

# A Versatile Method for the Hydrogen Peroxide Oxidation of Alcohols Using PTC Condition in *tert*-Butanol

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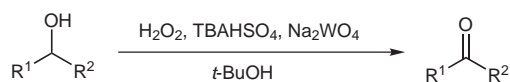
Dedicated to Prof. Sukh Dev, FNA.

**Abstract:** An efficient protocol for the oxidation of secondary and primary alcohols to the corresponding ketones and aldehydes and/or carboxylic acids using hydrogen peroxide as oxidant is described. A quasi-homogenous reaction system was obtained by *t*-butanol as solvent to achieve high yield of the product in short time.

**Key words:** oxidation, alcohols, hydrogen peroxide, sodium tungstate, phase transfer catalyst

Oxidation of alcohols to the corresponding aldehydes, carboxylic acids and ketones is one of the most important functional group transformations in organic synthesis.<sup>1</sup> Many catalyst systems, particularly those based on transition metal and heavy metal ions, are used for the oxidation of alcohols to the corresponding carbonyls.<sup>2</sup> Hydrogen peroxide is probably the best oxidant after dioxygen with respect to environmental and economic considerations.<sup>3</sup> H<sub>2</sub>O<sub>2</sub> oxidations catalyzed by easily available heteropolyanions and heteropolyacids such as Na<sub>2</sub>WO<sub>4</sub>, H<sub>2</sub>WO<sub>4</sub> and ammonium molybdate, constitute an environment friendly, feasible and economical procedure.<sup>4</sup>

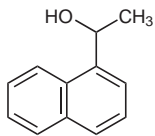
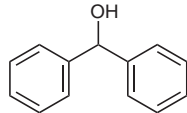
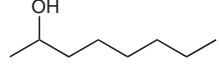
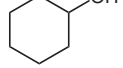
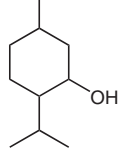
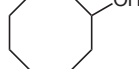
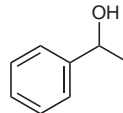
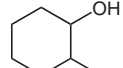
Recently, Noyori et al. have reported alcohol oxidation using sodium tungstate and methyl trioctyl ammonium hydrogen sulfate [CH<sub>3</sub>(*n*-C<sub>8</sub>H<sub>17</sub>)<sub>3</sub>N<sup>+</sup>HSO<sub>4</sub><sup>-</sup>(Q<sup>+</sup>HSO<sub>4</sub><sup>-</sup>)] as phase transfer catalyst (PTC) under heterogeneous conditions.<sup>5</sup> However, the choice of the phase transfer catalyst is critical; selection is made through trial and error and methyltrioctylammonium hydrogen sulfate required in this system is relatively costly. As the system is heterogeneous, the time required for completion of the reaction is generally long even at a very high stirring speed.<sup>6</sup> We report here a general method for the oxidation of alcohols in quasi-homogeneous mixture using easily available and cheap PTC tetrabutyl ammonium hydrogen sulfate (Schemes 1 and 2).



**Scheme 1** Oxidation of secondary alcohols with hydrogen peroxide in *tert*-butanol

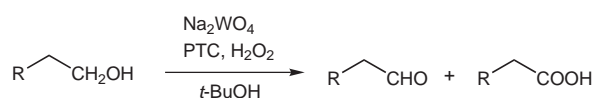
Reactions were performed by dissolving alcohols in *tert*-butanol, followed by addition of sodium tungstate and tetrabutyl ammonium hydrogen sulfate. The reaction mixture was heated to 90 °C and addition of 30% solution of hydrogen peroxide gave the respective carbonyl product in high yield. Reactions were monitored by gas chromatography and yields are based on the starting alcohol used (Tables 1 and 2).

**Table 1** Oxidation of Secondary Alcohols

| Entry | Alcohol  | Time (min) | Yield (%) |
|-------|--|------------|-----------|
| 1     |   | 30         | 98        |
| 2     |  | 30         | 100       |
| 3     |  | 30         | 100       |
| 4     |  | 30         | 100       |
| 5     |  | 30         | 89        |
| 6     |  | 30         | 100       |
| 7     |  | 30         | 100       |
| 8     |  | 30         | 100       |

Simple secondary alcohols have been converted to ketones under quasi-homogeneous condition using 30%  $\text{H}_2\text{O}_2$  (1:1.5 alcohol- $\text{H}_2\text{O}_2$ ) at 90 °C (Scheme 1). Diphenyl methanol was oxidized using substrate- $\text{H}_2\text{O}_2$ -PTC in 20:30:1:1 ratio to yield 100% diphenyl ketone within 30 minutes. Another advantage of this method is that 1-(1-naphthyl)ethanol, diphenyl methanol, 2-octanol, cyclohexanol, cyclooctanol, 1-phenyl ethanol and 2-methylcyclohexanol could be converted in 100% yield to the respective ketones in 30 minutes (Table 1).

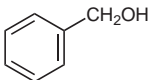
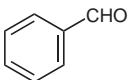
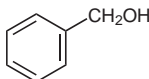
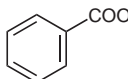
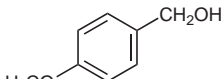
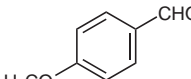
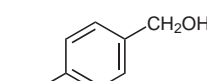
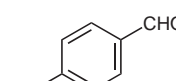

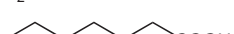
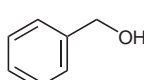
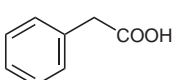
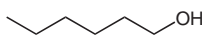
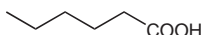
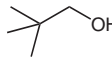
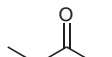
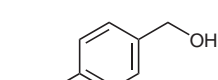
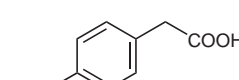
In a similar way, oxidation of benzylic alcohols gave the respective aldehydes or acids in good yield (Scheme 2). Benzyl alcohol was converted to benzaldehyde in 75% yield by slow addition of 1.5 equivalents of hydrogen peroxide.



**Scheme 2** Oxidation of primary alcohols with hydrogen peroxide in *tert*-butanol

Benzoic acid was obtained in 100% yield with 2 equivalents of hydrogen peroxide. Further substitution of the aromatic ring influenced the final product yield. *p*-Methoxybenzyl alcohol was converted to 87% *p*-methoxybenzaldehyde in four hours, the remaining material being unreacted alcohol and further conversion to acid did not occur; whereas *p*-nitrobenzyl alcohol was converted into *p*-nitrobenzaldehyde (62%) and *p*-nitrobenzoic acid (30%). Non-benzylic primary alcohols on oxidation under similar conditions (Table 2, entry 5–8) were directly converted to their respective carboxylic acids with the intermediate carbonyls being detected in trace quantities. For example, 1-heptanol on oxidation with 1.5 equivalents of hydrogen peroxide gave heptanoic acid as the major product with only traces of heptanal. Slow or portion-wise addition of hydrogen peroxide led to similar results. In comparison to secondary alcohols, primary alcohols in general appeared to be less reactive towards oxidation. This is the first time that tertiary butanol has been used as a solvent for the oxidation of alcohols using the  $\text{Na}_2\text{WO}_4$  system. By rendering the reaction mixture semi-homogeneous, total reaction time decreases appreciably.

**Table 2** Oxidation of Primary Alcohols

| Entry | Substrate   | Product   | Reaction conditions<br>alcohol- $\text{H}_2\text{O}_2$ - $\text{Na}_2\text{WO}_4$ -PTC | Yield (%)       |
|-------|---|---|--|-----------------|
| 1     |  |  | 20:30:1:1 (8 h)  | 75 <sup>a</sup> |
| 2     |  |  | 20:40:1:1  | 100             |
| 3     |  |  | 20:30:1:1  | 87 <sup>b</sup> |
| 4     |  |  | 20:40:1:1 (18 h)<br>100:200:1:2 (18 h)   | 62<br>52        |
| 5     |  |  | 20:50:1:1  | 89 <sup>c</sup> |
| 6     |  |  | 20: 40: 1:1  | 84              |
| 7     |  |  | 20:50:1:1  | 87              |
| 8     |  |  | 20:50:1:1  | 59 <sup>d</sup> |
| 9     |  |  | 20:50:1:1  | 87              |

<sup>a</sup> Remaining 25%: benzoic acid.

<sup>b</sup> Rest is unreacted alcohol.

<sup>c</sup> Remaining 11%: heptanal.

<sup>d</sup> Yield calculated on basis of  $^1\text{H}$  NMR spectroscopy and GC.

Another advantage of *tert*-butanol is that it has a better range of solubility for organic compounds than hydrocarbons, which were used earlier as solvents. Hence the use of *tert*-butanol in our system makes the reaction easier and faster giving 100% conversion of alcohols into ketones within one hour as compared to the earlier reports where these reactions were taking place in 4–8 hours.

In conclusion, we describe herein an efficient protocol for oxidation of primary and secondary alcohols with hydrogen peroxide in quasi-homogenous system. This protocol is high yielding, clean, safe, operationally simple and cost effective.

#### Representative Procedure

Diphenylmethanol (1.84 g, 10 mmol), sodium tungstate (164 mg, 0.5 mmol) and tetrabutyl ammonium hydrogen sulfate (169 mg, 0.5 mmol) were taken in *t*-BuOH (2 mL). The reaction mixture was heated to 90 °C and H<sub>2</sub>O<sub>2</sub> added (30% soln, 1.72 mL, 15 mmol) drop-wise with rapid stirring. On complete addition of H<sub>2</sub>O<sub>2</sub>, small aliquots (10 µL) of reaction mixture were taken at different time intervals and monitored by gas chromatography.

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#### References

- (1) (a) Sheldon, R. A.; Kochi, J. K. *Metal-Catalyzed Oxidation of Organic Compounds*; Academic Press: London, **1981**. (b) Ley, S. V.; Madin, A. In *Comprehensive Organic Synthesis*, Vol 7; Trost, B. M.; Fleming, I., Eds.; Pergamon: Oxford, **1991**, 305–327. (c) Hollingwarth, G. J. In *Comprehensive Organic Functional Group Transformations*, Vol. 3; Katritzky, A. R.; Meth-Cohn, O.; Rees, C. W.; Pattenden, G., Eds.; Elsevier Science Ltd.: Oxford, **1995**, 81–109. (d) Hains, A. H. *Methods for the Oxidation of Organic Compounds*; Academic Press: New York, **1988**.
- (2) For an overview of alcohol oxidation catalysis, see: (a) Muzart, J. *Chem. Rev.* **1992**, *92*, 113. (b) Seddon, K. R.; Stark, A. *Green Chem.* **2002**, *4*, 119. (c) Shaabani, A.; Mirzaei, P.; Lee, D. G. *Catal. Lett.* **2004**, *97*, 119. (d) Chhikara, B. S.; Chandra, R.; Tandon, V. *Tetrahedron Lett.* **2004**, *45*, 7585. (e) Wan, Q. *Synlett* **2004**, 1847. (f) Adak, A. K. *Synlett* **2004**, 1651. (g) Oba, M.; Endo, M.; Nishiyama, K.; Ouchi, A.; Ando, W. *Chem. Commun.* **2004**, *10*, 1672. (h) Moorthy, J. N.; Singhal, N.; Venkatakrishnan, P. *Tetrahedron Lett.* **2004**, *45*, 5419. (i) Lee, J. C.; Lee, J. Y.; Lee, S. J. *Tetrahedron Lett.* **2004**, *45*, 4939. (j) Guo, M.-L. *Green Chem.* **2004**, *6*, 271. (k) Reddy, S. R.; Das, S.; Punniyamurthy, T. *Tetrahedron Lett.* **2004**, *45*, 3561. (l) Bressette, A. R.; Glover, L. C. I. V. *Synlett* **2004**, 738. (m) Chhikara, B. S.; Tehlan, S.; Kumar, A. *Synlett* **2005**, 63. (n) Pillai, U. R.; Sahle-Demessie, E. *Green Chem.* **2004**, *6*, 161. (o) Velusamy, S.; Punniyamurthy, T. *Org. Lett.* **2004**, *6*, 217. (p) Tehlan, S.; Hundal, M. S.; Mathur, P. *Inorg. Chem.* **2004**, *43*, 6589.
- (3) (a) Jones, C. W. *Application of Hydrogen Peroxide and Derivatives*; MPG Books Ltd.: Cornwall UK, **1999**. (b) Jorgensen, K. A. *Chem. Rev.* **1989**, *89*, 431. (c) Jones, C. W. *Application of Hydrogen Peroxide and Derivatives*; Royal Society of Chemistry: Cambridge, **1999**. (d) *Catalytic Oxidations with Hydrogen Peroxide as Oxidant*; Strukul, G., Ed.; Kluwer Academic: Dordrecht The Netherlands, **1992**.
- (4) For selected peroxometalate-catalyzed oxidation examples, see: (a) Schultz, H. S.; Freyermuth, H. B.; Buc, S. R. *J. Org. Chem.* **1963**, *28*, 1140. (b) Ishi, Y.; Tanaka, H.; Nisiyama, Y. *Chem. Lett.* **1994**, 1. (c) Stec, Z.; Zawadiac, J.; Skibinski, A. C.; Nogueira, H. I. S.; Parkin, B. C. *J. Mol. Catal.* **1997**, *117*, 185. (d) Ventruello, C.; Gambaro, M. *J. Org. Chem.* **1991**, *56*, 5924. (e) Arends, I. W. C. E.; Sheldon, R. A.; Wallau, M.; Schuchardt, U. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1144. (f) Zennaro, R.; Pinna, F.; Strukul, G.; Arzoumanian, H. *J. Mol. Catal.* **1991**, *70*, 269.
- (5) (a) Noyori, R.; Aoki, M.; Sato, K. *Chem. Commun.* **2003**, 16, 1977. (b) Sato, K.; Takagi, J.; Aoki, M.; Noyori, R. *Tetrahedron Lett.* **1998**, *39*, 7549. (c) Sato, K.; Aoki, M.; Takagi, J.; Noyori, R. *J. Am. Chem. Soc.* **1997**, *119*, 12386. (d) Sato, K.; Aoki, M.; Takagi, J.; Zimmermann, K.; Noyori, R. *Bull. Chem. Soc. Jpn.* **1999**, *72*, 2287. (e) Sato, K.; Hyodo, M.; Takagi, J.; Aoki, M.; Noyori, R. *Tetrahedron Lett.* **2000**, *41*, 1439.
- (6) Lane, B. S.; Burgess, K. *Chem. Rev.* **2003**, *103*, 2457.