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Oxidation of Benzene to Phenols with Molecular Oxygen promoted by Copper(I) Chloride

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Benzene suspended in aqueous sulphuric acid solution was hydroxylated with O_2 in the presence of copper(I) chloride to give phenol and hydroquinone in yields of 24 and 8%, respectively. The active species generated from the Cu^I–O_2 system was shown to be hydroxyl radical from two pieces of evidence. It was suggested that hydroquinone is produced *via* an intermediate peroxyl radical, which is formed by the reaction of hydroxycyclohexadienyl radical with O_2.

Benzene is resistant to oxidation with molecular oxygen under ambient conditions. Udenfriend found that aromatic compounds are hydroxylated by O_2 at room temperature if Fe^{II}, ascorbic acid, and EDTA are also present.[1] However, the yields are generally poor and this method does not have much synthetic utility.[2] Benzene undergoes hydroxylation with Fenton's reagent (consisting of Fe^{II} and H_2O_2) to give phenol in moderate yields.[3,4] The active species from Fenton's reagent is established to be the hydroxyl radical generated by reaction (1).[5]

$$Fe^{II} + H_2O_2 + H^+ \longrightarrow Fe^{III} + {}^{\bullet}OH + H_2O \qquad (1)$$

Lindsay Smith demonstrated that aromatic compounds can be hydroxylated with O_2 in the presence of metal ions such as Cu^I, Sn^{II}, Ti^{III}, or Fe^{II}–EDTA, which have a standard redox potential $E°$ *ca.* 0.15 V.[6] These metal ions–O_2 systems have been supposed not to involve H_2O_2 as an intermediate or $^{\bullet}OH$ radical as the attacking species[6–8] on the basis of observed isomer distributions different from those from Fenton's oxidation. In contrast to the extensive studies on hydroxylation with Fenton's reagent,[3,4,5,9] Udenfriend's reagent,[6–8] and its analogue,[10] there has been no report so far on the hydroxylation of benzene and related compounds with O_2 promoted by Cu^I ions, except those by Lindsay Smith *et al.*[6,10] and Ullrich *et al.*[8] Hydroxylation with Cu^I–O_2 is also of interest from the biological point of view, since some oxygenases (quercetin 2,3-dioxygenase, dopamine β-hydroxylase, and tyrosinases) contain copper ion as an active centre, though little is known about the role of copper ion in the activation of molecular oxygen.[11,12]

The purposes of the present study on the hydroxylation of benzene with the Cu^I–O_2 system are to elucidate the general feature of this reaction, to determine the active species generated from Cu^I–O_2, to find out the optimum conditions for the formation of phenols, and to present a reaction scheme which accounts for the observations with the Cu^I–O_2 system.

Results and Discussion

Oxidation of Copper(I) *Chloride in the Absence of Benzene.*—Copper(I) chloride itself is sparingly soluble (*ca.* 1mM) in water[13] and in 0.05M-sulphuric acid. When solid copper(I) chloride is immersed in 0.05M-sulphuric acid and stirred at 25 °C under aerobic conditions, it slowly dissolves to give copper(II) ion by oxidation with O_2 (Figure 1). Hydrogen peroxide was detected in the oxidation mixture but its concentration was < 1mM. After oxidation for 1 h, copper(I) chloride (1 mmol) completely dissolved to give copper(II) ion (1 mmol) and hydrogen peroxide (0.003 mmol) with absorption of O_2 (0.24 ± 0.01 mmol). In dilute sulphuric acid, < 0.01M, copper(I) chloride was not completely oxidized even after 2 h. The stoicheiometry of the oxidation of copper(I) chloride, therefore, can be written as (2).

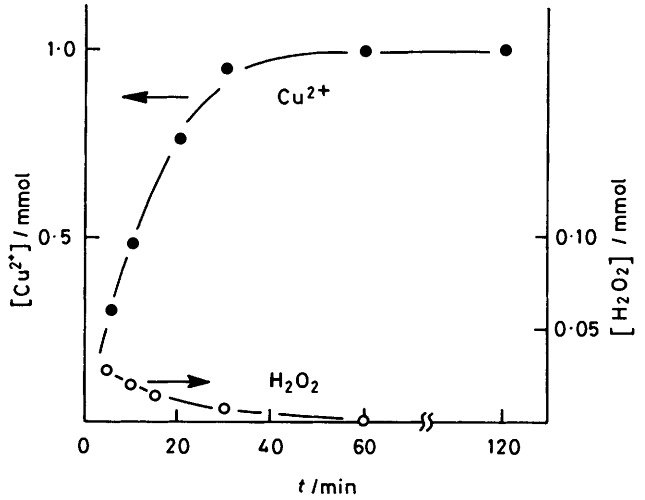


Figure 1. Time course of the oxidation of copper(I) chloride with O_2 in the absence of benzene. Copper(I) chloride, 1 mmol; solvent, 25 ml of 0.05M-H_2SO_4; atmosphere, air; temperature 25 °C

$$4\,Cu^I + O_2 + 4\,H^+ \longrightarrow 4\,Cu^{II} + 2\,H_2O \qquad (2)$$

Oxidation of Copper(I) *Chloride in the Presence of Benzene.*—When copper(I) chloride was oxidized with O_2 in the presence of benzene, three oxidation products, phenol, hydroquinone (HQ), and catechol (CA) were detected with reversed-phase high-performance liquid chromatography (h.p.l.c.). Neither resorcinol nor biphenyl, one of the main products in the oxidation of benzene with Fenton's reagent,[3,4] was detected at all. A small amount of *p*-benzoquinone was detected with h.p.l.c. but its yield was negligible except at higher O_2 pressure. The peak between HQ and CA in the chromatogram was estimated to be β-hydroxymucondialdehyde (HMDA)[14,15] since (1) it was completely depleted by addition by hydroxylamine or semicarbazide and (2) the absorption spectrum for the peak shows a broad band extending from 260 to 300 nm, while mucondialdehyde shows a sharp maximum at 270 nm.[14] The time courses of the accumulation of phenol, HQ, and CA shown in Figure 2 is parallel to that of the oxidation of copper(I) chloride with O_2 (Figure 1), suggesting that the rate-determining step in the oxidation of benzene with the CuCl–O_2 system is the oxidation of copper(I) chloride with O_2. The molar

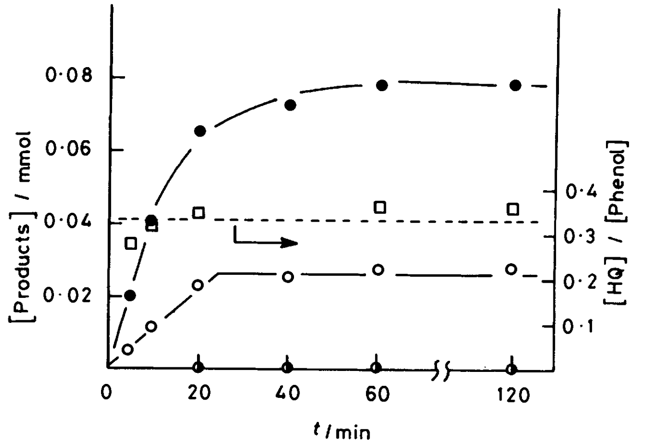


Figure 2. Accumulation curves of phenols in the oxidation of benzene with Cu^I–O_2. Benzene was oxidized under standard conditions (see Experimental section): ●, phenol; ○, HQ; ◑, CA; □, HQ/phenol

Table 1. Oxidation of benzene to phenols in the presence of copper salt at 25 °C[a]

Copper salt	H_2O_2 (mmol)	Atmosphere	Phenol (mmol)	HQ (mmol)
$CuCl_2$	0	Air	0	0
$CuSO_4$	0.5	Air	0	0
CuCl	0	N_2	0	0
CuCl	0	Air	0.08	0.027
CuCl	0.5	N_2	0.15	0.008

[a] [Copper salt] 40mM (1 mmol); [benzene] 8.4 mmol; solvent 25 ml of 0.05M-H_2SO_4; agitation shaking at 170 oscillation min^{-1}; reaction time 2 h

ratios of these products obtained under the typical reaction conditions described in the Experimental section were approximately independent of the reaction time, 100 (phenol), 33 (HQ), 2 (CA), and 2 (HMDA). The formation of an appreciable amount of HQ has not been reported in the oxidation of benzene with OH radical[3–5,14–18] and is characteristic of the CuCl–O_2 system. The detailed mechanism for the formation of HQ will be discussed in the later section. In the oxidation of benzene with Fenton's reagent,[3,4,9] biphenyl along with phenol were formed but addition of Cu^{II}, which is intrinsically present in the CuCl–O_2 system, effectively suppresses the formation of the dimeric product.[4] The γ-radiolysis of aerated aqueous solutions of benzene, which is established to involve OH radical as an active species,[16–18] yields phenol and HMDA.[14,15] Thus the oxidation products from the copper(I)–O_2 system are, except HQ, similar to those from the oxidation with $^{\bullet}OH$ radical. The quantitative relationship between the yield of phenols and the amount of Cu^{II} ion formed will be discussed in the later section.

Requirements for the Oxidation of Benzene.—With the intention of revealing requirements for the oxidation described above, benzene was treated with O_2 or H_2O_2 in the presence of either copper(I) or copper(II) species. The results in Table 1 clearly show that the coexistence of copper(I) and either O_2 or H_2O_2 is necessary for the hydroxylation of benzene. The yield of phenol in the oxidation of benzene with molecule oxygen in the presence of copper(I) chloride was 8% based on copper(I) chloride added. Copper(I) bromide and tetrakis(acetonitrile)-copper(I) perchlorate, a water-soluble complex of copper(I), were also effective for the oxidation of benzene but the yields of phenol based on copper(I) species were 2.1 and 2.3%, respectively. The iodide and thiocyanate of copper(I) gave no phenol because of their insolubility in water.[13] Copper(I) chloride, therefore, was used exclusively throughout this work. The active species from the CuCl–O_2 system is supposed to be hydroxyl radical generated from reactions (3) and (4), since

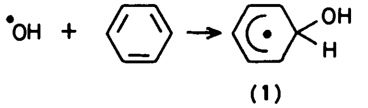
$$2\,Cu^I + O_2 + 2\,H^+ \longrightarrow 2\,Cu^{II} + H_2O_2 \qquad (3)$$

$$Cu^I + H_2O_2 + H^+ \longrightarrow Cu^{II} + {}^{\bullet}OH + H_2O \qquad (4)$$

copper(I) chloride is quantitatively converted into copper(II) ion by the oxidation with O_2 (Figure 1) and the oxidant, O_2, can be replaced by H_2O_2 as seen in Table 1. Reaction (4) is essentially the same as reaction (1) except Fe^{II} was replaced by Cu^I. The role of H_2O_2 will be fully analysed in the following section.

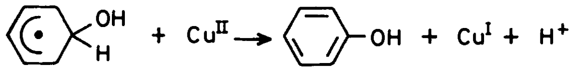
The Role of H_2O_2 *in the Oxidation of Benzene.*—As demonstrated in Table 1, benzene can be oxidized with H_2O_2 in the presence of copper(I) chloride under N_2 to give phenol in 30% yield based on H_2O_2 added. Further experiments on the oxidation of benzene with H_2O_2 showed that the yield of phenol was, as seen in Figure 3, proportional to the initial amounts of H_2O_2 with a slope of 0.34. These results suggest that about two-thirds of the $^{\bullet}OH$ radicals generated by reaction (4) are deactivated, presumably according to reaction (5),* and about one-third of the $^{\bullet}OH$ radicals are effectively used to attack the benzene nucleus to form hydroxycyclohexadienyl radical (1), as proposed by earlier workers,[19–21] according to reaction (6). Radical (1) is readily oxidized with the oxidant(s) in the reaction system, for instance, Cu^{II} ion.[4]

$$^{\bullet}OH + Cu^I + H^+ \longrightarrow H_2O + Cu^{II} \qquad (5)$$



(6)

(1)



(7)

The intercept in Figure 3 suggests that in the initial stage of the oxidation the concentration of Cu^{II} ion is too low to oxidize radical (1) effectively by reaction (7). In fact the addition of 40mM-copper(II) sulphate reduced the intercept as shown in Figure 3.

Provided that the active species in the Cu^I–O_2 system is hydroxyl radical generated from H_2O_2, the amount of $^{\bullet}OH$ radical produced by reaction (4) is expected to increase with increasing initial amount of copper(I) chloride since H_2O_2 is supplied by reaction (3). The yields of phenol and HQ in the aerial oxidation of benzene were actually proportional to the initial amount of copper(I) chloride, as shown in Figure 4. The linear relationship in Figure 4 is analogous to the plots for the oxidation with H_2O_2 in Figure 3, suggesting that the active species in the oxidation with the CuCl–O_2 system is $^{\bullet}OH$ radical and that phenol is formed through the same reaction path as in the CuCl–H_2O_2 system. It is noted that the molar ratios of HQ to phenol are constant (0.3) independent of the initial amount of copper(I) chloride. The constancy of the HQ:phenol ratio suggests that HQ and phenol are formed by a couple of competitive reactions.

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* The summation of equations (4) and (5) gives equation (19). Even if reaction (19) occurs instead of (5), the amount of H_2O_2 formed by reaction (3) can be calculated from equation (9).

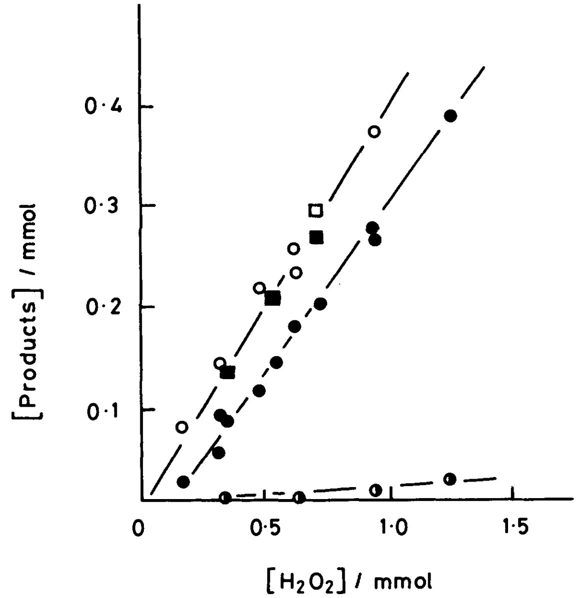


Figure 3. Plots of the amounts of phenols formed against the amounts of H_2O_2 used. Benzene was oxidized under standard conditions (see Experimental section) except for the initial amount of CuCl (for the Cu^I–H_2O_2 system) or the initial amount of H_2O_2 (for the Cu^I–H_2O_2 system). ●, Phenol obtained in the oxidation with Cu^I–H_2O_2; ◑, HQ obtained in the oxidation with Cu^I–H_2O_2; ○, phenol plus HQ obtained in the oxidation with Cu^I–H_2O_2 in the presence of 0.04M-$CuSO_4$; ■, phenol plus HQ obtained in the oxidation with Cu^I–O_2; □, phenol plus HQ obtained in the oxidation with Cu^I–O_2 in the presence of 0.04M-$CuSO_4$

The total amount of H_2O_2 formed during the whole sequence of the oxidation can be estimated from the stoicheiometric calculation^{22} as follows. By the oxidation of copper(I) chloride ($2a$ mmol) with O_2, H_2O_2 (a mmol) and copper(II) ion ($2a$ mmol) are formed [reaction (3)]. Since H_2O_2 does not accumulate in the reaction system as demonstrated in Figure 1, H_2O_2 (a mmol) is consumed by reaction (4) to give $^{\bullet}OH$ radical (a mmol) and copper(II) ion (a mmol). A fraction of $^{\bullet}OH$ radicals (αa mmol) is then converted into phenol (αa mmol) by reaction (6) followed by (7), consuming copper(II) ions (αa mmol). Competing with reactions (6) and (7), $^{\bullet}OH$ radical [$(1 - \alpha)a$ mmol] is deactivated by reaction (5) to give copper(II) ions [$(1 - \alpha)a$ mmol]. Accordingly the total amount of copper(II) ion formed, m_{Cu}, is given by equation (8). The amount of phenol formed, m_{Ph}, is equal to αa mmol as described above and elimination of α from equation (8) gives (9) where a is the amount of H_2O_2 formed by reaction (3). In the derivation of equation (9), the formation of HQ was not taken into account. Provided that HQ is, as discussed later, formed by reactions (10)—(12), the same equation as (9) can be derived as follows. A fraction of the radical (**1**) ($\beta\alpha a$ mmol) is converted into phenol, consuming $\beta\alpha a$ mmol of Cu^{II} ion [equation (7)], while $(1 - \beta)\alpha a$ mmol of the radical (**1**) is oxidized to HQ by equations (10)—(12) to yield Cu^{II} ion [$(1 - \beta)\alpha a$ mmol]. Thus the total amount of Cu^{II} ion formed can be written as in equation (13). Since the quantity $\beta\alpha a$ in equation (13) is equal to the amount of phenol formed (m_{Ph}), equation (9), can be obtained from (13). Therefore, the amount of H_2O_2 (a) formed by reaction (3) can be calculated from equation (9) using the experimental values of m_{Cu} and m_{Ph}, independent of the amount of HQ. The squares in Figure 3 are plots of the total amount of phenols ($m_{Ph} + m_{HQ}$) against the amount of H_2O_2 calculated from equation (9) and give a straight line with slope 0.4, indicating that α is approximately constant during the oxidation of benzene. The open circles in Figure 3 are plots of the total amount of phenols against the initial amount of H_2O_2 in the oxidation of benzene with CuCl–H_2O_2 in the presence of 40mM-copper(II) sulphate and are in good agreement with plots for the CuCl–O_2 system. From the results in Figure 3, it can be concluded that the active species in the oxidation of benzene with the Cu^I–O_2 system is generated from H_2O_2 and the most probable active species is hydroxyl radical produced by reaction (4). This conclusion is, however, inconsistent with that from Udenfriend's system.$^{6-8}$ The evidence against $^{\bullet}OH$ radical as an active species is that the isomer distribution of phenols in the

$$\begin{aligned} m_{Cu} &= 2a + a - \alpha a + (1 - \alpha)a \\ &= 4a - 2\alpha a \end{aligned} \tag{8}$$

$$a = (m_{Cu} + 2m_{Ph})/4 \tag{9}$$

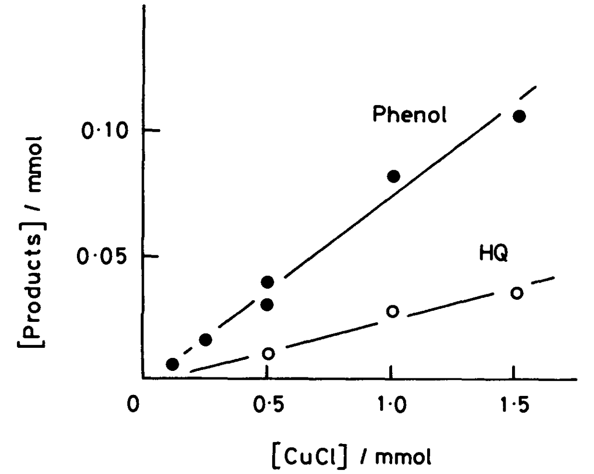
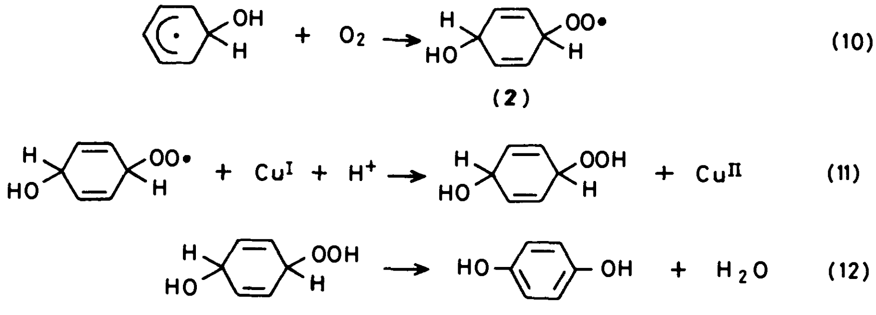


Figure 4. Effect of the initial amount of copper(I) chloride on the yield of phenols. Benzene was oxidized under standard conditions (see Experimental section) except for the initial amount of CuCl

$$\begin{aligned} m_{Cu} &= 2a + a - \beta\alpha a + (1 - \beta)\alpha a + (1 - \alpha)a \\ &= 4a - 2\beta\alpha a \end{aligned} \tag{13}$$



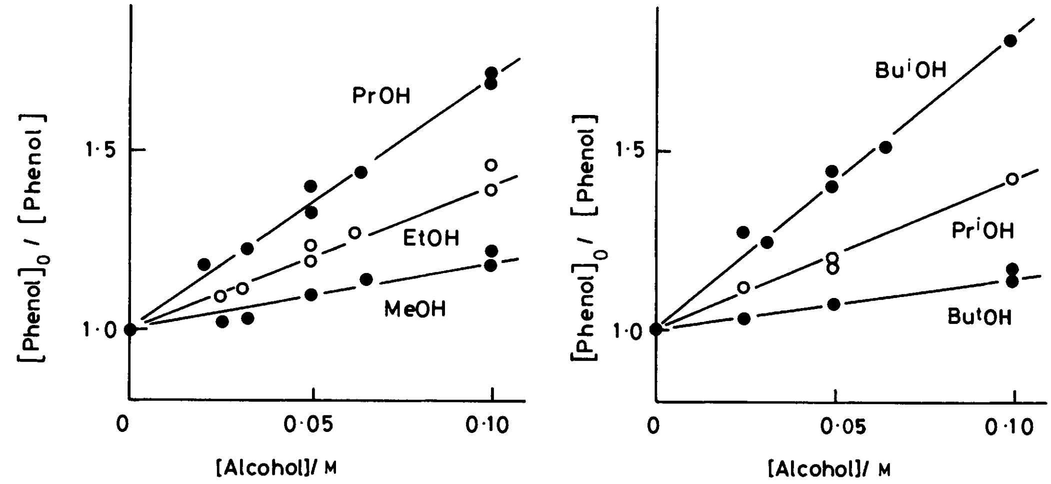
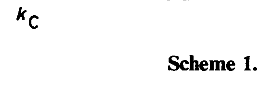


Figure 5. Linear relationships between [Phenol]$_0$/[Phenol] and [Alcohols]. Benzene was oxidized under the standard conditions (see Experimental section) except for the addition of extra alcohols

hydroxylation of monosubstituted benzenes is different from that of Fenton's oxidation. For the hydroxylation of toluene, for instance, the molar ratios of *o*-:*m*-:*p*-cresols are 45:30:24 for Udenfriend's[6] and 56:14:30 for Fenton's systems,[23] respectively. Eberhardt has demonstated, however, that O_2 plays a significant role in determining the isomer distribution of cresols produced by the radiolysis of aqueous solution of toluene.[24] When the radiolysis was carried out under O_2, the molar ratio of *o*-:*m*-:*p*-cresols was 37:42:21. On the other hand, the ratio 73:18:9 was obtained under N_2 through the active species is undoubtedly hydroxyl radical regardless of the atmosphere.[24] The result by Eberhardt indicates that the active species generated from the hydroxylating agent in problem cannot be univocally determined solely by the isomer distribution observed.

Effect of ˙OH *Radical Scavenger.*—In an oxidation which involves ˙OH radical as an active species, the addition of an ˙OH radical scavenger would decrease the yield of the oxidation product. Aliphatic alcohols have been conveniently used as effective scavengers for ˙OH radical.[25,26] In fact, the addition of methyl, ethyl, propyl, isopropyl, isobutyl, and t-butyl alcohols suppressed the oxidation of benzene with CuCl–O_2. The increasing order of the inhibition effect of the alcohols is as follows: t-butyl $\sim$ methyl $<$ isopropyl $\sim$ ethyl $<$ propyl $<$ isobutyl and almost parallel to the rate constants for the reaction of ˙OH radical with these alcohols.[5] In order to analyse the inhibition effect of these alcohols more quantitatively, a competitive reaction model for ˙OH radical with alcohol, benzene, and Cu^I ion is considered and shown in Scheme 1.



Scheme 1.

Assuming that the concentrations of the alcohol, benzene, and Cu^I ion are constant during the whole sequence of the reaction, one can derive relationship (14)[27] between the yield

$$\frac{[\text{Phenol}]_0}{[\text{Phenol}]} = \frac{k_A[\text{Alcohol}]}{k_B[\text{Benzene}] + k_C[\text{Cu}^I]} + 1 \qquad (14)$$

of phenol and the concentrations of alcohols added. [Phenol]$_0$ and [Phenol] stand for the concentrations of phenol formed in the absence and presence of the alcohol, respectively, and k_A—k_C are the rate constants for the reactions of ˙OH radical with the alcohol, benzene, and Cu^I ion, respectively. Plots of [Phenol]$_0$/[Phenol] against the concentration of added alcohol (Figure 5) gave straight lines with intercepts of 1.0, as expected from equation (14). The slopes of the straight lines in Figure 5 are a measure of the inhibition effect of the alcohols and correspond to $k_A/(k_B[\text{Benzene}] + k_C[\text{Cu}^I])$ in equation (14). The linear relationship in the plots of the slope for each alcohol obtained from Figure 5 against the rate constants k_A[5] (Figure 6) indicates that the active species generated from the oxidation of CuCl with O_2 is ˙OH radical. From equation (14), the slope of the straight line in Figure 6 is equal to $1/(k_B[\text{Benzene}] + k_C[\text{Cu}^I])$ and the numerical value of the slope obtained by the least-squares method from Figure 6 is 2.0×10^{-9}. As mentioned before, the fraction of OH radicals which is utilized for the oxidation of benzene (α) is *ca.* 0.3 and equal to $k_B[\text{Benzene}]/(k_B[\text{Benzene}] + k_C[\text{Cu}^I])$ [see equation (18)]. From these experimental values, $k_B[\text{Benzene}]$ 1.5×10^8 s^{-1} was obtained. Since the saturated concentration of benzene in 0.05M-H_2SO_4 is 0.022M, one can obtain k_B 6.8×10^9 l mol^{-1} s^{-1}. This value is in close agreement with the k_B hitherto reported, 7.7×10^9 l mol^{-1} s^{-1}.[28] Accordingly it is concluded that the active species in the oxidation with CuCl–O_2 system is hydroxyl radical.

The molar ratios of HQ:phenol observed in the oxidation of benzene in the presence of added alcohols were, as shown in Table 2, constant (0.33—0.36) regardless of their concentrations. This result indicates that linear relationship similar to Figure 6 holds for HQ as well as phenol and that HQ will be formed through the same intermediate, hydroxycyclohexadienyl radical (1).

Optimum Conditions for the Production of Phenols.—In the earlier studies on the hydroxylation of benzene with Fenton's reagent,[3,4] the effect of the initial amount of benzene on the yield of phenol was not fully understood since an excess of benzene

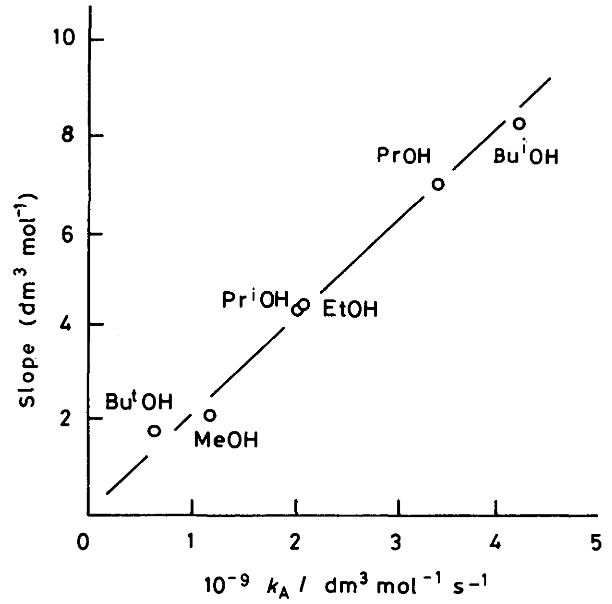


Figure 6. Linear relationship between the slopes of the straight lines obtained from Figure 5 and the rate constants (k_A) for the reaction of hydroxyl radicals with alcohols[5]

Table 2. Molar ratio hydroquinone:phenol in the presence of various amounts of alcohols[a]

Alcohol	0mM	25mM	50mM	100mM
Methyl	0.334	0.350	0.343	0.343
Ethyl	0.334	0.342	0.339	0.351
Propyl	0.350	0.338	0.353	0.359
Isopropyl	0.366	0.373	0.353	0.363
Isobutyl	0.352	0.352	0.348	0.333
t-Butyl	0.352	0.352	0.349	0.359

[a] Benzene was oxidized under the standard conditions (see Experimental section) except for the extra addition of the alcohols.

was usually added to the oxidizing system. Figure 7 shows that the amount of phenol formed in the oxidation of benzene with the CuCl–O_2 system increased with increasing the initial amount of benzene to reach a constant value above the saturated concentration of benzene (22mM), indicating that the oxidation occurs in the aqueous layer, and not in the benzene layer or at the interface between benzene and water. The yield of phenol based on benzene added increased on decreasing the initial amount of benzene, giving a maximum yield (24%) at 5mM-benzene (Figure 7). The result in Figure 7 suggests that most of the benzene remained unchanged in solution. The material balance of benzene was, therefore, determined in a larger scale reactor described in the Experimental section and summarized in Table 3. More than 98% of the benzene added was recovered as phenols and unchanged benzene in all experiments and the selectivities (yields based on benzene reacted) of phenol were 70—90% at 5—17% conversion of benzene. These selectivities obtained are the highest to our knowledge among several processes for the one-step oxidation of benzene to phenol.[29]

The effect of partial pressure of oxygen on the yield of phenol and HQ is mechanistically of interest since Fenton's reagent does not require oxygen and gives only a small amount of HQ (HQ:phenol 0.04—0.07) even in the presence of O_2.[9] In the CuCl–O_2 system, the yields of phenol and HQ increased on increasing the partial pressure of oxygen up to 0.21 atm, as

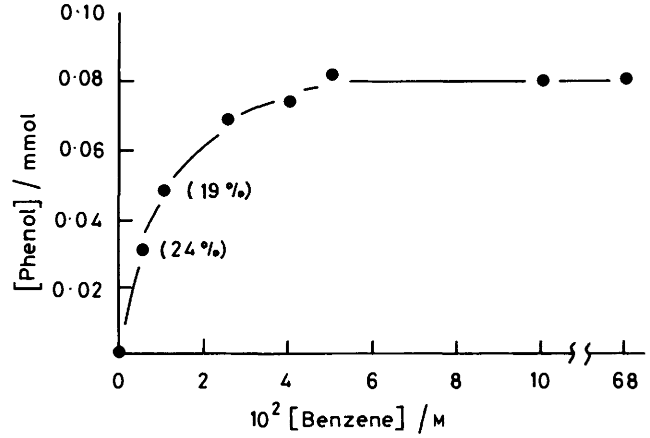


Figure 7. Effect of initial amount of benzene on the yield of phenol. Benzene was oxidized under standard conditions (see Experimental section) except for the initial amount of benzene. The figures in parentheses show the yields of phenol based on the benzene added

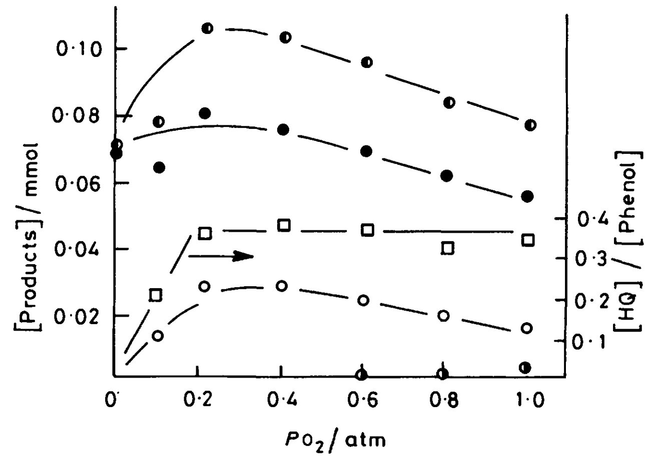


Figure 8. Effect of the partial pressure of oxygen on the yield of phenols. Benzene was oxidized under standard conditions (see Experimental section) except for the partial pressure of oxygen: ●, phenol; ○, HQ; ◑, benzoquinone; ◐, total; □, HQ/phenol

shown in Figure 8. At the higher partial pressure of O_2, the molar ratios of HQ:phenol was essentially constant (*ca.* 0.3) and a small amount of *p*-benzoquinone was detected. At the lower partial pressure of O_2, the HQ:phenol ratio was <0.1, though the yield of phenol was comparable with those obtained at the higher O_2 pressure. In the CuCl–H_2O_2 system where O_2 is absent, the ratio of HQ:phenol was *ca.* 0.05, as already shown in Figure 3. These results indicate that O_2 is necessary for the formation of HQ. A tracer experiment using $^{18}O_2$ revealed that the labeled oxygen atom was incorporated into HQ by the reaction of O_2 with radical (**1**) to form a peroxyl radical (**2**) according to equation (10).[30] The formation of the peroxyl radical (**2**) has been proposed by several workers on the basis of pulse-radiolysis experiments of aqueous benzene solutions.[15,21] The main reaction path for the formation of HQ is by no means the consecutive oxidation of phenol with $^{\bullet}OH$ radical, since a separate experiment on the oxidation of phenol under the same reaction conditions as for benzene showed that CA is formed as much as HQ (Table 4). The constancy of the molar ratios of HQ to phenol observed during the oxidation of benzene (Figure 2) is consistent with the competitive mechanism for the formation of HQ.

The effect of pH on the yield of phenol in the Fenton system

Table 3. Selective oxidation of benzene to phenols with CuCl–O_2 at 25 °C^a

CuCl (mmol)	Benzene (mmol) Used	Recovered	% Conversion	% Selectivity Phenol	HQ	CA	Total
5.0	1.249	1.037	17.0	74.1	12.3	2.4	88.7
5.0	1.563	1.315	15.9	73.8	15.3	2.4	91.5
5.0	1.876	1.600	14.7	73.6	12.3	2.2	88.1
5.0	2.188	1.917	12.7	70.5	15.9	2.2	88.6
10.0	1.563	1.469	6.0	90.4	4.3	2.1	96.8
10.0	2.188	2.079	5.0	89.9	6.4	1.8	98.2

^{a} In 0.05M-H_2SO_4 (125 ml).

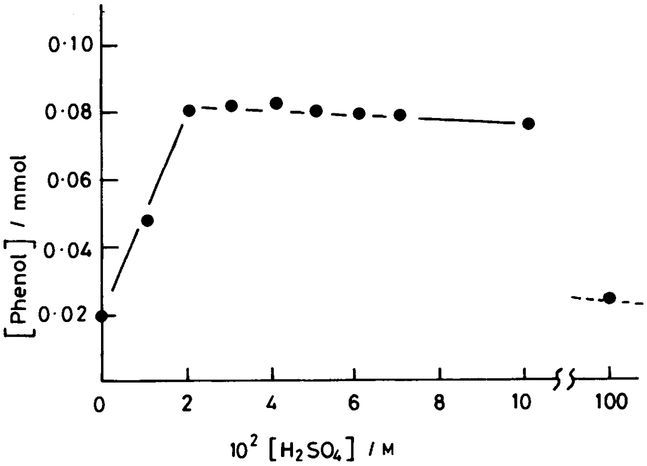
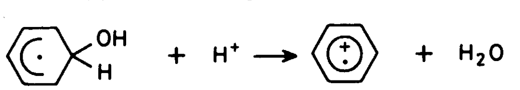


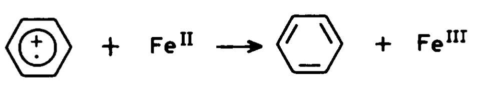
Figure 9. Effect of the concentration of H^+ ions on the yield of phenol. Benzene was oxidized under standard conditions (see Experimental section) except for the concentration of H^+

has been studied by Walling.[4] In the absence of any particular oxidants (Cu^{II} or Fe^{III}), the total yield of phenol plus biphenyl in 1M-H_2SO_4 was about one-sixth of that in 0.1M-H_2SO_4. Walling explained the 'inhibition' effect of H^+ ion in terms of the acid-catalysed dehydration of hydroxycyclohexadienyl radical (**1**) to form a cation radical (**3**), followed by the reduction of the cation radical (**3**) with Fe^{II} to give benzene.



(15)

(**3**)



(16)

The effect of H^+ ion on the total yield of phenol plus biphenyl becomes less marked in the presence of Cu^{II} ion, 57% in 0.1M-H_2SO_4 and 49% in 1M-H_2SO_4.[4] In the CuCl–O_2 system where an appreciable amount of Cu^{II} ion is present in the solution, the yield of phenol was independent of the concentration of H^+ ion in the range of 0.02—0.1M-H_2SO_4 as shown in Figure 9 and one might conclude that the deactivation reactions (15) and (16) are not operating under the present oxidizing system. Provided that hydroxycyclohexadienyl radical (**1**) undergoes the dehydration, reaction (15) will compete with (7) and the yield of phenol will be expected to increase by the addition of Cu^{II} ion. The result in Figure 10 shows a slight increase in the yield of phenol on increasing the concentration of Cu^{II} ion and the deactivation reactions (15) and (16) are supposed to contribute to the decrease in the yield of phenols but not sufficient to explain the low yield of phenol in Table 1. In 1M-H_2SO_4, the yield of phenol decreased to about one-third. At the lower concentrations of H^+ <0.02M, the yield of phenol again decreased. This is partly because the amount of H^+ is insufficient to complete the oxidation of copper(I) chloride by reaction (2) as described in the foregoing section.

Table 4. Oxidation of phenol with Cu^I–O_2 and Cu^I–H_2O_2 systems at 25 °C^a

Oxidant	Atmosphere	[HQ]/mM	[CA]/mM
Cu^I–O_2	Air	0.13	0.18
Cu^I–H_2O_2^{b}	N_2	0.26	0.28

^{a} [Phenol] 3.3mM; [CuCl] 40mM (1 mmol); solvent 25 ml of 0.05M-H_2SO_4, reaction time 1 h. ^{b} [H_2O_2] 20mM (0.5 mmol).

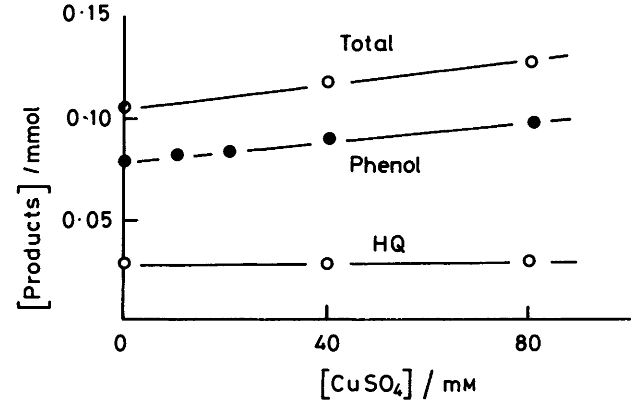


Figure 10. Effect of the amount of Cu^{II} ions added on the yield of phenols. Benzene was oxidized under standard conditions (see Experimental section) except for the extra addition of copper(II) sulphate

The effect of the reaction temperature on the yield of phenols was small (Figure 11) between 5 and 45 °C and the optimum temperature for the formation of phenol and HQ was 25—35 °C. In summary, the optimum conditions for the production of phenols are those described in Table 1.

Deactivation Reaction.—As described so far, the maximum yields of phenol and HQ in the oxidation of benzene with CuCl–O_2 were 8.0 and 2.8% based on CuCl added, respectively. Taking into account the fact that copper(I) chloride (3 mol) is required to generate ·OH radical (1 mol) according to reactions (3) and (4), these values should be tripled as 24.0 and 8.2%, respectively. The total yield of phenols thus calculated is still low (32%) and an unknown side-reaction besides (15) and (16) must be operating. The high selectivity of phenol (>90%, Table 3) rules out the possibility of the formation of an appreciable amount of by-products from benzene. It is also evident that H_2O_2 is quantitatively produced by the oxidation of Cu^I with O_2 according to reaction (3) since the yield of phenol in the oxidation with CuCl–H_2O_2 (34% based on H_2O_2 added) is in close agreement with that obtained in the CuCl–O_2 system (Figure 3). In Fenton's oxidation, the reaction of ·OH radical with Fe^{II} ion has been proposed to explain the lower yield of phenol observed without any direct evidence for the occurrence of this reaction. The deactivation reaction (5) of ·OH radical with Cu^I ion is analogous to reaction (17) and might take place

$$Fe^{II} + OH + H^+ \longrightarrow Fe^{III} + H_2O \qquad (17)$$

in oxidation with CuCl–O_2. The contribution of reaction (5) to

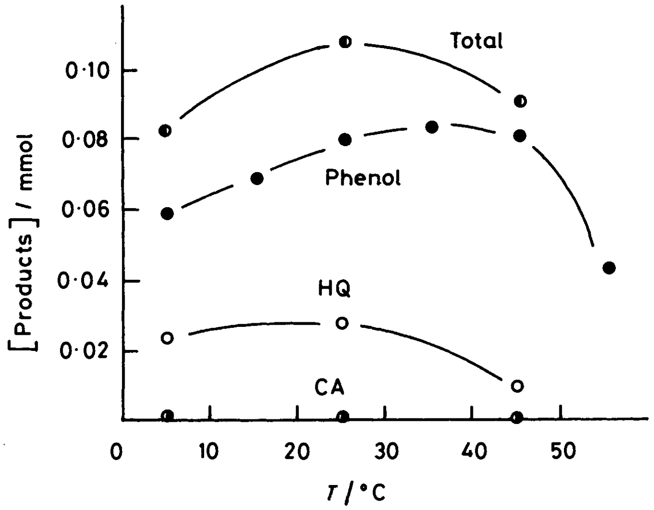
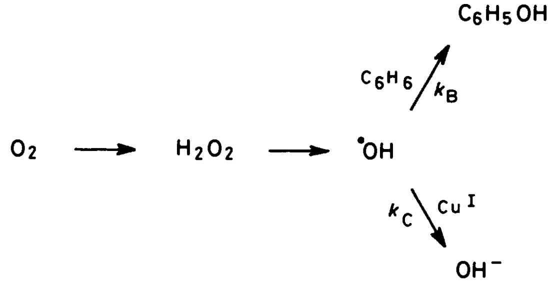


Figure 11. Effect of the reaction temperature on the yield of phenols. Benzene was oxidized under standard conditions (see Experimental section) except for the reaction temperature

the decrease in the yield of phenol will be determined by the relative reactivity of benzene and Cu^I toward •OH radical. The simplified competitive reaction model in Scheme 2 will be useful to estimate the contribution of reaction (5).



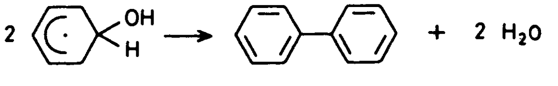
Scheme 2.

Assuming that the concentrations of both benzene and Cu^I ion are approximately constant during the whole sequence of the oxidation, one can derive equation (18) where $[Phenol]_0$ and [Phenol] are the theoretical and the observed yields of phenols, and $[Cu^I]$ and [Benzene] are the concentrations of Cu^I ion and benzene in the solution, respectively. The quantity of the left-hand side in equation (18) has been determined experimentally as *ca.* 3 (Figure 3). The saturated concentration of benzene at 25 °C is 0.022M and k_B is known to be 7.7×10^9 l mol^{-1} s^{-1}.[28] The concentration of Cu^I ion determined spectroscopically was *ca.* 2×10^{-4}M. Substituting these values into equation (18), k_C 1.8×10^{12} l mol^{-1} s^{-1} is obtained. The calculated value of k_C amounts to the upper limit of the second-order rate constant (*ca.* 10^{12} l mol^{-1} s^{-1}). Considering that the rate constant for the reaction of •OH radical with Fe^{II} ion [reaction (17)] is 3×10^8 l mol^{-1} s^{-1},[31] the value of k_C calculated above seems to be too high to be real. Therefore, there must be some deactivation reaction other than reaction (5). The most plausible deactivation reaction will be the reduction of H_2O_2 with Cu^I ion without generating free •OH radical as in equation (19). Equation (19) is equivalent to the combination of equations (4) with (5) and one cannot distinguish reaction (19) from the consecutive reactions (4) and (5) from the stoicheiometric point of view.

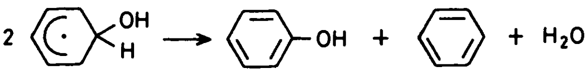
$$\frac{[\text{Phenol}]_0}{[\text{Phenol}]} = \frac{k_C[Cu^I]}{k_B[\text{Benzene}]} + 1 \qquad (18)$$

$$H_2O_2 + 2\,Cu^I + 2\,H^+ \longrightarrow 2\,H_2O + 2Cu^{II} \qquad (19)$$

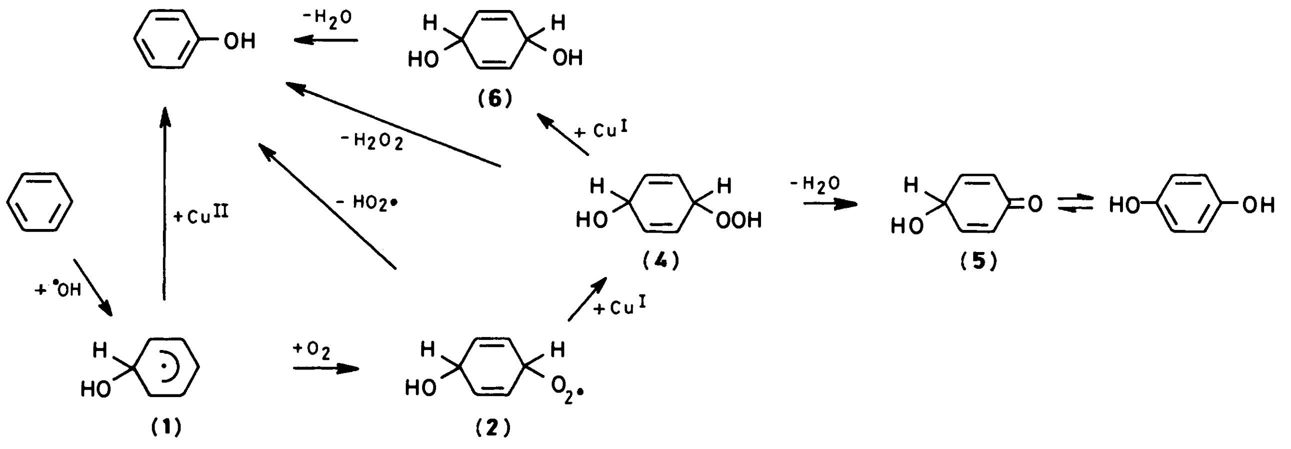
Reaction Mechanism.—In summary, all the observations described so far can be explained by the minimal reaction mechanism shown in Scheme 3. Hydroxycyclohexadienyl radical (**1**), which is formed by the addition of •OH radical to benzene nucleus, is a key intermediate. Depending upon the concentrations of the oxidants, Cu^{II} ion or O_2, radical (**1**) will react in a different manner. If there is not any particular oxidant in the system, radical (**1**) will be reduced back to benzene according to reactions (15) and (16), dimerize to give biphenyl,[3–5] or undergo disproportionation to phenol and benzene.[3] In the presence of a sufficient amount of Cu^{II} ion, radical (**1**) is easily oxidized with Cu^{II} ion to give phenol selectively.[4] Under aerobic conditions, radical (**1**) reacts with O_2 to yield the peroxyl radical (**2**), which is then converted into phenol or HQ depending on the concentration of Cu^I ion in the solution. In the absence of Cu^I ion, the peroxyl radical (**2**) will eliminate •O_2H to give



(20)



(21)



Scheme 3.

phenol as proposed by Dorfman *et al.*[21] If a sufficient amount of Cu^I ion is present as is in the CuCl–O_2 system, the peroxyl radical (**2**) will be reduced with Cu^I ion to give a hydroperoxide (**4**). Dehydration of the hydroperoxide (**4**) will produce a hydroxycyclohexadienone (**5**), which readily tautomerize to HQ. The reason why HQ is produced appreciably in the CuCl–O_2 system but not in Fenton's system may be related to the different redox behaviour of the two metal ions in reaction (11). Competing to the dehydration, the hydroperoxide (**4**) can be converted into phenol either by elmination of H_2O_2 or by the reduction with Cu^I ion to a diol (**6**) which readily aromatizes by dehydration.

Experimental

Materials.—All the materials were commercial reagent grade unless otherwise stated and obtained from Katayama Chemical Industries Co. Ltd. Copper(I) chloride was from Wako Pure Chemical Industries Ltd. Disodium bathocuproine disulphonate was obtained from Dojindo Laboratories. Tetrakis(acetonitrile)copper(I) perchlorate was prepared by refluxing the acetonitrile solution of copper(II) perchlorate with copper powder.[32] *p*-Benzoquinone was purified by sublimation.

Analysis.—Phenol, HQ, CA, hydroxymucondialdehydes (HMDA), *p*-benzoquinone, and benzene were determined with a reversed-phase h.p.l.c. using a Toyo Soda HLC-803D chromatograph coupled to a Toyo Soda UV-8 model II variable-wavelength u.v. detector, or a Hitachi 655 chromatograph coupled to a Hitachi 638-0410 variable-wavelength u.v. detector. The separation column was Cica-Merck Hibar LiChrosorb RP-18 (5 μm, 250 × 4 mm) or Toyo Soda TSK-gel ODS-120T (5 μm, 250 × 4 mm). The mobile phases were mixtures of acetonitrile (AN) and a phosphate buffer (0.05 mol dm^{-3}; pH 3.5) with ratios of 1:3 and 1:10 for the quantitative and qualitative analyses of the oxidation products, respectively, while a mixture of AN and water (5:3) was used for the determination of benzene. The chromatographic peaks were monitored with the u.v. detector at 270 nm for phenol, CA, and HMDA, 290 nm for HQ, 240 nm for *p*-benzoquinone, and 254 nm for benzene, respectively. The peak areas were recorded with a Shimazu Chromatopack C-R1B integrator. Since an authentic sample of HMDA was not available, titrimetric analysis of HMDA was made with a standard solution of semicarbazide, monitoring the peak area of HMDA in the chromatogram.

Biphenyl was determined by g.l.c. Hydrogen peroxide was analysed by titanium sulphate method at 410 nm (ε 800 dm^3 mol^{-1} cm^{-1}).[33]

The concentrations of copper(II) and copper(I) ions in the solution and the solubility of copper(I) chloride in 0.05M-H_2SO_4 were determined colorimetrically by the bathocuproine disulphonate method.[34] Disodium bathocuproine disulphonate complexes selectively with copper(I) ion, not with copper(II) ion, to give an orange colour with an absorption peak at 480 nm (ε 12 800 dm^3 mol^{-1} cm^{-1}). For the determination of copper(II) ion, a solution of L-ascorbic acid was added to an aliquot portion to reduce Cu^{II} to Cu^I ion.

Oxidation of Benzene with Cu^I–O_2.—A standard procedure is as follows. In an Erlenmeyer flask (100 ml) with a glass stopper were placed. 0.05 mol dm^{-3} H_2SO_4 (25 ml) and benzene (0.75 ml, 8.4 mmol). After addition of copper(I) chloride (99 mg, 1 mmol) to the solution, the flask was shaken for 2 h at 170 oscillations min^{-1} in a thermostatted bath (25 °C) in air. The oxidation mixture was then diluted to one-fourth with 0.017 mol dm^{-3} EDTA to suppress the tailing of the chromatographic peak due to Cu^{II} ion in the determination of the products with h.p.l.c.

In the experiment for the material balance of benzene (Table 2), CuCl (495 mg, 5 mmol) was added to 0.05 mol dm^{-3} H_2SO_4 (125 ml) containing a weighed amount of benzene in an Erlenmeyer flask (500 ml) with a glass stopper and the mixture was shaken for 1 h at 25 °C under aerobic conditions. The mixture was then cooled in an ice–salt-bath for 2 h to minimize the loss of benzene by evaporation, and ethyl alcohol (*ca.* 300 ml) was poured into the flask. After shaking for 10 min, the alcoholic solution was diluted to 500 ml and subjected to analysis by h.p.l.c.

Oxidation of Benzene with Cu^I–H_2O_2.—0.05 mol dm^{-3} H_2SO_4 (25 ml) was placed in an Erlenmeyer flask (100 ml) with a rubber stopper equipped with two glass capillaries to introduce N_2 gas. A stream of N_2 gas was passed for 20 min through the capillary and copper(I) chloride (99 mg, 1 mmol) and benzene (0.75 ml, 8.4 mmol) was added to the solution, which was then agitated with a magnetic stirrer at 1 000 r.p.m. After introducing N_2 a 0.2 mol dm^{-3} solution of H_2O_2 (0.3—2 ml) was added by the use of a syringe. The solution was stirred for 1 h at 25 °C under N_2 and subjected to h.p.l.c. analysis.

Oxidation of Phenol with Cu^I–O_2.—To 0.05 mol dm^{-3} H_2SO_4 (25 ml) containing phenol (3×10^{-3} mol dm^{-3}), copper(I) chloride (99 mg, 1 mmol) was added. The solution was shaken for 1 h at 25 °C in air. The analysis of HQ and CA was performed by h.p.l.c.

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