Catalatic Activity of Metal Chelates and Mixed-Ligand Complexes in the Neutral pH Region. I. Copper–Imidazole[1]

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Abstract: The catalatic activity of the copper complexes of the monodentate ligand, imidazole (Im), has been investigated by means of a differential manometric technique. The kinetic data, obtained from the initial rates of O_2 evolution, are consistent with a mechanism involving principally a reaction between $Cu(Im)_2^{2+}$ and the HOO^- anion. The concentrations of the catalytically active species were calculated using a computer program after taking into account the formation of 26 complexed and uncomplexed species existing in dynamic equilibrium with each other in Cu–Im–H_2O_2 phosphate-buffered systems. Evidence is presented for the involvement of a cupric–cuprous couple in the reaction mechanism. It is surmised that the species having two nitrogens coordinated to copper provide the lowest energy path for the reduction of the cupric ion to the cuprous ion. This presumably facilitates the rupture of the O–O bond in $Im_2Cu(OOH)^+$ because of an increase in the O–M–O bond angle in the change from the cupric to the cuprous state.

The catalytic decomposition of H_2O_2 to oxygen and water, *i.e.*, *catalatic* reactions, by metal salts and complexes has been extensively studied.[2] Catalatic activity is usually associated with catalase,[3] a hemoprotein, and iron compounds and chelates.[2,4–6] The nonheme, oxygen-carrying copper protein, hemocyanin, also exhibits catalatic activity[7–9] as do copper salts and chelates.[10–14]

Few significant quantitative studies on catalatic reactions of copper complexes in the neutral pH region exist from which reaction mechanisms can be deduced. We are investigating catalatic systems involving metal chelates in the pH region of ~6–8 in sodium dihydrogen phosphate buffer, taking into account the formation of simple, mixed, and hydrolyzed species. The inherent complexity of these systems, particularly in the neutral pH region, is exemplified by the fact that, depending on the nature of the metal ion and ligand, 18 to 26 species exist in solution in dynamic equilibrium with each other, necessitating the use of a computer to calculate the equilibrium concentration of these species. In a preliminary communication,[15] we reported the results of a study on the catalatic activities of the copper chelate of a bidentate ligand, histamine (Hm), in which the principal catalytically active species was the 1:1 chelate, Cu(II)–Hm. This report, in which we employ a monodentate ligand, imidazole (Im), leads to the conclusion that the decomposition of hydrogen peroxide by copper complexes involves a redox reaction, and, therefore, one critical factor in determining the catalytic activity of a complex species is its redox potential. The kinetic data confirm our previous work[15] which indicated that the predominantly active species were those in which two nitrogens are coordinated to the copper ion.

Experimental Section

Apparatus and Procedure. The rates of decomposition of H_2O_2 were determined from manometric measurements of O_2 by the use of a differential syringe manometer.[16] The reproducibility of our readings was ±5%, and the absolute accuracy as determined by measurement of known volumes of O_2 released from spectrophotometrically standardized solutions of H_2O_2 by crystalline catalase was ±4%. The rates of O_2 evolution were determined by presetting the micrometer syringe corresponding to a desired volume, generally from 3 to 20 μl, and recording the time required for the manometric fluid to reach the reference mark in a horizontal capillary. At this point, the micrometer was reset for the next reading, etc., until the run was complete. The apparatus was maintained on a single station of a Warburg bath, and the reaction reference flasks were completely immersed in the constant-temperature water bath. The rates of O_2 evolution were independent of shaking speeds above 80 cycles/min; a speed of 115 cycles/min was used throughout. Under the experimental conditions employed, only those solutions containing H_2O_2, copper, and imidazole possessed significant catalatic activity.

The observed rates of O_2 evolution, R, in μl sec^{-1}, obtained from the initial slopes of a plot of microliters of O_2 evolved *vs.* time, were converted to k_{obsd} in units of mol^{-1} l. sec^{-1} after correcting the O_2 volume to 0° and 760 mm by the factor 4.09×10^{-8}.

The kinetic runs were made at a total phosphate buffer concentration of 0.013 *M*. The catalatic activity has been found to vary

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Table I. Observed Rate, R, of Hydrogen Peroxide Decomposition at 25° as a Function of pH in Solutions Containing Copper, Imidazole, and Sodium Dihydrogen Phosphate

pH	$R \times 10^8$ l. mol^{-1} sec^{-1}	Molarity[a] $[Cu^{2+}]$	$[Im]$	$[PO_4^{3-}]$	$[HOO^-]$
$[Cu^{2+}]_T = 0.266 \times 10^{-3}$ *M*; $[Im]_T = 0.160 \times 10^{-2}$ *M*; [Sodium Phosphate Buffer]$_T$ = 0.013 *M*; $[H_2O_2]_T$ = 0.0333 *M*					
6.40	0.31	9.647×10^{-6}	2.188×10^{-4}	1.750×10^{-8}	2.100×10^{-7}
7.08	2.66	1.530×10^{-6}	5.765×10^{-4}	1.778×10^{-7}	1.005×10^{-6}
7.26	4.19	9.476×10^{-7}	6.784×10^{-4}	2.994×10^{-7}	1.521×10^{-6}
7.62	7.44	3.741×10^{-7}	8.441×10^{-4}	7.825×10^{-7}	3.483×10^{-6}
7.80	9.78	2.386×10^{-7}	9.029×10^{-4}	1.230×10^{-6}	5.271×10^{-6}
8.0	13.50	1.463×10^{-7}	9.509×10^{-4}	2.005×10^{-6}	8.353×10^{-6}
$[Cu^{2+}]_T = 0.53 \times 10^{-4}$ *M*; $[Im]_T = 0.160 \times 10^{-1}$ *M*; [Sodium Phosphate Buffer]$_T$ = 0.0133 *M*; $[H_2O_2]_T$ = 0.0333 *M*					
6.50	0.17	1.510×10^{-8}	3.068×10^{-3}	2.578×10^{-8}	2.645×10^{-7}
7.20	0.20	4.116×10^{-10}	8.646×10^{-3}	2.538×10^{-7}	1.326×10^{-6}
7.54	0.35	1.114×10^{-10}	1.147×10^{-2}	6.386×10^{-7}	2.900×10^{-6}
7.95	0.60	3.229×10^{-10}	1.380×10^{-2}	1.778×10^{-6}	7.453×10^{-6}

[a] The concentrations of these species for the conditions employed were calculated from the following formation constants expressed as log β as defined in the text. The constants for species marked with an asterisk were calculated from equations proposed in ref 21 and 22: HIm^+, 7.12;[23] H_3PO_4, 20.61; H_2PO_4, 18.5; HPO_4, 11.8;[24] H_2O_2, 11.6;[25] Cu(Im), 4.33; $Cu(Im)_2$, 7.87; $Cu(Im)_3$, 10.69; $Cu(Im)_4$, 12.72;[23] $Cu(H_2PO_4)$, 19.25; $Cu(HPO_4)$, 15.0;[24] Cu(OH), −6.5; $Cu_2(OH)_2$, −10.95; $-Cu_3(OH)_4$, 22.1;[26] $Cu(Im)(H_2PO_4)$*, 23.18; $Cu(Im)(HPO_4)$*, 18.63; $Cu(Im)_2(H_2PO_4)$*, 22.99; $Cu(Im)_2(HPO_4)$*, 18.44; $Cu(Im)_3(H_2PO_4)$*, 22.73; $Cu(Im)_3(HPO_4)$*, 18.18; Cu(HOO)*, 6.45; Cu(Im)(HOO)*, 9.95; $Cu(Im)_2$(HOO)*, 13.33; $Cu(Im)_3$(HOO)*, 16.65. The stability constant for the peroxy complex, $[Cu(HOO)]^+$, was obtained as described earlier.[15]

with changes in the total buffer concentration.[17] A high H_2O_2/Cu(II) ratio was maintained since the kinetics of H_2O_2 decomposition are dependent on the relative concentrations of H_2O_2 and the metal ion.[18] No visible precipitate or turbidity was observed in solutions at any stage of the work.

The final pH of solutions was checked with an Orion digital pH meter. The pH standards taken were 0.05 *M* potassium hydrogen phthalate, pH 4.00 ± 0.02 at 25°, and 0.05 *M* potassium phosphate monobasic sodium hydroxide buffer, pH 7.00 ± 0.02 at 25°. No attempt was made to convert the hydrogen ion activity into concentration, because the possible errors resulting from using the estimated values of several stability constants are considerably greater than that resulting from the neglect of activity correction.

Chemicals. Imidazole (Fluka puriss) was dried at 120° for 10 hr. A stock solution of copper (AR grade sulfate salt) was standardized volumetrically by complexometric titrations with the sodium salt of EDTA in the presence of murexide indicator as described by Schwarzenbach.[19] Sulfuric acid (AR) and carbonate-free sodium hydroxide were used for adjusting the pH of phosphate buffer solutions. The phosphate buffer was prepared from reagent grade sodium monohydrogen and sodium dihydrogen phosphate.

Results and Discussion

Solution Equilibria. In aqueous solutions containing copper(II), imidazole, and hydrogen peroxide in phosphate buffer, the following equilibria are considered: (a) ionization of imidazole and formation of 1:1, 1:2, 1:3, and 1:4 Cu–imidazole complexes; (b) ionization of hydrogen peroxide and the formation of a $[Cu \cdot OOH]^+$ complex; (c) ionization of H_3PO_4 into $H_2PO_4^-$, HPO_4^{2-}, and PO_4^{3-}; (d) the formation of the copper complexes of $H_2PO_4^-$ and HPO_4^{2-}; (e) hydrolysis of Cu(II) ions to give $[Cu(OH)]^+$, $[Cu_2(OH)_2]^{2+}$, and $[Cu_3(OH)_4]^{2+}$; (f) formation of mixed complexes of imidazole, phosphoric acid, and hydrogen peroxide with copper; (g) formation of hydrolyzed species of copper–imidazole complexes such as L_xCuOH. In all, we have taken into account the formation of 26 species existing in dynamic equilibrium with each other. The equilibrium concentrations of the various species were calculated on an IBM 360/50 computer by an iterative procedure from expressions for total metal, total imidazole, total phosphate, and total peroxide concentrations.[20] A listing of these species, together with the logarithms of their over-all stability constants obtained from the literature as cited, is given in the footnote to Table I.[21-26]

The over-all "practical constants" are defined as: $\beta = [M_mA_aB_b(H^+ \text{ or } OH^-)_w]/[M]^m[A]^a[B]^b[H^+ \text{ or } OH^-]^w$, where M, A, and B represent respectively metal ion, ligand A, and ligand B, while m, a, b, and w are positive integers or zero. The number of protons or hydroxyl ions in the complex species is given by H^+ and OH^-, respectively. From the knowledge of the stability constants, pH, and free ligand (Im, or PO_4^{3-} or HOO^-) and free metal ion concentration, the concentration of any species listed in the footnote to Table I can be calculated. The concentrations of $[Cu^{2+}]$, $[HOO^-]$, $[ImCu^+]$, $[ImCuOH^+]$, $[(Im)_2Cu^{2+}]$, and $[(Im)_2CuOH^+]$ as a function of pH are plotted in Figure 1. Constants for the hydrolyzed species of the type $L_xCu(OH)$ are relatively unaffected by the nature of the ligand,[27] and the value of $pK_a = 7$ was used as given in ref 27. It should be noted that the values of several of these constants are somewhat uncertain, and their cumulative effect on the calculated concentrations of the corresponding species will be a function of pH. Also, in alkaline regions, the solution equilibria of copper complexes are not very well understood. Therefore, the possibility of other species existing in this region cannot be excluded.

Kinetic Measurements. While the differential method employed gave a measure of the net O_2 evolved relative to the coppper-free controls, experiments were carried out to determine the degree to which all conceivable

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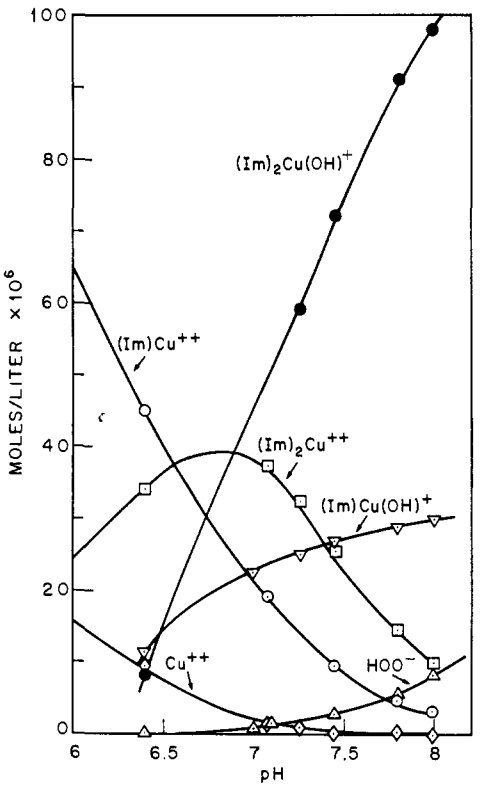

Figure 1. Concentration of $(Im)Cu^{2+}$, $(Im)_2Cu^{2+}$, $(Im)Cu(OH)^+$, $(Im)_2Cu(OH)^+$, free Cu^{2+}, and peroxide anion as a function of pH. $[Cu^{2+}]_T = 0.266 \times 10^{-3}$ *M*; $[Im]_T = 0.16 \times 10^{-2}$ *M*; $[H_2O_2]_T = 0.0333$ *M*; [sodium phosphate buffer]$_T = 0.013$ *M*.

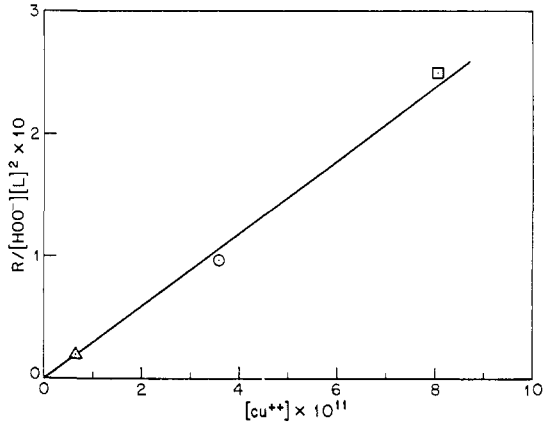

Figure 2. First-order dependence of rate of hydrogen peroxide decomposition on free copper concentration, $[Cu^{2+}]$: 25°, pH 7.95. $[H_2O_2]_T = 0.0333$ *M*; $[Im]_T = 2.67 \times 10^{-2}$ *M*; [phosphate buffer]$_T = 0.013$ *M*; $[Cu^{2+}]_T = 5.33 \times 10^{-4}$ *M* (⊡), 2.66×10^{-4} *M* (⊙), 5.33×10^{-5} *M* (△).

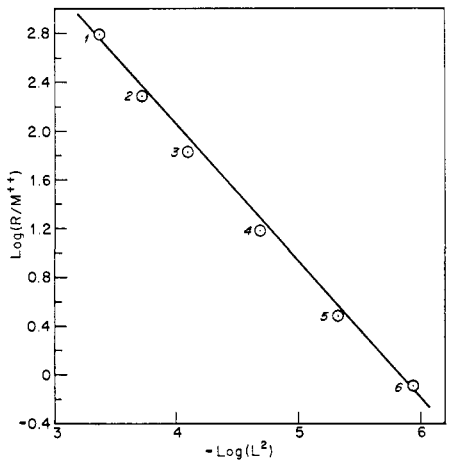

Figure 3. Second-order dependence of rate of hydrogen peroxide on free imidazole concentration at 25°. $[Cu^{2+}]_T = 5.30 \times 10^{-5}$ *M*; $[H_2O_2]_T = 0.033$ *M*; [phosphate buffer]$_T = 0.0133$ *M*; pH 7.95; $[Im]_T \times 10^2$ *M* = 2.67 (1), 1.60 (2), 1.07 (3), 0.533 (4), 0.266 (5), 0.133 (6).

combinations of the solution components decomposed H_2O_2. The only combinations which gave significant volumes of O_2 at the concentrations and pH's employed, were those which contained copper, imidazole, and H_2O_2. Therefore, nonimidazole-containing species of copper, uncomplexed imidazole, and various ionized and un-ionized buffer (H_3PO_4, $H_2PO_4^-$, HPO_4^{2-}, PO_4^{3-}, etc.) species need not be considered in the derivation of the rate equation. For reasons discussed later (such as reduced charge and free coordinating sites on the complexed species), the mixed complexes of copper with imidazole and H_2PO_4, HPO_4^{2-}, and PO_4^{3-} can also be ignored in the rate equation. The remaining complex species, therefore, which may contribute toward the O_2 evolution are $Cu(Im)^{2+}$, $Cu(Im)_2^{2+}$, $Cu(Im)_3^{2+}$, $Cu(Im)_4^{2+}$, and hydrolyzed species of 1:1, 1:2, and 1:3 Cu–imidazole complexes.

When pH, peroxide concentration, and imidazole concentration in 500- to 50-fold excess over copper concentration were kept constant, and the total copper concentration was varied tenfold in the range 5.3×10^{-4} to 5.3×10^{-5} *M*, the free $[Cu^{2+}]$ varied from 8.04×10^{-11} to 6.6×10^{12} *M*, and the rates of O_2 evolution were found to be first order in free copper concentration (Figure 2). When the pH and total copper and peroxide concentration were kept constant and total imidazole concentration was varied 20-fold in the range 1.33×10^{-3} to 2.66×10^{-2} *M*, the free imidazole concentration varied from 2.31×10^{-2} to 1.067×10^{-3} *M*, and the rates of O_2 evolution were found to be second order relative to the free imidazole concentration (Figure 3). When pH and copper and imidazole concentrations were kept constant, the rates of O_2 evolution were first order with respect to H_2O_2 concentration. The pH dependence of the rates of H_2O_2 decomposition as measured by O_2 evolution is shown in Figure 4.

Second-order dependence of rate of O_2 evolution as measured over a 20-fold variation in free and total imidazole (Figure 2) concentration indicates that the species ML^{2+}, ML_3^{2+}, and ML_4^{2+} contribute little toward the catalytic activity. However, $Cu(Im)_2^{2+}$ and $Cu(Im)_2OH^+$ both will give second-order dependence of rate of O_2 evolution on free imidazole concentration. The rate expression, therefore, can be written as

$$R = k_1[ML_2^{2+}][HOO^-] + k_1'[ML_2(OH^-)^+][HOO^-] \quad (1)$$

or

$$= k_1\beta_{12}[M^{2+}][L]^2[HOO^-] + k_1'\beta_{121}[M^{2+}][L]^2[OH^-][HOO^-] \quad (2)$$

If $Cu(Im)_2^{2+}$ and $Cu(Im)_2(OH^-)^+$ and HOO^- are the only active species, a plot of $R/[ML_2^{2+}][HOO^-]$ *vs.* $[ML_2(OH^-)^+]/[ML_2^{2+}]$ should give a straight line with intercept and slope giving the value of k_1 and k'_1, respectively. Figure 5 shows such a plot for which the con-

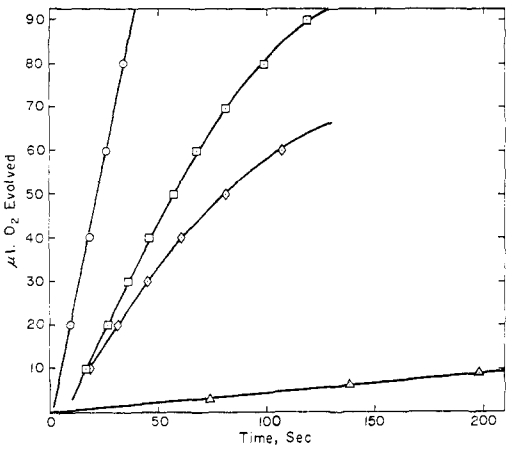

Figure 4. The effect of pH on the rate of hydrogen peroxide decomposition (25°): △, 6.4; ◇, 7.08; □, 7.26; ⊙, 8.0. The total initial concentrations $[Cu^{2+}]_T$, $[H_2O_2]_T$, $[Im]_T$, and [phosphate buffer]$_T$ are those given in Table I.

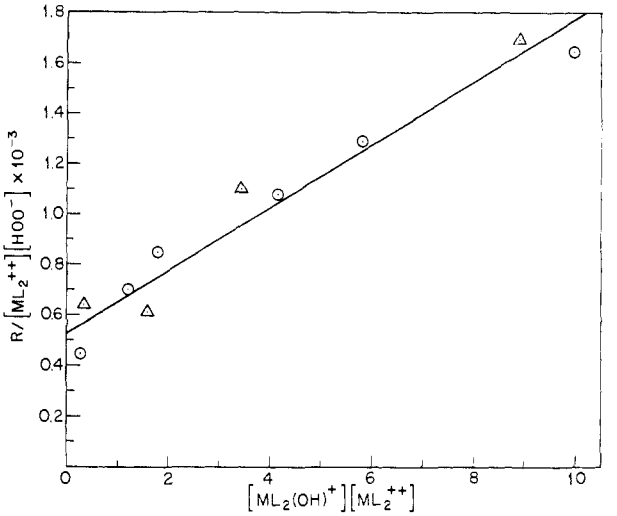

Figure 5. Graphical evaluation of k_1 and k_1' for the catalytic decomposition of hydrogen peroxide by $Cu(Im)_2^{2+}$ and $Cu(Im)_2(OH)^+$, respectively, at 25°. The total initial concentrations $[Cu^{2+}]_T$, $[H_2O_2]_T$, $[Im]_T$, [phosphate buffer]$_T$, and pH are those given in Table I.

centrations of $Cu(Im)^{2+}$, $Cu(Im)(OH^-)^+$, $Cu(Im)_2^{2+}$, $Cu(Im)_2(OH^-)^+$, and (HOO^-) change by factors of 590, 75, 350, 24.2, and 39.7, respectively. The pH range as shown in Figure 5 varied from 6.4 to 8.0. The rate constants k_1 and k_1', as obtained from the intercept and slope, are 530 and 120 l. mol^{-1} sec^{-1}, respectively. These values of k_1 and k_1' are relevant only to the present experimental conditions and depend on the values of the stability constants chosen for calculating the concentration of various species. Rather large scattering of points around the straight line in Figure 5 is presumably due to uncertainties in the values of the estimated constants.

Possible Mechanisms. The kinetic data fit eq 1 and 2 over a wide range of concentrations of active and possible active species. However, the data fit equally well to the equation

$$R = k_3[L_2Cu(II)HOO^+] + k_3'[L_2Cu(II)(OH)HOO] \quad (3)$$

or

$$= k_3\beta_{211}[L]^2[Cu^{2+}][HOO^-] + k_3'\beta_{2111}[L]^2[Cu^{2+}][OH^-][HOO^-] \quad (4)$$

In terms of free metal, free ligand, and free peroxide anion concentrations, the two sets of equations (1,2 and 3,4) are identical and differ only with respect to the formation constants β_{12}, β_{121}, β_{211}, and β_{2111}, respectively. From kinetic data alone, it is difficult to decide whether the reaction proceeds by either one or both of these steps. One can explain the kinetic data and obtain eq 1,2 and 3,4 by assuming the following sequence of reactions.

$$4H_2O_2 \overset{k_5}{\rightleftharpoons} 4HOO^- + 4H^+ \quad (5)$$

$$\underset{C}{L_2Cu^{II\ 2+}} + HOO^- \rightleftharpoons \underset{C_1}{L_2Cu^{II}HOO^+} \xrightarrow{k_3} \underset{C_2}{L_2Cu^{I}HOO^+} \quad (6)$$

$$\underset{C'}{L_2Cu^{II}OH^+} + HOO^- \rightleftharpoons \underset{C_1'}{L_2Cu^{II}OH\cdot HOO} \xrightarrow{k_3'} \underset{C_2'}{L_2Cu^{I}HOO^+} + OH^- \quad (7)$$

$$2L_2Cu^{I}HOO^+ + 2HOO^- \xrightarrow{k_8} 2L_2Cu^{II}(OH)_2 + 2O_2 \quad (8)$$

$$2L_2Cu^{II}(OH)_2 + 3H^+ \rightleftharpoons L_2Cu^{II}(H_2O)_2^{2+} + L_2Cu\begin{matrix}(OH)^+\\(H_2O)\end{matrix} \quad (9)$$

$$H^+ + OH^- \rightleftharpoons H_2O \quad (10)$$

In $[L_2Cu^{II}OOH^+]$, it is assumed that the peroxide anion is bidentate as was also assumed by Wang for iron chelates.[5] The O–O bond in $L_2M^{II}OOH^+$ will presumably rupture when stretched as a result of an increase in the O–M–O bond angle from 90° in the square-planar Cu(II) complex to 109° in tetrahedral cuprous complexes. The formation of the cuprous state was demonstrated by the fact that addition of 2,2′-biquinoline to the Cu–Im–H_2O_2 system instantaneously produced a pink color characteristic of the Cu(I) ions.[28]

The energy consumed in reactions 6 and 7 is compensated by the formation of the more stable Cu(I)–imidazole)$_2$ complex (log $\beta_{12Cu(II)}$ = 8.0; log $\beta_{12Cu(I)}$ = 11.0).[29] The intermediate C_2 contains electron-deficient oxygen, and, therefore, it can react rapidly with a second peroxide anion (eq 8). The reaction scheme described above is essentially the same as proposed by Wang[5a] for Fe(III)–H_2O_2 systems, except that our results suggest that in C_2 the metal ion is in its lower oxidation state. The mechanism proposed is probably not quantitatively cyclic since our observations and those of others[30] indicate that an oxidative destruction of ligand and complex does take place in the course of H_2O_2 decomposition. However, by confining our studies to the initial rates, the complications attributed to these side reactions can be neglected.

Using the steady-state approximation for the calculation of the concentration of the intermediate, $[L_2Cu^{I}OOH^+]$, we get

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$$d[L_2Cu^{I}OOH]^+/dt = k_3[L_2Cu^{II}HOO^+] + k_3'[L_2Cu^{II}\cdot OH\cdot HOO] - k_8[L_2Cu^{I}HOO^+]^2[HOO^-]^2 = 0 \quad (11)$$

Therefore

$$[L_2Cu^{I}HOO^+]^2 = \frac{k_3[L_2Cu^{II}HOO^+] + k_3'[L_2Cu^{II}OH\cdot HOO]}{k_8[HOO^-]^2} \quad (12)$$

$$R = d(O_2)/dt = k_3[L_2Cu^{II}HOO^+] + k_3'[L_2Cu^{II}OH\cdot HOO] \quad (13)$$

which is the same as expression 3. By assuming that in eq 6 and 7 of the reaction scheme C and C′ go directly to C_2 and C_2' ($C \rightarrow C_2, k_1$; $C' \rightarrow C_2', k_1'$), one obtains eq 1.

In studies on H_2O_2 decomposition by iron and its complexes at low pH (<2), Barb, Baxendale, George, and Hargrave[18] postulated free-radical mechanisms as a result of the reduction of ferric to the ferrous state. In the present investigation, the polymerization of acrylonitrile in the presence of Cu(II)–Im–H_2O_2 (pH 7) was employed to detect free-radical formation, but no polymerization was observed despite precautions to exclude oxygen from the system. When the level of cuprous ions is increased by direct addition, however, polymer formation took place. The esr studies on hydrogen peroxide decomposition by copper complexes do not show the presence of radicals or radical intermediates in these systems.[31] However, this does not exclude the presence of free radicals in the system. For example, the Fe(II)–H_2O_2 system has been investigated by the esr flow technique by Sicilio,[32] and no new radicals were observed due to the reaction of Fe(II) with H_2O_2 even though chemical tests have shown that free radicals are present. One explanation for the negative results is that the OH radical is extremely reactive and its concentration at any time is too small to be observed by usual esr methods. It is interesting to note that the free-radical reaction mechanism proposed by Barb, Baxendale, George, and Hargrave for Fe(III)–H_2O_2[18], if applied to Cu(II)–H_2O_2 systems under the steady-state condition for Cu(I) species, HOO, and HO radicals and with high peroxide to copper ratios, yields an over-all second-order rate expression, first order with respect to each reactant, M^{2+} and HOO^-. This is in agreement with rate expression 1 which reduces to $R = d(O_2)/dt = k_1[ML_2^{2+}][HOO^-]$ in the region in which hydrolyzed complex species are not formed (pH <3).

Hawkins and Perrin[33] and James and Williams[34] investigated the redox potentials of a number of copper complexes. It was observed that ligand characteristics such as lower charge on the ligand, larger ring size of the chelates, and small number of chelating groups (or nonchelating agents such as imidazole and ammonia) favor the product on the right side in the reaction

$$Cu(II) \underset{-e^-}{\overset{e^-}{\rightleftharpoons}} Cu(I) \quad (14)$$

These are the factors which also appear to favor the catalytic decomposition of H_2O_2. Thus, we have observed that bidentate neutral ligands, such as ethylenediamine and histamine, have greater catalytic activity than the corresponding complexes of glycine and α-alanine. The six-membered chelate ring of β-alanine was found to possess greater catalytic activity than Cu–α-alanine. These phenomena presumably arise from the fact that the linear or tetrahedral complexes of Cu(I) require a bond angle of ~180 and 109°, respectively, which are formed more easily by larger ring chelate systems.

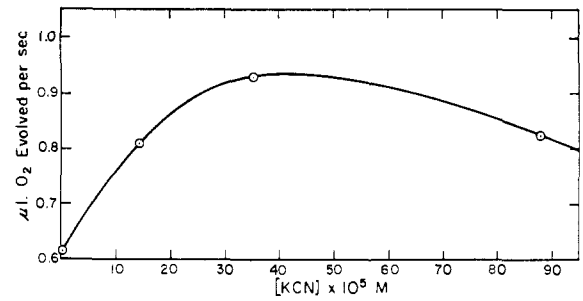

Figure 6. Effect of cyanide concentration on the rate of H_2O_2 decomposition: 25°, pH 7.0. [Phosphate buffer] = 0.013 *M*, $[Cu^{2+}]_T = 2.63 \times 10^{-4}$ *M*, $[Im]_T = 1.58 \times 10^{-3}$ *M*, $[H_2O_2]_T = 0.033$ *M*.

An interesting observation of the present study is the relative inertness of the 1:1, 1:3, and 1:4 copper–imidazole complexes. Considerations based on the number of free sites on a complex alone cannot explain it as the 1:1 copper–imidazole complex has three free coordinating positions on it. On the other hand, redox considerations predict that Cu–(imidazole)$_2$ should be the main catalytically active species. Thus, the standard potential of Cu(II)–Cu(I) couple in water of +0.167 V becomes more positive as the water molecules are replaced by up to two nitrogen donors.[34] Each donor nitrogen stabilizes the cuprous species by about 0.090 V. Cuprous ions have a tendency to be two coordinate and linear with saturated nitrogen ligands, while cupric ions may become at least four coordinate. The reduction potential becomes less positive for three or more coordinated monodentate ligands. Thus, two nitrogens coordinated to copper provide the lowest energy path for cupric redox reaction and *vice versa*. It is interesting to note, therefore, that with bidentate nitrogen ligands, *e.g.*, histamine, the 1:1 chelate with copper is the principal species responsible for catalatic activity.[15] The lower catalytic activity of $CuL_2(OH)^+$ is again explainable on redox potential considerations such as coordination of an anionic ligand (OH^-) and increase in the number of groups coordinated to the central metal ion.

Effect of Anions on Catalatic Activity. The observed rate of reaction was found to increase rapidly as the concentration of phosphate buffer was decreased. No simple stoichiometric relationship could be obtained as the effect cannot be explained on the basis of the fraction of total copper bound to various phosphate species. However, this strong inhibitory effect of phosphate buffer can be explained by redox considerations. Anions which stabilize the higher oxidation state of the complex will lower the reduction potential and hence reduce the observed rate of a redox reaction. Also, the mere presence of negative ions will make the approach of HOO^- toward $[L_2Cu]^{2+}$ or $[L_2CuOOH]^+$ more difficult.

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The effect of two Cu(I) preferring ligands,[35] chloride and cyanide ions, on the observed rate of H_2O_2 decomposition was investigated (Figure 6). In the concentration range $\approx 4 \times 10^{-4}$ *M*, chloride ion does not affect the observed rate of reaction. However, low concentrations of cyanide ion increased the rate, but when the concentration of cyanide was increased ($> 4 \times 10^{-5}$ *M*), an inhibitory effect was observed. It might be surmised that at low concentrations of CN^-, 1:1 copper–cyanide species are formed which are presumably catalytically active. At high cyanide concentrations, the extremely stable dicyano-, tricyano-, and tetracyanocuprate complexes are formed. Because of strong M–C π bonding,[36] these species would be catalytically inactive as they should show little tendency to react with peroxide anion to form the intermediate, $(CN)_xCuOOH$.

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Stereoselective Interaction of Optically Active Amino Acids and Esters with (L-Valine-N-monoacetato)copper(II)

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Abstract: Equilibrium constants for the coordination of optically active amino acidates (A^-) and their esters (E) to (L-valine-N-monoacetato)copper(II), Cu(L-ValMA) + L- or D-$A^- \rightleftharpoons$ Cu(L-ValMA)(A^-), have been determined. For leucine, phenylalanine, alanine, and serine, the value of K_f is 3.3–6.5 times larger for the L than for the D isomer. For valine the K_f value for the D enantiomer is 2.5 times greater than that for the L. For the ester, ethyl leucinate, the L isomer gives a K_f which is 3.4 times larger than that for the D ester. It has also been determined that the rate of hydrolysis of methyl leucinate and methyl phenylalaninate in the complexes, Cu(L-ValMA)(E), is higher for the D-amino acid ester than for the L isomer. The mechanisms and the origins of the stereoselective effects are discussed.

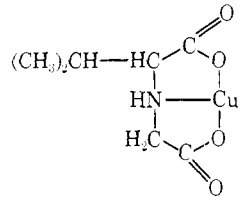
Like enzymes in general, metalloenzymes exhibit a high degree of specificity toward substrates of a particular structural type or optical configuration.[1] Since it is apparently the ligands surrounding the metal ion in these enzymes which are largely responsible for the over-all specificity of the enzyme, numerous attempts have been made to design simple metal complexes which also have some specificity. In this paper we shall be concerned with the specificity of labile metal complexes toward the two optical isomers of α-amino acids and their esters.[2] In some cases which have been studied, a metal complex which bears an optically active amino acidate, A^- ($NH_2CHRCO_2^-$), ligand shows no stereoselectivity in binding to a second L- or D-amino acidate. For example, the equilibrium constants for the reactions

$$\text{Cu(L-A)}^+ + \text{L-A}^- \rightleftharpoons \text{Cu(L-A)}_2$$

$$\text{Cu(L-A)}^+ + \text{D-A}^- \rightleftharpoons \text{Cu(L-A)(D-A)}$$

are identical for the amino acids alanine, phenylalanine, valine, and proline.[3] On the other hand, these equilibrium constants are reported to be different for asparagine.[4] Relative stabilities of analogous histidine complexes, M(L-Hist)$_2$ and M(L-Hist)(D-Hist), have been shown to be identical[5] when M is Ni^{2+} but different[6] when M is Co^{2+}. From these results it is not clear why stereoselectivity is observed in some cases but not in others.

In the present study, equilibrium constants for the coordination of optically active amino acids and esters to the complex (L-valine-N-monoacetato)copper(II), Cu-



(L-ValMA), have been determined. This complex does indeed form more stable complexes with one optical isomer than it does with the other enantiomer of most of the acids and esters examined. The Cu(L-ValMA) also exhibits some stereoselectivity in its catalysis of the hydrolysis of certain optically active amino acid esters.

Experimental Section

Materials. The amino acids, D- and L-valine (Val), D- and L-leucine (Leu), D- and L-serine (Ser), D- and L-alanine (Ala), and D- and L-phenylalanine (PhAla), were obtained from Mann Research Laboratories. The amino acid esters were prepared by the HCl-catalyzed reaction of the amino acid with the desired alcohol according to standard methods.[7] Proton nuclear magnetic resonance spectrometry was used to establish the identity of the isolated ester hydrochlorides. These spectra were measured on a

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