reaction scheme proposed in Figure 5.

In path B, the rate-determining step for the $Ni^{III}(H_{-2}Aib_3)$ reaction occurs at a later stage in the reaction sequence ([4] → [5] in Figure 5) than it does for the copper(III)-peptide oxidations of iodide. Also, path C, which will always exhibit a second-order dependence on the oxidant, carries the majority of the $Ni^{III}(H_{-2}Aib_3)-I^-$ reaction rate but is not present in the Cu(III) reactions. Thus, the oxidant reaction-rate order differences are attributable to the fact that the rate-determining step occurs at a later stage (between [4] and [5] in Figure 5) in the reaction sequence [1], [2], [4], and [5] when the oxidant is $Ni^{III}(H_{-2}Aib_3)$ rather than a copper(III)-peptide complex. The differing locations of the rate-determining steps also account for the apparent absence of reaction path A when $Ni^{III}(H_{-2}Aib_3)$ is the oxidant. Because the rate-determining step occurs late in the reaction sequence, the rate dependences of path A and path B are identical. That is, the two reaction paths, A and B, that are kinetically distinguishable in the copper(III)-peptide oxidations of iodide are merged into one combined reaction path, B, in the $Ni^{III}(H_{-2}Aib_3)$ reactions. Finally, the $M^{III}(I^-)$ species ([2] in Figure 5) is not formed in appreciable concentrations. Path C ([1] → [2] → [5]) involves the reaction of two $M^{III}(I^-)$ species, and as a consequence the rate of reaction via path C is very sensitive to the magnitude of the equilibrium constant K_0. The tetragonal d^7 nickel(III)-deprotonated peptide complexes of triglycinamide and *N*,*N*′-diglycylethylenediamine readily form axial adducts with ligands such as NH_3 and imidazole at room temperature and chloride in frozen ($N_2(l)$) aqueous glasses.[2,28] In contrast, the analogous adducts with the square-planar, d^8 copper(III) deprotonated peptides have not been detected. Thus, the equilibrium constant, K_0, is expected to be smaller for the copper(III) peptides than for the nickel(III) peptides. As a consequence, reaction paths A and B dominate the kinetics of the Cu(III) oxidations of iodide, while path C is the major kinetic pathway for the Ni(III) oxidation of iodide.

Conclusions

The oxidation of iodide to iodine by the nickel(III) complex of tri-α-aminoisobutyric acid, $Ni^{III}(H_{-2}Aib_3)$, is a thermodynamically favorable reaction that occurs by two kinetic pathways. Both pathways exhibit second-order Ni(III) and iodide dependences. The major pathway, path C, proceeds via a transition-state complex composed of two nickel-Aib_3 complexes and two iodides. The two-electron exchange between the two Ni(III) complexes and the two iodides is accomplished in one concerted reaction step. The minor reaction pathway, path B, is inhibited by the $Ni^{II}(H_{-2}Aib_3)^-$ product and proceeds via two discrete one-electron-transfer steps. The first step produces an I_2^- radical anion and $Ni^{II}(H_{-2}Aib_3)^-$. In contrast to the copper(III) reactions, the reduction of I_2^- by Ni(II) is faster than the oxidation of I_2^- to I_2 by the second equivalent of $Ni^{III}(H_{-2}Aib_3)$, and a second-order Ni(III) rate dependence is observed.

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Registry No. $Ni^{III}(H_{-2}Aib_3)(H_2O)_2$, 76757-47-6; I^-, 20461-54-5; $Ni^{II}(H_{-2}Aib_3)^-$, 76757-48-7; I_3^-, 14900-04-0.

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[28] Murray, C. K.; Margerum, D. W., to be submitted for publication.

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Rapid Electron-Transfer Reactions between Hexachloroiridate(IV) and Copper(II) Peptides

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The rates of oxidation of 12 copper(II)-peptide complexes by $IrCl_6^{2-}$ to give the copper(III) complexes are measured with use of a pulsed-flow spectrometer. The resulting second-order rate constants range from 3×10^7 to 1.1×10^9 M^{-1} s^{-1}. The rate constants for the tripeptides and tripeptide amides fit a Marcus plot corresponding to an apparent self-exchange rate constant greater than 10^8 M^{-1} s^{-1} for Cu(III)-Cu(II). However, this is more than 3 orders of magnitude larger than the directly determined self-exchange rate constant for these complexes and indicates a different mechanism for the iridium-copper cross-exchange reactions. A chloride bridge between iridium and copper is proposed. The rate constants reach limiting values as the free energy change becomes more favorable. The limiting values are consistent with an inner-sphere mechanism with substitution of an axial water of copper(II) by $IrCl_6^{2-}$.

Introduction

Copper(III) peptides are formed by hexachloroiridate(IV), $IrCl_6^{2-}$, oxidation of the corresponding copper(II) complexes,[1-3] but the reactions are too fast to be measured by stopped-flow techniques.[4] The recent development of a pulsed-flow instrument[5] permits the determination of rate constants for these reactions. The pulsed-flow method incorporates integrating observation of continuous flow[6,7] for short pulses using only 3-4 mL of each reagent per determination. Half-lives down to 40 μs for reactions under second-order conditions can be measured, allowing rate constants in excess of 10^9 M^{-1} s^{-1} to be determined. The present work complements the earlier study[4] of the reactions between copper(III) peptides and $IrCl_6^{3-}$ and extends the range of peptides by use of glycylglycyl-β-alanine (GGβA), the tripeptide of aminoisobutyric acid

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[1] Margerum, D. W.; Chellappa, K. L.; Bossu, F. P.; Burce, G. L. *J. Am. Chem. Soc.* **1975**, *97*, 6894.

[2] Bossu, F. P.; Chellappa, K. L.; Margerum, D. W. *J. Am. Chem. Soc.* **1977**, *99*, 2195.

[3] Margerum, D. W.; Wong, L. F.; Bossu, F. P.; Chellappa, K. L.; Czarnecki, J. J.; Kirksey, S. T., Jr.; Neubecker, T. A. *Adv. Chem. Ser.* **1977**, *No. 162*, 281.

[4] Owens, G. D.; Chellappa, K. L.; Margerum, D. W. *Inorg. Chem.* **1979**, *18*, 960.

[5] Owens, G. D.; Taylor, R. W.; Ridley, T. Y.; Margerum, D. W. *Anal. Chem.* **1980**, *52*, 130.

[6] Gerischer, H.; Heim, W. *Z. Phys. Chem. (Frankfurt/Main)* **1964**, *46*, 345.

[7] Gerischer, H.; Holzwarth, J.; Seifert, D.; Strohmaier, L. *Ber. Bunsenges. Phys. Chem.* **1969**, *73*, 952.

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(Aib_3),[8] and *c*-(β-alanylglycyl-β-alanylglycyl) (C).[9] The rate constants for the Ir(IV)–Cu(II) reactions are in good agreement with those calculated from the electrode potentials and the Ir(III)–Cu(III) reactions. A shift in the rate-determining step is confirmed as the free energy of the reactions changes.[4]

Copper(III)–deprotonated peptide complexes are readily prepared by chemical or electrochemical oxidation and are moderately stable in aqueous media.[1-3] The reduction potentials of these complexes are sensitive to the nature of the peptide ligand[2] spanning a range from 1.02 to 0.45 V. This permits the examination of the rate of redox reactions of the copper(III) peptides over a wide range of free energy values.

The electron-transfer characteristics of the copper(III)–peptide complexes have been examined with use of a number of reductants. In the initial investigation where $IrCl_6^{3-}$ was used, the rate constants for the reduction reactions of several uncharged copper(III) peptides exhibited a Marcus[10-14] type free energy dependence. On the basis of a self-exchange rate constant of 2.3×10^5 M^{-1} s^{-1} for the $Ir^{IV,III}Cl_6^{2-,3-}$ couple,[15] an apparent self-exchange rate constant of 7×10^7 M^{-1} s^{-1} was calculated for the copper(III, II) deprotonated peptide, $Cu^{III,II}(H_{-x}L)^{0,-}$, couple (25.0 °C, $\mu = 0.1$ M). Although the Marcus theory is derived for outer-sphere processes, a mechanism involving a chloride bridge could not be ruled out. Several negatively charged copper(III) peptides were used in the $IrCl_6^{3-}$ study to extend the range over which the rate could be examined as a function of free energy. The rate constants for the reactions of these peptide complexes with $IrCl_6^{3-}$ showed a much steeper dependence of log K_{12} than predicted by the Marcus correlation. It was suggested that the rate constants for the reverse reactions, between $IrCl_6^{2-}$ and $Cu^{II}(H_{-x}L)^{2-}$, might be diffusion limited, causing the steeper free energy dependence.

In the second study,[16] reduction of the same series of copper(III) complexes was performed with tris(1,10-phenanthroline)cobalt(II), $Co(phen)_3^{2+}$. Rapid outer-sphere electron transfer was observed. However, an unusual free energy dependence precluded a straightforward calculation of the $Cu^{III,II}(H_{-x}L)^{0,-}$ self-exchange rate.

In the third investigation the bis(2,9-dimethyl-1,10-phenanthroline)copper(I) complex was the reducing agent.[17] As in the first study,[4] the electron-transfer rate constant was observed to depend on the driving force of the reaction as predicted by Marcus for outer-sphere processes. However, the self-exchange rate for the $Cu^{II,I}(dmp)_2^{2+,+}$ couple is not well established; hence a reliable cross-check on the $Cu^{III,II}(H_{-x}L)^{0,-}$ self-exchange rate could not be made with use of this couple.

In each of these studies the thermodynamic driving force for the reactions was varied by changing the nature of the peptide ligand. The character of the correlations between the free energy and the rate constant indicated that the copper(III, II) self-exchange rate constants are very similar for all of the copper–peptide complexes.

A recent study[18] of the copper(III, II) deprotonated peptide self-exchange process using NMR line-broadening measurements and observations of copper(III) tetrapeptide + copper(II) tripeptide cross reactions shows that the self-exchange rate constant for the outer-sphere process is only 5.5×10^4 M^{-1} s^{-1} (25.0 °C, $\mu = 0.1$ M). However, the observed rate constants for the oxidation of copper(II) peptides by $IrCl_6^{2-}$ are many orders of magnitude larger than the rate constants calculated from the above self-exchange rate constant for the copper(III, II) peptide couples and the self-exchange rate constant of 2.3×10^5 M^{-1} s^{-1} for the hexachloroiridate(IV, III) couple. Hence, the cross reaction between the $IrCl_6^{2-,3-}$ couple and the copper(III, II) peptides must proceed by a mechanism other than simple outer sphere. A weak inner-sphere interaction with an axial chloride bridge between iridium and the copper peptide is proposed. The limiting rate constants for the reaction of $IrCl_6^{2-}$ and copper(II) peptides at the more favorable $\Delta E°$ values fit the inner-sphere model, with substitution of an axial H_2O on Cu(II), better than they fit a diffusion-limited process. The inner-sphere model also provides some rationale for the anomalous behavior of the copper(II) tetra-L-valine and copper(II) tetra-L-alanine complexes due to their steric characteristics.

Experimental Section

Reagents. Except for the tripeptide of α-aminoisobutyric acid,[8] all the oligopeptides were obtained from Vega Fox or Biosynthetika and were used without further purification. The following abbreviations are used for the amino acid residues (L isomers) of the peptides: glycyl, G; alanyl, A; β-alanyl, βA; valyl, V; leucyl, leu; prolyl, P; α-aminoisobutyric acid, Aib; *c*-(β-alanylglycyl-β-alanylglycyl), C; G_3a, glycylglycylglycylamide, etc. Millimolar solutions of the copper(II) complexes were prepared by the reaction of solutions of $Cu(ClO_4)_2$ (standardized by EDTA titration) with peptides in 5–10% excess. The pK_a values of these complexes[3] are such that the fully deprotonated form predominates above pH 10. Hence, the pH of the freshly prepared solutions was raised to pH 10.5. The resulting solutions were then diluted ($\sim 10^{-5}$ M) and their ionic strengths adjusted to 0.10 M with $NaClO_4$ at pH 10.5 before reaction with $IrCl_6^{2-}$. The above procedure was followed for each of the copper(II) peptides except $Cu^{II}(H_{-3}V_4)^{2-}$. Spectral changes show that this complex, unlike the others, has a pK_a value above 10. Hence, the pH of the freshly prepared solution was raised to 11 and its ionic strength adjusted to 0.1 M.

As in the previous investigation[4] using other copper(III) peptides, oxidation of the millimolar solution of $Cu^{II}(H_{-2}G_2\beta A)^-$ to the corresponding copper(III) complex was accomplished electrochemically by using obtained, system in which the electrode arrangement included a graphite-powder working electrode packed in a porous glass column, wrapped externally with a platinum-wire electrode.[19] The resulting copper(III) solution was diluted (3×10^{-5}) and its ionic strength adjusted to 0.1 M with $NaClO_4$.

Crystalline sodium hexachloroiridate(III) was prepared by the method of Poulsen.[20] The iridium content of the solid was evaluated by oxidation with $Cl_2(g)$ followed by spectrophotometric determination of $IrCl_6^{2-}$ ($\lambda_{max} = 490$ nm, $\epsilon = 4075$ M^{-1} cm^{-1}).[21] Solutions of $IrCl_6^{3-}$ (4×10^{-5} M) were prepared from the solid not more than 1 h before each kinetic determination and were buffered with 0.02 M acetic acid at pH 4.7. The ionic strength of the buffered $IrCl_6^{3-}$ solutions was adjusted to 0.1 M with $NaClO_4$, allowing for contribution from the buffer salt.

Commercial sources of Na_2IrCl_6 contain varying amounts of $Ir^{III}Cl_6^{3-}$, and therefore pure $Na_2Ir^{IV}Cl_6$ was obtained by bubbling Cl_2 through solutions which were then freeze-dried. Stock solutions of $IrCl_6^{2-}$ were freshly prepared before 0.2235 g set of experiments and kept slightly acidic to avoid decomposition. Solutions for kinetic runs were prepared by diluting the stock solution with 0.02 M borate buffer at pH 8 and $\mu = 0.1$ M. The stability of $IrCl_6^{2-}$ in this medium was monitored by the absorbance of the $IrCl_6^{2-}$ at 490 nm as a function of time. In a 10-min time period, after dilution of the stock solution in the pH 8 buffer, less than 2% loss of $IrCl_6^{2-}$ was observed. All kinetic runs were performed with $IrCl_6^{2-}$ solutions which had aged less than 10 min.

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(8) Kirksey, S. T., Jr.; Neubecker, T. A.; Margerum, D. W. *J. Am. Chem. Soc.* **1979**, *101*, 1631.
(9) Rybka, J. S.; Margerum, D. W. *Inorg. Chem.* **1980**, *19*, 2784.
(10) Marcus, R. A. *J. Chem. Phys.* **1956**, *24*, 966.
(11) Marcus, R. A. *Discuss. Faraday Soc.* **1960**, *29*, 21.
(12) Marcus, R. A. *J. Phys. Chem.* **1963**, *67*, 853, 2889.
(13) Marcus, R. A. *Annu. Rev. Phys. Chem.* **1964**, *15*, 155.
(14) Marcus, R. A. *J. Chem. Phys.* **1965**, *43*, 679.
(15) Hurwitz, P.; Kustin, K. *Trans. Faraday Soc.* **1966**, *62*, 427.
(16) DeKorte, J. M.; Owens, G. D.; Margerum, D. W. *Inorg. Chem.* **1979**, *18*, 1538.
(17) Lappin, R. G.; Youngblood, M. P.; Margerum, D. W. *Inorg. Chem.* **1980**, *19*, 407.
(18) Koval, C. A.; Margerum, D. W. *Inorg. Chem.*, in press.
(19) Clark, B. R.; Evans, D. H. *J. Electroanal. Chem.* **1965**, *69*, 181.
(20) Poulsen, I. A.; Garner, C. S. *J. Am. Chem. Soc.* **1962**, *84*, 2032.
(21) Thorneley, R. N.; Sykes, A. G. *Chem. Commun.* **1969**, 331.

The above procedure was used for all of the oxidation reactions except for that involving $Cu^{II}(H_{-3}V_4)^{2-}$. Because the pK_a for this complex is higher than the others, the $IrCl_6^{2-}$ solution was diluted in unbuffered 0.1 M $NaClO_4$. Upon mixture with the $Cu^{II}(H_{-3}V_4)^{2-}$ solution, at pH 11, the pH of the reaction mixture remained above 10.5, insuring complete production of the $Cu^{III}(H_{-3}V_4)^{-}$.

The reaction of $IrCl_6^{2-}$ (2×10^{-5} M) with 10^{-3} M NaOH was shown to be negligible during the pulsed-flow measurements with absorbance changes corresponding to those expected for dilution.

Kinetic Measurements. The rates of the oxidation–reduction reactions were measured with a pulsed-flow spectrometer interfaced to a Hewlett-Packard Model 2100A general-purpose computer.[5] The mixing cell and drive syringe block were thermostated at 25.0 °C. Reactions were monitored by following the formation or loss of $IrCl_6^{2-}$ at 490 nm. The velocities used with pulsed flow were varied in a random fashion in any given set of pushes to minimize the effect of optical system drift and decomposition of the $IrCl_6^{2-}$ at pH 8. All solutions were filtered and degassed by aspiration with stirring before introduction into the instrument. The absorbance of each reaction medium as a function of velocity was evaluated prior to performing kinetic determinations. These background absorbances were substracted from absorbance values obtained at the same velocity when a chemical process was being observed. Initial absorbance values, A_0, were determined by introducing the reactants separately into both drive syringes, rinsing the syringes and cell several times, and then acquiring the absorbance value at a low flow velocity where background absorbances are negligible. Final absorbance values, A_∞, were determined by mixing equal volumes by pipet of the reactants outside the instrument and then introducing the mixture into both drive syringes as above.

pH of Reaction Media. Several factors contributed to the choice of a reaction media at pH ~8. In this scheme, $IrCl_6^{2-}$ is buffered at pH 8 and the copper(II) peptide is held at higher pH until reaction in the pulsed flow. During the mixing process the Cu(II) solutions undergo a pH jump down to pH 8. Equilibration of the fully deprotonated form of the Cu(II) complex with various protonated species must be considered. The acid dissociation kinetics of $Cu^{II}(H_{-3}G_4)^{2-}$[22] and of several copper(II) deprotonated tripeptides[23] have been examined in detail. In the case of $Cu^{II}(H_{-3}G_4)^{2-}$, the rate constant for acid dissociation at pH 8 is <20 s^{-1}. The acid dissociation rate constants for the tripeptides are approximately 2 orders of magnitude lower under the same conditions. The slowest of the electron-transfer reactions in this study, between $IrCl_6^{2-}$ and $Cu^{II}(H_{-2}A_3)^-$, has a first half-life at $C_0 = 2.1 \times 10^{-5}$ M of 1.3 ms. Hence, the redox reactions are much faster than the most rapid acid dissociation reaction.

Higher pH values were avoided to prevent the rapid decomposition of $IrCl_6^{2-}$ and of the copper(III) peptide product. This allowed the measured values of A_0 and A_∞ to be more reliable, increasing the accuracy of the data analysis.

Data Treatment. Table I summarizes the absorbance values for the reactants and products as well as the steady-state absorbance as a function of flow velocity for each reaction mixture. The individual rate constant values are calculated in one of the following ways.

The reduction of $Cu^{III}(H_{-2}G_2\beta A)$ by $IrCl_6^{3-}$ and the oxidation of $Cu^{II}(H_{-2}A_3)^-$ by $IrCl_6^{2-}$ have small driving forces and must be treated as reversible reactions. The data analysis derived by Gerischer, Holzwarth, Seifert, and Strohmaier[24] for reversible second-order reactions, where the initial reactant concentrations are equal, was used. The appropriate relationships are summarized in eq 1–4. In these expressions A is the steady-state absorbance measured at constant flow velocity and A_0 and A_∞ are defined as in the Experimental Section. K is the equilibrium constant, k is the second-order rate constant, C_0 is the initial reactant concentration, l is the length of the flow cell (0.020 m), and v is the flow velocity.

$$M = (A - A_\infty)/(A_0 - A_\infty) \tag{1}$$

$$M = 1 - \frac{1}{Y}\left[\ln\,(\exp(Y) + Z) + \frac{1}{Z}\ln\,(1 + Z\exp(-Y)) - \frac{1+Z}{Z}\ln\,(1 + Z)\right] \tag{2}$$

$$Z = (1 - K^{1/2})/(1 + K^{1/2}) \tag{3}$$

$$Y = kC_0(l/v)\frac{2}{K^{1/2}} \tag{4}$$

The oxidations of $Cu^{II}(H_{-2}A_3)^-$, $(Cu^{II}(H_{-2}leu_3)^-$, and $Cu^{II}(H_{-3}G_4)^{2-}$ by $IrCl_6^{2-}$ were carried out under second-order conditions where the initial reactant concentrations were unequal. Hence, the data treatment derived by Gerischer and Heim[25] for the second-order-unequal case (eq 5–8) were used. In these expressions C_A and C_B are the initial concentrations of the reactants, A_A and A_B are the initial absorbances of the reactants, and A_P is the absorbance of the products of the reaction. The other terms are defined as above.

$$C_B = qC_A \tag{5}$$

$$M = \frac{A - A_A(1 - q) - A_P}{A_A + 1/q(A_B - A_P)} \tag{6}$$

$$M = (1 - q)(1/R)\ln\frac{1 - qe^{-R}}{1 - q} \tag{7}$$

$$R = k(l/v)C_A(1 - q) \tag{8}$$

The remainder of the reactions were carried out under second-order-equal concentration conditions. The relationships derived[6] for this case are given in eq 9–11.

$$M = (A - A_\infty)/(A_0 - A_\infty) \tag{9}$$

$$M = \ln\,(x + 1)/x \tag{10}$$

$$x = kC_0l/v \tag{11}$$

Previous work[5,26] has shown that eq 9–11 cannot be reliably applied to reactions whose half-lives are much less than 1 ms without incurring errors due to mixing effects. Hence, at initial concentration levels of 10^{-5} M, rate constants obtained from eq 9–11 with values much in excess of 10^8 M^{-1} s^{-1} would be prejudiced to lower values due to the mixing effect. An empirical correction scheme has been developed[5,26] which is based on a linear dependence of the absorbance quotient, $(A - A_\infty)/(A_0 - A_\infty)$, on the first half-life of a known system. Using a plot of $(A - A_\infty)/(A_0 - A_\infty)$ vs. half-life for the Ce(IV) + $Fe(CN)_6^{4-}$ system has allowed the pulsed-flow instrument to be calibrated for $t_{1/2}$ down to 40 μs.[5] Thus, half-lives less than 1 ms are obtained from such a calibration plot.

Equations 9–11 were applied to the reactions of $Cu^{II}(H_{-3}G_3AOCH_3)^-$, $Cu^{II}(H_{-3}AG_3)^{2-}$, $Cu^{II}(H_{-3}A_4)^{2-}$, and $Cu^{II}(H_{-3}V_4)^{2-}$. However, the calibration plot was used to obtain first half-lives for the reactions of $Cu^{II}(H_{-3}G_4a)^-$, $Cu^{II}(H_{-3}G_3a)^-$, and $Cu^{II}(H_{-3}PG_2a)^-$.

Results and Discussion

The redox rate constants reported previously[4] for copper(III) and Ir(III) correspond to k_1 in eq 12. In the present work

$$Cu^{III}(H_{-x}L)^{n-} + IrCl_6^{3-} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} Cu^{II}(H_{-x}L)^{(n+1)-} + IrCl_6^{2-} \tag{12}$$

the value of k_1 for the $G_2\beta A$ complex is measured and k_1 values are calculated for the Aib_3 and C complexes. Values of the reverse rate constant, k_{-1}, are determined for 12 Cu(II)-peptide complexes reacting with Ir(IV) as summarized in Table II. The ratios of the experimental values for k_1/k_{-1} permit electrode potentials to be calculated from the kinetic data, $E_{KIN}°$, which are in good agreement with the $\Delta E°$ values determined by cyclic voltammetry. As seen in Table II, these values agree within ±10 mV in most cases, with a larger but not serious disagreement noted for the A_3, G_4a, PG_2a, and V_4 complexes. Thus, the earlier conclusion that the uphill reactions between Cu(III) and Ir(III) corresponded to the redox step rather than to the acid dissociation reaction of the cop-

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(22) Youngblood, M. P.; Margerum, D. W. *Inorg. Chem.* **1980**, *19*, 3072.

(23) Hauer, H.; Dukes, G. R.; Margerum, D. W. *J. Am. Chem. Soc.* **1973**, *95*, 3515.

(24) Gerischer, H.; Holzwarth, J.; Seifert, D.; Strohmaier, L. *Ber. Bunsenges. Phys. Chem.* **1970**, *74*, 589.

(25) Gerischer, H.; Heim, W. *Ber. Bunsenges. Phys. Chem.* **1967**, *71*, 1040.

(26) Gerischer, H.; Holzwarth, J.; Seifert, D.; Strohmaier, L. *Ber. Bunsenges. Phys. Chem.* **1972**, *76*, 11.

Table I. Kinetic Data for the Reaction of Hexachloroiridate(IV) with Copper(II) Peptides As Determined by Pulsed Flow[a]

reactants	velocity, m/s	abs[b]	$10^{-8}k$,[c] $M^{-1}\ s^{-1}$
$IrCl_6^{3-} + Cu^{III}(H_{-2}G_2\beta A)$[d]	4.18	0.0967	0.042
	4.87	0.0904	0.039
	6.46	0.0881	0.048
	7.29	0.0845	0.048
	8.72	0.0812	0.051
	9.37	0.0826	0.058
$IrCl_6^{2-} + Cu^{II}(H_{-2}A_3)^-$[e,f]	3.95	0.0755	0.035
	4.74	0.0830	0.031
	5.46	0.0855	0.033
	6.28	0.0858	0.038
	7.23	0.0894	0.038
	7.86	0.0911	0.039
	8.54	0.0941	0.039
	9.39	0.0954	0.040
$IrCl_6^{2-} + Cu^{II}(H_{-2}L_3)^-$[e,g]	4.05	0.0491	0.66
	4.89	0.0502	0.75
	5.50	0.0523	0.76
	6.46	0.0589	0.64
$IrCl_6^{2-} + Cu^{II}(H_{-2}L_3)^-$[e,g]	7.20	0.0598	0.68
	8.06	0.0631	0.64
	9.31	0.0647	0.69
$IrCl_6^{2-} + Cu^{II}(H_{-3}G_3AOCH_3)^-$[e,h]	4.00	0.0335	1.1
	4.82	0.0354	1.1
	5.64	0.0362	1.2
	6.35	0.0380	1.1
	7.21	0.0393	1.3
	7.95	0.0402	1.3
	8.63	0.0440	1.1
	9.24	0.0430	1.3
$IrCl_6^{2-} + Cu^{II}(H_{-3}G_4a)^-$[e,h]	4.83	0.0208	9.4
	5.70	0.0204	11
	6.46	0.0204	13
	7.33	0.0224	11
	7.93	0.0233	11
	8.84	0.0241	11
	9.42	0.0251	11
$IrCl_6^{2-} + Cu^{II}(H_{-3}G_3a)^-$[e,i]	4.57	0.0225	6.8
	5.61	0.0231	6.8
	6.54	0.0239	6.8
	7.37	0.0245	7.7
	8.04	0.0253	7.9
	8.70	0.0241	9.3
	9.61	0.0272	7.7
$IrCl_6^{2-} + Cu^{II}(H_{-3}PG_2a)^-$[e,i]	4.81	0.0230	7.6
	5.69	0.0226	9.2
	6.58	0.0246	7.5
	7.33	0.0248	9.0
	8.10	0.0262	8.4
	8.79	0.0255	9.5
	9.45	0.0264	9.4
$IrCl_6^{2-} + Cu^{II}(H_{-3}G_4)^{2-}$[e,j]	4.84	0.0329	1.3
	5.75	0.0372	1.2
	6.44	0.0354	1.5
	7.25	0.0382	1.5
	7.91	0.0375	1.7
	8.68	0.0406	1.5
$IrCl_6^{2-} + Cu^{II}(H_{-3}AG_3)^{2-}$[e,k]	4.81	0.0348	1.1
	5.58	0.0372	1.1
	6.46	0.0372	1.3
	7.89	0.0385	1.5
	8.63	0.0398	1.5
	9.16	0.0384	1.7
$IrCl_6^{2-} + Cu^{II}(H_{-3}A_4)^{2-}$[e,l]	4.87	0.0478	0.41
	5.64	0.0511	0.38
	6.42	0.0497	0.48
	7.16	0.0516	0.47
	7.86	0.0524	0.48
	8.46	0.0536	0.48
	9.18	0.0536	0.52
$IrCl_6^{2-} + Cu^{II}(H_{-3}V_4)^{2-}$[m]	3.96	0.0557	0.25
	4.71	0.0544	0.33
	5.60	0.0592	0.27
	6.35	0.0600	0.29
	7.15	0.0617	0.28
	7.97	0.0624	0.30
	8.54	0.0625	0.32
	9.34	0.0657	0.26

[a] $T = 25.0\ °C$, $\mu = 0.1$ M ($NaClO_4$). For reactions under second-order equal conditions the initial concentration of both reactants is C_0. [b] Corrected for background absorbance due to media (see text). [c] Not corrected for diffusion effects. [d] pH 4.72, $[HOAc]_T = 0.01$ M, $C_0 = 2.0 \times 10^{-5}$ M, $A_0 = 0.0305$, $A_\infty = 0.1250$. [e] $[H_3BO_3]_T = 0.01$ M, pH 8.0. [f] $C_0 = 2.1 \times 10^{-5}$ M, $A_0 = 0.1524$, $A_\infty = 0.040$. [g] $[Cu^{II}(H_{-2}L_3)^-] = 1.5 \times 10^{-5}$ M, $[IrCl_6^{2-}] = 1.27 \times 10^{-5}$ M, $A_A = 0.0038$, $A_B = 0.1036$, $A_P = 0.0197$. [h] $C_0 = 9.25 \times 10^{-6}$ M, $A_0 = 0.0775$, $A_\infty = 0.0092$. [i] $C_0 = 9.25 \times 10^{-6}$ M, $A_0 = 0.0774$, $A_\infty = 0.0076$. [j] $[Cu^{II}(H_{-3}G_4)^{2-}] = 1.5 \times 10^{-5}$ M, $[IrCl_6^{2-}] = 1.25 \times 10^{-5}$ M, $A_A = 0.0030$, $A_B = 0.1016$, $A_P = 0.0115$. [k] $C_0 = 9.70 \times 10^{-6}$ M, $A_0 = 0.0809$, $A_\infty = 0.0073$. [l] $C_0 = 9.00 \times 10^{-6}$ M, $A_0 = 0.0755$, $A_\infty = 0.0090$. [m] $[NaOH] = 5 \times 10^{-4}$ M, $C_0 = 1.07 \times 10^{-5}$ M, $A_0 = 0.0803$, $A_\infty = 0.0132$.

per(II) peptides is verified. As the Ir(IV) oxidation reactions become more favorable (i.e., the $E°$ for eq 12 given in Table II become more negative) the rate constants (k_{-1}) first increase and then level off. This is seen in Figure 1 where log k_1 and log k_{-1} are plotted against log K_{12} (where K_{12} is the equilibrium constant for reaction 12). This plot can be divided roughly into two regions. For log $K_{12} > -4$, the rate constants for both oxidation of copper(II) and reduction of copper(III) are in qualitative agreement with the solid lines with slopes equal to ±0.5. In the region of log $K_{12} < -4$, the rate constants for the copper(III) reduction reactions show a steeper free energy dependence, with a slope of approximately 1. In this same region the rates of the copper(II) oxidation reactions show little dependence on K_{12}. The behavior of tetra-L-alanine and tetra-L-valine suggests that additional steric factors cause deviations for these complexes.

Attempts to measure the rate constant of the reaction between $IrCl_6^{3-}$ and $Cu^{III}(H_{-2}Aib_3)$ indicate that the reaction is biphasic, exhibiting a pH dependence from pH 4 to 5. These characteristics are consistent with a change in the rate step from electron transfer to acid dissociation of $Cu^{II}(H_{-2}Aib_3)^-$. Although the $Cu^{II}(H_{-2}G_3)^-$ acid dissociation is catalyzed by acetic acid,[27] this is not the case for the acid dissociation of $Cu^{II}(H_{-2}Aib_3)^-$. Thus, the magnitude of the acid dissociation rate constant at pH 5 (0.05 M $HOAc_T$, 25.0 °C, $\mu = 0.1$ M) is only ~30 s^{-1} for $Cu(H_{-2}Aib_3)^-$, and this accounts for the biphasic nature of the reduction with $IrCl_6^{3-}$ because the electron-transfer reaction is not rate determining for the entire reaction. Thus, a rate constant of $6.9 \times 10^4\ M^{-1}\ s^{-1}$ (calculated from $K_{12}k_{-1} = (1.3 \times 10^{-4})(5.8 \times 10^8\ M^{-1}\ s^{-1})$) is reported in Table II for k_1.

The characteristics of the $Cu^{III,II}(H_{-4}C)^{-,2-}$ couple are reported in more detail elsewhere.[28] Direct determination of the rate constant for $Cu^{III}(H_{-4}C)^-$ reacting with $IrCl_6^{3-}$ is possible at pH 3, but the results are complicated by the pos-

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(27) Bannister, C. E.; Margerum, D. W.; Raycheba, J. M. T.; Wong, L. F. *Symp. Faraday Soc.* **1975**, *10*, 78.

(28) Rybka, J. S.; Margerum, D. W. *Inorg. Chem.*, companion paper in this issue.

Table II. Rate Constants for the Reaction of Hexachloroiridate with Copper Peptides as a Function of Driving Force[a]

L	$\Delta E°$,[b] V	$10^{-4}k_1$,[c] M^{-1} s^{-1}	$10^{-8}k_{-1}$, M^{-1} s^{-1}	$\Delta E_{KIN}°$,[d] V
		$Cu^{III,II}(H_{-x}L)^{0,-}$		
$G_2\beta A$	0.05	5000 (±1000)	0.071[e]	
A_3	−0.08	54	0.37 (±0.03)	−0.11
leu_3	−0.12	51	0.69 (±0.05)	−0.13
G_3AOCH_3	−0.19	9.3	1.2 (±0.1)	−0.18
G_4a	−0.21	10.1	11 (±1)	−0.24
Aib_3	−0.23	7.4[e]	5.8 (±0.6)[f]	
G_3a	−0.25	3.4	7.6 (±0.9)	−0.26
VG_2a	−0.28	0.93		
G_2Aa	−0.29	0.92		
PG_2a	−0.29	0.58	8.7 (±0.8)	−0.31
		$Cu^{III,II}(H_{-x}L)^{-,2-}$		
G_4	−0.26	1.0	1.5 (±0.17)	−0.25
AG_3	−0.28	0.31	1.4 (±0.2)	−0.28
A_4	−0.29	0.075	0.46 (±0.05)	−0.28
V_4	−0.38	0.0020	0.29 (±0.03)	−0.36
C	−0.41	0.0047[e]	4.1 (±0.4)[g]	

[a] $T = 25.0$ °C, $\mu = 0.1$ M. [b] Defined for the reaction of copper(III) peptide + $IrCl_6^{3-}$ where $E° = 0.892$ V vs. NHE for the $Ir^{IV,III}Cl_6^{2-,3-}$ couple.[2] $E°$ values for the copper(III, II) couples are from refs 1, 4, 15, and 25. [c] Values of k_1 from ref 4 except for the reaction between $IrCl_6^{3-}$ and $Cu^{III}(H_{-2}G_2\beta A)$ determined in this work. [d] Calculated from $E° = 0.0591 \log (k_1/k_{-1})$. [e] Calculated from $E°$ and k_{-1} (see text). [f] This determination reported in detail in ref 18. [g] This determination reported in detail in ref 28.

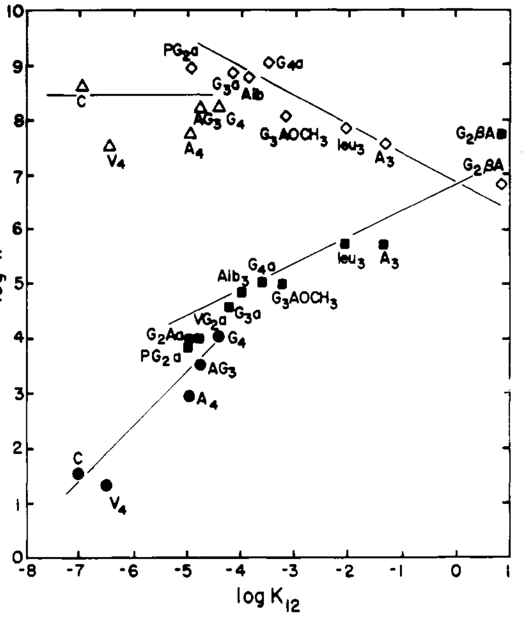

Figure 1. Free energy dependence for the rate of electron transfer for the partners of the copper(III, II) peptide and hexachloroiridate(IV, III) couples: △, $IrCl_6^{2-} + Cu^{II}(H_{-x}L)^{2-}$; ◇, $IrCl_6^{2-} + Cu^{II}(H_{-x}L)^-$; ■, $IrCl_6^{3-} + Cu^{III}(H_{-x}L)$ (value for Aib_3 is calculated; see text); ●, $IrCl_6^{3-} + Cu^{III}(H_{-x}L)^-$ (values for C and V_4 are calculated; see text).

sibility of contributions from protonated forms of the copper(III) species. Hence, the experimentally determined rate constant of 100 M^{-1} s^{-1} is suspect and a calculated value of 47 M^{-1} s^{-1} (from $K_{12}k_{-1} = (1.2 \times 10^{-7})(4.1 \times 10^8\ M^{-1}\ s^{-1})$) is reported in Table II for k_1.

Table II also shows a calculated k_{-1} value for the reaction of $IrCl_6^{2-}$ with $Cu^{II}(H_{-2}G_2\beta A)^-$. The value was determined from the quotient $k_1/K_{12} = 5.0 \times 10^7\ M^{-1}\ s^{-1}/7.0$ and could not be determined experimentally because the reaction is a thermodynamically unfavorable process with relatively stable products.

Models for the Electron-Transfer Process. In the previous investigation,[4] the reaction shown in eq 12 was initially expected to be a simple outer-sphere process for several reasons. Both partners in the $Ir^{IV,III}Cl_6^{2-,3-}$ couple have slow substitution reactions[29] and are known to undergo outer-sphere electron transfer with a variety of compounds.[30] The d^8, low-spin copper(III) complexes are also characterized by slow in-plane substitution reactions since redox decomposition is observed for these species rather than substitution.[31] The expectation of an outer-sphere reaction was supported by the fact that the free energy dependence for the reduction of the copper(III) peptides by $IrCl_6^{3-}$ showed Marcus[10–14] behavior. The steep slope of the free energy dependence of the rate constants, k_1, in the $\log K_{12} < -4$ region was rationalized by assuming that the reverse rate constants, k_{-1}, had reached a diffusion limit. However, the simple outer-sphere model has been discarded for the following reasons.

First, the outer-sphere model predicts a self-exchange rate constant $>10^8\ M^{-1}\ s^{-1}$ for the $Cu^{III,II}(H_{-x}L)^{0,-}$ couple. More direct evidence has recently been obtained which indicates that this value is several orders of magnitude too large. The self-exchange rate constant for the $Cu^{III,II}(H_{-2}Aib_3)^{0,-}$ couple was determined by NMR line broadening of the proton signals of the diamagnetic $Cu^{III}(H_{-2}Aib_3)$ complex as small amounts of the paramagnetic $Cu^{II}(H_{-2}Aib_3)^-$ complex were added.[18] From these observations a self-exchange rate constant of $5.5 \times 10^4\ M^{-1}\ s^{-1}$ (25.0 °C, $\mu = 0.1$ M) was calculated for the $Cu^{III,II}(H_{-2}Aib_3)^{0,-}$ couple. With this self-exchange rate constant and the value of $2.3 \times 10^5\ M^{-1}\ s^{-1}$ for the $Ir^{IV,III}Cl_6^{2-,3-}$ couple,[15] a cross-exchange rate constant of $6.9 \times 10^6\ M^{-1}\ s^{-1}$ is calculated from the Marcus theory[10–14] for the reaction of $IrCl_6^{2-}$ with $Cu^{II}(H_{-2}Aib_3)^-$. As shown in Table II, a rate constant of $5.8 \times 10^8\ M^{-1}\ s^{-1}$ is observed. This observation indicates that the reaction with $IrCl_6^{2-}$ proceeds via a different, more facile pathway than is observed in the self-exchange process. The cross reactions with the $Ir^{IV,III}Cl_6^{2-,3-}$ couple may proceed more rapidly because of the formation of an axial chloride bridge between iridium and copper.

Second, the outer-sphere model predicts a diffusion-limiting rate constant approximately 10 times larger than the observed limiting rate constant for the reaction of the 2− charged complexes with $IrCl_6^{2-}$. The diffusion limit for the oxidations of $Cu^{II}(H_{-3}G_4)^{2-}$, $Cu^{II}(H_{-3}AG_3)^{2-}$, and $Cu^{II}(H_{-4}C)^{2-}$ by $IrCl_6^{2-}$ is calculated as follows. The radius of the copper(II) complex in the plane of the peptide nitrogens can be taken to be approximately 4 Å (estimated by the metal to peptide oxygen distance in the crystal structure of $Cu^{II}(H_{-3}G_4)^{2-}$).[32] Evidence for axial hydration of copper(II)–peptide complexes has been found in the reaction entropies of several copper(III, II) peptide couples as determined by cyclic voltammetry.[33] From crystallographic data, Freeman[34] suggests that the axial $Cu{-}{-}{-}OH_2$ distance in several copper(II)–peptide complexes is from 2.3 to 2.5 Å. Thus, the radius of the copper(II) complexes in the axial direction can be approximated as the copper to water–hydrogen distance of 3.2 Å. The diffusion coefficient for these copper(II) complexes is estimated by the value of 4×10^{-6} cm^2/s for $Ni^{II}(H_{-2}G_3)^-$.[35] For $IrCl_6^{2-}$, the radius is 3.4 Å and the diffusion coefficient is 8.2×10^{-6} cm^2/s.[36] With these values for the radii and diffusion coefficients and the Debye equation (eq 13–15),[37] the diffusion-limited rate constant, k_D,

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(29) Bauer, R. A.; Basolo, F. *Inorg. Chem.* **1969**, *8*, 2237.
(30) Cecil, R.; Littler, J. S.; Easton, G. *J. Chem. Soc. B* **1970**, 626.
(31) Rybka, J. S.; Kurtz, J. L.; Neubecker, T. A.; Margerum, D. W. *Inorg. Chem.* **1980**, *19*, 2791.
(32) Freeman, H. C.; Taylor, M. R. *Acta Crystallogr.* **1965**, *18*, 939.
(33) Youngblood, M. P.; Margerum, D. W. *Inorg. Chem.* **1980**, *19*, 3068.
(34) Freeman, H. C. *Adv. Protein Chem.* **1967**, *22*, 257.
(35) Nag, K.; Banerjee, P. J. *J. Inorg. Nucl. Chem.* **1975**, *31*, 1521.
(36) Holzwarth, J.; Jurgensen, H. *Ber. Bunsenges. Phys. Chem.* **1974**, *78*, 526.

$$k_D = 4\pi(D_A + D_B)(r_A + r_B)\frac{N_0}{10^3}\frac{\delta}{e^{\delta} - 1} \times \exp[\epsilon\kappa(r_A + r_B)/(1 + \kappa(r_A + r_B))] \quad (13)$$

$$\delta = Z_A Z_B e_0^2/\epsilon k_B T(r_A + r_B) \quad (14)$$

$$\kappa = 8\pi N_0 e_0^2 \mu/10^3 \epsilon k_B T \quad (15)$$

can be calculated. This form of the Debye equation is modified for Coulombic interactions, and the standard shielding term[38] is used to correct for ionic media. Diffusion-limited rate constants of 2.9×10^9 and 1.9×10^9 M^{-1} s^{-1} are calculated for axial and equatorial interactions of the $Cu^{II}(H_{-x}L)^{2-}$ and $IrCl_6^{2-}$ species, respectively. These values are nearly 10 times larger than the approximate limit of 3×10^8 M^{-1} s^{-1} for k_{-1} in the reactions of $Cu^{II}(H_{-4}G_4)^{2-}$, $Cu^{II}(H_{-4}AG_3)^{2-}$, and $Cu^{II}(H_{-4}C)^{2-}$ with $IrCl_6^{2-}$ given in Table II.

Third, an inner-sphere model, that proceeds by axial substitution on the Cu(II) complex by $IrCl_6^{2-}$, provides a rationale for the behavior of the $Cu^{II}(H_{-3}A_4)^{2-}$ and $Cu^{II}(H_{-3}V_4)^{2-}$ reactions with $IrCl_6^{2-}$ on the grounds of steric hindrance. Construction of CPK space-filled models of the copper(II) tetra-L-valine and copper(II) tetra-L-alanine complexes suggests that significant steric crowding may occur if all the hydrophobic substituents on the α-carbon of the peptide are oriented toward the same side of the square-planar complex. This effect is especially evident in the case of the tetra-L-valine complex. If all four isopropyl substituents are oriented toward the same side of the square plane, then binding of the fourth peptide nitrogen to the metal is severely hindered. However, if the fourth isopropyl group is rotated toward the side of the plane opposite the first three, then complex formation is much easier. Orientation of the fourth isopropyl group toward the opposite side of the square plane causes some steric hindrance to any large molecules approaching either axial position. Hence, steric barriers to axial approach and bridging might explain the slower rate constants for the tetra-L-valine and, possibly, tetra-L-alanine complexes. Larger hydrophobic groups are present in the tri-L-leucine complex; however, all three of the residues are oriented in the same direction, leaving one axial site unhindered.

Because of the considerations outlined above, an inner-sphere model that proceeds via axial substitution on the Cu(II) complex is proposed. Equation 16 is the diffusion process

$$Cu^{III}(H_{-x}L)^{n-} + Ir^{III}Cl_6^{3-} \underset{k_{-D1}}{\overset{k_{D1}}{\rightleftharpoons}} [Cu^{III}(H_{-x}L)\cdot Ir^{III}Cl_6]^{(3+n)-} \quad (16)$$

resulting in the formation of the copper(II)–iridium(III) encounter complex. The electron-transfer step is given in eq 17,

$$[Cu^{III}(H_{-x}L)\cdot Ir^{III}Cl_6]^{(3+n)-} + H_2O \underset{k_{-e}}{\overset{k_e}{\rightleftharpoons}} [Cu^{II}(H_{-x}L)(H_2O)\cdot Ir^{IV}Cl_6]^{(3+n)-} \quad (17)$$

where the proposed reaction complex in Figure 2 adds an axial water either before or after the electron transfer. Equations 18 and 19 represent the movement of $Ir^{IV}Cl_6^{2-}$ from the inner

$$[Cu^{II}(H_{-x}L)(H_2O)\cdot Ir^{IV}Cl_6]^{(3+n)-} + H_2O \underset{k_{-s}}{\overset{k_s}{\rightleftharpoons}} [Cu^{II}(H_{-x}L)(H_2O)_2\cdot Ir^{IV}Cl_6]^{(3+n)-} \quad (18)$$

$$[Cu^{II}(H_{-x}L)(H_2O)_2\cdot Ir^{IV}Cl_6]^{(3+n)-} \underset{k_{-D2}}{\overset{k_{D2}}{\rightleftharpoons}} Cu^{II}(H_{-x}L)(H_2O)_2^{(n+1)-} + Ir^{IV}Cl_6^{2-} \quad (19)$$

coordination sphere of the copper(II) complex followed by separation of the products.

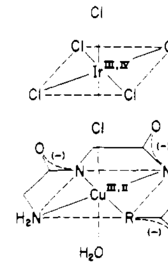

Figure 2. Proposed reaction complex for electron transfer with an inner-sphere chloride bridge between iridium and copper. R can be an oxygen (tripeptide), a NH (tripeptide amide), or an amino acid residue (tetrapeptide).

The mechanism in eq 16–19 is consistent with the behavior shown in Figure 1. In the region where log $K_{12} > -4$ and the electron-transfer step is rate determining, the rate constant for the oxidation reactions with $IrCl_6^{2-}$ is given by $k_{ox} = k_{-e}(k_{-s}k_{-D2})/(k_s k_{D2})$ if $k_{-e} \ll k_s$ and k_{D2}. The rate constant for the reduction reactions is $k_{red} = k_e(k_{D1}/k_{-D1})$ where $k_e \ll k_{-D1}$. In both cases the rate step is proportional to the electron-transfer process and a dependence on $K_{12}^{1/2}$ is expected from the Marcus theory.

In the region where log $K_{12} < -4$, the mechanism predicts different behavior for the oxidation and reduction reactions. For the oxidation of $Cu^{II}(H_{-x}L)^{2-}$ by $IrCl_6^{2-}$, the rate constant is given by the product $k_{-s}(k_{-D2}/k_{D2})$ if $k_{-s} \ll k_{D2}$. This product is essentially a substitution limit and is not expected to vary significantly as a function of the free energy change for the electron-transfer process. The substitution limit may, however, be sensitive to the different steric characteristics of the copper(II) peptides as suggested by the behavior of $Cu^{II}(H_{-3}A_4)^{2-}$ and $Cu^{II}(H_{-3}V_4)^{2-}$. If k_{-s} is the rate-determining step for the oxidation reactions, then the rate-determining step for the reduction reactions between $Ir^{III}Cl_6^{3-}$ and $Cu^{III}(H_{-x}L)^-$ is k_s. The overall rate constant for the reaction in this direction is given by $k_s(k_e k_{D1})/(k_{-e}k_{-D1})$ where $k_s \ll k_{-e}$ and k_{-D1}. In this region the rate is proportional to the ratio k_e/k_{-e} and thus varies with K_{12} to the first power.

A value for the substitution-limited rate constant for the oxidation of these Cu(II) complexes by $IrCl_6^{2-}$, given by $k_{-s}(k_{-D2}/k_{D2})$ above, can be estimated in the following manner. Equations 18 and 19 written in the reverse direction (eq 20 and 21) represent a simplified version of the Eigen and

$$Cu^{II}(H_{-x}L)(H_2O)_2^{n-} + IrCl_6^{2-} \overset{K_{os}}{\rightleftharpoons} [Cu^{II}(H_{-x}L)(H_2O)_2\cdot IrCl_6]^{(n+2)-} \quad (20)$$

$$[Cu^{II}(H_{-x}L)(H_2O)_2\cdot IrCl_6]^{(n+2)-} \xrightarrow{k^{Cu-H_2O}} [Cu^{II}(H_{-x}L)(H_2O)\cdot IrCl_6]^{(n+2)-} + H_2O \quad (21)$$

Tamm[39] substitution mechanism. In these expressions K_{os} is the outer-sphere association constant and k^{Cu-H_2O} is the rate of water exchange for the copper(II) complex. K_{os} values for labile metal ions are difficult to measure, but theoretical expressions are available.[38] The expression in eq 22 for the

$$K_{os} = \frac{4\pi N_0(r_A + r_B)^3}{3000} e^{-\delta} \exp[\delta\kappa(r_A + r_B)/(1 + \kappa(r_A + r_B))] \quad (22)$$

outer-sphere association constant has been derived from sta-

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(37) Debye, P. *Trans. Electrochem. Soc.* **1942**, *82*, 265.

(38) Margerum, D. W.; Cayley, G. R.; Weatherburn, D. C.; Pagenkopf, G. R. *ACS Monogr.* **1978**, *No. 174*, 1–220.

(39) Eigen, M.; Tamm, K. *Z. Elektrochem.* **1962**, *93*, 107.

tistical arguments[40] and the theory of diffusion.[41] With eq 22 and the center-to-center interaction distance of 6.6 Å for axial approach of $IrCl_6^{2-}$ to the copper(II) peptide discussed above, K_{os} values of 0.19 and 0.05 M^{-1} are calculated for 1–,2– and 2–,2– charges, respectively (25.0 °C, $\mu = 0.1$ M). The water exchange rate for Cu^{2+}(aq), k^{Cu-H_2O}, has been determined by NMR as 5×10^9 s^{-1}.[42,43] Use of the Cu^{2+}(aq) water-exchange rate for the copper(II)–peptide complexes would be valid only as a lower limit since the axial water molecules are probably more weakly bound in the case of the peptide complexes. A water-exchange rate of 10^{10} s^{-1} for the copper(II) peptides is used in further calculations and serves as an upper limit for the rate of this exchange process.[38] From the Eigen and Tamm mechanism the rate constant for the substitution process is $k^{Cu-H_2O}K_{os}$. For the reaction of $IrCl_6^{2-}$ with copper(II) peptides this product has values of 2×10^9 and 5×10^8 M^{-1} s^{-1} for 1–,2– and 2–,2– interactions, respectively. For comparison, the diffusion limit calculated from eq 13–15 for axial interaction of these same species is 4.1×10^9 and 1.9×10^9 M^{-1} s^{-1} for 1–,2– and 2–,2– charges, respectively. Equatorial substitution reactions of these species can be ruled out because in-plane substitution of complexes such as $Cu^{II}(H_{-3}G_4)^{2-}$ are much slower.[22] Hence, the axial substitution process can account, to within a good approximation, for the value of the limiting rate constant ($\sim 3 \times 10^8$ M^{-1} s^{-1}) that is observed for the reactions of $IrCl_6^{2-}$ with $Cu^{II}(H_{-3}G_4)^{2-}$, $Cu^{II}(H_{-3}AG_3)^{2-}$, and $Cu^{II}(H_{-4}C)^{2-}$.

If the diffusion and substitution limits discussed above are neglected, reasonable Marcus plots can be constructed for the $Cu^{III}(H_{-x}L)^0 + IrCl_6^{3-}$ and $Cu^{II}(H_{-x}L)^- + IrCl_6^{2-}$ reactions. According to the Marcus theory eq 23 and 24 give the relationship between the cross-reaction rate constant, the two self-exchange rate constants, and the equilibrium constant for the cross-exchange process. The same expression holds for k_{-1} if K_{12}^{-1} is used. Equations 23 and 24 were derived with assumption of an outer-sphere mechanism with negligible electrostatic work terms. Equation 23 requires that a plot of $\log (k/f^{1/2})$ vs. $\log K_{12}$ should be linear with a slope of 0.5 and an intercept of 0.5 $\log k_{11}k_{22}$.

$$k_1 = (k_{11}k_{22}K_{12}f)^{1/2} \qquad (23)$$

$$\log f = (\log K_{12})^2/[4 \log (k_{11}k_{22}/Z^2)] \qquad (24)$$

Figure 3 is a plot of $\log (k/f^{1/2})$ vs. $\log K_{12}$ for both the oxidation and reduction reactions of the $Cu^{III,II}(H_{-x}L)^{0,-}$ couple with the hexachloroiridate couple. For the reduction reactions of $Cu^{III}(H_{-x}L)$ by $IrCl_6^{3-}$, most of the data are from the earlier investigation[4] with the exception of the $Cu^{III}(H_{-2}G_2\beta A) + IrCl_6^{3-}$ reaction. The linear least-squares fit of these data has a slope of 0.56 (±0.04) and an intercept of 7.0 (±0.2). The oxidation reactions of $Cu^{II}(H_{-x}L)^-$ by $IrCl_6^{2-}$ give a similar linear free energy correlation with a slope of –0.5 (±0.09) and an intercept of 6.9 (±0.3). The *f* values used in these fits were calculated by successive approximations with use of eq 17 and 18 and ranged from 0.88 for A_3 to 0.19 for PG_2a.

Figure 3 suggests that the slope of the free energy dependence for both the oxidation and reduction reactions of the $Cu^{III,II}(H_{-x}L)^{0,-}$ couple with the $Ir^{IV,III}Cl_6^{2-,3-}$ couple obey the Marcus correlation. The average intercept value of 6.9 (±0.3) suggests a self-exchange rate constant of 3×10^8 M^{-1} s^{-1} for the $Cu^{III,II}(H_{-x}L)^{0,-}$ (standard deviation range is 7×10^7–10^9 M^{-1} s^{-1}) (25.0 °C, $\mu = 0.1$ M).

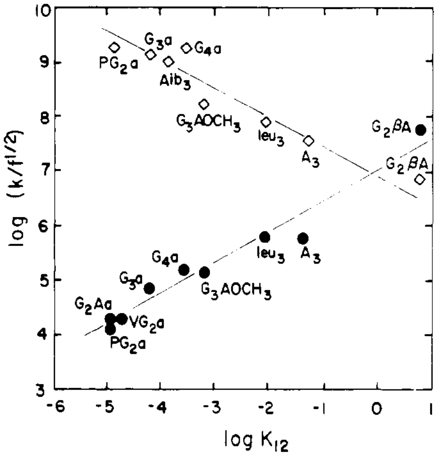

Figure 3. Marcus free energy correlation for the reactions of the $Cu^{III,II}(H_{-x}L)^{0,-}$ couple with the $Ir^{IV,III}Cl_6^{2-,3-}$ couple: ◇, $Cu^{II}(H_{-x}L)^- + IrCl_6^{2-}$; ●, $Cu^{III}(H_{-x}L) + IrCl_6^{3-}$.

Because of the approximate nature of the calculations of the limiting rate constants (i.e., substantial dependence on radii and effective charge), the Marcus treatment has been applied only to the experimentally observed rate constants. The rate constants in the vicinity of 10^9 M^{-1} s^{-1} clearly must have some contribution to the rate constant from the combination of diffusion of reactants and axial substitution processes. Hence, the self-exchange rate constant for this weak inner-sphere pathway may be larger, and it is safe to say that it is between 10^8 and 10^9 M^{-1} s^{-1}. The fact that a reasonable Marcus correlation is observed for a weak inner-sphere process is not entirely unexpected. These correlations have been observed previously for inner-sphere reactions as well as outer-sphere reactions, particularly in instances of weak inner-sphere coordination.[44-47]

The above considerations suggest that fast reactions might also be expected between copper(III, II) peptides and reaction partners other than $IrCl_6^{2-,3-}$ that are capable of an axial inner-sphere interaction. This appears to be the case for the reaction of copper(III) peptides with $Fe(CN)_6^{4-}$.[48]

Conclusions

Copper(II)–deprotonated peptide complexes are rapidly oxidized by hexachloroiridate(IV). The free energy dependence of the rate of these oxidations as well as that for the rate of the reductions of the corresponding copper(III) peptides by hexachloroiridate(III) shows two types of behavior. For $\log K_{12} > -4$ the slopes of the free energy dependences for both the oxidation and reduction rate constants are adequately accounted for by simple Marcus theory, even though these reactions do not involve simple outer-sphere electron transfers. For $\log K_{12} < -4$ the rates of the oxidation reactions reach a limiting value that is well below the diffusion limit calculated for the appropriate charge types and radii at an ionic strength of 0.1 and 25.0 °C. This behavior is more consistent with an inner-sphere mechanism that involves the substitution of an axial water on copper(II) peptide by $IrCl_6^{2-}$ rather than an outer-sphere mechanism for the following reasons. First, the rates of oxidation of the copper(II) peptides by $IrCl_6^{2-}$ are many orders of magnitude faster than the rate constants predicted from simple Marcus theory and the self-exchange rates for the copper(III, II) peptide and hexachloroiridate(IV, III) couples. Second, the limiting rate constants for $IrCl_6^{2-}$

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(40) Fuoss, R. M. *J. Am. Chem. Soc.* **1958**, *80*, 5059.
(41) Eigen, M. *Z. Phys. Chem. (Frankfurt/Main)* **1954**, *1*, 176.
(42) Lewis, W. B.; Alei, M., Jr.; Morgan, L. O. *J. Chem. Phys.* **1966**, *44*, 2409.
(43) Poupko, R.; Luz, Z. *J. Chem. Phys.* **1972**, *57*, 3311.
(44) Marcus, R. A. *J. Phys. Chem.* **1968**, *72*, 891.
(45) Woodruff, W. H.; Margerum, D. W. *Inorg. Chem.* **1974**, *13*, 2578.
(46) Sutin, N.; Gordon, B. M. *J. Am. Chem. Soc.* **1961**, *83*, 70.
(47) Haim, A.; Sutin, N. *J. Am. Chem. Soc.* **1966**, *88*, 434.
(48) Jacobs, S. A.; Margerum, D. W., unpublished data.

+ copper(II) peptide in the log $K_{12} < -4$ region fit an inner-sphere model better than they fit a diffusion-limited process. Third, the inner-sphere model provides some rationale for the anomalous behavior of the copper(II) tetra-L-alanine and copper(II) tetra-L-valine complexes due to steric interactions.

The steep slope of the free energy dependence for the copper(II) peptide reductions and the lack of a free energy dependence for the copper(II) peptide oxidations in the log $K_{12} < -4$ region are due to a shift of the rate-determining step away from the electron transfer. In the case of the reduction reactions the separation of the products of the electron transfer, the $Ir^{IV}Cl_6$–copper(II) peptide bridged complex, is rate limiting. The rate of the oxidation reactions is limited by substitution of $IrCl_6^{2-}$ for an axial water on the copper(II) peptide.

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Registry No. $Cu^{II}(H_{-2}A_3)^-$, 42179-70-4; $Cu^{II}(H_{-2}L_3)^-$, 29575-61-9; $Cu^{II}(H_{-3}G_3AOCH_3)^-$, 62882-66-0; $Cu^{II}(H_{-3}G_4a)^-$, 76861-95-5; $Cu^{II}(H_{-3}G_3a)^-$, 62801-35-8; $Cu^{II}(H_{-3}PG_2a)^-$, 76861-96-6; $Cu^{II}(H_{-3}G_4)^{2-}$, 57603-18-6; $Cu^{II}(H_{-3}AG_3)^{2-}$, 76899-38-2; $Cu^{II}(H_{-3}A_4)^{2-}$, 62959-95-9; $Cu^{II}(H_{-3}V_4)^{2-}$, 62959-94-8; $Cu^{III}(H_{-2}G_2\beta A)$, 69814-95-5; $Cu^{III}(H_{-2}Aib_3)$, 69990-31-4; $Cu^{III}(H_{-4}C)^-$, 76721-70-5; $IrCl_6^{2-}$, 16918-91-5; $IrCl_6^{3-}$, 14648-50-1.

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Reactions of the Trivalent Copper Complex of a Macrocyclic Tetrapeptide, *cyclo*-(β-Alanylglycyl-β-alanylglycyl)

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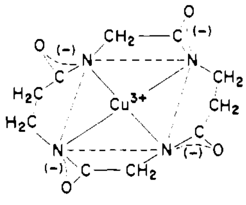
The electrode potential for the 14-membered macrocyclic peptide complex $Cu^{III,II}(H_{-4}C)^{1-,2-}$ is +0.48 V. $Cu^{III}(H_{-4}C)^-$ is relatively stable in neutral solution with a half-life of 5.7 weeks at 25.0 °C ($k_d = 2 \times 10^{-7}\ s^{-1}$). Its decomposition to copper(II) and oxidized ligand is acid catalyzed and base catalyzed. The latter reaction is first order in $[OH^-]$ and first order in $[Cu^{III}(H_{-4}C)^-]$ with $k_{OH} = 1.6 \times 10^{-2}\ M^{-1}\ s^{-1}$. Below pH 1 two intermediate copper(III) macrocyclic species form in rapid succession before a decomposition reaction occurs with a $[H^+]^2$ dependence where $k_{2H} = 1.0 \times 10^{-3}\ M^{-2}\ s^{-1}$. The $Cu^{III}(H_{-4}C)^-$ complex undergoes photochemical decomposition with a quantum yield of 8×10^{-3} at 278 nm. Electron-transfer reactions of $Cu^{II}(H_{-4}C)^{2-}$ with other Cu(III) peptides are rapid. These cross reactions lead to a calculated self-exchange rate constant of $6.0 \times 10^4\ M^{-1}\ s^{-1}$ for $Cu^{III}(H_{-4}C)^-$ and $Cu^{II}(H_{-4}C)^{2-}$ in 1.0 M $NaClO_4$ at 25.0 °C.

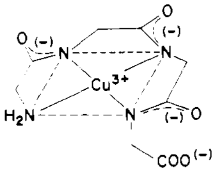
Introduction

Recent studies have shown that the macrocyclic tetrapeptide C (*cyclo*-(β-alanylglycyl-β-alanylglycyl)) reacts with divalent copper to form a quadruply deprotonated peptide complex.[1] The macrocycle helps to stabilize the $Cu^{II}(H_{-4}C)^{2-}$ complex, slowing down both acid attack on the deprotonated ligand and attack by other ligands on the metal. In the present work the macrocyclic complex is oxidized electrochemically to give the trivalent copper complex $Cu^{III}(H_{-4}C)^-$ with the proposed structure given in I. The electrode potential is only +0.48 V for this Cu(III)–Cu(II) couple in accord with a low potential expected[2] due to the presence of four deprotonated peptide donors. The $Cu^{III}(H_{-4}C)^-$ complex is characterized in regard to its UV–visible spectrum, its rate of redox decomposition as a function of pH, its photochemical decomposition, and its rate of electron-transfer reactions.



I

The trivalent oxidation state of copper has been observed in a number of compounds, many of which are not stable in aqueous solution.[3-6] Stabilization of the higher oxidation state by deprotonated peptide nitrogen donors makes copper(III) more easily accessible and long-lived.[2,7-10] The copper(III)–tetraglycine complex $Cu^{III}(H_{-3}G_4)^-$ (structure II) is stable in neutral solution with a half-life of 5.5 h.[11] The present macrocyclic peptide complex of copper(III) is about 200 times slower in undergoing redox decomposition under the same conditions. The reaction rate is both acid catalyzed and base catalyzed, giving rise to a U-shaped pH profile for the decomposition reaction. However, under all conditions it is slower to decompose than is $Cu^{III}(H_{-3}G_4)^-$.



II

Experimental Section

Reagents. The characterization of the 14-membered macrocyclic peptide (C) and the preparation of the copper(II) complex have been previously described.[1] Electrochemical oxidation to form $Cu^{III}(H_{-4}C)^-$ was accomplished with use of a flow electrolysis apparatus.[10] The

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(1) Rybka, J. S.; Margerum, D. W. *Inorg. Chem.* **1980**, *19*, 2784-2790.
(2) Bossu, F. P.; Chellappa, K. L.; Margerum, D. W. *J. Am. Chem. Soc.* **1975**, *97*, 6894-6896.
(3) Scholder, R.; Voelskow, U. *Z. Anorg. Allg. Chem.* **1951**, *266*, 256-268.
(4) Gray, E. T., Jr.; Taylor, R. W.; Margerum, D. W. *Inorg. Chem.* **1977**, *16*, 3047-3055.
(5) Olson, D. C.; Vasilevskis, J. *Inorg. Chem.* **1971**, *10*, 463-470.
(6) Bour, J. J.; Birker, P. J. M. W. L.; Steggerda, J. J. *Inorg. Chem.* **1971**, *10*, 1202-1205.
(7) Margerum, D. W.; Chellappa, K. L.; Bossu, F. P.; Burce, G. L. *J. Am. Chem. Soc.* **1977**, *99*, 2195-2203.
(8) Kirksey, S. T., Jr.; Neubecker, T. A.; Margerum, D. W. *J. Am. Chem. Soc.* **1979**, *101*, 1631-1633.
(9) Margerum, D. W.; Wong, L. F.; Bossu, F. P.; Chellappa, K. L.; Czarnecki, J. J.; Kirksey, S. T., Jr.; Neubecker, T. A. *Adv. Chem. Ser.* **1977**, *No. 162*, 281-303.