25:1:1:125 molar ratio for primary and 25:1:1:40 molar ratio for secondary alcohols in an open vessel. Then the reaction mixtures were placed inside a monomode microwave reactor<sup>11</sup> (Synthwave 402, Prolabo) and irradiated under a reflux condenser for specific time (i.e., 20 min for primary and 10 min for secondary alcohols). The best results were obtained when the temperatures of reaction mixtures were set to 90 °C and 100 °C for primary and secondary alcohols, respectively. The results are indicated in the Table.

Upon completion of the oxidation of primary alcohols, aqueous  $\text{Na}_2\text{CO}_3$  was added to the reaction mixture. Then, the mixture was extracted with ethyl acetate, the aqueous phase was acidified, and it was again extracted with ethyl acetate to afford carboxylic acids after the evaporation of the solvent.<sup>12a</sup> In the case of secondary alcohols, the work-up procedure was much simpler and reduced to the extraction of the reaction mixtures with ethyl acetate. The organic layer was then dried and the solvent was evaporated to give the desired ketone.<sup>12b</sup>

Primary alcohols are less reactive than secondary alcohols and need higher molar amounts of  $\text{H}_2\text{O}_2$  to give carboxylic acids. We have found that for those reactions, it was necessary to use 5 molar amounts of  $\text{H}_2\text{O}_2$  per alcohol to obtain satisfactory yields. When smaller amounts of  $\text{H}_2\text{O}_2$  were used, the final reaction mixtures contained unchanged alcohol, aldehyde, and, as the main products, dimeric esters. For example, during the oxidation of

**Table** Results of the Oxidation of Alcohols with Aqueous Hydrogen Peroxide<sup>a,b</sup>

Alcohol Structure	Amount [mmol]	Time [min]	Product Structure	Yield <sup>c</sup> [%]
<b>Primary Alcohols</b>				
	20	20		75
	15	20		80
	13	20		60
	18	20		84
<b>Secondary Alcohols</b>				
	15	10		94
	14	10		97
	18	10		92
	23	10		94
	20	10		77

<sup>a</sup>All the products were characterized by analytical and spectroscopic data;

<sup>b</sup>Under conventional conditions in the same temperature and time regime the reactions afforded mixtures of desired product and unreacted starting alcohol for example, the oxidations of 2-octanol and benzyl alcohol gave the mixtures of 2-octanone and 2-octanol in the molar ratio 1.6:1 and benzoic acid, benzaldehyde and benzyl benzoate in molar ratio 6:4.5:1, respectively; <sup>c</sup>Yield of isolated product

octanol-1 (octanol:Na<sub>2</sub>WO<sub>4</sub>: TBAHS:H<sub>2</sub>O<sub>2</sub> molar ratio 17:1:1:51) we obtained a mixture of 1-octanol, octanal-1, octyl octanoate, and octanoic acid in a ratio of 43:6:43:6. In contrast, secondary alcohols do not need these high amounts of H<sub>2</sub>O<sub>2</sub> and, in all cases, the molar ratio of alcohol to H<sub>2</sub>O<sub>2</sub> was adjusted to 1:1.6. The higher reactivity of secondary alcohols allows to oxidise them selectively even in the presence of primary hydroxyl group using a molar ratio diol:H<sub>2</sub>O<sub>2</sub> 1:1.6. For instance, the oxidation of 2-ethyl-1,3-hexanediol selectively gave 2-ethyl-1-hydroxy-3-hexanone in 97% yield (Table).

We have shown that the microwave protocol like the conventional one retains the alcohol/olefin chemoselectivity.<sup>4</sup> It was found that under microwave irradiation the epoxidation of olefins did not proceed at all. When olefins (i.e., 1-decene or 1-dodecene) and secondary alcohols in molar ratio 1:1 were added to the reaction mixtures, the olefins were recovered from the mixture with < 95% yield; furthermore, even small amounts of epoxides were not detected.

As far as the biphasic oxidation with aqueous H<sub>2</sub>O<sub>2</sub> is concerned the use of lipophilic quaternary ammonium salts is crucial for the process.<sup>4,13</sup> We have shown that in the mi-

crowave-assisted reactions there is no need for the preparation of such ammonium salts, and they could be successfully substituted with commercially available TBAHS. However, the test of other common PTC catalysts showed that, like under conventional conditions, the oxidation reactions occur most efficiently in the presence of hydrogen sulfate ions probably because of their sufficient acidity. We have observed only small amounts of 2-octanone in the oxidation of 2-octanol in the presence of triethylbenzylammonium chloride (TEBA), tetrabutylammonium bromide (TBAB), and polyethylene glycol as catalysts.

In conclusion, we have described a highly efficient the microwave-induced modification of Noyori's procedure for the oxidation of alcohols that allows for the rapid synthesis of carboxylic acid or ketones. The advantages of this environmentally benign and safe protocol include a simple reaction set-up, application of commercially available 30% aqueous hydrogen peroxide and catalysts, high product yields, short reaction times as well as the elimination of solvents and inorganic solid supports.

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- (11) The experiments can be done in a household microwave oven provided that the oven has to be modified and equipped with an upright condenser. The use of condenser is obligatory because, as in the most oxidation process, without accurate temperature and power adjustment the reactor can go out of control.
- (12) **a) The oxidation of 1-octanol is representative of the general procedure employed for primary alcohols:** The mixture of 1-octanol (2.6 g, 20 mmol),  $\text{Na}_2\text{WO}_4 \cdot 2\text{H}_2\text{O}$  (0.26 g, 0.79 mmol), TBAHS (0.27 g, 0.80 mmol), and 30% aqueous  $\text{H}_2\text{O}_2$  (11.3 g, 100 mmol) was irradiated and heated to 90 °C in the microwave reactor by the time indicated in the Table. At the end of the exposure to microwaves, the mixture was cooled to room temperature and 50 mL of aq.  $\text{Na}_2\text{CO}_3$  (20% w/w) was added followed by the extraction with AcOEt (2 × 20 mL). Then the aqueous phase was acidified with an aq. HCl, and extracted with AcOEt (2 × 20 mL) again. The organic phase was dried over  $\text{MgSO}_4$  and the evaporation of the solvent afforded crude octanoic acid, which was purified by Kugelrohr distillation. Yield 2.3 g (80%); **b) The oxidation of 2-octanol is representative of the general procedure employed for secondary alcohols:** The mixture of 2-octanol (1.95 g, 15 mmol),  $\text{Na}_2\text{WO}_4 \cdot 2\text{H}_2\text{O}$  (0.19 g, 0.58 mmol), TBAHS (0.20 g, 0.59 mmol), and 30% aqueous  $\text{H}_2\text{O}_2$  (2.72 g, 24 mmol) was irradiated and heated to 100 °C in the microwave reactor by the time indicated in Table 1. At the end of the exposure to microwaves, the mixture was cooled to the room temperature and extracted with AcOEt (2 × 20 mL). The organic phase was then dried over  $\text{MgSO}_4$  and evaporation of the solvent gave crude 2-octanone which was purified by Kugelrohr distillation. Yield 1.9 g (94%).
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Article Identifier:

1437-2096,E;2000,0,01,0143,0145,ftx,en;G24599ST.pdf