

An efficient aerobic oxidation of various organic compounds catalyzed by mixed addenda heteropolyoxometalates containing molybdenum and vanadium

Shin-ya Fujibayashi, Kouichi Nakayama, Masatoshi Hamamoto, Satoshi Sakaguchi, Yutaka Nishiyama, Yasutaka Ishii *

Department of Applied Chemistry, Faculty of Engineering, Kansai University, Suita, Osaka 564, Japan

Received 4 August 1995; accepted 2 February 1996

Abstract

Various organic compounds were oxidized by molecular oxygen in the presence of a catalytic amount of mixed-addenda heteropolyoxometalates containing molybdenum and vanadium. The catalytic activity of the molybdovanadophosphate was found to be greatly enhanced by supporting on charcoal. The supported catalyst has high catalytic activity for oxidative dehydrogenation of benzylic and allylic alcohols to the corresponding aldehydes and ketones (46–92%), nevertheless, the non-supported catalyst was inactive for the same oxidations under these conditions. 2,3,6-Trimethylphenol was selectively oxidized to trimethyl-*p*-benzoquinone, which is a precursor of vitamin E, in the presence of a catalytic amount of molybdovanadophosphate. In addition, the aerobic oxidation of amines, alkyl-substituted phenols, and alkanes were also examined.

Keywords: Molecular oxygen; Oxidation; Heteropolyoxometalate; Molybdovanadophosphate

1. Introduction

In recent years, heteropolyoxometalate-catalyzed reactions have undergone markedly rapid progress in organic reactions, and have been applied to various transformations of organic compounds [1]. The characteristic features of heteropolyoxometalates as catalysts in organic synthesis have been divided into two types; (i) strong oxidation ability and (ii) strong Brønsted acidity. In particular, the utilization of het-

eropoly compounds as homogeneous liquid-phase oxidation catalysts has recently been developed e.g., (i) oxidative dehydrogenations by polyoxotungstate under photochemical or normal thermal conditions [2,3]; (ii) hydrogen peroxide oxidations by molybdo- and tungstophosphates having a Keggin structure and peroxotungstophosphates with quaternary ammonium counter cations [4]; (iii) oxidation by transition metal substituted heteropolyoxometalates [5]; (iv) aerobic oxidation by mixed-addenda heteropolyoxometalates [6].

Molecular oxygen (dioxygen) is considered to be the best oxidant from both economical and

* Corresponding author.

environmental points of view. Therefore, the usage of dioxygen as the oxidant is an especially rewarding goal in oxidation chemistry. A number of homogeneous transition metal catalysts have been developed for this purpose [7]. Recently, Hill, Neumann, and Brégeault groups have reported heteropolyoxometalate-catalyzed aerobic oxidations (e.g., oxidative dehydrogenation of dienes [6](a), alcohols, and amines [6](b); oxidative coupling of phenols [6](c); oxidation of sulfides [6](d); oxidative cleavage of ketones and diols [6](e); and the oxidative dehydrogenation of alkanes [2] and alcohols [3] under photochemical or thermal conditions).

Previously, we have shown that mixed addenda 12-metallophosphates such as molybdovanadophosphate and tungstovanadophosphate were excellent catalysts for the aerobic oxidation of olefins and cyclic ketones in the presence of aldehydes [8]. During the course of our studies on the utilization of these catalysts in aerobic oxidation, we found that aerobic oxidations of various benzylic derivatives were efficiently promoted by molybdovanadophosphate [9], and that the catalytic activity of molybdovanadophosphate was markedly enhanced by supporting on activated carbon [10]. In this paper, we report full details on the aerobic oxidations of amines, alcohols, and phenols catalyzed by molybdovanadophosphates.

2. Experimental section

NMR spectra were recorded on JEOL JNM-GSX-400, JNM-PMX 60, JNM-EX-270 and Hitachi R-90H. ^1H -NMR (400, 270 or 60 MHz) and ^{13}C -NMR (100, 67.5 or 22.5 MHz) spectra were obtained with Me_4Si as an internal standard. ^{31}P -NMR spectra were obtained in D_2O with H_3PO_4 as an external standard. GLC analysis was performed with Shimadzu GC-14A and 12A equipped with a flame ionization detector with PEG-HF, silicone SE-30 and OV-1. HPLC analysis was performed on Shimadzu SPD-6A with a Shimadzu CLC-ODO column. IR spectra

were measured on Perkin Elmer 1600 and JEOL JIR-7000 and obtained with NaCl pellets or the KBr method. TG analysis was performed on Shimadzu DTG-50/50H. Energy dispersive X-ray analysis was performed with JEOL JEO-2001. Prior to the examination the surfaces of molybdovanadophosphate supported on active charcoal were coated with a thin layer (150 Å) of gold in order to improve conductivity and prevent charging. Accelerating voltage of 20 kV, probe current of 1.5×10^{-10} A, and counting time of 200 s were used.

All compounds and solvents were purchased from commercial sources and used without further treatment.

2.1. Preparation of catalysts

Various mixed addenda heteropolyoxometalates, $(\text{NH}_4)_5\text{H}_4\text{PV}_6\text{W}_6\text{O}_{40} \cdot 6\text{H}_2\text{O}$ [11], $(\text{NH}_4)_3\text{HPVMo}_{11}\text{O}_{40} \cdot 6\text{H}_2\text{O}$ [12], $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40} \cdot 32\text{H}_2\text{O}$ [12], and $\text{H}_4\text{PVMo}_{11}\text{O}_{40} \cdot 34\text{H}_2\text{O}$ [12] were prepared by published procedures.

An ammonium molybdovanadophosphate (NPVMO) was prepared by modifying the method described for the preparation of $(\text{NH}_4)_5\text{H}_4\text{PV}_6\text{W}_6\text{O}_{40} \cdot 6\text{H}_2\text{O}$: To a solution of NaVO_3 (7.32 g, 60 mmol) in water (38 ml) was added $\text{Na}_2\text{MoO}_4 \cdot 2\text{H}_2\text{O}$ (8.22 g, 34 mmol) in water (12 ml). To the resulting solution was added dropwise 85% H_3PO_4 (7.6 g, 66 mmol) in water (10 ml), and the mixture was stirred at 95°C for 1 h. After cooling to room temperature, the solution was added to a saturated ammonium chloride solution (150 ml) to give a brown precipitate (ca. 8 g). The resulting precipitate was recrystallized twice from 0.25 M H_2SO_4 to afford molybdovanadophosphate, NPVMO (**1a**). The **1a** is a reproducible material, as indicated by almost the same combustion analysis as follows: H, 1.76; N, 4.76. IR (KBr): 3158, 1621, 1401, 1058, 947, 874, 795 cm^{-1} . Molar ratio: P:Mo:V = 1.0:4.0:7.8.

NPVMO/C (**1b**) was prepared as follows: To a solution of **1a** (1 g) in an excess water was

added 9 g of active charcoal (Wako Pure Chemical, surface area: 1450 m²/g, pore size: 15–25 Å, pore volume: 0.58 ml/g) and the suspended solution was stirred vigorously for 0.5 h. After filtration, the precipitate was dried overnight in vacuo (20 mmHg) at ca. 90°C to obtain **1b** in which 10 wt% of **1a** was supported on the active charcoal. The surface area and pore volume of **1b** were estimated as 1250 m²/g and 0.52 ml/g, respectively. IR (KBr): 1059, 943, 854, 777 cm⁻¹ (around 1100–700 cm⁻¹).

2.2. General procedure for oxidative dehydrogenation of amines by dioxygen catalyzed by NPVMO (**1a**) and NPVMO/C (**1b**)

A toluene (4 ml) or benzonitrile (6 ml) solution of amines (2 mmol) and **1a** (35 mg) or **1b** (350 mg), respectively, was placed in a three necked flask equipped with a balloon filled with O₂. The mixture was stirred at 100°C for 20 h. After the reaction, the catalyst was filtered off and the resulting solution was extracted with diethyl ether (20 ml × 3). The combined extracts were dried over MgSO₄ and analyzed by GLC with an internal standard. Removal of the solvent under reduced pressure afforded a crude product. Purification by column chromatography on activated alumina with hexane eluent gave the corresponding Schiff bases and/or aldehydes.

2.3. General procedure for dehydrogenation of alcohols by dioxygen catalyzed by **1b**

A toluene solution (6 ml) of substrate (2 mmol) was added to **1b** (350 mg) in a three necked flask equipped with a balloon filled with O₂. The mixture was stirred at 100°C for 15 h. The same workup described for the **1a** catalyzed oxidative dehydrogenation of amines was carried out, and the resulting extracts were purified by column chromatography on silica gel with hexane/ethyl acetate (4/1) to give the corresponding carbonyl compounds.

2.4. General procedure for oxidation of various phenols by dioxygen catalyzed by **1a** or **1b**

To acetic acid (6 ml) or mixed solvent of acetic acid/water (5/1 v/v%) were added phenol (2 mmol) and **1a** (35 mg) or **1b** (350 mg), and a balloon filled with O₂ was fitted to the reaction flask. The mixture was stirred at 80°C for 1 h. After the reaction, the catalyst was filtered off and the solution was neutralized with aqueous NaHCO₃. The resulting solution was extracted with diethyl ether. The combined extracts were dried over MgSO₄. Removal of the solvent under reduced pressure afforded a crude product, which was purified by column chromatography on silica gel with hexane/ethyl acetate (4/1).

2.5. General procedure for oxidation of 2,4,6-trimethylaniline (**23**) by dioxygen catalyzed by **1b**

To acetic acid (6 ml) were added 2,4,6-trimethylaniline (2 mmol) and **1b** (350 mg), and a balloon filled with O₂ was fitted to the reaction flask. The mixture was stirred at 80°C for 20 h. After the reaction, the catalyst was filtered off and the solution was neutralized with aqueous NaHCO₃. The resulting solution was extracted with CH₂Cl₂. The combined extracts were dried over MgSO₄. Removal of the solvent under reduced pressure afforded a crude product, which was purified by column chromatography on activated alumina with CH₂Cl₂ eluent.

2.6. General procedure for oxygenation of hydroaromatic compounds by dioxygen catalyzed by **1a**

A toluene (4 ml) solution of substrate (2 mmol) and **1a** (35 mg) was placed in a three necked flask equipped with a balloon filled with O₂. The mixture was stirred at 100°C for 20 h. After the reaction, the catalyst was filtered off and the resulting solution was extracted with diethyl ether (20 ml × 3). The combined ex-

tracts were dried over MgSO_4 and analyzed by GLC with an internal standard. Removal of the solvent under reduced pressure afforded a crude product. Purification by column chromatography on activated alumina with hexane/ethyl acetate (4/1) gave the corresponding carbonyl compounds.

2.7. General procedure for aerobic oxidation of alkanes by $1a-O_2$ system in the presence of 2-methylpropanal

A 1,2-dichloroethane (10 ml) solution of alkane (2 mmol), 2-methylpropanal (8 mmol), and **1a** (35 mg) was placed in a three necked flask equipped with a balloon filled with O_2 . The mixture was stirred at 25°C for 15 h. After the reaction, the catalyst was filtered off and the resulting solution was extracted with CH_2Cl_2 (20 ml \times 3). The combined extracts were dried over MgSO_4 and analyzed by GLC with an internal standard. Removal of the solvent under reduced pressure afforded a crude product. Purification by column chromatography on silica gel with hexane/ethyl acetate (4/1) gave the corresponding oxidized products.

3. Results and discussion

3.1. Spectroscopic analysis of NPVMO (**1a**) and NPVM/C (**1b**)

A mixed-addenda tungstovanadophosphate, $(\text{NH}_4)_5\text{H}_4\text{PV}_6\text{W}_6\text{O}_{40} \cdot 6\text{H}_2\text{O}$, has been prepared by Pope et al. [11]. We attempted to prepare the corresponding molybdenum compound, $(\text{NH}_4)_5\text{H}_4\text{PV}_6\text{Mo}_6\text{O}_{40} \cdot n\text{H}_2\text{O}$, according to the Pope method using Na_2MoO_4 in place of Na_2WO_4 . Recrystallization of the resulting molybdovanadophosphate (NPVMO) (**1a**) from 0.25 M H_2SO_4 gave a clean brown precipitate which is reproducible material. The elemental analysis by ICP measurement showed that the composition of the resulting NPVMO, **1a**, consists of P:Mo:V = 1.0:4.0:7.8, deviating from a desired molybdovanadophosphate having P:Mo:V = 1:6:6. From the elemental analysis the average composition of the NPVMO prepared by the above method was approximately indicated as $(\text{NH}_4)_5\text{H}_6\text{PV}_8\text{Mo}_4\text{O}_{40}$ (anhydrous salt) (calcd. N 4.50, H 1.67, P 1.99, V 26.2, Mo 24.6%; found N 4.76, H 1.76, P 1.91, V 24.6, Mo 23.8%).

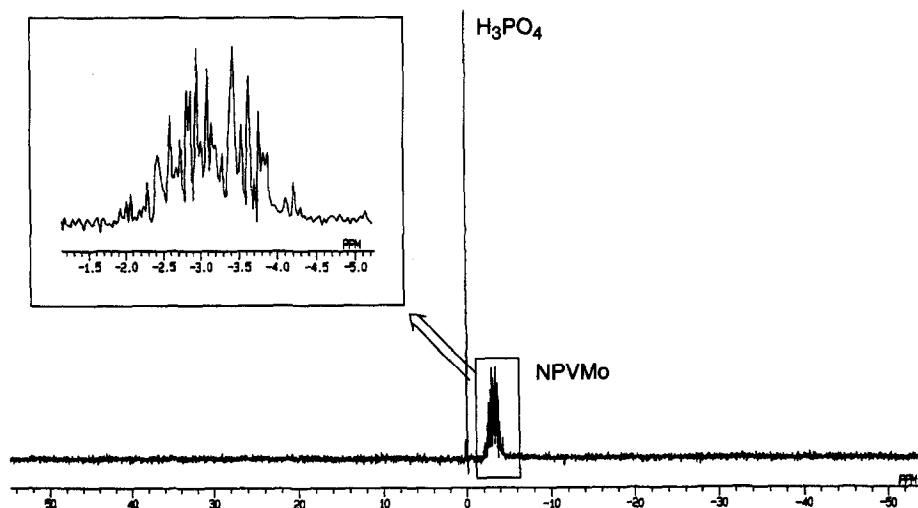


Fig. 1. ^{31}P NMR spectrum of NPVMO (**1a**) in D_2O with external standard, H_3PO_4 .

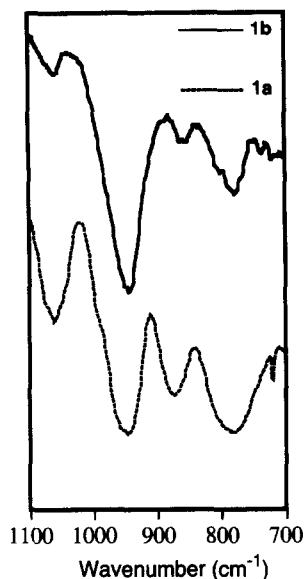


Fig. 2. IR spectra of NPVMO (**1a**) and NPVMO/C (**1b**).

Fig. 1 shows the ^{31}P NMR of the **1a** obtained here. The ^{31}P NMR gave a spectrum consisting of a number of signals which indicate that the resulting **1a** is a complex mixture. In the case of a disubstituted Keggin complex such as $[\text{PV}_2\text{Mo}_{10}\text{O}_{40}]^{5-}$, there are 66 possible ways of arranging the constituent ions, which after allowance for degeneracy leads to five distinct isomers [13]. Recently, Grate et al., have shown ^{31}P NMR of five positional isomers for α -Keggin $[\text{PV}_2\text{Mo}_{10}\text{O}_{40}]^{5-}$ [14]. Accordingly, it is probable that many positional isomers are present for the molybdovanadophosphate, NPVMO **1a**, which is prepared by the present method.

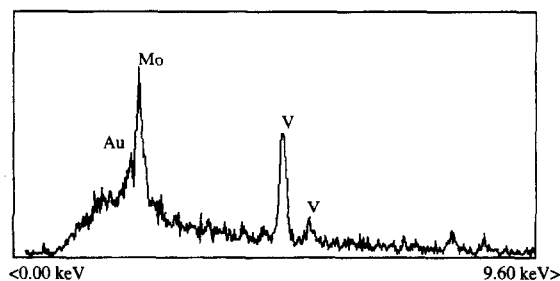


Fig. 3. EDX spectrum of NPVMO/C (**1b**).

Fig. 2 shows IR spectra of **1a** and NPVMO/C, **1b**, in the range of $700\text{--}1100\text{ cm}^{-1}$. The IR spectrum of **1a** shows four peaks for different types of oxygen bonds, although **1a** is not a pure complex; that is P–O (internal oxygen connecting P) at 1059 cm^{-1} , M–O (terminal oxygen bonding to M) at 943 cm^{-1} , M–O–M at 854 cm^{-1} and 777 cm^{-1} [15]. The characteristic absorption bands of the supported catalyst, **1b**, were similar to those of **1a**, although the absorptions were weaker than those of **1a**. This observation indicates that the structure of NPVMO was preserved after supporting on the active charcoal.

In order to obtain information on the distribution of **1a** on the active charcoal, the energy dispersive X-ray analysis (EDX) of **1b** was carried out. The EDX spectra of four different parts of the sample were the same. This fact shows that the **1a** is uniformly dispersed on the active charcoal Fig. 3.

Thus molybdovanadophosphate, NPVMO **1a**, which consisted of different positional and structural isomers, was used for the aerobic

Table 1
Aerobic oxidation of benzylamine (**2**) by various heteropolyoxometalates under several conditions

run	catalyst (mg)	solvent	yield, % ^a
1	$(\text{NH}_4)_3\text{H}_4\text{PV}_6\text{W}_6\text{O}_{40} \cdot 6\text{H}_2\text{O}$ (21)	toluene	46
2	NPVMO (1a) (16)	toluene	81
3 ^b	1a (16)	toluene	91
4	1a (16)	benzonitrile	>99
5 ^c	1a (16)	benzonitrile	63
6 ^c	1a (16)	acetonitrile	34
7 ^c	1a (16)	1,2-dichloroethane	31
8	$(\text{NH}_4)_3\text{HPVMO}_{11}\text{O}_{40} \cdot 7.5\text{H}_2\text{O}$ (39)	toluene	36
9	$\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40} \cdot 32\text{H}_2\text{O}$ (22)	toluene	39
10	$\text{H}_4\text{PVMO}_{11}\text{O}_{40} \cdot 34\text{H}_2\text{O}$ (22)	toluene	26
11	$\text{H}_3\text{PW}_{12}\text{O}_{40} \cdot n\text{H}_2\text{O}$ (17)	toluene	trace
12	$\text{H}_3\text{PMo}_{12}\text{O}_{40} \cdot n\text{H}_2\text{O}$ (27)	toluene	12

^a GLC yields based on substrate.

^b 40 h.

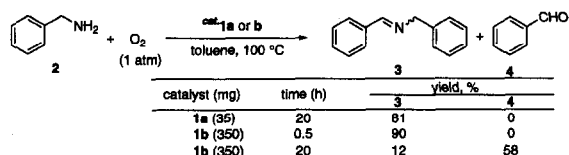
^c Reaction at 75°C .

oxidation of various organic compounds as the catalyst.

3.2. Oxidation of benzylamine by NPVMO(1a) and NPVM/C(1b)-O₂ system

The aerobic oxidation of benzylamine (**2**) was chosen as a model reaction to evaluate the catalytic potential of various heteropolyoxometalate catalysts. Table 1 shows the aerobic oxidation of **2** by a variety of heteropoly compounds under selected reaction conditions.

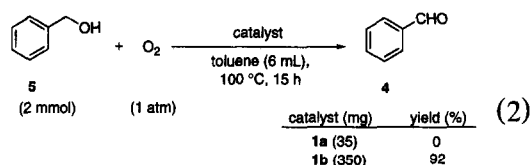
The oxidation of **2** with dioxygen (1 atm) in the presence of (NH₄)₅H₄PV₆W₆O₄₀ · 6H₂O (1 mol%, 21 mg) in toluene at 100°C for 20 h gave Schiff base, *N*-benzylidenebenzylamine (**3**), in 46% yield (run 1). The catalyst of NPVMO **1a** was found to be more active than that of (NH₄)₅H₄PV₆W₆O₄₀ · 6H₂O under these conditions (run 2). The catalytic activities of mixed addenda heteropolyoxometalates such as (NH₄)₃HPVMO₁₁O₄₀ · 7.5H₂O, H₅PV₂Mo₁₀O₄₀ · 32H₂O, and H₄PVMO₁₁O₄₀ · 34H₂O were lower than that of **1a** (runs 8–10). The usual heteropoly acids having a Keggin structure, H₃PW₁₂O₄₀ · *n*H₂O and H₃PMo₁₂O₄₀ · *n*H₂O, were inert in this oxidation (runs 11 and 12). It was found that the yield of **3** was markedly affected by the solvent and the reaction temperature (runs 2 and 4–7). Among the solvents examined, toluene and benzonitrile were found to be good solvents (runs 2 and 4). When NPVMO supported on the active carbon, NPVMO/C **1b**, was employed in the oxidation of **2** with dioxygen, benzaldehyde (**4**) was formed in 58% yield in preference to Schiff base **3** (Eq. 1).



(1)

3.3. Oxidation of benzylic and allylic alcohols by NPVMO/C(1b)-O₂ system

Since the oxidative dehydrogenation of benzylic amines by dioxygen could be achieved with high selectivity by **1a**, the aerobic oxidation of benzyl alcohol (**5**) was examined under the same conditions as the oxidation of **2**. However, it was found that the aerobic oxidation of benzyl alcohol (**5**) is not catalyzed by **1a** (Eq. 2). Neumann et al., have reported that Na₅PV₂Mo₁₀O₄₀ on active carbon is an efficient catalyst for the oxidative dehydrogenation of benzylic alcohols to benzaldehydes [6]. The same strategy for the **1a** provided an interesting result, i.e., the **1a** supported on the active carbon, NPVMO/C, **1b**, likewise showed excellent catalytic activity for the oxidation of **5** which failed to be oxidized by non-supported catalyst, **1a** (Eq. 2).



Thus, the oxidation of benzylic and allylic alcohols with molecular oxygen by **1b** was carried out. Representative results are shown in Table 2.

Interestingly, the recovered **1b** catalyst maintains a high catalytic activity even after 5 recycles (run 3). Substituted benzyl alcohols such as 4-methoxy-, 4-methyl-, and 2-methylbenzyl alcohols were oxidized to the corresponding benzaldehydes in good yields (83–92%) (runs 4–6). It is important to note that these benzyl alcohols were converted into the corresponding aldehydes without formation of carboxylic acids which are overoxidation products of aldehydes. Neumann suggests that these dehydrogenations proceed via a process other than the free radical process, because aldehydes are more easily oxidized to carboxylic acids than alcohols under

Table 2
Aerobic oxidation of various alcohols catalyzed by NPVMO/C (**1b**)^a

Run	Substrate	Product	Yield (%) ^b
1	benzyl alcohol (5)	benzaldehyde (4)	92
2 ^c	5	4	20
3 ^d	5	4	93
4	4-methoxybenzyl alcohol	<i>p</i> -anisaldehyde	92
5	4-methylbenzyl alcohol	<i>p</i> -tolualdehyde	92
6	4-methylbenzyl alcohol	<i>o</i> -tolualdehyde	83
7	α -phenethyl alcohol	acetophenone	79
8	benzoin	benzil	89
9	2-hexen-1-ol	2-hexenal	46
10	3-phenyl-2-propen-1-ol	cinnamaldehyde	87 ^e

^a Substrate (2 mmol) was allowed to react in the presence of **1b** (350 mg) under oxygen atmosphere (1 atm) in toluene (6 ml) at 100°C for 15 h.

^b Determined by GLC.

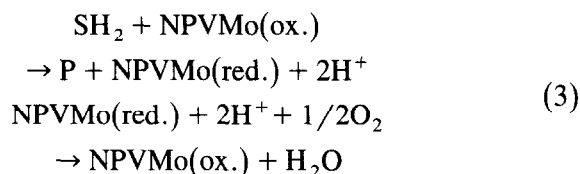
^c A mixture of **1a** (35 mg) and charcoal (315 mg) was used as catalyst.

^d Reaction by the recovered catalyst after 5 times recycles.

^e Determined by HPLC.

free radical autooxidation [6] [16]. 1-Phenethyl alcohol was converted into the corresponding ketone, acetophenone, in 79% yield (run 7). In the oxidation of the α -hydroxy ketone benzoin, benzil was obtained in good yield (run 8). The supported catalyst, **1b**, was also efficient for the selective dehydrogenation of the allylic alcohols to α,β -unsaturated carbonyl compounds (runs 9 and 10).

In the aerobic oxidation of amines and alcohols by mixed molybdovanadophosphates, the reaction is considered to proceed by transfer of electrons and a protons from substrate to the catalyst, yielding product and a proton and reduced catalyst. The reduced catalyst is reoxidized by dioxygen, yielding water and completing the catalytic cycle [6](b,f).



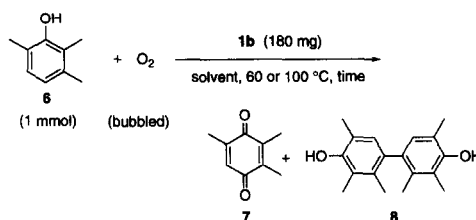
Hence, the enhancement of catalytic activity by supporting **1a** on the active carbon is believed to be due to the higher concentration of

substrates and oxygen by the adsorption in the vicinity of the active site. In addition, it is important to note that the electron can easily transfer from the substrate to the catalyst by supporting **1a** on the active charcoal, since the active carbon serves as a good mediator of the electron transfer. Thus, a rapid redox cycle of V(IV) to V(V) or vice versa may be effected in the oxidation on **1b**. The oxidation of **5** using a simple mixture of **1a** and active charcoal as catalyst resulted in **4** in low yield (run 2).

3.4. Aerobic oxidation of various phenols

The selective oxidation of alkyl-substituted phenols to the corresponding benzoquinones is an important transformation from the synthetic

Table 3
Aerobic oxidation of 2,3,6-trimethylphenol (**6**) catalyzed by NPVMO/C (**1b**)



Run	Solvent (ml)	Time (h)	Temp. (°C)	Conversion (%)	Yield (%) ^a	
					7	8
1 ^b	toluene (6)	20	100	0	0	0
2	toluene (6)	20	100	95	17	53
3 ^c	benzonitrile (6)	10	100	100	21	10
4	acetic acid (3)	1	60	77	13	61
5	acetic acid/ H ₂ O (3/3)	5	60	100	66	16
6	acetic acid/ H ₂ O (2/4)	5	60	100	75	3
7 ^{b,c}	acetic acid/ H ₂ O (2/4)	5	60	100	15	0
8 ^d	acetic acid/ H ₂ O (3/3)	5	60	100	68	7
9	DMF	5	60	100	19	0

^a HPLC yields based on substrate

^b **1a** was used as catalyst.

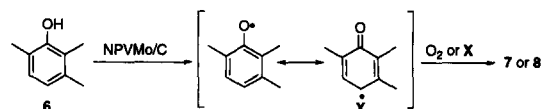
^c Overoxidation products were formed.

^d Recovered **1b** was used.

and industrial points of view. Therefore, many methods have been reported for the oxidation of these compounds using various oxidants [17]. However, there are few reports on the catalytic oxidation of these compounds by dioxygen as the oxidant [18].

Recently, Takehira et al., have reported that a copper(II)–amine catalyst is efficient for the aerobic oxidation of 2,3,6-trimethylphenol (**6**) to trimethyl-*p*-benzoquinone (**7**), which is an important compound as a precursor of vitamin E [19]. More recently, Kozhevnikov et al., have shown that the same oxidation can be carried out by molybdovanadophosphate catalyst [20]. Therefore, the development of an efficient catalyst for the transformation of **6** into **7** by dioxygen is especially of interest from the industrial aspect. Thus, the possibility of the oxidation of **6** to **7** with dioxygen catalyzed by **1a** and **1b** was investigated (Table 3).

In contrast to the aerobic oxidation of amines and alcohols where toluene and benzonitrile served as good solvents, the oxidation of **6** in these solvents led to unfavorable results. The oxidation of **6** by dioxygen catalyzed by **1b** in toluene afforded the coupling product 2,2',3,3',6,6'-hexamethylbiphenyl-4,4'-diol (**8**) (53%) in preference to quinone **7** (17%) (run 2). However, no oxidation of **6** by **1a** took place



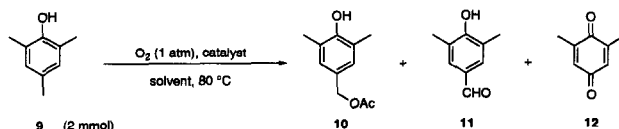
Scheme 1.

under these conditions (run 1). The same oxidation in acetic acid by **1b** gave **8** rather than **7** (run 4). The use of a mixed solvent of acetic acid and water was found to be suitable for the transformation of **6** to **7** (runs 5 to 6). Under these conditions, the oxidation of **6** in acetic acid/water (2/4 v/v%) produced **7** in 75% yield (run 6). When **1a** was employed as catalyst in the oxidation of **6** using the mixed solvent (AcOH/H₂O), **7** was obtained in low yield (run 7). According to patents, the oxidation of **6** with dioxygen to **7** is successfully carried out in *N,N*-dimethylformamide (DMF) by (salen)Co(II) and CuCl₂ [21] [21]. In the present study, however, the reaction in DMF led to the formation of large amounts of undesired products (run 9).

The oxidation of **8** to examine the reaction path of **6** to *p*-benzoquinone **7** resulted in a complex mixture of degraded products of **6** along with a small amount of **7** (7%). Therefore, the formation of **7** via **8** is considered to be a minor route. Probably, **7** is produced via reac-

Table 4

Aerobic oxidation of 2,4,6-trimethylphenol (**9**) catalyzed by NPVMo (**1a**) and NPVMo/C (**1b**)^a



Run	Catalyst	Solvent (ml)	Time (h)	Conversion (%)	Yield (%)		
					10	11	12
1	1a	AcOH (6)	20	100	75	5	trace
2	1a	AcOH/H ₂ O (5/1)	5	99	9	36	31
3	1b	AcOH (6)	10	99	3	80	4
4 ^c	1b	AcOH (6)	5	100	0	85	1

^a **9** (2 mmol) was allowed to react in the presence of **1a** (35 mg) or **1b** (350 mg) under oxygen atmosphere at 80°C.

^b Determined by GLC.

^c **10** was employed as substrate.

tion of phenoxy radical and molecular oxygen. The outline of the oxidation is shown in Scheme 1.

Izumi et al., have reported that about 10 wt% of 12-tungstophosphoric acid supported on active carbon is entrapped in the active charcoal after extraction by hot water or methanol [22]. NPVMO catalyst is extraordinarily soluble in water and acetic acid/water. In order to test the elution of the metal ions from **1b** in the mixed solvent of acetic acid/water (2/4 v/v%), the supported catalyst, **1b**, was treated in the acetic acid/water solvent under the same conditions as the oxidation of **6** (60°C for 5 h). The total weight loss of **1b** after the treatment was within 1%. From the quantitative analysis by UV measurement of the solution, the amount of the NPVMO **1a** eluted from the support in the solvent was estimated as 7% of the **1a** supported on the charcoal corresponding to 0.7% based on the **1b** used. In addition, leaching of **1a** is negligible small in toluene and acetic acid solution, because **1a** is insoluble in these solvents. The oxidation of **6** by the recovered **1b** led to almost the same results as that by the original **1b** (run 8 in Table 3).

The selective synthesis of *p*-hydroxybenzaldehydes is an important reaction from or-

ganic and industrial aspects, since these products are used as intermediates of perfumes and pharmaceutical derivatives [23]. Thus, the aerobic oxidation of 2,4,6-trimethylphenol (**9**) to 3,5-dimethyl-4-hydroxybenzaldehyde (**11**) catalyzed by **1a** and **1b** was examined (Table 4). The oxidation of **9** under oxygen atmosphere in the presence of **1a** in acetic acid for 20 h gave 4-(acetoxymethyl)-2,6-dimethylphenol (**10**) in 75% yield (run 1). The oxidation of **9** in a mixed solvent (AcOH/H₂O = 5/1) afforded 3,5-dimethyl-4-hydroxybenzaldehyde (**11**) (36%) and 2,6-dimethylbenzoquinone (**12**) (31%) (run 2). Interestingly, the oxidation catalyzed by **1b** in acetic acid gave **11** with high selectivity (80%) (run 3).

In order to elucidate the reaction path from **9** to **11**, the oxidation of **9** catalyzed by **1b** was followed by GLC (Fig. 4). It was found that the substrate **9** is consumed at the early stage of the oxidation (within 1 h) to form **10**. The resulting **10** gradually decreased and **11** increased. On the basis of the time-dependence curves of the products, **10** is considered to be a precursor to **11**. Indeed, the oxidation of **10** gave **11** in 85% yield (Table 4, run 4).

A plausible reaction path is shown in Scheme 2. The reaction may be initiated by hydrogen

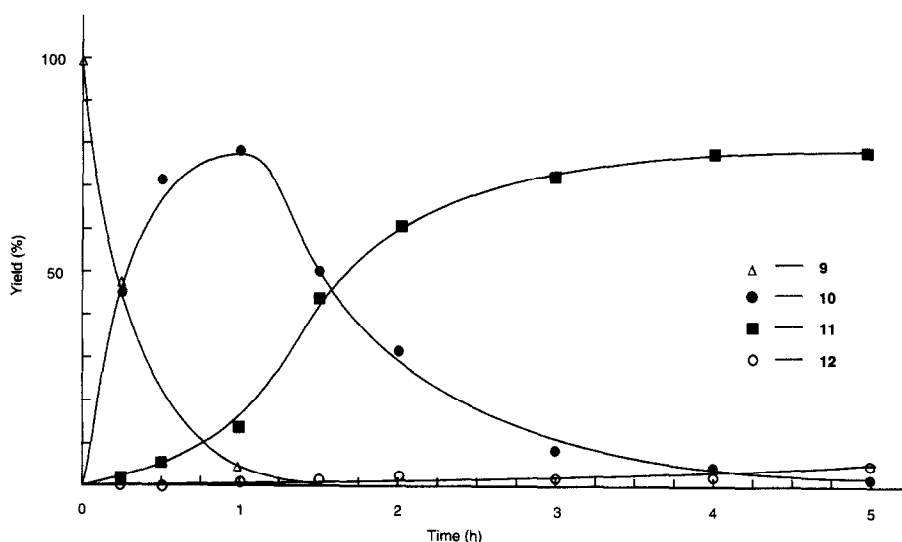
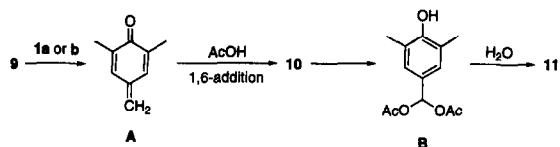


Fig. 4. Time-dependence curves for aerobic oxidation of 2,4,6-trimethylphenol (**9**) catalyzed by NPVMO/C (**1b**).



abstraction from **9** by **1a**. The resulting phenoxy radical tautomerizes to 2,5-cyclohexadien-4-one radical on which subsequent dehydrogenation by **1a** gives a quinone methide intermediate (**A**). Then, the 1,6-addition of acetic acid to **A** pro-

duces **10**, and hydroxyaldehyde **11** may be produced by the hydrolysis of diacetate intermediate (**B**) derived from **10** and acetic acid via a similar reaction path as the formation of **10**.

The oxidation of various phenol derivatives with dioxygen by **1a** or **1b** is shown in Table 5.

2,6-Di-*t*-butyl-*p*-cresol (**13**) was selectively oxidized with dioxygen by **1a** in acetic acid at 80°C for 5 h to form 4-(acetoxymethyl)-2,6-di-*t*-butylphenol (**14**) (61%) along with 3,5-di-*t*-butyl-4-hydroxybenzaldehyde (**15**) (12%) (run 1). The reaction in a mixed solvent of acetic

Table 5
Aerobic oxidation of various phenols catalyzed by NPVMO (**1a**) and NPVMO/C (**1b**)^a

run	substrate	solvent (mL)	product(s) / (yield, %) ^b		
1 ^c		AcOH (6)			
2 ^c		AcOH / H ₂ O (5 / 1)	(61)	(12)	(0)
3		AcOH (6)	(0)	(59)	(3)
4		AcOH (6)			16 (98)
5		AcOH (6)		15 (85)	
6		AcOH (6)	12 (29) ^d		(52) ^d
7		AcOH (6)			(81) ^d

^a Substrate (2 mmol) was allowed to react in the presence of **1b** (350 mg) under oxygen atmosphere at 80°C for 5 h.

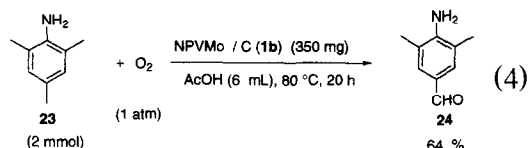
^b Determined by GLC.

^c 35 mg of **1a** was used instead of **1b**.

^d Isolated yield.

acid/water (5/1 v/v%) afforded **15** (35%) and 2,6-di-*t*-butylbenzoquinone (**16**) (25%) (run 2). When **1b** was used as the catalyst, the yield of **15** was improved to 59% yield (run 3). 2,6-Di-*t*-butyl-4-methoxyphenol (**17**) was quantitatively oxidized by **1b** to **16** under these conditions (run 4). The selective oxidations of **13** and 2,6-di-*t*-butylphenol (**21**) to **16** are difficult by conventional methods [6,24]. 2,6-Dimethylphenol (**19**) gave **12** and coupling product 2,2',6,6'-dimethylbiphenylquinone (**20**) (run 6). However, **21** afforded exclusively 2,2',6,6'-tetra-*t*-butylbiphenylquinone (**22**) in high yield (run 7).

In addition, 2,4,6-trimethylaniline (**23**) was converted to 4-amino-2,6-dimethylbenzaldehyde (**24**), which is difficult to prepare by conventional methods, by the **1b**-O₂ system (Eq. 4).



3.5. Oxidation of hydroarenes by NPVMO(**1a**)-O₂ system and NPVMO(**1a**)-aldehyde-O₂ system

We next examined the oxygenation of several hydroaromatic compounds (hydroarenes) by the **1a**-O₂ system. It was found that the oxygenation of hydroarenes was achieved with dioxygen by **1a** (Table 6).

In the oxidation of tetralin (**25**), **1a** catalyzed the selective oxygenation of the benzylic carbon of **5** to form 1-tetralone (**26**) and 1-hydroxy-1,2,3,4-tetrahydro-1-naphthol (**27**) in 70% and 21% selectivities, respectively, in 33% conversion of **25** (run 1). Unlike **25**, indan (**28**) was converted into 1-indanone (**29**) in relatively higher conversion (74%) (run 2). In the oxidation of **30** and **32** by **1b**-O₂ system, no oxidations were observed.

Despite higher catalytic activities of **1b**, the oxidation of **28** by **1b** did not occur. This is

Table 6
Oxygenation of various substrates catalyzed by NPVMO (**1a**)^a

run	substrate	conv., %	product(s)	select, % ^{b)}
1		33		70
				21
2		74		62
3		81		88
4		98		40

^a Substrate (2 mmol) was allowed to react in the presence of **1a** (35 mg) under oxygen atmosphere in toluene (4 ml) at 100°C for 20 h.

^b Based on substrate reacted.

believed to arise from the remarkable differences in the polarity of the starting **28** and the resulting **29**. That is, **28**, having a small polarity becomes difficult to adsorb on the active carbon owing to the very slow desorption of the resulting **29** bearing the polar carbonyl group. For hydroarenes bearing oxygen at their β -positions such as isochroman (**30**) and 1,3-dihydrobenzofuran (**32**), oxidations were accomplished in high conversions. 3,4-Dehydroisocoumarin (**31**) was obtained from **30** in good yield (run 3). However, the oxidation of **32** resulted in cleavage of the C-H bond to give phthalide (**33**) in slightly lower yield (run 4). Diphenylmethane (**34**) was not oxidized by this system.

More recently, Murahashi et al., have reported that ruthenium and iron-catalyzed oxidations of alkanes with molecular oxygen (1 atm) in the presence of an aldehyde and a catalytic amount of an acid at room temperature give the corresponding ketones and alcohols [25]. Thus, for substrates which were difficult to oxidize by the **1a**-O₂ system, 2-methylpropanal was added

to this system and the reaction was carried out at room temperature (Table 7).

Aerobic oxidation of tetralin **25** by **1a** in the presence of 2-methylpropanal in 1,2-dichloroethane at 25°C gave **26** in high selectivity, though the conversion was low (30%) (run 1). In the same oxidation in toluene at 100°C, however, **25** was converted in higher conversion (63%) to give **26** along with **27** (run 2). The oxygenation of **34** and fluorene (**36**) afforded benzophenone **35** and 9-fluorenone (**37**), respectively, in relatively high selectivity (runs 3 and 4). **36** is reported to be oxidized with dioxygen in basic medium such as Toriton B/pyridine [26] or Cu(II)-amine/sodium methoxide [27]. Cyclohexane (**38**) was converted into cyclohexanone (**39**) and cyclohexanol (**40**) in 7% conversion (run 5). It is reported that the oxidation of **38** with dioxygen (1 atm) by iron powder in the presence of heptanal produces **39** (66%) and **40** (29%) in 11% conversion [25]. Heptane (**41**)

failed to be oxidized by the present system (run 6).

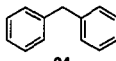
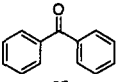
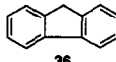
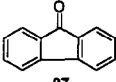



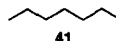
In conclusion, NPVMO **1a** and NPVMO/C **1b** were found to be excellent aerobic oxidation catalysts for various organic compounds. From synthetic and industrial points of view, **1a** and **1b** are considered to be novel catalysts for direct oxidations of various organic compounds by dioxygen.

Acknowledgements

This work was partly supported by a Grant-in-Aid for Scientific Research (No. 06453143) from the Ministry of Education, Science and Culture, Japan and the Science Research Promotion Fund from Japan Private School Promotion Foundation. We also thank to Dr. H. Oda and Dr. J. Shibata for measurement of surface areas and ICP measurement.

Table 7

Aerobic oxidation of various alkanes catalyzed by NPVMO (**1a**) in the presence of 2-methylpropanal

run	substrate	conv., %	product (selectivity, %) ^b	
1	25	30	26 (79)	27 (<1)
2 ^c	25	63	26 (76)	27 (6)
3	 34	13	 35	(62)
4	 36	46	 37	(87)
5	 38	7	 39	(58)  40 (30)
6	 41		d)	

^a Substrate (2 mmol) was allowed to react in the presence of **1a** (35 mg) and 2-methylpropanal (8 mmol) under oxygen atmosphere in 1,2-dichloroethane (10 ml) at 25°C for 15 h.

^b Determined by GLC.

^c The reaction was carried out in toluene (10 ml) at 100°C.

^d Most of substrate was recovered unchanged.

References

- [1] (a) M. Misono, *Catal. Rev.*, 29 (1987) 269. (b) M.T. Pope and A. Müller, *Angew. Chem., Int. Ed. Engl.*, 30 (1991) 34. (c) I.V. Kozhevnikov and K.I. Mateev, *Appl. Catal.*, 5 (1983) 135. (d) Y. Izumi, K. Urabe and M. Onaka, *Zeolite, Clay, and Heteropoly Acid in Organic Reactions*, Kodansha-VCH, Tokyo/Elsevier, New York, 1992 p. 99. (e) Y. Ishii, *Polyoxometalates Chemistry*, Kikan Kagaku Sosetu, No 20, Gakkai Shuppan Senta, Tokyo, 1993, p. 77.
- [2] (a) M.A. Fox, R. Cardona and E. Gaillard, *J. Am. Chem. Soc.*, 109 (1987) 6347. (b) C.L. Hill and D.A. Bouchard, *J. Am. Chem. Soc.*, 107 (1985) 5148.
- [3] (a) R.F. Ranneke and C.L. Hill, *J. Am. Chem. Soc.*, 110 (1988) 5461. (b) R.F. Ranneke and C.L. Hill, *Angew. Chem., Int. Ed. Engl.*, 27 (1988) 1526. (c) R. Chambers and C.L. Hill, *Inorg. Chem.*, 28 (1989) 2511.
- [4] (a) K. Yamawaki, T. Yoshida, H. Nishihara, Y. Ishii, Y. and M. Ogawa, *Synth. Commun.*, 16 (1986) 53. (b) M. Dumas, Y. Vo-Quang, L. Vo-Quang and F. Le Goffic, *Synthesis*, (1989) 64; (c) Y. Ishii, K. Yamawaki, T. Ura, H. Yamada, T. Yoshida and M. Ogawa, *J. Org. Chem.*, 53 (1988) 3587. (d) C. Venturello, R. D'Aloiso, J.C. Bart and M. Ricci, *J. Mol. Catal.*, 32 (1985) 107. (e) F.P. Balistreri, S. Failla, E. Spina and G.A. Tomaselli, *J. Org. Chem.*, 54 (1989) 947. (f) Y. Sakata and Y. Ishii, *J. Org. Chem.*, 56 (1991) 6233. (g) J.-M. Brégeault, C. Aubry, G. Chottard, N. Platzler, F. Chauveau, C. Huet and H. Ledon, in L.I. Simandi (Ed.), *Dioxygen Activation and Homogeneous Catalytic Oxidation*, Elsevier, Amsterdam, 1991, p 521.
- [5] (a) D.P. Katsoulis and M.T. Pope, *J. Am. Chem. Soc.*, 106 (1984) 2737. (b) C.L. Hill and R.B. Brown, *J. Am. Chem. Soc.*, 108 (1986) 536. (c) D.E. Katsoulis and M.T. Pope, *J. Chem. Soc., Dalton Trans.*, (1989) 1483. (d) R. Neumann and C. Abu-Gnim, *J. Am. Chem. Soc.*, 112 (1990) 6025.
- [6] (a) R. Neumann and M. Lissel, *M. J. Org. Chem.*, 54 (1989) 4607. (b) R. Neumann and M. Levin, *J. Org. Chem.*, 56 (1991) 5707. (c) M. Lissel, H. Jansen in de Wal and R. Neumann, *Tetrahedron. Lett.*, 33 (1992) 1795. (d) I.V. Kozhevnikov, V.I. Simanga, G.V. Varnakova and K.I. Matveev, *Kinet. Katal.*, 20 (1979) 506. (e) A. Atlamsani and J.-M. Brégeault, *J. Org. Chem.*, 58 (1993) 5663. (f) R. Neumann and M. Levin, *J. Am. Chem. Soc.*, 114 (1992) 7278.
- [7] For reviews: (a) R.A. Sheldon and J.K. Kochi, *Metal Catalyzed Oxidations of Organic Compounds*, Academic Press, New York, 1981, p. 271. (b) F. Centi and G. Trifiro (Eds.), *New Developments in Selective Oxidation, Studies in Surface Science and Catalysis*, Vol. 55, Elsevier, Amsterdam, 1990. (c) H. Simándi (Ed.), *Dioxygen Activation and Homogeneous Catalytic Oxidation, Studies in Surface Science and Catalysis*, Vol. 66, Elsevier, Amsterdam, (1990); (d) T. Mukaiyama and T. Yamada, *Bull. Chem. Soc. Jpn.*, 68 (1995) 17.
- [8] M. Hamamoto, K. Nakayama, Y. Nishiyama and Y. Ishii, *J. Org. Chem.*, 58 (1993) 6421.
- [9] K. Nakayama, M. Hamamoto, Y. Nishiyama and Y. Ishii, *Chem. Lett.*, (1993) 1699.
- [10] S. Fujibayashi, K. Nakayama, Y. Nishiyama and Y. Ishii, *Chem. Lett.*, (1994) 1345.
- [11] D.P. Smith and M.T. Pope, *Inorg. Chem.*, 12 (1973) 331.
- [12] G.E. Tsigdinos and C.J. Hallada, *Inorg. Chem.*, 7 (1968) 437.
- [13] M.T. Pope, S.E. O'Donnell and R.A. Prados, in R.F. Gould (ed.), *Advances in Chemistry Series: Inorganic Compounds with Unusual Properties*, American Chemical Society, Washington, DC, 1976, Ch. 8, p. 85.
- [14] L. Pettersson, I. Andersson, A. Selling and J.H. Grate, *Inorg. Chem.*, 33 (1994) 982.
- [15] C. Rocchicciolini-Detcheff, M. Fournier, R. Frank and R. Thouvenot, *Inorg. Chem.*, 22 (1983) 207.
- [16] R.A. Sheldon and N. de Heij, in W. Ando and Y. Moro-oka, eds., *The Role of Oxygen in Chemistry and Biochemistry*, Elsevier, Amsterdam, 1988, p. 243.
- [17] (a) C.R.H.I. de Jonge, H.M. van Dort and L. Vollbracht, *Tetrahedron Lett.*, (1970) 1881. (b) L.I. Smith and D.J. Byers, *J. Am. Chem. Soc.*, 63 (1941) 612. (c) H.-D. Becker, *J. Org. Chem.*, 30 (1965) 982.
- [18] (a) A.J. de Jong and R. van Helden, *Ger. Pat.* 2460665 and 2517870. (b) V. Kothari and J.J. Tazuma, *J. Catal.*, 41 (1976) 180. (c) A. Nishinaga, K. Watanabe and T. Matuura, *Tetrahedron Lett.*, (1974) 1291. (e) see in Ref. [7](a).
- [19] M. Shimizu, Y. Watanabe, H. Orita, T. Hayakawa and K. Takehira, *Bull. Chem. Soc. Jpn.*, 65 (1992) 1522.
- [20] O.A. Kholdeeva, A.V. Golvin, R.I. Maksimouskaya and I.V. Kozhevnikov, *J. Mol. Catal.*, 75 (1992) 235.
- [21] (a) Ref. [7](a), p. 373. (b) Ref. [7](a), p. 369.
- [22] Y. Izumi and K. Urabe, *Chem. Lett.*, (1981) 663.
- [23] M. Shimizu, Y. Watanabe, H. Orita, T. Hayakawa and K. Takehira, *Bull. Chem. Soc. Jpn.*, 66 (1993) 251.
- [24] M. Hirano, T. Ishii and T. Morimoto, *Bull. Chem. Soc. Jpn.*, 64 (1991) 1434.
- [25] S. Murahashii, Y. Oda and T. Naota, *J. Am. Chem. Soc.*, 114 (1992) 7913.
- [26] Y. Sprinzak, *J. Am. Chem. Soc.*, 80 (1958) 5449.
- [27] D.L. Allara, *J. Org. Chem.*, 37 (1972) 2448.