# Mechanism for Aerobic Oxidation of 3,5-Di-*tert*-butylcatechol to 3,5-Di-*tert*-butyl-*o*-benzoquinone Catalyzed by Di-$\mu$-hydroxo-dicopper(II) Complexes of Peralkylated Ethylelnediamine Ligands

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The aerobic oxidation of 3,5-di-*tert*-butylcatechol ($H_2$dbc) to the corresponding quinone (dbq), catalyzed by di-$\mu$-hydroxo-dicopper(II) complexes $[Cu_2(OH)_2L_2](ClO_4)_2$ [L = *N*,*N*′-tetramethylethylenediamine (tmeda) (**1**) and *N*,*N*′-tetraethylethylenediamine (teeda) (**2**)], has been spectroscopically and kinetically studied to gain some insight into the reaction mechanisms. The ESR spectra show that catecholato complexes [Cu(dbc)L] [L = tmeda (**3**) or teeda (**4**)] are formed upon reactions of **1** or **2** with $H_2$dbc, respectively. The UV–vis and ESI mass spectra show that **3** is converted to a semiquinonato complex $[Cu(dbsq)tmeda]^+$ (**5**) in the aerobic oxidation, while $[Cu(dbsq)teeda]^+$ (**6**) is only a minor species. In the presence of acid, **3** and **4** are aerobically oxidized to dbq quantitatively. Kinetic studies show that rate constants for the catalytic aerobic oxidation of $H_2$dbc are proportional to the second or the first order with **1** or **2**, respectively, and to the first-order with the $O_2$-partial pressure. Based on these data, different reaction mechanisms are proposed for **1** and **2**, and may be caused by the steric hindrances around the copper center of **1** and **2**.

The copper-catalyzed aerobic oxidation of catechols to quinones is an important chemical process in biological systems and medical diagnosis.[1–9] In biological systems, catechol is converted to quinone by catechol oxidase and tyrosinase,[1–8] which are enzymes having dicopper centers similar to the hemocyanin $O_2$-transport protein in arthropods and mollusks.[10] The mechanism for the oxidation of catechol by catechol oxidase is postulated to be as follows.[8] Catechol is bound at the dicopper(II) center ($Cu(II)_2$) to be oxidized to quinone, then $Cu(II)_2$ is reduced to $Cu(I)_2$. The resultant $Cu(I)_2$ binds the $O_2$-molecule to form a $\mu$-$\eta^2$:$\eta^2$-peroxo-dicopper(II) intermediate, which oxidizes a catechol to a quinone. Thus, two catechol molecules are oxidized by one $O_2$-molecule, which is reduced to two water molecules.

Although the enzymatic reaction mechanism for the oxidation of catechol seems to be simple, the aerobic oxidation of catechol catalyzed by copper complexes in artificial systems is much more complicated because of the generation of various intermediates in the stepwise one-electron oxidation of catechol via the binding of catechol to the copper complex. Many mechanistic studies on the aerobic oxidation of catechols catalyzed by copper complexes have been reported, with some pioneering work by using self-assembling dicopper complexes of bidentate ligands, such as peralkylated ethylenediamines, bipyridine derivatives, and related compounds.[11–24] The reaction intermediates proposed so far are catecholato complexes,[12–15] semiquinonato complexes,[11,16] and copper dioxygen species postulated as being responsible for formation of quinone and $H_2O_2$.[17–24] The chemical structures of these intermediates are shown in Chart 1.

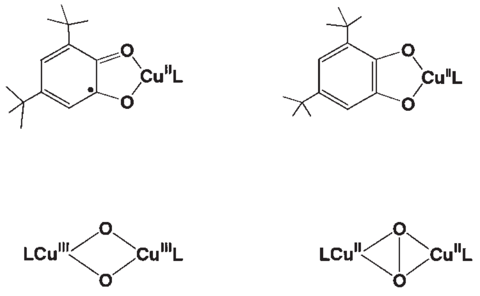

Chart 1.

Thompson et al. isolated the semiquinonatocopper(II) complexes of *N*,*N*′-tetramethylethylenediamine (tmeda) and *N*,*N*′-tetraethylethylenediamine (teeda) upon reactions of a $\mu$-methoxo-$\mu$-hydroxo-dicopper(II) complex of tmeda with 3,5-di-*tert*-butylcatechol ($H_2$dbc) and a ethylenecopper(I) complex of teeda with 3,5-di-*tert*-butyl-*o*-benzoquinone (dbq) under anaerobic conditions as shown in Eqs. 1 and 2, respectively, and claimed that the semiquinonate complexes are key intermediates responsible for the formation of dbq in the Cu-catalyzed aerobic oxidation of $H_2$dbc.[11]

$$[Cu_2(tmeda)_2(OH)(OMe)](ClO_4)_2 + H_2dbc \rightarrow [Cu(tmeda)(dbsq)](ClO_4) + [Cu(tmeda)](ClO_4) \qquad (1)$$

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$$[\mathrm{Cu(teeda)(C_2H_4)}](\mathrm{ClO_4}) + \mathrm{dbq} \rightarrow [\mathrm{Cu(teeda)(dbsq)}](\mathrm{ClO_4}) + \mathrm{C_2H_4} \quad (2)$$

Here, we report on spectral and kinetic studies for the reactions of $H_2$dbc with di-$\mu$-hydroxo-dicopper(II) complexes $[Cu_2(OH)_2L_2](ClO_4)_2$ [L = tmeda (**1**) and teeda (**2**)] in MeCN under both anaerobic and aerobic conditions to gain some insight into the mechanism for the Cu-catalyzed aerobic oxidation of catechol. We found that the catecholato complexes [Cu(dbc)L] [L = tmeda (**3**) or teeda (**4**)] are generated as reaction intermediates at the early stages of the reactions of **1** or **2** with $H_2$dbc, respectively, under both anaerobic and aerobic conditions. Moreover, we found that **3** is aerobically oxidized to a semiquinonato complex [Cu(dbsq)tmeda]($ClO_4$) (**5**), which is responsible for formation of dbq, while **4** is aerobically oxidized to directly give dbq without the formation of a semiquinonato complex [Cu(dbsq)teeda]($ClO_4$) (**6**).

## Experimental

**Materials.** All ordinary reagents and solvents were purchased and used as received, unless otherwise noted. MeCN was dried over $P_2O_5$ and distilled. Di-$\mu$-hydroxo-dicopper(II) complexes $[Cu_2(OH)_2L_2](ClO_4)_2$ [L = *N*,*N*′-tetramethylethylenediamine (tmeda) (**1**) and *N*,*N*′-tetraethylethylenediamine (teeda) (**2**)] were synthesized according to a literature method.[25,26] The peralkylated ethylenediamine ligand was dissolved in MeOH, and $Cu(ClO_4)_2 \cdot 6H_2O$ was added to the solution. To the resultant mixture was added two equivalents of triethylamine, then blue solid presipitated. The crude products were purified by recrystallization from AcOEt/MeCN/$CH_2Cl_2$. 3,5-Di-*tert*-butylcatechol ($H_2$dbc) was recrystallized from petroleum ether just before use. The catecholato complexes[11] [Cu(dbc)L] [L = tmeda (**3**) and teeda (**4**)] and the semiquinonato complexes[27] [Cu(dbsq)L]($ClO_4$) [L = tmeda (**5**) and teeda (**6**)] were prepared according to literature methods.

**Measurements.** UV–vis absorption spectra were recorded on BECKMAN DU 7400 and Otsuka Electronics MCPD-7000 spectrophotometers. Electro-spray ionization (ESI) mass spectra were obtained on a PE SCIEX API 150EX spectrometer using MeCN solutions. ESR spectra were recorded on a JEOL JES-TE 200 spectrometer in MeCN at 77 K.

**Generation and Decomposition of Catecholatocopper(II) Complexes in the Reactions of 1 or 2 with $H_2$dbc.** The generation and decomposition of the catecholato-copper(II) complexes in reactions of **1** or **2** with $H_2$dbc were monitored by the ESR and electronic absorption spectra under anaerobic and aerobic conditions. To a MeCN solution (5 mL) of **1** or **2** ($3.0 \times 10^{-4}$ M) was added a MeCN solution (5 mL) of $H_2$dbc ($4.0 \times 10^{-3}$ M), and rapidly mixed. The ESR spectra were measured at 77 K by taking an aliquot of the mixed solution just after mixing and after 30, 60, 120, 240, and 360 seconds. The electronic absorption spectra were measured in the same manner.

**Product Analysis for the Aerobic Oxidation of the Catecholatocopper(II) Complexes in the Presence and the Absence of Acid.** The catecholatocopper(II) complex of tmeda **3** (50 mg) was dissolved in 10 mL of MeCN, and the solution was allowed to stand for 2 days in contact with air. It was concentrated to dryness. The FAB MS spectrum of the residue shows a major peak at 432 corresponding to $[Cu(dbc)(O_2 + H)(temda)]^+$, suggesting that $O_2$ is incorporated into the dbc moiety. To the residue was added 5 mL of aqueous HCl (3.0 M). The mixture was extracted by $Et_2O$ (3 mL × 5). The extracts collected were concentrated to dryness to afford oily residue (25 mg). The $^1$H NMR, FAB MS, and IR data of the oily residue show that the ring-open product is a major product. The spectral data of the oily residue, IR data [$\nu$/cm$^{-1}$] on KBr disk: 2966 (aliphatic C–H) and 1755 (C=O). $^1$H NMR data ($\delta$/ppm vs $Me_4Si$) in $CDCl_3$: 6.96 (s, 1H, aromatic H), 2.98, 2.81 (d, 2H, $-CH_2-$), 1.24 (s, 3H, $-C(CH_3)_3$), and 0.99 (s, 3H, $-C(CH_3)_3$). FAB-MS data: *m*/*z* 255 $[M + H]^+$ and 195 $[M - CH_2CO_2H]^+$.

A MeCN solution of **3** (50 mg) was allowed to stand for 1 h after the addition of $O_2$, and was concentrated to dryness. The FAB MS spectrum of the residue shows a major peak at 399, corresponding to $[Cu(dbc)(temda)]^+$, suggesting that $O_2$ is not incorporated into the dbc moiety. To the residue was added 5 mL of aqueous HCl (3.0 M), and the mixture was extracted with $Et_2O$ (3 mL × 5). The collected extract was concentrated to dryness to afford an oily residue. The $^1$H NMR and FAB MS spectra of the residue show that dbq and $H_2$dbc are mainly contained and a small amount of the ring-open product is detected. To the resultant solution after a 1 h reaction of **3** (50 mg) with $O_2$, before concentration, was added 2.0 equivalents of $HClO_4$. After concentration, to the residue were added 5 mL of aqueous HCl (3.0 M) and $Et_2O$ (3 mL × 5). From the $Et_2O$ extract, dbq (22 mg) was obtained as a main product.

Almost the same results were obtained in the case of **4**.

**General Procedure for the Rate Measurements and Calculation of Pseudo-First-Order Rate Constants. Rate Measurements for Formation of dbq in the Reactions of 1 or 2 with $H_2$dbc.** A MeCN (2 mL) solution of $H_2$dbc was placed in a quartz-cell, and was degassed and refilled with a previously prepared $O_2/N_2$ mix gas. To the solution was added a MeCN solution (2 mL) of **1** or **2** by using a syringe. After mixing the solution, the increase of 3,5-di-*tert*-butylquinone (dbq) ($\lambda_{max}$ ($\varepsilon$) = 400 nm (1800 M$^{-1}$ cm$^{-1}$)) was followed by monitoring the change in the visible absorption at 400 nm. Quantitative conversion of $H_2$dbc to dbq was observed. All rate measurements were performed under pseudo-first-order conditions of excess $H_2$dbc and constant $O_2$-partial pressure at 25 ± 0.2 °C. Pseudo-first-order rate constants ($k_{obs}$) were obtained from fits of $-\ln(1 - A_t/A_\infty)$ vs time. A plot of the kinetic data gave straight lines in each kinetic measurement.

**Rate Dependence on Concentration of 1 and 2.** The rates were measured under the following conditions listed below: [**1**] = $5.0 \times 10^{-5}$–$3.0 \times 10^{-4}$ M, [**2**] = $1.0 \times 10^{-4}$–$4.0 \times 10^{-4}$ M, [$H_2$dbc] = $4.0 \times 10^{-3}$ M, under $O_2$ atmosphere.

**Rate Dependence on Concentration of $H_2$dbc.** The rates were measured under the following conditions listed below: [**1**] or [**2**] = $2.0 \times 10^{-4}$ M, [$H_2$dbc] = $2.0 \times 10^{-3}$–$5.0 \times 10^{-3}$ M, under $O_2$ atmosphere.

**Rate Dependence on $O_2$-Partial Pressure.** The rates were measured under the following conditions: [**1**] = $2.0 \times 10^{-4}$ M, [**2**] = $4.0 \times 10^{-4}$ M, [$H_2$dbc] = $4.0 \times 10^{-3}$ M, under $O_2/N_2$ atmosphere ($O_2$ partial pressure = 0, 0.25, 0.5, 0.75, 1 atm).

**Stopped-Flow Measurements for the Formation of the Catecholaocopper(II) Complexes upon the Reactions of 1 or 2 with $H_2$dbc.** The kinetic studies for the initial reactions of **1** or **2** with $H_2$dbc were carried out by using a UNISOKU stopped-flow apparatus with a multi-channel photodiode array under the same conditions as given in the general procedures for the rate measurements.

**Determination of $H_2O_2$ Generated in Aerobic Oxidation of $H_2$dbc.**[28] A peroxyoxalate chemiluminescent assay was used for the determination of $H_2O_2$ generated in the reactions according to a literature method. An aqueous phosphate buffer solution (pH = 7.0) of $\gamma$-cyclodextrin ($\gamma$-CD, 0.1 M), an aqueous phosphate solution (pH = 7.0) of dansyl acid (0.1 M) and a MeCN solution of bis(2,4,6-trichlorophenyl) oxalate (TCPO, $5.0 \times 10^{-3}$ M) were prepared. 135 μL of the $\gamma$-CD solution, 20 μL of the dansyl acid solution, and 20 μL of the TCPO were mixed in a cell, and the cell is placed in the Aroka Model BLR-301 emission spectrophotometer. To the cell was added a reaction mixture of **1** (or **2**) and $H_2$dbc in MeCN just after mixing, and after 1–5 min. the emission was counted. By using a calibration curve (emission vs $H_2O_2$), the $H_2O_2$ generated in the reactions was determined from the observed emission count number.

**Structure Determination of Single Crystals.** The structures of **1** and **2** were determined on a Rigaku AFC7R diffractometer with graphite monochromated Mo K$\alpha$ radiation ($\lambda = 0.71069$) and a 12 kW rotating anode generator. The cell constants and an orientation matrix for data collection were typically obtained from a least-squares refinement using the setting angles of 25 carefully centered reflections with $2\theta$ near 25°. The key facets of the structure determinations for the Cu(II) complexes **1** and **2** are given in Table 1. The data were collected at 296(1) K using the $\omega$–$2\theta$ scan technique to a maximum $2\theta$ value of 55.0°.

Table 1. Summary of Crystallograpic Data for **1** and **2**

| | **1** | **2** |
|---|---|---|
| Empirical formula | $C_{12}H_{34}Cl_2Cu_2N_4O_{10}$ | $C_{20}H_{50}Cl_2Cu_2N_4O_{10}$ |
| Formula weight | 592.42 | 704.63 |
| Crystal system | monoclinic | monoclinic |
| Space group | $P2_1/n$ (No. 14) | $P2_1/n$ (No. 14) |
| $a$/Å | 7.656(7) | 7.603(5) |
| $b$/Å | 14.820(7) | 17.876(3) |
| $c$/Å | 11.572(5) | 11.821(4) |
| $\beta$/deg | 108.03(5) | 90.62(4) |
| $V$/Å$^3$ | 1248(1) | 1606.4(9) |
| $Z$ | 2 | 2 |
| $T$/°C | 20.0 | 20.0 |
| $D_{calc}$/g cm$^{-1}$ | 1.576 | 1.457 |
| Radiation/Å | Mo K$\alpha$ ($\lambda = 0.71069$) | Mo K$\alpha$ ($\lambda = 0.71069$) |
| $\mu$/cm$^{-1}$ | 19.67 | 15.41 |
| $R$, $R_w$ | 0.066, 0.070 | 0.046, 0.047 |
| Goodness of Fit Indicator | 1.99 | 0.77 |

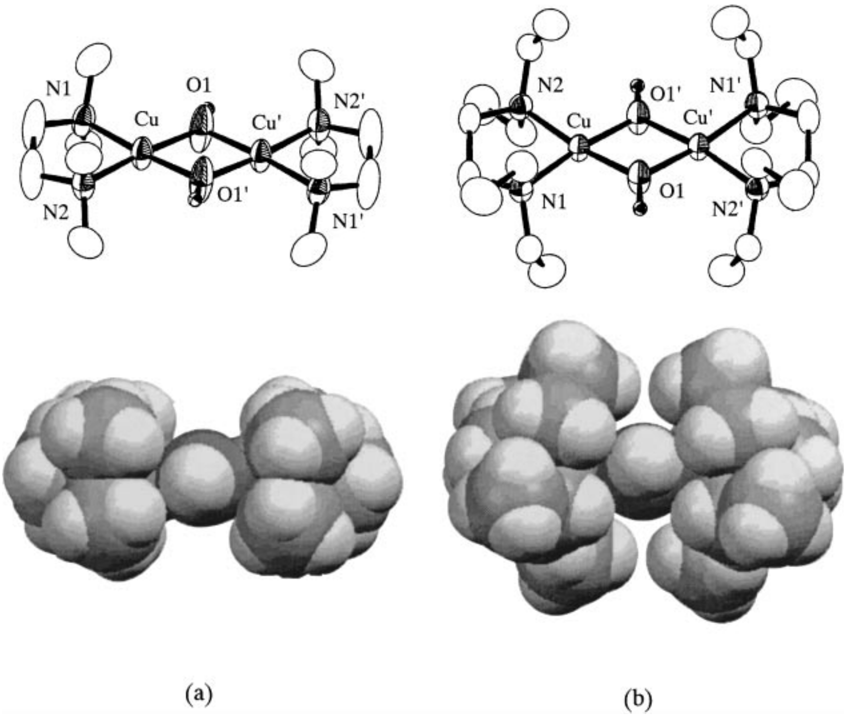
$R = \Sigma||F_o| - |F_c||/\Sigma|F_o|$, $R_w = [\Sigma w(|F_o| - |F_c|)^2/\Sigma w(F_o)^2]^{1/2}$, $w = 1$.

## Results and Discussion

**Crystal Structures of 1 and 2.** The crystal structures[25,26] of the di-$\mu$-hydroxo-dicopper(II) complexes $[Cu_2(OH)_2L_2](ClO_4)_2$ [L = *N*,*N*′-tetramethylethylenediamine (tmeda) (**1**) and *N*,*N*′-tetraethylethylenediamine (teeda) (**2**)] were determined to examine the structural influences of the tetraalkyl groups of the ligands, tmeda and teeda. The selected bond distances and angles are given in Table 2. ORTEP diagrams and space-filling models are shown in Fig. 1. The ethyl groups in **2**

Table 2. Selected Bond Distances (Å) and Angles (deg) for **1** and **2**

| **1** | | **2** | |
|---|---|---|---|
| Cu···Cu′ | 2.975(2) | Cu···Cu′ | 2.9979(7) |
| Cu–O(1) | 1.900(1) | Cu–O(1) | 1.9159(7) |
| Cu–O(1)′ | 1.9320(9) | Cu–O(1)′ | 1.9284(3) |
| Cu–N(1) | 2.0255(9) | Cu–N(1) | 2.0318(4) |
| Cu–N(2) | 2.016(1) | Cu–N(2) | 2.0226(7) |
| O(1)–Cu–O(1)′ | 78.13(4) | O(1)–Cu–O(1)′ | 77.51(1) |
| O(1)–Cu–N(1) | 98.14(4) | O(1)–Cu–N(1) | 98.05(2) |
| O(1)′–Cu–N(1) | 175.616(3) | O(1)′–Cu–N(1) | 172.789(3) |
| O(1)–Cu–N(2) | 175.037(3) | O(1)–Cu–N(2) | 172.068(5) |
| O(1)′–Cu–N(2) | 97.24(4) | O(1)′–Cu–N(1) | 172.789(3) |
| N(1)–Cu–N(2) | 86.56(4) | N(1)–Cu–N(2) | 87.84(2) |
| Cu–O(1)–Cu′ | 101.87(4) | Cu–O(1)–Cu′ | 102.49(1) |



(a) (b)

Fig. 1. ORTEP diagrams (top) and space filling models (bottom) of the cationic portions of **1** (a) and **2** (b).

are projected into spaces at both sides of the $Cu_2(OH)_2$ core plane like picket fences, being a much larger steric hindrance than methyl groups in **1**. The large steric hindrance of ethyl groups in **2** is clearly shown by the space-filling model (see Fig. 1), and as shown later, drastically affects the reactivity. The ethyl groups influence the bond distances and angles in **2**. The Cu–Cu distance of **2** is slightly elongated to avoid the steric repulsion between the ethyl groups: the Cu–Cu distances of **1** and **2** are 2.978 and 2.998 Å, respectively. Similarly, the Cu–O and Cu–N bond distances in **2** are slightly elongated: the average Cu–O bond distances of **1** and **2** are 1.916 and 1.922 Å, and the average Cu–N bond distances of **1** and **2** are 2.021 and 2.027 Å, respectively. The steric influences are also found in the bond angles: the Cu–O–Cu and the N–Cu–N bond angels of **2** are slightly larger than the corresponding angles of **1**.

**ESR Studies for the Reactions of 1 or 2 with $H_2$dbc under Anaerobic and Aerobic Conditions.** The reactions of **1** or **2** with $H_2$dbc in MeCN under anaerobic and aerobic conditions were followed by the ESR spectra. The dicopper(II) complexes **1** and **2** are ESR-silent due to the antiferromagnetic interaction between two Cu(II) ions. Upon the addition of $H_2$dbc to solutions of **1** or **2** in MeCN, clear ESR signals typical of mononuclear copper(II) complexes appeared immediately, as shown in Fig. 2. These ESR spectra are identical to those of catecholatocopper(II) complexes [Cu(L)(dbc)] [L = tmeda (**3**) and teeda (**4**)], which were independently prepared according to a literature method.[27] The amounts of **3** and **4** were determined by the intensity of the ESR signals observed with aliquots of the reaction mixtures during the course of the reactions. The time-courses of **3** and **4** are shown in Fig. 3.

The yields of the catecholato complexes at the beginning of the reactions were nearly 50% per copper ion of the dicopper complexes used. This indicates that **1** and **2** are quantitatively converted to **3** and **4** and an aquacopper(II) complexes $[Cu(L)(H_2O)_2](ClO_4)_2$ (L = tmeda and teeda) in a 1:1 ratio as shown in Eq. 3. The aquacopper(II) complexes might form dicopper(II) complexes to be ESR silent because the ESR spectra observed for the reactions do not show any other signals than those of **3** and **4**.

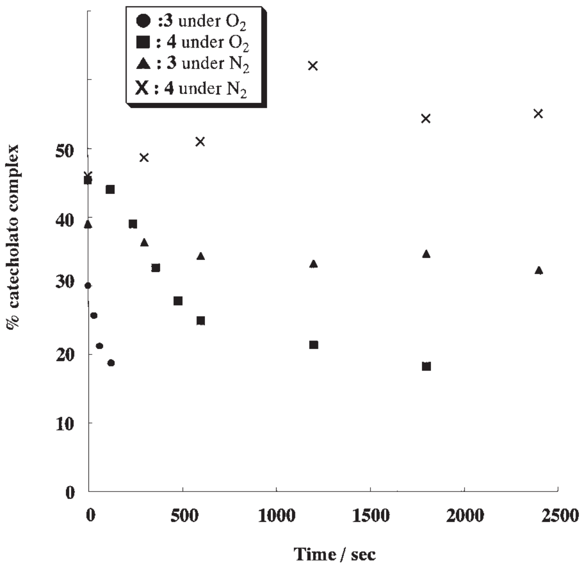


Fig. 3. Time-courses of **3** and **4** upon reactions of **1** or **2** with $H_2$dbc under both anaerobic and aerobic conditions in MeCN.

$$\underset{\substack{\mathbf{1}\ (L = \text{tmeda})\\ \text{or}\\ \mathbf{2}\ (L = \text{teeda})}}{[Cu_2L_2(OH)_2](ClO_4)_2} + H_2dbc \rightarrow \underset{\substack{\mathbf{3}\ (L = \text{tmeda})\\ \text{or}\\ \mathbf{4}\ (L = \text{teeda})}}{[CuL(dbc)]} + 1/n\{[Cu(OH)_2(dbc)](ClO_4)_2\}_n \tag{3}$$

Under anaerobic conditions, the catecholato complex of tmeda, **3**, was decreased in the half-life time of ca. 2 h, while the amount of the catecholato complex of teeda, **4**, was almost constant for more than 6 h. In a preparative scale reaction of **1** with $H_2$dbc under anaerobic conditions, a semiquinonato complex $[Cu(dbsq)tmeda](ClO_4)$ (**5**) and a Cu(I) complex $[Cu(tmeda)](ClO_4)$ were isolated as reported by Thompson

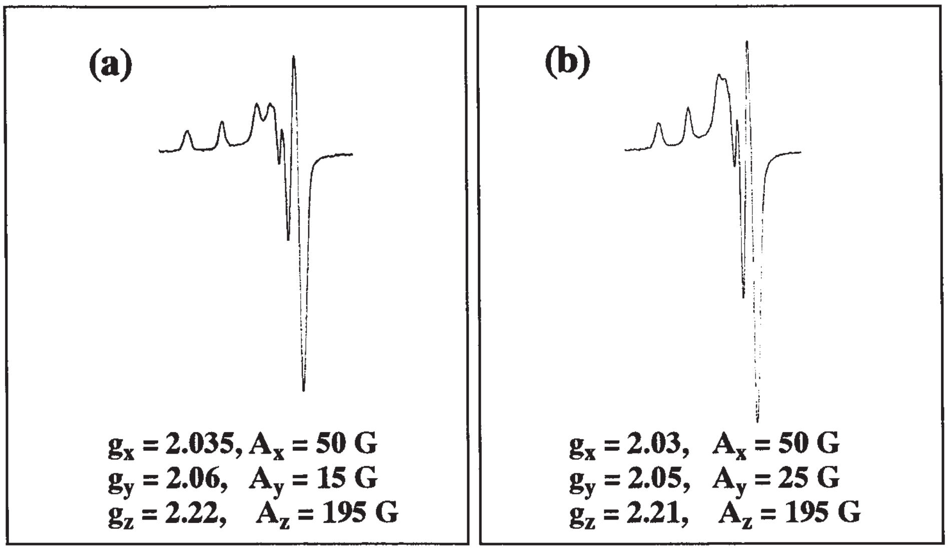


Fig. 2. ESR spectra of **3** (a) and **4** (b) generated from **1** and **2** upon reactions with $H_2$dbc.

et al. while in the case of **2**, a semiquinonato complex [Cu(dbsq)teeda]($ClO_4$) (**6**) was not obtained upon reaction of **2** with $H_2$dbc at all.[11] These results are consistent with the ESR observations. Thus, the decrease of **3** under anaerobic conditions is due to a redox reaction between **3** and the aqua-copper(II) complex to form **5** and the Cu(I) complex. The large steric hindrance of ethyl groups in teeda may prevent the reaction between **4** and the aqua copper(II) complex, leading to the high stability of **4** under anaerobic conditions. This indicates that the steric hindrance of ethyl groups in teeda exerts a drastic influence on the reactivity of the copper complexes. The decreases of **3** and **4** are much faster under aerobic conditions than under anaerobic conditions. This is direct evidence that $O_2$ is responsible for the oxidation of the catecholato complex. Under aerobic conditions, decomposition of **3** is much faster than that of **4**, indicating that **3** is more reactive to $O_2$ than **4**. As shown later, this may be also explained by the fact that the steric hindrance of ethyl groups in teeda is much larger than that of the methyl groups in tmeda.

**Early Stages of the Aerobic Reactions of 1 or 2 with $H_2$dbc.** The stopped-flow method was used to observe the early stages of the aerobic oxidation of $H_2$dbc catalyzed by **1** or **2**. The formations of the catecholato complexes **3** and **4** monitored at 400 nm obey good first-order kinetics with $k = 3.7 \times 10^2$ $sec^{-1}$ and 2.2 $sec^{-1}$, respectively. The pseudo-first-order rate constants are proportional to the first-order with **1** or **2** and with $H_2$dbc. The formation of **3** is nearly 170-fold faster than that of **4**, indicating that the large steric hindrance of the ethyl groups in teeda retards the reaction. The UV–vis spectra of the reaction mixtures after 2 sec were obtained by the stopped-flow method and are shown in Fig. 4. The Fig. 4(a) obtained for the aerobic reaction of $H_2$dbc with **1** shows a new band at 390 nm assignable to the semiquinonato complex **5**, while the Fig. 4(b) obtained for the aerobic reaction of $H_2$dbc with **2** shows only a broad signal assignable to **4**. These results clearly show that **3** is partly converted to **5**, while the semiquinonato complex **6** is not generated from **4**. The spectral data for **3**, **4**, and **5** in MeCN are independently obtained and shown in Table 3. The catecholato and the semiquinonato complexes have different absorption maximums at around 400 nm,[11,27] and it is possible to separate and determine each component in the UV–vis spectra of the reaction mixtures. The ratio of **3** and **5** in the reaction mixture after 2 sec is estimated to be 4:1. Therefore, **3** is the major species at the early stage of the aerobic oxidation of $H_2$dbc catalyzed by **1**.

The ESI mass spectra observed during the aerobic reactions of $H_2$dbc catalyzed by **1** or **2** show mass peaks ($m/z$) at 399 due to **5** as a major signal, but at 455 due to **6** as only a minor signal (see Fig. 5). This suggests that **5** is generated as an intermediate in the major reaction path, while **6** is only a minor species. In ESI mass spectroscopy, the electrically neutral catecholato complexes **3** and **4** are less sensitive for observation than the monocationic semiquinonato complexes **5** and **6**, resulting in almost no signals of **3** and **4**, though the catecholato complexes are the main species in the reaction mixtures. The UV–vis and the ESI mass spectra demonstrate that **3** is aerobically oxidized to **5** while **4** is not converted to **6** in the main reaction path.

Table 3. UV–Vis Spectral Data for **3**–**5** in MeCN

| Compound | $\lambda_{max}$/nm | $\varepsilon$/$M^{-1}$ $cm^{-1}$ |
|---|---|---|
| **3** | 403 | 790 |
| **4** | 390 | 900 |
| **5** | 390 | 2800 |

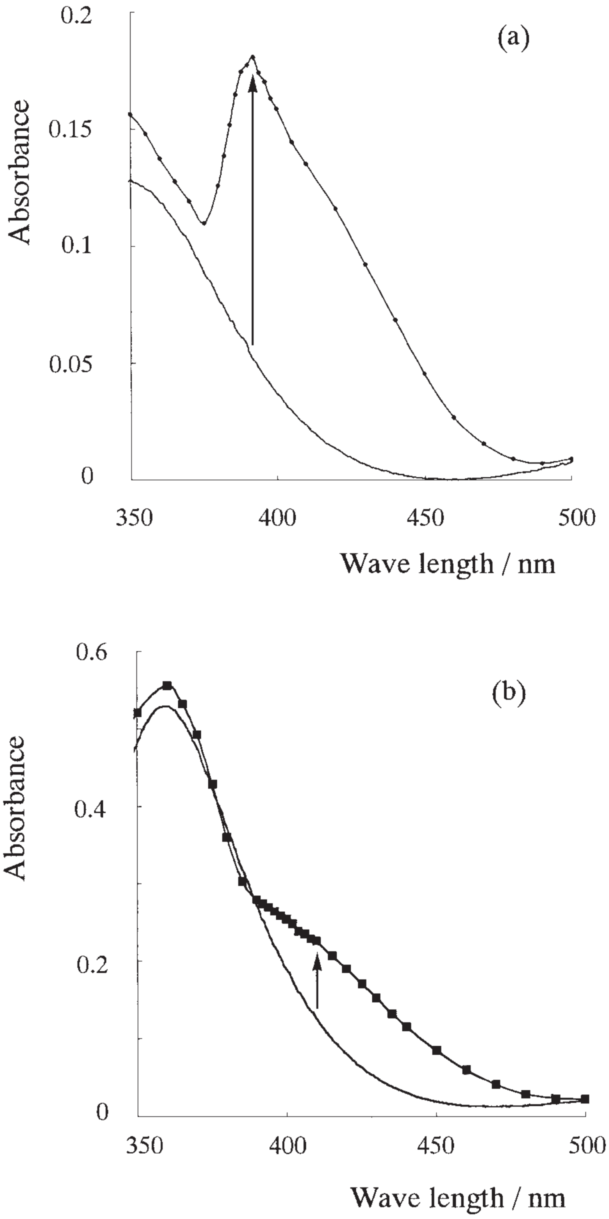


Fig. 4. UV–vis spectral changes after 2 sec upon addition of $H_2$dbc to MeCN solutions of **1** (a) or **2** (b) by stopped-flow method.

**Aerobic oxidation of 3 or 4.** The catecholato complexes **3** and **4** were independently prepared and used to examine the reactions with $O_2$. **3** and **4** in MeCN solutions are stable under anaerobic conditions, and oxidized upon the addition of $O_2$, as shown in Scheme 1. In the absence of an acid, **3** and **4** were converted to a ring-open product,[29] while in the presence of acid, **3** and **4** gave dbq, as described at Experimental section.

Pierpont et al. reported an aerobic oxidation of a phenanthrenediolatocopper(II) complex of tmeda, which

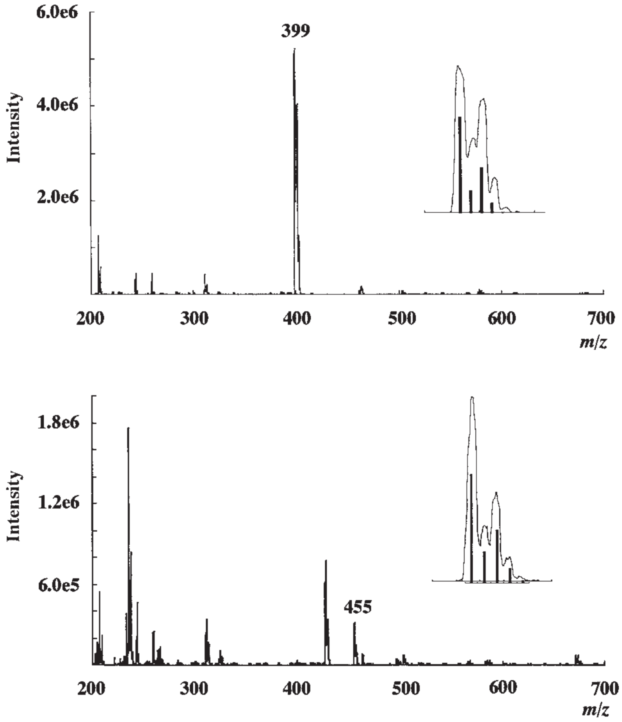
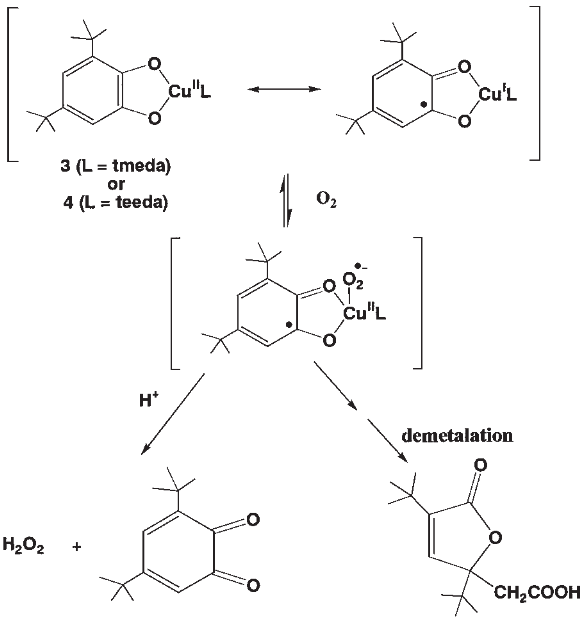


Fig. 5. ESI mass spectra observed in the course of the aerobic oxidation of $H_2$dbc catalyzed by **1** (top) or **2** (bottom). Isotope patterns of the semiquinonate complexes **5** and **6** are shown in the spectra.

is in a resonance of two valence tautomers of the phenanthrenediolatocopper(II) and the phenanthrenesemiquinonatocopper(I) states.[30] The phenanthrenesemiquinonatocopper(I) tautomer can bind a $O_2$-molecule to form a dioxygen complex, which is decomposed to phenanthrenequinone in the presence of an acid and to a ring-open product in the absence of acid. The reaction features and the products in the Pierpont's system are very similar to those in the aerobic oxidation of **3** and **4**. This indicates that the aerobic oxidation of **3** and **4** proceeds via dioxygen complexes similar to that of Pierpont's system.

The aerobic oxidation of the catecholato complexes **3** and **4** in the absence of an acid was followed by the UV–vis absorption spectra. Upon the addition of $O_2$ to a solution of **3** in MeCN, a new absorption band appeared at 393 nm. The spectral change was completed in ca. 1 h, and then the new band decreased very slowly. After 2 days, the reaction mixture was treated with aqueous HCl to demetalate, and gave the ring-open product as a major product. After a 1 h reaction of **3** with $O_2$, the intermediate was decomposed upon the addition of $HClO_4$, and dbq was isolated as a major product. These results indicate that the intermediate is a dioxygen complex, and in the absence of acid, the $O_2$ moiety in the intermediate is slowly incorporated into the catecholate to afford the ring-open product. Although either the Cu(I) or the carbon radical in the semiquinonate tautomers of **3** could be a $O_2$-binding site, the dioxygen molecule is probably bound at the Cu(I) center because the acid decomposition of the intermediate gives dbq, but not the ring-open product. Kinetic studies for the formation of the intermediate from **3** reveal that the formation rate is first-order with **3**. The product analysis for the aerobic oxidation of **4** gave almost the same results as that of **3**. Interestingly, however, the formation rate of the intermediate from **4** is zero-order with **4**. The difference in the rate dependence on the concentration of the catecholatocopper(II) complexes may be due to the large steric hindrance of the ethyl groups in **4**. It is noteworthy that the difference in the steric hindrance of the ligands tmeda and teeda exerts a drastic effect on the kinetics and the mechanisms of the aerobic oxidation of **3** and **4**, but there is no difference in the products.



Scheme 1.

**Kinetics and Mechanisms of the Aerobic Oxidation of $H_2$dbc Catalyzed by 1 or 2.** In order to clarify the reaction mechanisms for the aerobic oxidation of $H_2$dbc catalyzed by **1** or **2**, the catalytic aerobic reactions were kinetically investigated. The reactions were followed an increase of dbq at 400 nm. The rate constants are proportional to the second order with **1** and proportional to the first order with **2**, as shown in Fig. 6. Thus the reaction catalyzed by **1** is much faster at relatively high concentrations of the catalyst than that by **2**. Since the reaction intermediates for the reaction of **1** are **3** and **5**, two molecules of **3** or **5** are involved in the rate-determining step. Since the intermediate for the reaction of **2** is **4**, one molecule of **4** is involved in the rate-determining step. The rate dependence on the $O_2$-partial pressure was examined, and the rate constants for the reactions of **1** or **2** are proportional to the first-order with the $O_2$-partial pressure, as shown in Fig. 7. Thus, one molecule of $O_2$ is involved in the rate-determining steps.

In the present systems, $O_2$-molecule consumed for the oxidation of $H_2$dbc is converted to hydrogen peroxide. The generation of hydrogen peroxide is determined by a peroxyoxalate chemiluminescent assay.[28] As shown in Fig. 8, hydrogen peroxide is increased proportionally with the formation of dbq.

The spectral and kinetic data demonstrate that two molecules of the intermediate generated from **1** and one molecule of $O_2$ are involved in the rate-determining step of the aerobic

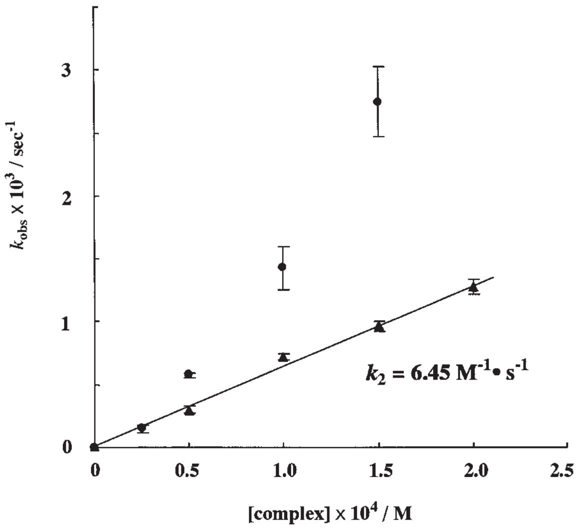


Fig. 6. Dependences of the rate constants ($k_{obs}$) on concentration of **1** and **2** in the aerobic oxidation of $H_2$dbc (2.0 mM) catalyzed by **1** (●) or **2** (▲) in MeCN under $O_2$ at 25 °C.

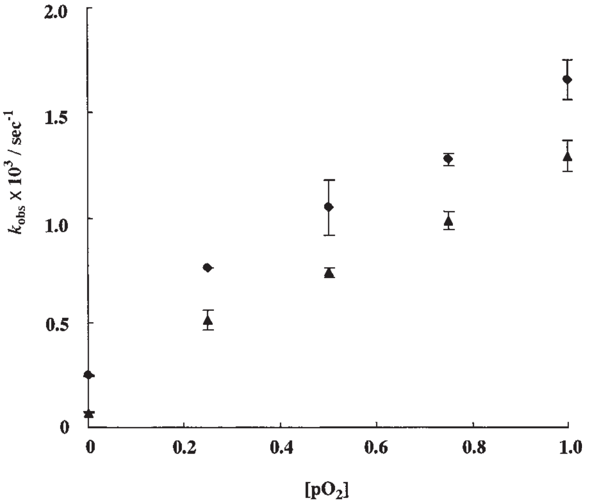


Fig. 7. Dependence of the rate constant ($k_{obs}$) on the $O_2$-partial pressure in the aerobic oxidation of $H_2$dbc (2.0 mM) catalyzed by **1** (0.1 mM) (●) or **2** (0.2 mM) (▲) in MeCN at 25 °C.

oxidation of $H_2$dbc catalyzed by **1**. Thus, two possible reactions may be considered for the rate-determining step. One of them is the reaction of **3** with the dioxygen complex of **3** to give two molecules of **5** and hydrogen peroxide in the presence of a proton donor, for example $H_2$dbc. Another is a reaction of two molecules of **5** with $O_2$ to give two molecules of dbq and hydrogen peroxide in the presence of the proton donor. Since **3** is the major species at the early stage of the reaction, as shown above, we propose that the former reaction is the rate-determining step of the aerobic oxidation of $H_2$dbc catalyzed by **1**. For the aerobic oxidation of $H_2$dbc catalyzed by **2**, we propose that the rate-determining step is the unimolecular decomposition of the dioxygen complex of **4** to directly give dbq and hydrogen peroxide in the presence of the proton donor.

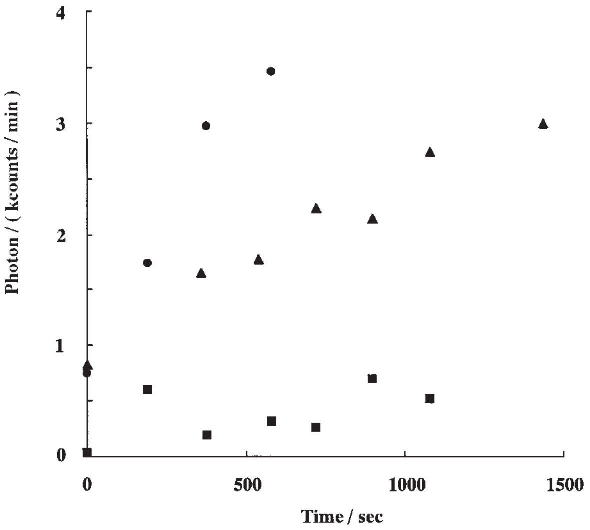


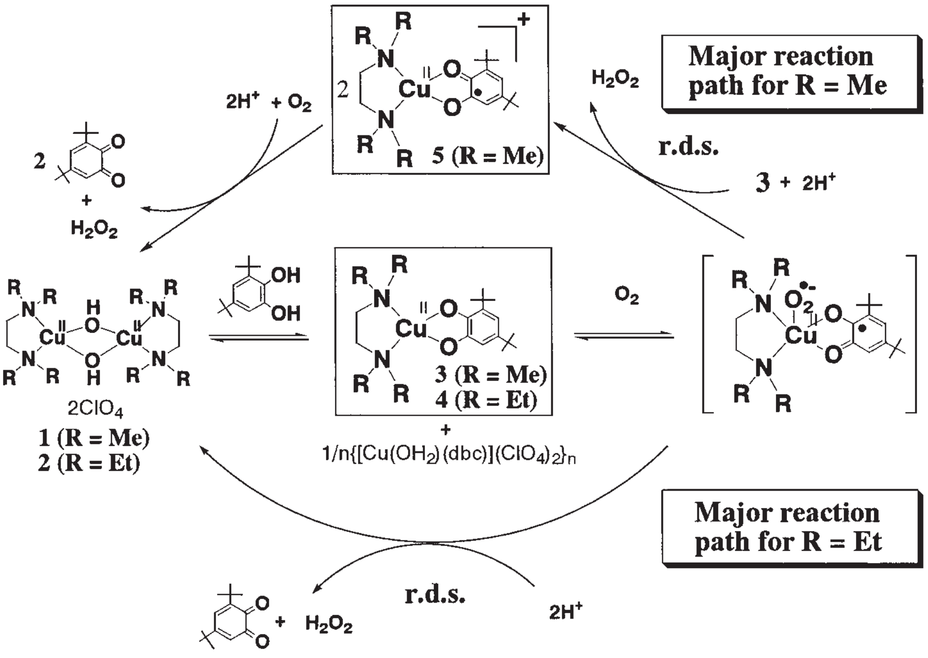
Fig. 8. Determination of $H_2O_2$ generated in the aerobic oxidation of $H_2$dbc catalyzed by **1** (●) or **2** (▲) and without catalyst (■).

Based on these considerations, the mechanisms for the aerobic oxidation of $H_2$dbc catalyzed by **1** or **2** are proposed in Scheme 2. At first the dicopper(II) complexes, **1** and **2**, react with $H_2$dbc to generate the catecholato complexes **3** and **4**. Next, **3** and **4** bind $O_2$ to form the dioxygen complexes. The dioxygen complex of **3** reacts with **3** via protonation to give two molecules of **5** and hydrogen peroxide, and **5** is aerobically converted to dbq as reported by Thompson et al. though the mechanism for the conversion of **5** to dbq has not been clarified yet.[11] The dioxygen complex of **4** is directly converted to dbq and hydrogen peroxide via protonation.

The difference of these two reaction mechanisms may be due to difference in the steric hindrance of the tetraalkyl groups between tmeda and teeda. The sterically less hindered complex of tmeda, **3**, is able to undergo the bimolecular reaction, which is thermodynamically favorable because of the two-electron reduction of $O_2$. In the sterically more hindered complex of teeda, **4**, the bimolecular reaction must be retarded and the unimolecular decomposition of the dioxygen complex of **4** proceeds preferentially.

## Conclusion

We have spectroscopically and kinetically investigated the anaerobic and aerobic reactions of **1** or **2** with $H_2$dbc. The spectral data demonstrate that the catecholato complexes **3** and **4** are the first intermediate in the aerobic oxidation of $H_2$dbc catalyzed by **1** or **2**. In the reaction of **1**, the less-sterically hindered ligand tmeda enables **3** to undergo bimolecular aerobic oxidation to lead to the formation of the semiquinonato complex **5** as the second intermediate. However, the large steric hindrance of the ethyl groups in teeda prevents the bimolecular reaction, resulting in the unimolecular two-electron oxidation of **4** by $O_2$ to dbq. Although Thompson et al. reported that the semiquinonato complex is responsible for the formation of dbq,[11] the semiquinonato complex is not detected at all in the case of the reaction catalyzed by **2**. Here, it is concluded that the catecholato complex is a key intermediate in the aerobic oxidation of $H_2$dbc catalyzed by **1** or **2**. Moreover,



Scheme 2.

the present results demonstrate that the semiquinonato complex is generated from the catecholato complex, but not directly from the reaction of **1** with $H_2$dbc.

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