cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.87 (s, 1 H, H-2), 4.16 (quartet, J = 7.2 Hz, 2 H, H-9), 2.90 (dd, J = 5.2 Hz, 1 H, H-7), 2.80–2.70 (m, 1 H, H-6), 2.50–2.16 (m, 5 H, H-4, H-7, H-11), 2.15–2.08 (m, 1 H, H-5), 1.83–1.70 (m, 1 H, H-5), 1.48 (quintet, J = 8.0 Hz, 2 H, H-12), 1.33 (sextet, J = 7.2 Hz, 2 H, H-13), 1.27 (t, J = 7.2 Hz, 3 H, H-10), 0.92 (t, J = 7.2 Hz, 3 H, H-14); ^{13}C NMR ($CDCl_3$) δ 199.43 (C-1), 172.69 (C-8), 166.04 (C-3), 124.95 (C-2), 60.46 (C-9), 42.97 (C-6), 37.53 (C-11), 34.66 (C-7), 29.75 (C-4), 29.09 (C-12), 28.68 (C-5), 22.34 (C-13), 14.22 (C-10), 13.85 (C-14). Anal. Calcd for $C_{14}H_{22}O_3$: C, 70.56; H, 9.30. Found: C, 70.55; H, 9.27.

6-(Carbethoxymethyl)-3-phenyl-2-cyclohexen-1-one (9). The reaction of 3-phenyl-2-cyclohexen-1-one[14a,b] (3.0 g, 17.4 mmol) with LDA (19.2 mmol) and ethyl bromoacetate (3.5 g, 20.9 mmol) was conducted in a fashion similar to that of method A. The crude material was purified by Kugelrohr distillation to yield 3.90 g (87%) of **9**: bp 100–130 °C/0.01 mmHg; IR (film) 1720, 1650, 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.58–7.50 (m, 2 H, Ar protons), 7.47–7.38 (m, 3 H, Ar protons), 6.43 (s, 1 H, H-2), 4.18 (quartet, J = 7.2 Hz, 2 H, H-9), 3.00–2.75 (m, 4 H, H-4, H-6, H-7), 2.40–2.25 (m, 2 H, H-5, H-7), 2.03–1.80 (m, 1 H, H-5), 1.29 (t, J = 7.2 Hz, 3 H, H-10); ^{13}C NMR ($CDCl_3$) δ 199.39 (C-1), 172.50 (C-8), 159.06 (C-3), 138.39 (Ph), 130.01 (Ph), 129.97 (Ph), 128.84 (Ph), 128.74 (Ph), 126.03 (Ph), 124.56 (C-2), 60.49 (C-9), 42.89 (C-6), 34.61 (C-7), 28.64 (C-5), 28.06 (C-4), 14.22 (C-10). Anal. Calcd for $C_{16}H_{18}O_3$: C, 74.40; H, 7.02. Found: C, 74.55; H, 7.12.

6-(Carbethoxymethyl)-3-ethoxy-2-cyclohexen-1-one (10). The reaction of 3-ethoxy-2-cyclohexen-1-one (3.0 g, 21.4 mmol) with LDA (23.5 mmol) and ethyl bromoacetate (4.3 g, 25.7 mmol) was conducted in a fashion similar to that of method A. The crude material was purified by flash chromatography on silica gel eluted with 10% to 40% ethyl acetate in hexane to yield 2.70 g (56%) of **10**:[10c] IR (film) 1720, 1655, 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.35 (s, 1 H, H-2), 4.16 (quartet, J = 7.5 Hz, 2 H, H-9), 3.95–3.85 (m, 2 H, H-11), 2.93 (dd, J = 4.5 Hz, 1 H, H-7), 2.79–2.65 (m, 1 H, H-6), 2.63–2.50 (m, 1 H, H-4), 2.45–2.35 (m, 1 H, H-4), 2.27 (dd, J = 7.8 Hz, 1 H, H-7), 2.15–2.07 (m, 1 H, H-5), 1.87–1.70 (m, 1 H, H-5), 1.36 (t, J = 7.5 Hz, 3 H, H-12), 1.27 (t, J = 7.5 Hz, 3 H, H-10); ^{13}C NMR ($CDCl_3$) δ 198.96 (C-1), 177.53 (C-3), 172.72 (C-8), 101.99 (C-2), 64.38 (C-11), 60.44 (C-9), 42.33 (C-6), 34.79 (C-7), 29.03 (C-4), 27.15 (C-5), 14.23 (C-10), 14.15 (C-12).

Simplified Procedure Utilized in the Excess Cyclohexenone Low-Temperature Study, Method B. The reaction of 2-cyclohexen-1-one (3.0 g, 31.2 mmol) with LDA (25 mmol) and ethyl bromoacetate (5.21 g, 31.2 mmol) was conducted in a fashion similar to that of method A. The normal isolation and purification procedure yielded 3.70 g (65%) of **6**. In a similar fashion the other 3-substituted-2-cyclohexen-1-ones were examined under these conditions, and the yield of the alkylated product is shown in Table I.

Simplified Procedure Utilized in the Excess LBTSA Low-Temperature Study, Method C. The reaction of 2-cyclohexen-1-one (2.0 g, 20.8 mmol) with LBTSA (22.9 mmol) and ethyl bromoacetate (4.60 g, 27.5 mmol) was conducted in a fashion similar to that of method A, with the exception that the dienolate was stirred for 30 min at −78 °C before ethyl bromoacetate was added. The normal isolation and purification procedure yielded 2.65 g (70%) of **6**. In a similar fashion the other 3-substituted-2-cyclohexen-1-ones were examined under these conditions, and the yield of the alkylated product is shown in Table I.

Registry No. **1**, 930-68-7; **2**, 1193-18-6; **3**, 6301-49-1; **4**, 10345-87-6; **5**, 5323-87-5; **6**, 111248-50-1; **7**, 83108-31-0; **8**, 123540-67-0; **9**, 123540-68-1; **10**, 58775-57-8; ethyl iodoacetate, 623-48-3; ethyl bromoacetate, 105-36-2.

Does the Reaction of Cu^+ with H_2O_2 Give OH Radicals? A Study of Aromatic Hydroxylation

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The reaction of Cu^+ with H_2O_2 was studied by using the isomer distribution obtained with fluorobenzene, anisole, and nitrobenzene as a probe for OH radicals. The reaction with benzene in presence of 5×10^{-2} M Cu^{2+} gave a maximum yield of 69% phenol. The isomer distributions obtained with fluorobenzene, anisole, and nitrobenzene are almost identical with those obtained in the radiation-induced hydroxylation under similar conditions. In experiments with benzene and nitrobenzene we have shown that Cu^{3+} produced via Cu^{2+} + OH does not hydroxylate these aromatic compounds in neutral or weakly acidic solutions (pH 5.0–6.0). We therefore conclude that in the reaction of Cu^+ with H_2O_2 the OH radical is the major reactive species that reacts with aromatic compounds.

The Cu^+ autoxidation has been studied extensively[1,2] ever since the hydroxylating properties of the Cu^+–O_2 system were discovered.[3,4] Evidence for[4] and against[5] the intermediate formation of OH radicals has been presented.[6] Recently a group of Japanese workers[7] have examined the Cu^+–O_2-induced hydroxylation of benzene and concluded that the reaction proceeds via OH radicals. At the same time we published a paper[8] on the reaction of Cu^+–O_2 using DMSO as a OH radical probe, reaching the same conclusion as the Japanese workers. It was suggested by both groups that the H_2O_2 produced in the autoxidation reacts with Cu^+ to give OH radical in a Fenton-type reaction. There is considerable evidence for this reaction in the literature.[9-12] It is frequently quoted without any references. However, contrary evidence was presented by

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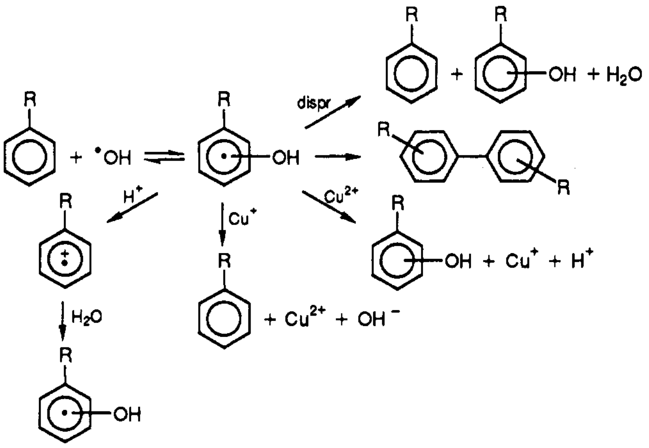
0022-3263/89/1954-5922$01.50/0

Scheme I



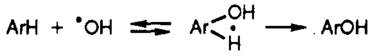
Johnson et al.[13] These authors postulate the formation of a Cu^{3+} species. To decide between these two possible pathways, we have examined the hydroxylation of a number of aromatic compounds by Cu^+–H_2O_2, comparing the isomer distributions obtained with those obtained in the radiolysis of dilute aqueous solutions.

Results and Discussion

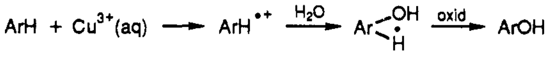
In the present study we wish to distinguish between the possible reaction steps in eq 1–4.

$$Cu^+ + H_2O_2 \rightarrow Cu^{2+} + OH^- + {}^{\bullet}OH \qquad (1)$$

$$Cu^+ + H_2O_2 \rightarrow Cu^{3+}(aq) \qquad (2)$$



$$\mathrm{ArH} + {}^{\bullet}\mathrm{OH} \rightleftharpoons \mathrm{Ar}\overset{\mathrm{OH}}{\underset{\mathrm{H}}{\overset{\bullet}{<}}} \longrightarrow \mathrm{ArOH} \qquad (3)$$



$$\mathrm{ArH} + \mathrm{Cu}^{3+}(\mathrm{aq}) \longrightarrow \mathrm{ArH}^{\bullet+} \xrightarrow{\mathrm{H_2O}} \mathrm{Ar}\overset{\mathrm{OH}}{\underset{\mathrm{H}}{\overset{\bullet}{<}}} \xrightarrow{\mathrm{oxid}} \mathrm{ArOH} \qquad (4)$$

Aromatic hydroxylation can take place via OH radicals and via radical cations.[14,15] In previous work[15] we have shown that the radical cation pathway does not occur with anisole and nitrobenzene. In the case of fluorobenzene and toluene however, the radical cation pathway leads to an isomer distribution completely different from that of the hydroxylation via OH radicals.[15] A careful analysis of the isomer distribution may therefore serve to distinguish between the two mechanisms.

Aromatic hydroxylation is a complicated process. It has been shown by us and others in a series of papers[15-17] that the isomer distribution obtained depends on a number of factors, including the presence of oxidizing or reducing metal ions, oxygen, and pH (Scheme I). Because of this great variability in the isomer distribution depending on the reaction conditions, one has to be extremely careful in using isomer distribution as an OH radical probe. Properly applied, however, the isomer distribution can be a very sensitive measure of the nature of the attacking radical. It has recently been suggested as a probe for OH radicals in vivo.[18]

Table I. Phenol Yields in the Reaction of Benzene with Cu^+–H_2O_2. Effect of Cu^{2+} and pH

expt	reactants,[a] M		pH[b]	time, h	phenol, mol × 10^6
	Cu^+	Cu^{2+}			
1	2×10^{-3}	5×10^{-2}		0.5	469
2	2×10^{-3}	5×10^{-2}		0.5	586
3	2×10^{-3}	5×10^{-2}		0.5	513
4	2×10^{-3}	5×10^{-2}		0.5	498
5	2×10^{-3}	5×10^{-2}		0.5	454
6	2×10^{-3}	0.1		0.5	308
7	2×10^{-3}	0.1		0.5	340
5	2×10^{-3}	0.1		0.5	332
9	2×10^{-3}	0.1	2.2	0.5	537
10	2×10^{-3}	0.1	2.2	0.5	537
11	2×10^{-3}	0.1	2.2	0.5	483
12	2×10^{-4}	5×10^{-2}		1	60
13	2×10^{-4}	5×10^{-2}		2	79
14	2×10^{-4}	5×10^{-2}		24	109
15	2×10^{-4}	5×10^{-2}	3.1	1	147
16	2×10^{-4}	5×10^{-2}	3.1	2	218
17	2×10^{-4}	5×10^{-2}	3.1	24	300

[a] All experiments were carried out in 500 mL of deoxygenated aqueous solutions containing 0.88×10^{-3} mol of H_2O_2. [b] The pH was adjusted by adding 50 or 500 μL of concentrated $HClO_4$, respectively.

We have examined the hydroxylation of benzene, fluorobenzene, and anisole with Cu^+–H_2O_2 in the presence of excess Cu^{2+} in dilute aqueous solutions. These results are shown in Tables I–III. Nitrobenzene was hydroxylated by Cu^+–H_2O_2 in the absence and presence of oxygen (Table IV) and in the presence of Cu^{2+} and H^+ (Table V). The hydroxylation of benzene gives a 69% yield of phenol in presence of Cu^{2+} to oxidize the intermediate hydroxycyclohexadienyl radical. A quantitative conversion is not expected for several reasons. At low Cu^{2+} concentrations not all the OH radical adducts are oxidized to the corresponding phenols, and excess Cu^+ can reduce the adducts back to starting material. With increasing Cu^{2+}, the Cu^{2+} competes with the aromatic for OH radicals, thus lowering the yield. These many competing reactions are summarized in Scheme I.

The rate of reduction by Cu^+ is different for the different isomeric OH radical adducts, thus leading to different isomer distributions depending on the Cu^+ concentration. This effect is particularly evident in the hydroxylation of nitrobenzene, where with increasing Cu^+ concentration the total yields become very low with a marked decrease in the percentage of *o*-nitrophenol. We have previously reported a similar effect of $K_4Fe(CN)_6$ and Fe^{2+} in the radiation-induced hydroxylation of nitrobenzene.[16b] Bhatia and Schuler[19] presented evidence for reduction of hydroxycyclohexadienyl radicals by Cu^+ in the radiation-induced hydroxylation of benzene.

Cu^{2+} has been used by a number[19,20] of investigators to oxidize intermediate hydroxycyclohexadienyl radicals. Bhatia and Schuler[19] have found that Cu^{2+} is much less effective in oxidizing these radicals than is $Fe(CN)_6^{3-}$. They observed with $Fe(CN)_6^{3-}$ a quantitative conversion of OH radicals to phenol, whereas with Cu^{2+} the yield dropped off substantially with increasing dose (only about 70% conversion at a dose of 5×10^{17} eV/g). In our own work on the radiation-induced hydroxylation of fluorobenzene and anisole[16d] we also observed a less than

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Table II. Product Yields in the Reaction of Fluorobenzene with Cu^+–H_2O_2–Cu^{2+}

	reactants,[a] M		products, mol × 10^6					% of isomers			
			fluorophenols								
expt	Cu^+	Cu^{2+}	ortho	meta	para	total	phenol	ortho	meta	para	FPhOH/PhOH
1	2×10^{-3}	10^{-2}	70	24	97	191	22	36.6	12.6	50.8	8.7
2	2×10^{-3}	2×10^{-2}	137	27	144	308	27	44.5	8.8	46.7	11.4
3	2×10^{-3}	5×10^{-2}	155	17	143	315	21	49.2	5.4	45.4	15.0
4	5×10^{-3}	10^{-2}	78	tr[b]	120	198	25	39.5		60.6	7.9
5	5×10^{-3}	2×10^{-2}	100	tr	148	248	28	40.3		59.7	8.9
6	5×10^{-3}	5×10^{-2}	138	tr	147	285	21	48.4		51.6	13.6
7	5×10^{-3}	5×10^{-2}	149	tr	163	312	27	47.8		52.2	11.6
8	5×10^{-3}	5×10^{-2}	134	tr	150	284	26	47.2		52.8	10.9
9	5×10^{-3}	5×10^{-2}	144	tr	162	306	29	47.1		52.9	10.6
10	5×10^{-3}	5×10^{-2}	135	tr	155	290	26	46.6		53.4	11.2
11[c]	5×10^{-3}	5×10^{-2}	84	tr	56	140	356	60.0		40.0	0.39
12[c]	5×10^{-3}	5×10^{-2}	84	tr	57	141	363	59.6		40.4	0.39

[a] All reactions were carried out in 500 mL of deoxygenated solutions containing 0.88×10^{-3} mol of H_2O_2. The products were extracted after 30 min of reaction time. [b] All experiments showed trace amounts of meta isomer as a small shoulder on a huge para isomer peak. [c] These experiments contained 5 mL of concentrated $HClO_4$ (pH = 1.0).

Table III. Product Yields in the Reaction of Anisole with Cu^+–H_2O_2–Cu^{2+}

	reactants,[a] M		products,[b] mol × 10^6					% of isomers			
			hydroxyanisoles								
expt	Cu^+	Cu^{2+}	ortho	meta	para	total	phenol	ortho	meta	para	HA/PhOH
1	2×10^{-4}	10^{-2}	44	2	20	66	8	66.7	3.0	30.3	8.3
2	2×10^{-4}	5×10^{-2}	45	4	11	60	8	75.0	6.7	18.3	7.5
3	2×10^{-4}	5×10^{-2}	48	4	13	65	10	73.8	6.2	20.0	6.5
4	2×10^{-3}	5×10^{-3}	250	16	188	454	45	55.1	3.5	41.4	10.1
5	2×10^{-3}	5×10^{-3}	259	14	178	451	43	57.4	3.1	39.5	10.5
6	2×10^{-3}	5×10^{-2}	264	24	186	474	41	55.7	5.1	39.2	11.6
7	2×10^{-3}	5×10^{-2}	275	16	178	469	45	58.6	3.4	38.0	10.4
8	5×10^{-3}	5×10^{-3}	300	9	207	516	52	58.1	1.7	40.1	9.9
9	5×10^{-3}	5×10^{-2}	267	14	179	460	40	58.0	3.0	38.9	11.5
10[c]	2×10^{-3}	5×10^{-2}	3				29				
11[c]	2×10^{-3}	5×10^{-2}	3				23				

[a] All reactions were carried out in 500 mL of deoxygenated solutions containing 0.88×10^{-3} mol of H_2O_2. [b] Products were extracted after 30 min of reaction time. [c] These experiments contained 5 mL of concentrated $HClO_4$ (69–72%, pH = 1.0).

Table IV. Reaction of Cu^+–H_2O_2 with Nitrobenzene. Effect of O_2 and Cu^+ Concentration

	reactants,[a] M			nitrophenols, mol × 10^6				% of isomers		
expt	Cu^+	Ar/O_2	time, h	ortho	meta	para	total	ortho	meta	para
1	2×10^{-4}	Ar	1	9.9	4.2	5.0	19.1	51.8	22.0	26.2
2	2×10^{-4}	Ar	24	26.8	10.2	12.2	49.2	54.5	20.7	24.8
3	2×10^{-3}	Ar	1	3.2	4.7	5.5	13.4	23.9	35.1	41.0
4	5×10^{-3}	Ar	1	0.9	2.6	2.5	6.0	15.0	43.3	41.7
5	2×10^{-4}	O_2	1	16.8	9.2	9.9	35.9	46.8	25.6	27.6
6	2×10^{-4}	O_2	1	16.7	9.0	10.2	35.9	46.5	25.1	28.4
7	2×10^{-4}	O_2	1	16.0	9.0	9.9	34.9	45.8	25.8	28.4
8	2×10^{-4}	O_2	2	19.7	10.6	12.8	43.1	45.7	25.6	29.7
9	2×10^{-4}	O_2	24	34.0	15.2	19.1	68.3	49.8	22.2	28.0
10		O_2	24	3.1	1.1	1.3	5.4	57.4	20.4	22.2

[a] All reactions were carried out in 500-mL aqueous solutions saturated with Ar (30 min) or O_2 (15 min). Then Cu^+ and nitrobenzene (500 μL) were added, and finally 10 mL of 0.3% H_2O_2 (0.88×10^{-3} mol) was injected.

quantitative conversion by Cu^{2+}, contrary to $Fe(CN)_6^{3-}$, which gave a quantitative conversion in both cases. $K_3Fe(CN)_6$ has first been used by Volkert and Schulte-Frohlinde[21] in the hydroxylation of benzoic acid, and it is clearly the most effective oxidizing agent in aromatic hydroxylation. This oxidizing agent cannot be used in our present work since it oxidizes Cu^+ to Cu^{2+}. We have therefore used Cu^{2+} in the hydroxylation of benzene (Table I), fluorobenzene (Table II), and anisole (Table III).

Since in the hydroxylation of nitrobenzene Cu^{2+} does not oxidize the intermediates at low concentrations (5×10^{-4} M)[16b] and at high Cu^{2+} concentrations the Cu^{2+} competes efficiently with nitrobenzene for OH radicals, we have used O_2 as oxidizing agent (Table IV).

Previous results on the radiation-induced hydroxylation of fluorobenzene, anisole, and nitrobenzene under similar conditions are summarized in Table VI. The isomer distributions for fluorobenzene and anisole with Cu^+–H_2O_2 in presence of Cu^{2+} as well as those for nitrobenzene in the presence of oxygen are indeed very close to those obtained via OH radicals in presence of Cu^{2+} or O_2 (Table VI).

From these results we can conclude that the hydroxylating species in these aromatic hydroxylation reactions is the OH radical. The OH radical however can be formed via the following pathways:

$$Cu^+ + H_2O_2 \rightarrow Cu^{2+} + OH^- + {}^\bullet OH \quad (5)$$

$$Cu^+ + H_2O_2 \rightarrow Cu^{3+}(aq) \quad (6)$$

$$Cu^{3+}(aq) \rightarrow {}^\bullet OH + H_3O^+ + Cu^{2+}(aq) \quad (7)$$

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Table V. Reaction of Cu^+–H_2O_2 with Nitrobenzene. Effect of O_2, Cu^{2+}, and pH

	reactants,[a] M					nitrophenols, mol × 10^6				% of isomers		
expt	Cu^+	Ar/O_2	Cu^{2+}	pH[b]	time, h	ortho	meta	para	total	ortho	meta	para
1	2 × 10^{-4}	Ar			1	9.9	4.2	5.0	19.1	51.8	22.0	26.2
2	2 × 10^{-4}	Ar	5 × 10^{-2}		1	5.6	2.1	2.7	10.4	53.8	20.2	26.0
3	2 × 10^{-4}	Ar	5 × 10^{-2}	3.1	1	10.3	4.0	4.8	19.1	53.9	20.9	25.1
4	2 × 10^{-4}	Ar	5 × 10^{-2}	3.1	24	215	64	116	395	54.4	16.2	29.4
5	2 × 10^{-4}	Ar	5 × 10^{-2}		24	26.8	10.2	12.2	49.2	54.5	20.7	24.8
6	2 × 10^{-4}	O_2			1	16.5	9.1	10.0	35.6	46.3	25.6	28.1
7	2 × 10^{-4}	O_2	5 × 10^{-2}		1	6.3	2.4	2.8	11.5	54.8	20.9	24.3
8	2 × 10^{-4}	O_2	5 × 10^{-2}		24	35.3	14.1	15.6	65.3	54.1	21.6	24.3
9	2 × 10^{-4}	O_2	5 × 10^{-2}	3.1	1	12.8	4.7	5.7	23.2	55.2	20.3	24.6
10	2 × 10^{-4}	O_2	5 × 10^{-2}	3.1	2	21.4	7.4	8.8	37.6	56.9	19.7	23.4
11	2 × 10^{-4}	O_2	5 × 10^{-2}	3.1	24	245	99	123	467	52.5	21.2	26.3
12	2 × 10^{-4}	O_2	5 × 10^{-2}	2.2	1	5.9	2.2	2.8	10.9	54.1	20.2	25.7
13	2 × 10^{-4}	O_2	5 × 10^{-2}	1.2	1	tr	tr	tr				
14	2 × 10^{-4}	O_2	5 × 10^{-2}	1.2	24	8.6	3.5	3.8	15.9	54.1	22.0	23.9
15	2 × 10^{-3}	Ar	5 × 10^{-2}		1	13.5	11.9	13.7	39.1	34.5	30.4	35.0
16	2 × 10^{-3}	Ar	0.1		1	10.3	8.2	9.6	28.1	36.7	29.2	34.2

[a] See footnote 1, Table IV. [b] The pH was adjusted by adding 50 μL of concentrated $HClO_4$ (pH 3.1), 500 μL of $HClO_4$ (pH 2.2), or 5 mL of $HClO_4$ (pH 1.2).

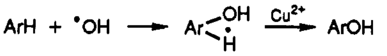
Table VI. Products Formed in the Radiolysis of Aqueous Solutions of Fluorobenzene, Anisole, and Nitrobenzene[a]

	hydroxylated products, g					% of isomers			
reactants	ortho	meta	para	total	phenol	ortho	meta	para	lit.
PhF + 2 × 10^{-3} M Cu^{2+}	0.55	tr	0.72	1.27	0.38	43.3	0	56.7	16d
PhF + 5 × 10^{-3} M Cu^{2+}	0.94	tr	0.81	1.75	0.25	53.7	0	46.3	16d
PhF + 5 × 10^{-2} M Cu^{2+}	0.98	tr	1.02	2.00	0.36	49.0	0	51.0	16d
PhF + 5 × 10^{-3} M Cu^{2+} + $HClO_4$ (pH 2.3)	0.40	tr	0.34	0.74	1.70	54.1	0	45.9	16d
$PhOCH_3$ + 5 × 10^{-2} M Cu^{2+}	1.36	0.1	0.80	2.26	0.26	60.2	4.4	34.4	16d
$PhOCH_3$ + $HClO_4$ (pH 1.4)	tr	tr	tr	tr	tr				16d
$PhNO_2$ + O_2 (saturated)	0.70	0.36	0.46	1.52		46.0	23.6	30.4	16a
$PhNO_2$ + O_2 (saturated)	0.82	0.38	0.49	1.69		48.5	22.6	28.9	16a

[a] For details see original literature.

Evidence supporting the formation of OH radicals from Cu^{3+}(aq) has been presented by Anbar and Pecht.[22] Meyerstein[23] has found that reaction 7 is pH dependent, OH being formed only at low (pH 3.4) and not in neutral or weakly acidic solutions (pH 5.2). Since most of our experiments were carried out in unbuffered solutions without addition of any acid (at pH 4.5 or higher), we conclude that OH radicals are formed via reaction 5 and not via reactions 6 and 7.

Additional evidence in favor of reaction 5 was obtained by studying the effect of Cu^{2+} and pH on the hydroxylation of benzene (Table I) and nitrobenzene (Table V). In the presence of Cu^{2+} we have the following competing reactions:

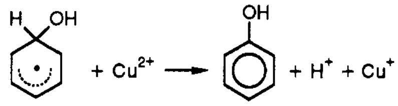


$$ArH + {}^{\bullet}OH \longrightarrow Ar\overset{OH}{\underset{H}{\dot{<}}} \xrightarrow{Cu^{2+}} ArOH \tag{8}$$

$$Cu^{2+} + {}^{\bullet}OH \longrightarrow Cu^{3+}(aq) \tag{9}$$

In the hydroxylation of benzene we find with increasing Cu^{2+} concentration a decrease in phenol yield due to the above competition between reactions 8 and 9. This result clearly shows that Cu^{3+}(aq) produced in this experiment does not hydroxylate benzene. Upon addition of $HClO_4$ (pH 3.2) however, the yield of phenol increases again due to the decomposition of Cu^{3+}(aq) to OH (reaction 7).

In our benzene hydroxylation experiments (Table I, experiments 1–5) we expect to obtain a maximum yield of 730 × 10^{-6} mol of phenol assuming that all H_2O_2 is converted to OH radicals and taking into consideration the competition between benzene and Cu^{2+} for OH (based on the rate constants 83% react with benzene[24]). This means that in our experiments (Table I, experiments 1–5) the average yield of 504 × 10^{-6} mol represents a yield of 69%. This calculation does not take into consideration the reduction of the hydroxycyclohexadienyl radical by Cu^+. Our observed yield of 69% is in excellent agreement with the yield obtained by Bhatia and Schuler[19] in the radiation-induced hydroxylation of benzene in presence of Cu^{2+}. We can therefore conclude that the reaction of Cu^+ with H_2O_2 gives exclusively OH radicals. Since Cu^{2+} oxidizes the hydroxycyclohexadienyl radical to phenol and Cu^+ (eq 10 and 11), we can expect a chain reaction. Excess H_2O_2 is consumed by small initial concentrations of Cu^+ (Table I, experiments 15–17).



(10)

$$Cu^{+} + H_2O_2 \longrightarrow Cu^{2+} + OH^{-} + {}^{\bullet}OH \tag{11}$$

In the hydroxylation of nitrobenzene we have also studied the effect of Cu^{2+} (Table V). In presence of 5 × 10^{-2} M Cu^{2+} this result again shows that Cu^{3+}(aq) in neutral or weakly acidic pH (5.0–6.0) does not hydroxylate nitrobenzene, and therefore the nitrophenols formed in the absence of Cu^{2+} must be formed via OH radicals. Upon addition of acid (pH 3.1) the yield of nitrophenol increases again dramatically due to OH formation via reaction 7 (Table V, experiments 9–11). If however the pH is decreased further (pH 1.2), the nitrophenol yield decreases due to irreversible dehydration (Table V, experiments 12 and 13).

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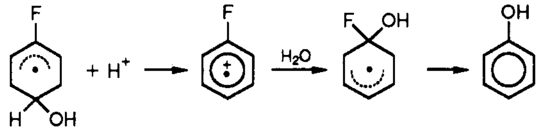
The effect of pH on the hydroxylation of fluorobenzene and anisole is also in accordance with previous results on the radiation-induced hydroxylations.[16d] In the hydroxylation of fluorobenzene the yield of phenol increases with decreasing pH (Table II, experiments 11 and 12):



(12)

The main position of attack by H_2O on the radical cation of fluorobenzene is at the ipso position, giving phenol as the main product in agreement with SCF MO calculations.[15] In the hydroxylation of anisole (Table III, experiments 10 and 11) and nitrobenzene (Table V, experiment 13) on the other hand, a low pH gives only small amounts of phenol and nitrophenols, due to the irreversibility of the dehydration.[15,25]

In conclusion we have shown that the hydroxylations of aromatics by Cu^+–H_2O_2 proceeds via OH radicals (reactions 1 and 3) and not via a Cu^{3+}(aq) species (reactions 2 and 4).

Experimental Section

General Procedure. Triply distilled water (500 mL) containing Cu^{2+} was deoxygenated by bubbling Ar through the solution for 30 min. After deoxygenation 500 μL of the aromatic was added, and the solution shaken to dissolve the aromatic. Then Cu^+ ($Cu(CH_3CN)_4ClO_4$) was added, and 10 mL of a 0.3% H_2O_2 solution (0.88×10^{-3} mol) was injected through a rubber stopper. The solution was shaken for 30 min and then extracted once with 200 mL and three times with 100 mL ether. The ether extracts were dried over Na_2SO_4 for 24 h and then concentrated to 10 mL in a rotary evaporator.

Preparation of Cu^+. The $Cu(CH_3CN)_4ClO_4$ was prepared according to the procedure described by Hemmerich and Sigwart.[26]

Analysis. The concentrated extracts were analyzed by gas chromatography using a 6-ft FFAP column (10% on Chromosorb W, AWDMCS) at 150 °C for phenol and fluorophenols and 170 °C for hydroxyanisoles. The nitrophenols were first reacted with 10 mL of diazomethane solution (prepared from Diazald, Aldrich Chemical Co.). Analysis was carried out using the same column as above at 165 °C and a flow rate of 20 mL of He/min. In the experiment using oxygen as oxidizing agent oxygen was bubbled through the solution before addition of Cu^+ and H_2O_2. Standards containing known amounts of products were worked up and analyzed under the same conditions as the experimental samples.

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Registry No. Cu^+, 17493-86-6; H_2O_2, 7722-84-1; fluorobenzene, 462-06-6; anisole, 100-66-3; nitrobenzene, 98-95-3; benzene, 71-43-2.

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Reactions of an *o*-Quinone Monoimide with Anthracenes, Phencyclone, and 1,3-Diphenylisobenzofuran

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The *o*-quinone monoimide *N*-(2,4-dichloro-6-oxo-2,4-cyclohexadien-1-ylidene)-4-nitrobenzamide (**1**) reacts at ambient temperature and in the absence of light with anthracene, 9-substituted anthracenes, and 9,10-diphenylanthracene to give the 4π + 4π cycloadducts dibenz[*b,f*][1,4]oxazocines (**6**). Compounds **6** when treated with acid isomerize into 9,10-disubstituted anthracenes. Compound **1** also undergoes 4π + 4π cycloaddition with 1,3-diphenylisobenzofuran and phencyclone. Admixing of 9,10-dimethylanthracene with **1** results in an abstraction of a hydrogen from one of the methyl groups by the nitrogen of **1** followed by the bonding of the oxygen of **1** with the erstwhile methyl carbon to give the ether **17**. A similar reaction occurs between **1** and hexamethylbenzene. The adduct of **1** with 1,3-diphenylisobenzofuran, namely, **26**, undergoes an isomerization to **28** in refluxing benzene.

The only known example of a thermal 4π + 4π cycloaddition of anthracene involves its interaction with the *o*-quinodimethane **2** (generated from **1**) to produce 9,10-*endo*-*o*-xylylene-9,10-dihydroanthracene (**3**) in 12% yield (Scheme I).[1] Photochemically induced 4π + 4π cycloadditions of anthracene are more common. For example, irradiation of a mixture of anthracene and 1,3-cyclohexadiene gave **4**[2] (Scheme I). Similar photochemical additions occur between anthracene and 2,5-dimethyl-2,4-hexadiene,[2] 1,3-diphenylisobenzofuran,[3] and derivatives of 1,3-cyclohexadienes.[4] This paper describes the relatively easy 4π + 4π thermal cycloadditions of anthracene and some 9-substituted anthracenes when the latter are treated with the *o*-quinone monoimide *N*-(2,4-dichloro-6-oxo-2,4-cyclohexadien-1-ylidene)-4-nitrobenzamide (**5**). Compound **5** also forms 4π + 4π thermally generated cycloadducts when it is admixed with 1,3-diphenylisobenzofuran and phencyclone.

Results and Discussion

The addition of **5** to methylene chloride solutions of anthracene, 9-methyl-, 9-phenyl-, 9-bromo-, 9-*trans*-styryl-, 1,4-dimethoxy-, and 9,10-diphenylanthracenes (**6a–g**) produced dark-colored reaction mixtures. The color faded gradually (1–2 days), and removal of the solvent left good yields of the 4π + 4π cycloadducts dibenz[*b,f*][1,4]oxazocines (**7a–g**) (Scheme II). Reaction of **5** with **6a–g** in the

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