Articles

Applicability of the Marcus Relationship to Copper(II/I) Electron Transfer. Comparison of NMR Self-Exchange Relaxation and Reduction and Oxidation Cross-Reaction Kinetics for a Macrocyclic Amino Tetrathiaether–Copper(II/I) Complex in Aqueous Solution

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Received May 12, 1992

The value of the electron self-exchange rate constant for $Cu^{II/I}([15]aneNS_4)$ {$[15]aneNS_4$ = 1,4,7,10-tetrathia-13-azacyclopentadecane, a quinquedentate macrocycle} has been determined directly by NMR line-broadening measurements in D_2O over the temperature range 5–45 °C at pD values ranging from 5.3 to 8.5. The results are independent of acidity over the range studied with a mean value (at 25 °C, μ = 0.10) of $k_{11(ex)}$ = 1.4 (±0.4) × 10^5 M^{-1} s^{-1}, ΔH^* = 23 (±4) kJ mol^{-1}, and ΔS^* = −69 (±11) J K^{-1} mol^{-1}. The cross-reaction kinetics for both $Cu^{II}L$ reduction and $Cu^{I}L$ oxidation have also been determined by stopped-flow techniques in aqueous solution using $Ru^{III/II}(NH_3)_5py$ (py = pyridine) as the counter reagent. Application of the Marcus cross relation to these data yields calculated self-exchange rate constants for the $Cu^{II/I}([15]aneNS_4)$ system of $k_{11(Red)}$ = 2.8×10^4 M^{-1} s^{-1} and $k_{11(Ox)}$ = 1.4×10^5 M^{-1} s^{-1}, respectively, at 25 °C, μ = 0.10 M. This is the first known Cu(II/I) system for which the agreement among the self-exchange rate constant values obtained by all three approaches is within experimental error (i.e., $k_{11(ex)} \approx k_{11(Red)} \approx k_{11(Ox)}$). This level of consistency indicates that both the reduction and oxidation reactions, as measured in this study, occurred by a single pathway unimpeded by rate-limiting configurational changes which have recently been identified for Cu(II/I) complexes of this type. These results support the applicability of the Marcus equation to cross reactions involving Cu(II/I) systems, provided the cross reactions are conducted under conditions where configurational changes in the copper complexes are not rate limiting.

Introduction

Interest in the electron-transfer properties of Cu(II/I) systems has been stimulated both by the prevalence of copper-containing enzymes in biological oxidation–reduction reactions[2–5] and the apparent discrepancies which have been noted between the oxidation and reduction kinetics of low molecular weight inorganic Cu(II/I) complexes.[6,7] Since Cu(II) tends to be 6-coordinate (tetragonal) or 5-coordinate (square pyramidal) while Cu(I) is most commonly 4-coordinate (tetrahedral),[8] a large change in coordination geometry will normally accompany electron transfer at a copper site. This is expected to result in a large Franck–Condon barrier which should be manifested in the form of reduced rate constants for self-exchange reactions of the type

$$^*Cu^{II}L + Cu^{I}L \overset{k_{11(ex)}}{\rightleftharpoons} {}^*Cu^{I}L + Cu^{II}L \qquad (1)$$

where L represents a coordinated ligand or apoprotein and $k_{11(ex)}$ is the characteristic self-exchange rate constant.

More than 20 years ago, Vallee and Williams suggested that the coordination geometry of the copper site in redox-active copper proteins might be constrained by the protein matrix and that this constraint might then account for the enhanced electron-transfer kinetics of these enzymes.[9] Subsequent crystal structures of some blue copper proteins have revealed the apparent presence of such constraints for the type 1 copper site which has been shown to be elongated trigonal pyramidal (4-coordinate) in plastocyanins[10] or elongated trigonal bipyramidal (5-coordinate) in azurins.[11] However, very few studies have yet been made which test the effect of specific ligand parameters upon the electron-transfer rate constants for the Cu(II/I) redox couple.[12]

The best examples of constrained low molecular weight Cu(II/I) systems for which electron-transfer kinetics have been reported to date would appear to be those of Wilson, Stanbury, and co-workers.[13] Their investigations have centered on the copper complexes formed with a series of related quinquedentate pyridylimine ligand species in which the copper atom appears to maintain a coordination number of 5 for both $Cu^{II}L$ and $Cu^{I}L$. On the basis of cross-reaction kinetics between closely related compounds as well as NMR relaxation studies in acetonitrile, these complexes have been found to exhibit k_{11} values of 10^3 to 4×10^4 M^{-1} s^{-1} at 25 °C. Interestingly, these values are not significantly different from aqueous k_{11} values reported for other Cu(II/I) complexes in which the coordination number is believed

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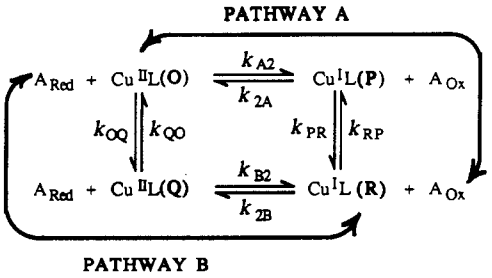


Figure 1. Proposed dual-pathway "square scheme" mechanism for electron-transfer cross reactions involving Cu(II/I) systems. The species designated as $Cu^{II}L(O)$ and $Cu^{I}L(R)$ represent the stable conformers of the two oxidation states, while $Cu^{II}L(Q)$ and $Cu^{I}L(P)$ represent metastable intermediates. The conformation of each of the latter species is assumed to approximate the coordination geometry of the stable conformer for the opposite oxidation state. As a result, these intermediates are more easily reduced and oxidized, respectively, than their corresponding stable conformers.

to change during electron transfer.[14] Thus, it may be inferred that a significant Franck–Condon barrier still accompanies electron transfer in these Cu(II/I) systems.

In investigating the kinetics of Cu(II/I) systems in which the coordination number is believed to change upon electron transfer, we have studied a series of copper complexes involving macrocyclic and acyclic polythiaether ligands reacting with selected counter reagents, A_{Ox} or A_{Red}:[15]

$$Cu^{II}L + A_{Red} \underset{k_{21}}{\overset{k_{12}}{\rightleftharpoons}} Cu^{I}L + A_{Ox} \qquad (2)$$

In these studies, we found that application of the Marcus square root relationship to both k_{12} and k_{21} values yielded considerably larger self-exchange rate constants in the former case than in the latter; that is, $k_{11(Red)} \gg k_{11(Ox)}$. To explain this phenomenon, we proposed that the electron-transfer step and configurational changes for these $Cu^{II/I}L$ systems occur sequentially rather than concertedly. The result is a dual-pathway square scheme, as shown in Figure 1, in which configurational changes can become rate-determining under specified circumstances.[15,16] This mechanism has recently been verified in a thorough investigation of a macrocyclic tetrathiaether complex, $Cu^{II/I}([14]aneS_4)$, using a combination of rapid-scan cyclic voltammetry, NMR relaxation measurements, and cross-reaction kinetic studies with a wide range of counter reagents.[17,18]

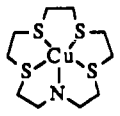
In the square scheme mechanism, the choice of the favored pathway is normally dependent upon the relative stabilities of the two metastable configurations designated as $Cu^{II}L(Q)$ and $Cu^{I}L(P)$ in Figure 1. For the polythiaether complexes studied to date, the intermediate Q appears to be much less stable than P, which indicates that pathway A is intrinsically preferred.[17] In conformance with recent general theoretical treatments of square scheme electron-transfer mechanisms,[19,20] an increase in the overall reaction potential and/or in the self-exchange rate constant (or concentration) of the counter reagent, A_{Ox}, can cause the rate of the configurational change R → P to become the rate-limiting process in $Cu^{I}L$ oxidation reactions.[18] Further increases can ultimately bring about a switch to the alternate pathway.[18] The consequence will be an apparent retardation in the reaction rate. It is to this phenomenon that we attribute the general observation that $k_{11(Red)} \gg k_{11(Ox)}$ for the copper–polythiaether complexes.

We have recently postulated that the square scheme mechanism is generally applicable to all Cu(II/I) complexes[18] so that configurationally-controlled reduction or oxidation may be manifested with essentially all copper systems. Unfortunately, since most investigators have tended to study only $Cu^{II}L$ reduction kinetics, the data available in the literature at this time are insufficient to establish the validity of this hypothesis for more than a very few systems.

Regardless of which intermediate species (Q or P) is the more stable, theoretical considerations dictate that configurationally-limited behavior will be observed *in only one direction* for thermodynamically favored reactions.[18,20] Under these circumstances, the *larger* value of $k_{11(Red)}$ or $k_{11(Ox)}$ should be within experimental error of the rate constant determined from direct self-exchange, $k_{11(ex)}$ (reaction 1). To date, we have established the validity of this relationship for two systems, $Cu^{II/I}([15]aneS_5)$[21] and $Cu^{II/I}([14]aneS_4)$.[18]

Whereas the square scheme mechanism provides an explanation for discrepancies between $k_{11(Red)}$ and $k_{11(Ox)}$ values, it also implies that both reduction and oxidation cross reactions with Cu(II/I) systems should yield consistent k_{11} values under conditions where the configurational change is *not* rate limiting, that is, when both processes proceed by the same pathway. Thus, upon application of the Marcus relationship to the resultant cross-reaction rate constants, k_{12} and k_{21} (reaction 2), the result should be that $k_{11(Red)} \approx k_{11(Ox)} \approx k_{11(ex)}$ as is normally expected with other metal redox couples (e.g., Fe(III/II), Co(III/II), Ru(III/II), etc.). Surprisingly, we have been unable to find *any* concrete examples in which the self-exchange rate constant for a Cu(II/I) system has been determined by all three approaches to yield a consistent k_{11} value. We note from our own studies, however, that such behavior was most closely approached by $Cu^{II/I}([15]aneS_5)$ where $k_{11(ex)} \approx k_{11(Red)} \approx 30k_{11(Ox)}$.[21]

The current study was specifically undertaken to demonstrate that consistent k_{11} values could be obtained for a single Cu(II/I) system from all three types of measurements (i.e., NMR relaxation and reduction and oxidation cross reactions). For this purpose, a system with reasonably rapid rates of configurational change was desired so that all studies could be conducted under conditions which were not configurationally limited. The system which has been selected is $Cu^{II/I}([15]aneNS_4)$



(14) Since there are no coordinated solvent molecules in these complexes, the magnitude of the solvent effect may not be exceptionally large. By correlation to recent studies by Swaddle and co-workers on a Cu(II/I)-substituted phenanthroline complex in both acetonitrile and aqueous solvents (Doine, H.; Yano, Y.; Swaddle, T. W. *Inorg. Chem.* **1989**, *28*, 2319–2322), the aqueous self-exchange rate constant would be expected to be no more than 1 order of magnitude larger than the acetonitrile value. Several aqueous Cu(II/I) systems have been reported to have k_{11} values of 10^5–10^6 M^{-1} s^{-1} (e.g.: Holwerda, R. A. *Inorg. Chem.* **1982**, *21*, 2107–2109. Allan, A. E.; Lappin, A. G.; Laranjeira, M. C. M. *Inorg. Chem.* **1984**, *23*, 477–482. Pulliam, E. J.; McMillin, D. R. *Inorg. Chem.* **1984**, *23*, 1172–1174. Cf., ref 15).

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{[15]aneNS$_4$ = 1,4,7,10-tetrathia-13-azacyclopentadecane} on the basis that its self-exchange rate constant was expected to be reasonably large ($\geq 10^5$ M^{-1} s^{-1}) by analogy to the previously studied Cu$^{II/I}$([15]aneS$_5$); we surmised that the rate constant for configurational change involved in oxidation via pathway A (designated as k_{RP} in Figure 1) in the square scheme mechanism is also reasonably large. For such a system, it was presumed possible to carry out selected oxidation reactions under conditions in which the rate of configurational change would not be exceeded. In an attempt to ensure this behavior, a counter reagent was chosen which would yield a thermodynamically unfavorable reaction potential in order to slow the oxidation reaction.

Studies on this system are facilitated by the greatly increased solubility of the [15]aneNS$_4$ ligand over that of [15]aneS$_5$ and by the fact that the Cu^{II}([15]aneNS$_4$) complex is much more stable than Cu^{II}([15]aneS$_5$), making it unnecessary to add large amounts of excess Cu(II) to prevent complex dissociation. It should also be noted that the substitution of an amine nitrogen donor atom for a thiaether sulfur results in a considerably lower redox potential for Cu$^{II/I}$([15]aneNS$_4$) compared to that for Cu$^{II/I}$([15]aneS$_5$) (0.46 versus 0.68 V, respectively).[22] Moreover, by analogy Cu(II) is presumed to be coordinated to all five donor atoms in the Cu^{II}L species in a square pyramidal geometry, and one Cu–S bond is presumed to rupture upon reduction to Cu^{I}L as observed in crystal determinations for Cu$^{II/I}$([15]aneS$_5$).[23]

In the current investigation, cross-reaction kinetic measurements have been obtained for both Cu^{II}L reduction and Cu^{I}L oxidation using a single counter reagent, Ru$^{III/II}$(NH$_3$)$_5$py. We have also conducted NMR relaxation measurements to obtain a direct determination of $k_{11(ex)}$, the latter measurements having been carried out over the range of pD 5.3–8.5 to establish the efficacy of the data. The results reveal that, within experimental error, $k_{11(Red)} \approx k_{11(ex)} \approx k_{11(Ox)}$. To the best of our knowledge, *this represents the first system for which equivalent values of the self-exchange rate constant for a Cu(II/I) system have been generated independently from all three types of measurements in aqueous solution.*

Experimental Section

The synthesis of the [15]aneNS$_4$ ligand will be described elsewhere.[24] All NMR measurements were conducted in deuterium oxide (99.8% D, Aldrich Chemical Co.), while all stopped-flow kinetic experiments were conducted in conductivity-grade distilled-deionized water. The reagents Ru^{III}(NH$_3$)$_5$py and Ru^{II}(NH$_3$)$_5$py were synthesized by the method outlined by Gaunder and Taube[25] with modifications as previously described.[18] The preparations of all solutions utilized have also been described.[18,21] Since the Cu^{II}([15]aneNS$_4$) complex is very stable, even at the lowest pH values studied (log $K_{Cu^{II}L}$ = 9.80, log $K_{Cu^{I}L}$ = 15.6),[22,26] it was not necessary to add an excess of Cu^{II}(aq) to the solutions used for the NMR measurements. However, since the ligand is protonable (log K_H = 8.14),[26] each solution used for NMR measurements was adjusted to the desired pD value using sodium deuteroxide (40% solution in D$_2$O) or perchloric acid-d (68% w/w solution in D$_2$O), both obtained from Sigma Chemical Co. Measurements were made at several different pD values to ascertain the effect of acidity upon the self-exchange rate constant value obtained. For the stopped-flow kinetic studies, a noncomplexing borate–mannitol buffer was used to maintain constant pH, unless otherwise indicated, and ionic strength was controlled at μ = 0.10 M using NaClO$_4$.

All pD measurements of D$_2$O solutions were made using an Orion Model 601A digital ionalyzer equipped with a micro Ag/AgCl combination pH electrode. The pD values were calculated using the scale of Glasoe and Long[27] where the pH meter was standardized with two or three aqueous buffers and the appropriate correction factor was applied.[21] All pD values reported are for 25 °C. No corrections were made for changes in pD with temperature since the kinetics proved to be unaffected by the pD level over the range studied. For the aqueous solutions used in the stopped-flow kinetics experiments, the pH values were checked using an Orion 901 microprocessor ionalyzer equipped with an Orion Ross combination pH electrode in which the usual 3 M KCl filling solution was replaced by 3 M NaCl solution to prevent possible precipitation of KClO$_4$ at the liquid junction. All other instrumentation and conditions used for both the NMR (including the pulse sequences)[21] and stopped-flow measurements[26] have been previously described.

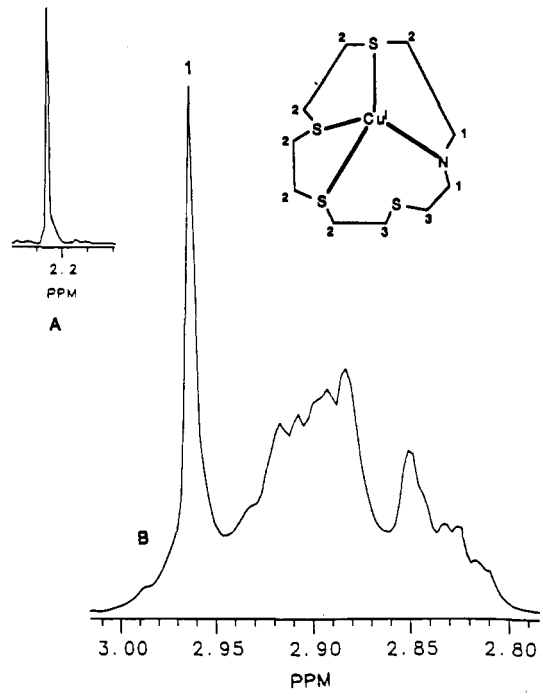

Figure 2. ^{1}H NMR spectra of the free [15]aneNS$_4$ ligand (spectrum A) and the Cu^{I}([15]aneNS$_4$) complex in D$_2$O (spectrum B). The major peak at 2.96 ppm was used for the line-broadening measurements.

Results

Cu^{I}([15]aneNS$_4$) Spectra. The ^{1}H spectrum of [15]aneNS$_4$ in D$_2$O shows a single peak analogous to that previously observed for [15]aneS$_5$[21] (Figure 2A). The proton bonded to the nitrogen atom exchanges rapidly with the deuterated solvent so that the NH proton does not couple with the protons on adjacent carbon atoms.[28] The single resonance line observed for the free ligand also indicates that nitrogen and sulfur have virtually identical effects on the CH protons, making them all magnetically equivalent.

As illustrated in Figure 2B, the ^{1}H spectrum of the Cu^{I}L complex (pH $\geq$ 5) is considerably more complicated showing a sharp peak at 2.96 ppm and overlapping multiplets with smaller downfield shifts. The crystal structure of Cu^{I}([15]aneS$_5$), previously determined by X-ray diffraction methods, revealed that four sulfur atoms are coordinated to the central copper ion in a distorted tetrahedral array while the fifth is unbonded; the same structure is presumed to be prevalent in solution.[23] The NMR spectrum for the S$_5$ complex consisted of a single peak,

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indicating that the five sulfur donor atoms were equivalent and, therefore, were interchanging rapidly on the NMR time scale. A low-resolution crystal structure for $Cu^{I}([15]aneNS_4)$[29] indicated a similar geometry (see inset in Figure 2B) in which the site occupied by the nitrogen donor atom varied. Moreover, recent evidence suggests that Cu(I) shows no significant preference between aliphatic amine nitrogens and thiaether sulfurs.[26] Thus, it is likely that the inner-coordination sphere of $Cu^{I}([15]aneNS_4)$ is a mixture of both S_4 and NS_3 donor groups on a time-averaged basis. In view of the apparent equivalence of the nitrogen and sulfur atoms upon the adjacent CH protons in the uncomplexed ligand, the assignment of the 2.96 ppm peak to the protons on C-1, adjacent to the nitrogen atoms, is a tenuous one. No attempt has been made to resolve or assign the other peaks.

Determination of Self-Exchange Rate Constants. The self-exchange rate constants were determined by measuring the changes in $Cu^{I}L$ resonance line widths as a function of the concentration of added $Cu^{II}L$, the latter quantity being determined from spectrophotometric absorbance measurements. In the calculation of the $k_{11(ex)}$ values, the equation of McConnell and Berger[30] was used in the following modified form:[21]

$$W_{DP}\mathcal{Q}\pi = W_D\mathcal{Q}\pi + k_{11(ex)}[Cu^{II}L] \quad (3)$$

In this equation, W_{DP} is the width at half-height ($T_2^{-1} = \pi W_{1/2}$) of a specific proton resonance peak for a solution containing both the diamagnetic ($Cu^{I}L$) and paramagnetic ($Cu^{II}L$) species, W_D is the corresponding value for a solution containing only the diamagnetic species, and $\mathcal{Q}$ is a correction factor used to correct the extent of outer-sphere complex formation at the specific ionic strength used (represented by the outer-sphere equilibrium constant $K_{OS(s)}$) to a common ionic strength value of 0.1 M (represented by the constant $K_{OS(0.1)}$):[31]

$$\mathcal{Q} = K_{OS(0.1)}/K_{OS(s)} \quad (4)$$

In the application of eq 3, it was determined that all of the required conditions were met.[32]

The width of the sharpest ^1H peak (at 2.96 ppm, Figure 2B) was determined using the Curve Analysis program.[33] Due to the difficulty in resolving the line width and the possible dependence of the properties of $Cu^{II}([15]aneNS_4)$ on acidity,[26] four series of measurements were made with the first two series run under very similar conditions and the third and fourth at markedly higher pD values. All four series used D_2O as the solvent with the temperature varied in 10° increments from +5 to +45 °C. Typical plots of eq 3 as applied to the line width data for series III (pD 7.4) are illustrated in Figure 3. The variable conditions used and the resultant $k_{11(ex)}$ values obtained for all four series are listed in Table I.

Measurement of Cross-Reaction Kinetics for $Cu^{II/I}([15]aneNS_4)$. No kinetic results have previously been reported for electron-transfer reactions involving the $Cu^{II/I}([15]aneNS_4)$ system. Therefore, a kinetic study of the cross reaction of this system with (pyridyl)pentaammineruthenium(III/II) was undertaken

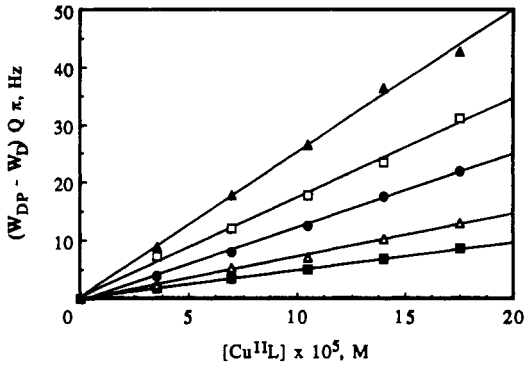

Figure 3. Typical plots of the NMR line width data plotted according to eq 3. The data shown are for series III (pD = 7.4). The slopes represent the value of $k_{11(ex)}$, while, in all cases, the intercepts are essentially zero. The five lines shown represent the data for 5 (smallest slope), 15, 25, 35, and 45 °C (largest slope), respectively.

Table I. Resolved $k_{11(ex)}$ Values for $Cu^{II/I}([15]aneNS_4)$ As Obtained from NMR Line-Broadening Measurements in D_2O at Variable Temperature, Corrected to μ = 0.1 M[a]

	series I	series II	series III	series IV
	Conditions Utilized			
pD (25 °C)	5.34 (8)	5.35 (6)	7.4 (1)	8.47 (4)
$[Cu^{I}L]$, mM	7.0	18	120	20
$[Cu^{II}L]$, mM	0–0.175	0–0.102[b]	0–0.175	0–0.254
	Resolved Values of $k_{11(ex)} \times 10^{-5}$, $M^{-1}\ s^{-1}$			
5 °C	1.01 (2)	0.59 (5)	0.48 (1)	0.61 (2)
15 °C	1.47 (6)	0.85 (4)	0.73 (3)	0.83 (2)
25 °C	1.83 (3)	1.20 (3)	1.24 (3)	1.14 (2)
35 °C	2.4 (1)	1.68 (2)	1.68 (5)	1.60 (3)
45 °C	3.35 (8)	2.30 (9)	2.44 (9)	2.25 (4)
	Activation Parameters[c]			
$\Delta H^{\ddagger}$, kJ mol^{-1}	19 (1)	23 (6)	28 (1)	21.7 (5)
$\Delta S^{\ddagger}$, J $mol^{-1}\ K^{-1}$	−79 (4)	−70.2 (2)	−53 (4)	−75 (2)

[a] In this and the succeeding tables, values listed in parentheses represent standard deviations in terms of the last significant figure shown. [b] Series II consisted of only three $[Cu^{II}L]$ values; all other series involved six values (see supplementary material). [c] Mean values: $\Delta H^{\ddagger}$ = 23 (±4) kJ mol^{-1}; $\Delta S^{\ddagger}$ = −69 (±11) J $mol^{-1}\ K^{-1}$.

as part of this investigation:

$$Cu^{II}L + Ru^{II}(NH_3)_5py \underset{k_{21}}{\overset{k_{12}}{\rightleftharpoons}} Cu^{I}L + Ru^{III}(NH_3)_5py \quad (5)$$

As expected, both the forward and reverse reactions were found to obey second-order kinetics conforming to the differential rate expression

$$-\frac{d[Cu^{II}L]}{dt} = k_{12}[Cu^{II}L][Ru^{II}] - k_{21}[Cu^{I}L][Ru^{III}] \quad (6)$$

where $[Ru^{II}]$ and $[Ru^{III}]$ represent the concentrations of the corresponding pyridyl pentaammine complexes.

The forward reaction was studied under pseudo-first-order conditions, with $Cu^{II}L$ in large excess, at 25 °C, pH 5.0 (borate–mannitol buffer system),[34] 0.10 M ionic strength ($NaClO_4$). Under these conditions, the last term in eq 6 was negligible and the integrated rate equation was of the form

$$\ln\{[Ru^{II}]_0/[Ru^{II}]_t\} = k_{obs}t \quad (7)$$

where $[Ru^{II}]_0$ and $[Ru^{II}]_t$ represent the concentrations of the Ru(II) complex at the time of reaction initiation and at any time, t, respectively, and k_{obs} is defined as

$$k_{obs} = k_{12}[Cu^{II}L]_0 \quad (8)$$

At measurable concentration levels, the pseudo-first-order reaction

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(32) The conditions required for eq 3 include $(T_2)_D \geq \tau_D \gg \tau_P \gg \tau_p$ and $(\delta\omega\tau_P/2)^2 \gg 1$, where τ_D and τ_P are the mean lifetimes of the diamagnetic and paramagnetic species, respectively, following electron transfer, τ_p is the paramagnetic spin–lattice relaxation time, $\delta\omega$ is the hyperfine splitting of the electron resonance of the paramagnetic species due to the proton, and $(T_2)_D$ is the spin–spin relaxation time of the diamagnetic species (cf. ref 21).
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Table II. Pseudo-First-Order Kinetic Data for the Reduction of $Cu^{II}([15]aneNS_4)$ with $Ru^{II}(NH_3)_5py$ at 25 °C, with pH = 5.0, and $[Ru^{II}]$ = 10.7 μM

μ = 0.1 M ($NaClO_4$)		μ = 0.03 M ($NaClO_4$)	
$[Cu^{II}L]_0$, mM	$10^{-2}k_{obs}$, s^{-1} [a]	$[Cu^{II}L]_0$, mM	$10^{-2}k_{obs}$, s^{-1} [a]
k_{obs} Values			
0.0775	0.63 (6)	0.344	0.86 (11)
0.155	1.9 (2)	0.516	1.9 (2)
0.232	3.4 (2)	0.688	2.3 (7)
0.310	3.8 (4)	0.860	2.9 (7)
Linear Regression Values[b]			
$k_{12(0.10)}$ = 1.4 (2) × 10^6 M^{-1} s^{-1}		$k_{12(0.03)}$ = 3.8 (5) × 10^5 M^{-1} s^{-1}	
		$k_{12(0.10)}$ = 9.1 × 10^5 M^{-1} s^{-1} [c]	

[a] Values shown represent the means of six repetitive runs. [b] Calculated using eq 8; for both sets of data, the intercept is not statistically different from zero. [c] Corrected to μ = 0.10 M using eq 9.

Table III. Pseudo-First-Order Kinetic Data for the Oxidation of $Cu^{I}([15]aneNS_4)$ with $Ru^{III}(NH_3)_5py$ at 25 °C, with μ = 0.10 M ($NaClO_4$), pH = 3.5 (unbuffered), and $[Cu^{I}L]_0$ = 0.038 mM[a]

$[Ru^{III}]_0$, mM	k_{obs}', s^{-1} [b]	$[Ru^{III}]_0$, mM	k_{obs}', s^{-1} [b]
0.426	10.2 (6)	1.279	14.8 (2)
0.639	11.0 (7)	1.492	16.3 (6)
0.853	14.0 (2)	1.918	20.9 (6)
1.066	14.8 (2)	2.131	26.8 (9)

[a] Linear regression value based on last five entries: k_{21} = 1.3 (2) × 10^4 M^{-1} s^{-1} (see text).[b] For all eight entries: k_{21} = 8 (1) × 10^3 M^{-1} s^{-1}.[c] [b] Values shown represent the means of 5–6 repetitive runs. [c] Calculated using expression equivalent to eq 8; intercept is not statistically different from zero (see Figure 3). [d] Intercept = 5 (±2) s^{-1}.

was found to be very rapid with a mean lifetime on the order of a few milliseconds, thereby severely limiting the range of excess reagent which could be utilized. In an attempt to extend this range, a second series of kinetic measurements were conducted at 0.03 M ionic strength, resulting in a decreased reaction rate. In order to compare the two data sets, the mean k_{12} value obtained at 0.03 M ionic strength ($k_{12(0.03)}$) was corrected to 0.10 M ($k_{12(0.10)}$) using the following relationship:

$$k_{12(0.10)} = k_{12(0.03)}\frac{\gamma_{Cu(0.10)}\gamma_{Ru(0.10)}}{\gamma_{Cu(0.03)}\gamma_{Ru(0.03)}} \quad (9)$$

Here γ_{Cu} and γ_{Ru} represent the activity coefficients for the two reagents at the designated ionic strengths as calculated from the extended Debye–Hückel equation:

$$\log \gamma_i = \frac{-A(z_i)^2\sqrt{\mu}}{1 + Ba\sqrt{\mu}}$$

In the latter expression, $A = 0.51_4$ and $B = 3.3_0 \times 10^7$ in aqueous solution at 25 °C,[31] z_i is the ionic charge (+2 for both reactants in this study), μ is the ionic strength, and "a" is the ionic diameter equal to approximately 8.8 × 10^{-8} and 7.6 × 10^{-8} cm for $Cu^{II}L$ and Ru(II), respectively, according to our earlier estimates.[15,18] The resulting k_{12} values for both data sets (including the final correction to 0.10 M ionic strength) are included in Table II.

In the attempt to determine the value of k_{21}, the reverse reaction was studied by mixing $Cu^{I}L$ with a large excess of $Ru^{III}(NH_3)_5$-py (to force reaction 5 to the left) resulting in a pseudo-first-order expression equivalent to eq 7

$$\ln \{[Cu^{I}]_0/[Cu^{I}]_t\} = k_{obs}'t \quad (10)$$

where $k_{obs}' = k_{21}[Ru^{III}]_0$. Using conditions in which $[Cu^{I}L]_0$ = 0.038 mM and $[Ru^{III}]_0 \leq 2.13$ mM, pH = 3.5 (unbuffered), reaction 5 still did not proceed more than 50% to the left; but estimated k_{obs}' values were obtained from the rate data for the first 50% of the reaction (Table III). (Although such pseudo-first-order plots should not be strictly linear, due to the second-order nature of the "forward" reaction, the curvature was not obvious). The application of linear regression to a plot of these k_{obs}' values against $[Ru^{III}]_0$ yielded k_{21} = 8 (1) × 10^3 M^{-1} s^{-1} with an intercept of 5 (±2) (dashed line in Figure 4). However, this plot should be linear only if the forward reaction (i.e., the k_{12} contribution) were a first-order process. Since the latter process is actually second-order, the plot should, in fact, be curved (as is apparent), ultimately reaching a limiting slope equal to k_{21} and a negligible intercept as the contribution of the forward reaction becomes negligible (i.e., as the oxidation of $Cu^{I}L$ proceeds to essential completion). Since this latter condition was not actually reached in our studies, the specific value of k_{21} should be less than the limiting slope observed in Figure 4. The solid line shown in this figure represents the linear regression line for the last five points as forced to pass through the origin. Thus, the two lines in Figure 4 presumably establish the outside limits for the value of k_{21}, that is, 0.8 × 10^4 < k_{21} < 1.3 × 10^4 M^{-1} s^{-1}.

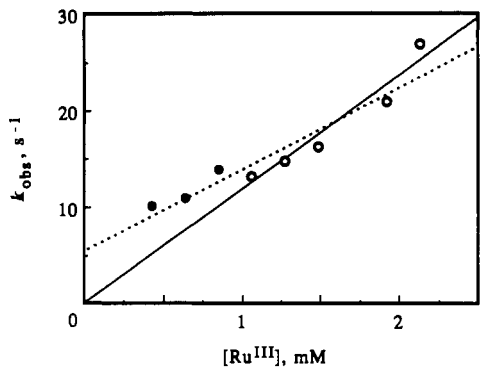

Figure 4. Plot of pseudo-first-order kinetic data for $Cu^{I}([15]aneNS_4)$ oxidation by $Ru^{III}(NH_3)_5py$ at 25 °C, with μ = 0.10 M and pH = 3.5 (Table III). The solid line represents the linear regression for the higher $[Ru^{III}]$ values only (open circles) forced through the origin (the theoretical intercept), while the dotted line represents the unrestricted regression line for all values.

In order to improve on our estimate of k_{21}, the reaction between $Cu^{I}L$ and Ru^{III} was studied under second-order conditions in which the forward reaction involving k_{12} was taken into account. Although the desired reaction did not proceed far to completion under the conditions used, this approach still provided sensitive measurements since only the reaction products, $Cu^{II}L$ and Ru^{II}, absorb significantly at 414 nm, the wavelength used to monitor the reaction (molar absorptivity values of $\epsilon_{Cu^{II}L}$ = 6100 and $\epsilon_{Ru^{II}}$ = 7550, respectively). Commencing with a solution mixture in which only $Cu^{I}L$ and Ru^{III} are present in significant concentrations at the time of reaction initiation, the applicable differential expression for the back reaction of eq 5 may be written in the form

$$dx/dt = k_{21}(a - x)(b - x) - k_{12}x^2 \quad (11)$$

where a and b are the initial concentrations of $Cu^{I}L$ and Ru^{III}, respectively, and

$$x = [Cu^{II}L]_t = [Ru^{II}]_t = A_t/l(\epsilon_{Cu^{II}L} + \epsilon_{Ru^{II}}) \quad (12)$$

where A_t represents the absorbance at any time, t, and l represents the cell path length (2.00 cm). If x_e is defined as the concentration of either product at equilibrium, the following expression can be generated for k_{12}

$$k_{12} = k_{21}(a - x_e)(b - x_e)/x_e^2 \quad (13)$$

which can then be substituted into eq 11 to yield, upon rearrangement:

$$\int x_e^2 dx/\{(a - x)(b - x)x_e - (a - x_e)(b - x_e)x^2\} = \int k_{21}dt \quad (14)$$

An exact numerical solution to eq 14 was obtained in the form

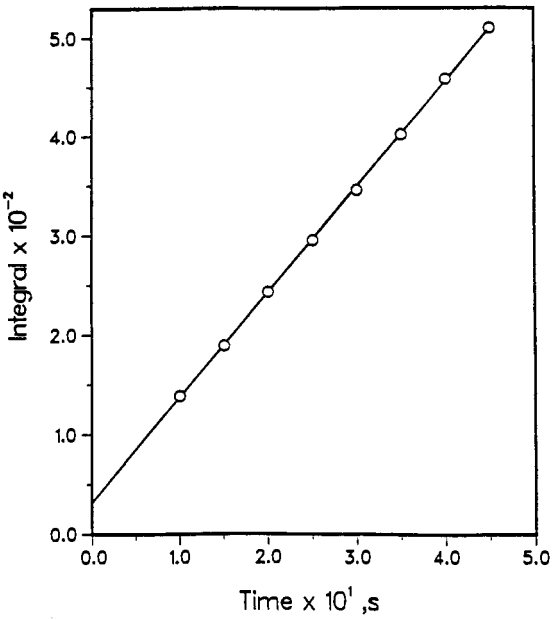

Figure 5. Sample plot of the second-order kinetic data from a single run for the reaction of $Cu^{I}([15]aneNS_4)$ with $Ru^{III}(NH_3)_5py$ showing the application of Simpson's rule to solve eq 14.

Table IV. Second-Order Kinetic Data for the Oxidation of $Cu^{I}([15]aneNS_4)$ with $Ru^{III}(NH_3)_5py$ at 25 °C, with μ = 0.10 M ($NaClO_4$), pH = 5.0, $[Cu^{I}L]_0$ = 0.12 mM, and $[Ru^{III}]_0$ = 0.17 mM

$10^{-4}k_{21}$, M^{-1} s^{-1}	intercept[a]	corr coeff (r^2)
1.28 (9)	−25 (37)	0.970
1.00 (1)	31 (3)	0.999
1.01 (3)	35 (7)	0.996
1.06 (6)	31 (2)	0.999
1.04 (2)	3.3 (6)	0.998
1.03 (7)[b,c]		

[a] Intercept values are presented only for comparative purposes; in all cases, the theoretical intercept values should be zero. [b] Mean value. [c] The mean value shown does not include the first entry listed since it can be eliminated using Dixon's Q parameter at the 95% confidence level (Rorabacher, D. B. *Anal. Chem.* **1991**, *63*, 139–146); inclusion of all five values yields k_{21} = 1.1 (1) × 10^4 M^{-1} s^{-1}.

of Simpson's rule.[35] This method offers the advantage of being applicable to a wide variety of integral expressions encountered in kinetics and is exact for polynomials of degree three or lower. A modular programming approach was used to solve the problem.[36] The second-order rate constant, k_{21}, was determined from the slope of the regression line of eq 14 as illustrated in Figure 5. The results obtained in this manner from five independent kinetic runs (Table IV) gave a mean value of k_{21} = 1.03 (7) × 10^4 M^{-1} s^{-1}, in good agreement with the limits established from the rate studies under pseudo-first-order conditions. This latter value has been utilized in subsequent calculations.

Discussion

Structural Changes Accompanying Electron Transfer. No direct evidence for the actual structures of the $Cu^{II}([15]aneNS_4)$ and $Cu^{I}([15]aneNS_4)$ species in solution phase has yet been generated. However, several pieces of pertinent evidence exist. The crystal structures for the closely related S_5 species (i.e., Cu^{II}-$([15]aneS_5)$ and $Cu^{I}([15]aneS_5)$) have been previously published.[23] The structure of the $Cu^{II}L$ species shows all five sulfurs to be coordinated in a distorted square pyramidal geometry (the distortion being caused by the fact that the ethylene linkages are too short to permit the fifth donor atom to reach a perpendicular apical position). This species is believed to maintain a similar five-coordinate geometry in solution with no solvent molecules bonded in the inner-coordination sphere. The latter assumption is supported by the observation that this species is the only Cu(II)–polythiaether complex, among those which we have tested, which has not shown evidence of forming adducts with a variety of "noncomplexing" anions, the latter adducts being presumed to represent a displacement of an inner-sphere solvent molecule.[37,38] Thus, we have inferred that there are no solvent molecules coordinated to this species. As noted under Results, the crystal structure of $Cu^{I}([15]aneS_5)$ is four-coordinate, exhibiting a somewhat distorted tetrahedral geometry with one sulfur not coordinated. Similar geometries are deemed likely for the corresponding $Cu^{II}([15]aneNS_4)$ and $Cu^{I}([15]aneNS_4)$ complexes. Therefore, a change in coordination number is presumed to accompany electron transfer in which one Cu–S (or Cu–N) bond is ruptured upon reduction.

Applicability of the Marcus Relationship. As noted in the Introduction, the Marcus cross relation has frequently been utilized for the purpose of calculating k_{11} values for Cu(II/I) systems.[39] In particular, we have utilized this relationship to calculate apparent k_{11} values for several Cu(II/I)–polythiaether complexes from cross-reaction rate constants involving both $Cu^{II}L$ reduction and $Cu^{I}L$ oxidation.[15] Although the original formulation of the Marcus relationship did not include considerations of bond formation and rupture during a reaction process, subsequent investigators have derived the same relationship without resorting to this limitation and have shown the applicability of this relationship to such processes as nucleophilic substitution reactions.[40]

The direct applicability of the Marcus equation to Cu(II/I) systems has been challenged by Lee and Anson[6] on the basis of the apparent discrepancies between calculated $k_{11(Red)}$ and $k_{11(Ox)}$ values for systems in which both values have been reported. They proposed that $Cu^{II}L$ and $Cu^{I}L$ species do not contribute equally to the reorganizational parameters due to the bond formation or rupture accompanying the electron-transfer process. On this basis, Lee and co-workers have recalculated all of our previously published k_{11} values to obtain "corrected" values.[7] As we have previously noted,[15-18] however, we believe that the discrepancies which exist are the result of a dual pathway mechanism as formalized in Figure 1. Since different thermodynamic conditions are required to promote $Cu^{II}L$ reduction or $Cu^{I}L$ oxidation, the preferred pathway exhibited for these two reaction processes may differ.[18] If the values obtained for $k_{11(Red)}$ and $k_{11(Ox)}$ do, in fact, represent different reaction pathways, they will not only be of different magnitude but will have no intrinsic relationship to each other.

In a thorough study on the $Cu^{II/I}([14]aneS_4)$ system, we have recently been able to provide a definitive demonstration of the square scheme mechanism depicted in Figure 1. Under specified limiting conditions, the oxidation of $Cu^{I}([14]aneS_4)$ species becomes rate limited by the R → P configurational change and the reaction rate is then first-order in $Cu^{I}L$ and independent of the counter reagent. Although apparent $k_{11(Ox)}$ values can be calculated, the application of the Marcus relationship (which assumes second-order behavior) to such data becomes totally inappropriate. Upon increase of (i) the potential, (ii) the self-exchange rate constant, and/or (iii) the concentration of the counter reagent, a switch to the alternate $Cu^{I}L$ oxidation pathway

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can be brought about, the latter pathway (pathway B) having a different characteristic k_{11} value.[17,18] At that point, the Marcus relationship is again applicable if the k_{11} value representative of this alternate pathway is utilized. Such issues have been disregarded by Lee in his approach.[7]

For reactions in which the intermediate species (P or Q) are at all times equilibrated with the corresponding stable configurations (O and R), both $Cu^{II}L$ reduction and $Cu^{I}L$ oxidation should proceed by a constant pathway. Under such circumstances, we propose that the Marcus equation should yield consistent k_{11} values for both oxidation and reduction regardless of the change in coordination number. It is our premise that the current study represents this latter situation.

To illustrate the foregoing point, the Marcus relationship has been applied to both the k_{12} and k_{21} cross-reaction rate constants in the form of the following expressions:[41]

$$k_{11(\mathrm{Red})} = (k_{12})^2/[k_{22}K_{12}f_{12}(W_{12})^2] \quad (15)$$

$$k_{11(\mathrm{Ox})} = (k_{21})^2/[k_{22}K_{21}f_{21}(W_{21})^2] \quad (16)$$

In these expressions, k_{22} represents the self-exchange rate constant for the $Ru^{III/II}(NH_3)_5py$ counter reagent (1.1×10^5 M^{-1} s^{-1}),[42] K_{12} and K_{21} represent the equilibrium constants for the forward and reverse processes in reaction 5 {$K_{12} = (K_{21})^{-1} = 2.3 \times 10^2$ based on E^f = 0.46 V for $Cu^{II/I}([15]aneNS_4)$[22] and 0.32 V for $Ru^{III/II}(NH_3)_5py$},[43] f_{12} = 0.78 and f_{21} = 0.77 are calculated nonlinear correction factors, and $W_{12} = W_{21} = 1.4_3$ is the calculated work term correction based on ionic radii of 4.4 and 3.8 Å for the copper and ruthenium complexes, respectively.[18]

With utilization of the "best" values of $k_{12} = 1.0 \times 10^6$ M^{-1} s^{-1} and $k_{21} = 1.0 \times 10^4$ M^{-1} s^{-1} for reaction 5 (Tables II–IV), eqs 15 and 16 yield $k_{11(\mathrm{Red})} = 2._8 \times 10^4$ M^{-1} s^{-1} and $k_{11(\mathrm{Ox})} = 1._4 \times 10^5$ M^{-1} s^{-1}. The latter value is in direct agreement with the NMR value obtained at 25 °C, $k_{11(\mathrm{ex})} = 1.4 \times 10^5$ M^{-1} s^{-1}, while the former value is within a factor of 5. In fact, this is the first Cu(II/I) system for which a consistent k_{11} value has been generated using all three methods (i.e., $Cu^{II}L$ reduction, $Cu^{I}L$ oxidation, and direct self-exchange). Since all three values agree within experimental error, we conclude that all three studies represent reaction by a single pathway with no evidence of configurationally-limited behavior. Moreover, this level of agreement supports the hypothesis that *the Marcus relationship does apply to Cu(II/I) systems* (provided that the cross reactions are carried out under conditions where any metastable intermediates are equilibrated with the ground-state species).

Of the limited number of Cu(II/I) systems for which both reduction and oxidation cross-reaction kinetics have been provided, the majority show discrepancies between $k_{11(\mathrm{Red})}$ and $k_{11(\mathrm{Ox})}$.[44] As noted above, however, these discrepancies may represent data obtained under conditions where the two self-exchange rate constants represent differing pathways or where one value was obtained under conditions where a configurational change has become rate limiting.[18] In the absence of independent data (such as we have recently generated using rapid-scan cyclic voltammetry),[17] the onset of configurationally-limited behavior and/or the energy relationships between competing pathways cannot be predicted. However, whenever the $k_{11(\mathrm{Red})}$ and $k_{11(\mathrm{Ox})}$ values for a single Cu(II/I) system are in disagreement, the existence of such behavior must be suspected. Under such circumstances, any attempt to derive a correlation between $k_{11(\mathrm{Red})}$ and $k_{11(\mathrm{Ox})}$ values will lead to erroneous conclusions. Thus, the "corrected" k_{11} values of Lee et al.[7] must be viewed with suspicion.

Acknowledgment. This work was supported, in part, by a contract from the J. Paul Getty Conservation Institute. We wish to acknowledge the contributions of the Wayne State University Central Instrumentation Facility in making available the nuclear magnetic resonance spectrometers and the ancillary equipment utilized in this work.

Supplementary Material Available: Tables listing original NMR line width measurements and original stopped-flow kinetic data (3 pages). Ordering information is given on any current masthead page.

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