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Mechanistic Study of Air Oxidation of Benzene in Sulfuric Acid Catalyzed by Cuprous Ions

Atsutaka Kunai, Shintaro Hata, Sotaro Ito, and Kazuo Sasaki*

Department of Applied Chemistry, Faculty of Engineering, Hiroshima University, Saijo, Higashi-Hiroshima 724, Japan

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The aerial oxidation of benzene in a 0.05 M H_2SO_4 solution in the presence of CuCl produces phenol and hydroquinone, the latter of which is not found in Fenton reactions. The present study was carried out for elucidation of the mechanism of the reaction in the presence of Cu^+ ions by the aid of ^{18}O-tracer technique. Results obtained are consistent with the reaction mechanism of the Fenton reaction currently accepted, and no peculiar mechanism inherent to Cu^+ ions is observed. The isotope incorporation in both phenol and hydroquinone was in good agreement with the simple probability rule as if there was no isotope scrambling during the whole reaction sequence. This is in accordance with the mechanism in which hydroquinone is derived from the oxygen adduct of a hydroxycyclohexadienyl radical almost exclusively. Under our conditions, however, equilibration between hydroxycyclohexadienyl radicals and benzene cation radicals is not observed, presumably because the latter, if formed, are rapidly reduced by Cu^+ ions.

We have reported that benzene is oxidized to form phenol and hydroquinone under ambient conditions.[1] The reaction proceeds in aqueous acidic solutions containing cuprous ions and oxygen.

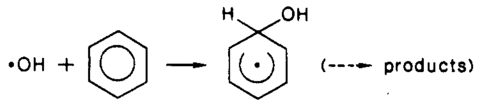
Mechanistically, the reaction has a close resemblance to the Fenton reaction and without doubt OH radicals play a role of primary importance. Although the Fenton reaction (Fe^{2+}/H_2O_2) of aromatic compounds has been studied extensively and the reaction mechanism is almost established,[2-5] there are no systematic data for elucidating the reaction mechanism in the Cu^+/O_2 system.

Besides the difference in reactivities of Fe^{2+} and Cu^+ ions, the apparent difference between the two reaction systems appears in the oxidant being used, oxygen for the former and hydrogen peroxide for the latter. These differences cause some change in the reaction products. For instance, an appreciable amount of hydroquinone is produced[1b,c] in the Cu^+/O_2 system while it is not in the Fenton system. Biphenyl, which is one of the main products in the Fenton reaction under certain conditions, is hardly seen in the Cu^+/O_2 system. It will be interesting whether the two reactions concerned are occurring independently with their own mechanism or whether the problem is merely a matter of appearance.

There is another point to be elucidated. According to our experience,[1] the yield of phenol based on Cu^+ ions consumed is near to 10%, which is almost one-third of the theoretical value expected from the stoichiometry in eq 1–3. When the reaction is started from H_2O_2 instead of oxygen under a nitrogen atmosphere, the percentage yield of phenol based on H_2O_2 is only 30%. The latter figure seems nearly one-half of the corresponding value with Fe^{2+} ions (Fenton reaction). The reason why the efficiency is lower with Cu^+ ions than Fe^{2+} ions may also be explained if the reaction mechanism is established. We thus attempted to study the isotope incorporation in the products of the Cu^+/O_2 system. It should be noted that, even in the Fenton reaction, some uncertainty remains about the effect of oxygen.[4] Since an appreciable amount of hydroquinone, which has never attracted attention in the past, is produced in the Cu^+/O_2 system, the isotope incorporation in hydroquinone will provide useful information not only for the present system but also for the Fenton reaction.

$$2Cu^+ + O_2 + 2H^+ \longrightarrow 2Cu^{2+} + H_2O_2 \qquad (1)$$

$$Cu^+ + H_2O_2 + H^+ \longrightarrow Cu^{2+} + H_2O + \cdot OH \qquad (2)$$



(3)

Experimental Section

Analyses. Isotope contents in both the reacting gas and the phenolic products were determined by a Hitachi RMU-6D mass spectrometer. For the analysis of phenolic products, a Hitachi 655 high-pressure liquid chromatograph (HPLC) was employed. The separation column was a Merck Hibar Lichrosorb RP-18 (10 μm). The eluent was a mixture of acetonitrile (33%) and aqueous phosphate buffer (pH 3.5, 67%). In the chromatogram, three peaks corresponding to hydroquinone, catechol, and phenol appeared in that order. Biphenyl was not detected at all.

Tracer Experiments. Experimental apparatus consisted of mainly two parts, the reactor and the gas reservoir systems (see Figure 1). By separate experiments, it was confirmed that isotope exchange between gaseous oxygen and solution components (H_2O and H_2O_2) was negligible.

Preparation of Reacting Gas. Heavy oxygen gas was obtained by electrolysis of ^{18}O water of 98.4% purity supplied by Amersham International. A sample of the labeled water (1 mL) was placed in a small U-tube electrolysis cell (E) of which the anode branch was connected to the reservoir system composed of a ca. 30 mL glass cylinder and a 100 mL ground-glass syringe (GS 1), being separated by an electromagnetic valve (EMV). The valve interlocked with an optical device (L) to maintain the pressure inside the cylinder equal to external atmosphere. Another syringe (GS 2) was set to the bottom of the cylinder through two three-way cocks (C1 and C2). Prior to electrolysis, the system was evacuated and filled with He. Labeled oxygen gas evolved by electrolysis was first led to the syringe (GS 1) to read its volume and then mixed with a known amount of ordinary oxygen preliminarily taken in GS 2.

Reactor System. The system was composed of a 500-mL round-bottom flask with four openings to which a gas buret, a gas sampler, and a dropping funnel were attached. The reservoir system was connected through the fourth opening. Oxygen gas stored in the reservoir system was diluted with a mixture of He and Ar stored separately in the reactor system by opening the stopcock C3. Ar was used as the internal standard. After mixing the three gases homogeneously, the stopcock C3 was again closed

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Table I. Material Balance of Benzene in the Reaction of the Cu/O_2 System[a]

			products[b]		molar ratio based on benzene			
benzene reacted	CuCl reacted	oxygen absorbed	phenol	hydroquinone	Cu^+	O_2	PhOH	HQ
0.490	3.80	1.20	0.253	0.078	7.76	2.45	0.52	0.16

[a] All data are expressed in mmoles. [b] Besides these, a trace amount of catechol and an unknown product estimated to be hydroxymucondialdehyde were detected.

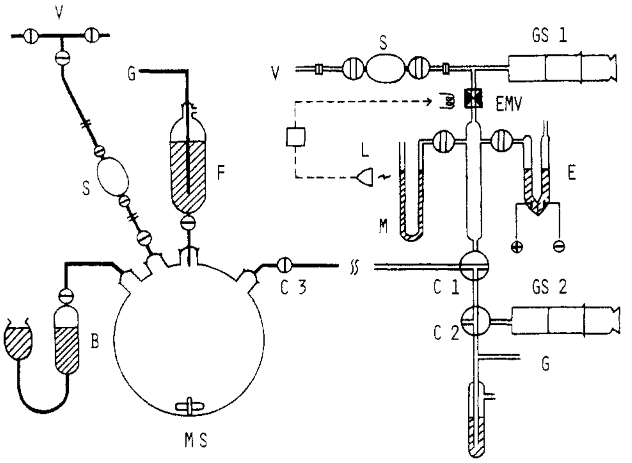

Figure 1. Reactor system of isotope experiments: (E) electrolysis cell; (GS 1 and GS 2) 100-mL glass syringes; (EMV) electromagnetic valve; (L) photo sensor; (S) gas sampler; (M) micromanometer; (F) dropping funnel; (B) gas buret; (MS) magnetic spin bar; (C1 and C2) three-way cocks; (C3) stopcock; (G) gas inlet; (V) vacuum system.

to separate the reservoir from the reactor system. The initial composition of the reacting gas was analyzed at this stage with particular attention on the O_2 to Ar ratio, which gave the best proof for the apparatus being free from leakage when compared with the ratio at the final stage of the reaction.

Cuprous chloride (792 mg; 8 mmol) had been placed preliminarily in the reactor flask. After the preparation of the reaction gas as described above, a deaerated solution of 0.05 M H_2SO_4 (200 mL) was introduced into the flask from a dropping funnel. The reaction was started by addition of 10 mL of benzene under vigorous agitation. After complete dissolution of CuCl (30 min), a sampling of the gas phase was taken for mass spectrometry, nitrogen was flushed into the solution to remove benzene and oxygen and the reaction was stopped. The resultant solution was extracted with dichloromethane to isolate phenols. Hydroquinone was separated from the condensed extract and recrystallized from benzene. Phenol was isolated by vacuum sublimation from the residual extract.

Material Balance. Experiments for determining material balance were carried out in a 200-mL Erlenmeyer flask. A benzene solution (20 mM) in 0.05 M H_2SO_4 was prepared in advance. This solution (100 mL) was transferred carefully into an ice-cooled flask to which a micromanometer and a gas-tight glass syringe were installed. A known amount of CuCl had been preliminarily placed in a small Teflon pan which hung inside the flask by a string. Before the reaction was started the flask was warmed to room temperature (20 °C), and the whole system was equilibrated. By a vigorous stirring of the solution, CuCl in the pan was conveniently transferred to the solution, and the reaction was started. The volume of oxygen consumed was continuously followed during the reaction.

Since benzene is volatile, the amount of benzene in the gas space and on the wall surface of the apparatus affected the result seriously. Because of this, it was necessary to cool the whole apparatus after finishing the reaction to minimize benzene in the gas space. It was also necessary to wash the walls of every part of the apparatus carefully with hexane. By these precautions it was possible to recover 98% of benzene used.

Results and Discussion

Material Balance and Some Characteristics of the Reaction. Under ordinary conditions, products detectable by HPLC are hydroquinone, phenol, and catechol. Besides these, a distinctive peak appeared between hydroquinone and catechol, whenever oxygen was present in the reaction system. We could not, however, identify the species responsible for this peak. Upon addition of carbonyl reagent, semicarbazide, or hydroxylamine, the peak decreased, definitely suggesting the product to be hydroxymucondialdehyde.[6] The yield of it estimated from the amount of carbonyl reagent reacted was, however, negligibly small (less than 1%).

Acidity of the reaction medium affected seriously the product distribution in the Cu/O_2 system. For instance, the reaction in 0.05 M H_2SO_4 produced phenol and hydroquinone in a molar ratio of approximately 3:1. The ratio changed monotonously with increasing pH, and at pH 3.5 the ratio was almost inverted.[7] It should be noted, however, that the data cited in the following part of this paper are restricted to those obtained in 0.05 M H_2SO_4 solutions.

In the absence of benzene, the molar ratio of oxygen absorbed against CuCl reacted was 4, in agreement with the stoichiometry in eq 4.

$$O_2 + 4H^+ + 4Cu^+ \rightarrow 2H_2O + 4Cu^{2+} \qquad (4)$$

When benzene was present in the system, however, the material balance became as listed in Table I. In this particular experiment, 1.94 mmol of benzene was initially taken in 100 mL of 0.05 M H_2SO_4 to make the concentration slightly less than saturated. After the reaction, the amount of benzene recovered was 1.45 mmol, showing that the remaining 0.49 mmol was consumed during the reaction. During this period, the amount of CuCl reacted was 3.80 mmol.

The selectivities with respect to phenol and hydroquinone are indicated at the right extreme of Table I. The value for phenol (52%) is slightly higher than the corresponding value in the Fenton system (43–45%, see Table II of the succeeding paper.[8] Overall selectivity of phenols including hydroquinone (*p*-benzoquinone in Fenton reaction) is still higher (ca. 70%) than in the Fenton system (ca. 50%). In contrast, the yield of total phenolic products on the base of Cu^+ ions is very low (0.331/3.80 = 0.09). Higher selectivity and lower yield of phenolic products seem to be one of the characteristics of the Cu^+/O_2 system. Other characteristic features of this system appear, for instance, in a poor yield of catechol and complete disappearance of biphenyl. The selective formation of hydroquinone and its pH dependence should be regarded as the remarkable character of this reaction.

Tracer Study. Undoubtedly, the characteristic features that appeared in the reaction of the Cu^+/O_2 system are closely related to the presence of oxygen. In the Fenton reaction, too, it is well-known that biphenyl is not produced or markedly decreased by the presence of oxygen.[4,5]

Although there are several pieces of evidences[1] that the reactions occurring in the Cu^+/O_2 system are basically the

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[6] Jacob, N.; Balakrishnan, I.; Reddy, M. P. *J. Phys. Chem.* **1977**, *81*, 17.

[7] Ito, S.; Okada, H.; Sasaki, K., to be published.

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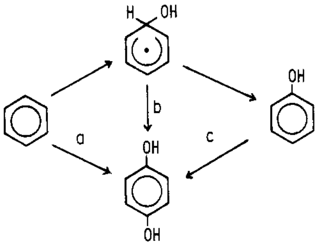
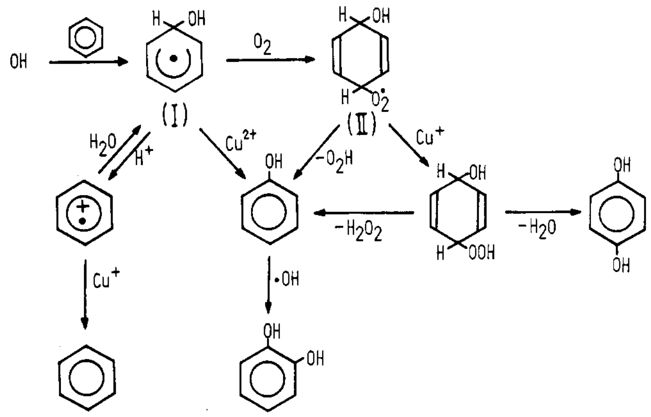
Table II. ^{18}O Content (%) in the Reacting Gas and Products in the Cu/O_2 System

	O_2			phenol			hydroquinone		
run	m/e	before	after	m/e	obsd	calcd	m/e	obsd	calcd
1	32	92.9	93.0	94	92.2	92.9	110	88.8	86.1
	34	0	0	96	7.8	7.1	112	10.9	13.4
	36	7.1	7.0				114	0.3	0.5
2	32	78.8	79.3	94	79.0	79.3	110	67.4	62.8
	34	0	0	96	21.0	20.7	112	30.5	32.9
	36	21.2	20.7				114	2.1	4.3

Scheme I



Scheme II



same as those in an ordinary Fenton reaction and OH radicals are of primary importance, there still remain possibilities of assuming some active species other than OH radicals. In this connection, it should be noted that the special reactivity of metal ion–oxygen complex has often been postulated in the past, mainly in the biochemical field.[9-12] Through a series of studies on the autoxidation of Cu(I) complex salts, Zuberbühler[13-15] concluded the formation of Cu(I)–O_2 complex at the transition state. A similar conclusion was also reached by Gray.[16] These studies suggest that some specific mechanism might be operating in the Cu^+/O_2 system. In this respect, it is of particular interest to find the route by which hydroquinone is produced.

Generally speaking, three different routes can be considered for producing hydroquinone as illustrated in Scheme I: (a) a direct path in which two oxygen atoms of hydroquinone come from a single oxygen (or H_2O_2) molecule; (b) a stepwise path in which a hydroxycyclohexadienyl radical (radical I) is converted to hydroquinone without passing through phenol; (c) a stepwise path in which phenol is first formed and then is converted to hydroquinone.

Among these three, the path c can be safely ignored. This is because when phenol was oxidized in place of benzene in the Cu^+/O_2 system, the amount of hydroquinone decreased to almost one in eight and, instead, catechol increased drastically and its yield was almost twice as much as the amount of hydroquinone.[7] A similar result was also reported by Varagnut[17] who studied the reaction of phenol with Fenton's reagent. Accordingly, if hydroquinone were derived from phenol, a lower yield of hydroquinone would be resulted and more catechol would have been produced than those actually observed (Table I). Presumably, the yield of catechol, which is very low in the reaction of benzene, may represent the degree of the contribution of path c. Another support for this assumption is, in the reaction of benzene in the Cu^+/O_2 system, that phenol and hydroquinone accumulate independently of each other to make the molar ratio unchanged irrespective of the reaction time.[7] This also indicates that phenol and hydroquinone are formed competitively, and the consecutive formation of the latter compound can be ruled out.

Accordingly, our tentative task is how to distinguish the other two paths, a and b. This can be accomplished by use of doubly labeled oxygen, $^{18}O_2$. If path a operates preferentially, hydroquinone produced should consist only of doubly labeled (*m/e* 114) and ordinary (*m/e* 110) molecules, but no singly labeled species (*m/e* 112) can be expected. The molar fraction of the doubly labeled species in the total hydroquinone should be the same as the fractional content of labeled oxygen in the reacting gas. On the other hand, if the reaction proceeds via path b, hydroquinone will contain doubly labeled molecules at a lesser percentage.

Table II shows the results of two series of experiments using oxygen of two different isotope contents (0.07 and 0.21, respectively). As for phenol, it is clearly indicated that the isotope content after the reaction preserves the isotope content in the reacting gas. This is in some sense reasonable because, as far as the isotope scrambling at any stage of the passage from OH radicals to phenol is negligible, the tracer content in phenol should be equal to the gaseous composition. Accordingly, attention should rather be focused on the data of hydroquinone which indicate that the singly labeled species (*m/e* 112) greatly exceeds the doubly labeled one (*m/e* 114). Relative abundance of the three species (*m/e* 110, 112, and 114) precisely coincide with the probability (last column) calculated on the assumption of two-step reaction. This tells us that the path a can safely be excluded.

Arguments developed above lead us to postulate the reaction sequence as is outlined in Scheme II, which is basically the same as the mechanism proposed for the Fenton reaction.[4,5] According to the currently accepted theory, radical I is the primary intermediate in the reaction of OH radicals with benzene. Phenol is produced by oxidation of radical I when certain oxidants such as Cu^{2+} or Fe^{3+} ions are in the system. When oxygen is present,

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(12) Hamilton, G. A. *Ibid.* **1964**, *86*, 3391.

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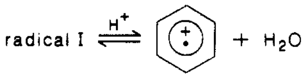
(17) Varagnut, J. *Ind. Eng. Chem., Prod. Res. Dev.* **1976**, *15*, 212.

radical I is rapidly converted to peroxy radical (radical II), which according to Dorfman[3] also produces phenol by releasing an HO_2 radical. These mechanisms seem applicable without any modification to the formation of phenol in the Cu^+/O_2 system.

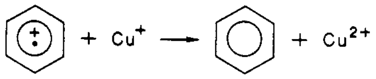
As for hydroquinone, its formation route was found to be competitive with that of phenol, and the isotope incorporation satisfied the simple probability rule so that the fraction of doubly labeled product was equal to the square of the fractional isotope content in the reacting gas. Undoubtedly, the first isotope is incorporated at the stage of radical I, and the second incorporation occurs at radical II. No peculiar mechanism inherent to the Cu^+/O_2 system is necessarily taken into account.

There is another point to be noted. According to Norman[18,19] and Walling,[4,5] a hydroxycyclohexadienyl radical (radical I), which is believed to be the primary intermediate in the reaction, suffers the acid-catalyzed dehydration reaction shown in eq 5. The dehydration step is thought to be in quasi-equilibrium with the reverse hydration reaction. If the rate of the backward reaction is large enough, the isotope content in radical I should be lowered because the backward reaction produces nonlabeled radical I. Along this line, Vysotskaya[20] studied the ^{18}O incorporation in phenols produced during the Fenton reaction of some substituted benzenes and reported that the isotopes scrambling due to eq 5 was confirmed. Although we may be somewhat skeptical[21] about the accuracy of their experiment we still have no reason to deny their result.



(5)

The data in Table I, however, do not show such a scrambling effect. We are left with the question why the scrambling takes place in the Fenton system but not in the Cu^+ system. A tentative but consistent explanation for this apparent contradiction may be obtained if we assume a rapid electron transfer between the cation radicals produced by eq 5 and Cu^+ ions (eq 6).



(6)

A similar reaction with Fe^{2+} ions in place of Cu^+ was originally proposed by Walling.[4,5] The electron-transfer reaction may be faster with Cu^+ than Fe^{2+} ions so that the reverse reaction back to radical I can safely be ignored and the isotope concentration in phenol will become equal to that of the reacting gas. If this is true, it may also be true that some of the Cu^+ ions and thus radical I are wasted by this mechanism. This may be an answer to the question why the efficiency is lower with Cu^+ ions than Fe^{2+} ions, which was raised in the introduction of this paper. Unfortunately, however, we have not got any further information yet to give a certain answer to this problem.

In any case, we believe that almost all of the apparent differences found between the Cu^+/O_2 and Fe^{2+}/H_2O_2 systems can be attributed to the different redox behavior of the $Cu^{+/2+}$ and $Fe^{2+/3+}$ couples; i.e., while the Cu^+ reduction of O_2 is fast, Fe^{2+} reduction of O_2 is too slow to be important. This is the reason why hydrogen peroxide is necessary in the Fenton reaction. The reason why hydroquinone is produced appreciably in the present system but not in the Fenton system may also be related to the different redox behavior of the two metal ion couples, though the details are left for further study.

The absence of biphenyl in the present system should be ascribed to the effect of oxygen which rapidly converts radical I to II. Direct oxidation of radical I by Cu^{2+} ions may also be responsible for the absence of biphenyl.

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Registry No. CuCl, 7758-89-6; benzene, 71-43-2.

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[20] Vysotskaya, N. A.; Shevchuk, L. G. *Zh. Org. Khim.* **1973**, *9*, 2080.

[21] The isotope levels used in their experiments seems too low to draw any accurate conclusion. In addition, according to their result at pH 1.5 (run 13 of their table), which was done at conditions more or less similar to our experiments,[8] 99% of phenol produced contain hydroxyl groups originated from water; i.e., 99% of phenol is formed by passing through the benzene cation radical. This is not only incredible in itself but also disagrees with our result described in the succeeding paper (See Table I, ref 8).

Effect of Dihydroaromatic Compounds on the Cation Radical Chain Oxygenation of Tetraalkyl Olefins

Stephen F. Nelsen* and Mark F. Teasley

S. M. McElvain Laboratories of Organic Chemistry, Department of Chemistry, University of Wisconsin, Madison, Wisconsin 53706

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Ionic chain hydrogenation of *syn*-sesquinorbornene (**7**) to **13** by 1,4-cyclohexadiene (**11**) may be initiated by tris(2,4-dibromophenyl)aminium ($\mathbf{9}^{\bullet+}$) hexachloroantimonate at −78 °C and is efficient enough to inhibit cation radical catalyzed oxygenation of **7** by oxygen. The chain-carrying steps appear not to involve radicals, and the reaction can be initiated by HBF_4 at low temperature or TFA at above room temperature. *anti*-Sesquinorbornene (**8**) is considerably less reactive and requires HBF_4 to initiate hydrogenation. Isopropylideneadamantane (**16**) requires FSO_3H for initiation, but biadamantylidene (**1**) is not hydrogenated under our conditions. Nevertheless, addition of 5 equiv of **11** intercepts the kinetic chain for cation radical catalyzed oxygenation of **1** to dioxetane **2**; the chain length for consumption of **1** drops from over 800 to less than 2, and epoxide **19** becomes a major product. It is proposed that the open peroxy carbocation $B^{\bullet+}$ is trapped by **11** to lead to the observed results.

Tetraalkyl olefins containing α-branched alkyl groups which hold their C_α–H bonds near the nodal plane of the olefin π system, such as biadamantylidene (**1**), give unusually kinetically stable cation radicals,[1] making their

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