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The Dual Roles of Oxodiperoxovanadate Both as a Nucleophile and an Oxidant in the Green Oxidation of Benzyl Alcohols or Benzyl Halides to Aldehydes and Ketones

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Sulfoxides and tertiary amine oxides have similar structures in that the oxygen atom is partially negatively charged. Both can react as a nucleophilic oxidant toward halides, which are converted into aldehydes or ketones. Recently, we found that dimethylsulfoxide (DMSO) is capable of oxidizing benzyl alcohols to benzaldehydes in high yields when catalyzed by acid. DMSO is believed to function as a nucleophilic oxidant.[1] Traditionally, Mn^{+4}, Mn^{+6}, Cr^{+6}, and Fe^{+6} reagents are the commonly used oxidants for alcohols.[2,3] These reagents must be used in stoichiometric amounts and yield side products that require costly disposal. In these oxidations, the metal oxides or metalates react as an electrophile toward the alcohols in most of the cases.[3] Similarly, the peroxides of $NaMoO_4$ and Na_2WO_4, which are excellent catalysts in the oxidation of alcohol by H_2O_2, were proposed to act as an electrophile towards alcohols.[4]

Vanadium peroxide was reported to be involved in a number of reactions[5] such as the oxidation of ethanol to

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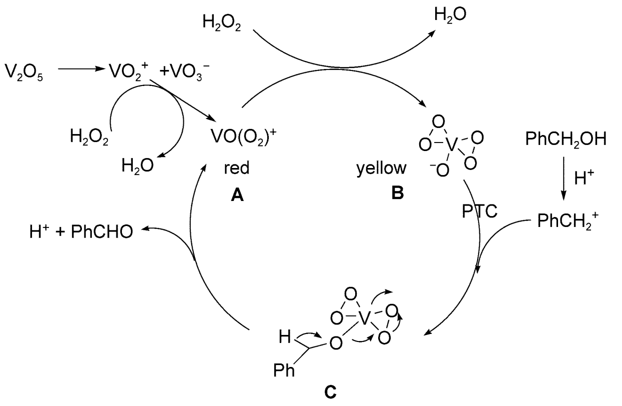
acetaldehyde, and 2-propanol to acetone with H_2O_2 and $VO(OiPr)_3$,[6] the oxidation of alcohols to aldehydes or ketones by using H_2O_2 and vanadium silicate xerogel,[7] and the aerobic oxidation of propargylic alcohols to ketones catalyzed by $VO(acac)_2$ (Hacac = acetylacetone).[8] The discovery of vanadium bromoperoxidase (V–BrPO) in marine organisms has stimulated more active research on vanadium peroxide chemistry.[5,8–12] Although it is well documented that under acidic conditions V_2O_5 can be oxidized by H_2O_2 into vanadium peroxide,[5] there is no report of the oxidation of alcohols with H_2O_2 catalyzed by V_2O_5. We envisioned that $VO(O_2)_2^-$ could behave in a similar way to DMSO as a nucleophilic oxidant toward alcohols (Scheme 1). But this type of reaction has never been reported in the literature for metalates.



Scheme 1. Proposed mechanism for the oxidation of alcohols with H_2O_2 catalyzed by V_2O_5 and PTC.

In addition, the oxidation of benzyl halides to aldehydes is a significant reaction because aromatic aldehydes are used widely. For example, benzaldehyde alone produced in the United States, Western Europe, and Japan in 1983 amounted to 19500 tons.[13] There are two major methods of production of aromatic aldehydes in use. The first method is the hydrolysis of benzal chloride. The problem is that benzal chloride is often contaminated by benzyl chloride and trichloromethyl benzene. In addition, benzal chloride is toxic and carcinogenic.[13] The second method is the oxidation of the methyl group on the aromatic ring, which involves the use of complicated equipment and catalysts. The yield for benzaldehyde is only 40–60% and side products such as maleic anhydride, citraconic anhydride, phthalic anhydride, anthraquinone, CO and CO_2 are produced.[13]

Several oxidations of organic halides to carbonyl compounds are known. These include the Hass–Bender reaction,[14] the Sommelet reaction,[15] the Krohnke reaction,[16] the Kornblum reaction,[17] oxidations by using amine N-oxide,[18] the Masaki photooxidation,[19] and oxidations by using $NaIO_4$.[20] Stoichimetric amount of oxidants have to be used in most of these oxidations. Although the Masaki photooxidation offers the advantage that oxygen is used as the oxidant, volatile organic solvents such as acetone or CH_2Cl_2 are also used in the oxidation.

To solve these existing problems, we started our research by treating benzyl alcohol with dilute H_2O_2, V_2O_5 (0.05 equiv), and BTEAB (benzyltriethylammonium bromide; 0.05 equiv) as the catalysts. The reaction did not take place at room temperature or at reflux. On acidification to pH 4 with HBr, HCl, H_2SO_4, or H_3PO_4, the oxidation of benzyl alcohol to benzaldehyde readily took place at 60 °C. Above pH 5 there was almost no oxidation. A plot of TOF against pH indicates that the reaction rate increases with the acidity of the reaction mixture (Figure 1). The reaction mixture was initially red and became yellow as the reaction proceeded. In the work up, the vanadium reagents were removed by simply washing with aqueous NaOH. A total of 15 liquid alcohols were oxidized by dilute aqueous H_2O_2 (1.2 to 2.8 equiv), with V_2O_5 (0.05 equiv), and BTEAB (0.05 equiv) catalysts at 60 °C at pH 2 without the use of any organic solvents. Table 1 presents the reaction times and

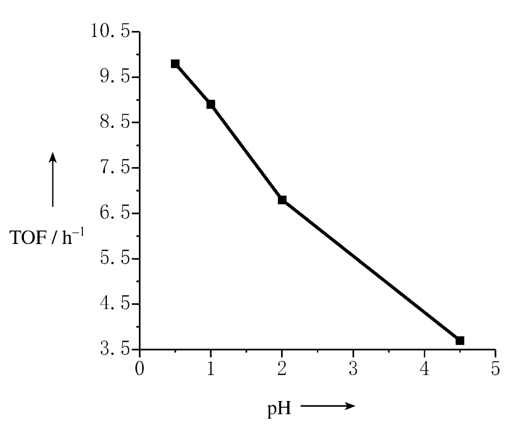


Figure 1. Plot of TOF (h^{-1}) against pH in the oxidation of benzyl alcohol to benzaldehyde using H_2O_2 catalyzed by V_2O_5 and PTC.

Table 1: BTEAB and V_2O_5 catalyzed oxidation of benzyl alcohols to aldehydes or ketones by H_2O_2.

Entry	Alcohol	Time [h]	Yield [%][a]
1	$PhCH_2OH$	6.0	84
2	$PhCH(OH)CH_3$	2.0	81
3	$PhCH(OH)(CH_2)_3CH_3$	1.5	81
4	*p*-$MeOC_6H_4CH_2OH$	8.0	83
5	*p*-$ClC_6H_4CH_2OH$	7.0	84
6	*o*-$ClC_6H_4CH_2OH$	7.5	82
7	*p*-$MeC_6H_4CH_2OH$	10.0	83
8	*o*-$BuOC_6H_4CH_2OH$	7.0	90
		34.0	81
10	2,5-$Br_2C_6H_3CH_2OH$	8.5	87
11	Ph_2CHOH	2.5	88
12	*p*-$ClC_6H_4CH(OH)(CH_2)_3Me$	2.4	85
13	*p*-$MeC_6H_4CH(OH)(CH_2)_3Me$	2.2	87
14	cyclohexanol	30.0	84
15	menthol	36.0	88
16	Menthol[b]	40	0
17	BnCl[c]	6	85

[a] A mixture of benzyl alcohol (0.5 g), H_2O (10 mL), V_2O_5 (0.05 equiv), H_2O_2 (30%, 1.2–2.8 equiv), and BTEAB (0.05 equiv) adjusted to pH 4 with H_2SO_4 and was heated to reflux for the indicated time. After the reaction mixture was cooled to room temperature, it was added to aqueous NaOH (20%, 5 mL) and extracted with ether three times. The organic layer was combined and dried and the solvents were removed by evaporation to give the desired product, which was analyzed by IR and ^{1}HNMR. [b] Aliquat 336 (0.05 equiv) used instead of BTEAB. [c] Benzaldehyde as product.

yields for these reactions. All the alcohols were oxidized into the corresponding aldehydes or ketones with excellent yields. The benzyl alcohols are oxidized much faster than aliphatic alcohols (entries 14 and 15) and secondary alcohols are oxidized faster than primary alcohols (entries 1, 4–8 versus entries 2 and 3). The presence of the electron-withdrawing group on the aromatic ring (entry 9) leads to a lower rate of oxidation of the *m*-nitrobenzyl alcohol.

When the oxidation was performed under a nitrogen atmosphere, a similar reaction rate was observed. The reaction did not proceed under an oxygen atmosphere when hydrogen peroxide was not present. These results indicate that oxygen is not the oxidant in these reactions, although this was proposed by Conte et al. in the oxidation of alcohols by $VO(OiPr)_3$ and oxygen.[21] To determine the effect of bromide, we used *n*-butoxybenzylalcohol as the substrate and replaced BTEAB with Aliquat 336 (0.05 equiv) in both the absence and presence of potassium bromide (0.05 equiv). Both reactions proceeded at almost the same rate (8.5 h), but without the catalytic amount of V_2O_5, the oxidation was very sluggish. This suggests that the primary function of BTEAB is a phase transfer catalyst (PTC) and the oxidation of alcohol by bromine can be ignored.

As indicated in Table 1, the oxidation rate of *m*-nitrobenzyl alcohol is only one fifth that of benzyl alcohol (entry 9 versus entry 1). This suggests that this oxidation does not occur by a radical pathway but most probably by a nucleophilic oxidation pathway (Scheme 1). Under acidic conditions, benzyl alcohol is protonated and produces a benzyl cation, which is attacked by $VO(O_2)_2^-$ to form intermediate **C**. Losing a proton, intermediate **C** decomposes into benzaldehyde. The rate-determining step is the formation of benzyl cation. This is supported by the fact that the secondary benzyl alcohols are oxidized three to four times faster than the primary benzylalcohols and 16 times faster than the aliphatic alcohols.

To further prove the mechanism, we subjected benzyl chloride to the same oxidation conditions. Benzaldehyde was formed in 85 % yield in 6 h. Therefore it is easy to understand why the oxidations of menthol and cyclohexanol occur at much lower reaction rates. When menthol was treated with H_2O_2 (2.5 equiv) catalyzed by V_2O_5 at pH 2 in the presence of Aliquat 336 (0.05 equiv) instead of BTEAB, no reaction took place after 40 h (entry 16). This result suggests that the low concentration of bromine is the oxidant here (entry 15) and $VO(O_2)_2^-$ is not a good enough nucleophile to substitue efficiently the protonated hydroxyl group of aliphatic alcohols. Our attempt at trapping $VO(O_2)_2^-$ with TrCl or TsCl failed, which suggests that $-OV(O_2)_2$ is a very good leaving group and intermediate **C** is extremely unstable.

Therefore, we have for the first time demonstrated the dual roles of $VO(O_2)_2^-$ both as a nucleophile and oxidant toward alcohols. This reaction mechanism is rare among metal oxides and metalate oxidants. We have established a new green oxidation procedure of alcohols with H_2O_2 catalyzed by V_2O_5 and BTEAB. Although several green oxidation procedures of alcohols are known,[22] in most cases expensive metals such as Ru,[23] Pd,[24] Pt,[25] Ir[26] and Rh[27] are used as catalysts. This makes the oxidation process an expensive one. We used H_2O_2 as the oxidant because it has high oxygen content, is inexpensive and stable. V_2O_5 is also inexpensive and stable. Unfortunately, this oxidation is limited to benzyl alcohol because of the unique mechanism related to oxodiperoxovanadate.

To broaden the potential application of oxodiperoxovanadate, we oxidized both primary and secondary benzyl chlorides and bromides to aldehydes and ketones in boiling water using H_2O_2 (1.5 equiv) catalyzed by V_2O_5 (0.05 or 0.1 equiv) and Aliquat 336 (0.05 equiv). The 22 organic halides (Table 2) were all oxidized in good yields to the corresponding aldehydes or ketones. The oxidation is compatible with amides (entry 9), esters (entries 8 and 11), ethers (entries 5, 6, 7 and 13), aryl halides (entries 2, 3, 10, 18 and 11) and phenolic (entries 4 and 12) groups. Primary halide are oxidized faster than secondary halides, which suggests that the $OV(O_2)_2^-$ anion is a bulky nucleophile and is sensitive to steric hindrance. The reaction is faster with benzyl chlorides than with benzyl bromides. A possible reason is that $-OV(O_2)_2$ is such a good leaving group that it is more easily substituted by the better nucleophile, bromide ion, than by the chloride ion. The following equilibrium exists [Eq. (1)].

$$ArCH_2Br + VO(O_2)_2^- \rightleftharpoons ArCH_2OV(O_2)_2 + Br^- \tag{1}$$

A comparative experiment was carried out to verify this. When benzyl chloride was oxidized by H_2O_2 (1.5 equiv) catalyzed by V_2O_5 (0.05 equiv) and Aliquat 336 (0.05 equiv)

Table 2: Oxidation of benzyl halides to aldehydes and ketones by H_2O_2 catalyzed by V_2O_5 and Aliquat 336.[a]

Entry	Benzyl Halide	Time [h]	Yield [%][b]
1	$PhCH_2Cl$	6.0(3.5)	70(90)
2	*p*-$ClC_6H_4CH_2Cl$	6.0 (3.5)	73(90)
3	*o*-$ClC_6H_4CH_2Cl$	7.0	75
4	*o*-$HOC_6H_4CH_2Cl$	5.0	81
5	*o*-$BnOC_6H_4CH_2Cl$	6.0	87
6	*o*-*n*$BuOC_6H_4CH_2Cl$	8.0	82
7	*o*-*i*$BuOC_6H_4CH_2Cl$	11.0	80
8	*o*-$BzOC_6H_4CH_2Cl$	8.0	73
9	*p*-$AcNHC_6H_4CH_2Cl$	6.0	83
10	2,5-$Br_2C_6H_3CH_2Cl$	10.0	82
11	*p*-$BzOC_6H_4CH_2Cl$	8.0	76
12	1-chloromethyl-2-hydroxynaphthalene	13.0	80
13	1-benzyloxy-2-chloromethylnaphthalene	12.0	82
14	PhCHClMe	10.0	77
15	PhCHClEt	10.0	72
16	PhCHClBu	12.0	81
17	*p*-$MeC_6H_4CHClBu$	10.0	78
18	*p*-$ClC_6H_4CHClBu$	12.0	81
19	$PhCH_2Br$[c]	14.0	84
20	*p*-$BrC_6H_4CH_2Cl$	15.0	85
21	1-bromomethylnaphthalene	20.0	75
22	PhCHBrMe	24.0	75

[a] Typical procedure: A mixture of *p*-chlorobenzyl halide (10 g), H_2O (10 mL), H_2O_2 (30%, 1.5 equiv), V_2O_5 (0.005 equiv) and Aliquat 336 (0.05 equiv) was refluxed for 6 h. After cooling to room temperature, the oil layer was separated and distillated to give pure *p*-chlorobenzaldehyde in 73% yield. The aqueous phase was reused for the subsequent oxidation. For the eight subsequent oxidations, the reaction time was 3.5 h and the yield was more than 90%. [b] The conversion for chlorides was quantitative. [c] 0.1 equivalents of V_2O_5 were used for bromide.

and KBr (1.0 equiv), the reaction took 2 h longer than in the absence of KBr (entry 1). In addition, this result agrees well with the fact that the $OV(O_2)_2^-$ anion could not be trapped with TrCl (see above). We also found that $OV(O_2)_2^-$ ion is an excellent catalyst. The separated aqueous phase containing $OV(O_2)_2^-$ ions and PTC was used in the subsequent eight oxidation runs. In the first run of the oxidation of benzyl chloride and *p*-chlorobenzyl chloride, the yield was 70% and 73% respectively, the reaction time was 6 h. In the subsequent eight runs the yield was 90% and the reaction time was shortened to 3.5 h. The reaction is self-accelerated by the accumulated HCl. In the catalytic oxidation of *p*-chlorobenzyl chloride, the substrate/catalyst ratio reached 1000:5 and the reaction rates and the yields remained unchanged.

In our oxidation, only water was used to dilute the H_2O_2, no organic solvents were used in the whole process. This represents the first green oxidation of benzyl halides, which is operationally simple and produces high yields and is well suited for a variety of functionalized benzyl halides. Our new green oxidation reaction provides a better solution for the existing problems in the oxidation of benzyl halides. The conversion of organic chlorides to aromatic aldehydes is quantitative. The yields are more than 90%. The whole process does not need any organic solvents. The two waste products are water and HCl. The latter provides acidic conditions to accelerate the reaction. The catalysts (V_2O_5 and Aliquat 336) are inexpensive, stable and efficient (S/C 1000:5) and can be reused without losing its efficiency.

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[1] C. Li, Y. Xu, M. Lu, Z. Zhao, L. Liu, Z. Zhao, Y. Cui, P. Zheng, X. Ji, G. Gao, *Synlett* **2002**, 2041.
[2] R. C. Larock, *Comprehensive Organic Transformations, Vol. 1*, Wiley, New York, **1999**, pp. 1205–1261.
[3] M. Hudlicky, *Oxidations in Organic Chemistry*, American Chemical Society, Woshington, DC, **1990**, pp. 114–159.
[4] K. Sato, M. Aoki, J. Takagi, K. Zimmermann, R. Noyori, *Bull. Chem. Soc. Jpn.* **1999**, *72*, 2287.
[5] A. Butler, M. J. Clague, G. E. Meister, *Chem. Rev.* **1994**, *94*, 625.
[6] O. Bortolini, V. Conte, F. Di Furia, G. Modena, *Nouv. J. Chim.* **1985**, *9*, 147.
[7] R. Neumann, M. Levin-Elad, *Appl. Catal. A* **1995**, *122*, 85.
[8] Y. Maeda, N. Kakiuchi, S. Matsumura. T. Nishimura. T. Kawamura, S. Uemura, *J. Org. Chem.* **2002**, *67*, 6718.
[9] R. Wever, M. B. E. Krenn in *Vanadium in Biological System* (Ed.: N. D. Chasteen), Kluwer Academic Publishers, Dordrecht, The Netherlands, **1990**, p. 81.
[10] U. Bora, G. Bose. M. K. Chaudhurl, S. S. Dahr, R. Gopinath, A. T. Khan, B. K. Patel, *Org. Lett.* **2000**, *2*, 247.
[11] H. Kelm, H.-J. Krueger, *Inorg. Chem.* **1996**, *35*, 3553.
[12] G. J. Colpas, B. J. Hamstra, J. W. Kampf, V. L. Pecoraro, *J. Am. Chem. Soc.* **1996**, *118*, 3469.
[13] *Ullmann's Encyclopedia of Industrial Chemistry*, 7th ed., Electronic release, Wiley, VCH, **2003**.
[14] R. A. Sheldon, I. W. C. E. Arends, A, Dijksman, *Catal. Today* **2000**, *57*, 157.
[15] R. C. Larock, *Comprehensive Organic Transformations, Vol. 2*, Wiley, New York, **1999**, pp. 1222–1225.
[16] T. Nishimura, T. Onoue, K. Ohe, S. Uemura, *J. Org. Chem.* **1999**, *64*, 6750.
[17] N. Kornblum, W. J. Jones, G. J. Anderson, *J. Am. Chem. Soc.* **1959**, *81*, 4113.
[18] M. G. Edwards, J. M. J. Williams, *Angew. Chem.* **2002**, *114*, 4934; *Angew. Chem. Int. Ed.* **2002**, *41*, 4740.
[19] A. Itoh, T. Kodana, S. Inagaki, Y. Masaki, *Org. Lett.* **2000**, *2*, 2455.
[20] H. B. Hass, M. L. Bender, *J. Am. Chem. Soc.* **1949**, *71*, 1767.
[21] V. Conte, F. Di Furia, G. Modena, *J. Org. Chem.* **1988**, *53*, 1665.
[22] F. Kröhnke, *Angew. Chem.* **1963**, *75*, 317; *Angew. Chem. Int. Ed. Engl.* **1963**, *2*, 380.
[23] a) H. Ji, T. Mizugaki, K. Ebitani, K. Kaneda, *Tetrahedron Lett.* **2002**, *43*, 7179; b) K. Yamaguchi, N. Mizuno, *Angew. Chem.* **2002**, *114*, 4720; *Angew. Chem. Int. Ed.* **2002**, *41*, 4538.
[24] S. Suzuki, T. Onishi, Y. Fujita, H. Misawa, J. Otera, *Bull. Chem. Soc. Jpn.* **1986**, *59*, 3287.
[25] C.-G. Jia, F.-Y. Jing, W.-D. Hu, M.-Y. Huang, Y.-Y. Jiang, *J. Mol. Catal.* **1994**, *91*, 139.
[26] S. Das, A. K. Panigrahi, G. C. Maikap, *Tetrahedron Lett.* **2003**, *44*, 1375.
[27] J. Martin, C. Martin, M. Faraj, J.-M. Bregeault, *Nouv. J. Chim.* **1984**, *8*, 141.