

Vanadium-catalyzed Atmospheric Oxidation of Benzyl Alcohols Using Water as Solvent

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A vanadium complex combined with 4,4'-di-*tert*-butyl-2,2'-bipyridyl as a ligand exhibited excellent catalytic activity in atmospheric oxidation of benzhydrols using water as solvent to afford benzophenones in good yields.

Oxidation of alcohols is one of the most important reactions in organic synthesis. Traditionally, stoichiometric amounts of heavy metal reagents (e.g., chromium(VI)) are used as oxidants. From a green chemical viewpoint, oxidation of alcohols using catalytic amounts of metal complexes in the presence of molecular oxygen (O₂) has attracted much attention in recent years.¹ However, most of the reactions are performed in organic solvent, such as acetonitrile, dichloromethane, and toluene. Water is the most abundant and eco-friendly solvent available. It is also nonflammable, and therefore, oxidation using water as solvent could be cheaper, more eco-friendly, and safer than current oxidation processes in organic solvents.² But examples of metal-complex-catalyzed oxidation of alcohols with O₂ using water as solvent are still rare,^{3–6} and precious metals (e.g., palladium, ruthenium, and gold), high pressure of air or O₂, and a stoichiometric amount of base are often required in the reactions.

Vanadium exists on the surface of the earth more abundantly than copper, and pentavalent vanadium acts as an oxidant. Recently, some vanadium catalyst systems have been developed for the oxidation of alcohols with O₂.⁷ However, there has been no report of an efficient catalytic system with vanadium for aerobic oxidation of alcohols using water as the only solvent under atmospheric conditions.

Herein, we report that oxovanadium complexes bearing bipyridyl derivatives have excellent catalytic activity in oxidation of benzhydrol derivatives using water as the only solvent under an atmospheric pressure of O₂. Furthermore, we found that the vanadium-catalyzed atmospheric oxidation of various benzyl alcohols proceeded successfully by the use of catalytic amounts of benzhydrols as additives.

Oxidation of benzhydrol (**1a**) using different vanadium catalysts and ligands (Figure 1) was examined using water as solvent under O₂ atmosphere (0.1 MPa) at 90 °C, and the results are shown in Table 1. VOSO₄ and VO(Hhpic)₂ were not effective as catalysts for the oxidation (Entries 2 and 3).⁸ Also, 3-hydroxypicolinic acid (H₂hpic) was found to be ineffective as an additional ligand to VOSO₄ (Entry 4). In sharp contrast, when VOSO₄ was combined with 4,4'-di-*tert*-butyl-2,2'-bipyridyl (4,4'-*t*Bubpy), the oxidation of **1a** with atmospheric oxygen proceeded successfully, affording benzophenone (**2a**) in 47% yield (Entry 5). When the reaction time was prolonged to 6 h, the yield of **2a** increased to 83% yield (Entry 6). Among bipyridyl ligands screened (4,4'-*t*Bubpy, 5,5'-Mebpy, 4,4'-Mebpy,

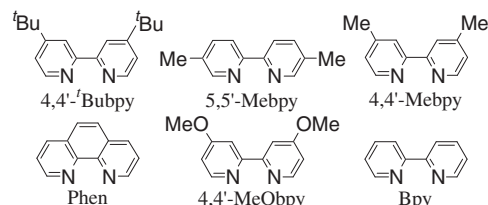


Figure 1. Structures of ligands in Table 1.

Table 1. Catalytic activities for oxidation of benzhydrol with different catalysts and ligands^a

Entry	Catalyst	Ligand	Yield of 2a /%	Recovery of 1a /%
1	None	None	ND	>99
2	VOSO ₄	None	Trace	94
3	VO(Hhpic) ₂	None	ND	>99
4	VOSO ₄	H ₂ hpic	Trace	>99
5	VOSO ₄	4,4'- <i>t</i> Bubpy	47	40
6 ^c	VOSO ₄	4,4'- <i>t</i> Bubpy	83	ND
7 ^c	VOSO ₄	5,5'-Mebpy	76	4
8 ^c	VOSO ₄	4,4'-Mebpy	33	56
9 ^c	VOSO ₄	Phen	22	77
10 ^c	VOSO ₄	4,4'-MeObpy	19	76
11 ^c	VOSO ₄	Bpy	17	76

^aReaction conditions: catalyst (0.005 mmol), ligand (0.01 mmol), benzhydrol (**1a**) (0.1 mmol), H₂O (0.5 mL), O₂ (0.1 MPa), 90 °C, 3 h. ^bDetermined by ¹H NMR. ND: Not detected.

^cReaction time was 6 h.

Phen, 4,4'-MeObpy, and Bpy),⁹ 4,4'-*t*Bubpy was found to be the most effective as a ligand (Entries 6–11).

Various benzhydrol derivatives **1b–1d** bearing electron-withdrawing and electron-donating groups could be oxidized effectively in the presence of catalytic amounts of VOSO₄ and 4,4'-*t*Bubpy using water as solvent under an atmosphere of O₂ (Table 2, Entries 1–5).¹⁰ In the case of the oxidation of 1-phenylethanol (**1f**), however, a trace amount of acetophenone (**2f**) was detected as an oxidation product (85% of **1f** was recovered) (Entry 6). The yield of **2f** slightly increased to 3% by prolonging the reaction time to 22 h, but this condition was not practical. When a catalytic amount of **1a** was employed as an additive, to our surprise, **2f** was obtained in 22% yield in 13 h. As a result of further optimization of the reaction conditions by using sat. MgSO₄(aq)¹¹ and scaling up from 0.1 mmol of

Table 2. Vanadium-catalyzed oxidation of alcohols under O₂

Entry	R ¹	R ²	2	Time/h	Yield/% ^c
1 ^a	Ph	Ph	a	6	83 (87)
2 ^a	4-MeC ₆ H ₄	4-MeC ₆ H ₄	b	8	83
3 ^a	4-MeOC ₆ H ₄	Ph	c	6	83 (84)
4 ^a	4-BrC ₆ H ₄	Ph	d	8	90 (83)
5 ^a	4-NO ₂ C ₆ H ₄	Ph	e	6	86
6 ^a	Ph	Me	f	3	Trace
7 ^b	Ph	Me	f	22	67
8 ^{b,d}	4-MeOC ₆ H ₄	Me	g	22	31
9 ^{b,d}	4-BrC ₆ H ₄	Me	h	22	92
10 ^{b,d}	4-NO ₂ C ₆ H ₄	Me	i	48	75
11 ^{b,d}	2-Thienyl	Me	j	40	48
12 ^{b,d}	Ph	ⁿ Bu	k	23	86 (76)
13 ^{b,d}	Ph	^c Pr	l	22	55
14 ^{b,d}	Ph	^c Hex	m	23	77
15 ^{b,d}	4-MeOC ₆ H ₄	H	n	22	77
16 ^{b,d}	4-BrC ₆ H ₄	H	o	22	65
17 ^{b,d,e}	Ph	H	p	22	24 ^f

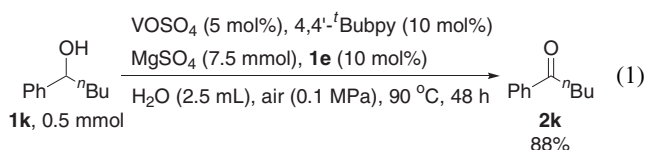
^aReaction conditions: VOSO₄ (0.005 mmol), 4,4'-tBubpy (0.01 mmol), **1** (0.1 mmol), H₂O (0.5 mL), O₂ (0.1 MPa), 90 °C.

^bReaction conditions: VOSO₄ (0.025 mmol), 4,4'-tBubpy (0.05 mmol), **1a** (0.05 mmol), H₂O (2.5 mL), MgSO₄ (7.5 mmol), substrate **1** (0.5 mmol), O₂ (0.1 MPa), 90 °C. ^cDetermined by ¹H NMR. Isolated yields were shown in parentheses.

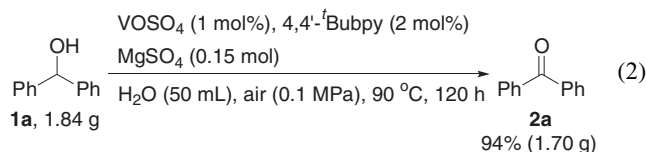
^d**1e** (0.05 mmol) was added instead of **1a**. ^e2.0 mmol scale reaction. ^fBenzoic acid (61%) was obtained as the major product.

substrate to 0.5 mmol, the yield of **2f** increased to 67% yield (Entry 7). In the case of 1-(*p*-substituted phenyl)ethanols **1g–1i** as substrates, *p*-nitrobenzhydrol (**1e**) acted as effective additive and the corresponding ketones **2g–2i** were obtained in moderate to high yields (Entries 8–10). The catalytic system of VOSO₄–4,4'-tBubpy–**1e** could be applied to the oxidation of other secondary benzyl alcohols **1j–1m**, and the oxidation products **2j–2m** were obtained in moderate to good yields, respectively (Entries 11–14). The vanadium-catalyzed oxidation of primary benzyl alcohols also proceeded. In the case of *p*-substituted benzyl alcohols **1n** and **1o** as substrates, the corresponding aldehydes **2n** and **2o** were obtained as the major products (Entries 15 and 16). When benzyl alcohol (**1p**) was employed as substrate, benzoic acid (61%) was generated as the major product (Entry 17).

Furthermore, we examined the catalytic oxidation of 1-phenylpentan-1-ol (**1k**) under air (0.1 MPa). Interestingly, the oxidation of **1k** proceeded successfully by prolonging the reaction time to 48 h, affording the corresponding ketone **2k** in a good yield (eq 1).



In addition, the gram-scale aerobic oxidation of benzhydrol (**1a**) was examined. As a result, benzophenone (**2a**) was obtained in an excellent yield (eq 2).



In conclusion, we found a novel vanadium catalyst system for oxidation of benzyl alcohols using water as the only solvent under an atmospheric pressure of O₂ as the oxidant¹² in the presence of catalytic amounts of benzhydrols.^{13,14} Further studies of the reaction mechanism, role of benzhydrols as additives, catalyst recycling, and application to oxidation of other organic compounds are in progress. Results will be reported in due course.

This research was supported by JST Research Seeds Quest Program (Lower Carbon Society), from the Ministry of Education, Culture, Sports, Science and Technology, Japan, and Kansai Research Foundation for Technology Promotion (KRF). S.K. acknowledges Research Fellowships of the Japan Society for the Promotion of Science (JSPS) for Young Scientists.

References and Notes

- For reviews concerning oxidation reactions of alcohols catalyzed by transition-metal complexes with molecular oxygen, see: a) S.-I. Murahashi, N. Komiya, in *Modern Oxidation Methods*, ed. by J.-E. Bäckvall, Wiley-VCH, Weinheim, **2004**, Chap. 6, pp. 165–191. b) K. M. Gligorich, M. S. Sigman, *Chem. Commun.* **2009**, 3854. c) J. Piera, J.-E. Bäckvall, *Angew. Chem., Int. Ed.* **2008**, *47*, 3506. d) M. J. Schultz, M. S. Sigman, *Tetrahedron* **2006**, *62*, 8227.
- For reviews concerning organic reactions using water as solvent, see: a) R. N. Butler, A. G. Coyne, *Chem. Rev.* **2010**, *110*, 6302. b) A. Chanda, V. V. Fokin, *Chem. Rev.* **2009**, *109*, 725. c) K. H. Shaughnessy, *Chem. Rev.* **2009**, *109*, 643.
- Recently, oxidation reactions of alcohols using water as solvent catalyzed by transition-metal complexes Pd,³ Ru,⁴ Cu,⁵ Au,⁶ with molecular oxygen were reported. a) T. Osako, Y. Uozumi, *Chem. Lett.* **2009**, *38*, 902. b) B. P. Buffin, J. P. Clarkson, N. L. Belitz, A. Kundu, *J. Mol. Catal. A: Chem.* **2005**, *225*, 111. c) G.-J. ten Brink, I. W. C. E. Arends, R. A. Sheldon, *Science* **2000**, *287*, 1636.
- a) N. Komiya, T. Nakae, H. Sato, T. Naota, *Chem. Commun.* **2006**, 4829. b) C. N. Kato, A. Shinohara, N. Moriya, K. Nomiya, *Catal. Commun.* **2006**, *7*, 413.
- P. J. Figiel, M. Leskelä, T. Repo, *Adv. Synth. Catal.* **2007**, *349*, 1173.
- H. Li, B. Guan, W. Wang, D. Xing, Z. Fang, X. Wan, L. Yang, Z. Shi, *Tetrahedron* **2007**, *63*, 8430.
- Oxidation reactions of alcohols using organic solvent,^{7a–7g} ionic liquids as solvent,^{7h} or water as solvent⁷ⁱ catalyzed by oxovanadium complexes with molecular oxygen were reported. a) M. Kirihara, Y. Ochiai, S. Takizawa, H. Takahata, H. Nemoto, *Chem. Commun.* **1999**, 1387. b) Y. Maeda, N. Kakiuchi, S. Matsumura, T. Nishimura, S. Uemura, *Tetrahedron Lett.* **2001**, *42*, 8877. c) Y. Maeda,

- N. Kakiuchi, S. Matsumura, T. Nishimura, T. Kawamura, S. Uemura, *J. Org. Chem.* **2002**, *67*, 6718. d) S. Velusamy, T. Punniyamurthy, *Org. Lett.* **2004**, *6*, 217. e) S. R. Reddy, S. Das, T. Punniyamurthy, *Tetrahedron Lett.* **2004**, *45*, 3561. f) A. T. Radosevich, C. Musich, F. D. Toste, *J. Am. Chem. Soc.* **2005**, *127*, 1090. g) Z. Du, H. Miao, H. Ma, Z. Sun, J. Ma, J. Xu, *Adv. Synth. Catal.* **2009**, *351*, 558. h) N. Jiang, A. J. Ragauskas, *Tetrahedron Lett.* **2007**, *48*, 273. i) Z. Du, J. Ma, H. Ma, J. Gao, J. Xu, *Green Chem.* **2010**, *12*, 590.
- 8 a) M. Nakai, M. Obata, F. Sekiguchi, M. Kato, M. Shiro, A. Ichimura, I. Kinoshita, M. Mikuriya, T. Inohara, K. Kawabe, H. Sakurai, C. Orvig, S. Yano, *J. Inorg. Biochem.* **2004**, *98*, 105. b) S. Kodama, Y. Ueta, J. Yoshida, A. Nomoto, S. Yano, M. Ueshima, A. Ogawa, *Dalton Trans.* **2009**, 9708. c) S. Kodama, J. Yoshida, A. Nomoto, Y. Ueta, S. Yano, M. Ueshima, A. Ogawa, *Tetrahedron Lett.* **2010**, *51*, 2450.
- 9 a) J. Selbin, *Chem. Rev.* **1965**, *65*, 153. b) H. Sakurai, H. Tamura, K. Okatani, *Biochem. Biophys. Res. Commun.* **1995**, *206*, 133. c) O. J. D'Cruz, Y. Dong, F. M. Uckun, *Biol. Reprod.* **1999**, *60*, 435. d) G. D. Triantafillou, E. I. Tolis, A. Terzis, Y. Deligiannakis, C. P. Raptopoulou, M. P. Sigalas, T. A. Kabanos, *Inorg. Chem.* **2004**, *43*, 79. e) M. Salavati-Niasari, M. R. Elzami, M. R. Mansournia, S. Hydarzadeh, *J. Mol. Catal. A: Chem.* **2004**, *221*, 169. f) C. R. Waidmann, A. G. DiPasquale, J. M. Mayer, *Inorg. Chem.* **2010**, *49*, 2383.
- 10 We examined the oxidation of **1a** by addition of a radical inhibitor, 2,6-di-*tert*-butylphenol (10 mol % of substrate), according to the conditions of Table 2, Entry 1. As a result, **1a** was completely consumed after 6 h, and **2a** was obtained in 84% yield. This suggests that our vanadium-catalyzed aerobic oxidation of benzyl alcohols using water as solvent might not involve a radical pathway.^{7b,7c}
- 11 In our reaction system, VOSO₄ was soluble in water, but in contrast, ligands and substrates were insoluble in water, and these materials floated on the aqueous solution of vanadium before heating the reaction mixture. The complexation of vanadium with ligands started by heating the mixture to form the vanadium complex with ligands. This complex was insoluble in water but soluble in alcohols (substrates). From these results, we presume that the present oxidation reaction proceeds in organic layer. Therefore, we expected that the oxidation on water would proceed smoothly by using sat. MgSO₄(aq) as solvent to inhibit partial transfer to the aqueous layer. Actually, we found that the yields of oxidation products increased. Hence, we feel that the high concentration of SO₄²⁻ ion or Mg²⁺ ion is desirable in our reaction system.
- 12 A weak and broad peak was detected at ca. -510 ppm by taking ⁵¹V NMR spectra (CDCl₃) of the reaction mixture after the reaction, under the conditions of Table 2, Entry 1. From this, we assume the formation of vanadium(V) species in this reaction.⁷ⁱ VOSO₄ is vanadium(IV) species, and vanadium(V) species may be formed by oxidation of vanadium(IV) species with molecular oxygen. There is a possibility that the vanadium(V) species acts as active species in the oxidation reaction.
- 13 Time course change of the vanadium-catalyzed oxidation of 1-phenylethanol (**1f**) using a catalytic amount of benzhydrol (**1a**) as an additive was investigated by taking ¹H NMR spectra. As a result, the yield of acetophenone (**2f**) continued to increase after consuming **1a** completely. Also, benzophenone (**2a**) was generated from the oxidation of **1a**. Hence, we examined the oxidation of **1f** using **2a** as an additive, but the reaction scarcely proceeded. In addition, the substituents on aromatic rings of benzhydrols as additives may affect the activity of vanadium catalysts, because the oxidation of **1h** using **1a** as an additive instead of *p*-nitrobenzhydrol (**1e**), under the conditions of Table 2, Entry 9, proceeded slowly to afford **2h** (22 h, 51%). From these results, we believe that benzhydrols may act as ligands for the vanadium complexes to improve catalytic activity in our reaction system.
- 14 Supporting Information is available electronically on the CSJ-Journal Web site, <http://www.csj.jp/journals/chem-lett/index.html>.