Catalytic Activity of Copper(II)-Ethylenediamine Complexes in Autoxidation of Phenols

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Studies of the autoxidation of *tert*-butylphenols 1–4 with molecular oxygen in the presence of Cu(II) complexes of N-substituted ethylenediamines indicate that the most catalytically active complexes are sterically crowded around the nitrogen atoms. The principal primary oxidation products formed in the presence of these complexes are substituted biphenyls **5**, **7**, **10**, and **14**, the first three of which are converted into secondary products on prolonged oxidation. Only in the oxidation of **2** is a diphenyl ether (**9**) formed, in quantities that increase little after the first 5 min of oxidation.

Complexes of copper with aliphatic and heterocyclic amines are known to catalyze the autoxidation of substituted phenols. Studies of copper complexes with pyridines and aliphatic and heterocyclic amines have shown that both the catalytic activity and the nature of the oxidation products are influenced by the basicity and steric properties of the ligand.[1-6] In our previous studies of the oxidation of 2,4-di-*tert*-butylphenol (**1**), the catalytic activity of Cu(II) complexes with aliphatic amines decreased in the order $RNH_2 > R_2NH > R_3N$.[7] Moreover, while the complex with piperazine was somewhat less active than those of primary aliphatic amines, that with morpholine was more than twice as active as those with primary aliphatic amines. Studies of the donor properties of heterocyclic molecules[8] and of the stabilities of Cu(II) complexes with substituted iminodiacetic acids[9] suggest that the coordination of oxygen to copper is weaker than that of nitrogen and that the catalytic activity of the morpholine–Cu(II) complex reflects its relative instability.

The activity of Cu(II) complexes with some primary α,ω-alkylenediamines in the oxidation of 2,6-di-*tert*-butyl-4-methylphenol has been shown to increase with the length of the alkylene group.[5] As an extension of our studies on Cu(II) complexes with aliphatic amines, we have investigated Cu(II) complexes of a series of ethylenediamines bearing *N*-alkyl substituents to determine the effect of the number and type of alkyl groups on the activity of the complex in catalyzing the oxidation of 4-*tert*-butylphenols **1**–**4**, as well as on the nature of the oxidation products formed.

Results and Discussion

The Cu(II)–diamine complexes were prepared and the oxidations conducted under a set of standard conditions (see Experimental Section) except where minor deviations from these conditions are indicated. The relative activities of the complexes were determined by measuring the quantities of oxidation products formed from a standard quantity of the phenol.

Table I. Oxidation of 2,4-Di-*tert*-butylphenol in the Presence of Ethyl-Substituted Ethylenediamine-Cu(II) Complexes[a]

diamine	product 5,[b] mol × 10⁶
$H_2N(CH_2)_2NH_2$	0.4
$C_2H_5NH(CH_2)_2NH_2$	1.7
$C_2H_5NH(CH_2)_2NHC_2H_5$	5.6
$(C_2H_5)_2N(CH_2)_2NH_2$	8.3
$(C_2H_5)_2N(CH_2)_2NHC_2H_5$	41.5
$(C_2H_5)_2N(CH_2)_2N(C_2H_5)_2$	93.5

[a] Standard conditions. [b] Analysis by GLC.

Table II. Competitive Oxidation of 2,4-Di-*tert*-butylphenol[a]

run	diamine (oxidation time)[b,c]	product 5,[d] mol × 10⁶
1	EDA (30 min)	0.4
2	TEEDA (30 min)	93.5
3	EDA + TEEDA (30 min)	1.5
4	TEEDA (10 min), then EDA (20 min)	51.7
5	TEEDA (10 min)	52.4

[a] Standard conditions. [b] EDA = ethylenediamine; TEEDA = *N*,*N*′-tetraethylethylenediamine. [c] All diamines used at 1.94×10^{-5} mol. [d] Analysis by GLC.

Ethyl-Substituted Ethylenediamine–Cu(II) Complexes. Results of the oxidation of **1** in the presence of Cu(II) complexes of *N*-ethyl-substituted ethylenediamines are shown in Table I. Although the activity increased with the number of ethyl substituents, the sharp increase at three and four ethyl groups implies that steric crowding around nitrogen is more important than electronic effects of the ethyl groups. We believe that steric crowding leads to less stable complexes and greater catalytic activity. This conclusion was reinforced by studies of competitive oxidations, using ethylenediamine and tetraethylethylenediamine as ligands, with the results shown in Table II. Run 3 indicates that Cu(II) complexes preferentially with ethylenediamine to form a stable, relatively inactive catalyst. Runs 4 and 5 show that addition of ethylenediamine during the oxidation withdraws the Cu(II) ion from the active, less stable tetraethylethylenediamine complex and interrupts the oxidation.

Effect of Diamine/Cu(II) Ratio. Visible absorption spectra of 1:1 and 2:1 mixtures of diamine and $CuCl_2$ in methanol showed maxima at 680–790 and 555–670 nm, respectively. These spectra indicate the formation of 1:1 and 2:1 complexes, although the presence of some 2:1 complex in the 1:1 mixtures cannot be excluded. There was no spectral evidence for complexes of 3:1 or higher ratio.

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Table III. Diamine/Cu(II) Ratio in Oxidation of 2,4-Di-*tert*-butylphenol[a]

		products, mol × 10^6			
	mole ratio[b] diamine/	3 min		13 min	
run	Cu(II)	5	6	5	6
1	0:1	0.5	0	1.1	0
2	0.5:1	1.1	0	7.5	0
3	1:1	6.7	0	25.5	0.9
4	1:4	1.5	0	4.9	0
5	2:1	17.5	1.6	37.1	12.2
6	4:1	13.1	2.4	21.5	11.2
7	8:1	10.9	2.0	18.2	9.2

[a] 4.85×10^{-4} mol phenol in 10 mL of methanol.
[b] Unity = 9.7×10^{-6} mol.

The results of oxidizing 1 with various ratios of *N,N'*-diisopropylethylenediamine to Cu(II) are shown in Table III. The yield of the initial oxidation product 5 was greatest at a diamine/Cu(II) ratio of 2:1, implying that the 2:1 complex is the active catalyst species.

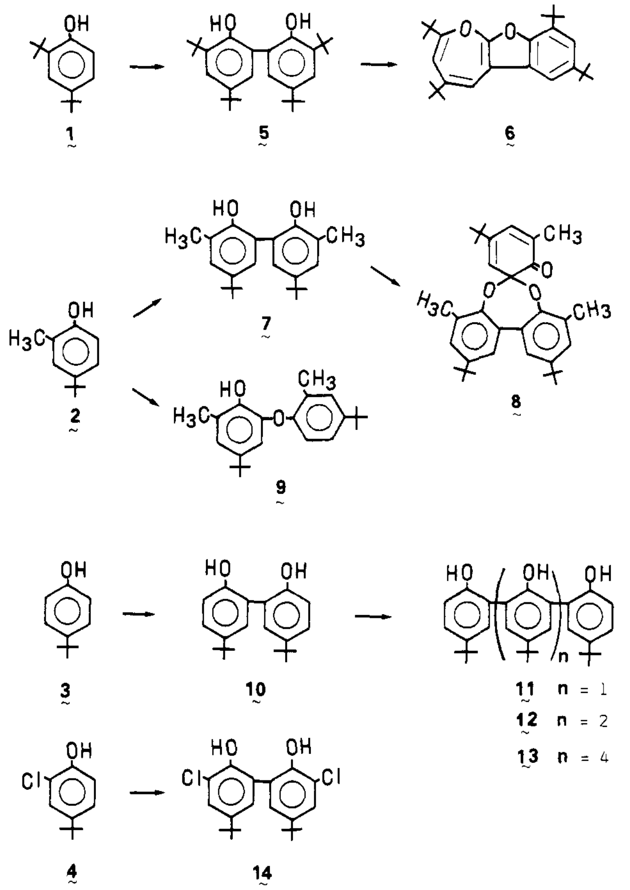
Catalytic Activity of *N,N'*-Dialkylethylenediamine Complexes. The 2:1 complexes of a series of *N,N'*-dialkylethylenediamines with Cu(II) were examined in the oxidation of phenols 1–4, and the relative activities of the complexes are indicated in Table IV. The most active complexes were those derived from the diamines *N,N'*-$(C_4H_9\text{-}t)_2$ > *N,N'*-$(C_3H_7\text{-}i)_2$ > *N,N'*-$(C_4H_9\text{-}sec)_2$, in which there is steric crowding at the carbon attached to nitrogen. Complexes of the uncrowded *N,N'*-dialkylethylenediamines were substantially less active.

Examination of CPK models indicates that the less active 2:1 complexes have square-planar geometry, whereas the more active complexes with alkyl branching on the carbon attached to nitrogen are forced into a tetrahedral configuration. Copper ion in a tetrahedral complex is expected to undergo facile electron transfer because no large change in the geometry of the ion is required.[10]

The oxidation products of the four phenols examined are shown in Scheme I and Table IV. The relative activities of the alkylethylenediamine complexes were the same for all four phenols, but the oxidizability of the phenols varied considerably. Although the oxidation of 1 in the presence of various Fe, Co, and Cu complexes is reported to involve the 2- and/or 4-positions,[5,11] under our conditions neither these products nor a diphenyl ether was detected. We isolated only 5 and its oxidation product 6. Likewise, the phenols 2–4, with CH_3, H, or Cl in the 2-position, gave the substituted biphenyls 7, 10, and 14, respectively, as the principal primary oxidation products. Only 2 gave a diphenyl ether (9). Of the four phenols, 1 was the most readily oxidized, giving an 89% yield of 5 + 6 with the *N,N'*-di-*tert*-butylethylenediamine–Cu(II) complex. The 2-methyl analogue 2 gave 7 + 8 + 9 in a combined yield of 57%. On the other hand, the analogues 3 and 4 were oxidized to only a minor extent, even with increased catalyst concentration and extended oxidation times. Polyphenols 11 and 12 were formed in very small amounts in the oxidation of 3. An independent oxidation of biphenol 10 likewise gave very small yields of 12 and 13.

The differences in oxidizability of the four phenols appear to be related to electronic effects of the 2-substituents rather than to their bulk. Methyl and chloro, which have almost the same bulk, affected the oxidizability quite differently. However, the electron-donating *tert*-butyl and methyl groups in the 2-position enhanced the oxidation rate over that of 3, whereas the electron-withdrawing chlorine substituent did not. An electronic basis for these differences is supported by comparison of the oxidation potentials ($E_{1/2}$) of the phenols. The potentials of 1 (0.487 V) and 2 (0.501 V) are significantly lower than that of 3 (0.578 V).[12] A calculated $E_{1/2}$ for 4 (0.570 V) is similar to that of 3.

Scheme I. Products Derived from 2-Substituted-4-*tert*-butylphenols



Experimental Section

GLC analyses were carried out on a JEOL Model JGC-20K equipped with 3% Apiezone L grease on Celite 545 NAW column. HPLC analyses were performed on a Shimadzu Model LC-3A liquid chromatograph. The columns used in HPLC were as follows: (1) Zorbax ODS for the determinations of 5-9 (methanol), (2) Permaphase ODS for 10 (water/methanol/acetonitrile, 2:1:1, v/v) and 14 (methanol/water, 13:7, v/v). Preparative GLC was performed on a JEOL Model JGC-1100 instrument. Visible spectra were recorded on a Shimadzu UV-300 spectrophotometer. Melting points were determined on a Mitamura Riken Kogyo micro hot-stage and are uncorrected. Electron-impact (EIMS) (16 eV) and isobutane chemical-ionization (CIMS) mass spectra were measured on a Hitachi Model M-70 mass spectrometer. ^1H NMR spectra were recorded on a JEOL MH-100 spectrometer with Me_4Si as an internal standard.

Materials. Anhydrous copper(II) chloride was prepared by heating the dihydrate in an oven at 100 °C for 20 h. 4-*tert*-Butyl-2-methylphenol (2) was prepared according to the literature.[13] 4-*tert*-Butyl-2-chlorophenol (4) was purified by chromatography on Florisil with benzene. Substituted ethylenediamines were

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Table IV. Oxidation of Phenols in the Presence of *N*,*N*′-Dialkylethylenediamine–Cu(II) Complexes[a, b]

2-R′-4-*tert*-butylphenol, R′	product	alkyl grp of *N*,*N*′-dialkylethylenediamine								
		H	CH_3	C_2H_5	*n*-C_3H_7	*i*-C_3H_7	*n*-C_4H_9	*i*-C_4H_9	*sec*-C_4H_9	*t*-C_4H_9
t-C_4H_9	**5**	0.4	1.3	5.6	6.0	55.6	5.8	7.7	39.1	18.1
	6	tr	tr	tr	tr	19.2	tr	tr	7.8	197
CH_3	**7**	tr	tr	tr	tr	19.3	tr	tr	16.6	12.5
	8	tr	tr	tr	tr	8.7	tr	tr	4.4	75.3
	9	tr	tr	tr	tr	4.8	tr	tr	4.1	12.4
H[c]	**10**	tr	tr	tr	tr	0.8	tr	tr	0.4	3.8
Cl	**14**	tr	tr	tr	tr	0.3	tr	tr	tr	3.0

[a] Standard conditions. [b] Yields of products in moles × 10^6. [c] Terphenol **11** and quaterphenol **12** were also identified.

prepared by literature procedures and distilled before use: *N*,*N*,*N*′,*N*′-tetraethylethylenediamine[14] and *N*,*N*′-dipropyl- and dibutylethylenediamines.[15]

Standard Conditions. 2-Substituted-4-*tert*-butylphenols (4.85×10^{-4} mol), anhydrous copper(II) chloride (9.7×10^{-6} mol), and the ethylenediamine (1.94×10^{-5} mol) were dissolved in methanol, and the volume was made up to 10 mL with methanol. Oxygen was bubbled through the mixture at atmospheric pressure and 25 °C for 30 min.

Effect of Diamine/Cu(II) Ratio on the Oxidation of 2,4-Di-*tert*-butylphenol. The phenol was oxidized in the presence of *N*,*N*′-diisopropylethylenediamine–Cu(II) complexes of different ratios under standard conditions for periods of 3 and 13 min. The results are shown in Table III. The products were identified as follows.

3,3′,5,5′-Tetra-*tert*-butyl-2,2′-dihydroxybiphenyl (5): mp 195–196.5 °C (lit.[16] mp 199 °C), no depression when mixed with an authentic sample; EIMS, *m*/*z* 410 (M^+).

2,4,7,9-Tetra-*tert*-butyloxepino[2,3-*b*]benzofuran (6): mp 156–158 °C (hexane and methanol) (lit.[16,17] mp 156–162 °C), no depression when mixed with an authentic sample; CIMS, *m*/*z* 409 (M^+ + H).

Oxidation of 2-Substituted-4-*tert*-butylphenols in the Presence of *N*,*N*′-Dialkylethylenediamine–Cu(II) Complexes. The catalytic effectiveness of various 2:1 *N*,*N*′-dialkyl-substituted-ethylenediamine–Cu(II) complexes in promoting the oxidation of 2-substituted-4-*tert*-butylphenols under standard conditions is shown in Table IV.

To obtain pure samples, the oxidations of 2,4-di-*tert*-butylphenol and 4-*tert*-butyl-2-methylphenol were performed for 2 h. The initial products **5** and **7** were further oxidized to **6** and **8**, respectively. The oxidations were interrupted by addition of dilute hydrochloric acid after 5 min, and the mixture was extracted with ether. After evaporation of the ether, **5** was obtained by chromatography (Florisil/light petroleum), and **7** and **9** were separated by GLC. The yield of **9** reached a maximum within 5 min and increased little at longer oxidation times. Products **6** and **8** precipitated within 2 h; the precipitates were filtered and recrystallized. The oxidation products of 4-*tert*-butyl-2-methylphenol were identified as follows.

5,5′-Di-*tert*-butyl-2,2′-dihydroxy-3,3′-dimethylbiphenyl (7): mp 112–113 °C (lit.[18] mp 115–116 °C), no depression when mixed with an authentic sample.

2,5′,10-Tri-*tert*-butyl-3′,4,8-trimethyldibenzo[*d*,*f*][1,3]-dioxepin-6-spirocyclohexa-3′,5′-dien-2′-one (8): mp 235.5–236 °C (light petroleum) (lit.[18] mp 238–240 °C), no depression when mixed with an authentic sample; CIMS, *m*/*z* 487 (M^+ + H).

4′,5-Di-*tert*-butyl-2-hydroxy-2′,3-dimethyldiphenyl ether (9): liquid;[19] ^1H NMR (CCl_4) δ 1.20 (s, 9 H, 4′-*t*-C_4H_9), 1.32 (s, 9 H, 5-*t*-C_4H_9), 2.27 (s, 6 H, CH_3), 5.35 (s, 1 H, OH), 6.50 (d, *J* = 2 Hz, 1 H, 6-H), 6.64 (d, *J* = 8 Hz, 1 H, 6′-H), 6.76 (d, *J* = 2 Hz, 1 H, 4-H), 7.03 (dd, *J* = 8 and 2 Hz, 1 H, 5′-H), 7.15 (d, *J* = 2 Hz, 1 H, 3′-H); EIMS, *m*/*z* 326 (M^+).

On the other hand, in oxidations of 4-*tert*-butylphenol and 4-*tert*-butyl-2-chlorophenol, the concentration of catalyst was increased by a factor of 4, and the reaction times were 1 and 4 h, respectively. Other conditions were the same as standard. The products from both phenols formed complexes with Cu(II), which precipitated and were filtered and decomposed by concentrated HCl. They were purified by TLC (PSC-Fertigplatten Kieselgel $60F_{254}$, Merck).

5,5′-Di-*tert*-butyl-2,2′-dihydroxybiphenyl (10): mp 200–205 °C (lit.[20] mp 204–205 °C), no depression when mixed with an authentic sample; EIMS, *m*/*z* 298 (M^+). Dibenzoate: EIMS, *m*/*z* 506 (M^+), 402 (M^+ − C_6H_5CO + H).

5,5′-Di-*tert*-butyl-3,3′-dichloro-2,2′-dihydroxybiphenyl (14): mp 159.5–160 °C; ^1H NMR (CCl_4) δ 1.33 (s, 18 H, *t*-C_4H_9), 6.44 (s, 2 H, OH), 7.09 (d, *J* = 2 Hz, 2 H, 6- and 6′-H), 7.20 (d, *J* = 2 Hz, 2 H, 4- and 4′-H); EIMS, *m*/*z* 366 (M^+). Anal. Calcd for $C_{20}H_{24}O_2Cl_2$: C, 65.40; H, 6.59; Cl, 19.30. Found: C, 65.10; H, 6.74; Cl, 19.28. Dibenzoate: mp 198.5–199 °C.

5,5′,5″-Tri-*tert*-butyl-2,2′,2″-trihydroxy-1,1′:3′,1″-terphenyl (11): EIMS, *m*/*z* 446 (M^+). Dibenzoate: mp 76–77 °C; EIMS, *m*/*z* 654 (M^+), 550 (M^+ − C_6H_5CO + H). The tribenzoate could not be prepared.

Oxidation of Biphenol 10. The oxidation was conducted under the conditions used for 4-*tert*-butylphenol. After addition of dilute hydrochloric acid to the reaction mixture, the solution was extracted with ether and the ether evaporated, and products **12** and **13** were isolated by TLC.

5,5′,5″,5‴-Tetra-*tert*-butyl-2,2′,2″,2‴-tetrahydroxy-1,1′:3′,1″:3″,1‴-quaterphenyl (12): mp 99–99.5 °C; EIMS, *m*/*z* 594 (M^+). Tribenzoate: mp 100–100.5 °C; EIMS, *m*/*z* 906 (M^+), 802 (M^+ − C_6H_5CO + H). The tetrabenzoate could not be prepared.

5,5′,5″,5‴,5⁗,5′⁗-Hexa-*tert*-butyl-2,2′,2″,2‴,2⁗,2′⁗-hexahydroxy-1,1′:3′,1″:3″,1‴:3‴,1⁗:3⁗,1′⁗-sexiphenyl (13): EIMS, *m*/*z* 892 (M^+ + 2 H).

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Registry No. **1**, 96-76-4; **2**, 98-27-1; **3**, 98-54-4; **4**, 98-28-2; **5**, 6390-69-8; **6**, 65355-46-6; **7**, 32569-81-6; **8**, 15175-44-7; **9**, 37971-56-5; **10**, 22385-96-2; **10** dibenzoate, 87586-48-9; **11**, 62224-34-4; **11** dibenzoate, 87586-60-5; **12**, 87586-49-0; **12** tribenzoate, 87586-61-6; **13**, 87586-50-3; **14**, 87586-51-4; **14** dibenzoate, 87586-52-5; $Cu[H_2N(CH_2)_2NH_2]_2^{2+}$, 13426-91-0; $Cu[C_2H_5NH(CH_2)_2NH_2]_2^{2+}$, 24646-14-8; $Cu[C_2H_5NH(CH_2)_2NHC_2H_5]_2^{2+}$, 52918-69-1; $Cu[(C_2H_5)_2N(CH_2)_2NH_2]_2^{2+}$, 46754-10-3; $Cu[(C_2H_5)_2N(CH_2)_2NHC_2H_5]_2^{2+}$, 87586-53-6; $Cu[(C_2H_5)_2N(CH_2)_2N(C_2H_5)_2]_2^{2+}$, 49857-21-8; $Cu[CH_3NH(CH_2)_2NHCH_3]_2^{2+}$, 36421-65-5; Cu[*n*-$C_3H_7NH(CH_2)_2NH$-*n*-$C_3H_7]_2^{2+}$, 87586-54-7; Cu[*i*-$C_3H_7NH(CH_2)_2NH$-*i*-$C_3H_7]_2^{2+}$, 87586-55-8; Cu[*n*-$C_4H_9NH(CH_2)_2NH$-*n*-$C_4H_9]_2^{2+}$, 87586-56-9; Cu[*i*-$C_4H_9NH(CH_2)_2NH$-*i*-$C_4H_9]_2^{2+}$, 87586-57-0; Cu[*s*-$C_4H_9NH(CH_2)_2NH$-*s*-$C_4H_9]_2^{2+}$, 87586-58-1; Cu[*t*-$C_4H_9NH(CH_2)_2NH$-*t*-$C_4H_9]_2^{2+}$, 87586-59-2.

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