

Tetranuclear vanadium complex, $(VO)_4(\text{hpic})_4$: a recyclable catalyst for oxidation of benzyl alcohols with molecular oxygen

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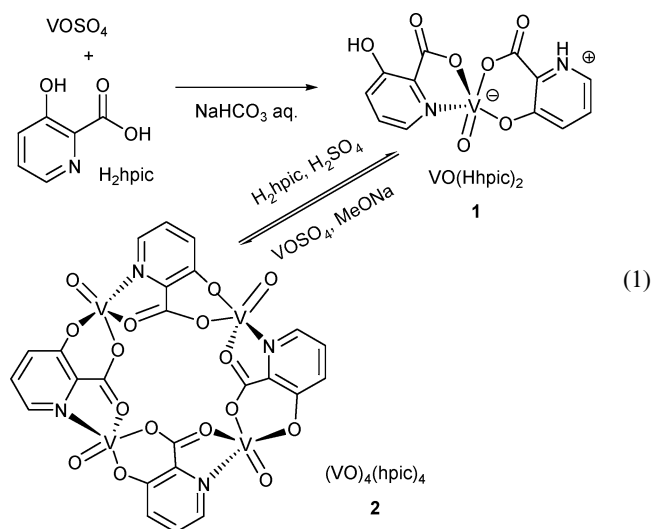
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Vanadium(IV) complexes bearing 3-hydroxypicolinic acid (H_2hpic) as ligands, $\text{VO}(\text{Hhpic})_2$ (**1**) and the cyclic tetramer $(\text{VO})_4(\text{hpic})_4$ (**2**), have excellent catalytic ability for the oxidation of a variety of primary and secondary benzyl alcohols with molecular oxygen in acetonitrile or protic solvents such as ethanol and water, affording the corresponding aldehydes and ketones, respectively. Construction of multi-nuclear complexes by the selection of ligands attains higher turnover numbers and recycling of the catalyst.

Highly selective oxidation of organic compounds is a fundamental transformation in synthetic organic chemistry.¹ In recent years, considerable efforts have been devoted to the development of transition-metal-catalyzed oxidation systems of organic compounds with molecular oxygen as the oxidant.^{2–10} However, expensive metals (*e.g.* palladium and ruthenium) and toxic organic solvents have been traditionally used to accomplish most of these oxidation systems. Vanadium exists on the surface of the earth more abundantly than copper, palladium, or ruthenium, and pentavalent vanadium complexes, vanadium(V), act as oxidants.^{2a} In addition, there is great interest in the coordination chemistry of vanadium because vanadium plays an important role in various biological systems, and in particular, vanadium(V) is stereochemically flexible.¹¹ Vanadium(IV) complexes **1** and **2** were synthesized and characterized by Yano *et al.* in 2002 (eqn (1)).¹² The tetranuclear vanadium complex **2** is of interest as a new catalyst for oxidation of organic substrates. This is because its unique robust structure is the first example of a vanadium molecular square, and it may be possible to use **2** as a recyclable catalyst. In addition, the ligand 3-hydroxypyridine-2-carboxylic acid (3-hydroxypicolinic acid, H_2hpic) has a good affinity for water, and therefore it is expected that **2** will have catalytic activity in non-toxic protic solvents such as ethanol and water.^{5f}

Herein, we report the catalytic activity of vanadium complexes **1** and **2** in the oxidation of benzyl alcohols using molecular oxygen for the purpose of developing a new green oxidation system in organic chemistry.

Firstly, we examined the catalytic activity of vanadium complexes **1** and **2** and other vanadium complexes using benzyl alcohol



as the substrate and molecular oxygen as the co-oxidant. The oxidation of benzyl alcohol (1.5 mmol) was conducted under oxygen pressure (1.0 MPa) at 120 °C for 3 h in the presence of various vanadium complexes (2 mol%) in acetonitrile (6 mL) using a 50 mL stainless steel autoclave (Table 1).[†]

Commercially available vanadium complexes such as V_2O_5 and VOSO_4 did not show any catalytic activity towards the oxidation of benzyl alcohol under these reaction conditions (entries 1 and 2). When $\text{VO}(\text{acac})_2$ and $\text{VO}[\text{OCO}(\text{CH}_2)_{16}\text{CH}_3]_2$ were employed as the catalysts, benzaldehyde was formed in low yields (entries 4 and 5).

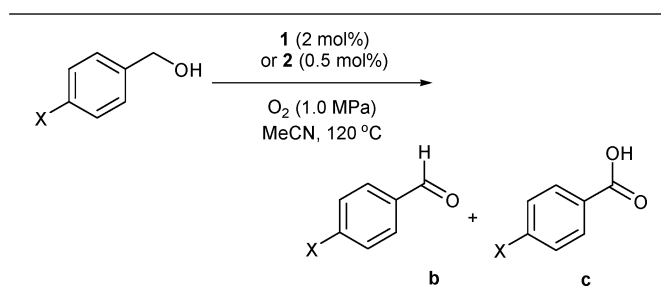
Table 1 Oxidation of benzyl alcohol using various vanadium complexes

Entry	Catalyst	V (mol%)	Solvent	Yield (%) ^a	
				b	c
1	V_2O_5	2	MeCN	—	—
2	VOSO_4	2	MeCN	—	—
3	$\text{VO}(\text{OEt})_3$	2	MeCN	Trace	—
4	$\text{VO}(\text{acac})_2$	2	MeCN	17	—
5	$\text{VO}[\text{OCO}(\text{CH}_2)_{16}\text{CH}_3]_2$	2	MeCN	12	—
6	$\text{VO}(\text{Hhpic})_2$ (1)	2	MeCN	61	—
7	$(\text{VO})_4(\text{hpic})_4$ (2)	0.5	MeCN	62	—
8	$\text{VO}(\text{Hhpic})_2$ (1)	2	EtOH	36	29
9	$(\text{VO})_4(\text{hpic})_4$ (2)	0.5	EtOH	49	22

^a GC yield.

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Table 2 Oxidation of various benzyl alcohols using **1** or **2**

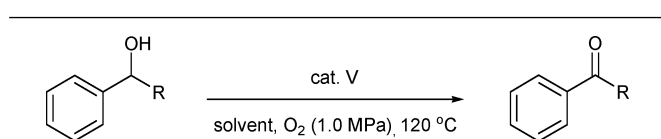
Entry	X	Catalyst	Time/h	Yield (%) ^a	
				b	c
1	H	1	3	(61)	—
2	H	2	3	(62)	—
3	Me	1	6	(86)	(2)
4	Me	2	3	(75)	—
5	OMe	1	4	92	—
6	OMe	2	3	39	—
7	Cl	1	9	82	11
8	Cl	2	3	52	32
9	NO ₂	1	9	88	Trace
10	NO ₂	2	3	91	6

^a Isolated (GC) yield.

In contrast, the oxidation of benzyl alcohol in the presence of the vanadium complex catalysts **1** and **2** gave benzaldehyde selectively in good yields (entries 6 and 7). When ethanol was employed as solvent, the over-oxidation of benzaldehyde was observed to afford benzoic acid (entries 8 and 9).

Catalysts **1** and **2** also catalyzed the oxidation of various benzyl alcohols bearing electron-withdrawing and electron-donating groups in acetonitrile (Table 2). In most cases, the corresponding aldehydes were provided selectively, and no formation of over-oxidation products (carboxylic acids) was observed.

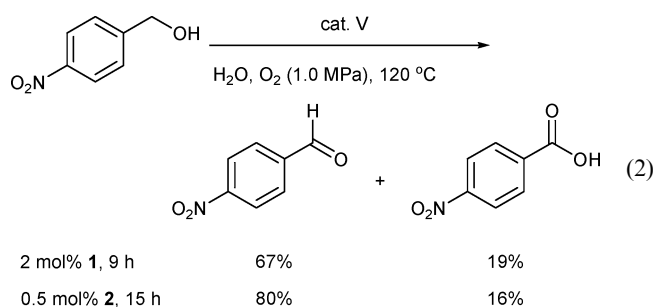
In addition, various secondary benzyl alcohols could be oxidized by the use of **1** or **2** as catalysts (Table 3). Compared with the results of oxidation in acetonitrile, the oxidation in ethanol successfully proceeded in a shorter reaction time with higher yields of the corresponding ketones.

Table 3 Oxidation of secondary benzyl alcohols using **1** or **2** in acetonitrile or ethanol

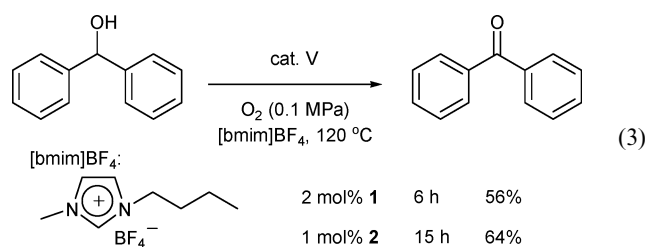
Entry	R	Time/h	Catalyst (mol%)	Solvent	Yield (%) ^a
1	Ph	15	1 (2)	MeCN	51
2	Ph	40	1 (2)	MeCN	71
3	Ph	15	1 (2)	EtOH	(90)
4	Ph	15	2 (0.5)	EtOH	(89)
5	Me	15	1 (2)	MeCN	51
6	Me	12	1 (2)	EtOH	(88)
7	Me	15	2 (0.5)	EtOH	(83)
8	<i>i</i> -Pr	12	1 (2)	EtOH	98
9	<i>i</i> -Pr	15	2 (0.5)	EtOH	59

^a Isolated (GC) yield.

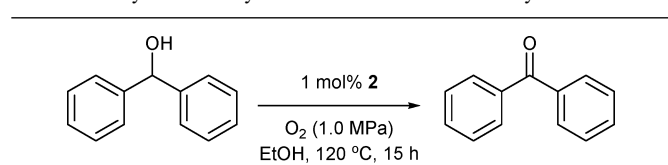
Furthermore, we examined the catalytic oxidation reaction in water as water is a more environmentally friendly solvent. Interestingly, vanadium complexes **1** and **2** exhibited excellent catalytic activity towards the oxidation of *p*-nitrobenzyl alcohol in water (eqn (2)).



Recently, ionic liquids have attracted much attention as green solvents in organic syntheses. When we examined the oxidation of benzhydrol using the ionic liquid [bmim]BF₄^{13,14} as solvent in the presence of vanadium catalysts **1** and **2**, the desired oxidation of benzhydrol proceeded under an atmosphere of oxygen, affording benzophenone in 56% and 64% yields, respectively (eqn (3)).



Vanadium complexes **1** and **2** are soluble in polar solvents like acetonitrile and ethanol, but insoluble in other organic solvents like chloroform and diethyl ether. Therefore, we are interested in the reuse of vanadium complexes **1** and **2** in the oxidation of benzhydrol by using ethanol as the reaction solvent and diethyl ether as the extract solvent. Unfortunately, vanadium complex **1** could not be employed as a recycling catalyst. In sharp contrast, the reuse of vanadium complex **2** could be conducted without a significant decrease in catalytic activity (Table 4). In addition, it has been revealed that for the oxidation of benzhydrol by the catalytic system of vanadium complex **2**, the turnover number (TON) reaches 2500 and the turnover frequency (TOF) reaches 52 h⁻¹ (Table 5). These results show that vanadium complex **2** has superior durability and high catalytic activity for the oxidation of

Table 4 Recyclable ability of **2** in the oxidation of benzhydrol in ethanol

Reaction run	1	2	3	4	5
Yield ^a (%)	79	81	86	77	87 (82)
Recovery of catalyst	Quant.	Quant.	Quant.	Quant.	Quant.

^a GC (Isolated) yield.

Table 5 Comparison of TON and TOF

Entry	System	TON	TOF/h ⁻¹
1	0.024 mol% 2	2500	52
2	0.1 mol% 1	860	18

cf. VO(acac)₂: TON 45, TOF 15 h⁻¹; V₂O₅: TON 19, TOF 2 h⁻¹.

alcohols in comparison with other vanadium-catalyzed oxidation systems (*cf.* VO(acac)₂: TON 45, TOF 15 h⁻¹; V₂O₅: TON 19, TOF 2 h⁻¹).

In conclusion, we have found several unique characteristics of vanadium complexes **1** and **2** as oxidation catalysts of benzyl alcohols with molecular oxygen. For example, they can be employed as catalysts for the oxidation of benzyl alcohols in non-toxic solvents such as ethanol, water, and ionic liquids. In particular, tetranuclear vanadium complex **2** is useful as a recycling catalyst with excellent TON and TOF. These results suggest that it is possible to control the oxidation potential of vanadium and affinity of the vanadium catalysts to solvents by the selection of appropriate ligands in vanadium complexes. In addition, we believe that the preparation of the multi-nuclear catalyst such as **2** enables us to develop economically and environmentally friendly oxidation systems with a recycling catalyst having superior durability. We are now challenging the development of further useful oxidation of alcohols and amines by designing the catalysts based on the results described in this paper.

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Notes and references

† General procedure for the vanadium-catalyzed oxidation of benzyl alcohols in acetonitrile or ethanol is as follows: In a 50 mL stainless steel autoclave with a magnetic stirring bar were added VO(Hhpic)₂ (2 mol%) or VO₄(hpic)₄ (0.5 mol%), solvent (6 mL) and benzyl alcohols (1.5 mmol). Oxygen was purged twice and then charged at 1.0 MPa. The reaction was conducted with magnetic stirring for the appropriate time upon heating at 120 °C. The resulting mixture was filtered through a Celite pad and the filtrate was analyzed by GC. Purification of the product was carried out on a short pad of silica gel using ethyl acetate and hexane as eluent to afford the analytically pure aldehydes and carboxylic acids, respectively. All products were commercially available and identified by comparison of the isolated products with authentic samples.

1 (a) S. V. Ley and A. Medin, in *Comprehensive Organic Synthesis*, ed. B. M. Trost and I. Fleming, Pergamon, Oxford, 1991, vol. 7, ch. 2.7;

- (b) T. V. Lee, in *Comprehensive Organic Synthesis*, ed. B. M. Trost and I. Fleming, Pergamon, Oxford, 1991, vol. 7, ch. 2.8; (c) G. Procter, in *Comprehensive Organic Synthesis*, ed. B. M. Trost and I. Fleming, Pergamon, Oxford, 1991, vol. 7, ch. 2.9.
- 2 Recently, highly selective oxidations using transition-metal V²⁺, Pt³⁺, Rh⁴⁺, Pd⁵⁺, Ru⁶⁺, Co⁷⁺, Ni⁸⁺, Cu⁹⁺, and Os¹⁰⁺ complexes with molecular oxygen were reported; (a) T. Hirao, *Chem. Rev.*, 1997, **97**, 2707; (b) M. Kirihara, Y. Ochiai, S. Takizawa, H. Takahata and H. Nemoto, *Chem. Commun.*, 1999, 1387; (c) Y. Maeda, N. Kakiuchi, S. Matsumura, T. Nishimura and S. Uemura, *Tetrahedron Lett.*, 2001, **42**, 8877; (d) Y. Maeda, N. Kakiuchi, S. Matsumura, T. Nishimura, T. Kawamura and S. Uemura, *J. Org. Chem.*, 2002, **67**, 6718; (e) S. Velusamy and T. Punniyamurthy, *Org. Lett.*, 2004, **6**, 217; (f) S. R. Reddy, S. Das and T. Punniyamurthy, *Tetrahedron Lett.*, 2004, **45**, 3561; (g) A. T. Radosevich, C. Musich and F. D. Toste, *J. Am. Chem. Soc.*, 2005, **127**, 1090.
- 3 C.-G. Jia, F.-Y. Jing, W.-D. Hu, M.-Y. Huang and Y.-Y. Jiang, *J. Mol. Catal.*, 1994, **91**, 139.
- 4 J. Martin, C. Martin, M. Faraj and J.-M. Bregeault, *Nouv. J. Chim.*, 1984, **8**, 141.
- 5 (a) T. F. Blackburn and J. Schwartz, *J. Chem. Soc., Chem. Commun.*, 1977, 157; (b) K. Kaneda, M. Fujii and K. Morioka, *J. Org. Chem.*, 1996, **61**, 4502; (c) T. Nishimura, T. Onoue, K. Ohe and S. Uemura, *Tetrahedron Lett.*, 1998, **39**, 6011; (d) T. Nishimura, T. Onoue, K. Ohe and S. Uemura, *J. Org. Chem.*, 1999, **64**, 6750; (e) K. P. Peterson and R. C. Larock, *J. Org. Chem.*, 1998, **63**, 3185; (f) G.-J. ten Brink, I. W. C. E. Arends and R. A. Sheldon, *Science*, 2000, **287**, 1636; (g) Y. Uozumi and R. Nakao, *Angew. Chem., Int. Ed.*, 2003, **42**, 194; (h) M. J. Schultz, C. C. Park and M. S. Sigman, *Chem. Commun.*, 2002, 3034; (i) T. Nishimura, Y. Maeda, N. Kakiuchi and S. Uemura, *J. Chem. Soc., Perkin Trans. 1*, 2000, 4301; (j) T. Nishimura, N. Kakiuchi, M. Inoue and S. Uemura, *Chem. Commun.*, 2000, 1245; (k) D. R. Jensen, M. J. Schultz, J. A. Mueller and M. S. Sigman, *Angew. Chem., Int. Ed.*, 2003, **42**, 3810; (l) T. Iwasawa, M. Tokunaga, Y. Obora and Y. Tsuji, *J. Am. Chem. Soc.*, 2004, **126**, 6554; (m) M. Yang, K.-T. Yip, J.-H. Pan, Y.-C. Chen, N.-Y. Zhu and D. Yang, *Synlett*, 2006, 3057; (n) S. Shimazu, T. Uehara, A. Asami, T. Hara and N. Ichikuni, *J. Mol. Catal. A: Chem.*, 2008, **282**, 28.
- 6 (a) M. Matsumoto and N. Watanabe, *J. Org. Chem.*, 1984, **49**, 3435; (b) I. E. Markó, P. R. Giles, M. Tsukazaki, I. Chellé-Regnaud, C. J. Urch and S. M. Brown, *J. Am. Chem. Soc.*, 1997, **119**, 12661; (c) K. Kaneda, T. Yamashita, T. Matsushita and K. Ebitani, *J. Org. Chem.*, 1998, **63**, 1750; (d) B. Hinzen, R. Lenz and S. V. Ley, *Synthesis*, 1998, 977; (e) T. Matsushita, K. Ebitani and K. Kaneda, *Chem. Commun.*, 1999, 265; (f) M. Pagliaro and R. Ciriminna, *Tetrahedron Lett.*, 2001, **42**, 4511; (g) K. Masutani, T. Uchida, R. Irie and T. Katsuki, *Tetrahedron Lett.*, 2000, **41**, 5119; (h) M. Lee and S. Chang, *Tetrahedron Lett.*, 2000, **41**, 7507; (i) K. Yamaguchi, K. Mori, T. Mizugaki, K. Ebitani and K. Kaneda, *J. Am. Chem. Soc.*, 2000, **122**, 7144; (j) A. Miyata, M. Murakami, R. Irie and T. Katsuki, *Tetrahedron Lett.*, 2001, **42**, 7067; (k) A. Hanyu, E. Takezawa, S. Sakaguchi and Y. Ishii, *Tetrahedron Lett.*, 1998, **39**, 5557; (l) H.-Y. Shen, S.-C. Zhou, M.-H. Wei and H.-X. Zong, *React. Funct. Polym.*, 2006, **66**, 827; (m) C. N. Kato, A. Shinohara, N. Mori and K. Nomiyama, *Catal. Commun.*, 2006, **7**, 413; (n) C. N. Kato, M. Ono, T. Hino, T. Ohmura and W. Mori, *Catal. Commun.*, 2006, **7**, 673.
- 7 (a) T. Iwahama, S. Sakaguchi, Y. Nishiyama and Y. Ishii, *Tetrahedron Lett.*, 1995, **36**, 6923; (b) V. B. Sharma, S. L. Jain and B. Sain, *Tetrahedron Lett.*, 2003, **44**, 383; (c) T. Yamada and T. Mukaiyama, *Chem. Lett.*, 1989, 519; (d) V. B. Sharma, S. L. Jain and B. Sain, *J. Mol. Catal. A: Chem.*, 2004, **212**, 55; (e) G. Blay, L. Cardona, I. Fernández and J. R. Pedro, *Synthesis*, 2007, 3329.
- 8 B. M. Choudary, M. L. Kantam, A. Rahman, C. V. Reddy and K. K. Rao, *Angew. Chem., Int. Ed.*, 2001, **40**, 763.
- 9 (a) E. Saint-Aman, S. Ménage, J.-L. Pierre, E. Defrancq and G. Gellon, *New J. Chem.*, 1998, **22**, 393; (b) P. Chaudhuri, M. Hess, J. Müller, K. Hildenbrand, E. Bill, T. Weyhermüller and K. Wieghardt, *J. Am. Chem. Soc.*, 1999, **121**, 9599; (c) I. E. Markó, P. R. Giles, M. Tsukazaki, S. M. Brown and C. J. Urch, *Science*, 1996, **274**, 2044; (d) R. C. Pratt and T. D. P. Stack, *J. Am. Chem. Soc.*, 2003, **125**, 8716; (e) P. Gamez, I. W. C. E. Arends, J. Reedijk and R. A. Sheldon, *Chem. Commun.*, 2003, 2414; (f) I. E. Markó, A. Gautier, R. Dumeunier, K. Doda, F. Philippart, S. M. Brown and C. J. Urch, *Angew. Chem., Int. Ed.*, 2004, **43**, 1588; (g) S. Velusamy, A. Srinivasan and T. Punniyamurthy, *Tetrahedron Lett.*, 2006, **47**, 923; (h) N. Lu and Y.-C. Lin, *Tetrahedron Lett.*, 2007, **48**, 8823.

- 10 (a) K. S. Coleman, M. Coppe, C. Thomas and J. A. Osborn, *Tetrahedron Lett.*, 1999, **40**, 3723; (b) P. A. Shapley, N. Zhang, J. L. Allen, D. H. Pool and H.-C. Liang, *J. Am. Chem. Soc.*, 2000, **122**, 1079.
- 11 (a) D. C. Crans, J. J. Smee, E. Gaidamauskas and L. Yang, *Chem. Rev.*, 2004, **104**, 849; (b) K. H. Thompson, J. H. McNeill and C. Orvig, *Chem. Rev.*, 1999, **99**, 2561.
- 12 (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 and S. Yano, *J. Inorg. Biochem.*, 2004, **98**, 105; (b) S. Yano, M. Nakai, F. Sekiguchi, M. Obata, M. Kato, M. Shiro, I. Kinoshita, M. Mikuriya, H. Sakurai and C. Orvig, *Chem. Lett.*, 2002, 916.
- 13 (a) M. Earle, in *Ionic Liquids in Synthesis*, ed. P. Wasserscheid and T. Welton, Wiley-VCH, Weinheim, 2008, vol. 1, pp. 350–356; (b) V. Conte, B. Floris and A. Silvangri, in *Vanadium: The Versatile Metal*, ed. K. Kustin, J. C. Pessoa and D. C. Crans, ACS Symposium Series 974, American Chemical Society, Washington, DC, 2007, ch. 2.
- 14 Oxidations using transition-metal complexes with molecular oxygen in ionic liquids were reported: (a) X.-E. Wu, L. Ma, M.-X. Ding and L.-X. Gao, *Chem. Lett.*, 2005, **34**, 312; (b) N. Jiang and A. J. Ragauskas, *Org. Lett.*, 2005, **7**, 3689; (c) N. Jiang and A. J. Ragauskas, *Tetrahedron Lett.*, 2007, **48**, 273; (d) N. Jiang and A. J. Ragauskas, *J. Org. Chem.*, 2007, **72**, 7030; (e) A. Shaabani, E. Farhangi and A. Rahmati, *Appl. Catal., A*, 2008, **338**, 14.