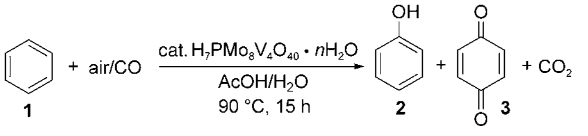
Phenol Synthesis

Hydroxylation of Benzene to Phenol under Air and Carbon Monoxide Catalyzed by Molybdovanadophosphoric Acid**

*Masayuki Tani, Takao Sakamoto, Shuichi Mita, Satoshi Sakaguchi, and Yasutaka Ishii**

Phenols are one of the most important classes of raw materials in the chemical industry, and a variety of compounds are derived from them, such as resins, dyes, and pharmaceuticals.[1] In 2000, the worldwide production of phenol was 6.6 megatons. Most of this phenol is produced by the cumene process reported by Hock and Lang in 1944.[2] The direct conversion of benzene to phenol by hydroxylation with O_2 is the most desirable method among phenol syntheses. However, indirect phenol production through the formation of cumene hydroperoxide and oxidative decomposition of benzoic acid are currently employed. The direct synthesis of phenol from benzene and nitrous oxide has been described,[3] but this method is only cost-effective when nitrous oxide is available cheaply as a by-product.[4] Therefore, for a long time much attention has been paid to the direct synthesis of phenol by the hydroxylation of benzene with O_2, which is referred to as a dream oxidation in the chemical industry. There have been many attempts at the direct conversion of benzenes to phenols with H_2O_2[5] or O_2,[6] under the influence of a reducing agent, such as H_2[7] or CO[8] and transition metals, such as Cu, Pd, or Pt,[9] or heteropolyoxometalates.[10] Recently, Mizukami et al. reported a one-step conversion of benzene to phenol with O_2 and H_2 at a palladium membrane.[7]

In the course of our study on the coupling of benzene with acrylates in the presence of O_2 by $Pd(OAc)_2$ combined with molybdovanadophosphates, we found that a small amount of phenol is formed as a by-product.[11] Thus, our attention has been focused on the direct conversion of benzene (**1**) into phenol (**2**), and an efficient simple catalytic method for the synthesis of **2** from **1** using molybdovanadophosphoric acids as catalysts has been established [Eq. (1)].



(1)

The reaction of **1** under air (15 atm) and CO (5 atm) with $H_7PMo_8V_4O_{40}\cdot n\,H_2O$[12] catalyst in acetic acid/water (9:1; 13.5/1.5 mL) at 90 °C for 15 h afforded **2** in 27.3 % yield (turnover number (TON) = 21.8), along with a small amount of 1,4-benzoquinone (**3**; 3.4 % yield), which was a further oxidation product of **2** (Table 1, run 2). About 70 % of the CO was recovered in this reaction, and the selectivity for **2** based on CO consumed was approximately 35 %. This is the first successful conversion of **1** into **2** in high yield by molybdovanadophosphoric acid under mild conditions.[13] It was found that the yield of **2** was influenced by the partial pressures of air and CO. For instance, the reaction under high air pressure (17.5 atm) and low CO pressure (2.5 atm) resulted in a decrease of the conversion of **1** into **2** (20.9 %; run 1). Under a CO pressure of 10 atm and an air pressure of 15 or 10 atm (runs 3 and 4, respectively), the results were almost the same as those for run 2. In the absence of CO, no reaction was induced (run 5). The reaction was considerably influenced by the amount of solvent mixture and the water content (runs 6–9). No reaction took place in anhydrous acetic acid (run 9). The reaction without sodium acetate resulted in a slight decrease in the yield of **2** (run 10). No reaction took place with a combination of air and H_2 in place of CO as the reducing agent (run 11). It is thought that CO, which can be easily obtained from abundant cheap carbon resources, such as asphalt and pitch, is a superior reducing agent to H_2 derived from methane and naphtha,[14] although the present method brought about the concurrent formation of phenol and a stoichiometric amount of CO_2.

Table 1: Oxidation of benzene (**1**) to phenol (**2**) under air and CO by $H_7PMo_8V_4O_{40}$.[a]

Run	Air:CO [atm]	AcOH/H_2O [mL]	Conv. [%][b]	Yield [%][c] **2**	Yield [%][c] **3**	TON [mol/mol]
1	17.5:2.5	13.5/1.5	33.0	20.9	3.2	16.7
2	15:5	13.5/1.5	41.6	27.3	3.4	21.8
3	15:10	13.5/1.5	47.4	28.1	4.0	22.4
4	10:10	13.5/1.5	44.5	25.9	2.8	20.7
5	20:0	13.5/1.5	n.r.			
6	15:5	18/2	41.4	26.9	3.5	21.5
7	15:5	9/1	41.0	21.0	3.7	16.8
8	15:5	4.5/0.5	44.7	18.1	4.1	14.5
9	15:5	15.0/0	n.r.			
10[d]	15:5	13.5/1.5	35.8	23.3	3.6	18.6
11[e]	15:5	13.5/1.5	n.r.			

[a] **1** (2 mmol) was reacted under air and CO in aqueous acetic acid in the presence of AcONa (0.1 mmol) with $H_7PMo_8V_4O_{40}\cdot n\,H_2O$ (25 µmol, 1.25 mol% based on $H_7PMo_8V_4O_{40}\cdot 24\,H_2O$) at 90 °C for 15 h. [b] n.r. = no reaction. [c] Based on **1** used. [d] Without NaOAc. [e] Air:H_2 = 15:5 (atm); H_2 was used instead of CO.

Figure 1 shows the time-dependence of the hydroxylation of **1**. The production of **2** increased smoothly with time up to five hours and then continued at a constant level, while, **2** was slowly converted into **3** at the same time. The fact that **2** was converted into the overoxidized products including **3** by its individual exposure to CO and air in the presence of the catalyst supports this interpretation.

---

[*] M. Tani, T. Sakamoto, S. Mita, S. Sakaguchi, Prof. Y. Ishii
Department of Applied Chemistry
Faculty of Engineering and High Technology Research Center
Kansai University
Suita, Osaka 564-8680 (Japan)
Fax: (+81) 6-6339-4026
E-mail: ishii@ipcku.kansai-u.ac.jp

[**] This work was partially supported by MEXT.KAKENHI (No.15750095).

Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.

DOI: 10.1002/ange.200462769

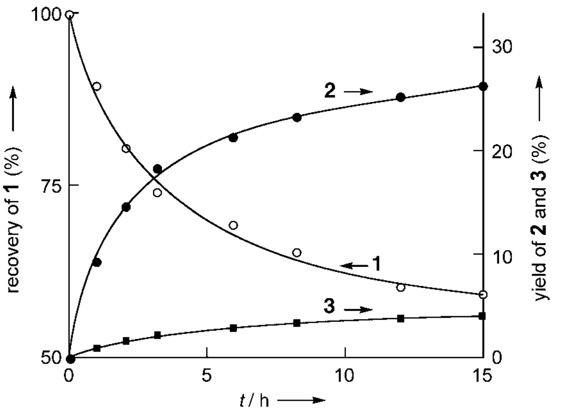


Figure 1. Time-dependence curve for the hydroxylation of **1** under the same conditions as run 6 in Table 1.

Table 2 shows the results of the hydroxylation of **1** in the presence of several molybdovanadophosphoric acids. The reaction was also promoted by $H_{3+n}PMo_{12-n}V_nO_{40}\cdot nH_2O$ (n = 1–3)[12] to give **2** in yields of 13–22%, but $H_3PMo_{12}O_{40}\cdot nH_2O$, which lacked the vanadium atom, did not catalyze the hydroxylation. These results indicate that the vanadium species is a key element for the hydroxylation of benzene, although an active species is not identified because of the complexity of the molybdovanadophosphoric acids used as catalysts. Their ^{31}P NMR spectra (see Supporting Information) attest to the existence of many molybdovanadophosphoric acids that contain varying compositions of P, Mo, and V. However, no reaction occurred by using [VO(acac)$_2$] (acac = acetylacetonate) as a catalyst (run 5). This result will be discussed later.

Table 2: Oxidation of benzene (**1**) to phenol (**2**) under air and CO catalyzed by several molybdovanadophosphoric acids.[a]

Run	Catalyst	Conv. [%]	Yield [%][b]	
			2	**3**
1	$H_3PMo_{12}O_{40}$		n.r.	
2	$H_4PMo_{11}V_1O_{40}$	22.8	13.6	1.2
3	$H_5PMo_{10}V_2O_{40}$	36.8	21.3	3.0
4	$H_6PMo_9V_3O_{40}$	33.6	22.2	2.1
5	VO(acac)$_2$		n.r.	

[a] Reactions were carried out under the same conditions as those for run 2 in Table 1. [b] Based on **1** used.

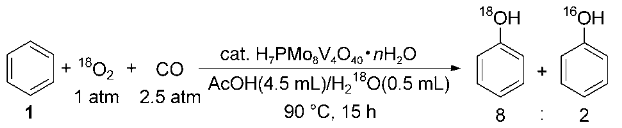
From a practical synthetic viewpoint, reuse of the recovered catalyst is very important. Thus, the hydroxylation was repeated with recovered catalyst under the same conditions as those for run 2 in Table 1. The yields of **2** and **3** were almost the same throughout five runs, that is, 27–29% for **2** and 2–5% for **3**, in the 40–42% conversion of **1** (Table 3). The ^{31}P NMR spectrum of the recovered catalyst was only slightly different from that of the fresh one (see Supporting Information).

Two labeling experiments were carried out to obtain mechanistic information on the hydroxylation. The reaction using $H_2{}^{18}O$ in place of $H_2{}^{16}O$ afforded an 8:2 mixture of Ph^{16}OH and Ph^{18}OH. This finding shows that a nucleophilic attack of $H_2{}^{18}O$ to form a cationic benzene intermediate seems to be unlikely as a major route to **2**. Second, the hydroxylation of **1** under CO and $^{18}O_2$ instead of $^{16}O_2$ in acetic acid and $H_2{}^{18}O$ was examined [Eq. (2)].

Table 3: Oxidation of benzene (**1**) to phenol (**2**) under air and CO by recovered catalyst.[a]

Run	Recovery	Yield [%][b]	
		2	**3**
1	1st	27.5	4.3
2	2nd	27.5	5.3
3	3rd	28.5	2.0
4	4th	28.9	2.5
5	5th	28.0	3.2

[a] Reactions were carried out under the same conditions as those for run 2 in Table 1. [b] Based on **1** used. The conversion of **1** was 40–42%.



(2)

GC–MS measurement of the resulting phenol indicated that an approximate 8:2 mixture of Ph^{18}OH and Ph^{16}OH is formed. The preferential formation of Ph^{18}OH indicates that gas-phase oxygen ($^{18}O_2$) serves as an oxygen source in this hydroxylation reaction. Also, it is likely that the ^{16}O atom in the Ph^{16}OH comes from the oxygen in the $H_7PMo_8V_4O_{40}\cdot nH_2O$ structure. In fact, it was found that $H_7PMo_8V_4O_{40}$ was easily reduced with CO under these conditions. For example, when $H_7PMo_8V_4O_{40}\cdot nH_2O$ (0.5 mmol) in acetic acid was treated with CO (5 atm, ca. 11 mmol) at 90°C for 5 h, about 1 mmol of CO_2 was formed, and the color of the solution changed from orange to dark green. The formation of CO_2 and this color change of the catalyst solution suggest that $H_7PMo_8V_4O_{40}$ is easily reduced to $H_7PMo_8V_4O_{40-x}$, in which the oxygen is partially reduced as well. On the other hand, no such color change of the catalyst was observed when H_2 instead of CO was used for the reduction of $H_7PMo_8V_4O_{40}$. This is in agreement with the fact that the hydroxylation of **1** to **2** did not take place when H_2 was employed in place of CO (Table 1, run 11).

It may be assumed that the oxidation proceeds through a Fenton-type reaction of **1** with H_2O_2 generated in situ ($CO + O_2 + H_2O \rightarrow H_2O_2 + CO_2$), since H_2O_2 is reported to be formed with high turnover frequency from CO, O_2, and H_2O in the presence of a Pd catalyst.[15] Thus, we examined the hydroxylation of benzene with H_2O_2 catalyzed by molybdovanadophosphoric acid. Treatment of **1** with 35% H_2O_2 (1 equiv) in the presence of $H_6PMo_9V_3O_{40}$ in AcOH at 90°C for 8 h produced **2** in low yield (6–7%) based on the amount of **1** used. However, hydroxylation by H_2O_2 with [VO(acac)$_2$] in place of the heteropoly acid afforded **2** in 3–4% yield, whereas the reaction under CO and air was not catalyzed by [VO(acac)$_2$] at all (see Table 2, run 5). This fact may indicate that the formation of H_2O_2 from CO, O_2, and H_2O is unlikely in the present hydroxylation reaction. In addition, the reaction using $^{16}O_2$ and $H_2{}^{18}O$ gave an 8:2 mixture of $Ph^{16}OH$ and $Ph^{18}OH$ as shown above. If H_2O_2 is formed in this reaction, $H^{16}O^{18}OH$ would be generated from $^{16}O_2$ and $H_2{}^{18}O$, and as a consequence an approximate 1:1 mixture of $Ph^{16}OH$ and $Ph^{18}OH$ would be obtained. Therefore, the in situ generation of H_2O_2 is thought to be unlikely in the present hydroxylation reaction.

On the basis of these results, it can be concluded that O_2 is activated on the partially reduced $H_7PMo_8V_4O_{40-x}$ and that the activated oxygen reacts with **1** to eventually form **2**. In addition, since the reaction is not promoted by $H_3PMo_{12}O_{40}$, which lacks the V ion, it seems likely that O_2 is activated on the V species in $H_7PMo_8V_4O_{40-x}$.

In conclusion, we have developed a simple, direct synthetic method of producing phenol (**2**) from benzene (**1**) with air in the presence of CO by using molybdovanadophosphoric acids as catalysts. This method may provide a promising alternative route to **2** from **1** in place of the cumene process, which needs three reaction steps.

Experimental Section

Oxidation of benzene: in a typical procedure, the reaction was carried out in a teflon autoclave. Benzene (2 mmol) was added to a solution of $H_7PMo_8V_4O_{40}\cdot 24\,H_2O$ (26.5 μmol) and AcONa (0.1 mmol) in AcOH (13.5 mL) and water (1.5 mL). The mixture was stirred at 90 °C for 15 h under air (15 atm) and CO (5 atm). After the reaction, GC and GC–MS analyses were performed. The conversions and yields of products were estimated from the peak areas, based on the GC internal standard technique.

Recovery of the catalyst: After the reaction, H_2O (5 mL) was added to the mixture, followed by extraction with iPr$_2$O (40 mL). The aqueous layer was washed with iPr$_2$O (40 mL), and the combined aqueous extracts were concentrated by evaporation under reduced pressure. The green solid obtained was dried in vacuo to give the recovered catalyst. The ^{31}P NMR spectra of the fresh and recovered catalysts were similar.

Received: December 1, 2004

Keywords: hydrocarbons · hydroxylation · oxidation · oxygen · synthetic methods

---

[1] a) R. A. Sheldon, J. K. Kochi, *Metal-Catalyzed Oxidations of Organic Compounds*, Academic, New York, **1981**; b) W. Jordan, H. Barneveld, O. van Gerlich, M. Kleine-Boymann, J. Ullrich in *Ullmann's Encyclopedia of Industrial Chemistry*, *Vol. A19*, VCH, Weinheim, **1991**, p. 307.

[2] H. Hock, S. Lang, *Ber. Desch. Chem. Ges.* **1944**, *B77*, 257.

[3] a) M. Iwamoto, J. Hirata, K. Matsukami, S. Kagawa, *J. Phys. Chem.* **1983**, *87*, 903; b) E. Suzuki, K. Nakashiro, Y. Ono, *Chem. Lett.* **1988**, 953; c) R. Burch, C. Howitt, *Appl. Catal. A* **1992**, *86*, 139; d) R. Burch, C. Howitt, *Appl. Catal. A* **1993**, *103*, 135; e) G. I. Panov, A. S. Kharitonov, V. I. Sobolev, *Appl. Catal. A* **1992**, *82*, 31; f) G. I. Panov, A. S. Kharitonov, V. I. Sobolev, *Appl. Catal. A* **1993**, *98*, 33; g) G. I. Panov, A. S. Kharitonov, V. I. Sobolev, *Appl. Catal. A* **1996**, *141*, 185; h) B. Liptakova, M. Hronec, Z. Cvengrosova, *Catal. Today* **2000**, *61*, 143.

[4] A. K. Uriarte, M. A. Rodkin, M. J. Gross, A. S. Kharitonov, G. I. Panov, *Stud. Surf. Sci. Catal.* **1997**, *110*, 857.

[5] a) C. Walling, *J. Am. Chem. Soc.* **1975**, *97*, 363; b) C. Walling, *Acc. Chem. Res.* **1975**, *8*, 125; c) J. R. L. Smith, R. O. C. Norman, *J. Am. Chem. Soc.* **1963**, *85*, 2897; d) N. A. Milas, *J. Am. Chem. Soc.* **1937**, *59*, 2342; e) H. Mimoun, L. Saussine, E. Daire, M. Postel, J. Fischer, R. Weiss, *J. Am. Chem. Soc.* **1983**, *105*, 3101; f) K. Nomiya, H. Yanagibayashi, C. Nozaki, K. Kondoh, E. Hiramatsu, Y. Shimizu, *J. Mol. Catal. A* **1996**, *114*, 181; g) L. W. Lee, W. J. Lee, Y. K. Park, S. E. Park, *Catal. Today* **2000**, *61*, 137; h) M. Stockmann, F. Konietzni, J. U. Notheis, J. Voss, W. F. Maier, *Appl. Catal. A* **2001**, *208*, 343.

[6] a) N. Herron, C. A. Tolman, *J. Am. Chem. Soc.* **1987**, *109*, 200; b) T. Kitano, Y. Kuroda, M. Mori, S. Ito, K. Sasaki, M. Nitta, *J. Chem. Soc. Perkin Trans. 2* **1993**, 981.

[7] S. Niwa, M. Eswaramoorthy, J. Nair, A. Raj, N. Itoh, H. Shoji, T. Namba, F. Mizukami, *Science* **2002**, *295*, 105.

[8] a) T. Jintoku, H. Taniguchi, Y. Fujiwara, *Chem. Lett.* **1987**, 1865; b) T. Jintoku, K. Takaki, Y. Fujiwara, Y. Fuchita, K. Hiraki, *Bull. Chem. Soc. Jpn.* **1990**, *63*, 438; c) T. Tsunami, M. Nakamura, H. Tominaga, *J. Chem. Soc. Chem. Commun.* **1992**, 1446; d) W. Laufer, J. P. M. Niederer, W. F. Hoelderich, *Adv. Synth. Catal.* **2002**, *344*, 1084.

[9] a) T. Kitano, T. Nakai, M. Nitta, M. Mori, S. Ito, K. Sasaki, *Bull. Chem. Soc. Jpn.* **1994**, *67*, 2850; b) T. Miyake, M. Hamada, Y. Sasaki, M. Oguri, *Appl. Catal. A* **1995**, *131*, 33; c) T. Miyake, M. Hamada, H. Niwa, M. Nishizuka, M. Oguri, *J. Mol. Catal. A* **2002**, *178*, 199; d) I. Yamanaka, T. Nabeta, S. Takenaka, K. Otsuka, *Stud. Surf. Sci. Catal.* **2000**, *130*, 815; e) T. Fukushi, W. Ueda, Y. Moro-oka, T. Ikawa, *Ind. Eng. Chem. Res.* **1989**, *28*, 1587; f) R. Hamada, Y. Shibata, S. Nishiyama, S. Tsuruya, *Phys. Chem. Chem. Phys.* **2003**, *5*, 956; g) H. Yamanaka, R. Hamada, H. Nibuta, S. Nishiyama, S. Tsuruya, *J. Mol. Catal. A* **2002**, *178*, 89; h) I. Yamanaka, S. Katagiri, S. Takenaka, K. Otsuka, *Stud. Surf. Sci. Catal.* **2002**, *130*, 809.

[10] a) K. Nomiya, K. Yagishita, Y. Nemoto, T. Kamataki, *J. Mol. Catal. A* **1997**, *126*, 43; b) L. C. Passoni, A. T. Cruz, R. Buffon, U. Schuchardt, *J. Mol. Catal. A* **1997**, *120*, 117; c) Y. J. Seo, Y. Mukai, T. Tagawa, S. Goto, *J. Mol. Catal. A* **1997**, *120*, 149.

[11] T. Yokota, M. Tani, S. Sakaguchi, Y. Ishii, *J. Am. Chem. Soc.* **2003**, *125*, 1476.

[12] a) G. A. Tsigdinos, C. J. Hallada, *Inorg. Chem.* **1968**, *7*, 437; b) L. Pettersson, I. Anderesson, A. Selling, J. H. Grate, *Inorg. Chem.* **1994**, *33*, 982; c) V. F. Odyakov, E. G. Zhizhina, R. I. Maksimovskaya, K. I. Matveev, *Kinet. Catal.* **1995**, *36*, 733; d) K. Nomiya, K. Yagishita, Y. Nemoto, T. Kamataki, *J. Mol. Catal. A* **1997**, *126*, 43; e) M. Vennat, P. Herson, J.-M. Brégeault, G. B. Shul'pin, *Eur. J. Inorg. Chem.* **2003**, 908.

[13] For example, the Pd-catalyzed synthesis of phenol from benzene under CO (5 atm) and O_2 (65 atm) in $H_2O/MeCOCH_2CHMe_2$ at 70 °C gave phenol in 3.2 % yield based on benzene used: R. Tassiniari, D. Bianchi, R. Ungarelli, E. Battistel, R. D'Aloisio (Enichem S.P.A.), EP894783, **1999** [*Chem. Abstr.* **1999**, *130*, 155248].

[14] Evolution of about 0.9 kg of CO_2 is estimated to accompany the production of 1 m^3 of H_2 from CH_4.

[15] a) D. Bianchi, R. Bortolo, R. D'Aloisio, M. Ricci, *Angew. Chem.* **1999**, *111*, 734; *Angew. Chem. Int. Ed.* **1999**, *38*, 706; b) D. Bianchi, R. Bortolo, R. D'Aloisio, M. Ricci, S. Soattini (Enichem S.P.A.), EP808796, **1997** [*Chem. Abstr.* **1997**, *128*, 50358]; c) R. Vignola, E. Battistel, D. Bianchi, R. Bortolo, R. Tassinari (Enichem S.P.A.), EP861688, **1998** [*Chem. Abstr.* **1998**, *129*, 218223].