5020

J. Am. Chem. Soc. **1988,** *110,* 5020–5024

Copper-Mediated Hydroxylation of an Arene: Kinetics and Mechanism of the Reaction of a Dicopper(II) m-Xylyl-Containing Complex with H₂O₂ To Yield a Phenoxodicopper(II) Complex

Richard W. Cruse,[†] Susan Kaderli,[†] Charles J. Meyer,[†] Andreas D. Zuberbühler,*[,†] and Kenneth D. Karlin*[,‡]

Contribution from the Institute of Inorganic Chemistry, University of Basel, CH-4056 Basel, Switzerland, and Department of Chemistry, State University of New York (SUNY) at Albany, Albany, New York 12222. Received October 15, 1987

Abstract: The kinetics and mechanism of the hydroxylation by H_2O_2 of a dicopper(II) complex $\{Cu_2(L-H)\}^{4+}$ (**5**) to the phenoxo and hydroxo doubly bridged product $\{Cu_2(L-O)(OH)\}^{2+}$ (**3**) are reported. In 50% $H_2O/N,N$-dimethylformamide the reaction is second order in complex, first order in H_2O_2, and inversely first order in $[H^+]$. The complete rate law is given by

$$v = k[\{Cu_2(L-H)\}^{4+}]^2[H_2O_2]/([H^+](1 + K[\{Cu_2(L-H)\}^{4+}]))$$

$$k = 0.4 \ M^{-1} \ s^{-1} \qquad K = 4500 \ M^{-1}$$

The absence of a deuterium effect with $\{Cu_2(L-D)\}^{4+}$ in the place of $\{Cu_2(L-H)\}^{4+}$ eliminates hydrogen abstraction as the rate-limiting step and points to an attack by a reactive and probably electrophilic hydroxylating agent. The second-order dependence in complex **5** and the pH dependence are explained by the formation of a hydroperoxide intermediate, $\{Cu_2(L-H)(OOH)\}^{3+}$ (**6**). The intermediate is subsequently transformed into **3** under the influence of a second molecule of **5** which acts as a Lewis acid and promotes O–O bond rupture in the hydroperoxide complex.

The interaction and subsequent reactivity of dioxygen (O_2) with copper ions is of great interest due to the importance and prominence of O_2-binding and/or activating proteins in biological systems and the utility of copper compounds in oxidative synthetic reactions.[1–4]

Hemocyanins (Hc's) bind and transport O_2,[5–7] and we have recently described several types of synthetic dinucleating ligand systems where the dicopper(I) complexes are able to bind O_2 and CO reversibly at low temperatures in dichloromethane.[8,9]

We have also described a synthetic system where O_2 activation occurs, in which an aromatic ring, which is part of a dinucleating ligand, is hydroxylated.[10] Here, the dinucleating ligand, L-H (**1**), (PY = 2-pyridyl), in which two tridentate bis[2-(2-
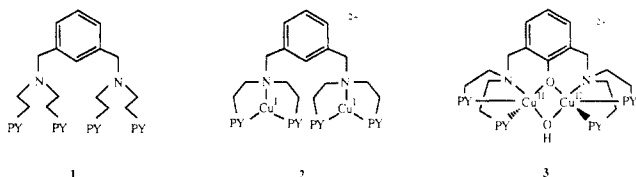
pyridyl)ethyl]amine units are connected by a m-xylyl group, is employed. The three-coordinate dinuclear copper(I) complex, $\{Cu_2(L-H)\}^{2+}$ (**2**), reacts with dioxygen, resulting in the oxygenation of the ligand and concomitant formation of the phenoxo- and hydroxo-bridged dinuclear Cu(II) complex, $\{Cu_2(L-O)(OH)\}^{2+}$ (**3**). The free phenol **4** can be isolated by removal of the copper
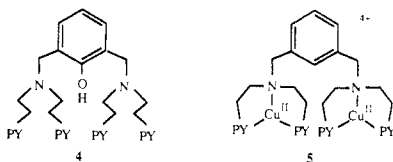
ions from **3** using a base extraction procedure.[10] The hydroxylation reaction, $2 + O_2 \rightarrow 3$, is analogous to the reactions mediated by the copper monooxygenases[7,11–15] such as tyrosinase[7,11–13] and dopamine β-hydroxylase[11,14] since labeling studies on the enzymes and this model system show that one atom of O_2 is incorporated

into the organic substrate and the stoichiometry of the reaction is $Cu:O_2 = 2:1$.

We have already presented some evidence for the intermediacy of a peroxodicopper(II) complex in the hydroxylation reaction, $2 + O_2 \rightarrow 3$. When a 2-fluoro substituted m-xylyl ligand is used

(1) Gampp, H.; Zuberbühler, A. D. *Met. Ions Biol. Syst.* **1981,** *12,* 133–190.

(2) Sheldon, R. A.; Kochi, J. K. *Metal-Catalyzed Oxidation of Organic Compounds;* Academic Press: New York, 1981.

(3) (a) Karlin, K. D.; Gultneh, Y. *J. Chem. Educ.* **1985,** *62 (11),* 983–990. (b) Karlin, K. D.; Gultneh, Y. *Prog. Inorg. Chem.* **1987,** *35,* 219–327.

(4) (a) *Biological & Inorganic Copper Chemistry;* Karlin, K. D., Zubieta, J., Eds.; Adenine Press: Guilderland, NY, 1986; Vol. 1 and 2. (b) *Copper Coordination Chemistry: Biochemical & Inorganic Perspectives;* Karlin, K. D., Zubieta, J., Eds.; Adenine Press: Guilderland, NY, 1983.

(5) (a) Solomon, E. I. *Metal Ions in Biology;* Spiro, T. G., Ed.; Wiley-Interscience: New York, 1981; Vol. 3, pp 41–108. (b) Solomon, E. I.; Penfield, K. W.; Wilcox, D. E. *Struct. Bonding (Berlin)* **1983,** *53,* 1–57.

(6) Lontie, R.; Witters, R. *Met. Ions Biol. Syst.* **1981,** *13,* 229–258.

(7) Solomon, E. I. In *Copper Coordination Chemistry: Biochemical & Inorganic Perspectives;* Karlin, K. D., Zubieta, J., Eds.; Adenine Press: Guilderland, NY, 1983; pp 1–22.

(8) (a) Karlin, K. D.; Cruse, R. W.; Gultneh, Y.; Farooq, A.; Hayes, J. C.; Zubieta, J. *J. Am. Chem. Soc.* **1987,** *109,* 2668–2679. (b) Blackburn, N. J.; Strange, R. W.; Cruse, R. W.; Karlin, K. D. *J. Am. Chem. Soc.* **1987,** *109,* 1235–1237. (c) Pate, J. E.; Cruse, R. W.; Karlin, K. D.; Solomon, E. I. *J. Am. Chem. Soc.* **1987,** *109,* 2624–2630. (d) Karlin, K. D.; Haka, M. S.; Cruse, R. W.; Gultneh, Y. *J. Am. Chem. Soc.* **1985,** *107,* 5828–5829. (e) Karlin, K. D.; Haka, M. S.; Cruse, R. W.; Meyer, G. J.; Farooq, A.; Gultneh, Y.; Hayes, J. C.; Zubieta, J. *J. Am. Chem. Soc.* **1988,** *110,* 1196–1207.

(9) A system for which an X-ray crystal structure of the dioxygen/copper complex is reported is given in: Jacobson, R. R.; Tyeklar, Z.; Farooq, A.; Karlin, K. D.; Liu, S.; Zubieta, J. *J. Am. Chem. Soc.* **1988,** *110,* 3690–3692.

(10) Karlin, K. D.; Gultneh, Y.; Hayes, J. C.; Cruse, R. W.; McKown, J. W.; Hutchinson, J. P.; Zubieta, J. *J. Am. Chem. Soc.* **1984,** *106,* 2121–2128.

(11) Lerch, K. *Met. Ions. Biol. Syst.* **1981,** *13,* 143–186.

(12) Robb, D. A. *Copper Proteins and Copper Enzymes;* Lontie, R., Ed.; CRC: Boca Raton, FL, 1984; Vol. 2, pp 207–241.

(13) (a) Wilcox, D. E.; Porras, A. G.; Hwang, Y. T.; Lerch, K.; Winkler, M. E.; Solomon, E. I. *J. Am. Chem. Soc.* **1985,** *107,* 4015–4027. (b) Sugimoto, H.; Spencer, L.; Sawyer, D. T. *Proc. Natl. Acad. Sci. U.S.A.* **1987,** *84,* 1731–1733.

(14) Villafranca, J. J. *Metal Ions in Biology;* Spiro, T. G., Ed.; Wiley-Interscience: New York, 1981; Vol. 3, pp 263–290.

(15) A copper-containing phenylalanine hydroxylase has been recently described: Pember, S. O.; Villafranca, J. J.; Benkovic, S. J. *Biochemistry* **1986,** *25,* 6611–6619.

†University of Basel.

‡State University of New York (SUNY) at Albany.

Copper-Mediated Hydroxylation of an Arene

J. Am. Chem. Soc., Vol. 110, No. 15, 1988 5021

(i.e., L-F, in which a fluorine atom is placed in the position that is hydroxylated), little or no hydroxylation occurs in the reaction of $\{Cu_2(L\text{-}F)\}^{2+}$ with O_2. At -80 °C a spectrum of the adduct identified as $\{Cu_2(L\text{-}F)(O_2)\}^{2+}$, a peroxo dicopper(II) complex,[8d,e] is observed.[16]

A peroxo dicopper(II) intermediate was also implicated in experiments where a dicopper(II) species, formed by the reaction of $2CuY_2$ ($Y = BF_4^-$, NO_3^-) with L-H in aqueous N,N-dimethylformamide (DMF), reacted with H_2O_2 to again produce near quantitative yields of $\{Cu_2(L\text{-}O)(OH)\}^{2+}$ (3).[17] Here we expand upon this latter observation, and a detailed kinetic/mechanistic study of the reaction of $\{Cu_2(L\text{-}H)\}^{4+}$ (5) with H_2O_2 is reported.

Experimental Section

Kinetics. Most kinetic measurements, including those involving the effects of various buffers and buffer concentrations were followed at 380 nm on a Varian Techtron UV–vis spectrophotometer (Model 635) by using stopped-flow techniques. The data (500 absorbances per curve) were read automatically by a Dolphin microprocessor and stored on a cassette by using a Sanyo tape recorder (Microcorder ZE 601). The data were then transferred to an Apple IIe computer for numerical analysis and curve-fitting. Initial reaction rates, $v_o = -d[\{Cu_2(L\text{-}H)\}^{4+}]/dt$ for the conversion of $\{Cu_2(L\text{-}H)\}^{4+}$ to $\{Cu_2(L\text{-}O)(OH)\}^{2+}$ were calculated by a special procedure after fitting the initial parts of the reaction to a double exponential decay with a background term.[18] Final calculations and plots were done on a Hewlett-Packard 9835A computer by using a general nonlinear least-squares program, CURFIT. The uncertainties of all parameters are indicated by twice their calculated standard errors, 2σ.

A multiwavelength stopped-flow kinetic technique was used to observe the transition toward a first-order dependence in complex at high initial complex concentrations and to check for the formation of any intermediates. A Canterbury SF-3A stopped flow system, coupled to a Zeiss MCS 512 VIS diode array detector and a Hewlett-Packard 300 computer, was used for data collection. The data were analyzed by the computer with the program KINFIT.[19] All experiments were done in 50% DMF/H_2O at 25.0 °C and with an ionic strength of 0.1 (LiClO$_4$).

The rapid initial interaction of H_2O_2 with the complex was followed spectrophotometrically at 340 nm on a Durrum D110 stopped-flow system. Data were automatically recorded on a Datalab DL901 transient recorder and transferred to the Apple IIe computer for analysis as above.

Reagents. Hydrogen peroxide (30%, Perhydrol, Merck), collidine (2,4,6-trimethylpyridine, p.a., Merck), perchloric acid (60%, Merck), and lithium perchlorate (purum, Fluka) were used without further purification. The solvent mixture was prepared by dilution of 1 vol of prepurified DMF to 2 vol with distilled water (22 °C). Equal volumes of the separate solutions of complex and H_2O_2 were prepared by using equal volumes of a buffer stock to ensure a well-defined pH and a maximum degree of homogeneity in the mixed solutions in the stopped-flow experiment. This was critical with the particular system due to the high viscosity of the solvent and to the large differences in the indices of refraction between buffered and unbuffered solutions. A noticeable increase in noise was observed in the measurements when the proportion of buffer to solvent was not identical in the two solutions mixed in the stopped-flow experiment.

Because of the instability of 5 in H_2O, organic solvents had to be used. For pH control, a mixed aqueous/organic solvent was preferable. Methanol, dimethyl sulfoxide, and DMF were tested with various amounts of H_2O. 50% DMF/H_2O was selected on the basis of reproducibility and completeness of the reaction. The quantitative conversion of 5 into 3 was checked by comparison of the product with an authentic sample.[10,17]

The acidities of all solutions were determined with a glass electrode which was calibrated in the usual way by using standard buffers. Proton activities were calculated directly from the pH readings and used for the values of $[H^+]$ throughout. Linearity and correct slope of the electrode were checked with buffers of different acid-to-base ratios.

DMF had to be purified prior to use to remove any contamination by dimethylamine which might coordinate to the complex and interfere with

the kinetics. This was accomplished by addition of water and toluene (DMF/water/toluene, 1000 mL/40 mL/12 mL), which were removed by azeotropic distillation from an oil bath (150 °C) until the distillate came off at 110 °C (ca. 100 mL of fraction). Small amounts of toluene remaining in the DMF did not interfere with the kinetics. The DMF was then distilled from an oil bath at 85 °C under reduced pressure (2400 Pa, bp 45 °C) in the absence of light. The first 70-mL fraction was discarded. The DMF and all of its subsequent solutions were then used fresh and minimally exposed to light. L-H was obtained as described.[10]

2-Deuterio-m-xylene.[21] 2-Bromo-m-xylene (Aldrich, 25 g, 0.135 mol) was added dropwise to a stirred suspension of magnesium chips (6.56 g, 0.27 mol) in dry THF (100 mL). The reaction mixture was stirred for 2 more h and then quenched with D_2O (Aldrich, 7 mL, 0.405 mol). After addition of 100 mL of H_2O the crude compound was extracted with 300 mL of ether, the solvent was removed at atmospheric pressure, and 2-deuterio-m-xylene was purified by distillation: 11.76 g (81%), bp 130–135 °C; ^{1}H NMR (CDCl$_3$) 2.2 (6 H, s), 6.6–7.1 (3 H, m).
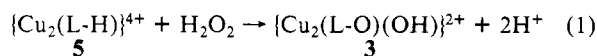
1,3-Bis(bromomethyl)-2-deuteriobenzene.[21] 2-Deuterio-m-xylene (11.76 g, 0.1097 mol) were refluxed in 200 mL of CCl$_4$ with N-bromosuccinimide (39 g, 0.219 mol) in the presence of a trace of dibenzoyl peroxide. After cooling, the mixture was filtered, and the solvent was removed in vacuo. Recrystallization at 0 °C from CCl$_4$ (20 mL) and hexane (80 mL) gave 8.71 g (30%) of crystalline product: ^{1}H NMR (CDCl$_3$) 4.4 (4 H, s), 7.1 (3 H, s).

L-D. The deuteriated ligand, L-D, was obtained from 1,3-bis(bromomethyl)-2-deuteriobenzene (3 g, 11 mmol) and bis(2-(2-pyridyl)-ethyl)amine (5.14 g, 22 mmol) in ethyl acetate (150 mL) as described for L-H,[10] giving 3.64 g (58%) of pure deuterio compound: ^{1}H NMR (CDCl$_3$) 2.9 (16 H, s), 3.6 (4 H, s), 6.8–7.5 (15 H, m), 8.3 (4 H (py-6), d br).

$\{Cu(L\text{-}H)(NO_3)_4\}\cdot 4H_2O$ (amounts given in brackets) and $\{Cu_2(L\text{-}D)\text{-}(NO_3)_4\}\cdot 4H_2O$[21] were synthesized by the reaction of 2 mol-equiv of Cu(NO$_3$)$_2\cdot$3H$_2$O (0.97 g, 4.02 mmol) with L-H (1.12 g, 2.01 mmol) or L-D in methanol (50 mL), stirred for 30 min, precipitated with isopropyl alcohol (i-PrOH, 150 mL), and left standing for 2 days at 0 °C. Blue crystals were filtered off, washed with ethanol, dried in air, and recrystallized from MeOH/i-PrOH (1:1) giving 1.51 g (75%) pure product.[20]

Results and Discussion

The overall reaction of 5 to yield 3 (eq 1) involves the liberation of two protons, necessitating the use of buffers for pH control.

$$\{Cu_2(L\text{-}H)\}^{4+} + H_2O_2 \rightarrow \{Cu_2(L\text{-}O)(OH)\}^{2+} + 2H^+ \quad (1)$$
$$\qquad\quad \mathbf{5} \qquad\qquad\qquad\qquad\qquad \mathbf{3}$$

The following buffers were tested in preliminary experiments: 2,6-lutidine-4-sulfonate, $H_2PO_4^-/HPO_4^{2-}$, 2,4,6-collidine (COLL), and $H_3BO_3/B(OH)_4^-$. None of the buffers were completely free of interaction with reaction 1, but the collidine buffer proved by far the most satisfactory with respect to influence on rates and spectra as well as to the completeness of the hydroxylation. The lutidine and phosphate buffers strongly inhibit the reaction, probably because of their low apparent pK^H (4.5 and 5.3, respectively) in 50% DMF/H_2O. With borate ($pK^H = 11.0$) both the starting and final spectra differed strongly from buffer-free mixtures.[22] All subsequent kinetics experiments were done with COLL buffer, limiting the accessible pH range to 6–7. With this buffer, a twofold excess of H_2O_2 was sufficient to ensure complete and stoichiometric hydroxylation. On the basis of diode-array stopped flow experiments (vide infra) the bulk of complex remains in the 2+ state throughout the reaction. Formation of Cu(I), e.g., through reduction by H_2O_2, was specifically excluded by running identical experiments in the presence of air or oxygen and under completely anaerobic conditions: O_2 has no influence on either rate or products of the reaction.

Effect of H_2O_2. The influence of H_2O_2 on the rate was studied for $[\{Cu_2(L\text{-}H)\}^{4+}] = 10^{-4}$ M in a 1:1 COLL buffer with a large

(16) Karlin, K. D.; Cruse, R. W.; Haka, M. S.; Gultneh, Y.; Cohen, B. I. *Inorg. Chim. Acta* **1986**, *125*, L43–L44.

(17) Blackburn, N. J.; Karlin, K. D.; Concannon, M.; Hayes, J. C.; Gultneh, Y.; Zubieta, J. *J. Chem. Soc., Chem. Commun.* **1984**, 939–940.

(18) Gampp, H.; Maeder, M.; Zuberbühler, A. D. *Talanta* **1980**, *27*, 1037–1045.

(19) Meyer, C. J.; Kaden, T. A.; Siegfried, L.; Zuberbühler, A. D., manuscript in preparation.

(20) Farooq, A.; Karlin, K. D., unpublished results. Anal. Calcd for C$_{36}$H$_{48}$Cu$_2$N$_{10}$O$_{16}$: C, 43.07; H, 4.79; N, 13.96. Found: C, 43.54; H, 4.33; N, 13.94. VIS spectrum: $\lambda_{max} = 630$ nm, $\epsilon_{max} = 310$ M^{-1} cm^{-1}.

(21) Cohen, B. I. Ph.D. Dissertation, State University of New York at Albany, 1987.

(22) Potentiometric titration reveals that above pH 7.5 up to four protons are liberated from $\{Cu_2(L\text{-}H)\}^{4+}$. Starting material and possibly end product would therefore be different around pH 11 of borate buffers. In addition, borate might interfere directly with 5 and 3.

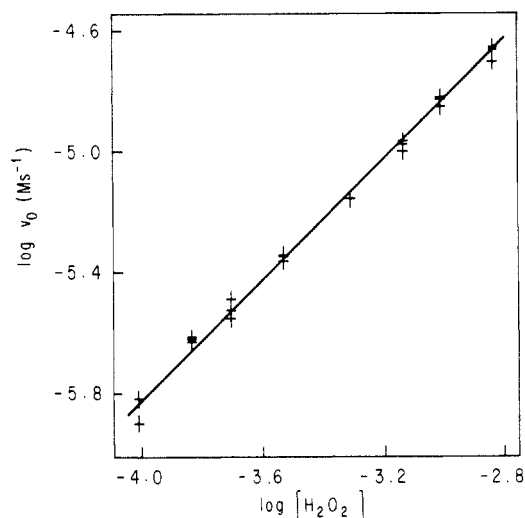**Figure 1.** Initial rate of hydroxylation, v_0 as a function of $[H_2O_2]$: $[\{Cu_2(L-H)\}^{4+}] = 10^{-4}$ M, $[COLL] = 0.05$ M, $[HClO_4] = 0.025$ M, pH = 6.61, (+) experimental points, (—) best line with slope 1.
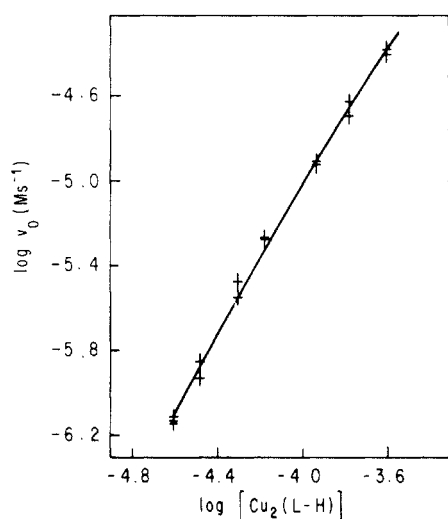

Figure 2. Rate of hydroxylation as a function of $[\{Cu_2(L-H)\}^{4+}]$: $[H_2O_2]$ = 10^{-3} M, $[COLL] = 0.05$ M, $[HClO_4] = 0.025$ M, pH = 6.58, (+) experimental points, (—) calculated with eq 3.

excess of H_2O_2. As shown in Figure 1, a slope of unity is obtained[23a] for a plot of log v_0 against log $[H_2O_2]$, establishing a strict first-order dependence in H_2O_2.

$$v = -d[\{Cu_2(L-H)\}^{4+}]/dt = +d[\{Cu_2(L-O)(OH)\}^{2+}/dt \qquad (2)$$

Effect of $\{Cu_2(L-H)\}^{4+}$. The dependence of v_0 on the complex concentration was studied for $[H_2O_2] = 10^{-3}$ M in 1:1 (pH 6.58) COLL buffer. A second-order dependence was observed[23b] with some deviation at higher complex concentrations, as shown in Figure 2. A more complete dependence on $[\{Cu_2(L-H)\}^{4+}]$, consistent with the data at all concentrations considered, is given by

$$v = k_{obsd}[\{Cu_2(L-H)\}^{4+}]^2/(1 + K[\{Cu_2(L-H)\}^{4+}]) \qquad (3)$$

$$k_{obsd} = 1420 \pm 130 \text{ M}^{-1} \text{ s}^{-1} \qquad K = 4500 \pm 1400 \text{ M}^{-1}$$

(23) (a) For the H_2O_2 dependence the linear least-squares estimate for the slope is 0.98 ± 0.03(2σ). No deviation from unity is thus implied according to statistical criteria. (b) Using only results with $[\{Cu_2(L-H)\}^{4+}] < 10^{-4}$ M (cf. Figure 2), the best line has a slope of 2.03 ± 0.12(2σ). Again, this deviation is not significant in relation to the ideal value of 2. (c) Best slope for pH dependence = 1.09 ± 0.13(2σ); deviation from unity is not significant.

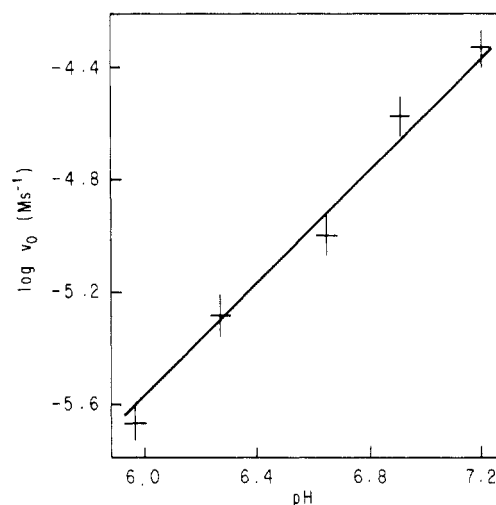**Figure 3.** pH dependence of hydroxylation: $[\{Cu_2(L-H)\}^{4+}] = 10^{-4}$ M, $[H_2O_2] = 10^{-3}$ M, (+) calculated from buffer dependences extrapolated to zero buffer concentration, $[COLL]/[COLL\cdot HClO_4] = 1:4, 1:2, 1:1, 2:1,$ and 4:1, (—) best line with slope 1.

Effect of pH. When the effect of pH was studied directly at buffer concentrations around 0.05 M, apparent slopes around 1.3–1.5 were obtained for plots of log v_0 against pH in experiments with different concentrations of complex and hydrogen peroxide. Such slopes do not correspond reasonably well with expected rate laws and mechanisms, and they were subsequently traced to small but significant effects of the COLL buffer. In order to separate buffer and pH effects, the following procedure was adapted: Buffer dependences were studied for five series of measurements with $[COLL]/[COLL\cdot HCLO_4]$ ratios of 4:1, 2:1, 1:1, 1:2, and 1:4. The total $[COLL]$ was varied between 0.0025 and 0.040 M within each series. Depending on the ratio of protonated and deprotonated COLL, an accelerating or inhibiting effect of the buffer was observed. Obtaining information with respect to general acid or base catalysis from these buffer dependences is unfortunately precluded by the multitude of possible effects such as direct competition with H_2O_2 for binding to copper, change of the reactivity of $\{Cu_2(L-H)\}^{4+}$ by additional coordination, or interaction with intermediates.

The results of the individual series were therefore extrapolated to zero buffer concentration. As is shown in Figure 3, these extrapolated reaction rates are proportional to $[H^+]^{-1}$, i.e., the slope of log v_0 against pH is unity.[23c] The complete rate law is thus given by eq 4,

$$v = k[\{Cu_2(L-H)\}^{4+}]^2[H_2O_2]/([H^+](1 + K[\{Cu_2(L-H)\}^{4+}])) \qquad (4)$$

$$k = 0.40 \pm 0.10(2\sigma) \text{ M}^{-1} \text{ s}^{-1} \qquad K = 4500 \pm 1400(2\sigma) \text{ M}^{-1}$$

where k is calculated from the data presented in Figure 3, extrapolated to zero buffer concentration. The results of the H_2O_2 and complex dependences are not directly compatible since they were obtained at relatively high buffer concentrations. Nevertheless, rate constants corresponding to k can be calculated. The results are 0.62 ± 0.08 M^{-1} s^{-1} and 0.38 + 0.04 M^{-1} s^{-1} for the data of Figures 1 and 2, respectively. As expected from the small influence of COLL, the values are rather close to the buffer-independent rate constant. Of course, buffer-independent complex and H_2O_2 dependences could, in principle, also be obtained. This would, however, require the determination of each data point presented in Figures 1 and 2 from a complete buffer dependence for the given condition. As this procedure would be tedious and add little to the mechanistic understanding of the system, such experiments were not undertaken.

Stopped-Flow Experiments. The data discussed so far were collected on the Varian Techtron spectrophotometer. The reactions had relaxation times in the range of seconds to minutes, and the data were analyzed by using the method of initial rates in order to avoid any interference of side products or secondary reactions.

Copper-Mediated Hydroxylation of an Arene

J. Am. Chem. Soc., Vol. 110, No. 15, 1988 5023

In addition, some experiments were done on a Durrum (single wavelength) and on a Canterbury (diode array) stopped-flow instrument. With the former, a very rapid initial reaction could be observed in the high-energy region (300–340 nm) of the spectrum. This reaction could, however, only be followed at high dilution: $[\{Cu_2(L\text{-}H)\}^{4+}] < 10^{-4}$ M, $[H_2O_2] < 2 \cdot 10^{-4}$ M. The reaction was observable consistently, but the actual rates and absorbance changes were rather irreproducible. On the basis of a second-order model $v = k_2[\{Cu_2(L\text{-}H)\}^{4+}][H_2O_2]$, k_2 could be estimated to be about 10^4 M^{-1} s^{-1}, but since the quality of the data and the range of accessible concentrations was insufficient for the establishment of a rate law, this matter was not investigated in more detail.

Complete spectra between 360 and 750 nm were collected with the diode array stopped-flow setup. In this range, the rapid initial reaction does not interfere, and only two absorbing species were present according to the abstract factor analysis[24] built into the program KINFIT.[19] Therefore, a significant buildup of absorbing intermediates may be excluded. Experiments were done both with 5 and its deuteriated analogue, $\{Cu_2(L\text{-}D)\}^{4+}$. Spectra were followed up to 98% completion of the reaction. The whole set of data was subjected to numerical analysis in a manner described in detail for spectrophotometric equilibrium studies[25] after substituting the appropriate kinetics models. Relatively high concentrations in complex (0.15 mM) and H_2O_2 (3.23 mM) were used in a 25 mM COLL buffer of pH 6.57. Under such conditions, a marked deviation from second-order dependence in $[\{Cu_2(L\text{-}H)\}^{4+}]$ would be expected from the initial rates experiments, cf. Figure 2. In fact, simple kinetics models such as third- or rather pseudo-second-order kinetics were not appropriate to describe the data. Since H_2O_2 was present in a 20-fold excess, its concentration could be treated as constant throughout the reaction. Excellent fits with consistent rate constants and spectra, independent of the total reaction time considered, were obtained by directly applying eq 3 which had been derived from initial rates, however. The following results were obtained for the complexes with normal (L-H) and deuteriated (L-D) ligand: $k_{obsd}(L\text{-}H)/k_{obsd}(L\text{-}D) = 1.08 \pm 0.16$; $K(L\text{-}H)/K(L\text{-}D) = 1.14 \pm 0.26$.

Three conclusions may be drawn from these multiwavelength stopped-flow experiments: First, no deuterium effect is observed in the hydroxylation of the aromatic ring, 5 → 3. Second, the general rate law 4 deduced from initial rates is fully supported by the complete analysis of multiwavelength spectra, giving additional weight to the otherwise less well-defined second term described by K. Third, no intermediates are observed spectrophotometrically on the time scale employed for the complex, hydrogen peroxide, and pH dependences.
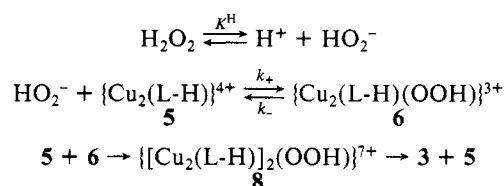
Mechanism. The general rate law 4 has interesting and perhaps surprising implications. The second-order dependence in $[\{Cu_2(L\text{-}H)\}^{4+}]$ has to be explained with a transition state containing two molecules of 5, i.e., a total of four copper ions. This is somewhat unexpected since dinuclear copper centers as are present in 5 are thought to be generally sufficient to form reactive copper peroxides both in biological systems such as tyrosinase as well as in model reactions.[1-4] In fact, purely intramolecular electron transfer within a dinuclear peroxo complex, $\{Cu_2(L\text{-}H)(O_2)\}^{2+}$ (7),


6   7
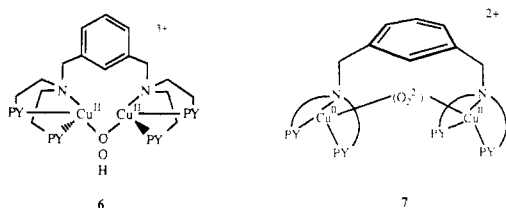
has been postulated for the closely related reaction, 2 → 3, starting from Cu(I) and O_2.[9,10,16,17,26] In addition, a peroxo complex 7

is excluded from the mechanistic scheme by the result of the pH dependence. Since neither $\{Cu_2(L\text{-}H)\}^{4+}$ nor H_2O_2 are significantly deprotonated in the pH-range studied and since no intermediate builds up in significant amounts during the reaction, hydrogen peroxide must be bound in the form of the monoanion, HO_2^-, in the reactive species. The complete copper dependence (eq 3) could in principle be explained by the formation of a hydroperoxide $\{Cu_2(L\text{-}H)(OOH)\}^{3+}$ (6) in a rapid equilibrium reaction followed by reaction with a second $\{Cu_2(L\text{-}H)\}^{4+}$ or by steady-state kinetics based on 6. However, the first possibility is excluded by the fact that no leveling off is found with respect to H_2O_2 and that no such intermediate is observed in the diode-array stopped-flow experiments.[27]

The absence of a significant deuterium effect suggests that the actual attack on the arene ring takes place after the rate-determining step of the overall reaction. It is thus induced by a highly reactive, probably electrophilic[13] intermediate. A minimum mechanistic scheme for the H_2O_2-induced hydroxylation, 5 → 3, is

$$H_2O_2 \xrightleftharpoons{K^H} H^+ + HO_2^-$$

$$HO_2^- + \underset{5}{\{Cu_2(L\text{-}H)\}^{4+}} \xrightleftharpoons[k_-]{k_+} \underset{6}{\{Cu_2(L\text{-}H)(OOH)\}^{3+}}$$

$$5 + 6 \rightarrow \underset{8}{\{[Cu_2(L\text{-}H)]_2(OOH)\}^{7+}} \rightarrow 3 + 5$$

This scheme is in complete agreement with the experimental rate law 4. Since, however, the deprotonation constant K^H of H_2O_2 is unknown for the reaction medium, no numerical values may be assigned to the individual rate constants. 6 is an unstable intermediate. Its structure is unknown, but a 1,1-binding of HO_2^- with a terminal OH group looks most attractive for both thermodynamic and kinetic reasons. Precedence for the formation of such hydroperoxides is found[28] in the ability of 3 to bind H_2O_2 efficiently by displacement of the bridging OH^-.

$$3 + H_2O_2 \rightarrow \{Cu_2(L\text{-}O)(OOH)\}^{2+} + H_2O$$
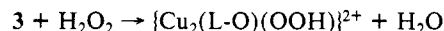
Besides its composition, $\{[Cu_2L\text{-}H]_2(OOH)\}^{7+}$, very little is known about the tetracopper species 8. It may equally represent

8
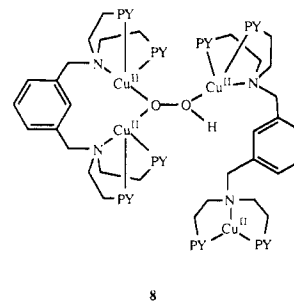
another unstable intermediate or a mere transition state. As it is difficult to assign a convincing role to the second molecule of 5 with respect to the actual electron transfer, we propose that this species is needed as a Lewis acid rather than as a direct mediator of electron flow. Complex 5 can be easily envisaged to bind to the terminal OH group of the hydroperoxide, strongly promoting its potential as a leaving group. The remaining oxene-like oxygen atom would of course be a highly reactive electrophile, in con-

(24) Malinowski, E. K.; Howery, D. G. Wiley-Interscience: New York, 1980.

(25) (a) Gampp, H.; Maeder, M.; Meyer, C. J.; Zuberbühler, A. D. *Talanta* **1985**, *32*, 95–101. (b) Gampp, H.; Maeder, M.; Meyer, C. J.; Zuberbühler, A. D. *Talanta* **1985**, *32*, 257–264.

(26) The mechanistic scheme proposed in ref 9 and 10 is fully supported by a detailed kinetic study of reaction 2 → 3 in dichloromethane (Cruse, R. W.; Kaderli, S.; Karlin, K. D.; Zuberbühler, A. D., manuscript submitted) where no indication of second-order complex dependence is found.

(27) The very fast initial absorbance changes around 340 nm observed on the Durrum instrument are no contradiction to this statement. Nothing is known about their nature and possible relation to the hydroxylation reaction, and no evidence is available to conclude that substantial amounts of the complexes are involved.

(28) (a) Karlin, K. D.; Cruse, R. W.; Gultneh, Y. *J. Chem. Soc., Chem. Commun.* **1987**, 599–600. (b) Karlin, K. D.; Ghosh, P.; Cruse, R. W.; Farooq, A.; Gultneh, Y.; Jacobson, R. R.; Blackburn, N. J.; Strange, R. W.; Zubieta, J. *J. Am. Chem. Soc.*, in press.

cordance with the earlier suggestions of an electrophilic species derived from peroxodicopper(II) in tyrosinase[13a] and the recently described Fe(III) mediated electrophilic activation of hydrogen peroxide toward oxygenation of organic substrates.[13b] No unique assignment of oxidation states is possible for the time between O–O bond rupture and oxygenation. No free oxygen atom is expected to form in view of the 100% selectivity of the reaction, and coordination of O to $2Cu^{2+}$ would be equivalent to O^{2-} coordinating to $2Cu^{3+}$ or even to one Cu^{4+} as CuO^{2+}. Whether splitting off OH^- and oxygenation of the aromatic ring are in fact two sequential steps or one synchronous reaction may remain experimentally ambiguous due to the high reactivity of all species involved.

Experiments presently in progress[26] will shed further light on the relation of the H_2O_2 induced reaction presented in this paper with the analogous reaction, **2 → 3**, starting from Cu(I) and O_2.

Isomerization in Metal–Metal Bonded M_2L_{10} Systems Involving Cis and Trans Sets of Bis(diphenylphosphino)methane Ligands

Ann R. Cutler, Daniel R. Derringer, Phillip E. Fanwick, and Richard A. Walton*

Contribution from the Department of Chemistry, Purdue University, West Lafayette, Indiana 47907. Received November 9, 1987

Abstract: The reactions of the dirhenium(III) complexes $Re_2(O_2CR)_4X_2$ (R = CH_3, C_2H_5, C_6H_5; X = Cl, Br), $Re_2(O_2CR)_2X_4L_2$ (R = CH_3, C_2H_5; X = Cl, Br; L = H_2O, 4-methylpyridine, DMF, DMSO), and $(n\text{-Bu}_4N)_2Re_2X_8$ (X = Cl, Br) with $Ph_2PCH_2PPh_2$ (abbreviated dppm) or, in the case of $(n\text{-Bu}_4N)_2Re_2X_8$, $Ph_2CH_2PPh_2$/acetate mixtures affords the reduced complexes Re_2-$(O_2CR)X_4(dppm)_2$ and cis- and trans-$Re_2(O_2CR)_2X_2(dppm)_2$ depending upon the choice of reaction conditions. The thermolysis of $Re_2(O_2CR)X_4(dppm)_2$ provides a high yield synthetic route to $Re_2X_4(dppm)_2$ (X = Cl, Br), a procedure that can be adapted to produce $Re_2I_4(dppm)_2$ directly from $Re_2(O_2CCH_3)_2I_4 \cdot nH_2O$. The cis and trans isomers of the triply bonded dirhenium(II) compounds $Re_2(O_2CR)_2X_2(dppm)_2$ can be oxidized to paramagnetic cis-$[Re_2(O_2CR)_2X_2(dppm)_2]PF_6$ and trans-$[Re_2$-$(O_2CR)_2X_2(dppm)_2]PF_6$ by $[(\eta^5\text{-}C_5H_5)_2Fe]PF_6$ and $(C_7H_7)PF_6$, respectively. The structures of representative members of these groups of new complexes have been established by X-ray crystallography, viz., $Re_2(O_2CCH_3)Cl_4(dppm)_2 \cdot 2(CH_3)_2CO$ (1), cis-$Re_2(O_2CCH_3)_2Cl_2(dppm)_2$ (2), and trans-$[Re_2(O_2CCH_3)_2Cl_2(dppm)_2]PF_6 \cdot CH_2Cl_2$ (3). Complex 1 crystallizes in the monoclinic space group $P2_1/c$ with the following unit cell dimensions: $a = 12.720$ (2) Å, $b = 35.593$ (5) Å, $c = 9.405$ (2) Å, $\beta = 104.36$ (1)°, $V = 5610$ (3) Å^3, and $Z = 4$. The structure was refined to $R = 0.036$ and $R_w = 0.055$ for 5822 data with $F^2 > 3.0\sigma(F^2)$. The structure contains symmetrically bridging acetate and dppm ligands and is based upon an eclipsed M_2L_{10} geometry, with two axial and two equatorial Re–Cl bonds. The Re–Re distance is 2.300 (1) Å, which is in accord with the presence of a Re–Re bond of order 3.5. The unit cell dimensions for complexes 2 and 3, which crystallize in the monoclinic space groups $P2_1/c$ and $C2/c$, respectively, are as follows: for **2**, $a = 14.634$ (6) Å, $b = 15.190$ (5) Å, $c = 24.281$ (6) Å, $\beta = 107.24$ (3)°, $V = 5155$ (6) Å^3, and $Z = 4$; for **3**, $a = 22.853$ (5) Å, $b = 18.712$ (3) Å, $c = 14.236$ (4) Å, $\beta = 107.48$ (2)°, $V = 5807$ (4) Å^3, and $Z = 4$. The structure of **2** was refined to $R = 0.045$ and $R_w = 0.061$ for 4468 data with $F^2 > 3.0\sigma(F^2)$, whereas for **3** the refinement gave $R = 0.034$ and $R_w = 0.049$ for 2936 data with $F^2 > 3.0\sigma(F^2)$. Both complexes contain pairs of bridging acetate and dppm ligands and axial Re–Cl bonds. In **2** the pairs of acetate (and dppm) ligands are cis to one another, while they assume a trans disposition in **3**. The Re–Re distance is 2.315 (1) Å in **2** and 2.275 (1) Å in **3**.

Complexes that contain pairs of metal atoms spanned by two bridging bidentate phosphine ligands of the type $R_2PCH_2PR_2$ constitute an important and extensive class of molecules that range from those that contain no metal–metal interactions to those in which the metal–metal bond order may be 1, 2, 3, or 4.[1–3] From the extensive body of data that has accumulated we are not aware of any reports that describe the isolation and characterization of isomers in which the $R_2PCH_2PR_2$ ligands span a metal–metal bond and are in cis and trans arrangements to one another. Upon examining the reactions of the dirhenium(III) carboxylates $Re_2(O_2CR)_4X_2$ and $Re_2(O_2CR)_2X_4L_2$ (R = alkyl or aryl; X = Cl or Br; L = monodentate neutral donor)[4,5] toward the ligand

$Ph_2PCH_2PPh_2$ (abbreviated dppm) we have discovered the existence of pairs of cis and trans isomers of stoichiometry Re_2-$(O_2CR)_2X_2(dppm)_2$. We now report the synthesis, properties, and structural characterization of this novel class of triply bonded dirhenium(II) complexes.

Experimental Section

Starting Materials. The compounds $(n\text{-Bu}_4N)_2Re_2X_8$ (X = Cl, Br, or I) were synthesized as described in the literature.[6–9] In the case of X = Cl or Br, these salts were converted into the bis-carboxylate complexes $Re_2(O_2CR)_2X_4L_2$ (R = CH_3 or C_2H_5; L = H_2O, 4-Mepy, DMF, or DMSO) with use of the published procedures.[10] The iodide complex

(1) Puddephatt, R. J. *Chem. Soc. Rev.* **1983**, 99 and references cited therein.

(2) Cotton, F. A. *Polyhedron* **1987**, 6, 667 and references cited therein.

(3) Price, A. C.; Walton, R. A. *Polyhedron* **1987**, 6, 729 and references cited therein.

(4) Cotton, F. A.; Walton, R. A. *Multiple Bonds Between Metal Atoms*; Wiley: New York, 1982, and references cited therein.

(5) Cotton, F. A.; Walton, R. A. *Struct. Bonding (Berlin)* **1985**, 62, 1 and references cited therein.

(6) Barder, T. J.; Walton, R. A. *Inorg. Chem.* **1982**, 21, 2510; *Inorg. Synth.* **1985**, 23, 116.

(7) Cotton, F. A.; Curtis, N. F.; Johnson, B. F. G.; Robinson, W. R. *Inorg. Chem.* **1965**, 4, 326.

(8) Glicksman, H. D.; Walton, R. A. *Inorg. Chem.* **1978**, 17, 3197.

(9) Preetz, W.; Rudzik, L. *Angew. Chem., Int. Ed. Engl.* **1979**, 18, 150.