Reactions Between Copper(II) and 2-Mercaptosuccinic Acid in Aqueous Perchlorate Solution

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The anaerobic oxidation of 2-mercaptosuccinic acid (H_3L) by copper(II) in aqueous acidic perchlorate media (pH 2—4) proceeds by the formation of a sulphur-bonded transient $[CuL]^-$ which absorbs maximally at 350 nm with an absorption coefficient of 1 600 ± 50 $dm^3 mol^{-1} cm^{-1}$. In conditions of a large excess of substrate the major redox path involves the acid-catalysed dimerization of $[CuL]^-$, equation (i), with a rate constant k_3 = 3 dm^3

$$[Cu(HL)] + [CuL]^- \longrightarrow [Cu_2HL_2]^- \qquad (i)$$

$mol^{-1} s^{-1}$ at I = 0.1 mol dm^{-3} and 25 °C. Subsequent attack by substrate according to the overall equation (ii)

$$[Cu_2HL_2]^- + 2H_3L \longrightarrow [Cu_2(H_2L)_2] + [H_2L'\text{–}L'H]^- \qquad (ii)$$

results in formation of the corresponding disulphide and a copper(I) dimer which is fully formed when the ratio $[H_3L]_0 : [Cu^{2+}]_0$ exceeds 2 : 1. The mechanism is discussed in terms of the formation of a two-electron redox template which allows direct production of disulphide without formation of high-energy radical species. Various side reactions are noted.

SINCE the appearance of a paper [1] describing the properties of a mixed-valence complex of 2-mercaptosuccinic acid, a large number of studies of the interactions of copper(II) with sulphur-containing reductants have been reported. Many of these studies concern the amino-acids cysteine and penicillamine (3-mercaptovaline) due to the biological importance of the Cu–S chromophore.[2]

In anaerobic alkaline cysteine solution an e.s.r.-active complex ($\lambda_{max.}$ 330 nm) containing Cu^{II} : cysteine in the ratio 1 : 2 decomposes with apparent second-order kinetics and is reported [3] to be the intermediate in the copper-catalysed oxidation of cysteine.[4,5] At lower pH an e.s.r.-active transient ($\lambda_{max.}$ 530 nm) containing Cu^{II} : cysteine in the ratio 1 : 1 is also observed.[6,7] Comparable species have been noted [8-11] in the case of penicillamine ($\lambda_{max.}$ 333 and 520 nm respectively) although the latter peak has been interpreted as due to a mixed-valence complex for which a number of structures and stoicheiometries have been suggested.[8,12-15] Studies of the interactions of copper with cysteamine have been reported [16-18] and stable complexes of Cu^{II} with 2-mercaptopropionylglycine have also been examined.[19,20]

This paper forms part of a series in which the roles of metal ions in the oxidation of mercaptocarboxylic acids have been investigated.[21-23] Reactions of metal-ion complexes, intermediates in these oxidations, are often important in determining the mechanisms. The kinetics and mechanism of the decomposition of a transient

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sulphur-bound copper(II) complex in conditions of an excess of substrate are now described. The substrate, 2-mercaptosuccinic acid, is particularly useful in the study of the redox interaction of Cu^{II} with sulphur-containing ligands since the copper(I) products of the reactions are soluble in water.

EXPERIMENTAL

Copper(II) perchlorate was prepared by the action of excess of CuO (Hopkin and Williams, AnalaR) in perchloric acid and recrystallized from water. Its solutions were standarized by iodimetric titration.[24] All the other reagents were obtained and used as described previously.[21]

Reactant solutions were prepared daily and were outgassed by freezing and thawing under reduced pressure, then stored under a positive pressure of nitrogen gas. Aliquot portions were withdrawn into all-glass syringes through a Teflon adaptor and were transferred to a stopped-flow apparatus.[23] Typical experiments involved copper(II) and 2-mercaptosuccinic acid concentrations of 10^{-5}—10^{-3} mol dm^{-3} and the hydrogen-ion concentration was maintained constant either in excess or at higher pH by utilizing the self-buffering properties of the substrate. The pH of solutions was measured, after mixing, using a Radiometer-26 pH meter.

E.s.r. measurements were made on aqueous glasses at −150 °C using a Varian E-104 spectrometer. Absorbances were measured on a Unicam SP 800 spectrophotometer, the sample compartment of which was continually flushed with nitrogen gas.

At least four reaction half-lives were followed in kinetic measurements. Rate constants were evaluated using conventional linear least-squares procedures. All the measurements were made at 25 ± 0.1 °C at an ionic strength of 0.1 mol dm^{-3} using $Na[ClO_4]$ as the background electrolyte.

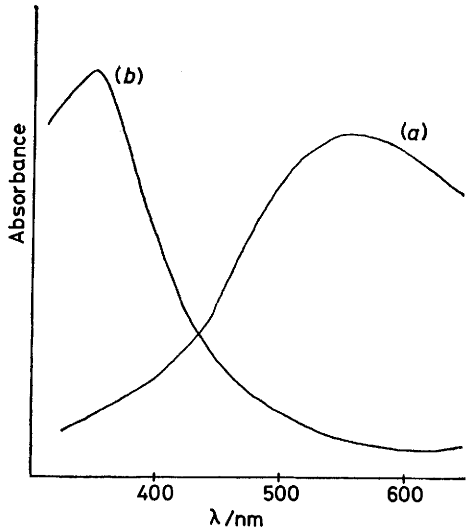

FIGURE 1 Absorption spectra of copper–mercaptosuccinate chromophores: (a) the reaction product in conditions of excess of Cu^{II}; (b) the transient intermediate formed in conditions of excess of Cu^{II} or of substrate

RESULTS

(a) *Reaction Products and Stoicheiometry.*—In the presence of an excess of 2-mercaptosuccinic acid, H_3L, copper(II) is reduced to a yellow copper(I) complex which has an absorption coefficient of 670 dm^3 mol^{-1} cm^{-1} at 350 nm. Spectrophotometric titration at this wavelength shows that the maximum formation of the product occurs when the ratio $[Cu^{2+}]_0 : [H_3L]_0 = >1 : 2$. One mol of the mercaptide is reduced to the corresponding disulphide while a second mol is incorporated into the copper(I) product [equation (1)], thereby stabilizing the lower-valence state.[2] The exact nature of this yellow copper(I)–mercaptide complex has not

$$2Cu^{2+} + 4H_3L \rightarrow [Cu_2(H_2L)_2] + H_2L'\text{–}L'H_2 + 4H^+ \quad (1)$$

been investigated but it seems likely that the immediate redox product is a dimer which subsequently oligomerizes.

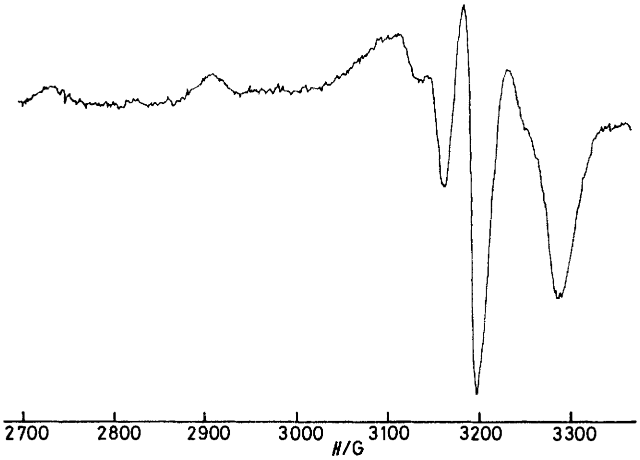

FIGURE 2 E.s.r. spectrum of the transient intermediate formed in the reaction of 2-mercaptosuccinic acid with Cu^{II} at ν = 9.081 G, Hz, −150 °C, and pH = 3

The product obtained with an excess of Cu^{II} is a purple diamagnetic complex absorbing maximally at 525 nm as shown in Figure 1(a). This species has an absorption coefficient $>2 \times 10^3$ dm^3 mol^{-1} cm^{-1} based on the total copper concentration and has previously been characterized [1] as a mixed-valence complex $[Cu^I_4Cu^{II}(H_2L)_4]$.

(b) *Characterization of the Intermediate.*—In conditions of either excess of Cu^{II} or 2-mercaptosuccinic acid a transient absorbing strongly at 350 nm is detected within the time of mixing. The spectrum in Figure 1(b) was obtained by a point-by-point scan using a stopped-flow spectrophotometer. The rapid rate of formation of the transient ($>10^7$ dm^3 mol^{-1} s^{-1}) and its unusually high absorption coefficient of 1.6×10^3 dm^3 mol^{-1} cm^{-1} at 350 nm suggest a sulphur-bonded complex of Cu^{II}. An e.s.r. spectrum of the complex is presented in Figure 2 and supports the assignment of oxidation state. It is consistent with an approximately axially symmetric co-ordinate system with $g_{\parallel} = 2.170$, $g_{\perp} = 2.24$, $a_{\parallel} = 175$ G, and $a_{\perp} = 38$ G.*

Spectrophotometric titration of the intermediate at 350 nm shows complete formation of this species between pH 2 and 4, and the available e.s.r. and kinetic measurements are

$$Cu^{2+} + H_3L \overset{K_1}{\rightleftharpoons} [CuL]^- + 3H^+ \quad (2)$$

consistent with equilibrium (2) where $K_1 = 10^{-2.4}$ mol^2 dm^{-6}. It is likely that the intermediate protonated species

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* Throughout this paper: 1 G = 10^{-4} T.

[24] A. I. Vogel, 'A Textbook for Quantitative Inorganic Analysis,' 3rd edn., Longmans, London, 1961.

[Cu(HL)] is dominant in solution at lower pH, but no measurements below pH 1 are available because the nature of the reaction changes.

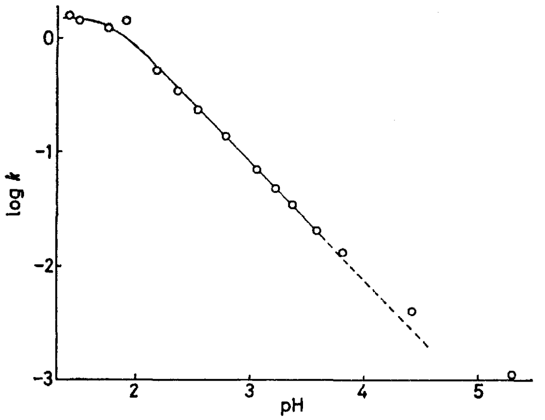


FIGURE 3 Dependence of the rate of decomposition of $[CuL]^-$ on pH at $[Cu^{2+}] = 9.35 \times 10^{-5}$, $[H_3L] = 9.35 \times 10^{-3}$, $I = 0.1$ mol dm^{-3}, and 25 °C

At pH > 4, in conditions of excess of substrate, the species in solution changes as revealed by an increase in the molar absorption coefficient at 350 nm ($>10^5$ dm^3 mol^{-1} cm^{-1}). This is attributed to bis complex formation, and an

$$[CuL]^- + H_3L \overset{K_2}{\rightleftharpoons} [CuL_2]^{4-} + 3H^+ \qquad (3)$$

upper limit of 10^{-11} mol^2 dm^{-6} for K_2 in equation (3) can be calculated. The e.s.r. spectrum of the fully formed bis complex $[CuL_2]^{4-}$ was obtained in 0.1 mol dm^{-3} Na[OH] and shows $g_{\parallel} = 2.133$, $g_{\perp} = 2.028$, $a_{\parallel} = 125$ G, and $a_{\perp} = 25$ G.

TABLE

Second-order rate constants for the decay of $[CuL]^-$ at 25 °C and $I = 0.1$ mol dm^{-3}

$10^5[Cu^{2+}]_0$ / mol dm^{-3}	$10^3[H_3L]_0$ / mol dm^{-3}	pH [a]	*k* [b] / dm^3 mol^{-1} s^{-1}
9.35	1.48	3.08	0.017
	1.74	2.01	0.213
		2.28	0.128
		2.52	0.081
		2.85	0.042
		3.06	0.025
		3.28	0.013
		3.49	0.009
		3.80	0.005
	3.87	2.86	0.070
	7.44	2.71	0.149
	9.35	1.41	1.563
		1.50	1.420
		1.75	1.238
		1.92	1.388
		2.13	0.582
		2.32	0.385
9.35	9.35	2.54	0.231
		2.78	0.133
		3.05	0.069
		3.22	0.048
		3.36	0.034
		3.58	0.021
		3.80	0.013
		4.42	0.004
		5.29	0.001
4.68	8.08	2.73	0.223
23.4	8.08	2.67	0.110
46.8	8.08	2.62	0.065

[a] The relation pH = $-\log[H^+]$ was found to hold within experimental error. [b] Evaluated using $\varepsilon_{350} = 1.6 \times 10^3$ dm^3 mol^{-1} cm^{-1} with a pathlength of 1.75 cm.

(*c*) *Kinetic Measurements*.—The kinetics of decomposition of the transient $[CuL]^-$ to form the yellow copper(I)–mercaptide product were followed at 350 nm in the presence of an excess of substrate. The reaction rate has an apparent second-order dependence on the transient concentration, and second-order rate constants obtained under various conditions are presented in the Table.

When the dominant copper(II) species in solution is $[CuL]^-$ the rate has a linear dependence on $[H^+]$, Figure 3, and the dependence on excess of substrate is first order changing to zero order at higher concentrations. The rate also shows a slight inhibition as the ratio $[Cu^{2+}]_0 : [H_3L]_0$ is increased and a plot of $[H^+]/k$ against $[Cu^{2+}]_0/[H_3L]_0$ was found to be linear (Figure 4). At low pH the rate attains a value which is independent of acidity but which shows a dependence on excess of substrate similar to that observed at pH > 2.

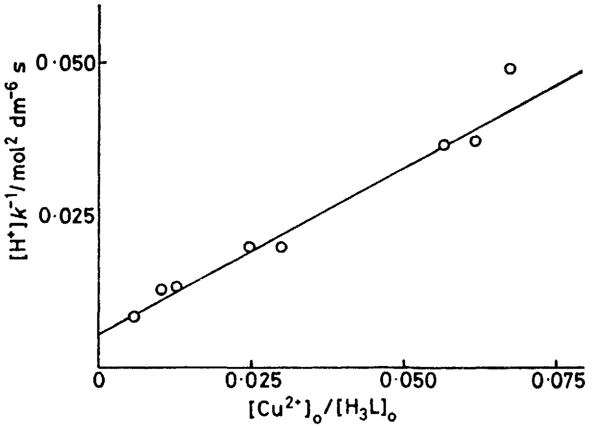


FIGURE 4 Plot derived from the reciprocal of equation (15) at 25 °C and $I = 0.1$ mol dm^{-3}

DISCUSSION

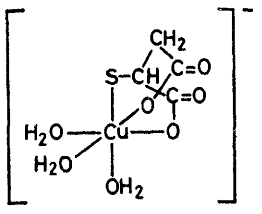
The substrate has three ionizable protons only two of which are directly important in the pH range considered.[25] Formation of the tridentate chelate complex

$$H_3L \rightleftharpoons [H_2L]^- + H^+;\ K_{a1} = 10^{-3.64}\ \text{mol dm}^{-3} \qquad (4)$$

$$[H_2L]^- \rightleftharpoons [HL]^{2-} + H^+;\ K_{a2} = 10^{-4.64}\ \text{mol dm}^{-3} \qquad (5)$$

$$[HL]^{2-} \rightleftharpoons L^{3-} + H^+;\ K_{a3} = 10^{-10.37}\ \text{mol dm}^{-3} \qquad (6)$$

$[CuL]^-$ is favourable, equation (2), with $K_1 = 10^{-2.4}$ mol^2 dm^{-6}. The probable structure contains both five- and six-membered rings and has four equatorial oxygen



donors and an axial sulphur donor consistent with the e.s.r. results. Combination of equations (2) and (4)—(6)

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[25] G. R. Lenz and A. E. Martell, *Inorg. Chem.*, 1965, **4**, 378.

gives a value of $10^{16.2}$ dm^3 mol^{-1} for the formation constant of the tridentate *OOS* chelate [equation (7)]. The

$$Cu^{2+} + L^{3-} \rightleftharpoons [CuL]^- \qquad (7)$$

stability of this chromophore is enhanced greatly over the corresponding *NOO* system as represented by aspartic acid ($10^{8.6}$ dm^3 mol^{-1}).[26] Reasons for the enhancement might be found by considering the difference in charge (2– against 3–) of the two substrates or the relief of ring strain with the larger sulphur atom. It is, however, obvious that the affinity of copper for sulphur exceeds that for nitrogen. In contrast, the corresponding equilibrium constant for bis-complex formation ($<10^{7.6}$ mol^2 dm^{-6}) is comparable to the aspartate value ($10^{6.8}$). In this case, charge and steric effects are unfavourable.

The decomposition of $[CuL]^-$ is second order in the transient concentration which is interpreted in terms of dimer formation. The reaction is acid-catalysed suggesting that opening of the chelate ring is necessary before reaction can proceed. Redox is initiated by attack by a further mol of substrate on the dimer. Since the rate is similar no matter whether the excess of substrate is in its ionized form or not, it is concluded that attack is by the sulphydryl end of the molecule. Using the value $10^{-3.64}$ mol dm^{-3} for the first K_a of 2-mercaptosuccinic acid, the ratio $k_5 : k_4$ is *ca.* 1.1 : 1 and for convenience the two rate constants will be treated as identical.

$$[CuL]^- + H^+ \rightleftharpoons [Cu(HL)]; \quad K_{a4} = 10^{-1.8}\ \text{dm}^3\ \text{mol}^{-1} \qquad (8)$$

$$[CuL]^- + [Cu(HL)] \xrightarrow{k_3} [Cu_2HL_2]^- \qquad (9)$$

$$[Cu_2HL_2]^- + H_3L \xrightarrow{k_4} [(Cu^I)_2HL] + [HL'\text{-}L'H_2]^- \qquad (10)$$

$$[Cu_2HL_2]^- + [H_2L]^- \xrightarrow{k_5} [(Cu^I)_2HL] + [HL'\text{-}L'H]^{2-} \qquad (11)$$

The initial redox product $[Cu_2(HL)]$ is further stabilized by the rapid reaction (12), thereby forming the

$$[Cu_2(HL)] + H_3L \xrightarrow{\text{fast}} [Cu_2(H_2L)_2] \qquad (12)$$

stoicheiometric product. Steps (10) and (11) provide evidence for the absence of bis complexes in the pH range under investigation. Reaction of a bis complex would involve a minimum stoicheiometric ratio of 2.5 : 1.

As the ratio $[Cu^{2+}]_0 : [H_3L]_0$ is increased a further path (13) becomes significant and the reaction ceases to be second order in the transient concentration. This

$$[Cu_2(H_2L)]^- + [CuL]^- \xrightarrow{k_6} 3[CuL]^- \qquad (13)$$

curious reaction is reversible in the presence of an excess of substrate but it is suggested that this may be the path leading to formation of the mixed-valence product $[Cu^I{}_4Cu^{II}(HL_2)_4]$. It should be noted that at pH < 2 the mixed-valence product is unstable.

Assuming the dimer to be a steady-state species leads to the rate law (14) for the reaction which reduces to (15) when $K_{a4} \gg [H^+]$. Taking the value for K_{4a} to be $10^{-1.8}$ dm^3 mol^{-1}, it is found that $k_3 = 3$ dm^3 mol^{-1} s^{-1} and $k_4/k_6 = 10^{-2}$.

$$-\frac{d[CuL^-]}{dt} = \frac{k_3k_4[H_3L][H^+]}{k_4[H_3L] + k_6[CuL^-]} \cdot \frac{K_{a4}[CuL^-]^2}{(K_{a4} + [H^+])^2} \qquad (14)$$

$$-\frac{d[CuL^-]}{dt} = \frac{K_{a4}{}^{-1}k_3k_4[H^+][CuL^-]^2}{k_4 + (k_6[CuL^-]/[H_3L])} \qquad (15)$$

At lower pH the mechanism differs only with respect to the reactive species in the oligomerization processes [equations (16) and (17)]. For conditions of $[H^+] \gg K_{a4}$

$$[Cu(HL)] + [Cu(HL)] \xrightarrow{k_7} [Cu_2HL_2]^- + H^+ \qquad (16)$$

$$[Cu_2HL_2]^- + [Cu(HL)] \xrightarrow{k_8} [Cu_2(HL)_2] + [CuL]^- \qquad (17)$$

$$-\frac{d[Cu(HL)]}{dt} = \frac{k_7k_4[Cu(HL)]^2}{k_4 + (k_8[Cu(HL)]/[H_3L])} \qquad (18)$$

the rate law becomes (18) and values of 1.6 dm^3 mol^{-1} s^{-1} and 0.15 are calculated for k_7 and k_4/k_8 respectively.

The similarity of rates k_3 and k_7 suggests that the necessary acid-catalysed ring opening involves only one of the dimer-forming reactants.

The formation of dimeric intermediates in the oxidation of mercaptocarboxylic acids by one-electron oxidants is a well characterized process.[23] Dimerization provides a two-electron template on which direct oxidation of the mercaptide to the disulphide can occur without invoking high-energy radical species. In the case of Cu^{II} the dimeric template cannot undergo spontaneous redox as was found with Fe^{III} but instead requires further reaction with substrate to stabilize the Cu^I.

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[26] S. Chabereck and A. E. Martell, *J. Amer. Chem. Soc.*, **1952**, **74**, 6021.