

Electron Transfer by Copper Centers

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1. Introduction

1.1. Scope of the Current Review

All electron-transfer reactions are presumed to involve a significant reorganizational energy representing a combination of (i) the internal changes in bond lengths and angles due to changes in electron density and orbital configurations and (ii) the reorganization of the surrounding solvent matrix due to changes in the dipoles of the redox species. As a d^9 system, Cu(II) tends to adopt a six-coordinate tetragonal (distorted octahedral) geometry or a five-coordinate (square pyramidal or trigonal bipyramidal) geometry, whereas Cu(I), as a d^{10} system, is generally found to be four-coordinate (tetrahedral).^{1,2} Thus, as illustrated in Figure 1, electron transfer in unconstrained Cu(II/I) systems is presumed to involve the rupture of one or two coordinate bonds and a twisting of the remaining bond angles. As a result, internal reorganizational energies are presumed to be particularly significant in the electron-transfer behavior of copper. On the other hand, the d^{10} electronic configuration of Cu(I) should not exhibit a strong preference for any specific geometry and the Jahn–Teller distortion in Cu(II) complexes is a dynamic process,³ which suggests that the geometry of Cu(II) complexes is somewhat plastic.⁴

The current review examines the influence of coordination geometry upon both (i) the thermo-

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David Rorabacher was born in Ypsilanti, Michigan, in 1935 and received his B. S. degree in chemistry from the University of Michigan in 1957. After a two-year interlude as a research engineer with the Ford Motor Company, he entered the graduate chemistry program at Purdue University, receiving his Ph.D. degree in analytical chemistry under Dale Margerum in 1963. He spent a year as a faculty member at Wayne State University in Detroit, Michigan, before departing for an NIH-sponsored postdoctorate in relaxation methods with Manfred Eigen at the Max Planck Institute for Physical Chemistry in Göttingen, Germany. He then returned to Wayne State where his research has primarily focused on the thermodynamics and mechanisms of fast metal ion reactions in solution, including complex formation and dissociation and electron-transfer processes. Other emphases have included the investigation of solvent effects and macrocyclic ligands upon reaction properties and the development of noncomplexing buffers and selective complexing agents with biomedical applications. The unusual mechanistic behavior of copper(II/I) electron-transfer reactions has been a major focus of his research for the past two decades.

dynamic potentials and (ii) electron-transfer kinetics for Cu(II/I) systems involving a single copper center. Since specific structures may have an impact upon these parameters, relevant crystal structures or other structural information is cited throughout this document. The major emphasis, however, is on the interpretation of the kinetic behavior in terms of the stepwise mechanisms.

The literature on systems involving dicopper centers or those with single copper centers reacting with dioxygen is not included. There are two reasons for these latter omissions: (i) most such systems react by inner-sphere mechanisms, which are more difficult to analyze rigorously, and (ii) the thermodynamic and kinetic parameters are less well characterized as a function of structure. Such systems differ significantly from those discussed in this review and deserve to be treated separately.

The only previous attempt to review the literature on Cu(II/I) electron-transfer rate constants in terms of the influence of structure was that authored by Yandell in 1983.⁵ (More recently, Stanbury and co-workers compiled a table of self-exchange rate constants for 24 inorganic Cu(II/I) systems and 16 copper enzymes.)⁶ Yandell's review was not comprehensive, and more recent work has added significantly to our understanding of the possible role of structure in these processes. Therefore, the systems that were reviewed by Yandell are revisited in the current work, which attempts to cover the pertinent kinetic literature on Cu(II/I) electron transfer from 1977 to the present (plus two early publications from 1956 and 1967).

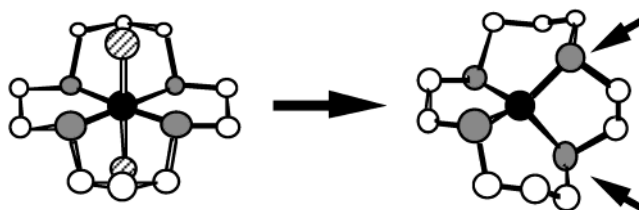


Figure 1. Coordination change commonly occurring in Cu(II/I) electron transfer. This example shows the macrocyclic tetrathiaether [14]aneS₄ as the coordinated ligand. The Cu(II) complex on the left is tetragonally distorted with the four sulfur donor atoms (shaded circles) coordinated in the plane and two solvent molecules or anions (striped circles) coordinated to the copper atom (solid circle) at the axial positions. Upon reduction to the Cu(I) complex (right), the two axial donor bonds rupture and the remaining four donor atoms twist toward a tetrahedral arrangement. This process involves inversion of the two donor atoms designated by arrows. (Open circles represent carbon atoms and the hydrogen atoms have been omitted for clarity.)

Although a few studies have been reported on electron-transfer reactions involving Cu(III/II), this area is much less well explored and the amount of existing data does not permit broad conclusions to be drawn about the relationships between structure and electron-transfer properties. Therefore, this topic is treated only briefly at the end of this review.

Throughout this review, an attempt has been made to analyze and interpret the significance of the reported studies rather than merely catalog them. However, in a review of this magnitude, it is likely that the conclusions of some authors will have been misinterpreted or overlooked. For these, and other sins of omission and commission, the author of this review expresses his sincere apologies.

1.2. Correlation to Enzymatic Systems and the "Entatic State" Concept

Copper is second only to iron in its prevalence in redox-active metalloproteins. This fact alone has stimulated much interest in the study of the electron-transfer properties of low molecular weight complexes of copper. Although the current review is principally focused upon inorganic Cu(II/I) systems, the relevance to biological Cu(II/I) systems has been recognized by nearly every investigator who has been active in this field, and possible correlations between the behavior of low molecular weight and enzymatic systems have been used to justify many inorganic studies reported in the literature. Of the various copper enzymes, the type 1 copper sites in blue copper proteins have been the most extensively investigated in terms of their structures, their thermodynamic potentials, and their electron-transfer kinetics. An examination of several electron-transfer studies on blue copper proteins is included to demonstrate the extent to which low molecular weight complexes both compare and differ in their behavior.

In an often-quoted paper published in 1968,⁷ Vallee and Williams postulated that in all enzymes the active site is constrained by the surrounding protein matrix to adopt a geometry similar to that anticipated for the corresponding transition state geom-

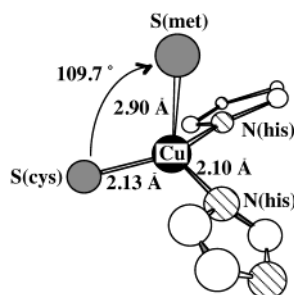


Figure 2. Schematic representation of the geometry of the Cu site in the blue copper protein plastocyanin. The copper atom (solid circle) sits above the plane of the two histidine nitrogens (striped circles) and the cysteine sulfur (shaded) with an elongated axial bond to a methionine sulfur. The coordination geometry in azurin is similar with an elongated bond to a carboxylic oxygen from a glycine residue situated at an axial site opposite to the methionine sulfur. The open circles represent the carbon atoms in the histidine imidazole groups. (Hydrogens and peripheral atoms have been omitted for clarity.)

etry of an unconstrained system. As a result, the reorganizational energy required to reach the transition state would be minimized and the reaction kinetics would be maximized. These authors claimed that redox-active metalloenzymes with iron and copper at the active sites should represent prime examples of this “entatic (constrained) state.” For the Fe(III/II) redox couple, they noted that the bond lengths normally exhibited by Fe(III) are significantly shorter than those for Fe(II). Thus, they suggested that in heme proteins the porphyrin ring might be expected to maintain Fe–N bond lengths that were intermediate between the normal bond lengths for unconstrained Fe(II)–N and Fe(III)–N bonds. As a more extreme example, they noted that Cu(II) generally changes both its coordination number and its coordination geometry upon reduction to Cu(I) as noted above.

Williams⁸ later expounded on this theme and suggested that in the type 1 copper sites in blue copper proteins the Cu atoms might be constrained to an intermediate five-coordinate geometry. Subsequent crystal structures of a large number of blue copper proteins have lent credibility to this prophecy as such sites have been found to be four-coordinate trigonal pyramidal (distorted tetrahedral)—as in plastocyanins—or five-coordinate trigonal bipyramidal—as in azurins.^{9–17} In those type 1 Cu sites that are four-coordinate, the Cu atom is coordinated to two imine nitrogens from histidine residues and the mercaptide sulfur from a cysteine residue with an elongated axial bond to the thioether sulfur from a methionine residue (Figure 2) or, less commonly, to a glutamine oxygen. For sites exhibiting a coordination number of five, an elongated bond to a carboxylic oxygen from a glycine residue occupies the opposite axial site to generate a trigonal bipyramidal geometry. Although it was long thought that the apparent distortion evident in these unusual geometries arose from matrix constraints, as originally proposed by Vallee and Williams, recent analyses by Solomon and co-workers^{18–21} and by Ryde and co-workers^{22–24} have led to the conclusion that the geometries of these copper sites are not the result of

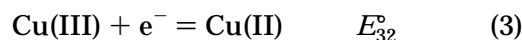
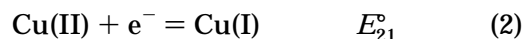
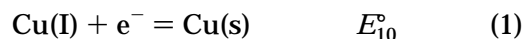
strain but are induced by the nature of the covalent Cu–S(cysteine) bond itself.

The conclusions of Solomon and Ryde imply that the attempts reported in the literature to generate low molecular weight complexes that duplicate the geometries of the type 1 copper site are unlikely to generate similar thermodynamic and kinetic behavior since none of the studies reported to date involve mercaptide sulfur donor atoms. In that sense, they are not truly biomimetic. Nonetheless, the influence of coordination geometry upon the potentials and kinetics of electron transfer in Cu(II/I) systems is a matter of fundamental importance to both inorganic copper and copper enzyme chemistry, and several parallels between the two are noted.

2. Characterization of Electron-Transfer Processes

Electron-transfer processes inevitably require the participation of both an electron donor and an electron acceptor. To characterize the contribution of the copper system to an overall electron-transfer process, it is necessary to factor out the individual contributions of the two reacting partners. For potential values in aqueous media, this is generally accomplished by referencing all potentials to the standard hydrogen electrode (SHE). In nonaqueous solvents, the ferrocene–ferricenium ion redox couple is the reference system recommended by the International Union of Pure and Applied Chemistry (IUPAC) as a more easily reproducible reference system,²⁵ although many investigators simply report their Cu(II/I) potentials relative to the reference electrode used in their specific measurements.

The electrochemistry of copper can be expressed by three one-electron processes:



Standard potential values for solvated copper have been determined as thermodynamic values in terms of activities. For the majority of electrochemical measurements, however, relatively high ionic strengths (≥ 0.01 M) are used so that the experimental values are obtained as concentration potentials, designated by $E^{\circ'}$ values:

$$E = E_{21(\text{solv})}^{\circ'} - \frac{RT}{n\mathcal{F}} \ln \frac{[\text{Cu}^+]}{[\text{Cu}^{2+}]} \quad (4)$$

Thus,

$$E_{21(\text{solv})}^{\circ'} = E_{21}^{\circ} - \frac{RT}{n\mathcal{F}} \ln \frac{\gamma_{\text{Cu}^+}}{\gamma_{\text{Cu}^{2+}}}$$

where γ_{Cu^+} and $\gamma_{\text{Cu}^{2+}}$ represent the appropriate activity coefficients.

In the presence of complexing agents, the potential values are usually reported in terms of the concentrations of the complexed species:



$$E = E_{21}^{\circ'} - \frac{RT}{n\mathcal{F}} \ln \frac{[\text{Cu}^{\text{I}}\text{L}]}{[\text{Cu}^{\text{II}}\text{L}]} \quad (6)$$

where L represents a coordinated ligand. If the fraction of uncomplexed copper ion is relatively small in both oxidation states, the relationship between the concentration potential, $E_{21}^{\circ'}$, for any Cu(II/I) complex system and that for the solvated Cu(II/I) couple, $E_{21}^{\circ'}(\text{solv})$, can be represented as

$$E_{21}^{\circ'} = E_{21}^{\circ'}(\text{solv}) + \frac{RT}{n\mathcal{F}} \ln \frac{K_{\text{Cu}^{\text{I}}\text{L}}}{K_{\text{Cu}^{\text{II}}\text{L}}} \quad (7)$$

In practice, most potential values for Cu(II/I) systems are estimated from the average potentials of the cathodic and anodic peaks ($E_{1/2}$) observed in slow scan cyclic voltammetric (CV) measurements. This is reasonably reliable for reversible systems involving a single form of the Cu(II) and Cu(I) species providing that the ionic strength and temperature are well controlled and that the species do not adsorb on the electrode surface. For such systems, the value of $E_{1/2}$ is presumed to approximate $E^{\circ'}$.

For electron-transfer kinetics, the contribution of the copper redox couple is represented by the so-called electron self-exchange rate constant, designated as k_{11} throughout this review. This parameter is defined as the rate constant for the exchange of an electron between two copper atoms in the two oxidation states of interest:



This rate constant is independent of any thermodynamic driving force (since $\Delta G^{\circ} = 0$). Such values tend to be difficult to obtain directly since the reactants and products are identical. Both NMR line broadening and isotope scrambling can be used to resolve these values under favorable circumstances as discussed later. However, most k_{11} values are calculated from experimental rate constants measured from reactions between the Cu(II/I) species and appropriately selected oxidizing or reducing agents as discussed in section 4.

3. Correlation of Copper(II/I) Potential Values to Ligand Morphology

Although this review is primarily focused on the electron-transfer kinetics of copper systems, their redox thermodynamics are also of interest, particularly since the calculation of self-exchange rate constants from cross-reaction kinetics requires a knowledge of the redox potentials of both reactants. Potential values for literally hundreds of copper complexes have been reported in the literature, both in aqueous and in nonaqueous solvents. Two limited compilations (both sponsored by the International

Table 1. Empirical Parameters Affecting Copper(II/I) Potential Values^a

ligand feature	ΔE_{L} (mV)	mod ΔE_{L} (mV)	significance level (%)
thioether donor	+141 ± 12	170	>99.99
aromatic N-donor	+52 ± 13		>99.9
aliphatic N-donor	-75 ± 12		>99.99
carboxylate O-donor	-26 ± 23		70
macrocyclic ligand	+24 ± 44	-120, ^b -360 ^c	40
5-memb chelate rings	-46 ± 10		>99.99
tripodal ligand	+291 ± 52		>99.99

^a Values from ref 30 except as noted. ^b Macrocyclic effect as evaluated for tetrathiaether complexes (ref 31). ^c Macrocyclic effect as evaluated for tetraamine complexes (ref 31).

Union of Pure and Applied Chemistry) are noteworthy. That by Milazzo and Caroli²⁶ is the more comprehensive as it provides potentials for complexes formed with a variety of ligands, some being reported in more than one solvent. This source also includes references to the original literature. The compilation by Bertocci and Wagman²⁷ includes only simple complexing agents in aqueous solution and provides fewer literature references, although it focuses more strongly on the overall thermodynamic parameters. A much more comprehensive list of copper redox potentials has recently been compiled.²⁸

Patterson and Holm²⁹ made the first attempt to generate an extensive correlation of Cu(II/I) redox potentials to the coordination geometry imposed by various coordinated ligands. On the basis of polarographic measurements on 37 copper complexes in DMF, they observed that (i) nonplanar bis-chelate complexes underwent reduction at higher potentials than their planar analogues and (ii) planar quadridentate complexes showed a marked dependence on the nature of the donor atoms with the potentials increasing in the order $\text{N}_4 < \text{N}_2\text{O}_2 < \text{N}_2\text{S}_2$. Addison³⁰ compared the potentials of 45 copper complexes in water and methanol (plus two in acetonitrile)—including those with N, S, and O donor atoms—from which he generated an empirical equation relating Cu(II/I) potentials to a number of features of the complexed ligand. These included the number of donor atoms of specific types (thioether sulfur, aromatic nitrogen, aliphatic nitrogen, carboxylic oxygen) and the morphology of the ligand (macrocyclic, tripodal, number of five-membered vs six-membered chelate rings). The resulting empirical relationship was of the form

$$E_{1/2} = E_{(\text{solv})}^{\circ'} + \sum (n\Delta E_{\text{L}}) \quad (9)$$

where $E_{(\text{solv})}^{\circ'}$ represents the concentration potential of the aequated Cu(II/I) redox couple (0.13 V vs SHE),³¹ ΔE_{L} represents the change in the Cu(II/I) potential brought about by various ligand features (such as donor atom type, number of five-membered chelate rings, etc.), and n represents the number of times that specific feature appears in a coordinated ligand. A tabulation of the values generated by Addison for a number of ligand features is given in Table 1. Also included are modified parameters subsequently suggested by Bernardo et al.³¹ as a result of their observation that the magnitude of the

macrocyclic effect appeared to vary with the number of amine nitrogen donor atoms in the macrocycle, presumably due to the differing degree of nitrogen atom solvation in acyclic and macrocyclic ligands.³²

More recently, Comba and Jakob³³ attempted to correlate the potentials of 26 copper(II/I) tetramine complexes to calculated strain energies. They emphasized that each conformer of a given $\text{Cu}^{\text{II/I}}\text{L}_n$ system should give rise to a different redox potential. However, they also noted that, for conformers with small variations in strain, the potential differences were minor while highly strained conformers would be present in such small quantities that they could not be accessed experimentally.

The relatively high potentials observed for both thioether sulfur-containing ligands and tripodal ligands has led many investigators to conclude that both features tend to stabilize the Cu(I) oxidation state. However, this conclusion appears to be incorrect. In a series of related quadridentate macrocyclic ligand complexes, Bernardo et al.³¹ determined that the Cu(II/I) potentials increased by an average of 0.3 V each time a thioether sulfur was substituted for an amine nitrogen donor atom. Since the stability constants of these complexes had also been determined independently,³⁴ these authors were able to demonstrate that the potential changes were due entirely to the *destabilization of the Cu(II) oxidation state* by thioether sulfur, that is, the Cu(I) stability constants remained virtually constant regardless of whether S or N donor atoms were included in the macrocyclic ring. Subsequently, Ambundo et al.³⁵ demonstrated that, for 12 tripodal ligands of copper containing a tertiary amine nitrogen bridgehead and both thioether sulfur and pyridyl nitrogen donor atoms on the legs, the potentials were governed almost entirely by the destabilization of Cu(II) rather than the stabilization of Cu(I) by the tripodal geometry. Furthermore, they demonstrated that the potentials of more than 35 Cu(II/I) systems, covering a range of 1.5 V, were essentially linear when plotted against the logarithmic stability constants of the $\text{Cu}^{\text{II/L}}$ complexes. An expanded version of their original plot is shown in Figure 3, which includes over 50 macrocyclic, acyclic, and tripodal ligands containing amine and imine nitrogens and thioether sulfur donor atoms. All ligands represented are uncharged to exclude the influence of electrostatic effects. The line drawn in this plot has the Nernstian slope (-0.059) in accordance with the concept that the values of $K_{\text{Cu}^{\text{I/L}}}$ are relatively constant as indicated by a rearrangement of eq 7 for 25 °C:

$$E_{21}^{\circ'} = E_{(\text{soln})}^{\circ'} + \frac{2.303RT}{nF}(\log K_{\text{Cu}^{\text{II/L}}} - \log K_{\text{Cu}^{\text{I/L}}})$$

$$E_{21}^{\circ'} = \text{constant} - 0.059 \log K_{\text{Cu}^{\text{II/L}}} \quad (10)$$

It is presumed that other Cu(II/I) systems would also cluster about this line, but reliable stability constant values are lacking for the majority of Cu(II) complexes for which potential measurements have been reported.

The net conclusion from these various studies is that, as a d^{10} system, Cu(I) has little preference for

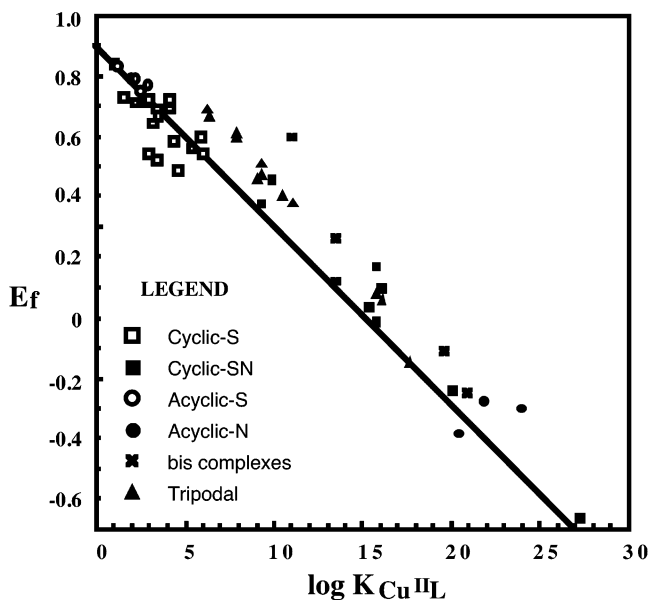


Figure 3. Plot of the $\text{Cu}^{\text{II/L}}$ redox potential versus the logarithmic $\text{Cu}^{\text{II/L}}$ stability constant (eq 10) for 50 complexes with uncharged ligands. The ligands represented in this plot include macrocyclic, acyclic, and tripodal ligands, which contain thioether, amine nitrogen, and pyridine nitrogen donor atoms. The solid line has the Nernstian slope (-0.059), indicating that the stability constants for all $\text{Cu}^{\text{I/L}}$ complexes are relatively constant. The solid line represents a $\text{Cu}^{\text{I/L}}$ stability constant of 10^{13} . (Plot expanded from ref 35).

specific coordination geometries or donor atom types. As a result, Cu(I) complexes exhibit little variation in their overall stability constants for complexes involving a wide variety of ligand structures in aqueous solution. When the solvent matrix is altered, however, significant changes do occur since the complexing ligand competes with the solvent for inner-sphere coordination sites on both Cu(II) and Cu(I) ions. For example, in acetonitrile, for which Cu(I) has a strong affinity, the stabilities of many Cu(I) complexes decrease by approximately 10^6 relative to their aqueous values whereas the stabilities of the corresponding Cu(II) complexes tend to increase by a similar magnitude.³⁶

The potential values for the majority of Cu(II/I) complexes included in this review have been reported in the literature, most commonly in either aqueous solution or acetonitrile. These values are listed in Table 2. The potential values in acetonitrile are referenced against ferrocene as recommended.²⁵

4. Treatment of Electron-Transfer Kinetic Data for Inorganic Copper(II/I) Complexes

4.1. Determination of Self-Exchange Rate Constants—The Marcus Approach

In the vast majority of studies, the electron self-exchange rate constant (k_{11}) for the copper complex of interest, as defined by eq 8, is derived from reactions with selected counterreagents involving the transfer of a single electron:



Table 2. Formal Potential Values for Cu(II/I) Complexes Discussed in This Review

complexed ligand	table	solvent			ref
		H ₂ O	CH ₃ CN	other	
		V vs SHE	V vs Fc	V vs std listed	
water	3	0.13			31
bpy	5	0.12			5
dipa	5	0.20			5
pyim	5	0.08			5
phen	5	0.17			5
4,4'-Me ₂ bpy	5	0.09			78
4,7-Me ₂ phen	5	0.10			78
5-NO ₂ -phen	5	0.26			5
terpy	5	-0.02			78
6,6'-Me ₂ bpy	5		0.56	0.59 (D1 vs SHE)	113, 112
Me ₄ bpy	6			0.60 (D1 vs SHE)	112
2,9-Me ₂ phen	6	0.60	0.28		5, 119
Me ₂ Φ ₂ phen (dpmp)	6	0.62	0.27		100, 121
Me ₂ (ΦSO ₃) ₂ phen (dpsmp)	6	0.62			100
2,9-Φ ₂ phen	6		0.30		120
diphen	6		-0.15, 0.40 (E _{pc} , E _{pa})		126
Me ₂ -2,3,2-S ₄	7	0.89			132
Et ₂ -2,3,2-S ₄	7	0.89			132
Me ₂ -3,2,3-S ₄	7	0.83			141
<i>cis</i> -cyhx-Me ₂ -3,2,3-S ₄	7	0.75			141
<i>trans</i> -cyhx-Me ₂ -3,2,3-S ₄	7	0.77			141
[12]aneS ₄	7	0.64			132
[13]aneS ₄	7	0.52			133
[14]aneS ₄	7	0.59			56
[14]aneS ₄ - <i>b</i>	7	0.69			152
[15]aneS ₄	7	0.64			133
[16]aneS ₄	7	0.71			132
[15]aneS ₅	7	0.69			168
<i>syn</i> -[14]aneS ₄ -diol	7	0.54			134
<i>anti</i> -[14]aneS ₄ -diol	7	0.49			134
<i>cis</i> -cyhx-[14]aneS ₄	7	0.54			136
<i>trans</i> -cyhx-[14]aneS ₄	7	0.60			136
<i>syn-cis, cis</i> -dicyhx-[14]aneS ₄	7	0.57			137
<i>anti-cis, cis</i> -dicyhx-[14]aneS ₄	7	0.67			137
<i>meso-trans, trans</i> -dicyhx-[14]aneS ₄	7	0.58			137
<i>dl-trans, trans</i> -dicyhx-[14]aneS ₄	7	0.69			137
<i>cis, trans</i> -dicyhx-[14]aneS ₄	7	0.60			137
<i>cis</i> -cypt-[14]aneS ₄	7	0.56			135
<i>trans</i> -cypt-[14]aneS ₄	7	0.67			135
<i>syn-cis, cis</i> -dicypt-[14]aneS ₄	7	0.57			138
<i>anti-cis, cis</i> -dicypt-[14]aneS ₄	7		0.28		138
<i>meso-trans, trans</i> -dicypt-[14]aneS ₄	7		0.34		138
<i>dl-trans, trans</i> -dicypt-[14]aneS ₄	7		0.39		138
<i>cis, trans</i> -dicypt-[14]aneS ₄	7	0.63			138
pdto	9	0.59			5
ta	9	0.19			5
1dta	9	0.27			5
2dta	9	0.30			5
3dta	9	0.31			5
tta	9	0.44			5
[14]aneNS ₃ - <i>a</i>	9	0.38			31
[14]aneNS ₃ - <i>b</i>	9	0.41			152
[14]aneNSSN	9	-0.01			31
[14]aneNSNS	9	0.10			153
(py) ₂ DAP	10		-0.14 (SCE)		154
(imidH) ₂ DAP	10		-0.27 (SCE)		154
(imidR) ₂ DAP	10		-0.26 (SCE)		154
W ₁₂ O ₄₀ ⁸⁻	10	-0.02			47
bib	10		0.27 (Ag/AgCl)		6
bite	10		0.32		142
TMMEA	11	0.69			163

Table 2 (Continued)

complexed ligand	table	solvent			ref
		H ₂ O	CH ₃ CN	other	
		V vs SHE	V vs Fc	V vs std listed	
PMMEA	11	0.38			165
PMAS	11	0.40			165
PEMEA	11	0.60			165
PEAS	11	0.61			165
BPEMEA	11	0.46			165
TPMA	11	-0.15			165
TPEA	11	0.51			165
TAAB	12	0.23			167
[15]aneS ₅	12	0.69			175
[15]aneNS ₄	12	0.46			31
[13]aneS ₄	12	~0.52			175
oxathiane-[12]aneS ₄	12	0.72			171
[9]aneS ₃	13	0.72			176
Cupredoxins					
azurin	14	0.31			182
stellacyanin	14	0.19			182
plastocyanin	14	0.37			182
pseudoazurin	14	0.28			211
umecyanin	14	0.29			182
rusticyanin	14	0.68			212, 213
amicyanin	14	0.26			211

where the counterreagent, A_{Red} or A_{Ox}, is selected on the basis of its favorable properties including the fact that it will not readily undergo inner-sphere substitution nor form inner-sphere bridges to the copper complex. For such reactions, the overall rate equation is generally observed to be first-order with respect to each reactant for either Cu^{II}L reduction,

$$\text{rate} = -\frac{d[\text{Cu}^{\text{II}}\text{L}]}{dt} = k_{12}[\text{Cu}^{\text{II}}\text{L}][\text{A}_{\text{Red}}] \quad (12)$$

or Cu^IL oxidation,

$$\text{rate} = -\frac{d[\text{Cu}^{\text{I}}\text{L}]}{dt} = k_{21}[\text{Cu}^{\text{I}}\text{L}][\text{A}_{\text{Ox}}] \quad (13)$$

If the reaction takes place by an outer-sphere mechanism, the electron transfer can be conceived to occur at the intersection of the potential energy surfaces for the (nonbridged) reactants and products. Based on this concept, the theoretical relationship between the observed cross-reaction rate constants and the self-exchange rate constants for the specific redox couples involved have been formulated by Marcus into the well-known cross-relationship (or "square root relationship"), which can be conveniently rearranged to the form³⁷

$$k_{11} = \frac{(k_{12})^2}{k_{22}K_{12}f_{12}(W_{12})^2} \quad \text{or} \quad k_{11} = \frac{(k_{21})^2}{k_{22}K_{21}f_{21}(W_{21})^2} \quad (14)$$

In these expressions, k_{22} represents the self-exchange rate constant for the selected counterreagent:



K_{12} (or K_{21}) is the equilibrium constant for reaction

11 as determined from the potentials of the two reactants; f_{12} (or f_{21}) is a nonlinear correction term (to account for the fact that the two potential energy surfaces are not linear in the region of their intersection); W_{12} (or W_{21}) is the electrostatic work term function. The last two terms are dependent upon the effective contact radii of the two reacting partners, as well as the distance between their centers of charge at the time of electron transfer. These latter parameters are generally regarded as rough estimates only. Due to the uncertainty of the several parameters involved in eq 14 (i.e., k_{12} or k_{21} ; k_{22} ; the potentials of the two reactants; the effective contact radii; the distance between charge centers) and the fact that k_{11} varies as the square of k_{12} or k_{21} , the difference in k_{11} values obtained for a single Cu(II/I) system from different cross-reactions may vary by as much as 1 order of magnitude.³⁸

The impact of structural changes upon the electron-transfer processes for both Cu(II/I) electron self-exchange reactions and Fe(III)/Cu(I) cross-reactions are illustrated schematically in Figure 4. Based on the normal concept of the Marcus treatment, the coordination geometries of the two reactants are conceived to rearrange to an intermediate structure prior to the transfer of the electron itself. The extent of reorganization for a single redox couple is presumed to be identical for both self-exchange and cross-reactions.

According to the Marcus relationship, the same value for k_{11} should be obtained for a specific Cu^{II/I}L system from any of three possible approaches if outer-sphere reactions are involved: (i) direct measurement of a self-exchange reaction by NMR relaxation measurements (reaction 8), (ii) reduction of the Cu^{II}L species using a suitable reducing reagent, A_{Red} (reaction 11), or (iii) oxidation of the Cu^IL species with an oxidizing agent, A_{Ox} (reverse of reaction 11). For the purposes of this review, values obtained from these

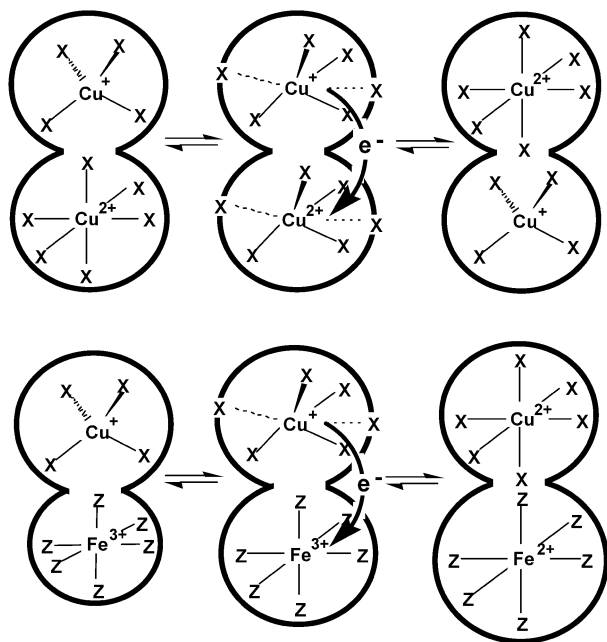


Figure 4. Schematic diagram of outer-sphere reactions as normally conceived for a single-step electron-transfer process showing the reorganization of the inner-sphere coordination geometry in a Cu(II)–Cu(I) self-exchange process (top) and in a cross-reaction between Cu(I) and Fe(III) complexes (bottom). In the case of Fe(III/II), the bond lengths change upon changing the oxidation state whereas for Cu(II/I) the bond lengths remain relatively constant but the number of coordinate bonds changes. The solid circles represent the first layer of solvent molecules surrounding the complexes, these two layers having merged in forming the outer-sphere complex. In each diagram, the left figure represents the precursor complex, the middle diagram represents the transition state at the time of electron transfer, and the right diagram represents the successor complex. The same extent of reorganization is perceived to take place at the copper center in both the self-exchange and cross-reactions. Donor atoms attached to the Cu center that are shown as part of the outer-sphere solvent layer are perceived to be in the process of forming or breaking (depending upon the direction in which the reaction is proceeding). This diagram does not attempt to show the metastable intermediates.

three approaches are designated as $k_{11(\text{NMR})}$, $k_{11(\text{Red})}$, and $k_{11(\text{Ox})}$, respectively. Agreement among the k_{11} values obtained by these different approaches is considered to verify the applicability of Marcus theory to any specific system. In earlier studies on Cu(II/I) systems, k_{11} values were generally derived solely from kinetic studies on cross-reactions involving the reduction of the Cu^{II}L species ($k_{11(\text{Red})}$). It is now recognized that both oxidation and reduction reaction kinetics must be investigated if the system is to be fully characterized since a major part of the reorganization accompanying electron transfer may occur as a discrete step either preceding or succeeding the electron-transfer step.

As originally presented by Marcus, the derivation of eq 14 was based on the treatment of chemical bonds as harmonic oscillators. In nearly all cases, inorganic Cu(II/I) systems involve the rupture or formation of one or two coordinate bonds upon electron transfer. Since bond rupture or formation does not lend itself to the oscillator approach, some

researchers have questioned the validity of the Marcus relationship when applied to Cu(II/I) reactions as noted below.^{39,40} However, the same relationship can be generated without the assumption of harmonic oscillators, and Brauman,⁴¹ among others, has used the Marcus approach for nucleophilic substitution reactions in which bond breakage and formation occurs. Evidence for the applicability of the Marcus relationship to Cu(II/I) electron-transfer reactions is presented in the sections that follow.

4.2 Problems in Obtaining and Interpreting Kinetic Data

Electron-transfer reactions involving monomeric copper complexes reacting with a counterreagent—in which both reactants undergo a one-electron change—tend to be first-order with respect to each reactant as noted in eqs 12 and 13. A large majority of kinetic studies on such processes are conducted under pseudo-first-order conditions in which one reactant is maintained in relatively large excess over the other so that only the more dilute species undergoes an appreciable change in concentration during the kinetic measurements. Under these conditions, the pseudo-first-order rate constant is expected to vary linearly with the concentration of the excess reagent with a zero intercept. Deviations from such behavior may indicate the onset of mechanistic complications (as discussed in the following section) or problems with interfering reactions. To establish the kinetic dependence on the concentration in an unequivocal manner, the reagent in excess should be varied over at least a 10-fold concentration range; but many studies reported in the literature involve much smaller concentration variations. Ideally, the reaction kinetics should also be studied under conditions in which each reactant, in turn, is kept in large excess. This is rarely done, however, and may be impossible to achieve in many cases due to solubility limitations or monitoring signal restrictions.

Incomplete Complexation. For metal complexes that have relatively small stability constants (generally on the order of $\leq 10^6 \text{ M}^{-1}$), the complex may not be fully formed under the conditions utilized for the kinetic study. If a reactant species is incompletely formed, complex formation will appear as a coupled reaction during the electron-transfer process. This situation worsens as the reactant concentrations decrease since the stability constants of even 1:1 complexes have units of reciprocal molarity. Utilization of a large excess of either the metal ion or the ligand makes it possible to minimize this problem, although it should be recognized that *it is the absolute concentration of the ligand or metal ion in excess—and not the ratio of the two—that is the determining factor*. Even for complexes that exhibit large thermodynamic stability constant values, a decrease in pH can cause the conditional complex stability constant to decrease to the point where complex dissociation becomes significant if the ligand is extensively protonated. This latter problem can usually be minimized by buffering the solution at a sufficiently

high pH. However, caution must be taken to utilize a buffer that will not complex the copper ion itself.⁴² A study of the kinetic behavior with respect to a variation in the buffer concentration as well as a variation in pH will tend to reveal the presence of any problems. If a product species is incompletely formed under the reaction conditions used, the product may dissociate as the reaction proceeds, but this is generally not a problem unless this same product is being used to monitor the reaction kinetics.

Dependence of Mechanistic Behavior on Reagent Concentration. For the specific mechanisms described in the next section, additional complications may arise because the choice of reaction pathway may depend on the specific concentration range of the counterreagent; and the order of the reaction with respect to this reagent may vary within different concentration ranges. For this reason, a careful study of the effect of changing the counterreagent concentration is essential if meaningful results are to be obtained.

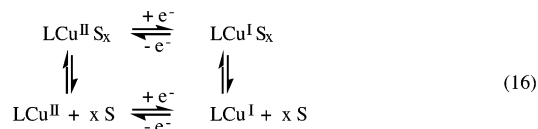
Avoidance of Inner-Sphere Pathways. As noted in the preceding section, most kinetic investigations on Cu(II/I) electron transfer utilize reactions with a specific counterreagent for the purpose of calculating the magnitude of the Cu^{II/I}L self-exchange rate constants by means of the Marcus cross-relation (eq 14). This approach is viable only if the reactions proceed by an outer-sphere mechanism in which there is no direct linking of the two metal ions. In the case of Cu(II) and Cu(I) complexes, for which the inner-coordination sphere is very labile, it is advisable to utilize substitutionally inert counterreagents such as Ru(III/II) complexes to ensure that no inner-sphere bridging occurs. For solvents of lower dielectric or for reactants having high charges of opposite sign, or both, the extent of ion pairing must also be taken into account.

Physical Parameters of Reactants. In many publications involving Cu(II/I) electron-transfer kinetics, the experimental details are not presented in sufficient detail to permit a critical evaluation as to whether the foregoing conditions have been rigorously met. The physical parameters required for eq 14 (especially the ion size parameters assumed by the investigators) are also frequently not specified with sufficient detail to permit a check on the veracity of the calculations made. Until recently, many studies utilized a single counterreagent so that no cross-check of the validity of the calculated self-exchange rate constants was possible.

For all of the foregoing reasons, it is difficult to provide a detailed evaluation of the veracity of the reported self-exchange rate constants for many of the copper complexes that have been based on reaction with a single counterreagent. In the current review, however, results from studies conducted by different investigators on several series of closely related complexes make it possible to obtain an overview of the various types of kinetic behavior encountered and to permit these to be compared to the physical features of the systems involved.

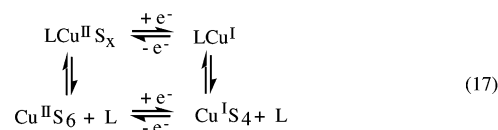
4.3. Summary of Proposed Mechanisms for Copper(II/I) Systems

In his 1983 review,⁵ Yandell noted that not only do the coordination number and stereochemistry of Cu(II) and Cu(I) differ, but both oxidation states are also labile. The lability of the inner-sphere sites dictates that, when Cu(II/I) systems are reacted with counterreagents, care must be taken to select reagents that themselves are substitutionally inert as noted above. It is particularly interesting to note that, even in the absence of inner-sphere mechanisms, Yandell suggested that a dual pathway mechanism might be manifested in which the expansion or contraction of the coordination number of copper could occur as a discrete step either preceding or following the electron-transfer step. A similar mechanism had also been proposed by Al-Shatti, Lappin, and Sykes.⁴³ Based on a hypothetical system involving five- or six-coordinate Cu(II), this mechanism can be represented as a simple square scheme,



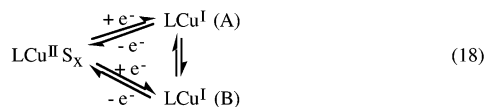
where L represents a quadridentate ligand, "S" represents a solvent molecule (or other labile unidentate species), $x = 1$ or 2 , LCu^{II} represents a possible Cu(II) intermediate species with reduced coordination number, and $\text{LCu}^{\text{I}}\text{S}_x$ represents a Cu(I) intermediate with expanded coordination number. Based on the literature available at the time of his review, Yandell concluded that there was "no convincing theoretical argument or experimental observations to support the case for either $\langle \text{LCu}^{\text{II}} \rangle$ or $\langle \text{LCu}^{\text{I}}\text{S}_x \rangle$ as 'real' intermediates."⁵

Appearing back to back with Yandell's review and, therefore, not included in his data was our own summary⁴⁴ on the investigation of a series of Cu(II/I)-polythiaether complexes, which included a study of both their reduction and their oxidation kinetics. At that time, we had observed discrepancies in the self-exchange rate constants calculated from cross-reactions involving Cu^{II}L reduction ($k_{11(\text{Red})}$) and Cu^IL oxidation ($k_{11(\text{Ox})}$) when using Cu(II/I) potential measurements obtained from slow-scan cyclic voltammetric (CV) measurements; but we had also observed the appearance of at least one additional anodic peak in some CVs as the scan rate was increased. As one possible explanation of the CV behavior, a related dual pathway mechanism was considered in which the coordinated multidentate ligand dissociated from the Cu^{II}L species in a discrete step prior to the heterogeneous electron-transfer reaction of the aquated species ($\text{Cu}^{\text{II}}\text{S}_6$ or $\text{Cu}^{\text{I}}\text{S}_4$ where S represents a solvent molecule and $x = 1$ or 2):



This mechanism was rejected on the basis of its

incompatibility with known values for substitution rates for Cu(II) and Cu(I). Instead, the unusual appearance of the CVs was attributed to the interconversion of two Cu(I) species to produce a triangular mechanism:



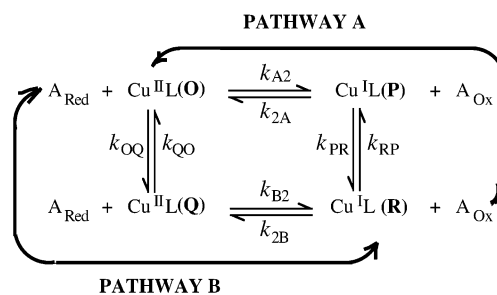
In view of the uncertainties in the E° values generated from the CVs for these Cu^{II/I} redox couples, the Marcus equations for the oxidation and reduction cross-reaction rate constants were, at that time, combined to generate a single “average” k_{11} value.

Nearly all of the studies summarized by Yandell involved the reduction of Cu(II) complexes by various reducing agents. A lone exception was the study by Yoneda, Blackmer, and Holwerda⁴⁵ on the oxidation of Cu(phen)₂⁺ and Cu(bpy)₂⁺ (phen = 1,10-phenanthroline, bpy = 2,2'-bipyridine) by Co^{III}(EDTA)⁻. From their studies, Yoneda et al. calculated $k_{11(\text{Ox})}$ values of 5×10^7 and $4 \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$, respectively, for these two Cu(II/I) systems. These latter values contrast dramatically with the corresponding $k_{11(\text{Red})}$ values of 43 and $1.4 \times 10^2 \text{ M}^{-1} \text{ s}^{-1}$ that Augustin and Yandell had subsequently measured for these same two systems from the reduction of the Cu(II) complexes with cytochrome-*c*^{II}.⁴⁶ These latter authors were unable to explain the huge differences in the apparent self-exchange rate constants obtained from the oxidation and reduction of these two systems. It should be noted, however, that, immediately thereafter, Lappin and Peacock⁴⁷ suggested that the discrepancy might be “rationalized in terms of a concomitant structural change which may participate in the rate-determining step of the cross-reaction.”

Almost simultaneously with the appearance of Yandell's review, Lee and Anson published a paper³⁹ in which they focused on the discrepancies in the k_{11} values obtained by Yoneda, Blackmer, and Holwerda for the oxidation of Cu^I(phen)₂⁺ and Cu^I(bpy)₂⁺ and those obtained by Augustin and Yandell for the corresponding reduction kinetics as noted above. Lee and Anson concluded that, due to the need to form and rupture coordinate bonds during electron transfer, the Marcus cross-relationship did not apply to Cu(II/I) systems because the Cu(II) and Cu(I) species did not contribute equally to the reorganizational barrier. Instead, they suggested that the correct k_{11} value should be the geometric mean of the values obtained by Yoneda et al. and by Augustin and Yandell. At the end of their paper, Lee and Anson acknowledged “helpful discussions with Prof. R. A. Marcus”, which suggested that Marcus himself had agreed with their conclusions.

In a subsequent study, Lee and Anson⁴⁸ attempted to obtain a direct measurement of the self-exchange rate constant for Cu^{II/I}(phen)₂ using an electrochemical technique in which the Cu(I) species was adsorbed on the surface of a graphite electrode and exchanged

Scheme 1



electrons with the corresponding Cu(II) species in solution. They reported that their data were consistent with an estimated k_{11} value of $10^5 \text{ M}^{-1} \text{ s}^{-1}$, which being similar to the geometric mean of the k_{11} values reported by the previous workers (i.e., $4.6 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$) convinced them of the correctness of their hypothesis. Lee and Anson's conclusions impeded further kinetic studies on Cu(II/I) cross-reactions since it implied that self-exchange rate constant values calculated from the application of the Marcus relationship (eq 14) to cross-reaction rate constants were unreliable.

To examine the unusual CV behavior that had been observed earlier for Cu(II/I) polythiaether complexes, Bernardo et al.⁴⁹ used 80% methanol–20% water (by weight) as a solvent to allow the use of low temperatures (down to -77°C) as a means of slowing the chemical processes. Studies on the CV behavior of the Cu^{II}([14]aneS₄)²⁺ complex ([14]aneS₄ = 1,4,8,11-tetrathiacyclotetradecane) confirmed the presence of a metastable Cu^IL intermediate and suggested that a similar intermediate existed for Cu^{II}L. From the resultant data, it was concluded that the electron-transfer behavior of Cu^{II/I}([14]aneS₄) and related Cu(II/I) systems could be described in terms of a dual-pathway square scheme mechanism as illustrated for the case of homogeneous cross-reactions in Scheme 1. In this scheme, the species designated as Cu^{II}L(O) and Cu^IL(R) represent the thermodynamically stable species, while Cu^IL(P) and Cu^{II}L(Q) represent metastable intermediates the conformations of which are presumed to resemble more closely the stable configurations of the other oxidation state. This mechanism parallels that previously proposed by Yandell (eq 16), except that the intermediate species are presumed to include an alteration of the coordination geometry around the copper site and the possibility of a change in the conformation of the coordinated ligands occurring as discrete sequential steps rather than concertedly. The resulting potential energy surfaces for the favored reaction pathway should then be expanded to include the intermediate species (Figure 5).

Rapid-scan cyclic voltammetric measurements made with ultramicroelectrodes have since demonstrated the existence of both the O and P intermediates under ambient conditions.⁵⁰ With the aid of computer simulations, it has been possible to evaluate all of the stepwise rate and equilibrium constants represented in Scheme 1 for a few selected systems.⁵¹

The mechanism in Scheme 1 is of particular interest in that a parallel mechanism has been theoretic-

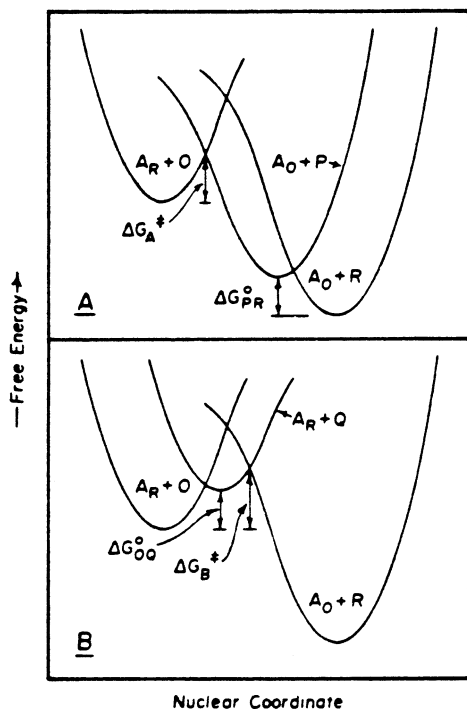


Figure 5. Qualitative potential energy surfaces illustrating the possible contribution of a conformational intermediate to an electron-transfer reaction involving a $\text{CuL}^{2+/+}$ system (Reprinted from ref 132. Copyright 1987 American Chemical Society.). In pathway A (top), electron-transfer produces a metastable conformational isomer (P) of the product species; in pathway B (bottom), a conformational preequilibrium precedes electron transfer. Terms are referenced to Scheme 1. The two-dimensional free-energy surfaces are drawn with distortions to reflect the very large amplitude nuclear displacements that accompany the net reaction.

cally proposed by Hoffman and Ratner⁵² to apply to biological electron-transfer processes. The existence of discrete steps for conformational change, as represented by the rate constants designated as k_{OQ} , k_{QO} , k_{PR} , and k_{RP} , suggests that the conformational changes can themselves become rate-limiting, leading to a condition known as “gated”⁵² or “directional”⁵³ electron transfer. Brunshwig and Sutin have generated three-dimensional projections of the overall potential energy surface for such a system, which is reproduced in Figure 6.⁵³ Theoretical considerations make it apparent that, for any given Cu(II/I) system, conformational gating can occur in only one direction. From this it has been proposed that such systems can act as a “molecular switch”⁵⁴ to control counterproductive back reactions.

4.4. Kinetic Description of a Square Scheme Mechanism

In the remainder of this review, we will examine the extent to which Cu(II/I) systems reported in the literature conform to the kinetic behavior predicted by the mechanism in Scheme 1. To do this, it is advantageous to examine the various types of kinetic behavior that may occur for such a scheme. Application of the steady-state approximation to the two metastable intermediate species, **P** and **Q**,

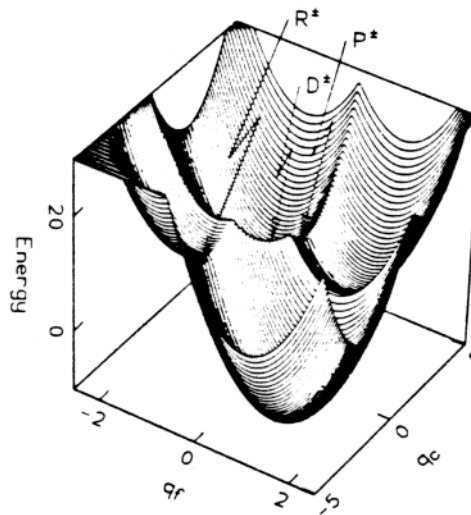


Figure 6. Potential energy surfaces for an electron-transfer reaction involving metastable intermediates (Reprinted from ref 53. Copyright 1989 American Chemical Society.). The “reactant” (e.g., $\text{Cu}^{\text{II}}\text{L}(\text{O})$ in Scheme 1) is represented by the front well and the “product” (e.g., $\text{Cu}^{\text{I}}\text{L}(\text{R})$ in Scheme 1) by the back well. The side pockets, designated as R^\ddagger and P^\ddagger in this diagram, represent metastable intermediates (e.g., $\text{Cu}^{\text{II}}\text{L}(\text{Q})$ and $\text{Cu}^{\text{I}}\text{L}(\text{P})$, respectively, in Scheme 1). The point D^\ddagger represents the transition state barrier for the direct reaction of $\text{Cu}^{\text{II}}\text{L}$ to $\text{Cu}^{\text{I}}\text{L}$ with concerted conformational changes.

results in the following general kinetic expressions:⁵⁵

Reduction

$$-\frac{d[\text{Cu}^{\text{II}}\text{L}]}{dt} = \left(\frac{k_{A2}k_{PR}}{k_{2A}[\text{A}_{\text{Ox}}] + k_{PR}} + \frac{k_{B2}k_{QO}}{k_{B2}[\text{A}_{\text{Red}}] + k_{QO}} \right) [\text{Cu}^{\text{II}}\text{L}(\text{O})][\text{A}_{\text{Red}}] \quad (19)$$

Oxidation

$$-\frac{d[\text{Cu}^{\text{I}}\text{L}]}{dt} = \left(\frac{k_{2A}k_{RP}}{k_{2A}[\text{A}_{\text{Ox}}] + k_{PR}} + \frac{k_{2B}k_{QO}}{k_{B2}[\text{A}_{\text{Red}}] + k_{QO}} \right) [\text{Cu}^{\text{I}}\text{L}(\text{R})][\text{A}_{\text{Ox}}] \quad (20)$$

Comparison to eqs 12 and 13 demonstrates that the parenthetical coefficients in eqs 19 and 20 represent k_{12} and k_{21} , respectively, with the first parenthetical term representing the kinetic contribution of pathway A and the second term representing that of pathway B. Whereas both reaction pathways are always available, the relative percentage of the overall reaction that proceeds by each pathway should primarily be a function of the relative stabilities of the two intermediate species, designated as $\text{Cu}^{\text{I}}\text{L}(\text{P})$ and $\text{Cu}^{\text{II}}\text{L}(\text{Q})$ in Scheme 1. Depending upon which parenthetical term is preferred (i.e., whether pathway A or pathway B is more favorable) and the relative magnitude of the two terms in the denominator of each of the two parenthetical terms, a number of limiting expressions may result. Since the

majority of electron-transfer reactions are studied under conditions where reaction 11 lies far to the right or left, a convenient manner in which to discuss the various types of limiting behavior is to consider separately the reduction and oxidation kinetic expressions under conditions in which the term representing either pathway A or B is dominant:

Reduction

Pathway A dominant:

$$\left(\frac{k_{A2}k_{PR}}{k_{2A}[A_{Ox}] + k_{PR}} \right) \gg \left(\frac{k_{B2}k_{OQ}}{k_{B2}[A_{Red}] + k_{QO}} \right)$$

If $k_{2A}[A_{Ox}] \ll k_{PR}$:

$$-\frac{d[Cu^{II}L]}{dt} = k_{A2}[Cu^{II}L(O)][A_{Red}] \quad (19a)$$

If $k_{2A}[A_{Ox}] \gg k_{PR}$:

$$-\frac{d[Cu^{II}L]}{dt} = K_{A2}k_{PR} \frac{[Cu^{II}L(O)][A_{Red}]}{[A_{Ox}]} \quad (19b)$$

Pathway B dominant:

$$\left(\frac{k_{A2}k_{PR}}{k_{2A}[A_{Ox}] + k_{PR}} \right) \ll \left(\frac{k_{B2}k_{OQ}}{k_{B2}[A_{Red}] + k_{QO}} \right)$$

If $k_{B2}[A_{Red}] \ll k_{QO}$:

$$-\frac{d[Cu^{II}L]}{dt} = K_{OQ}k_{B2}[Cu^{II}L(O)][A_{Red}] \quad (19c)$$

If $k_{B2}[A_{Red}] \gg k_{QO}$: $-\frac{d[Cu^{II}L]}{dt} = k_{OQ}[Cu^{II}L(O)] \quad (19d)$

Oxidation

Pathway A dominant:

$$\left(\frac{k_{2A}k_{RP}}{k_{2A}[A_{Ox}] + k_{PR}} \right) \gg \left(\frac{k_{2B}k_{QO}}{k_{B2}[A_{Red}] + k_{QO}} \right)$$

If $k_{2A}[A_{Ox}] \ll k_{PR}$:

$$-\frac{d[Cu^I L]}{dt} = K_{RP}k_{2A}[Cu^I L(R)][A_{Ox}] \quad (20a)$$

If $k_{2A}[A_{Ox}] \gg k_{PR}$: $-\frac{d[Cu^I L]}{dt} = k_{RP}[Cu^I L(R)] \quad (20b)$

Pathway B dominant:

$$\left(\frac{k_{2A}k_{RP}}{k_{2A}[A_{Ox}] + k_{PR}} \right) \ll \left(\frac{k_{2B}k_{QO}}{k_{B2}[A_{Red}] + k_{QO}} \right)$$

If $k_{B2}[A_{Red}] \ll k_{QO}$:

$$-\frac{d[Cu^I L]}{dt} = k_{2B}[Cu^I L(R)][A_{Ox}] \quad (20c)$$

If $k_{B2}[A_{Red}] \gg k_{QO}$:

$$-\frac{d[Cu^I L]}{dt} = K_{2B}k_{QO} \frac{[Cu^I L(R)][A_{Ox}]}{[A_{Red}]} \quad (20d)$$

(In these expressions, $K_{A2} = k_{A2}/k_{2A}$, $K_{OQ} = k_{OQ}/k_{QO}$, $K_{RP} = k_{RP}/k_{PR}$, and $K_{2B} = k_{2B}/k_{B2}$.) Of these eight

limiting expressions, eqs 19a and 20a represent electron transfer via pathway A with species **R** and **P** completely equilibrated (i.e., the conformational equilibrium is rapidly established relative to the rate of the electron-transfer step), while 19c and 20c represent the corresponding expressions for pathway B with species **O** and **Q** completely equilibrated. Under either of these limiting conditions, the observed second-order behavior is completely indistinguishable from a single pathway mechanism because the kinetic behavior will be identical to eqs 12 and 13 and the presence of the metastable intermediates will not be apparent. By contrast, eqs 19d and 20b represent the situation in which the conformational change *preceding* the electron-transfer step becomes the rate-limiting process. Both expressions are first-order, independent of the concentration of counter-reagent. The remaining two limiting expressions, described by eqs 19b and 20d, represent a situation in which a conformational change *following* the electron-transfer step becomes rate-limiting. Theoretical considerations suggest that this condition will never be observed for thermodynamically favorable reactions.⁵³ Since these terms do not contribute to the observed kinetic behavior, eqs 19 and 20 can be rewritten in the slightly abbreviated form shown:

Reduction Kinetic Expression (Revised)

$$-\frac{d[Cu^{II}L]}{dt} = \left(k_{A2} + \frac{k_{B2}k_{OQ}}{k_{B2}[A_{Red}] + k_{QO}} \right) [Cu^{II}L(O)][A_{Red}] \quad (19')$$

Oxidation Kinetic Expression (Revised)

$$-\frac{d[Cu^I L]}{dt} = \left(\frac{k_{2A}k_{RP}}{k_{2A}[A_{Ox}] + k_{PR}} + k_{2B} \right) [Cu^I L(R)][A_{Ox}] \quad (20')$$

4.5. Predicted Kinetic Behavior for a Square Scheme Mechanism

For systems that conform to the mechanism in Scheme 1, it should be noted that the Marcus approach is valid for all conditions in which the intermediate species is completely equilibrated with the corresponding ground-state species. Thus, eq 14 can be applied to reactions proceeding by pathway A if **P** and **R** are equilibrated or to those proceeding by pathway B under conditions in which **O** and **Q** are equilibrated. As noted above, theory predicts that a conformational change *following* the electron-transfer step will never become rate-limiting for thermodynamically favorable conditions.⁵³ Thus, *it is only when the intermediate is formed prior to electron transfer that unusual behavior may be observed*—that is, for oxidation reactions when pathway A is preferred or for reduction reactions when pathway B is preferred.

For reactions in which intermediate **P** is more stable than intermediate **Q**, the reaction will preferentially proceed via pathway A and all reduction reactions should conform to eq 19a. Thus, in all cases,

the cross-reaction rate constant, k_{12} , for all reduction reactions should yield the self-exchange rate constant representative of pathway A, $k_{11(A)}$, when subjected to eq 14. For the corresponding oxidation reactions, **R** and **P** will be equilibrated at all times if the oxidations are conducted sufficiently slowly and the reaction will be second-order in conformance with eq 20a. Insertion of the value of k_{21} into eq 14 will then yield the $\text{Cu}^{\text{II/L}}$ self-exchange rate constant representative of pathway A, designated as $k_{11(A)}$. However, upon (i) increase of the equilibrium constant for the reverse process in reaction 11, designated as K_{21} (which can be accomplished by increasing the potential of the oxidizing counterreagent, A_{Ox}), (ii) selection of a counterreagent with a larger self-exchange rate constant, k_{22} (eq 14), or (iii) increase of the concentration of the counterreagent, $[A_{\text{Ox}}]$, the limiting condition may be reached in which $k_{2A}[A_{\text{Ox}}] \gg k_{\text{PR}}$.⁵⁶ At that point, first-order behavior, as represented by eq 20b, may begin to be observed for the oxidation reactions. Under these first-order conditions, the Marcus relationship will no longer apply to the oxidation process since the reaction rate will then be controlled by the rate of conformational change rather than by electron transfer. When a reaction becomes limited by a conformational change (or a similar ancillary reaction such as proton transfer), it is said to be “gated.”

Since the value of k_{RP} places an absolute limit on how fast oxidation can proceed by pathway A, further increases in K_{21} , k_{22} , or $[A_{\text{Ox}}]$ or a combination of these will ultimately result in the condition where pathway B becomes favored and eq 20b will then be superseded by eq 20c (i.e., $k_{2B}[A_{\text{Ox}}] \gg k_{\text{RP}}$). At that point, oxidation reactions will again be second-order and eq 14 will once more apply. *The reaction is no longer considered to be “gated”,* although the change in pathway is clearly dictated by the rate limitations of the gated process (i.e., conformational change). The value of k_{11} obtained from eq 14 under these latter conditions will be representative of pathway B, $k_{11(B)}$. This value will necessarily be smaller than $k_{11(A)}$ for a system in which intermediate **P** is more stable than intermediate **Q** (i.e., pathway A is intrinsically favored). Thus, an important conclusion of the Scheme 1 mechanism is that, even for cross-reactions involving both the oxidation and reduction of a single $\text{Cu}(\text{II/I})$ system, for which the data in both cases obey second-order kinetics, it is possible that the application of the Marcus relationship may yield two different values for k_{11} (i.e., $k_{11(A)}$ and $k_{11(B)}$) for oxidation reactions (if **P** is more stable than **Q**) or for reduction reactions (if **Q** is more stable than **P**) since both reaction pathways may be sampled. It is for this reason that a variety of counterreagents and a variety of concentration conditions must be studied if reactions conforming to Scheme 1 are to be fully characterized.

If intermediate **Q** is more stable than **P**, electron transfer will preferentially occur by pathway B. Under this circumstance, however, “gated” electron transfer will only be observable for reduction reactions and $k_{11(B)} > k_{11(A)}$. Since the relative tendency of any specific reaction to proceed preferentially by pathway A or B will depend on the relative stabilities

of the intermediate species, **P** and **Q**, it is presumed that changes in the steric requirements of the coordinated ligands can alter the preferred pathway. Recent studies on the electron-transfer kinetics of a variety of $\text{Cu}(\text{II/I})$ systems with differing geometric constraints have shed some light on the conditions that affect the relative stabilities of these two intermediates and, therefore, result in either pathway A or pathway B being favored. These studies will be highlighted in the sections that follow.

4.6. Energetic Description of the Square Scheme Mechanism

The discussion in the foregoing subsection describes the electron-transfer behavior of a system conforming to Scheme 1 in terms of the overall kinetic expressions. However, the fact that the dominant pathway can be altered by altering the overall reaction potential or even by increasing the concentration of the counterreagent has often raised the question as to whether the principle of microscopic reversibility is being violated in such systems. Energy diagrams, such as that shown in Figure 6, are not easily adapted to illustrate the concepts involved in altering the preferred reaction pathway since they involve specific constraints placed upon the reactant and product concentrations and the nuclear coordinates. In an attempt to illustrate the salient points involved when two conformations of both the oxidized and reduced species exist, a simplistic energy diagram is presented in Figure 7. This diagram is intended to represent the complete ionization of $\text{Cu}(\text{I})$ (e.g., by spectral excitation) to eliminate complications introduced by the counterreagent—although it is recognized that the electron is actually being transferred to the counterreagent.

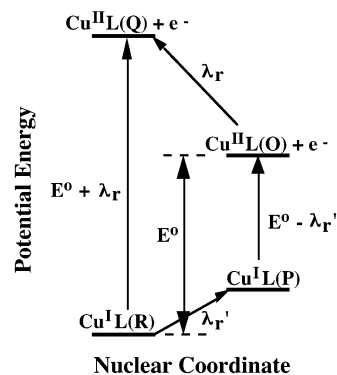


Figure 7. Simplified schematic energy diagram for the loss of an electron from a $\text{Cu}(\text{I})$ complex involving discrete metastable intermediate species for $\text{Cu}^{\text{I}}\text{L}$ and $\text{Cu}^{\text{II}}\text{L}$. The potential E^0 represents the electrochemical potential for the overall $\text{Cu}^{\text{II/L}}$ system (i.e., $\text{Cu}^{\text{II}}\text{L}(\text{O}) + e^- = \text{Cu}^{\text{I}}\text{L}(\text{R})$). The terms λ_r and λ_r' represent the reorganizational barriers for $\text{Cu}^{\text{II}}\text{L}(\text{O}) \rightarrow \text{Cu}^{\text{II}}\text{L}(\text{Q})$ and $\text{Cu}^{\text{I}}\text{L}(\text{R}) \rightarrow \text{Cu}^{\text{I}}\text{L}(\text{P})$, respectively, which, in turn, are proportional to the logarithmic values of the rate constants k_{OQ} and k_{RP} , respectively. The example shown is for a $\text{Cu}(\text{II/I})$ system in which $\lambda_r > \lambda_r'$ resulting in pathway A being preferred over pathway B. Pathway B would be preferred for the case where $\lambda_r < \lambda_r'$ (see text). Since all processes shown in this diagram are first-order (i.e., participation of the counterreagent is not represented), this diagram does not illustrate the onset of “gated” electron transfer.

The intermediate species $\text{Cu}^{\text{I}}\text{L}(\mathbf{P})$ is always more readily oxidized than species $\text{Cu}^{\text{I}}\text{L}(\mathbf{R})$, but it is also less populated than $\text{Cu}^{\text{I}}\text{L}(\mathbf{R})$, the actual population (at a specific temperature) being dependent upon the reorganizational energy of the reduced species, λ_r' . The diagram shown represents the specific situation in which intermediate \mathbf{P} is more stable than intermediate \mathbf{Q} , that is, $\lambda_r > \lambda_r'$, so that pathway A is preferred. The oxidation of $\text{Cu}^{\text{I}}\text{L}(\mathbf{P})$ to $\text{Cu}^{\text{II}}\text{L}(\mathbf{O})$ requires a driving force equal only to $E^\circ - \lambda_r'$. However, when the driving force of the overall reaction exceeds $E^\circ + \lambda_r$, the direct oxidation of $\text{Cu}^{\text{I}}\text{L}(\mathbf{R})$ to $\text{Cu}^{\text{II}}\text{L}(\mathbf{Q})$ becomes feasible. Under these conditions, both oxidation processes readily occur (i.e., $\text{Cu}^{\text{I}}\text{L}(\mathbf{P}) \rightarrow \text{Cu}^{\text{II}}\text{L}(\mathbf{O})$ and $\text{Cu}^{\text{I}}\text{L}(\mathbf{R}) \rightarrow \text{Cu}^{\text{II}}\text{L}(\mathbf{Q})$) but the latter process—representative of pathway B—dominates since the population of $\text{Cu}^{\text{I}}\text{L}(\mathbf{R})$ greatly exceeds that of $\text{Cu}^{\text{I}}\text{L}(\mathbf{P})$. Thus, although the dominant pathway shifts from pathway A to pathway B, microscopic reversibility is never violated in these reactions.

For the corresponding reduction process, the energy difference for the reduction of $\text{Cu}^{\text{II}}\text{L}(\mathbf{O})$ is seen to be less than that for the reduction of $\text{Cu}^{\text{II}}\text{L}(\mathbf{Q})$. Since $\text{Cu}^{\text{II}}\text{L}(\mathbf{O})$ is the more populated species, its direct reduction will always dominate. Corresponding arguments can be made for reactions in which intermediate \mathbf{Q} is more stable than intermediate \mathbf{P} , that is, $\lambda_r < \lambda_r'$.

5. Electron-Transfer Kinetic Studies on Inorganic Copper(II/I) Complexes

5.1. Organization of Tables

As suggested by the complexity of eqs 19 and 20, characterization of the electron-transfer kinetic behavior for Cu(II/I) redox couples that conform to Scheme 1 generally requires a determination of cross-reaction kinetic data for both $\text{Cu}^{\text{II}}\text{L}$ reductions and $\text{Cu}^{\text{I}}\text{L}$ oxidations. The availability of kinetic results from reactions involving multiple counterreagents, which provide driving forces of varying magnitude, are particularly valuable since the consistency—or lack thereof—of calculated self-exchange rate constant values can be a sign of a change in the reaction pathway, the onset of conformationally controlled (“gated”) first-order behavior, or both. The appearance of inner-sphere electron-transfer mechanisms should also be revealed by such comparisons since application of eq 14 to cross-reactions involving inner-sphere reactions would be expected to yield different k_{11} values with differing counterreagents. For the proper analysis of gated behavior, it is also extremely useful to have data that represent a wide range of counterreagent concentrations. For systems in which different k_{11} values are obtained from Cu(II) reduction and Cu(I) oxidation reactions, electron self-exchange rate constants determined directly from NMR line broadening data (or related techniques) are particularly valuable since, according to Scheme 1, the $k_{11(\text{NMR})}$ value should always represent the “preferred” reaction pathway and should be in agreement with the largest $k_{11(\text{Red})}$ or $k_{11(\text{Ox})}$ values obtained from cross-reactions. For these various reasons, the tables

in this review include each individual cross-reaction kinetic study reported in the literature for each $\text{Cu}^{\text{II/I}}\text{L}$ system.

Electron self-exchange rate constants determined directly by NMR line-broadening are listed in bold-face in the tables. These $k_{11(\text{NMR})}$ values are independent of eq 14 and, therefore, do not require the estimation of ion-size parameters. For each cross-reaction study, the individual counteroxidant or -reductant used in the study is indicated and the cross-reaction rate constant (k_{12} or k_{21}) is listed followed by the calculated self-exchange rate constant (k_{11}) derived from it by means of eq 14.

At the beginning of the tabulation of kinetic data for each specific Cu(II/I) system, the ligand coordinated to the copper is designated by its chemical name and a commonly accepted abbreviation. This is followed by the potential value that Cu(II/I) complex. Structural representations of all ligands included in the tables are provided in Figures 8–13 for greater clarity. Abbreviations for ligand moieties associated with the counterreagents are as follows:

[14]aneN ₄	= 1,4,8,11-tetraazacyclotetradecane (cyclam)
acac ⁻	= acetylacetonate
bpy	= 2,2'-bipyridine
bpyO ₂	= <i>N,N</i> -dioxo-2,2'-bipyridine
Cp	= cyclopentadiene
cyt- <i>c</i> (II)	= cytochrome- <i>c</i> ^{II}
(dmg) ₃ BC ₄ H ₉	= tris(dimethylglyoximate)- <i>n</i> -butylborate
EDTA ⁴⁻	= ethylenediamine- <i>N,N,N,N</i> -tetraacetate
HECp	= hydroxyethylcyclopentadiene
hfac ⁻	= hexafluoroacetylacetonate
isn	= isonicotinamide
MeCp	= 1-methylcyclopentadiene
4,7-Me ₂ phen	= 4,7-dimethyl-1,10-phenanthroline
Me ₄ [14]tetraeneN ₄	= TIM (see below)
Me ₆ [14]dieneN ₄	= 5,7,7,12,14,14-hexamethyl-1,4,8,11-tetraazacyclotetradeca-4,11-diene
(nox) ₃ BC ₆ H ₅	= tris(1,2-cyclohexanedioximate)-phenylborate
(nox) ₃ BC ₄ H ₉	= tris(1,2-cyclohexanedioximate)- <i>n</i> -butylborate
phen	= 1,10-phenanthroline
PMcP	= pentamethylcyclopentadiene
py	= pyridine
pyz	= pyrazine
sep	= 1,3,6,8,10,13,16,19-octaazabicyclo[6.6.6]icosane (sepulchrate)
tacn	= [9]aneN ₃ = 1,4,7-triazacyclononane
terpy	= 2,2'-6',2''-terpyridine
TIM	= 2,3,9,10-tetramethyl-1,4,8,11-tetraazacyclotetradeca-1,3,8,10-tetraene

The temperature for all rate constants listed is 25 °C with the ionic strength maintained at $\mu = 0.1$ unless otherwise indicated. For tables in which the

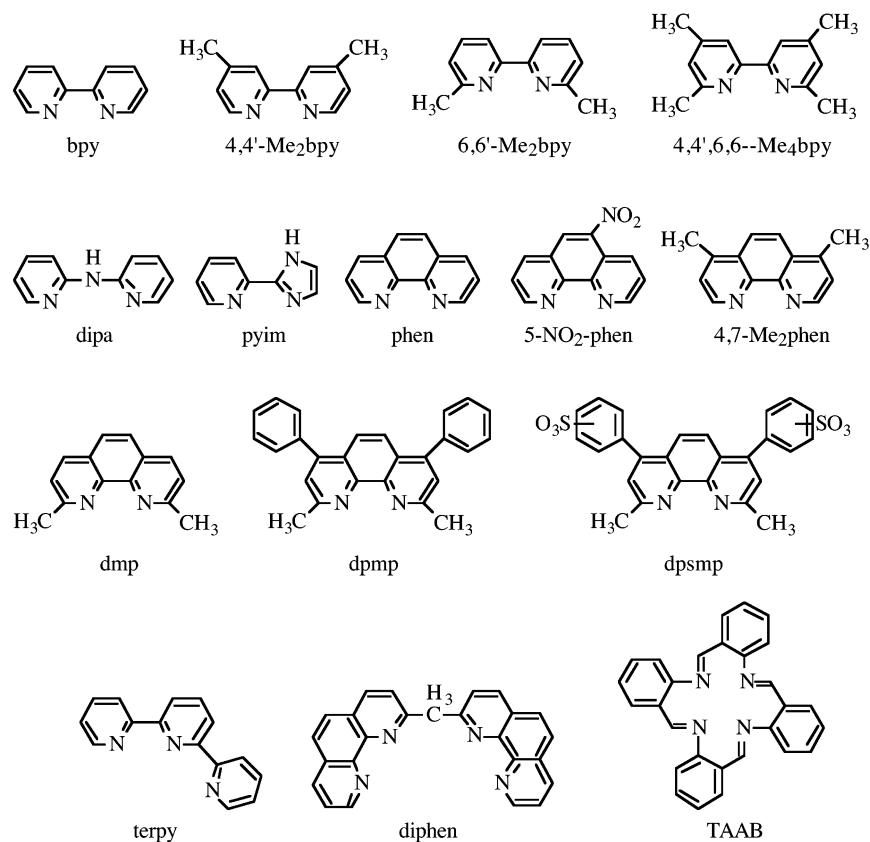


Figure 8. Polypyridyl ligands and a related cyclic tetraimine ligand (TAAB) for which electron-transfer kinetic data have been reported for their Cu(II/I) complexes.

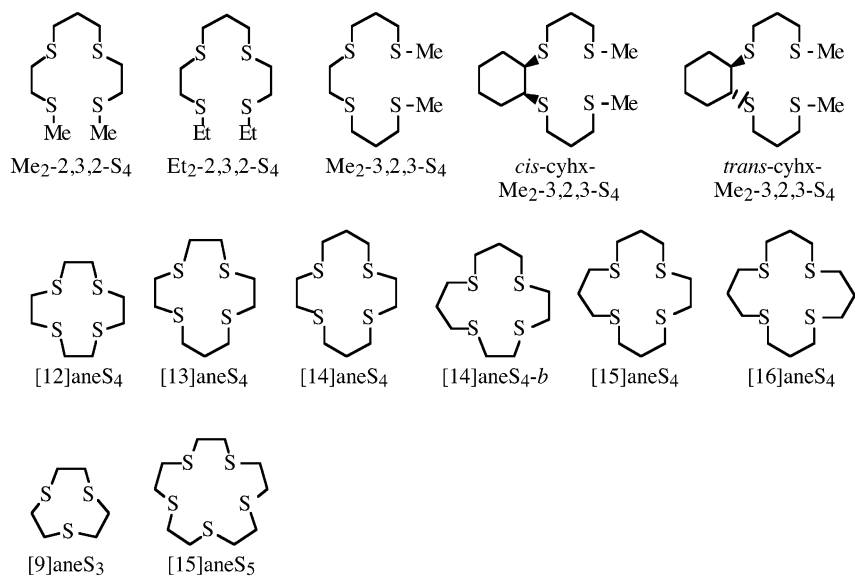


Figure 9. Acyclic and unsubstituted macrocyclic polythiaether ligands for which the electron-transfer kinetic behavior of their Cu(II/I) complexes have been reported.

listed studies were conducted in more than one solvent, the solvents utilized are designated as follows:

- A = water
- B = acetonitrile
- C = acetone
- D1 = 20% methanol–80% water (by volume?)
- D2 = 50% methanol–50% water (by volume)
- D3 = 80% methanol–20% water (by weight)
- D4 = 100% methanol
- E = DMSO

All rate constant values are given in units of $M^{-1} s^{-1}$ unless otherwise noted. Some nonaqueous data—particularly in acetonitrile—are reported in units of $m^{-1} s^{-1}$ (i.e., $kg mol^{-1} s^{-1}$) and are so identified by a footnote. (Since the density of acetonitrile is $0.784 g mL^{-1}$ at $25 ^\circ C$, rate constants can be converted from $kg mol^{-1} s^{-1}$ to $M^{-1} s^{-1}$ by dividing by a factor of 1.28; however, this conversion is relatively insignificant in view of the other experimental errors involved.)

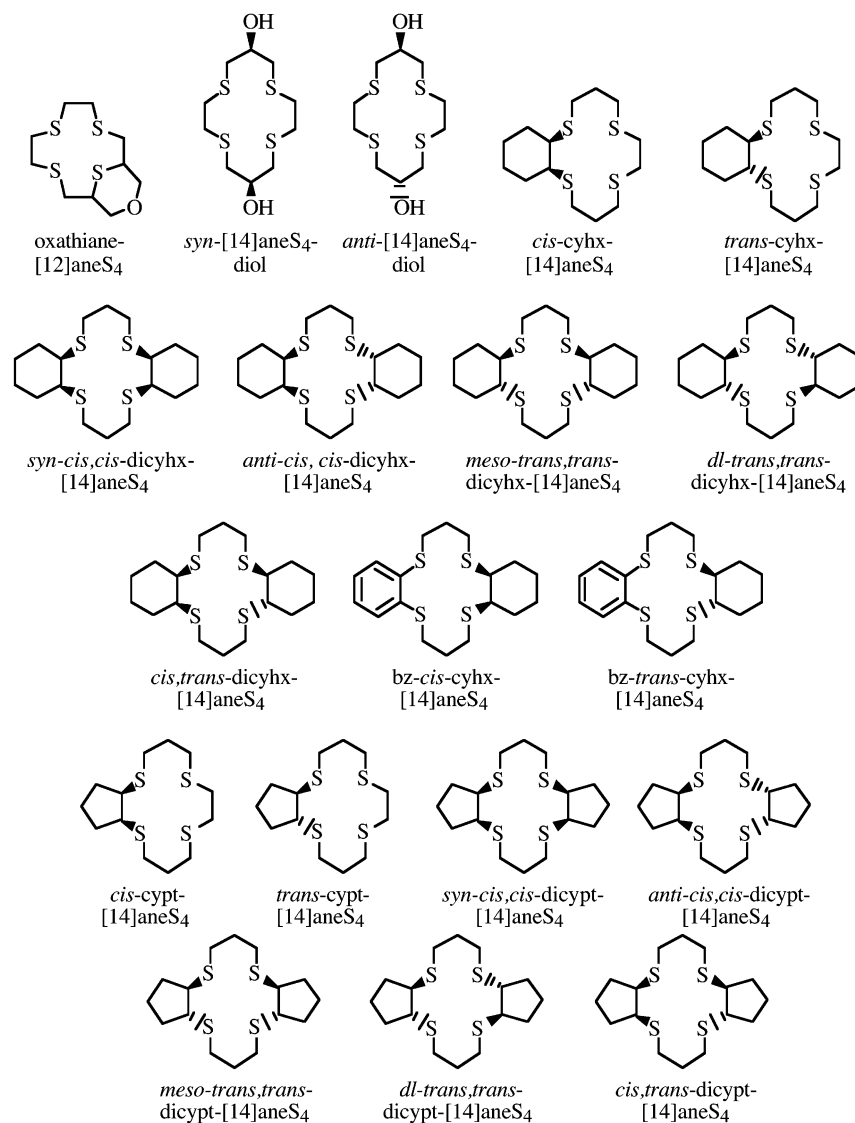


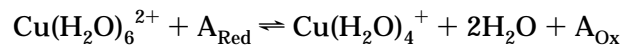
Figure 10. Substituted macrocyclic tetrathiaethers for which $\text{Cu}^{\text{II/I}}$ electron-transfer kinetics have been reported.

Electron self-exchange rate constants (k_{11}) calculated from cross-reaction data by means of eq 14 are generally those reported by the original investigators and have not been rechecked. (In many cases, the ion size parameters applied for the calculation of k_{11} from cross-reaction data have not been specified by the investigators.) Since most of the rate constant data are limited in accuracy and the range of rate constants covers several orders of magnitude, all cross-reaction and self-exchange rate constants are reported as logarithmic values for ease of comparison. In many cases, only one digit is reported in the mantissa since the calculated k_{11} values are often limited to one significant figure as is evident when repetitive determinations are reported.

5.2. The Aquacopper(II/I) and Acetonitrilecopper(II/I) Systems

From a conceptual standpoint, the simplest $\text{Cu}(\text{II/I})$ system in aqueous solution is that of aquacopper(II/I). The divalent ion is generally considered to be six-coordinate although a recent neutron diffraction study has indicated that it may be only five-

coordinate.⁵⁷ (There is some question as to whether these latter data are the result of the fluxionality of the Jahn–Teller distortion in solution since a crystal structure of $(\text{NH}_4)_2[\text{Cu}(\text{OH}_2)_6](\text{SO}_4)_2$ showed the aquated ion to be in a distorted octahedral geometry as expected.)⁵⁸ The univalent species is presumed to be four-coordinate. Early attempts to measure the self-exchange rate constant for the aquacopper(II/I) redox couple,



such as the studies reported by Parker and Espenson involving the oxidation of $\text{Cu}^{\text{I}}_{\text{aq}}$ by aquated iron(III)⁵⁹ or the reduction of $\text{Cu}^{\text{II}}_{\text{aq}}$ by aquated vanadium(II),⁶⁰ resulted in reactions that appeared to proceed by an inner-sphere mechanism (Table 3), presumably with hydroxide serving as the bridging ligand. A 1981 study by Yandell,⁶¹ involving the reduction of $\text{Cu}^{\text{II}}_{\text{aq}}$ by cytochrome-*c*^{II}, also resulted in very rapid electron transfer, which presumably does not represent an outer-sphere reaction.

In 1978, as part of a study on the quenching of polypyridylruthenium(II) complexes by aquacopper(II)

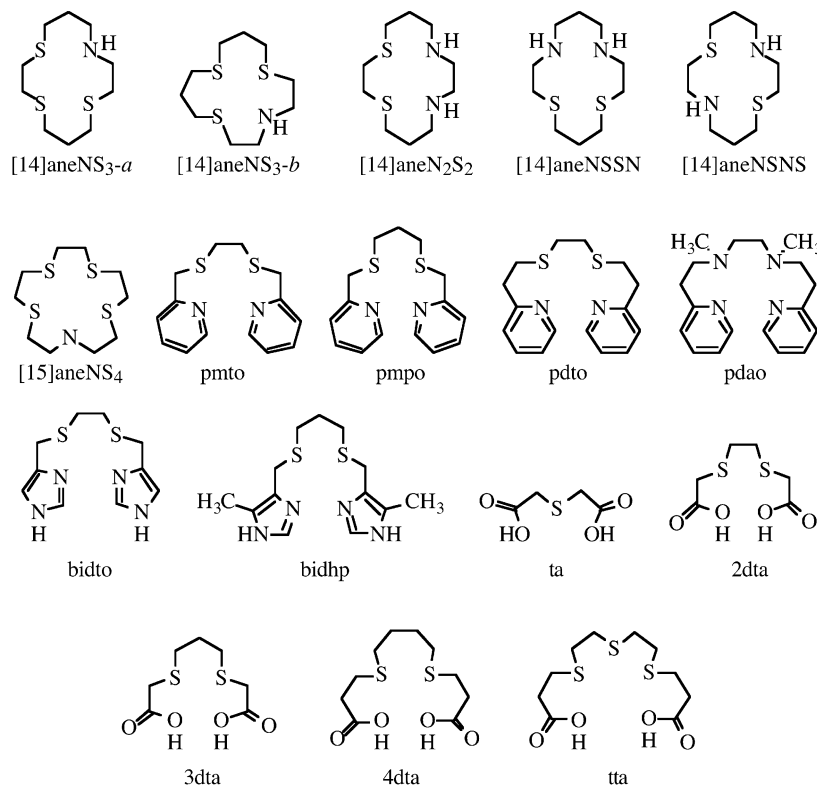


Figure 11. Ligands containing mixed donor atoms for which Cu(II/I) complex electron-transfer kinetics have been reported.

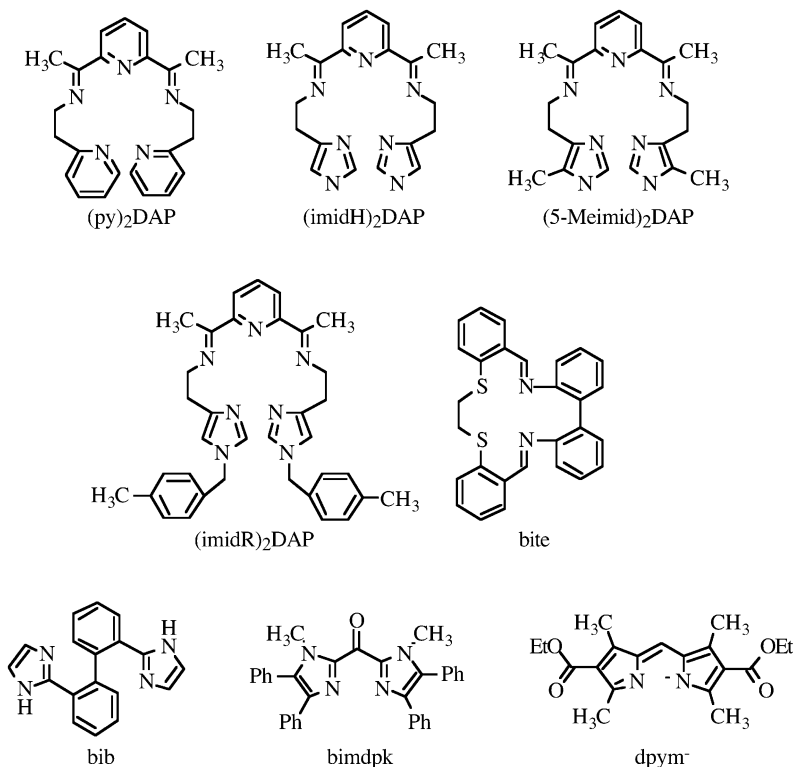


Figure 12. Ligands for which it is hypothesized that the Cu complexes retain the same coordination number and similar geometries in both oxidation states.

ion, Sutin and co-workers⁶² obtained an estimate of $k_{11(\text{Ox})} \approx 1 \times 10^{-5} \text{ M}^{-1} \text{ s}^{-1}$ for the Cu^{II/I}_{aq} couple at 25 °C (in 0.5 M HClO₄–LiClO₄) by fitting the rate constant data for the back reaction of Cu^I_{aq} with various Ru^{III}L₃ complexes to the Marcus relationship. In view of the substitutional inertness of the ruthe-

nium complexes, this latter value was assumed to represent an outer-sphere pathway. Subsequently, Davies⁶³ measured the oxidation kinetics of aquacopper(I) ion with several Ru(III) complexes in 1.0 M LiClO₄–HClO₄. From the combination of his own data with that of Sutin and co-workers, Davies

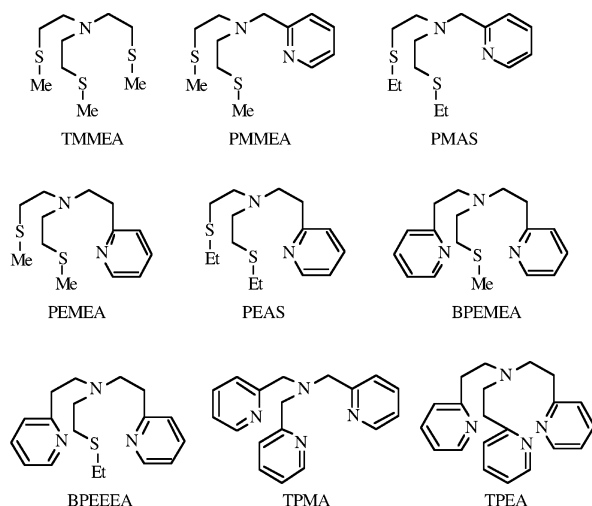


Figure 13. Tripodal ligands for which Cu(II/I) complex electron-transfer kinetics have been reported.

Table 3. Electron-Transfer Rate Constants Reported in the Literature for Aquacopper(II/I) in Aqueous Solution, 25 °C, $\mu = 0.10$ M (Except as Noted)

oxidant	reductant	$\log k_{12}$ or k_{21} ($M^{-1} s^{-1}$)	$\log k_{11}$ ($M^{-1} s^{-1}$)	ref
Water: $Cu^{II/I}(H_2O)_x$ [$E^\circ = 0.13$ V]				
$Cu^{II}_{aq}{}^{2+}$	Cyt ^{II}	0.76	0.72	61
$Cu^{II}_{aq}{}^{2+}$	hemoglobin	too fast to measure		122
$Cu^{II}_{aq}{}^{2+}$	$V^{II}_{aq}{}^{2+}$	1.43 ^a	-1.7 [IS] ^{a,b}	60
$Cu^{II}_{aq}{}^{2+}$	$Co^{II}(\text{sep})^{3+}$	0.9	-5.6 (-6.3) ^c	66
$Cu^{II}_{aq}{}^{2+}$	$Co^{II}(\text{sep})^{3+}$	0.70 ^d	-6.3 ^d	64
$Cu^{II}_{aq}{}^{2+}$	ascorbate	0.64 ^a	(~5.3) [IS] ^{a,b}	76
$Fe^{III}_{aq}{}^{3+}$	$Cu^I_{aq}{}^{+}$	5.21 ^a	[IS] ^{a,b}	59
$Fe^{III}(H_2O)_5F^{2+}$	$Cu^I_{aq}{}^{+}$	$\geq 8^a$	[IS] ^{a,b}	59
$Fe^{III}(H_2O)_5N_3^{2+}$	$Cu^I_{aq}{}^{+}$	$\geq 6.7^a$	[IS] ^{a,b}	59
$Ru^{III}L_3^{3+ e}$	$Cu^I_{aq}{}^{+}$	8.41–8.67 ^d	-5.0 ^d	62
$Co^{III}(\text{TIM})^{3+}$	$Cu^I_{aq}{}^{+}$	4.63 {pH 1}	< -5	131
		5.52 {pH 2}		
$Ru^{III}(\text{NH}_3)_5py^{3+}$	$Cu^I_{aq}{}^{+}$	1.68 ^a	-3.72 ^{a,f} -6.77 ^{a,g}	63
$Ru^{III}(\text{NH}_3)_5isn$	$Cu^I_{aq}{}^{+}$	2.73 ^a	-3.72 ^{a,f} -4.92 ^{a,g}	63
$Ru^{III}(\text{NH}_3)_4bpy$	$Cu^I_{aq}{}^{+}$	3.58 ^a	-3.72 ^{a,f} -6.60 ^{a,g}	63
$Ru^{III}(\text{NH}_3)_4(isn)_2^{3+}$	$Cu^I_{aq}{}^{+}$	4.64 ^a	-3.72 ^{a,f} -6.06 ^{a,g}	63

^a $\mu = 1.0$. ^b IS = inner-sphere mechanism. ^c Cu^{II}_{aq} adduct with ClO_4^- . ^d $\mu = 0.5$. ^e L represents bpy, phen, 4,4'-Me₂bpy, and 5-Cl-phen. ^f Average self-exchange rate constant reported by Davies. ^g Self-exchange rate constant values recalculated by Sisley and Jordan using different Ru(III/II) potential values for 1.0 M ionic strength.

obtained an average value of $k_{11}(\text{Red}) = 1.9 \times 10^{-4} M^{-1} s^{-1}$. In this connection, it should be noted that Davies did not clearly define the E° values and ionic radii for the reactants that he utilized in making his calculations.

Sisley and Jordan⁶⁴ carried out extensive kinetic measurements on the reduction of Cu^{II}_{aq} by $Co^{II}(\text{sep})$ (sep = S-[1,3,6,8,13,16,19-octaazabicyclo[6.6.6]eicosane]), the latter counterreagent being substitutionally inert and, therefore, favoring electron transfer only by an outer-sphere pathway. Their reactions were carried out in the presence of ClO_4^- concentrations ranging from 0.1 to 1.0 M. From their cross-

reaction rate data, Sisley and Jordan calculated a value of $k_{11} = 5 \times 10^{-7} M^{-1} s^{-1}$ for the Cu^{III}_{aq} couple. These authors also reexamined Davies' calculations using potential values for the ruthenium reagents, which were determined in 1 M KCl,⁶⁵ to generate k_{11} values of 1.7×10^{-7} to 8.7×10^{-7} for three of Davies' four systems (see Table 3). Sisley and Jordan suggested that the difference in their calculated k_{11} values and those previously reported by Davies was primarily because Davies had utilized E° values determined for 0.10 M ionic strength whereas his kinetic studies were conducted in 1.0 M $LiClO_4-HClO_4$.

An earlier, and much more limited, study on the reduction of Cu^{II}_{aq} by $Co^{II}(\text{sep})$ was conducted by Koenigbauer⁶⁶ in 0.1 and 0.3 M ClO_4^- . The results indicated the possible formation of a weak adduct between aquated Cu(II) and ClO_4^- , similar to the perchlorate adducts formed by Cu(II)-tetrathiaether complexes.⁶⁷ Direct evidence for such outer-sphere adducts has been reported for aqueous solutions of copper perchlorate by Nomura and Yamaguchi.⁶⁸ Resolution of Koenigbauer's limited data suggested that the k_{11} values attributable to the Cu^{II}_{aq} and $Cu^{II}_{aq}(ClO_4)$ adduct species were 2.6×10^{-6} and $5.4 \times 10^{-7} M^{-1} s^{-1}$, respectively (Table 3). The latter value is identical to the value reported by Sisley and Jordan and suggests that their reported k_{11} value for Cu^{II}_{aq} may be underestimated because of the influence of an outer-sphere perchlorate adduct.

From an examination of all of the available data, the upper limit for the self-exchange rate constant value for the pure Cu^{III}_{aq} system (in the absence of a perchlorate adduct) can doubtless be set at $k_{11} \leq 2 \times 10^{-4} M^{-1} s^{-1}$ for 25 °C, $\mu = 0.1$ M, with a more likely upper limit of about $5 \times 10^{-6} M^{-1} s^{-1}$. It appears that Sisley and Jordan's value of $k_{11} = 5 \times 10^{-7} M^{-1} s^{-1}$ should be accepted as the benchmark value for $\mu = 1.0$ M (ClO_4^-).

Acetonitrile represents the second most common solvent for the study of Cu(II/I) electron transfer reactions and a knowledge of the self-exchange rate constant of the solvated couple in this solvent would be extremely useful. Manahan⁶⁹ made an early attempt to determine this value by mixing the perchlorate salts of hydrated Cu(II) and acetonitrile-solvated Cu(I) in acetonitrile using ⁶⁴Cu as a tracer. The reaction was then quenched by lowering the temperature to -40 °C in a dry ice bath, causing the immediate precipitation of $Cu(CH_3CN)_4ClO_4$ which was then filtered and measured with a scintillation counter. The isotopic exchange appeared to be complete within the time of separation, leading Manahan to conclude that $k_{11} \geq 0.3 M^{-1} s^{-1}$. It is suspected that this value reflects an acceleration of electron exchange during the separation process. Jordan and Irangu⁷⁰ have recently studied the reaction kinetics of solvated Cu(II) reacting with ferrocene and dimethylferrocene in water/acetonitrile mixtures containing from 50% to 97.5% CH_3CN and have obtained a preliminary estimate of $k_{11} \approx 5 \times 10^{-9} M^{-1} s^{-1}$ for acetonitrile-solvated Cu(II/I).

Table 4. Electron-Transfer Rate Constants for Chlorocopper(II/I) and Imidazolylcopper(II/I) Couples in Aqueous Solution at 25 °C, $\mu = 0.10$ M (Except as Noted)

oxidant	reductant	$\log k_{12}$ or k_{21} ($M^{-1} s^{-1}$)	$\log k_{11}$ ($M^{-1} s^{-1}$)	ref
	Monochloride: $Cu^{II}Cl$			
$Cu^{II}Cl^+$	cyt- c^{II}	2.76 ^a	0.82 ^a	63
$Cu^{II}Cl^+$	$Co^{II}(sep)^{2+}$	3.20 ^c	-3.70 ^c	64
	Dichloride: $Cu^{II}Cl_2$			
$Cu^{II}Cl_2$	cyt- c^{II}	3.6	1.30	63
$Cu^{II}Cl_2$	$Co^{II}(sep)^{2+}$	4.18 ^b	-3.70 ^b	64
	Trichloride: $Cu^{II}Cl_3$			
$Cu^{II}Cl_3^-$	$Co^{II}(sep)^{2+}$	5.65 ^b	-3.70 ^b	64
$Ru^{III}(NH_3)_4phen^{3+}$	$Cu^I Cl_3^{2-}$	3.04	-4.5	78
$Co^{III}ZCl_2^{+e}$	$Cu^I Cl_3^{2-}$	5.89 ^c	[IS] ^c	78
	Tetrachloride: $Cu^{II}Cl_4$			
$Cu^{II}Cl_4^{2-}$ (?)	$Cu^I Cl_4^{3-}$ (?), 12 M HCl		7.7	71
	Imidazoles (im)			
$Cu^{II}(im)_2^{2+}$	$Co^{II}(sep)^{2+}$	1.54 ^d	-7.0 ^d	64
$Cu^{II}(im)_3^{2+}$	$Co^{II}(sep)^{2+}$	1.85 ^d	-7.0 ^d	64
$Cu^{II}(im)_4^{2+}$	$Co^{II}(sep)^{2+}$	2.08 ^d	-7.0 ^d	64

^a $\mu = 1.0$. ^b $\mu = 0.5$. ^c $\mu = 0.2$. ^d $\mu = 0.15$. ^e Z represents $Me_4[14]tetraeneN_4$.

5.3. Copper(II/I) Complexes with Unidentate Ligands

5.3.1. Chlorocopper(II/I) Systems

The first direct measurement of a Cu(II/I) self-exchange rate constant was that reported by McConnell and Weaver in 1956 using ^{63}Cu NMR line broadening of cuprous–cupric ion solutions in 12 M HCl.⁷¹ In this medium, they obtained a self-exchange rate constant of $5 \times 10^7 M^{-1} s^{-1}$ (Table 4). Interestingly, this k_{11} value has never been exceeded by any subsequent Cu(II/I) redox couple.

McConnell and Weaver suggested that the chloride ion catalyzed the electron-transfer process, and it has generally been assumed by subsequent authors that this measurement represented an inner-sphere mechanism. It is worth noting, however, that in this medium of extremely high chloride concentration both oxidation states are probably coordinatively saturated by four chloride ions and $Cu^{II}Cl_4^{2-}$ ion is one of the few low-molecular-weight Cu(II) complexes that is known to be tetrahedral.^{72–74} Since both oxidation states are likely to be tetrahedral in McConnell and Weaver's study, a small Franck–Condon barrier is to be expected. Thus, even in the absence of chloride bridging, the self-exchange rate constant for this redox couple might be exceptionally large.

In a study on the oxidation kinetics of ferrocyclochrome-*c* by Cu^{II}_{aq} , Yandell reported that the reaction was catalyzed by the addition of chloride ion.⁶¹ Since the iron center is about 3.4 Å below the protein surface,⁷⁵ it seems unlikely that chloride bridging would be effective with cytochrome-*c*. Therefore, Yandell ascribed the observed acceleration to the greater reactivity of the $CuCl^+$ and $CuCl_2$ species, their enhanced reactivity being attributed to their more favorable redox potentials. In fact, as shown in

Table 4, upon correction for the effects of potential, Yandell's estimates of the self-exchange rate constants for $Cu^{II}Cl$ and $Cu^{II}Cl_2$ differ only slightly from the value that he calculated for the Cu^{II}_{aq} redox couple. (However, as noted in Table 3, his aquacopper(II/I) self-exchange rate constant appears to be several orders of magnitude too large.)

Xu and Jordan⁷⁶ found that the addition of chloride ion also enhanced the oxidation of ascorbate by aquacopper(II) ion. The effect that they observed exceeded that to be expected on the basis of the higher potential for the $Cu^{II}Cl_n$ redox couples. However, they were hesitant to assign this enhancement to a higher Cu(II/I) self-exchange rate constant in view of the possibility that an inner-sphere reaction might be involved in the ascorbate reaction. Sisley and Jordan⁶⁴ subsequently reexamined the effect of coordinated chloride in their studies involving the reduction of aquacopper(II) by $Co^{II}(sep)$, the latter reagent being limited to outer-sphere pathways. Using literature values for the stepwise complex formation constants and the potential values for the various $Cu^{II}Cl_n$ species, Sisley and Jordan concluded that, within experimental error, $CuCl^+$, $CuCl_2$, and $CuCl_3^-$ exhibited self-exchange rate constants of $k_{11} = 2.0 \times 10^{-4} M^{-1} s^{-1}$ (Table 4).

If only outer-sphere electron transfer were involved, it seems surprising that the coordination of the first chloride ion should result in a large increase in k_{11} while subsequent chloride complexation has no apparent effect. However, a reexamination of Sisley and Jordan's data raises some questions regarding their analysis of the reactivity of the trichlorocuprate(II) species in particular. On the basis of the various equilibrium constants reported in aqueous solution, Sharma and Millero⁷⁷ have generated a series of "best" values for the formation of $CuCl^+$, $CuCl_2$, and $CuCl_3^-$ in aqueous solution at both 0 and 5 M ionic strength. These consensus values indicate that the stepwise formation of the $CuCl_3^-$ species is much less than unity, so the maximum concentration of $Cu^{II}Cl_3^-$ achieved was never more than 10% of the $Cu^{II}Cl_2$ concentration. Since Sisley and Jordan utilized potential values for $Cu^{II}Cl_2$ and $Cu^{II}Cl_3^-$ that differed by only 0.015 V, the difference in driving force for the latter two species is virtually insignificant. Thus, according to their own calculations, the contribution of $Cu^{II}Cl_3^-$ to the overall reaction rate never exceeded a few percent, which suggests that it was barely significant within the limits of their experimental error. The latter observation may still be regarded as being of interest, however, because it implies that the self-exchange rate constant for the $Cu^{II}Cl_3^-$ species is several orders of magnitude smaller than the values found for most multidentate ligand complexes.

Munakata and Endicott⁷⁸ reported a rate constant for the oxidation of Cu(I) in the presence of varying amounts of chloride using $Ru^{III}(NH_3)_4phen$ as oxidant. They found a significant acceleration in the oxidation rate as the chloride ion concentration was increased and attributed this to the dominant reactivity of the $Cu^I Cl_3^{2-}$ species based on their conclusion that $Cu^I Cl_2^-$ and $Cu^I Cl_3^{2-}$ were the prevalent species

in solution over a wide range of chloride ion concentration. This assignment led them to calculate a self-exchange rate constant of $k_{11} = 3.5 \times 10^{-5} \text{ M}^{-1} \text{ s}^{-1}$ for the $\text{Cu}^{\text{II}}/\text{Cu}^{\text{I}}\text{Cl}_3(\text{H}_2\text{O})^{-2}$ redox couple, a value that is within an order of magnitude of the value suggested by Sisley and Jordan but is also similarly erroneous since the available equilibrium constant data indicate that only the mono- and dichloro-copper(I) species form in appreciable amounts in aqueous solution.⁷⁷ Therefore, it is presumed that the acceleration in their observed oxidation rate was due to the dichloro species.

5.3.2. Imidazolylcopper(II/I) Systems

In the course of their study on aquacopper(II/I), Sisley and Jordan⁶⁴ also studied the effect of added imidazole (im) on the electron-transfer rates between Cu^{II} and $\text{Co}^{\text{II}}(\text{sep})$. They concluded that the self-exchange rate constants for each of the $\text{Cu}^{\text{II}}(\text{im})_n$ species were approximately constant at $1 \times 10^{-7} \text{ M}^{-1} \text{ s}^{-1}$ (Table 4), a value that is 5-fold smaller than the value they obtained for aquacopper(II/I). In analyzing the data for the imidazole complexes, Sisley and Jordan admitted that there was considerable uncertainty regarding the choice of potential values used for the $\text{Cu}^{\text{II}}/\text{Cu}^{\text{I}}(\text{im})_3$ and $\text{Cu}^{\text{II}}/\text{Cu}^{\text{I}}(\text{im})_4$ couples since appropriate stability constants are not available for the $\text{Cu}^{\text{I}}-\text{imidazole}$ complexes. To circumvent this deficiency, they utilized the corresponding values for the pyridine complexes. Whereas this may result in considerable error, the conclusion that the self-exchange rate constants for the imidazole complexes are not significantly different from that of the aquacopper(II/I) couple would appear to be valid in view of the relatively slow cross-reaction kinetics that were observed upon the addition of the imidazole ligand.

5.4. Polypyridyl Complexes

Among the most widely studied $\text{Cu}^{\text{II}}/\text{Cu}^{\text{I}}$ systems are those with various polypyridyl ligands including 2,2'-bipyridine (bpy), 1,10-phenanthroline (phen), and a number of substituted derivatives (Figure 8). Some of these systems exhibit relatively high redox potentials ($E_{21}^{\circ} > 0.5 \text{ V}$), so the $\text{Cu}^{\text{I}}\text{L}_2$ species are stable with respect to oxidation. However, there are several concerns regarding the reported electron-transfer kinetic studies for $\text{Cu}^{\text{II}}/\text{Cu}^{\text{I}}$ polypyridyl systems: (a) For $\text{Cu}^{\text{II}}(\text{phen})_2^{2+}$ reduction studies, the product of the conditional stability constant for the addition of the second phenanthroline molecule, K_2' , multiplied by the excess phen concentration must be $\geq 10^2$ to ensure that 99% of the complex exists as the 1:2 complex, $\text{Cu}^{\text{II}}(\text{phen})_2^{2+}$ {i.e., $[\text{Cu}^{\text{II}}(\text{phen})_2^{2+}]/[\text{Cu}^{\text{II}}(\text{phen})^{2+}] = K_2'[\text{phen}] \geq 10^2$ }. In aqueous solution, K_2 is approximately 6×10^6 ,⁷⁹ which implies that the excess phen concentration should exceed $5 \times 10^{-5} \text{ M}$, and even larger concentrations of excess phen are required as the phen becomes significantly protonated below pH 5. (b) The use of a significant excess of ligand could generate interfering amounts of the 1:3 complex, $\text{Cu}^{\text{II}}\text{L}_3^{3+}$, since the reported value for the third stepwise stability constant is $K_3 \approx 10^5 \text{ M}^{-1}$.⁷⁹ (c) The aromatic rings in the polypyridyl

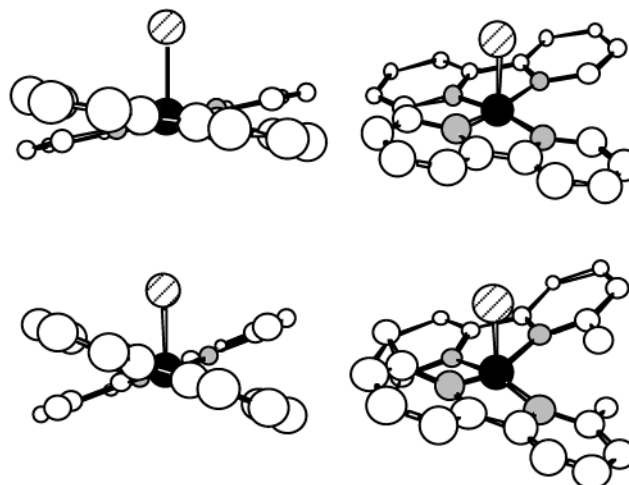


Figure 14. Schematic side and tilted views of the $\text{Cu}^{\text{II}}(\text{phen})_2(\text{H}_2\text{O})_2^{2+}$ (top views) and $\text{Cu}^{\text{II}}(2,9\text{-Me}_2\text{phen})_2(\text{H}_2\text{O})_2^{2+}$ (bottom views) cations showing the noncoplanarity of the nitrogen donor atoms as a result of the steric hindrance provided by the respective hydrogen atoms and methyl groups in the 2,9 positions.

ligands may participate in the electron-transfer process. Few of the publications that have appeared have made note of these potential problems, and none has considered the possibility that the 1:3 complex may be present in significant concentrations.

5.4.1. Bis(2,2'-bipyridyl)copper(II/I) and Bis(1,10-phenanthroline)copper(II/I) Structures

Crystal structures show that both the $\text{Cu}^{\text{I}}(\text{bpy})_2^{+}$ ⁸⁰ and $\text{Cu}^{\text{I}}(\text{phen})_2^{+}$ ⁸¹ cations exist as flattened tetrahedra in the solid state with dihedral angles ranging from 49.9 to 76.8°. This flattening has been attributed to "stacking interactions" between adjacent aromatic ligands in the crystal.⁸²⁻⁸⁴ In solution, all $\text{Cu}^{\text{I}}-\text{polypyridyl}$ complexes are believed to adopt nearly regular D_{2d} symmetry (i.e., with a dihedral angle of 90°).⁸⁵ In fact, the closely related complex of bis(6,6'-dibromo-2,2'-bipyridine)copper(I) perchlorate has been shown to have a nearly perfect tetrahedral symmetry even in the solid state with a dihedral angle of 87.9° between the two CuN_2 planes.⁸⁴

In the corresponding $\text{Cu}^{\text{II}}(\text{phen})_2^{2+}$ and $\text{Cu}^{\text{II}}(\text{bpy})_2^{2+}$ complexes, the four N-donor atoms would be expected to be coplanar except for the fact that steric interactions between the α -hydrogens prevent this (Figure 14).⁸⁶ The specific geometry exhibited by these complexes appears to depend on the nature of the other ligands available as well as the solvent. As early as 1984, Hathaway and co-workers⁸⁷ noted that, of the 34 bis(bipyridyl)copper(II) complexes characterized crystallographically at that time, the majority of structures showed that the bis(bipyridyl)copper(II) moiety tends to be five-coordinate, having the general formula $[\text{Cu}^{\text{II}}(\text{bpy})_2\text{X}]Y_n$ (where $n = 1$ or 2 depending upon whether X has a charge of -1 or 0). A number of related structures published subsequently show the same structural tendency.⁸⁸⁻⁹³ Crystal structures of complexes in which X represents a coordinated water molecule are particularly pertinent to the electron-transfer studies reported to date. Such complexes exhibit either distorted square pyramidal or

Table 5. Electron-Transfer Rate Constants for Bis(2,2'-bipyridyl)copper(II/I), Bis(1,10-phenanthroline)copper(II/I) and Related Copper(II/I) Polypyridyls in Aqueous Solution at 25 °C, $\mu = 0.10$ M (Except as Noted)

oxidant	reductant	$\log k_{12}$ or k_{21} ($M^{-1} s^{-1}$)	$\log k_{11}$ ($M^{-1} s^{-1}$)	ref
Bis(2,2'-bipyridine): $Cu^{II/I}(bpy)_2$ [$E^{\circ'} = 0.12$ V] ^a				
$Cu^{II}L_2^{2+}$	cyt-c ^{II}	0.76	0.82	61
$Cu^{II}L_2^{2+}$	cyt-c ^{II}	0.15		46
		0.3		103
			2.15	107
$Co^{III}(EDTA)^-$	$Cu^IL_2^+$	2.41 ^{b,c}	6.60 ^{b,c} (?)	45
$Co^{III}(bpy)_3^{3+}$	$Cu^IL_2^+$	3.46 ^d	1.60 ^d	78
		3.63 ^e		78
		3.26 ^{d,f}		78
Bis(2,2'-dipyridylamine): $Cu^{II/I}(dipa)_2$ [$E^{\circ'} = 0.20$ V] ^a				
$Cu^{II}L_2^{2+}$	cyt-c ^{II}	2.20	2.83	5
Bis(2,2'-pyridylimidazole): $Cu^{II/I}(pyim)_2$ [$E^{\circ'} = 0.08$ V] ^a				
$Cu^{II}L_2^{2+}$	cyt-c ^{II}	0.23	1.08	5
Bis(1,10-phenanthroline): $Cu^{II/I}(phen)_2$ [$E^{\circ'} = 0.17$ V] ^a				
$Cu^{II}L_2^{2+/+}$			~5.0 ^h (?)	48
$Cu^{II}L_2^{2+}$	cyt-c ^{II}	0.43	1.83	46
			1.7	103
			1.63	107
$Cu^{II}L_2^{2+}$	deoxymyoglobin	2.17		46
$Cu^{II}L_2^{2+}$	hemoglobin	"fast"		122
$Co^{III}(EDTA)^-$	$Cu^IL_2^+$	2.49 ^{b,c}	7.7 ^{b,c} (?)	45
$Co^{III}(EDTA)^-$	$Cu^IL_2^+$	2.65 ^h		104
$Co^{III}(acac)_3$	$Cu^IL_2^+$	2.88 ^h		104
$Co^{III}(bpy)_3^{3+}$	$Cu^IL_2^+$	3.38 ^d	2.23 ^d	78
		3.08 ^{d,f}		78
Bis(4,4'-dimethyl-2,2'-bipyridyl): $Cu^{II/I}(4,4'-Me_2bpy)_2$ [$E^{\circ'} = 0.09$ V] ⁱ				
$Co^{III}(bpy)_3^{3+}$	$Cu^IL_2^+$	4.69 ^d	3.60 ^d	78
		4.15 ^{d,f}	3.60 ^{d,f}	78
Bis(4,7-dimethyl-1,10-phenanthroline): $Cu^{II/I}(4,7-Me_2phen)_2$ [$E^{\circ'} = 0.10$ V] ⁱ				
$Co^{III}(bpy)_3^{3+}$	$Cu^IL_2^+$	4.26 ^d	3.0 ^d	78
		3.59 ^{d,f}	3.0 ^{d,f}	78
Bis(5-nitro-1,10-phenanthroline): $Cu^{II/I}(5-NO_2-phen)_2$ [$E^{\circ'} = 0.26$ V] ^a				
$Cu^{II}L_2^{2+}$	cyt-c ^{II}	2.20	1.97	103
			1.93	107
2,2',2''-terpyridyl: $Cu^{II/I}(terpy)$ [$E^{\circ'} = -0.02$ V] ⁱ				
$Co^{III}X(H_2O)_2^{3+j}$	$Cu^IL(H_2O)^+$	2.72 ^g	0.9 ^g	78

^a Reference 5. ^b $\mu = 0.5$. ^c Yoneda et al. used 0.5 M sodium acetate as a buffer and ionic strength control. ^d Solution contained 10% (v/v) acetone to solubilize the Cu^IL_2 species. ^e Solution contained 2% (v/v) acetone to solubilize the Cu^IL_2 species. ^f $\mu = 0.01$. ^g Lee and Anson's measurements on the self-exchange rate constant for $Cu^{II/I}(phen)_2^{2+/+}$ were made at 22 ± 2 °C in the presence of 0.02 M acetate buffer; most experiments were conducted in the presence of Cl^- electrolytes since substitution of $CF_3SO_3^-$ indicated that Cl^- had no effect upon the results. ^h $\mu = 0.25$. ⁱ Reference 78. ^j X represents $Me_6[14]dieneN_4$.

distorted trigonal bipyramidal geometries.^{91,94–96} The same range of geometries exists for the majority of other Cu(II) bis-bipyridyl and bis-phenanthroline complexes as well. {Interestingly, for those complexes that appear to be distorted square pyramidal, the water molecule (or other unidentate ligand) may occupy an equatorial site.} The distinction between the latter two geometries is one of degree as noted by Carugo and Castellani⁹⁷ in their summary of the structural parameters of 25 structures of $[Cu^{II}(bpy)_2X]Y$ crystals. They formulated an approach for classifying these structures in terms of their placement along an ideal pathway for the isomerization reaction from the trigonal bipyramidal geometry to the square pyramidal one. In studies on $Cu^{II}(phen)_2(H_2O)^{2+}$, $Cu^{II}(bpy)_2(H_2O)^{2+}$, and $Cu^{II}(bpy)_2Cl^+$, Bray and Drickamer⁹⁸ noted that the transition from a trigonal bipyramidal to a square pyramidal geometry could readily be induced by pressure.

In forming a crystal with hexafluorophosphate as anion, Foley, Tyagi, and Hathaway⁸⁷ obtained a four-coordinate $Cu^{II}(bpy)_2^{2+}$ cation, which exhibited a

compressed tetrahedral geometry with a dihedral angle of 44.6°, halfway between a planar and a regular tetrahedral geometry. This specific structure is of particular interest because it may approximate a reaction intermediate along the pathway of normal electron-transfer reactions.

5.4.2. Bis(2,2'-bipyridyl)copper(II/I) and Bis(1,10-phenanthroline)copper(II/I) Kinetics

As has been noted in an earlier section, the original data on the electron-transfer kinetics of the bis complexes formed by Cu(II/I) with the two simplest bidentate polypyridyl ligands, 2,2'-bipyridine and 1,10-phenanthroline, yielded controversial results. Table 5 contains the results of all known studies on the electron-transfer kinetics of the $Cu^{II/I}(phen)_2$ and $Cu^{II/I}(bpy)_2$ systems, as well as closely related systems involving substitutions on the "back side" of the ligand, which are presumed to be devoid of additional steric effects. The earliest such kinetic study, which has given rise to much controversy, is that by Yoneda, Blackmer, and Holwerda,⁴⁵ as cited earlier. Their

study involved the oxidation of $\text{Cu}^{\text{I}}(\text{bpy})_2^+$ and $\text{Cu}^{\text{I}}(\text{phen})_2^+$ by $\text{Co}(\text{EDTA})^-$, $\text{Co}(\text{PDTA})^-$, and $\text{Co}(\text{CyDTA})^-$. In applying the Marcus relationship to their cross-reaction rate constants with $\text{Co}(\text{EDTA})^-$, these investigators obtained calculated $k_{11(\text{Ox})}$ values of 4×10^6 and $5 \times 10^7 \text{ M}^{-1} \text{ s}^{-1}$ for the $\text{Cu}^{\text{II}}(\text{bpy})_2$ and $\text{Cu}^{\text{II}}(\text{phen})_2$ systems, respectively, as noted in section 4.3. These are among the largest k_{11} values reported for any Cu(II/I) system. (Although these authors did not make corrections for the nonlinear (f) and work term (W) functions in eq 14, those corrections are generally minor and do not account for the disagreement of their k_{11} values with those of other studies.) The corresponding kinetic study on the reduction of $\text{Cu}^{\text{II}}(\text{bpy})_2(\text{H}_2\text{O})^{2+}$ and $\text{Cu}^{\text{II}}(\text{phen})_2(\text{H}_2\text{O})^{2+}$ with cytochrome- c^{II} by Augustin and Yandell⁴⁶ yielded $k_{11(\text{Red})}$ values of 1.4×10^2 and 43, respectively. Holwerda⁹⁹ later suggested that the large discrepancy between his $k_{11(\text{Ox})}$ values and the $k_{11(\text{Red})}$ values obtained by Augustin and Yandell might be attributable to differences between the extent of $\text{Cu}^{\text{II}}\text{-H}_2\text{O}$ bond breaking and $\text{Cu}^{\text{I}}\text{-H}_2\text{O}$ bond making in the activated complexes of self-exchange and cross-reactions. This sentiment was later echoed by Lee and Anson in making their proposal that the Marcus treatment might not be valid for Cu(II/I) systems (see section 4.3).³⁹ Several other investigators^{43,63,100} have also added their comments regarding the disagreement between the foregoing $k_{11(\text{Red})}$ and $k_{11(\text{Ox})}$ data without arriving at a satisfactory consensus regarding the underlying cause.

The size and complexity of cytochrome- c^{II} , which was used as the reducing agent in Yandell's studies, raises the question as to whether the observed discrepancies can be attributed to the difficulties inherent in attempting to apply the Marcus relationship (eq 14) to reactions involving this reagent. It is noteworthy, however, that other workers have successfully applied Marcus theory to reactions involving this reagent and have reported consistent results.^{101,102} It is also significant that Yandell's data for the reduction of Cu(II)-2,9-dimethyl-1,10-phenanthroline with cytochrome- c^{II} yields a self-exchange rate constant that agrees very well with values calculated from cross-reactions with more conventional outer-sphere counterreagents (Table 6).¹⁰³

Yoneda, Blackmer, and Holwerda's kinetic experiments on the oxidation of $\text{Cu}^{\text{I}}(\text{phen})_2$ with $\text{Co}(\text{EDTA})^-$ have been repeated by de Araujo and Hodges.¹⁰⁴ Whereas the latter authors did not attempt to calculate the apparent k_{11} value for the $\text{Cu}^{\text{II}}(\text{phen})_2$ system, they observed a very similar cross-reaction rate constant ($k_{21} = 4.48 \times 10^2 \text{ M}^{-1} \text{ s}^{-1}$) to that reported by Yoneda et al. ($k_{21} = 3.12 \times 10^2 \text{ M}^{-1} \text{ s}^{-1}$). de Araujo and Hodges also studied the oxidation of $\text{Cu}^{\text{I}}(\text{phen})_2^+$ with $\text{Co}^{\text{III}}(\text{acac})_3$ (where acac represents acetylacetonate), but unfortunately, the self-exchange rate constant for $\text{Co}^{\text{III/II}}(\text{acac})_3^{0/-}$ does not appear to be available, so this latter cross-reaction study cannot be used as a cross-check on the $\text{Co}^{\text{III}}(\text{EDTA})^-$ result. Nonetheless, the study with $\text{Co}^{\text{III}}(\text{acac})_3$ is of specific interest in that these investigators were able to demonstrate that the reaction rate with $\text{Cu}^{\text{I}}(\text{phen})_2^+$ increased as the phenanthro-

line concentration increased, leveling off at a phenanthroline concentration of 0.1 mM, which represented about a 5:1 ratio of ligand to Cu(I) (the latter being maintained at 0.020 mM). This observation was interpreted to indicate that, in the absence of a sufficient amount of excess ligand, the 1:1 $\text{Cu}^{\text{I}}(\text{phen})_2(\text{H}_2\text{O})_2^+$ complex was present at a significant concentration level and that its oxidation rate is much smaller than for the 1:2 complex. This explanation suggests the possibility that other studies involving the $\text{Cu}^{\text{II}}(\text{phen})_2$ system and related analogues may have yielded erroneously small rate constants if the ligand concentration were insufficient (see section 4.2).

The other principle oxidation studies involving unsubstituted phenanthroline and bipyridyl complexes are those reported by Munakata and Endicott⁷⁸ for which they utilized $\text{Co}^{\text{III}}(\text{bpy})_3^{3+}$ as the oxidant. Application of eq 14 yielded $k_{11(\text{Ox})}$ values of 38 and 1.7×10^2 for $\text{Cu}^{\text{II}}(\text{bpy})_2$ and $\text{Cu}^{\text{II}}(\text{phen})_2$, respectively, both values being 5 orders of magnitude smaller than those of Yoneda et al. and both being within experimental error of the $k_{11(\text{Red})}$ values reported by Augustin and Yandell. Although Munakata's paper does not provide specific data on the reactant concentrations used in his study, an examination of Munakata's original notes indicates that he used a 1:2 stoichiometric ratio of Cu(I) to ligand with the copper concentration varied over the narrow range of 0.05 to 0.10 mM.^{105a} The solvent matrix contained 10% acetone-90% water (to improve ligand solubility). Lowering the acetone concentration to 2% caused only a slight increase in the cross-reaction rate constant. Munakata indicated in his paper that all solutions were prepared in 10^{-4} M HClO_4 , which would seem to imply that his kinetic studies may have been conducted at about pH 4, whereas his original notes state that all solutions were prepared in 10^{-5} M HClO_4 .^{105a} (At the latter level, the ligand itself would tend to buffer the solution at a pH slightly below 5 if the total ligand concentration were in the range of 0.10-0.20 mM.) Rough calculations based on literature values for the ligand protonation constants and complex stability constants^{105b} indicate that, even at pH 4 in the presence of 0.10 mM total Cu(I) and 0.20 mM total ligand, more than one-half of the Cu(I) will be in the form of the 1:2 complex for both the phenanthroline and bipyridine systems. Thus, it is presumed that Munakata's k_{11} values for the $\text{Cu}^{\text{II}}(\text{bpy})_2$ and $\text{Cu}^{\text{II}}(\text{phen})_2$ systems may be slightly too small, but they are presumably within the correct order of magnitude.

Munakata's $k_{11(\text{Ox})}$ value for $\text{Cu}^{\text{II}}(\text{bpy})_2$ appears to be in agreement with a "preliminary" value of $k_{11(\text{Ox})} = 28 \text{ M}^{-1} \text{ s}^{-1}$ reported by Davies⁶³ for the oxidation of $\text{Cu}^{\text{I}}(\text{bpy})_2^+$ using $\text{Ru}^{\text{III}}(\text{NH}_3)_5\text{py}$ as the oxidizing agent in aqueous solution. Although Davies did not specify the pH utilized for the latter study, it is apparent that his parallel study on the $\text{Cu}^{\text{II}}(\text{dmp})_2$ system (Table 6) was conducted in solutions buffered at pH 6.1.

In view of the intricacies of the kinetic behavior predicted by Scheme 1 and the discrepancies noted

Table 6. Electron-Transfer Rate Constants for Sterically Hindered Bis(bipyridyl) and Bis(phenanthroline) Complexes with Copper(II/I) in Aqueous and Acetonitrile Solution (Except as Specified) at 25 °C

oxidant	reductant	solvent	log k_{12} or k_{21} ($M^{-1} s^{-1}$)	log k_{11} ($M^{-1} s^{-1}$)	ref
Bis(6,6'-dimethyl-2,2'-bipyridyl): $Cu^{II/I}(6,6'-Me_2bpy)_2$ or $Cu^{II/I}(dmbp)_2$ [$E^{\circ'} = 0.59$ V (SHE) in 20% $CH_3OH-80\%$ H_2O] ^a					
$Cu^{II}L_2^{2+}$	$Ru^{II}(NH_3)_5isn^{2+}$	D1	5.53	3.43	112
$Cu^{II}L_2^{2+}$	$Ru^{II}(NH_3)_5py^{2+}$	D1	5.62	2.76	112
$Cu^{II}L_2^{2+}$	$Ru^{II}(NH_3)_4bpy^{2+}$	D1	5.62	1.89	112
[$E^{\circ'} = 0.56$ V (Fc) in CH_3CN] ^b					
$Cu^{III}L_2$		B		3.74^c	113
$Cu^{II}L_2^{2+}$	$Ru^{II}(hfac)_3^-$	B	3.77 ^c	-0.15 ^c	113
$Cu^{II}L_2^{2+}$	$Co^{II}(bpy)_3^{2+}$	B	3.28 ^c	0.15 ^c	113
$Cu^{II}L_2^{2+}$	$Fe^{II}(Cp)_3$	B	variable ^d	[$k_{OQ} = 50$]	113
$Ru^{III}(hfac)_3$	$Cu^IL_2^+$	B	3.38 ^c	-0.7 ^c	113
$Ni^{III}(tacn)_2^{3+}$	$Cu^IL_2^+$	B	4.97 ^c	2.83 ^c	113
$Mn^{III}(bpyO_2)_3^+$	$Cu^IL_2^+$	B	3.32 ^c	3.28 ^c	113
Bis(4,4',6,6'-tetramethyl-2,2'-bipyridyl): $Cu^{II/I}(Me_4bpy)_2$ [$E^{\circ'} = 0.60$ V (SHE) in 20% $CH_3OH-80\%$ H_2O] ^b					
$Cu^{II}L_2^{2+}$	$Ru^{II}(NH_3)_5isn^{2+}$	D1	5.40	3.36	112
$Cu^{II}L_2^{2+}$	$Ru^{II}(NH_3)_5py^{2+}$	D1	5.67	2.49	112
$Cu^{II}L_2^{2+}$	$Ru^{II}(NH_3)_4bpy^{2+}$	D1	5.17	1.86	112
<i>cis</i> - $Ru^{III}(NH_3)_4(isn)_2$	Cu^IL_2	D1	5.4	4.0	112
Bis(2,9-dimethyl-1,10-phenanthroline): $Cu^{II/I}(2,9-Me_2phen)_2$ or $Cu^{II/I}(dmp)_2$					
$Cu^{III}L_2^{2+/+}$		A ^{e,f}		5.3	116
$Cu^{II}L_2^{2+}$	cyt- <i>c</i> ^{II}	A	6.00	4.23	103
$Cu^{II}L_2^{2+}$	$Co^{II}(phen)_3^{2+}$	A	4.79	4.64	103
$Cu^{II}L_2^{2+}$	hydroquinones	A ^f	several	5.0	117
$Cu^{II}L_2^{2+}$	hydroquinone	A ^f	7.40	4.73	99
$Cu^{II}L_2^{2+}$	$Ru^{II}(NH_3)_5isn^{2+}$	A	5.66	[4.6]	63
$Cu^{II}L_2^{2+}$	$Ru^{II}(NH_3)_5py^{2+}$	A	5.74	[4.6]	63
$Cu^{II}L_2^{2+}$	$Ru^{II}(NH_3)_4bpy^{2+}$	A	5.57	[4.6]	63
$Cu^{II}L_2^{2+}$	$Ru^{II}(NH_3)_4phen^{2+}$	A ^g	5.46	4.6	78
Cu^{III} -peptides	$Cu^IL_2^{2+}$	A	4-8	???	100
$Cu^{III}L_2^{2+/+}$		B		3.70^c	116
$Cu^{II}L_2^{2+}$	$Co^{II}(bpy)_2^{2+}$	B	2.85 ^c	0.20 ^{c,d}	119
$Cu^{II}L_2^{2+}$	$Fe^{II}(Cp)_2$	B	gated ^c	[$k_{OQ} = 33$]	119
$Cu^{II}L_2^{2+}$	$Fe^{II}(PMCP)_2$	B	mixed	[$k_{OQ} = 34$]	119
$Ni^{III}(tacn)_2^{3+}$	Cu^IL_2	B	5.43 ^c	3.70 ^c	119
$Mn^{III}(bpyO_2)_3^+$	Cu^IL_2	B	4.46 ^{a,c}	4.46 ^c	119
$Cu^{III}L_2^{2+/+}$		C		3.48^c	116
Bis(2,9-dimethyl-4,7-diphenyl-1,10-phenanthroline): $Cu^{II/I}(Me_2\Phi_2phen)_2$ or $Cu^{II/I}(dpsmp)$					
$Cu^{III}L_2^{2+/+}$		B		3.15^c	121
$Cu^{II}L_2^{2+}$	hemoglobin	A	"very fast"		122
Bis(2,9-dimethyl-4,7-diphenyl-1,10-phenanthroline)disulfonate): $Cu^{II/I}(dpsmp)$ [$E^{\circ'} = 0.62$ V]					
$Cu^{III}L_2^{2-/3-}$		A		5.7	125
$Cu^{II}L_2^{2-}$	hydroquinone	A ^e	8.15	6.4	99
$Cu^{II}L_2^{2-}$	$Fe(CN)_6^{4-}$	A	limiting ^g	[$k_{OQ} = 229$]	43
$Cu^{II}L_2^{2-}$	$Fe(CN)_6^{4-}$	A	limiting ^g	[$k_{OQ} = 137$], 5.6	123
$Cu^{II}L_2^{2-}$	$Fe(EDTA)^{2-}$	A	limiting ^g	[$k_{OQ} = 139$]	123
$Cu^{II}L_2^{2-}$	$Fe(CN)_5(PPh_3)^{3-}$	A	limiting ^g	[$k_{OQ} = 130$]	123
$Cu^{II}L_2^{2-}$	$Ru(NH_3)_5pyz^{2+}$	A	limiting ^g	[$k_{OQ} = 136$]	123
$Cu^{II}L_2^{2-}$	$Ru^{II}(NH_3)_5py^{2+}$	A	7.2 ^h	1.0	123
$Cu^{II}L_2^{2-}$	Ni^IHZ^i	A		4.86	124
$Ni^{III}HZ^i$	$Cu^IL_2(H_2O)^{3-}$	A		5.90	124
$Ni^{III}Z^i$	$Cu^IL_2(H_2O)^{3-}$	A		7.26	124
Cu^{III} -peptides	$Cu^IL_2^+$	A	limiting		100
1,2-Bis(9-methyl-1,10-phenanthroline-2-yl)ethane): $Cu^{II}(diphen)/Cu^I_2(diphen)_2$					
$Cu^{III}L_2^{2+/+}$		B		4.96^c	127
$Ni^{III}(tacn)_2^{3+}$	$Cu^I_2L_2^+$	B	4.68 (biphasic)		127
Bis(2,9-diphenyl-1,10-phenanthroline): $Cu^{II/I}(2,9-\Phi_2phen)_2$ or $Cu^{II/I}(dpp)_2$					
$Cu^{II}L_2^{2+}$	$Co^{II}(bpy)_3^{2+}$	B	5.20	4.67 ^c	120
$Co^{III}(bpyO_2)_3^{3+}$	Cu^IL_2	B	4.28	5.72 ^c	120

^a Reference 112. ^b Reference 113. ^c Rate constants are in units of $kg\ mol^{-1}\ s^{-1}$. ^d Reaction appears to be limiting first-order indicating that the reaction is "gated". ^e Chloride used for ionic strength control. ^f Acetate used for ionic strength control; $\mu = 0.2$. ^g Solution contained 10% acetone to improve the solubility of the $Cu(I)$ species; $\mu = 0.01$. ^h Reaction is at the limit of the stopped-flow method. ⁱ Z represents an oxime-imine ligand.

above, it is tempting to suggest that the much larger $k_{11(Ox)}$ value reported by Yoneda et al. represents pathway B as the favored reaction pathway (Scheme

1) while the reduction studies by Augustin and Yandell represent the situation in which the rate of the limiting conformational change represented by

k_{OQ} (that is, the conversion of $Cu^{II}(phen)_2(O)$ to $Cu^{II}(phen)_2(Q)$) has been exceeded, thus forcing pathway A (the intrinsically less favored pathway) to become the predominant reaction path. However, the theory governing Scheme 1 dictates that the more favorable pathway (i.e., the one with the larger k_{11} value) is the only one that can be observed in both directions (i.e., for both oxidation and reduction) while the less favorable pathway (with the smaller k_{11} value) can only be observed in one direction, that being the direction in which the conformational change precedes the electron-transfer step for the favored reaction.⁵³ Accessing the less favored pathway will then occur when the overall reaction rate exceeds the rate of conformational change. Thus, the fact that the “smaller” $k_{11(Red)}$ value obtained by Augustin and Yandell agrees with the $k_{11(Ox)}$ values reported by Munakata and Endicott and by Davies implies that a k_{11} value larger than the values these investigators reported is not possible for the $Cu^{II}(phen)_2$ and $Cu^{II}(bpy)_2$ systems.

On the basis of the foregoing considerations, it seems likely that the $k_{11(Ox)}$ values obtained by Yoneda et al. for the oxidation of $Cu^I(bpy)_2$ and $Cu^I(phen)_2$ —and confirmed by de Araujo and Hodges—may represent an inner-sphere mechanism. Such an inner-sphere pathway could yield a larger cross-reaction rate constant, which in turn would generate a larger calculated k_{11} value for the $Cu^{II}(phen)_2^{2+/+}$ and $Cu^{II}(bpy)_2^{2+/+}$ couples when inserted into eq 14. This is a particularly significant conclusion in view of the controversy that these data have provoked. In discussing their own study, de Araujo and Hodges did, in fact, consider the possibility that a carboxylate moiety from the $Co(EDTA)^-$ oxidant might form a bridge to the copper center prior to electron transfer to generate an inner-sphere reaction. However, they argued that such an inner-sphere pathway would require the initial dissociation of a coordinated phen ligand. Since they observed no rate dependence with this counterreagent upon adding large concentrations of phenanthroline, they rejected the inner-sphere mechanism hypothesis. This conclusion ignores the possibility that an inner-sphere mechanism could, instead, involve an expansion of the $Cu(I)$ coordination sphere (from four to five) prior to the electron-transfer step, in which case no dissociation of phenanthroline would be required.

5.4.3. Related Polypyridylcopper(III) Systems Devoid of Additional Steric Factors

In view of the uncertainty surrounding the origin of the discrepancies in the k_{11} values for the phenanthroline and bipyridyl complex systems, an examination of the data obtained for $Cu(II/I)$ complexes with closely related substituted polypyridyls is of considerable interest. Table 5 includes the published electron-transfer studies on complexes involving polypyridyl ligands for which no additional steric factors apply, that is, the ring substituents are at the 4 through 7 positions on 1,10-phenanthroline and at the 4,4' or 5,5' positions on 2,2'-bipyridine so that, like bpy and phen, only the α -hydrogens should encounter steric hindrance when two ligands attempt to coordinate

in a coplanar fashion on $Cu(II)$. Such substitutions may alter the ligand K_a values, but the derived results would be expected to be closely analogous to those of the unsubstituted bpy and phen systems. Unfortunately, all of these systems have been studied in only one direction—either reduction or oxidation but not both—and each ligand system has been studied by only one research group. For the oxidation studies on $Cu^I(4,4'-Me_2bpy)_2^+$ and $Cu^I(4,7-Me_2phen)_2^+$, Munakata and Endicott⁷⁸ obtained $k_{11(Ox)}$ values that are roughly 1 order of magnitude larger than those for the corresponding nonsubstituted systems. This presumably reflects the positive inductive effect of the methyl substituents involved. From their limited study on the electron-transfer kinetics of the monoterpyridyl complex of $Cu(I)$ with $Co^{III}(Me_6[14]dieneN_4)^{3+}$, these same investigators calculated $k_{11(Ox)} = 8 M^{-1} s^{-1}$, which represents the smallest value in this series. The presence of an additional inner-sphere water molecule in this system may have a bearing on the reduced k_{11} value as noted in section 8 of this review.

Augustin and Yandell^{103,106,107} studied the reduction of bis(5-nitro-1,10-phenanthroline)copper(II) with cytochrome-*c*^{II} and reported a calculated value of $k_{11(Red)} \approx 86 M^{-1} s^{-1}$, which is in very close agreement with the value obtained for the corresponding unsubstituted system. Additional studies by Yandell (never published but included in his review)⁵ on the reduction of two $Cu(II)$ complexes involving ligands closely related to bipyridine yielded k_{11} values in the range of $12-600 M^{-1} s^{-1}$. It is to be noted that none of the $k_{11(Red)}$ values reported for these bpy and phen analogues by Munakata or Yandell approach the $k_{11(Ox)}$ values obtained by Yoneda et al. for $Cu^{II}(phen)_2$ and $Cu^{II}(bpy)_2$.

5.4.4. Complexes of Copper(III) Involving “Steric” Substitutions on Bipyridine and Phenanthroline

As noted above, the coordinated 2,2'-bipyridine or 1,10-phenanthroline ligands are distorted away from a planar configuration in the bis $Cu(II)$ complexes because of repulsive interactions between the α -hydrogens on the two coordinated polypyridyls. The introduction of methyl groups in the positions α to the donor atoms increases the dihedral angle between the two coordinated polypyridyl ligands to the point where the $Cu(II)$ complex more nearly approximates the tetrahedral geometry presumed to be favored in the corresponding $Cu(I)$ complex (Figure 14). As an example, Burke, Henrick, and McMillin¹⁰⁸ determined the structures for both the $Cu(II)$ and $Cu(I)$ bis complexes formed with 4,4',6,6'-tetramethyl-2,2'-bipyridine (Me_4bpy). The structure of $Cu^{II}(Me_4bpy)_2X$, where X was either H_2O or ClO_4^- , was found to be five-coordinate with a distorted trigonal bipyramidal structure, the unique ligand (H_2O or ClO_4^-) occupying a position in the equatorial plane. The corresponding $Cu(I)$ complex was in a flattened tetrahedron with a dihedral angle of 68° . Similarly, Burke, McMillin, and Robinson¹⁰⁹ reported the crystallographic structure of bis(6,6'-dimethyl-2,2'-bipyridyl)copper(I) tetrafluoroborate, in which the cationic unit, $Cu^I(6,6'-Me_2bpy)_2^+$, was found to exhibit a less flat-

tened tetrahedral structure with a dihedral angle of 80.9°. As noted earlier, this type of flattening has been attributed to crystal packing or, more specifically, to stacking interactions involving the aromatic rings, a factor that is presumed to be insignificant in dilute solutions.

McMillin's group¹¹⁰ has also reported that the crystal structure of $\text{Cu}^{\text{I}}(\text{dpmp})_2$ (dpmp = 2,9-dimethyl-4,7-diphenyl-1,10-phenanthroline = bathocuproin) exhibited a nearly perfect tetrahedral geometry with a dihedral angle of 87.6°. A number of related Cu(I) structures have also been reported by this group,¹¹¹ and the various types of distortions have been discussed.

Davies and Byers¹¹² studied the kinetics for the reduction of both bis(6,6'-dimethyl-2,2'-bipyridine)-copper(II) ($\text{Cu}^{\text{II}}(6,6'\text{-Me}_2\text{bpy})_2^{2+}$) and bis(4,4',6,6'-tetramethyl-2,2'-bipyridyl)copper(II) ($\text{Cu}^{\text{II}}(\text{Me}_4\text{bpy})_2^{2+}$) in 20% methanol–80% water. Three closely related Ru(II) compounds were utilized as the reductants (Table 6). The cross-reaction rate constants did not increase as rapidly with decreasing reagent potential as would be predicted by the Marcus relationship. Thus, the calculated $k_{11(\text{Red})}$ values decreased as the driving potential increased, the differences covering a range of about 30-fold.

Although Davies and Byers suggested that such lack of consistency is not uncommon when applying the Marcus relationship to systems involving wide ranges in reaction potentials, these results represent an unusually large discrepancy in k_{11} values for correlated systems in the absence of other problems and suggest the possibility that these reactions are approaching limiting first-order behavior due to the onset of conformational "gating." The authors reported that they did not observe rate saturation as the concentration of the Ru(II) reagent increased—as would be expected if "gated" behavior were operative—but, for the most rapid reaction they studied, involving the reduction of $\text{Cu}^{\text{II}}(\text{Me}_4\text{bpy})_2^{2+}$ by $\text{Ru}^{\text{II}}(\text{NH}_3)_5\text{py}^{2+}$, there was an apparent curving off of their observed pseudo-first-order rate constant as this value exceeded about 120 s^{-1} . It is also particularly interesting to note that the largest $k_{11(\text{Red})}$ value reported by Davies for $\text{Cu}^{\text{II}}(6,6'\text{-Me}_2\text{bpy})_2^{2+}$ is in very good agreement with the $k_{11(\text{NMR})}$ value obtained by Takagi in acetonitrile¹¹³ (see Table 6). Although the solvents differed in these two studies, similar k_{11} values have been observed for many Cu(II/I) systems in water and acetonitrile.¹¹⁴

Takagi and co-workers^{113,115} have conducted an extensive study on the electron-exchange kinetics of $\text{Cu}^{\text{II/I}}(6,6'\text{-Me}_2\text{bpy})_2^{2+/+}$ in acetonitrile, including both cross-reactions and the direct determination of k_{11} by NMR line broadening as noted above. The reduction of the Cu(II) complex with ferrocene was found to exhibit limiting first-order behavior (independent of the ferrocene concentration) as the ferrocene concentration was increased. As the authors noted, this type of behavior is consistent with the mechanism in Scheme 1 for a system in which pathway B is preferred if the conformational change represented by k_{OQ} , has become rate limiting in accordance with eq 19d.

The calculated $k_{11(\text{Red})}$ values that Takagi reported for the reductions carried out with $\text{Co}^{\text{II}}(\text{bpy})_3^{2+}$ and $\text{Ru}^{\text{II}}(\text{hfac})_3^-$ are much smaller than the NMR k_{11} value, supporting the suggestion that with these two reagents the calculated self-exchange rate constant is representative of pathway A (the "less favorable" pathway in this case) in accordance with eq 19a. Surprisingly, the authors did not address that possibility. More puzzling is the very small $k_{11(\text{Ox})}$ value reported for the oxidation of $\text{Cu}^{\text{I}}(6,6'\text{-Me}_2\text{bpy})_2^+$ with $\text{Ru}^{\text{III}}(\text{hfac})_3$. This small value cannot be the result of similar "gated" behavior since, according to the theory pertaining to the mechanism in Scheme 1, limiting first-order ("gated") behavior will only be observed in *one direction* for any reaction that is thermodynamically favorable.⁵³ Thus, if the reduction reaction can be "gated," as indicated by Takagi's data, the preferred reaction pathway is presumably pathway B (as the authors concluded). In corresponding oxidation reactions, the conformational change would follow electron transfer and not be observed. Moreover, despite the fact that the calculated $k_{11(\text{Ox})}$ values obtained from their other two oxidations with $\text{Ni}^{\text{III}}(\text{tacn})_3^{3+}$ and $\text{Mn}^{\text{III}}(\text{bpyO}_2)_3^{3+}$ appear to agree with the NMR k_{11} value within experimental error, these authors concluded that the latter reactions are also "gated." This is presumed to be a misstatement since it is inconsistent with Scheme 1 behavior if pathway B is the preferred reaction pathway for the $\text{Cu}^{\text{II/I}}(6,6'\text{-Me}_2\text{bpy})_2^{2+/+}$ system.

Three Cu(II/I) systems with closely related, sterically hindered bis-phenanthrolines have been studied by a variety of investigators: 2,9-dimethyl-1,10-phenanthroline (neocuproin, 2,9-Me₂phen, or dmp), 2,9-dimethyl-4,7-diphenyl-1,10-phenanthroline (bathocuproin, Me₂Φ₂phen, or dpmp), and 2,9-dimethyl-4,7-diphenyl-1,10-phenanthroline disulfonate (bathocuproin disulfonate or dpsmp). The kinetic data obtained for these three systems are included in Table 6. Of particular interest are the results reported by Doine (Takagi), Yano, and Swaddle¹¹⁶ for the determination of the $\text{Cu}^{\text{II/I}}(\text{dmp})$ self-exchange rate constant as obtained directly by NMR line broadening in deuterated water, acetone, and acetonitrile. For the latter two solvents, these workers reported k_{11} values of 3.0×10^3 and $4.9 \times 10^3 \text{ M}^{-1} \text{ s}^{-1}$, respectively, while the aqueous value was considerably larger at $2.0 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$. In other studies (vide infra), solvent effects seem to have a relatively minor effect on k_{11} values for Cu(II/I) systems as long as four inner-sphere sites are occupied by reasonably strong donor atoms. Therefore, there is some question as to whether the presence of chloride in the aqueous study (added to increase the complex solubility) may have contributed to an inner-sphere mechanism, which could then account for the larger aqueous $k_{11(\text{NMR})}$ value. From the data in Table 6, it is apparent that $k_{11(\text{Red})}$ values calculated from eight different $\text{Cu}^{\text{II}}(\text{dmp})_2^{2+}$ reduction studies, as reported by Augustin and Yandell, Holwerda and co-workers, and Munakata and Endicott,^{78,99,106,117} are all intermediate between the aqueous and nonaqueous $k_{11(\text{NMR})}$ values determined by Swaddle and co-workers.

The only oxidation study on $\text{Cu}^{\text{I}}(\text{dmp})_2^+$ in aqueous solution was that carried out by Lappin, Youngblood, and Margerum¹⁰⁰ in which they utilized $\text{Cu}(\text{III})$ –oligopeptides as oxidants. These investigators made no attempt to calculate the self-exchange rate constant for $\text{Cu}^{\text{II}}(\text{dmp})_2$ in their publication since the self-exchange rate constant for the $\text{Cu}(\text{III})$ –oligopeptides had not been determined at that time. However, their later evaluation of the self-exchange rate constant for the $\text{Cu}(\text{III}/\text{II})$ complex with deprotonated tri- α -aminoisobutyrate ($\text{H}_{-2}\text{Aib}_3^{3-}$), $5.5 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$,¹¹⁸ apparently applies to most other $\text{Cu}(\text{III}/\text{II})$ polypeptide complexes as well.¹⁰⁰ Application of this value to the cross-reaction rate constants with $\text{Cu}^{\text{II}}(\text{dmp})_2$ yields an estimated value of $k_{11(\text{Ox})} \approx 10^7 \text{ M}^{-1} \text{ s}^{-1}$ for the $\text{Cu}^{\text{II}}(\text{dmp})_2$ system. This very large value is similar to the large k_{11} values reported by Yoneda et al. for $\text{Cu}^{\text{II}}(\text{phen})_2$ and $\text{Cu}^{\text{II}}(\text{bpy})_2$ and is also presumed to represent an inner-sphere reaction.

Much more definitive data have been obtained on $\text{Cu}^{\text{II}}(\text{dmp})_2$ by Takagi and co-workers in acetonitrile.¹¹⁹ From reactions with two oxidizing agents, $\text{Ni}^{\text{III}}(\text{tacn})_2^{3+}$ and $\text{Mn}^{\text{III}}(\text{bpyO}_2)_3^{3+}$, they obtained $k_{11(\text{Ox})}$ values for the $\text{Cu}(\text{II}/\text{I})$ system that differed by 50-fold, spanning either side of the NMR k_{11} value. Since the NMR value was within an order of magnitude of the k_{11} values for each of these cross-reactions, they concluded that the differences merely represented experimental error. For the corresponding reduction kinetics with $\text{Fe}^{\text{II}}(\text{PMCP})_2$ and $\text{Fe}(\text{Cp})_2$,¹²⁰ however, mixed kinetic behavior was observed with the former reagent while first-order gated behavior was evident with the latter reagent. These results are again indicative of a system that conforms to Scheme 1 with pathway B being preferred. Thus, it appears that the conformational change is becoming rate-limiting with the latter reagents. The additional reduction study with $\text{Co}^{\text{II}}(\text{bpy})_3^{2+}$ as counterreagent gave a significantly smaller k_{11} value, which presumably represents a switch to pathway A (eq 19a).

Takagi and co-workers¹²¹ have also determined the self-exchange rate constant for the $\text{Cu}(\text{II}/\text{I})$ system with 2,9-dimethyl-4,7-diphenyl-1,10-phenanthroline (dpmp) in acetonitrile by NMR line-broadening and found the value to be similar to that for $\text{Cu}^{\text{II}}(\text{dmp})_2^{2+/+}$ in this same solvent¹¹⁶ despite the difference in the radii of these two systems. Unfortunately, the only cross-reaction study that has been reported is one involving reduction with hemoglobin by Eguchi and Saltman.¹²² The rate constant was reported to be “very fast”, and the authors concluded that the reaction probably proceeded via an inner-sphere mechanism.

The $\text{Cu}(\text{II}/\text{I})$ complex with the related ligand 2,9-dimethyl-4,7-diphenyl-1,10-phenanthroline disulfonate, $\text{Cu}^{\text{II}}(\text{dpsmp})_2$, has been studied by several research groups, largely because it is both commercially available and water-soluble. Al-Shatti, Lappin, and Sykes⁴³ studied the reduction kinetics with $\text{Fe}^{\text{II}}(\text{CN})_6^{4-}$ and observed limiting first-order kinetics with a rate constant of 229 s^{-1} . They ascribed this to a conformational change in which the five-coordinate $\text{Cu}^{\text{II}}\text{L}_2(\text{H}_2\text{O})^{2+}$ species converted to a tetrahedral or distorted tetrahedral geometry prior to

electron transfer in accordance with Scheme 1. In revisiting this system, Leupin, Al-Shatti, and Sykes¹²³ utilized a variety of reductants including $\text{Fe}^{\text{II}}(\text{CN})_6^{4-}$, $\text{Fe}^{\text{II}}(\text{EDTA})^{2-}$, $\text{Fe}^{\text{II}}(\text{CN})_5\text{PPh}_3$, and $\text{Ru}^{\text{II}}(\text{NH}_3)_5\text{py}^{2+}$. In all cases, they observed that at low concentrations of reagent the reactions were second-order but appeared to approach limiting first-order behavior as the concentration of the counterreagent was increased, the resolved first-order rate constant for all four systems being within the narrow range of 130 – 139 s^{-1} , which presumably represents the value of k_{OQ} in accordance with eq 19d. These results are again consistent with the mechanism in Scheme 1 in which pathway B is preferred. From their data for the reactions with $\text{Fe}(\text{CN})_6^{4-}$ and $\text{Fe}^{\text{II}}(\text{EDTA})^{2-}$, these authors also extrapolated an apparent second-order rate constant for the electron-transfer step itself of about $4 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$. Although Leupin, Al-Shatti, and Sykes did not specifically consider the square scheme mechanism in Scheme 1, they included an alternate reaction path involving the direct reduction of $\text{Cu}^{\text{II}}(\text{dpsmp})_2^{2+}$ without the formation of a prior intermediate, which is equivalent to pathway A (eq 19d). Their attempts to study reactions with additional ruthenium reductants, including $\text{Ru}^{\text{II}}(\text{NH}_3)_5(\text{py})^{2+}$, $\text{Ru}^{\text{II}}(\text{en})_3^{2+}$, $\text{Ru}^{\text{II}}(\text{NH}_3)_5(\text{isn})^{2+}$, and $\text{Ru}(\text{NH}_3)_5(\text{methyl nicotinate})^{2+}$, were thwarted by the fact that the reaction rates were so fast that they could not be resolved by the stopped-flow technique.

Allan, Lappin, and Laranjeira¹²⁴ reported evidence that, at higher pH values, the coordinated water in $\text{Cu}^{\text{II}}(\text{dpsmp})_2(\text{H}_2\text{O})^{2+}$ ionizes to produce the corresponding hydroxide for which they resolved a $\text{p}K_{\text{a}}$ value of 8.27. These investigators conducted a variable pH study of the reaction with $\text{Fe}^{\text{II}}(\text{CN})_6^{4-}$, in which the concentration of the latter reagent was from 2 to 200 times larger than that used in the earlier study by Al-Shatti et al. Allan et al. reported that they resolved their data to yield two limiting first-order rate constants of 334 and 26 s^{-1} , representing the species with axial H_2O and OH^- , respectively. They interpreted these latter values to represent the rate constants for loss of a coordinated water or hydroxide ion from these two species. However, these values appear to be too small to represent simple solvent loss from $\text{Cu}(\text{II})$. These investigators also carried out oxidation studies on $\text{Cu}^{\text{I}}(\text{dpsmp})_2$ using a $\text{Ni}(\text{IV})$ oxime imine complex as the counterreagent. The kinetic data were complex, and the apparent self-exchange rate constant obtained for this $\text{Cu}(\text{II}/\text{I})$ system of $5 \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$ is outside the range found by any other investigators on similar systems.

An independent NMR line-broadening study by Juntunen¹²⁵ on $\text{Cu}^{\text{II}}(\text{dpsmp})_2$ yielded $k_{11(\text{NMR})} \approx 5 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$. Holwerda obtained a similar $k_{11(\text{Red})}$ for the $\text{Cu}^{\text{II}}(\text{dpsmp})_2$ system using hydroquinone as the counterreagent.⁹⁹ The much smaller $k_{11(\text{Red})}$ value obtained by Leupin, Al-Shatti, and Sykes¹²³ when using $\text{Ru}^{\text{II}}(\text{NH}_3)_5\text{py}^{2+}$ as the reductant, $k_{11(\text{Red})} = 10 \text{ M}^{-1} \text{ s}^{-1}$, indicates that the latter reaction has switched to pathway A. This observation provides further support for the conclusion that their limiting first-

order kinetics for reduction by other counterreagents were conformationally limited.

Recently, Takagi and co-workers^{126–128} have studied a system in which two phenanthroline ligands are bridged by an ethylene group substituted at the 2,2' positions to generate a quadridentate ligand, which they have designated as diphen. The electron-transfer chemistry in acetonitrile was complicated by the fact that the reduced complex dimerizes to produce a $\text{Cu}_2\text{L}_2^{2+}$ species. A dicopper(II) intermediate with a high-energy tetrahedral coordination geometry was identified both spectrophotometrically and electrochemically as it was slow to convert to the monomer following $\text{Cu}^{\text{II}}\text{L}_2^{2+}$ oxidation. No successful measurements on the reduction kinetics of $\text{Cu}^{\text{II}}\text{L}_2^{2+}$ were reported. The reaction is gated, but since this process appears to involve a dimerization process, it is outside the realm of the conformational changes that are presumed to occur in the other systems discussed in this review.

5.5. Thiaether Complexes

Thiaether sulfur donor atoms have been the focus of specific interest in Cu(II/I) studies ever since the parallels between the spectral and electrochemical properties of thiaether ligand complexes and the blue copper proteins were first noted.^{129,130} Relative to the polypyridyl ligand systems, the polythiaether complexes (Figures 9 and 10) exhibit even higher $\text{Cu}^{\text{II/I}}$ potentials, which facilitate the study of their redox chemistry. As noted earlier (Figure 3), the high Cu(II/I) potentials of these complexes are attributable to the destabilization of the $\text{Cu}^{\text{II}}\text{L}$ species relative to saturated amine complexes³¹ rather than to a stabilization of the $\text{Cu}^{\text{I}}\text{L}$ species as has been frequently assumed.

The first report on the electron-transfer kinetics of a Cu(II/I) system involving thiaether sulfur donor atoms appeared in a 1981 paper by Augustin, Yandell, Addison, and Karlin.¹⁰⁷ This study included a single reduction of the macrocyclic tetrathiaether [14]aneS₄ (which they had obtained from our laboratory) with cytochrome-*c*^{II}. Our own studies on this and related macrocyclic polythiaether ligands had been conducted earlier,¹³¹ but since we had carried out both reduction and oxidation studies, which did not agree in terms of the resolved k_{11} values, our results were not published until 1983⁴⁴ and the definitive interpretation did not appear until 1987 when it was first proposed that all of these copper complexes might be undergoing electron transfer via Scheme 1.¹³²

In our original studies, both the $\text{Cu}^{\text{II}}\text{L}$ reduction and $\text{Cu}^{\text{I}}\text{L}$ oxidation kinetics were investigated for a series of complexes with cyclic tetrathiaethers ranging in ring size from 12 through 16 with two related acyclic ligands also included. For the $\text{Cu}^{\text{II/I}}([14]\text{aneS}_4)$ system, the corresponding $k_{11(\text{Red})}$ and $k_{11(\text{Ox})}$ values were 1.6×10^3 and $2.2 \text{ M}^{-1} \text{ s}^{-1}$, respectively, and all but one of these systems yielded $k_{11(\text{Ox})}$ values that were smaller than the corresponding $k_{11(\text{Red})}$ values by 3–7 orders of magnitude.¹³²

To corroborate the existence of Scheme 1 for the macrocyclic polythiaether complexes, Bernardo⁴⁹ in-

vestigated the cyclic voltammetric (CV) behavior of these systems as a function of sweep rate and temperature in 80% methanol–20% water (by weight), a solvent mixture that permitted the solution temperature to be lowered to -77°C . For slow scan rates at ambient temperature, completely reversible CVs were observed with the cathodic and anodic peaks representing equilibrated oxidant and reductant species. However, as the scan rate was increased or the temperature lowered, a separate anodic peak emerged at higher potentials, which was attributed to the oxidation of the stable $\text{Cu}^{\text{I}}\text{L}(\mathbf{R})$, which was no longer equilibrated with $\text{Cu}^{\text{I}}\text{L}(\mathbf{P})$, directly to $\text{Cu}^{\text{II}}\text{L}(\mathbf{Q})$. For solutions originally containing only the oxidized species, the use of extremely low temperatures showed that the $\text{Cu}^{\text{I}}\text{L}(\mathbf{R})$ anodic peak ultimately disappeared and a new anodic peak emerged at lower potential. This latter peak was attributed to un-equilibrated $\text{Cu}^{\text{I}}\text{L}(\mathbf{P})$, which, having been generated from $\text{Cu}^{\text{II}}\text{L}(\mathbf{O})$ reduction during the cathodic sweep, had not had time to convert to $\text{Cu}^{\text{I}}\text{L}(\mathbf{R})$ prior to the return anodic sweep. Although only a slight indication of the $\text{Cu}^{\text{II}}\text{L}(\mathbf{Q})$ intermediate was observed in this CV study, computer simulation of the overall CV behavior made it possible to estimate all of the rate constants in Scheme 1 for the system involving $\text{Cu}^{\text{II/I}}([14]\text{aneS}_4)$.^{49,50}

More extensive kinetic measurements were subsequently conducted on the 13-, 14-, and 15-membered ring tetrathiaethers and two dialcohol derivatives of [14]aneS₄.^{56,133,134} The electron-transfer kinetics for each of these five systems were measured with a total of four reductants and four oxidants, and independent k_{11} values were also obtained from NMR line broadening measurements.^{56,133,134} In all five systems, the calculated $k_{11(\text{Red})}$ values were in close agreement with the corresponding values obtained by NMR (Table 7). This observation was in sharp contrast to the original suggestion by Lee and Anson³⁹ that the k_{11} value for Cu(II/I) systems, as determined directly without invoking eq 14, should be the geometric mean of $k_{11(\text{Red})}$ and $k_{11(\text{Ox})}$ (see section 4.3). As confirmation of the hypothesis that these complexes conform to Scheme 1 with pathway A as the preferred reaction path, the cross-reaction kinetics for $\text{Cu}^{\text{I}}\text{L}$ oxidation produced $k_{11(\text{Ox})}$ values similar to those obtained from the reduction and NMR measurements *when the driving force of the reaction was small* (i.e., when the oxidation reaction was slow). However, as the driving force was increased (by increasing the potential or the self-exchange rate constant of the counterreagent), all five systems exhibited second-order kinetics with calculated $k_{11(\text{Ox})}$ values that were 2 or more orders of magnitude smaller than $k_{11(\text{NMR})}$. This last behavior was interpreted to represent a switch to the alternate pathway (pathway B) according to eq 20b. For three of these systems, it was also observed that with one specific oxidizing reagent, $\text{Ni}^{\text{III}}([14]\text{aneN}_4)^{3+}$, the reaction kinetics changed from second- to first-order as the counterreagent concentration was increased within a specific range, demonstrating the onset of gated kinetics; and further increases in $\text{Ni}^{\text{III}}([14]\text{aneN}_4)$ concentration resulted in a return to

Table 7. Electron-Transfer Rate Constants for Polythiaether Complexes with Copper(II/I) in Aqueous and Acetonitrile Solution at 25 °C

oxidant	reductant	solvent	$\log k_{12}$ ($M^{-1} s^{-1}$)	$\log k_{11}$ ($M^{-1} s^{-1}$)	ref
Acyclic Polythiaethers					
2,5,9,12-Tetrathiatridecane:					
$Cu^{II}(Me_2-2,3,2-S_4)$ [$E^{\circ'} = 0.89$ V]					
$Cu^{II}L^{2+}$	$Co^{II}(bpy)_3^{2+}$	A ^a	5.28	2.3	141
$Cu^{II}L^{2+}$	$Ru^{II}(NH_3)_4bpy^{2+}$	A ^a	5.71	0.8	141
$Cu^{II}L^{2+}$	$Ru^{II}(NH_3)_5isn^{2+}$	A ^a	5.3, 5.5, 5.6	1.3, 1.7, 2.0	141
$Cu^{II}L^{2+}$	$Ru^{II}(NH_3)_4py^{2+}$	A ^a	6.40	0.7	141
$Cu^{II}L^{2+}$	$Co^{II}(TIM)$	A	3.69	5.23 (?)	132
$Ni^{III}([14]aneN_4)^{3+}$	Cu^IL^+	A	2.76	-0.4	141
$Ru^{III}(NH_3)_2(bpy)_2^{3+}$	Cu^IL^+	A	4.60	-0.4	141
$Fe^{III}(4,7-Me_2phen)_3^{3+}$	Cu^IL^+	A	5.90	0.9	141
$Fe^{III}(4,7-Me_2phen)_3^{3+}$	Cu^IL^+	A	4.67	-1.19	132
3,6,10,13-Tetrathiapentadecane:					
$Cu^{II}(Et_2-2,3,2-S_4)$ [$E^{\circ'} = 0.89$ V]					
$Cu^{II}L^{2+}$	$Co^{II}(TIM)$	A	3.41	4.66 (?)	132
$Fe^{III}(4,7-Me_2phen)_3^{3+}$	Cu^IL^+	A	4.50	-1.53	132
$Fe^{III}(bpy)_3^{3+}$	Cu^IL^+	A	4.79	-3.40	132
$Fe^{III}(phen)_3^{3+}$	Cu^IL^+	A	6.0	-1.82	132
$Ru^{III}(NH_3)_4bpy^{3+}$	Cu^IL^+	A	>8	??	132
2,6,9,13-Tetrathiatetradecane:					
$Cu^{II}(Me_2-3,2,3-S_4)$ [$E^{\circ'} = 0.83$ V]					
$Cu^{II}L^{2+}$	$Co^{II}(phen)_3^{2+}$	A ^a	4.34	0.77	141
$Cu^{II}L^{2+}$	$Co^{II}(bpy)_3^{2+}$	A ^a	4.73	1.25	141
$Cu^{II}L^{2+}$	$Ru^{II}(NH_3)_4bpy^{2+}$	A ^a	6.18	1.24	141
$Cu^{II}L^{2+}$	$Ru^{II}(NH_3)_5isn^{2+}$	A ^a	6.36	0.75	141
$Ni^{III}([14]aneN_4)^{3+}$	Cu^IL^+	A	3.79	2.33	141
$Ru^{III}(NH_3)_2(bpy)_2^{3+}$	Cu^IL^+	A	4.51	2.07	141
$Fe^{III}(4,7-Me_2phen)_3^{3+}$	Cu^IL^+	A	6.18	2.04	141
7,8- <i>cis</i> -Cyclohexano-2,6,9,13-tetrathiatetradecane:					
$Cu^{II}(cis-cyhx-Me_2-3,2,3-S_4)$ [$E^{\circ'} = 0.75$ V]					
$Cu^{II}L^{2+}$	$Co^{II}(bpy)_3^{2+}$	A	4.71	1.58	141
$Cu^{II}L^{2+}$	$Ru^{II}(NH_3)_4bpy^{2+}$	A	5.51	0.96	141
$Cu^{II}L^{2+}$	$Ru^{II}(NH_3)_5isn^{2+}$	A	5.90	0.97	141
$Ni^{III}([14]aneN_4)^{3+}$	Cu^IL^+	A	4.00	1.51	141
$Ru^{III}(NH_3)_2(bpy)_2^{3+}$	Cu^IL^+	A	5.60	1.04	141
$Fe^{III}(4,7-Me_2phen)_3$	Cu^IL^+	A	6.40	1.32	141
7,8- <i>trans</i> -Cyclohexano-2,6,9,13-tetrathiatetradecane:					
$Cu^{II}(trans-cyhx-Me_2-3,2,3-S_4)$ [$E^{\circ'} = 0.77$ V]					
$Cu^{II}L^{2+}$	$Co^{II}(bpy)_3^{2+}$	A	4.56	1.01	141
$Cu^{II}L^{2+}$	$Ru^{II}(NH_3)_4bpy^{2+}$	A	5.63	0.93	141
$Cu^{II}L^{2+}$	$Ru^{II}(NH_3)_5isn^{2+}$	A	6.04	1.04	141
$Ni^{III}([14]aneN_4)^{3+}$	Cu^IL^+	A	3.76	1.32	141
$Ru^{III}(NH_3)_2(bpy)_2^{3+}$	Cu^IL^+	A	5.41	0.80	141
$Fe^{III}(4,7-Me_2phen)_3$	Cu^IL^+	A	6.20	1.22	141
Macrocyclic Polythiaethers					
1,4,7,10-Tetrathiacyclododecane:					
$Cu^{II}([12]aneS_4)$ [$E^{\circ'} \approx 0.64$ V]					
$Cu^{II}L^{2+}$	$Co^{II}(TIM)$	A	2.38	5.6	132
$Fe^{III}(4,7-Me_2phen)_3^{3+}$	Cu^IL^+	A	5.08	-2.0	132
1,4,7,10-Tetrathiacyclotridecane:					
$Cu^{II}([13]aneS_4)$ [$E^{\circ'} = 0.52$ V]					
$Cu^{II}L^{2+/+}$		A		5.51	133
$Cu^{II}L^{2+}$	$Co^{II}(TIM)^{2+}$	A	1.70	5.59	132
$Cu^{II}L^{2+}$	$Ru^{II}(NH_3)_4bpy^{2+}$	A	7.26	5.87	133
$Cu^{II}L^{2+}$	$Ru^{II}(NH_3)_5py^{2+}$	A	7.45	5.98	133
$Cu^{II}L^{2+}$	$Ru^{II}(NH_3)_6^{2+}$	A	8.1	5.3	133
$Co^{III}(TIM)^{3+}$	Cu^IL^+	A	1.74	5.52	133
$Ru^{III}(NH_3)_4bpy^{3+}$	Cu^IL^+	A	5.41	4.87	133
$Ni^{III}([14]aneN_4)^{3+}$	Cu^IL^+	A	6.69	4.32	133
$Ru^{III}(NH_3)_2(bpy)_2^{3+}$	Cu^IL^+	A	7.36	1.90	133
$Fe^{III}(4,7-Me_2phen)_3^{3+}$	Cu^IL^+	A	>8	>0.3	133
$Fe^{III}(4,7-Me_2phen)_3^{3+}$	Cu^IL^+	A	6.26	-2.0	132
1,4,8,11-Tetrathiacyclotetradecane:					
$Cu^{II}([14]aneS_4-a)$ [$E^{\circ'} = 0.59$ V]					
$Cu^{II}L^{2+/+}$		A		3.88	56
$Cu^{II}L^{2+}$	$Co^{II}(TIM)^{2+}$	A	0.88	3.41	132
$Cu^{II}L^{2+}$	$Ru^{II}(NH_3)_4bpy^{2+}$	A	5.68	3.79	132

Table 7 (Continued)

oxidant	reductant	solvent	$\log k_{12}$ ($M^{-1} s^{-1}$)	$\log k_{11}$ ($M^{-1} s^{-1}$)	ref
Macrocyclic Polythiaethers					
1,4,8,11-Tetrathiacyclotetradecane:					
Cu ^{III} ([14]aneS ₄ -a) [$E^{\circ'} = 0.59$ V]					
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ isn ²⁺	A	6.28	4.00	56
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ py ²⁺	A	6.65	3.89	56
Cu ^{II} L ²⁺	cyt- <i>c</i> (II)	A	6.38	4.88 ^b	107
Ru ^{III} (NH ₃) ₄ bpy ³⁺	Cu ^I L ⁺	A	4.99	2.58	56
Ni ^{III} ([14]aneN ₄) ³⁺	Cu ^I L ⁺	A	5.65 (mixed)	2.45	56
Ru ^{III} (NH ₃) ₂ (bpy) ₂ ³⁺	Cu ^I L ⁺	A	6.3	0.1	56
Fe ^{III} (4,7-Me ₂ phen) ₃ ³⁺	Cu ^I L ⁺	A	6.72	-0.38	56
Fe ^{III} (4,7-Me ₂ phen) ₃ ³⁺	Cu ^I L ⁺	A	6.90	0.0	132
Cu ^{II} L ²⁺	Co ^{II} (bpy) ₃ ²⁺	B	3.76	3.24	114
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₄ bpy ²⁺	B	5.43	3.55	114
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ isn ²⁺	B	6.41	3.53	114
Mn ^{III} (bpyO ₂) ₃ ⁺	Cu ^I L ⁺	B	4.62	3.23	114
Ni ^{III} ([14]aneN ₄) ³⁺	Cu ^I L ⁺	B	5.2, 5.1	0.6, 0.3	114
Fe ^{III} (4,7-Me ₂ phen) ₃ ³⁺	Cu ^I L ⁺	B	5.8, 6.0	-1.0, -0.5	114
Fe ^{III} (bpy) ₃ ³⁺	Cu ^I L ⁺	B	6.34	-0.7	114
1,4,7,11-Tetrathiacyclotetradecane:					
Cu ^{III} ([14]aneS ₄ -b) [$E^{\circ'} = 0.69$ V]					
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₄ bpy ²⁺	A	5.73	2.2	152
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ isn ²⁺	A	6.70	2.9	152
Ni ^{III} ([14]aneN ₄) ³⁺	Cu ^I L ⁺	A	5.7	3.0	152
Ru ^{III} (NH ₃) ₂ (bpy) ₂ ³⁺	Cu ^I L ⁺	A	7.7	3.1-4.9	152
1,4,8,12-Tetrathiacyclopentadecane:					
Cu ^{III} ([15]aneS ₄) [$E^{\circ'} = 0.64$ V]					
Cu ^{II} L ^{2+/+}		A		4.08	133
Cu ^{II} L ²⁺	Co ^{II} (TIM) ²⁺	A	2.34	3.70	133
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₄ bpy ²⁺	A	6.08	3.70	133
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ py ²⁺	A	6.08	4.00	133
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₆ ²⁺	A	7.52	3.11	133
Co ^{III} (TIM) ³⁺	Cu ^I L ⁺	A	0.15	3.76	132
Ru ^{III} (NH ₃) ₄ bpy ³⁺	Cu ^I L ⁺	A	3.89	3.26	133
Ni ^{III} ([14]aneN ₄) ³⁺	Cu ^I L ⁺	A	5.06	2.00	133
Ru ^{III} (NH ₃) ₂ (bpy) ₂ ³⁺	Cu ^I L ⁺	A	6.92	2.08	133
Fe ^{III} (4,7-Me ₂ phen) ₃ ³⁺	Cu ^I L ⁺	A	7.65	2.34	133
Fe ^{III} (4,7-Me ₂ phen) ₃ ³⁺	Cu ^I L ⁺	A	7.18	1.15	132
1,5,9,13-Tetrathiacyclohexadecane:					
Cu ^{III} ([16]aneS ₄) [$E^{\circ'} = 0.71$ V]					
Cu ^{II} L ²⁺	Co ^{II} (TIM) ²⁺	A	1.72	3.57	132
Fe ^{III} (4,7-Me ₂ phen) ₃ ³⁺	Cu ^I L ⁺	A	6.40	1.30	132
1,4,7,10,13-Pentathiacyclopentadecane:					
Cu ^{III} ([15]aneS ₅) [$E^{\circ'} = 0.69$ V]					
Cu ^{II} L ^{2+/+}		A		5.3	168
Cu ^{II} L ²⁺	Co ^{II} (TIM) ²⁺	A	2.77	5.54	132
Fe ^{III} (4,7-Me ₂ phen) ₃ ³⁺	Cu ^I L ⁺	A	6.66	3.87	132
Substituted Macrocyclic Polythiaethers					
<i>syn</i> -3,6,10,13-Tetrathiacyclotetradecane-1,8-diol:					
Cu ^{III} (<i>syn</i> -[14]aneS ₄ -diol) [$E^{\circ'} = 0.54$ V]					
Cu ^{II} L ^{2+/+}		A		3.40	134
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₄ bpy ²⁺	A	5.13	3.51	134
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₄ phen ²⁺	A	5.32	3.59	134
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ isn ²⁺	A	5.82	3.89	134
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ py ²⁺	A	6.23	3.72	134
Ru ^{III} (NH ₃) ₄ bpy ³⁺	Cu ^I L ⁺	A	4.28	2.04 (mixed)	134
Ni ^{III} ([14]aneN ₄) ³⁺	Cu ^I L ⁺	A	5.92 (mixed)	2.63	134
Ru ^{III} (NH ₃) ₂ (bpy) ₂ ³⁺	Cu ^I L ⁺	A	6.63	-0.15	134
Fe ^{III} (4,7-Me ₂ phen) ₃ ³⁺	Cu ^I L ⁺	A	7.08	-0.22	134
<i>anti</i> -3,6,10,13-Tetrathiacyclotetradecane-1,8-diol:					
Cu ^{III} (<i>anti</i> -[14]aneS ₄ -diol) [$E^{\circ'} = 0.49$ V]					
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₄ bpy ²⁺	A	5.18	4.23	134
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₄ phen ²⁺	A	5.11	4.08	134
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ isn ²⁺	A	5.72	4.43	134
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ py ²⁺	A	6.20	4.40	134
Ru ^{III} (NH ₃) ₄ bpy ³⁺	Cu ^I L ⁺	A	4.91	2.68	134
Ni ^{III} ([14]aneN ₄) ³⁺	Cu ^I L ⁺	A	6.23	2.54	134
Ru ^{III} (NH ₃) ₂ (bpy) ₂ ³⁺	Cu ^I L ⁺	A	6.26	-1.77	134
Fe ^{III} (4,7-Me ₂ phen) ₃ ³⁺	Cu ^I L ⁺	A	7.68	-1.85	134

Table 7 (Continued)

oxidant	reductant	solvent	$\log k_{12}$ ($M^{-1} s^{-1}$)	$\log k_{11}$ ($M^{-1} s^{-1}$)	ref
Substituted Macrocyclic Polythiaethers					
2,3- <i>cis</i> -Cyclohexanediyl-1,4,8,11-tetrathiacyclotetradecane: Cu ^{III} (<i>cis</i> -cyhx-[14]aneS ₄) [$E^{\circ\prime} = 0.54$ V]					
Cu ^{II/I} L ^{2+/+}		A		4.70	136
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₄ phen ²⁺	A	5.6	4.3	136
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ isn ²⁺	A	6.0	4.3	136
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ py ²⁺	A	6.5	4.0	136
Cu ^{II} L ²⁺	Co ^{II} (bpy) ₃ ²⁺	A	4.3	4.8	136
Ru ^{III} (NH ₃) ₄ bpy ³⁺	Cu ^I L ⁺	A	4.3	2.3	136
Ni ^{III} ([14]aneN ₄) ³⁺	Cu ^I L ⁺	A	6.3 (lim)	3.3 (lim)	136
Ru ^{III} (NH ₃) ₂ (bpy) ₂ ³⁺	Cu ^I L ⁺	A	6.4	-0.5	136
Fe ^{III} (4,7-Me ₂ phen) ₃ ³⁺	Cu ^I L ⁺	A	6.9	-0.7	136
2,3- <i>trans</i> -Cyclohexanediyl-1,4,8,11-tetrathiacyclotetradecane: Cu ^{III} (<i>trans</i> -cyhx-[14]aneS ₄) [$E^{\circ\prime} = 0.60$ V]					
Cu ^{II/I} L ^{2+/+}		A		≤3	136
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₄ bpy ²⁺	A	5.46	3.3	136
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₄ phen ²⁺	A	5.6	3.3	136
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ isn ²⁺	A	6.0	3.3	136
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ py ²⁺	A	6.3	2.8	136
Cu ^{II} L ²⁺	Co ^{II} (bpy) ₃ ²⁺	A	2.7	3.0	136
Ru ^{III} (NH ₃) ₄ bpy ³⁺	Cu ^I L ⁺	A	4.6	4.0	136
Ni ^{III} ([14]aneN ₄) ³⁺	Cu ^I L ⁺	A	5.8 (lim)	3.0	136
Ru ^{III} (NH ₃) ₂ (bpy) ₂ ³⁺	Cu ^I L ⁺	A	5.3	-2.0	136
Fe ^{III} (4,7-Me ₂ phen) ₃ ³⁺	Cu ^I L ⁺	A	5.7	-2.4	136
<i>syn</i> -2,3,9,10- <i>cis,cis</i> -Dicyclohexanediyl-1,4,8,11-tetrathiacyclotetradecane: Cu ^{III} (<i>syn-cis,cis</i> -dicyhx-[14]aneS ₄) [$E^{\circ\prime} = 0.57$ V]					
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₄ bpy ²⁺	A	4.95	4.0	137
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ isn ²⁺	A	5.75	3.7	137
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ py	A	6.00	4.0	137
Ru ^{III} (NH ₃) ₄ bpy ³⁺	Cu ^I L ⁺	A	5.48	3.9	137
Ni ^{III} ([14]aneN ₄) ³⁺	Cu ^I L ⁺	A	6.15	2.2	137
Ru ^{III} (NH ₃) ₂ (bpy) ₂ ³⁺	Cu ^I L ⁺	A	7.3	0.9	137
<i>anti</i> -2,3,9,10- <i>cis,cis</i> -Dicyclohexanediyl-1,4,8,11-tetrathiacyclotetradecane: Cu ^{III} (<i>anti-cis,cis</i> -dicyhx-[14]aneS ₄) [$E^{\circ\prime} = 0.67$ V]					
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₄ bpy ²⁺	A	4.58	1.9	137
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ isn ²⁺	A	5.38	1.9	137
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ py	A	5.66	2.2	137
Ru ^{III} (NH ₃) ₄ bpy ³⁺	Cu ^I L ⁺	A	4.30	2.8	137
Ni ^{III} ([14]aneN ₄) ³⁺	Cu ^I L ⁺	A	6.11	3.2	137
Ru ^{III} (NH ₃) ₂ (bpy) ₂ ³⁺	Cu ^I L ⁺	A	7.7	2.7	137
<i>meso</i> -2,3,9,10- <i>trans,trans</i> -Dicyclohexanediyl-1,4,8,11-tetrathiacyclotetradecane: Cu ^{III} (<i>meso-trans,trans</i> -dicyhx-[14]aneS ₄) [$E^{\circ\prime} = 0.58$ V]					
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₄ bpy ²⁺	A	4.26	2.1	137
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ isn ²⁺	A	5.26	2.0	137
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ py ²⁺	A	5.38	2.3	137
Ru ^{III} (NH ₃) ₄ bpy ³⁺	Cu ^I L ⁺	A	4.48	2.3	137
Ni ^{III} ([14]aneN ₄) ³⁺	Cu ^I L ⁺	A	5.04	2.3 (A)	137
Ru ^{III} (NH ₃) ₂ (bpy) ₂ ³⁺	Cu ^I L ⁺	A	6.23	-0.32 (B)	137
				-1.1	137
<i>dl</i> -2,3,9,10- <i>trans,trans</i> -Dicyclohexanediyl-1,4,8,11-tetrathiacyclotetradecane: Cu ^{III} (<i>dl-trans,trans</i> -dicyhx-[14]aneS ₄) [$E^{\circ\prime} = 0.69$ V]					
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₄ bpy ²⁺	A	5.49	2.6	137
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ isn ²⁺	A	5.94	2.0	137
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ py ²⁺	A	6.36	2.6	137
Ni ^{III} ([14]aneN ₄) ³⁺	Cu ^I L ⁺	A	3.8	3.0	137
Ru ^{III} (NH ₃) ₂ (bpy) ₂ ³⁺	Cu ^I L ⁺	A	5.7	3.3	137
Fe ^{III} (4,7-Me ₂ phen) ₃ ³⁺	Cu ^I L ⁺	A	7.6	3.5	137
2,3- <i>cis</i> -9,10- <i>trans</i> -Dicyclohexanediyl-1,4,8,11-tetrathiacyclotetradecane: Cu ^{III} (<i>cis,trans</i> -dicyhx-[14]aneS ₄) [$E^{\circ\prime} = 0.60$ V]					
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₄ bpy ²⁺	A	4.84	2.6	137
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ isn ²⁺	A	5.71	2.7	137
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ py ²⁺	A	5.00	3.0	137
Ru ^{III} (NH ₃) ₄ bpy ²⁺	Cu ^I L ⁺	A	4.41	2.8	137
Ni ^{III} ([14]aneN ₄) ³⁺	Cu ^I L ⁺	A	6.08	3.3	137
Ru ^{III} (NH ₃) ₂ (bpy) ₂ ³⁺	Cu ^I L ⁺	A	7.6	2.4	137

Table 7 (Continued)

oxidant	reductant	solvent	$\log k_{12}$ ($M^{-1} s^{-1}$)	$\log k_{11}$ ($M^{-1} s^{-1}$)	ref
Substituted Macrocyclic Polythiaethers					
2,3- <i>cis</i> -Cyclopentanediy-1,4,8,11-tetrathiacyclotetradecane: Cu ^{III} (<i>cis</i> -cypt-[14]aneS ₄) [$E^{\circ'} = 0.56$ V]					
Cu ^{II} L ^{2+/+}		A		4.7	135
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₄ bpy ²⁺	A	5.60	4.1	135
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ isn ²⁺	A	6.18	4.5	135
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ py ²⁺	A	6.57	4.2	135
Ru ^{III} (NH ₃) ₄ bpy ³⁺	Cu ^I L ⁺	A	5.38	3.7	135
Ni ^{III} ([14]aneN ₄) ³⁺	Cu ^I L ⁺	A	6.34	2.9	135
Ru ^{III} (NH ₃) ₂ (bpy) ₂ ³⁺	Cu ^I L ⁺	A	7.8	2.8	135
$k_{RP} < 2 \times 10^2 s^{-1}$					
2,3- <i>trans</i> -Cyclopentanediy-1,4,8,11-tetrathiacyclotetradecane: Cu ^{III} (<i>trans</i> -cypt-[14]aneS ₄) [$E^{\circ'} = 0.67$ V]					
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₄ bpy ²⁺	A	5.74	2.7	135
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₄ phen ²⁺	A	5.91	3.1	135
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ isn ²⁺	A	6.38	3.3	135
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ py ²⁺	A	6.76	3.1	135
Ni ^{III} ([14]aneN ₄) ³⁺	Cu ^I L ⁺	A	5.38	2.3 [A], 0.9 [B]	135
Ru ^{III} (NH ₃) ₂ (bpy) ₂ ³⁺	Cu ^I L ⁺	A	6.00	0.6	135
Fe ^{III} (4,7-Me ₂ phen) ₃ ³⁺	Cu ^I L ⁺	A	6.76	0.9	135
$k_{RP} = 1.3 \times 10^2 s^{-1}$					
<i>syn</i> -2,3,9,10- <i>cis</i> , <i>cis</i> -Dicyclopentanediy-1,4,8,11-tetrathiacyclotetradecane: Cu ^{III} (<i>syn-cis,cis</i> -dicypt-[14]aneS ₄) [$E^{\circ'} = 0.57$ V]					
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₄ bpy ²⁺	A	5.62	4.0	138
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₄ phen ²⁺	A	5.96	4.4	138
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ isn ²⁺	A	5.85	3.7	138
Ni ^{III} ([14]aneN ₄) ³⁺	Cu ^I L ⁺	A	gated	$k_{RP} = 0.4$	138
Ru ^{III} (NH ₃) ₂ (bpy) ₂ ³⁺	Cu ^I L ⁺	A	gated	$k_{RP} = 0.1$	138
Fe ^{III} (4,7-Me ₂ phen) ₃ ³⁺	Cu ^I L ⁺	A	3.90	-6.47 (?)	138
<i>anti</i> -2,3,9,10- <i>cis</i> , <i>cis</i> -Dicyclopentanediy-1,4,8,11-tetrathiacyclotetradecane: Cu ^{III} (<i>syn-cis,cis</i> -dicypt-[14]aneS ₄) [$E^{\circ'} = 0.28$ V vs ferrocene in CH ₃ CN)]					
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₄ bpy ²⁺	B	5.61	2.8	138
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ isn ²⁺	B	6.81	3.2	138
Ni ^{III} ([14]aneN ₄) ³⁺	Cu ^I L ⁺	B	5.51	2.2	138
Mn ^{III} (bpyO ₂) ₃ ³⁺	Cu ^I L ⁺	B	3.65	2.4	138
Fe ^{III} (4,7-Me ₂ phen) ₃ ³⁺	Cu ^I L ⁺	B	5.81	0.2	138
Fe ^{III} (bpy) ₃ ³⁺	Cu ^I L ⁺	B	6.26	0.2	138
<i>meso</i> -2,3,9,10- <i>trans,trans</i> -Dicyclopentanediy-1,4,8,11-tetrathiacyclotetradecane: Cu ^{III} (<i>meso-trans,trans</i> -dicypt-[14]aneS ₄) [$E^{\circ'} = 0.34$ V vs ferrocene in CH ₃ CN)]					
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₄ bpy ²⁺	B	4.6, 4.8	1.4, 1.8	138
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ isn ²⁺	B	5.96	2.0	138
Ni ^{III} ([14]aneN ₄) ³⁺	Cu ^I L ⁺	B	4.45	-0.6	138
Mn ^{III} (bpyO ₂) ₃ ³⁺	Cu ^I L ⁺	B	2.23	-1.2	138
Fe ^{III} (4,7-Me ₂ phen) ₃ ³⁺	Cu ^I L ⁺	B	5.28	-1.6	138
Fe ^{III} (bpy) ₃ ³⁺	Cu ^I L ⁺	B	4.82	-3.5	138
<i>dl</i> -2,3,9,10- <i>trans,trans</i> -Dicyclopentanediy-1,4,8,11-tetrathiacyclotetradecane: Cu ^{III} (<i>dl-trans,trans</i> -dicypt-[14]aneS ₄) [$E^{\circ'} = 0.39$ V vs ferrocene in CH ₃ CN)]					
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₄ bpy ²⁺	B	6.4	2.8	138
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₄ phen ²⁺	B	6.51	3.2	138
Ni ^{III} ([14]aneN ₄) ³⁺	Cu ^I L ⁺	B	3.78	0.2	138
Ni ^{III} ([9]aneN ₃) ₂ ³⁺	Cu ^I L ⁺	B	3.43	0.4	138
Fe ^{III} (4,7-Me ₂ phen) ₃ ³⁺	Cu ^I L ⁺	B	5.11	0.3	138
Fe ^{III} (bpy) ₃ ³⁺	Cu ^I L ⁺	B	5.41	-0.2	138
2,3- <i>cis</i> -9,10- <i>trans</i> -Dicyclopentanediy-1,4,8,11-tetrathiacyclotetradecane: Cu ^{III} (<i>cis,trans</i> -dicypt-[14]aneS ₄) [$E^{\circ'} = 0.63$ V]					
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₄ bpy ²⁺	A	6.05, 5.81	3.9, 3.4	138
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₄ phen ²⁺	A	6.38	3.7	138
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ isn ²⁺	A	5.81	3.3	138
Ni ^{III} ([14]aneN ₄) ³⁺	Cu ^I L ⁺	A	6.11	3.52	138
Ru ^{III} (NH ₃) ₂ (bpy) ₂ ³⁺	Cu ^I L ⁺	A	6.46, 6.70	1.0, 1.5	138
$k_{RP} = 1.4 \times 10^2 s^{-1}$					

^a $\mu = 0.20$. ^b Augustin et al. apparently used a higher potential for the Cu^{II}/L redox couple.

second-order behavior with the smaller calculated $k_{11(\text{Ox})}$ value characteristic of pathway B (eq 20c). All of this behavior is consistent with eq 20' in the following modified form:

$$k_{\text{obs}} = k_{21}[\text{A}_{\text{Ox}}] = \left(\frac{k_{2\text{A}}k_{\text{RP}}}{k_{2\text{A}}[\text{A}_{\text{Ox}}] + k_{\text{PR}}} + k_{2\text{B}} \right) [\text{A}_{\text{Ox}}] \quad (20'')$$

Under conditions where pathway B is not yet contributing to the reaction rate, eq 20'' reduces to

$$k_{\text{obs}} = k_{21}[\text{A}_{\text{Ox}}] = \left(\frac{k_{2\text{A}}k_{\text{RP}}}{k_{2\text{A}}[\text{A}_{\text{Ox}}] + k_{\text{PR}}} \right) [\text{A}_{\text{Ox}}] \quad (21)$$

which can be rearranged to the form

$$\frac{1}{k_{21}[\text{A}_{\text{Ox}}]} = \frac{1}{k_{\text{obs}}} = \frac{1}{K_{\text{RP}}k_{2\text{A}}[\text{A}_{\text{Ox}}]} + \frac{1}{k_{\text{RP}}} \quad (21')$$

or

$$\frac{1}{k_{21}} = \frac{[\text{A}_{\text{Ox}}]}{k_{\text{obs}}} = \frac{[\text{A}_{\text{Ox}}]}{k_{\text{RP}}} + \frac{1}{k_{2\text{A}}K_{\text{RP}}} \quad (21'')$$

Plots in the form of eq 21' or 21'' have been reported by various investigators, the latter yielding $K_{\text{RP}}k_{2\text{A}}$ ($\equiv k_{21(\text{A})}$) as the reciprocal intercept and k_{RP} as the reciprocal slope. Ultimately, the contribution of the $k_{2\text{B}}$ term ($\equiv k_{21(\text{B})}$) in eq 20'' should become increasingly important as the $k_{2\text{B}}[\text{A}_{\text{Ox}}]$ term increases. Of the five Cu(II/I) complex systems noted above, k_{RP} values of 50, 120, and 50 s^{-1} were reported for [14]aneS₄, *syn*-[14]aneS₄-diol, and *anti*-[14]aneS₄-diol, respectively, with limiting values of ≥ 200 and ≤ 5 s^{-1} for the complexes with [13]aneS₄ and [15]aneS₄, respectively.^{56,133,134} If all three terms in eq 20'' contribute to the reaction kinetics (i.e., second-order kinetics via pathway A, first-order kinetics due to rate-limiting conformational change, and second-order kinetics via pathway B) as the counterreagent concentration is varied, curve fitting can be used to resolve the individual values of $k_{21(\text{A})}$, $k_{21(\text{B})}$, and k_{RP} .¹³⁴ A prime example of such multifold behavior is illustrated in Figure 15 for the oxidation of Cu^I(*trans*-cypt-[14]aneS₄)⁺ by Ni^{III}([14]aneN₄)³⁺ for which the three limiting conditions overlap significantly as the oxidant concentration is varied.¹³⁵ The initial and final linear portions of this plot represent the limiting k_{21} values for pathways A and B, respectively, while the intermediate curved segment represents the onset of first-order "gated" electron-transfer mixing in with the second-order contribution. It is pertinent to note that both linear segments extrapolate through the origin.

More recently, rapid-scan CV measurements (up to 5 kV s^{-1}) were made by Villeneuve et al. on a series of substituted macrocyclic tetrathiaethers in which one or both of the ethylene bridges in [14]aneS₄ were replaced by *cis*- or *trans*-cyclohexane.⁵¹ The resulting seven ligands (*cis*- and *trans*-cyhx-[14]aneS₄ and *syn-cis,cis*-, *anti-cis,cis*-, *meso-trans,trans*-, *dl-trans,trans*-, and *cis,trans*-dicyhx-[14]aneS₄) exhibit different preferences for the orientations of the four

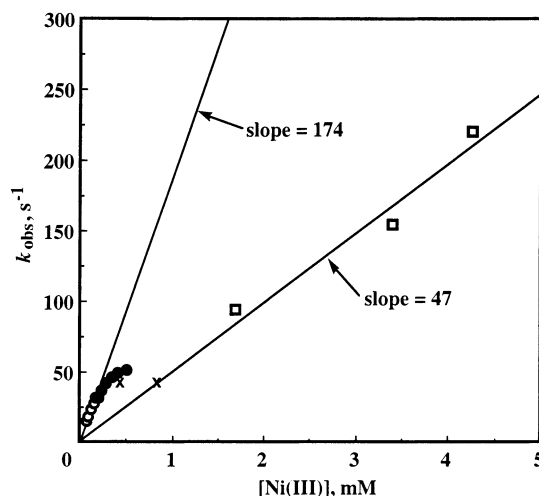


Figure 15. Plot of the observed pseudo-first-order rate constant for the oxidation of Cu^I(*trans*-cypt-[14]aneS₄)⁺ (see Figure 10 for ligand structure) by Ni^{III}([14]aneN₄)³⁺ as a function of the latter concentration. The initial slope yields $k_{21(\text{A})} = 174 \text{ M}^{-1} \text{ s}^{-1}$, the leveling off region yields $k_{\text{RP}} \approx 1 \times 10^2 \text{ s}^{-1}$, and the final slope yields $k_{21(\text{B})} = 47 \text{ M}^{-1} \text{ s}^{-1}$. Reprinted from ref 135. Copyright 2000 American Chemical Society.

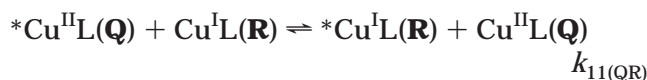
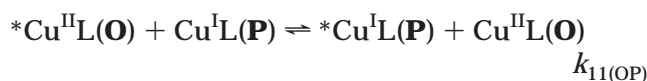
Table 8. Electron Self-Exchange Rate Constants for Pathways A and B and Specific Self-Exchange Rate Constants ($k_{11(\text{OP})}$ and $k_{11(\text{QR})}$) for the Metastable Intermediates Reacting with Their Stable Redox Partners for Eight Copper(II/I) Complexes with Closely Related Macrocyclic Tetrathiaethers in Aqueous Solution at 25 °C, $\mu = 0.10 \text{ M}$ [from Ref 137]

constant	complexed ligand ^a							
	L0	L2	L3	L7	L8	L9	L10	L11
log $k_{11(\text{A})}$	3.9	4.5	3.1	4.0	2.0	2.1	2.3	2.7
log $k_{11(\text{B})}$	0.0	1.0	1.0	0.9	2.8	-0.7	3.3	~0.2 ^b
log K_{RP}^c	-1.7	-1.7	-2.7	-1.2	-2.3	-1.6	-3.0	-2.2
log K_{OQ}^c	-4.4	-5.1	-3.7	-5.3	-4.1	-5.7	-2.8	-5.2
log $k_{11(\text{OP})}$	5.6	6.2	5.8	5.2	4.3 ^d	4.8	5.3	4.9
log $k_{11(\text{QR})}$	4.4	6.1	4.7	6.2	6.9 ^d	5.0	6.1	~5.3 ^b

^a L0 = [14]aneS₄; L2 = *cis*-cyhx-[14]aneS₄; L3 = *trans*-cyhx-[14]aneS₄; L7 = *syn-cis,cis*-dicyhx-[14]aneS₄; L8 = *anti-cis,cis*-dicyhx-[14]aneS₄; L9 = *meso-trans,trans*-dicyhx-[14]aneS₄; L10 = *dl-trans,trans*-dicyhx-[14]aneS₄; L11 = *cis,trans*-dicyhx-[14]aneS₄ (see Figure 10). ^b The log $k_{11(\text{B})}$ value listed is based on the limiting $k_{11(\text{Ox})}$ value obtained for Cu^I(L11) reacting with Fe^{III}(4,7-dmphe)₃ in acetonitrile (ref 140); this value, in turn, was used to calculate the value of log $k_{11(\text{QR})}$. ^c In ref 51, the values of K_{RP} and K_{OQ} were inadvertently listed with the incorrect sign on the exponents. ^d The extreme values obtained for log $k_{11(\text{OP})}$ and log $k_{11(\text{QR})}$ for Cu^{III}(L8) suggest the possibility of experimental error in one or more parameters.

sulfur donor atoms. These are reflected in the individual rate and equilibrium parameters for these systems as generated from the matching of computer simulations to a huge array of experimental CVs as shown in Table 8. Extensive cross-reaction kinetic studies were also made on these Cu(II/I) systems^{136,137} from which it became possible to calculate the self-exchange rate constants for each of the two pathways in Scheme 1, $k_{11(\text{A})}$ and $k_{11(\text{B})}$ (Table 8). The combination of these latter values with the equilibrium constants for the conformational changes, K_{OQ} (i.e., $k_{\text{OQ}}/k_{\text{QO}}$) and K_{RP} (i.e., $k_{\text{RP}}/k_{\text{PR}}$), as determined from the CV measurements,⁵¹ has permitted an estimation of the specific self-exchange rate constants repre-

sentative of the two stable oxidation states exchanging electrons directly with their metastable counterparts:¹³⁷



These latter values are included in Table 8. Whereas the overall self-exchange rate constants $k_{11(A)}$ and $k_{11(B)}$ for the two reaction pathways range over 5 orders of magnitude for this series of complexes, nearly all of the $k_{11(OP)}$ and $k_{11(QR)}$ rate constants fall within the narrow range of 10^5 – 10^6 $M^{-1} s^{-1}$,¹³⁷ the same range exhibited by many of the blue copper proteins. These results support the concept that, if ligands could be devised that “freeze” the Cu(II/I) coordination geometry to the approximate structures of the $Cu^I L(\mathbf{P})$ or $Cu^{II} L(\mathbf{Q})$ intermediates, exceptionally rapid electron transfer would be observed. On the other hand, ligands that are very flexible might be expected to exhibit small reorganizational energies and thereby promote large electron self-exchange rate constants. Neither concept has yet been extensively demonstrated.

A series of ligands parallel to those included in Table 8 has recently been generated in which the cyclohexane rings have been replaced by cyclopentane rings.^{135,138} Since cyclopentane is less flexible than cyclohexane, it was postulated that these more rigid systems might lead to more rapid electron transfer. Interestingly, the $k_{11(A)}$ values tend to parallel the values obtained with the corresponding cyclohexane derivatives, but the $k_{11(B)}$ values show several significant differences as shown in Table 7. Since independent data on the values of K_{OQ} and K_{RP} are not available for the cyclopentane-substituted systems, however, no detailed analysis of the origins of these differences has yet been made.

One of the most notable observations resulting from the kinetic studies on both the cyclohexane- and cyclopentane-substituted complexes is the fact that the ligands involving the *dl-trans,trans* derivatives appear to favor reaction pathway B over pathway A.^{137,138} This is particularly significant since the four sulfur donor atoms in these two derivatized ligands are not coplanar in the Cu(II) complexes but are skewed in the direction of a flattened tetrahedron. In fact, the crystal structure of the Cu(II) complex with the *dl-trans,trans*-cyp[14]aneS₄ complex¹³⁹ revealed that the ligand is in a rare conformation (designated as Conformer II) in which the lone pairs on three of the sulfur donor atoms are oriented on one side of the coordinated macrocycle while those on the fourth donor atom are oriented toward the opposite side. It has been speculated that this conformation must be an intermediate in all electron-transfer reactions with [14]aneS₄-type ligands,⁵¹ but this is the only system in which this conformation has been physically observed.

Dunn et al.¹⁴⁰ also studied three similar ligands in which a phenylene group replaced one ethylene

bridge in [14]aneS₄, the opposite two sulfurs being bridged by an ethylene, *cis*-cyclohexane, or *trans*-cyclohexane group. In all three systems, the $k_{11(A)}$ and $k_{11(B)}$ values were similar to those observed with the Cu(II/I) systems involving the singly derivatized *trans*-cyclohexane and *trans*-cyclopentane derivatives. In a separate study, Dunn et al.¹⁴¹ also studied the electron-transfer kinetics of four comparable noncyclic tetrathiaether complexes with Cu(II/I) in which the central bridging moiety was ethylene, propylene, *cis*-cyclohexane, or *trans*-cyclohexane (listed at the beginning of Table 7). The k_{11} values were surprisingly small (within the range of 10^{-2} to 10^2 $M^{-1} s^{-1}$) compared to the corresponding $Cu^{II/I}([14]aneS_4)$ values. Only the Me₂-2,3,2-S₄ ligand system provided any definitive evidence of two reaction pathways.

5.6. Mixed Donor Atom Complexes

5.6.1. Thiaether Sulfur–Imine Nitrogen Mixed Donor Ligand Systems

Since type 1 Cu sites in blue copper proteins are characterized by coordination of the copper to two unsaturated nitrogen donors (from histidine residues) and two sulfur donors (from cysteine and methionine), special attention has been given to ligands containing an N₂S₂ donor set (Figure 11). Xie, Wilson, and Stanbury¹⁴² have studied both the $Cu^{II}L$ reduction and $Cu^I L$ oxidation kinetics of the Cu(II/I) complex with bite (Figure 12), a 16-membered macrocyclic ligand containing two thiaether sulfurs and two imine nitrogens as donor atoms. These investigators also attempted to determine the k_{11} value directly from NMR line-broadening measurements.⁶ Since this system appears to form four-coordinate complexes with both Cu(II) and Cu(I) and is, therefore, considered to be coordination invariant, it is discussed in the next section. However, it is worth noting here that the electron self-exchange rate constant calculated from both reduction and oxidation reactions for this system is the smallest ever measured for a multidentate ligand system, being in the range of 0.01 – 0.07 $M^{-1} s^{-1}$.

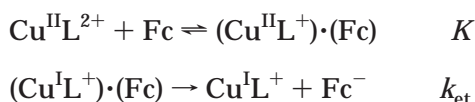
The acyclic ligand designated as pdto (Figure 11) also contains two thiaether sulfurs and two unsaturated nitrogens (from pyridines) as donor atoms. Brubaker and co-workers¹⁴³ determined the crystal structures of both the oxidized and reduced complexes and reported that the $[Cu^{II}(pdto)ClO_4]ClO_4$ complex is square pyramidal with the coordinated perchlorate anion in the axial position. The corresponding reduced complex, $[Cu^I(pdto)]PF_6$, is tetrahedral as expected. These authors suggested that a similar coordination change might occur in the type 1 sites of blue copper proteins (a hypothesis that is not supported by subsequent protein crystal structures). Davies and co-workers^{144–146} have studied the reduction kinetics of the $Cu^{II}(pdto)$ complex with multiple counterreagents in three different solvents. Additional reduction studies have been reported by Karlin and Yandell¹⁴⁷ and by Tanaka and co-workers.¹⁴⁸ The calculated $k_{11(Red)}$ values in aqueous solution and in acetonitrile are relatively small, being

within the range of $0.1\text{--}10\text{ M}^{-1}\text{ s}^{-1}$. The only known Cu^{II}L oxidation kinetic study involved a back reaction with Ru^{III}(NH₃)₄bpy³⁺.⁶⁶ The calculated aqueous self-exchange rate constant was $k_{11(\text{Ox})} = 0.3\text{ M}^{-1}\text{ s}^{-1}$, in line with the $k_{11(\text{Red})}$ values. Thus, no evidence has been observed for a dual-pathway mechanism.

Canthers and co-workers¹⁴⁹ have studied the Cu(II/I) complex with a related ligand, bidhp (Figure 11), in which the pyridine moieties have been replaced by methylimidazole. They determined the self-exchange rate constant by NMR line broadening in dimethyl sulfoxide and reported a value of $k_{11(\text{NMR})} = 4 \times 10^3\text{ M}^{-1}\text{ s}^{-1}$, 3 orders of magnitude larger than that for pdto. No other data involving this system are available for comparison.

In addition to their studies on the pdto system, Tanaka and co-workers¹⁴⁸ have reported electron-transfer kinetic studies in methanol on a closely related ligand in which the sulfur–pyridine linkages were decreased by one carbon (pmto, Figure 11), and a third correlated study involved the expansion of the bridge between the two sulfur donor atoms (pmpo, Figure 11). These investigators also reported electron-transfer kinetic studies on a similar ligand (bidto, Figure 11) involving terminal imidazole groups in place of the pyridines.¹⁵⁰ This latter ligand differs from Canthers' bidhp ligand only by (i) having an extra bridging carbon between the two sulfur donor atoms and (ii) lacking methyl groups on the imidazoles. Tanaka and co-workers have also studied several related bis-complexes in which each bidentate ligand contained one unsaturated nitrogen and a thiaether sulfur.^{148,150}

In most of the foregoing studies, Tanaka and co-workers observed that, in reduction of the Cu^{II}L or Cu^{II}L₂ complexes with excess ferrocene (or 1,2-dimethylferrocene) in either methanol or acetone, the observed pseudo-first-order rate constant curved off with increasing ferrocene concentration. In their original paper,¹⁵⁰ Tanaka and co-workers interpreted this behavior in terms of a mechanism in which the Cu^{II}L complex formed a strong equilibrated outer-sphere complex with the ferrocene reagent (characterized by the equilibrium constant, K) followed by electron-transfer as the rate-determining step, k_{et} :



On the basis of this model, these workers derived the following overall kinetic expression:

$$k_{\text{obs}} = \frac{Kk_{\text{et}}[\text{Fc}]}{1 + K[\text{Fc}]}$$

From a double reciprocal plot (k_{obs}^{-1} vs $[\text{Fc}]^{-1}$),

$$\frac{1}{k_{\text{obs}}} = \frac{1}{Kk_{\text{et}}[\text{Fc}]} + \frac{1}{k_{\text{et}}} \quad (22)$$

they assumed that the reciprocal intercept represented the rate constant for the electron-transfer step, k_{et} , and the reciprocal slope yielded Kk_{et} from which they calculated a value for K , the presumed

equilibrium constant for outer-sphere complex formation. It should be noted, however, that eq 22 is identical in form to the expression generated from eq 19' for the kinetics of a reduction reaction conforming to Scheme 1 in which only pathway B is contributing:

$$\frac{1}{k_{12}[\text{A}_{\text{Red}}]} = \frac{1}{k_{\text{obs}}} = \frac{1}{K_{\text{OQ}}k_{\text{B2}}[\text{A}_{\text{Red}}]} + \frac{1}{k_{\text{OQ}}} \quad (23)$$

Thus, it is assumed that the values that Tanaka and co-workers attributed to k_{et} actually represent the k_{OQ} rate constant for the conformational change $\text{O} \rightarrow \text{Q}$ and the values that they attributed to Kk_{et} are actually $K_{\text{OQ}}k_{\text{B2}} \equiv k_{12(\text{B})}$ from which $k_{11(\text{B})}$ can be calculated using eq 14.

In a subsequent paper,¹⁴⁸ Tanaka and co-workers recognized the possibility of an alternate mechanism in which the limiting first-order process was due to the desolvation of the Cu^{II}L complex. This latter mechanism is equivalent to pathway B in Scheme 1. Their limiting first-order rate constant values of 12, 50, and 860 s⁻¹ for the Cu(II/I) systems with pmto, pmpo, and pdto, respectively, appear to be reasonable values for k_{OQ} in light of studies on similar systems.

5.6.2. Thiaether Sulfur–Amine Nitrogen Mixed Donor Ligand Systems

Mixed donor ligand systems containing thiaether sulfur and amine nitrogen donor atoms have the advantage of generating larger Cu^{II}L stability constants while still retaining reasonably high Cu^{III}/L potentials. Vande Linde et al.¹⁵¹ studied the electron-transfer kinetics of a Cu(II/I) system involving a 15-membered macrocyclic ligand containing four thiaether sulfurs and one amine nitrogen ([15]aneNS₄, Figure 11). This system exchanged electrons very rapidly and, therefore, is treated in the section on rapidly reacting systems below. Two other macrocyclic complexes with three thiaether sulfurs and one amine nitrogen have recently been reported by Galijasevic et al.,¹⁵² both being 14-membered macrocycles. The difference between these two ligands is that [14]aneNS_{3-a} has the more common chelate ring sequence 5,6,5,6 while [14]aneNS_{3-b} has the sequence 5,5,6,6 (Figure 11). The latter system exhibits a slightly larger k_{11} value than does the former, but neither system gave evidence of differences in the $k_{11(\text{Red})}$ and $k_{11(\text{Ox})}$ values. Interestingly, the k_{11} values observed for these two systems (Table 9) are intermediate between the values obtained independently for pathways A and B in the Cu^{II}/([14]aneS₄) system.

Galijasevic¹⁵³ has also studied the electron-transfer kinetics of three systems involving N₂S₂ donor sets designated as [14]aneN₂S₂, [14]aneNSSN, and [14]aneNSNS (Figure 11).³⁴ All three of these 14-membered macrocyclic ligands form the normal 5,6,5,6 chelate ring sequence, but they differ in terms of the placement of the two nitrogen donors. Koenigbauer⁶⁶ had earlier noted a pH dependence when studying the electron-transfer kinetics of these systems in aqueous solution. More recently, it has become apparent that this effect is attributed to the fact that,

Table 9. Electron-Transfer Rate Constants for Copper(II/I) Couples with Mixed Donor Ligands at 25 °C

oxidant	reductant	solvent	$\log k_{12}$ ($M^{-1} s^{-1}$)	$\log k_{11}$ ($M^{-1} s^{-1}$)	ref
Acyclic Ligand Systems					
1,8-Bis(2-pyridyl)-3,6-dithiaoctane: Cu ^{III} (pdto)					
Cu ^{II} L ²⁺	cyt- <i>c</i> (II)	A	4.23	0.7	147
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₄ bpy ²⁺	A	3.99	1.0	147
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₄ bpy ²⁺	A	4.08	0.2	66
Cu ^{II} L ²⁺	<i>cis</i> -Ru ^{II} (NH ₃) ₄ (isn) ₂ ²⁺	D2	4.58	-1.2	144
Cu ^{II} L ²⁺	<i>cis</i> -Ru ^{II} (bpy) ₂ Cl ₂	D2	4.64	+1.2 [IS] ^a	144
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₄ bpy ²⁺	D2	3.30	-1.0	144
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ isn ²⁺	D2	4.15	-1.0	144
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ py ²⁺	D2	4.58	-0.8	144
Cu ^{II} L ²⁺	Fe ^{II} (Me ₂ Cp) ₂	B	5.21	0.2	148
Cu ^{II} L ²⁺	Fe ^{II} (Cp) ₂	B	4.32	1.2	146
Cu ^{II} L ²⁺	Fe ^{II} (Cp) ₂	C	4.96	3.4	146
Cu ^{II} L ²⁺	Fe ^{II} (Cp) ₂	D2	4.98	0.3	146
Ru ^{III} (NH ₃) ₄ bpy ³⁺	Cu ^I L ⁺	A	2.55	-0.5	66
Cu^{III}L^{2+/+}	1,7-Bis(5-methylimidazol-4-yl)-2,6-dithiaheptane: Cu ^{III} (bidhp)	E		3.60	149
Acyclic Sulfur–Oxygen Donor Ligand Complexes—Reduction Only					
Cu ^{II} (ta) ²⁺	cyt- <i>c</i> (II)	A	2.23	2.4	107
Cu ^{II} (2dta) ²⁺	cyt- <i>c</i> (II)	A	3.71	3.7	107
Cu ^{II} (3dta) ²⁺	cyt- <i>c</i> (II)	A	1.56	1.3	107
Cu ^{II} (tta) ²⁺	cyt- <i>c</i> (II)	A	3.85	1.8	5
Macrocyclic Ligand Systems					
1,4,8-Trithia-11-azacyclotetradecane: Cu ^{III} ([14]aneNS ₃ - <i>a</i>)					
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ isn ²⁺	A	3.38	1.5	152
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ py ²⁺	A	4.11	1.7	152
Ru ^{III} (NH ₃) ₄ bpy ³⁺	Cu ^I L ⁺	A	4.71, 4.99	0.3, 0.9	152
Ru ^{III} (NH ₃) ₄ phen ³⁺	Cu ^I L ⁺	A	4.43, 4.17	1.6, 1.1	152
1,7,11-Trithia-4-azacyclotetradecane: Cu ^{III} ([14]aneNS ₃ - <i>b</i>)					
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ isn ²⁺	A	4.1	2.5	152
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ py ²⁺	A	4.5, 4.6	2.1	152
Ru ^{III} (NH ₃) ₄ bpy ³⁺	Cu ^I L ⁺	A	5.3, 5.7	2.0, 2.8	152
Ru ^{III} (NH ₃) ₄ phen ³⁺	Cu ^I L ⁺	A	5.8	2.7	152
1,4-Dithia-7,11-diazacyclotetradecane: Cu ^{III} ([14]aneN ₂ S ₂)					
Cu ^{II} L ²⁺	Co ^{II} (sep) ²⁺	A		0.5 (pH 4.5)	153
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₆ ²⁺	A		0.9 (pH 3.5)	153
Ru ^{III} (NH ₃) ₅ py ³⁺	Cu ^I L ⁺	A		-5.3 (pH 1.0)	153
				-4.9 (pH 2.0)	153
			gated	-1.6 (pH 5.6)	153
1,11-Dithia-4,7-diazacyclotetradecane: Cu ^{III} ([14]aneNSSN)					
Cu ^{II} L ²⁺	Co ^{II} (sep) ²⁺	A		1.0 (pH 3.3)	153
				1.3 (pH 4.5)	153
Ru ^{III} (NH ₃) ₅ py ³⁺	Cu ^I L ⁺	A		-3.6 (pH 1.0)	153
				-3.9 (pH 2.0)	153
				-3.2 (pH 3.5)	153
1,7-Dithia-4,11-diazacyclotetradecane: Cu ^{III} ([14]aneNSNS)					
Cu ^{II} L ²⁺	Co ^{II} (sep) ²⁺	A		1.8 (pH 3.3)	153
				2.9 (pH 4.5)	153

^a Reaction is apparently inner-sphere.

in some of these systems, one of the nitrogen atoms is required to invert upon electron-transfer and this requires the abstraction of the attached hydrogen, a process that is retarded as the pH decreases. Galijasevic's data have confirmed this effect in a series of related studies in acetonitrile where hydrogen abstraction is made more difficult by the non-aqueous solvent but is facilitated as additional water is added. Because of the complexity of the acetonitrile data, only the aqueous values are recorded in Table 9. However, the limited data presented here for the [14]aneN₂S₂ and [14]aneNSSN systems make it clear that the oxidation kinetics are extremely slow at low pH in aqueous media, presumably reflecting a switch to pathway B in Scheme 1. Since it is likely that the more favorable mechanistic pathway for these N₂S₂

donor systems is pathway A—as has been established for the corresponding S₄ macrocycles—the difficulty of inverting a nitrogen preceding electron transfer during the oxidation process is presumed to be reflected in this behavior.

5.6.3. Thiaether Sulfur–Carboxylic Oxygen Mixed Donor Ligand Systems

In their studies on thiaether complexes, Yandell and co-workers¹⁰⁷ reported the only studies conducted to date on Cu(II/I) systems involving mixed sulfur–oxygen donors. Of the five ligands included in their studies, all were acyclic and contained one (ta), two (2dta, 3dta, 4dta), or three (tta) thiaether sulfur donors and two terminal carboxylates (Figure 11). A single reduction study, using cytochrome-*c*^{II} as the

Table 10. Cross-Reaction Kinetic Studies for Coordination Invariant Copper(II/I) Couples at 25 °C

oxidant	reductant	solvent	$\log k_{12}$ ($M^{-1} s^{-1}$)	$\log k_{11}$ ($M^{-1} s^{-1}$)	ref
Pentacoordinate Complexes					
$Cu^{II/L} 2^{+/+}$	Bis-2,6-[1-((2-pyridin-2-ylethyl)imino)ethyl]pyridine: $Cu^{II/(py)_2DAP}$	B ^a		3.23	154
				2.49^b	154
$Cu^{II/L} 2^{+/+}$ $Cu^{II}((py)_2DAP)^{2+}$	Bis-2,6-[1-((2-imidazol-4-ylethyl)imino)ethyl]pyridine: $Cu^{II/(imidH)_2DAP}$	B ²		4.11	155
		B ^a	4.81	3.20 ^c	154
$Cu^{II}((py)_2DAP)^{2+}$	Bis-2,6-[1-((2- <i>N</i> - <i>p</i> -xylylimidazol-4-yl)ethyl)pyridine: $Cu^{II/(imidR)_2DAP}$	B ^a	4.79	3.52 ^c	154
		$Cu^I L^+$			
$Cu^{II/L} 2^{+/+}$	Bis-2,6-[1-((2-(5-methyl)imidazol-4-ylethyl)imino)pyridine: $Cu^{II}((5-Meimid)_2DAP)$	B ²		4.54 (20 °C)	156
Tetrahedral Complexes					
$Fe^{III}(CN)_6^{3+}$	12-Tungstocuprate: $Cu^{II/I}W_{12}O_{40}^{6-/-}$	A	5.61	0.41	47
$Cu^{II}L_2^{2+}$ $Cu^{II}L_2^{2+}$ $Cu^{II}L_2^{2+}$	Bis(2,2'-bis(2-imidazolyl)biphenyl): $Cu^{II/(bib)_2}$	B	1.34	-0.44	6
		B	1.94	-0.31	6
		B	1.88	-1.62	6
$Cu^{II/L} 2^{2+/+}$	Bis((1-methyl-4,5-diphenylimidazol-2-yl)ketone): $Cu^{II/(bimdpk)_2}$	C		4.29	159
$Cu^{II/I}(dpym)_2^{0/-}$	3,3',5,5'-Tetramethyl-4,4'-dicarboethoxydipyrrromethene = Hdypm: $Cu^{II/I}(dpym)_2$	C ^d		3.77	160
$Cu^{II/L} 2^{+/+}$ $Cu^{II}L_2^{2+}$ $Cu^{II}L_2^{2+}$ $Cu^{II}L_2^{2+}$ $Cu^{II}L_2^{2+}$ $Fe(bpy)_3^{3+}$	Biphenyldiimino Dithiaether: $Cu^{II/I}(bite)$	C		[1.34 first-order]	161
		B	2.91	-1.16	142
		B	4.57	-1.39	142
		B	4.88	-1.92	142
		B	4.87	-1.92	142
		B	4.40	-1.54	142

^a $\mu = 0.05$. ^b $\mu = 0.02$. ^c Corrected to $\mu = 0$. ^d $\mu = 0.007$.

counterreagent, was reported in each case. As shown in Table 9, the self-exchange rate constant is largest for the 2dta system, which forms all five-membered chelate rings.

5.7. Coordination Invariant Systems

5.7.1. Five-Coordinate Systems

Stanbury, Wilson and co-workers^{154–156} studied the electron-transfer kinetics of a series of four closely related linear ligands containing five unsaturated nitrogen donor atoms. These ligands, designated as $(py)_2DAP$, $(imidH)_2DAP$, $(imidR)_2DAP$, and $(5-imidMe)_2DAP$ (Figure 12), are particularly interesting since the crystal structures reveal that both $Cu^{II}L$ and $Cu^I L$ are essentially trigonal bipyramidal (five-coordinate), although the $Cu^{II}L$ structures are less regular. For three of the four $Cu(II/I)$ systems that were studied in this series, the electron self-exchange rate constants were determined directly in acetonitrile from NMR line-broadening experiments. In this nonaqueous medium, some effect of ion pairing was observed for which corrections were made (but these effects are not exceptionally large since acetonitrile has a dielectric constant of 38.8 (at 20 °C)—similar to that of methanol). Since Cu retains the same coordination number and approximate geometry during the overall electron-transfer process, very large k_{11} values might be anticipated. Somewhat surprisingly, the k_{11} values obtained were in the range of 2×10^3 to $3 \times 10^4 M^{-1} s^{-1}$ (Table 10). The

consistency of the rate constants among the various reactants suggested that there was no tendency for these systems to undergo inner-sphere electron transfer under the conditions used. However, no cross-reactions were carried out other than reactions of three of these species with each other.

5.7.2. Four-Coordinate Systems

In line with the comments made earlier on the anticipated reactivity of the $Cu^{II/I}Cl_4$ system, in which the copper ion would be expected to remain tetrahedrally coordinated in both oxidation states, studies on $Cu(II/I)$ redox systems in which both oxidation states are tetrahedrally coordinated would appear to be particularly relevant to the blue copper proteins. Lappin and Peacock⁴⁷ were the first to attempt to measure the electron-transfer kinetics of a $Cu(II/I)$ system, which purportedly remains tetrahedral in both oxidation states. Their study involved the oxidation of the 12-tungstocuprate complex ion, $Cu^{II/I}W_{12}O_{40}^{7-/-}$, with $Fe^{III}(CN)_6^{3-}$. The central metal ion coordination site in $Cu^{II/I}W_{12}O_{40}^{6-/-}$ is buried about 5 Å beneath the surface of the polytungstate shell. Application of eq 14 to the observed cross-reaction rate constant yielded a value of $k_{11(Ox)} = 2.6 M^{-1} s^{-1}$ for the tungstocuprate(II/I) couple. The authors concluded that, in view of the limited structural change required for electron transfer, the relatively small self-exchange rate constant may reflect the nature of the polytungstate medium through which the electron must pass. A “hop” mechanism was proposed in

which the rate-determining process is the migration of the electron within the tungstate shell.

Knapp, Potenza, Schugar, and co-workers¹⁵⁷ generated 2,2'-bis(2-imidazolyl)biphenyl (bib) as a bidentate ligand (Figure 12), which because of steric constraints forms four-coordinate bis-complexes with both Cu(II) (pseudo-square planar) and Cu(I) (pseudo-tetrahedral) as revealed in their crystal structures. These investigators subsequently attempted to determine the self-exchange rate constant of the $\text{Cu}^{\text{II/I}}\text{L}_2^{2+/+}$ redox couple by NMR line broadening but found that the exchange rate was too slow for the time domain of this technique.¹⁵⁸ This led them to propose that $k_{11} \leq 10^2 \text{ M}^{-1} \text{ s}^{-1}$. Subsequently, Stanbury and Wilson and co-workers⁶ measured the rate constants for the reduction of $\text{Cu}^{\text{II}}(\text{bib})_2$ with three closely related substitution-inert Co(II) complexes. Application of eq 14 yielded an average $k_{11(\text{Red})}$ value of $0.16 \text{ M}^{-1} \text{ s}^{-1}$, one of the smallest values ever observed up to that time for a Cu(II/I) system involving a multidentate ligand. Utilizing newly developed copper force field constants, these workers concluded that, despite the invariant coordination number, the internal reorganizational energy is particularly large and appears to arise from angular distortions around the copper center.

Garner and co-workers¹⁵⁹ have generated another highly substituted ligand, bimdpk (Figure 12), which also forms four-coordinate complexes with both oxidation states of copper as shown by the crystal structures; and the electron paramagnetic resonance (EPR) and electronic spectra indicate that these cations have a very similar structure in the solid state and in solution. From NMR line broadening measurements in acetonitrile, these investigators found that this system exhibits a much larger k_{11} value of $1.9 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$. No cross-reactions have been reported with this system.

A similar tetrahedral system has been studied by Swaddle and co-workers^{160a} involving a diimidazole ligand known as Hdpym (Figure 12). When deprotonated, the dpym⁻ ligand forms bis complexes similar to those formed with bimdpk. A crystal structure has shown the $\text{Cu}^{\text{II}}(\text{dpym})_2$ complex to be close to tetrahedral.^{160b} Swaddle's NMR line-broadening measurements in acetone yielded a k_{11} value for this system of $5.9 \times 10^3 \text{ M}^{-1} \text{ s}^{-1}$.

Stanbury and Wilson's group¹⁶¹ has investigated the Cu(II/I) system with a macrocyclic diiminodithiaether ligand designated as bite (Figure 12). The crystal structure of the Cu(I) complex is distorted tetrahedral as expected. The crystal structure of the Cu(II) complex had the four ligand donor atoms arranged in a distorted plane with two distant axial BF_4^- ions completing the tetragonal coordination sphere. Extended X-ray absorption fine structure (EXAFS) measurements showed that the ligand donor atoms represented the primary coordination environment around both Cu(I) and Cu(II) from which these investigators concluded that the coordination number was virtually invariant. An attempt to measure the self-exchange rate constant by direct NMR line broadening in acetone showed no dependence upon the $\text{Cu}^{\text{II}}(\text{bite})$ concentration. From this

observation, these investigators concluded that the self-exchange rate constant was "gated" even in the absence of a thermodynamic driving force. Subsequently, this same group¹⁴² studied the cross-reaction kinetics of $\text{Cu}^{\text{II/I}}(\text{bite})$ reacting with four reducing agents and one oxidizing agent in acetonitrile. Both the oxidation and reduction cross-reactions gave consistent k_{11} values of approximately $0.02 \text{ M}^{-1} \text{ s}^{-1}$. The authors suggested that the difference between their consistently small k_{11} values from cross-reactions and their apparently larger first-order self-exchange rate constant, as obtained for the direct self-exchange in acetone, "implies a more efficient mechanism for the self-exchange reaction than for the cross-reactions, such as an inner-sphere mechanism."

The measurements made on the $\text{Cu}^{\text{II/I}}(\text{bite})$ system and the conclusions reached give rise to many questions regarding their interpretation. The fact that the k_{11} values calculated from the cross-reactions are extremely small would indicate that no electron exchange would be observable on the NMR time scale (as noted previously by Knapp et al. in their attempts to make similar measurements on the $\text{Cu}^{\text{II/I}}(\text{bib})_2$ system). This is consistent with the fact that Xie et al.¹⁴² did not observe any line broadening. This seems to represent a more plausible explanation for this observation than the suggestion that the self-exchange reaction itself is "gated". Moreover, the failure to detect axial coordination by solvent molecules in the $\text{Cu}^{\text{II}}(\text{bite})$ complex from EXAFS measurements is to be expected if the coordinate bonds are elongated. Therefore, this system may not represent a coordination invariant system as originally suggested.

5.8. Tripodal Ligand Systems

Tripodal ligands are branched acyclic quadridentate ligands in which each of the three branches is attached to a nitrogen bridgehead and each branch contains a donor atom (Figure 13). As a result of this arrangement, the four donor atoms cannot coordinate in a planar fashion and, therefore, cannot adapt to the coordination geometries normally preferred by Cu(II). However, depending upon the length of the branching chains, they can accommodate a reasonable tetrahedral geometry of the type anticipated in Cu(I) complexes. A number of crystal structures have demonstrated that, if all branches form five-membered chelate rings, the Cu(II) complexes tend to adopt a trigonal bipyramidal geometry with a fifth ligand, either a solvent molecule or an anion, at the axial site opposite to the bridgehead nitrogen.¹⁶² If one or more branches form six-membered chelate rings, the Cu(II) complexes tend to approximate a square pyramidal geometry. The symmetric ligand tris(2-(methylthioethyl)amine) (TMMEA) falls into the former category, and the crystal structure of the Cu(II) complex reveals that it has virtual C_{3v} symmetry with an anion in the fifth coordination site, which is presumed to be replaced by a solvent molecule in dilute solution.¹⁶³ Upon reduction, this fifth donor atom dissociates to produce a distorted tetrahedral complex that retains C_{3v} symmetry with

Table 11. Electron-Transfer Rate Constants for Tripodal Ligand Complexes with Copper(II/I) in Aqueous Solution at 25 °C

oxidant	reductant	solvent	$\log k_{12}$ ($M^{-1} s^{-1}$)	$\log k_{11}$ ($M^{-1} s^{-1}$)	ref
Tris(2-methylthioethyl)amine: Cu ^{III} (TMMEA)					
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₄ phen ²⁺	A	3.88	-1.3	163
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₄ bpy ²⁺	A	3.80	-1.5	163
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ isn ²⁺	A	4.01	-1.8	163
Ni ^{III} ([14]aneN ₄) ³⁺	Cu ^I L ⁺	A	4.72	1.3	163
Ru ^{III} (NH ₃) ₂ (bpy) ₂ ³⁺	Cu ^I L ⁺	A	5.9	0.5	163
Fe ^{III} (4,7-Me ₂ phen) ₃ ³⁺	Cu ^I L ⁺	A	6.53	0.9	163
2-Pyridylmethylbis(2-methylthioethyl)amine: Cu ^{III} (PMMEA)					
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₄ phen ²⁺	A	3.88	-1.3	165
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₄ bpy ²⁺	A	3.80	-1.5	165
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ isn ²⁺	A	4.01	-1.8	165
Ni ^{III} ([14]aneN ₄) ³⁺	Cu ^I L ⁺	A	4.72	1.3	165
Ru ^{III} (NH ₃) ₂ (bpy) ₂ ³⁺	Cu ^I L ⁺	A	5.9	0.5	165
Fe ^{III} (4,7-Me ₂ phen) ₃ ³⁺	Cu ^I L ⁺	A	6.53	0.9	165
2-Pyridylmethylbis(2-ethylthioethyl)amine: Cu ^{III} (PMAS)					
Cu ^{II} L ²⁺	cyt-c(II)	A	3.22	1.7	107
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ py ²⁺	A	3.77	1.6	147
Cu ^{II} L ²⁺	Co ^{II} (terpy) ₂ ²⁺	A	2.95	0.8	147
Cu ^I L ²⁺	Fe(HECp) ₂ ²⁺	A	4.11	1.7	164
2-Pyridylethylbis(2-methylthioethyl)amine: Cu ^{III} (PEMEA)					
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₄ phen ²⁺	A	3.25	-1.0	165
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₄ bpy ²⁺	A	3.25, 3.16	-1.1	165
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ isn ²⁺	A	4.08, 3.99	-0.3	165
Ru ^{III} (NH ₃) ₂ (bpy) ₂ ³⁺	Cu ^I L ⁺	A	6.43	0.3	165
Ru ^{III} (NH ₃) ₄ phen ³⁺	Cu ^I L ⁺	A	6.53, 6.49	-0.5	165
2-Pyridylethylbis(2-ethylthioethyl)amine: Cu ^{III} (PEAS)					
Cu ^{II} L ²⁺	cyt-c(II)	A	3.84	0.1	147
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ isn ²⁺	A	4.03	-0.5	165
Ru ^{III} (NH ₃) ₂ (bpy) ₂ ³⁺	Cu ^I L ⁺	A	3.51	0.6	165
Bis(2-pyridylethyl)-2-methylthioethylamine: Cu ^{III} (BPEMEA)					
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₄ phen ²⁺	A	2.59	0.0	165
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₄ bpy ²⁺	A	2.33	-0.5	165
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ isn ²⁺	A	2.91, 2.86	-0.5	165
Ru ^{III} (NH ₃) ₅ isn ₂ ³⁺	Cu ^I L ⁺	A	3.18	1.9	165
Ru ^{III} (NH ₃) ₄ bpy ³⁺	Cu ^I L ⁺	A	4.51	1.2	165
Ru ^{III} (NH ₃) ₄ phen ³⁺	Cu ^I L ⁺	A	4.40	1.0	165
Bis(2-pyridylethyl)-2-ethylthioethylamine: Cu ^{III} (BPEEEA)					
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ isn ²⁺	A	3.02	-0.4	165
Tris(2-pyridylmethyl)amine: Cu ^{III} (TPMA)					
Cu ^{II} L ²⁺	cyt-c(II)	A	-1.22	1.8	5
Tris(2-pyridylethyl)amine: Cu ^{III} (TPEA)					
Cu ^{II} L ²⁺	cyt-c(II)	A	3.13	1.9	5

only minimal changes in the remaining bond lengths and angles. Although such systems are not coordination invariant, the seemingly small changes in the Cu(II/I) complex geometry accompanying a change in oxidation state suggested that electron transfer might be rapid.

Augustin et al.¹⁰⁷ reported the first electron-transfer kinetic studies for Cu(II/I) complexes with the tripodal ligands PMAS and PEAS (Figure 13) using cytochrome-c^{II} as the reductant. Additional reductions on one or both of these systems were carried out by Karlin and Yandell¹⁴⁷ and by Garcia, Karlin, and Holwerda¹⁶⁴ with similar k_{11} values being obtained. To date, electron-transfer kinetics have been reported for a total of nine tripodal ligand systems (Table 11). For Cu^{III}(TMMEA), the kinetics of three reduction and three oxidation reactions were determined with appropriate counterreagents.¹⁶³ These results indicated that the self-exchange rate constant for reduction, $k_{11(\text{Red})}$, was about 2 orders of magnitude smaller than that for oxidation, $k_{11(\text{Ox})}$, consistent

with the conclusion that the oxidation reactions were proceeding by pathway B (as the preferred reaction pathway) whereas the reduction reactions were forced to proceed by pathway A due to the rate-limiting k_{OQ} value. Interestingly, similar results were obtained for Cu^{III}(BPEMEA), which forms two six-membered chelate rings.¹⁶⁵ In this regard, these systems resemble the polypyridyl systems discussed earlier, a point of particular interest since, in both cases, the ligand distorts the Cu(II) geometry away from planarity, thereby presumably lowering the reorganizational barrier required to generate the Cu^{II}L(Q) metastable intermediate. Of the other tripodal ligand systems that have been studied to date, Cu^{III}(PEMEA) showed small k_{11} values for both oxidation and reduction that were similar to the $k_{11(\text{Red})}$ values obtained for the TMMEA and BPEMEA systems. By contrast, Cu^{III}(PMMEA), which was expected to show similar behavior to Cu^{III}(TMMEA) since it forms all five-membered chelate rings, exhibited both $k_{11(\text{Red})}$ and $k_{11(\text{Ox})}$ values that were comparable in magnitude

Table 12. Copper(II/I) Redox Couples Exhibiting Electron Self-Exchange Rate Constants of $10^5 \text{ M}^{-1} \text{ s}^{-1}$ or Greater in Aqueous Solution at 25 °C

oxidant	reductant	solvent	$\log k_{12}$ ($\text{M}^{-1} \text{ s}^{-1}$)	$\log k_{11}$ ($\text{M}^{-1} \text{ s}^{-1}$)	ref
Cu^{III}L^{2+/+}	Tetrabenzob[<i>b,f,j,n</i>]-[1,5,9,13]tetraazacyclohexadecane: Cu ^{III} (TAAB)				
		A		5.7	166
Cu^{III}L^{2+/+}	1,4,7,10,13-Pentathiacyclopentadecane: Cu ^{III} ([15]aneS ₅)				
		A		5.0	168
Cu^{III}L^{2+/+}		D3		4.9	168
Cu ^{II} L ²⁺	Co ^{II} (TIM) ²⁺	A	2.78	5.5	132
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₄ bpy ²⁺	A	7.9	5.4	132
Fe ^{III} (4,7-Me ₂ phen) ₃ ³⁺	Cu ^I L ⁺	A	7.7	3.9	132
Cu^{III}L^{2+/+}	1,4,7,10-Tetrathia-13-azacyclopentadecane: Cu ^{III} ([15]aneNS ₄)				
		A		5.1	151
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ py ²⁺	A	5.96	4.4	151
Ru ^{III} (NH ₃) ₅ py ³⁺	Cu ^I L ⁺	A	4.11	5.1	151
Cu^{III}L^{2+/+} (see Table 6 for cross-reaction data)	1,4,7,10-Tetrathiacyclotridecane: Cu ^{III} ([13]aneS ₄)				
		A		5.5	133
Cu^{III}L^{2+/+}	Oxathiane-1,4,7,10-tetrathiacyclododecane: Cu ^{III} (oxathiane-[12]aneS ₄)				
		A		5.92	171
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₅ isn ²⁺	A	7.99	5.8	171
Cu ^{II} L ²⁺	Ru ^{II} (NH ₃) ₄ bpy ²⁺	A	7.63	5.7	171
Ru ^{III} (NH ₃) ₅ (bpy) ₂ ³⁺	Cu ^I L ⁺	A	8.11	5.9	171
Ni ^{III} ([14]aneN ₄) ³⁺	Cu ^I L ⁺	A	6.51	5.6	171

to the $k_{11(\text{Ox})}$ values obtained for the TMMEA and BPEMEA systems.

5.9. Copper(II/I) Systems Exhibiting Rapid Electron Exchange

As has been noted in the preceding discussion, most of the efforts to generate Cu(II/I) systems that would exhibit large self-exchange rate constants have proven unsuccessful. This suggests that the internal reorganizational energy barriers have generally been larger than anticipated as noted by Stanbury and co-workers in their study on the electron-transfer kinetics of Cu^{III}(bib)₂.⁶ Nonetheless, five systems exhibiting values of k_{11} equal to or greater than $10^5 \text{ M}^{-1} \text{ s}^{-1}$ have been reported (Table 12).

The first inorganic Cu(II/I) system for which a large k_{11} value was obtained was that reported by Pulliam and McMillin¹⁶⁶ using a highly conjugated macrocyclic tetramine, tetrabenzob[*b,f,j,n*]-[1,5,9,13]tetraazacyclohexadecane (TAAB, Figure 8). These investigators studied the exchange kinetics of the Cu(II/I) complex using NMR line broadening and obtained a value of $k_{11} = 5 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$. At the time of their study, Pulliam and McMillin noted that they could not rule out the possibility that an inner-sphere mechanism was involved. However, a subsequent cross-reaction study by Labuda and Sima,¹⁶⁷ using ascorbate ion as the reductant, was in excellent agreement with Pulliam and McMillin's $k_{11(\text{NMR})}$ value. This provides strong support for the premise that the $k_{11(\text{NMR})}$ value for Cu^{III}(TAAB) represents outer-sphere electron exchange.

Subsequently, two Cu(II/I) systems with quinque-dentate macrocyclic ligands have been studied in our laboratory. One, designated as [15]aneS₅ (Figure 9), contains five thiaether sulfur donors and has yielded a k_{11} value of $1 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$ as determined by NMR.¹⁶⁸ An identical value was determined in 80% methanol (w/w). This value was corroborated from

two cross-reactions involving the reduction of the Cu^{II}L complex, while a somewhat smaller value was calculated from a single oxidation study,¹³² but the latter value was not sufficiently different to provide definitive evidence for a change in reaction pathway. A closely related ligand, designated as [15]aneNS₄ (Figure 11), in which one of the sulfur donor atoms was replaced by an amine nitrogen donor atom, yielded $k_{11} = (1-2) \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$ by NMR, and this value was shown to be consistent with k_{11} values generated from both Cu^{II}L reduction and Cu^IL oxidation reactions.¹⁵¹

The Cu^{III}([13]aneS₄) system, which was cited earlier with the macrocyclic polythiaether complexes, also yielded a large k_{11} value of $3 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$ as determined by NMR with corroborative k_{11} values being generated from reduction reactions of Cu^{II}L.¹³³ An examination of the crystal structures shows that this system is structurally similar to the Cu^{III}([15]aneS₅) system in that both Cu^{II}([15]aneS₅)¹⁶⁹ and Cu^{II}([13]aneS₄)¹⁷⁰ are square pyramidal, the latter having a water molecule occupying the apical site. Upon reduction of the former complex, one of the Cu–S bonds in the plane dissociates to generate a tetrahedral complex in which none of the donor atoms is required to change the orientation of its lone electron pair.¹⁶⁹ No crystal structure has been determined for the reduced Cu^I([13]aneS₄) species, but the reduction process is presumed to involve a similar dissociation of a Cu–S bond while the apical Cu–OH₂ bond remains intact. This, again, would generate a tetrahedral Cu^IL complex without requiring donor atom inversion.

On the basis of the foregoing observations, it was concluded that the generation of a five-coordinate Cu(II) complex in which four of the coordinate bonds were restricted to a more restrained tetrahedral arrangement might lead to an even larger k_{11} value. Accordingly, Krylova et al.¹⁷¹ generated a [12]aneS₄

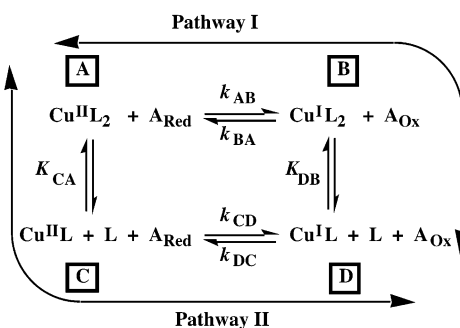
ligand with a fused oxathiane ring (Figure 10) to improve its aqueous solubility. Crystal structures demonstrate that reduction of the Cu(II) complex is accompanied by the rupture of a Cu–S bond while the unique apical donor atom (presumed to involve a solvent molecule in solution) remains intact.¹⁷¹ As determined by NMR, the self-exchange rate constant was found to be $8 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$, a value which was corroborated by both Cu^{II}L reduction and Cu^IL oxidation cross-reactions. This is the largest k_{11} value generated to date for an inorganic Cu(II/I) system and compares favorably with the largest values reported for any of the copper proteins. It is also interesting to note that for the Cu^{II/I}(oxathiane-[12]aneS₄) system there was no evidence for the onset of gated electron-transfer reactions even under conditions where the cross-reaction rate constant for Cu^IL oxidation exceeded $10^8 \text{ M}^{-1} \text{ s}^{-1}$. This indicates that the change in ligand conformation is exceptionally rapid with this system.

5.10. Copper(II/I) System Coupled with Ligand Dissociation

The three donor atoms in the small macrocyclic ligand 1,4,7-trithiacyclononane, [9]aneS₃ (Figure 9), are endodentate with a geometric arrangement that facilitates the coordination of two ligand molecules to the opposite faces of an octahedral coordination sphere. The crystal structure of the [Cu^{II}([9]aneS₃)₂](BF₄)₂·2CH₃CN complex, as reported by Wilson, Glass, and co-workers,¹⁷² shows that there is very little tetragonal distortion, a fact that the authors attributed to the geometrical requirements of the ligand. This group later determined the crystal structure of the corresponding Cu(I) complex, [Cu^I([9]aneS₃)₂]PF₆,¹⁷³ which showed that one ligand was triply coordinated to the copper while the second was attached through a single Cu–S bond. Subsequent crystal structures of several Cu^I([9]aneS₃)Y compounds, where Y was a unidentate ligand, showed that all such structures were similar.¹⁷⁴ Such results led these investigators to conclude that both oxidation states of Cu were coordinated to two ligand molecules in solution.

In focusing on the electrochemical behavior of the Cu(II/I)-[9]aneS₃ system, Wilson and co-workers observed CV behavior similar to that observed by Bernardo et al. for Cu(II/I) complexes with larger macrocyclic tetrathiaether ligands.^{49,175} From this they concluded that the [9]aneS₃ system involved a similar mechanism to that illustrated in Scheme 1 in which discrete conformational and electron-transfer steps occurred for the 1:2 complex. Subsequent studies by Kandedgedara et al.,¹⁷⁶ however, involving a wider range of Cu concentrations for the CV measurements and extensive thermodynamic determinations, showed that, in fact, the reduced species is a 1:1 complex in solution and that the behavior observed by Wilson and co-workers was due to the association and dissociation of the second ligand coupled to the electron-transfer process. As shown in Scheme 2, the applicable mechanism differs from that in Scheme 1 in that ligand association/

Scheme 2



dissociation represents the coordination change in the vertical processes. For the [9]aneS₃ ligand system, pathway I is the only viable pathway under normal conditions. By utilizing huge Cu(II) concentrations, Kandedgedara showed that, even when the 1:1 Cu(II) complex was dominant, this species always added a second ligand before undergoing electron transfer (i.e., C → A → B → D).

The data for the overall electron-transfer behavior of the Cu^{II/I}([9]aneS₃)_n system (where $n = 1, 2$) are presented in Table 13 for aqueous solutions. The first column of k_{11} values are those calculated from the overall cross-reaction rate constants. These values were then corrected for the equilibrium constant K_{DB} to generate k_{11} values representative of the Cu^{II/I}L₂ species (A ⇌ B). It is interesting that these latter values are on the order of $10^5 \text{ M}^{-1} \text{ s}^{-1}$, which is comparable both to the k_{11} values for the rapidly reacting systems in Table 12 and to the resolved $k_{11(\text{OP})}$ and $k_{11(\text{QR})}$ rate constants for the systems in Table 8. This is consistent with the presumption that the two 1:2 complexes (i.e., A and B) have nearly identical geometries so that minimal reorganization accompanies electron transfer.

On the basis of the fact that the cross-reaction studies gave no evidence of direct electron transfer of C ⇌ D, Kandedgedara et al. concluded that electron-transfer is extremely unfavorable for the 1:1 complex and that pathway II can only be accessed in oxidation reactions when a very large driving force is applied. This is consistent with the observation by Wilson et al. that, when Cu^IL was subjected to the extreme driving conditions of pulse radiolysis, a direct loss of the electron via pathway II could be observed.¹⁷⁴ The apparently sluggish electron-transfer behavior observed for the 1:1 Cu^{II/I}([9]aneS₃) complex is consistent with similar observations on other systems in which several coordinated solvent molecules are involved, such as the 1:1 Cu^{II/I}(phen) system, which appears to react much more slowly than Cu^{II/I}(phen)₂.¹⁰⁴

6. Copper(III/II) Systems

The Cu(III) oxidation state is relatively rare but has been observed as a stable species when Cu is coordinated to very hard bases. Since Cu(III), as a d⁸ system, tends to form square planar complexes and Cu(II) is presumed to be tetragonal, it is assumed that, during a self-exchange reaction, the ligand donor atoms tend to remain coordinated in the xy-

Table 13. Electron-Transfer Rate Constants for $\text{Cu}^{\text{III}}([\text{9]janeS}_3)_n$ in Aqueous Solution at 25 °C^a

oxidant	reductant	$\log k_{12}$ or k_{21} ($\text{M}^{-1} \text{s}^{-1}$)	$\log k_{11}$ ($\text{M}^{-1} \text{s}^{-1}$)	$\log k_{11}(\text{corrected})^b$ ($\text{M}^{-1} \text{s}^{-1}$)
$\text{Cu}^{\text{II}}\text{L}_2^{2+}$	$\text{Ru}^{\text{II}}(\text{NH}_3)_4\text{bpy}^{2+}$	6.28	4.98	4.19 (5.95)
$\text{Cu}^{\text{II}}\text{L}_2^{2+}$	$\text{Ru}(\text{NH}_3)_4\text{phen}^{2+}$	6.99	6.21	5.64
$\text{Cu}^{\text{II}}\text{L}_2^{2+}$	$\text{Ru}(\text{NH}_3)_5\text{isn}^{2+}$	7.04	5.75	5.05
$\text{Ni}^{\text{III}}([\text{14]janeN}_4)^{3+}$	$\text{Cu}^{\text{I}}\text{L}^+$	5.54	1.54	3.18
$\text{Ru}^{\text{III}}(\text{NH}_3)_2(\text{bpy})_2^{3+}$	$\text{Cu}^{\text{I}}\text{L}^+$	7.36	2.44	4.84
$\text{Fe}^{\text{III}}(4,7\text{-Me}_2\text{phen})_3^{3+}$	$\text{Cu}^{\text{I}}\text{L}^+$	8.06	2.87	4.60

^a Reference 176. ^b Corrected for the equilibrium constant for ligand addition to the $\text{Cu}^{\text{I}}\text{L}$ species prior to electron transfer.

plane while two loosely held solvent molecules associate/dissociate along the *z*-axis. This implies that a coordinated quadridentate ligand will not undergo significant conformational changes during an electron-transfer reaction. As a result, the self-exchange rate constants for $\text{Cu}(\text{III}/\text{II})$ systems are expected to show much less dependence on ligand structure.

Margerum and co-workers have conducted a series of studies on $\text{Cu}(\text{III}/\text{II})$ peptide complexes, which stabilize the formation of copper(III) upon deprotonation of the amide nitrogens. Koval and Margerum¹¹⁸ determined the first electron self-exchange rate constant for $\text{Cu}(\text{III}/\text{II})$ complex with tri- α -aminoisobutyric acid by means of NMR line broadening and obtained $k_{11} = 5.5 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$. In a subsequent study,¹⁷⁷ this group was able to generate self-exchange rate constants for five different tetrapeptide complexes. All five systems yielded k_{11} values within the range of $(0.4\text{--}2) \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$. Cross reaction studies involving the oxidation of $\text{Cu}(\text{II})$ peptide complexes with IrCl_6^{2-} resulted in very rapid kinetics, which were attributed to an inner-sphere mechanism in which a Cl^- ion served as a bridging donor atom.¹⁷⁸

Sulfab and co-workers¹⁷⁹ have shown that the $\text{Cu}(\text{III})$ oxidation state is also stabilized by coordination to imine-oxime ligands. In one definitive study,¹⁸⁰ they measured the reduction kinetics for a series of $\text{Cu}(\text{III})$ complexes with substituted imine-oximes and obtained k_{11} values in the range of $(5\text{--}7) \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$. No other studies have been located in which electron self-exchange rate constants for $\text{Cu}(\text{III}/\text{II})$ systems have been reported.

7. Comparative Copper(III) Blue Copper Protein Properties

A large percentage of papers reporting on the electron-transfer kinetics of inorganic copper complexes have claimed that these systems provide information relevant to the behavior of copper proteins, particularly those involving the type 1 copper site in the proteins classified as cupredoxins.¹⁰ However, it is recognized that because of their structural complexity the blue copper proteins may involve electron-transfer pathways that do not parallel those for smaller inorganic systems.¹⁸¹ Of these proteins, the most extensively studied representatives are plastocyanins, which are found in all green plants, and azurins, which are found in bacteria. As noted early in this review, the copper sites in plastocyanins generally involve coordination of the metal ion to two histidine nitrogens and a cysteine sulfur plus an elongated axial bond to a methionine sulfur (Figure

2). In stellacyanin and some other cupredoxins, the methionine sulfur bond is replaced by a glutamate oxygen, generally with a concomitant decrease in the $\text{Cu}(\text{II}/\text{I})$ redox potential. Azurin involves a similar copper coordination environment to that of plastocyanins except that a fifth coordination site, opposite to the axial methionine sulfur, is occupied by a glycinate oxygen. Although several of the inorganic copper complexes for which electron-transfer studies have been reported involve two nitrogen and two sulfur donors, none contain a thiolate sulfur such as that provided by cysteine and none closely approximate the geometry of the type 1 copper sites. Therefore, none can claim to duplicate the coordination environment in the proteins.

Despite these differences in the copper coordination sphere, a comparison of the electron-transfer properties between the inorganic systems and the proteins is of considerable interest. Many blue copper sites exhibit redox potentials within the relatively narrow range of 0.2–0.4 V (vs SHE);¹⁸² however, potentials as high as 1.0 V have been recorded.¹⁸³ The $\text{Cu}(\text{II}/\text{I})$ potentials of inorganic complexes in which the copper is coordinated to unsaturated nitrogen donors, to thioether sulfur donor atoms, or to both are generally comparable to, and often exceed, these potentials, the highest value reported being 0.83 V.¹⁴¹

Comparisons of the electron-transfer kinetic behavior of the cupredoxins to inorganic copper systems are somewhat problematic. The proteins normally function by having the substrate bind to a specific surface patch through electrostatic or hydrogen-bonding interactions. Such species have a finite lifetime during which the electron transfer occurs, and the actual path of the electron through a sequence of bonds may greatly affect the kinetic parameters. By contrast, the inorganic systems discussed in this review generally form short-lived outer-sphere complexes with their reaction partners. In the majority of cases, these outer-sphere complexes are electrostatically unfavorable, and the electron is presumed to transfer by means of direct orbital overlap between the donor and acceptor species.

Many reports have been made of kinetic studies involving cross-reactions of cupredoxins either with other proteins or with inorganic counterreagents. Attempts have been made to treat the resulting cross-reaction rate constants with the Marcus cross-reaction to generate electron self-exchange rate constants. Such values may vary over several orders of magnitude for a single protein reacting with different counterreagents.¹⁸⁴ This may reflect the fact that the

Table 14. Electron Self-Exchange Rate Constants Reported for Cupredoxins in Aqueous Solution at 25 °C^a

protein type	source	log k_{11} ($M^{-1} s^{-1}$)	ref
azurin	<i>Pseudomonas aeruginosa</i>	5.9–6.1	188,189
azurin	<i>Pseudomonas aeruginosa</i>	6.4 ^b	190
stellacyanin	<i>Rhus vernicifera</i>	5.1 ^b	191
plastocyanin	<i>Anabaena variabilis</i>	5.5–5.8	192
pseudoazurin	<i>Chromobacter cycloclastes</i>	3.5, 5.1 ^c	193,194
umecyanin	<i>Horseradish roots</i>	3.8	195
rusticyanin	<i>Thiobacillus ferrooxidans</i>	4.0	196
amicyanin	<i>Thiobacillus versutus</i>	4.8–5.1	197,198

^a All values determined by NMR measurements unless otherwise noted. ^b EPR measurements. ^c Stopped-flow measurements for a cross-reaction with cytochrome *c*(551) from *Pseudomonas aeruginosa*.

reactive site on the protein surface may differ for counterreagents of differing charge.^{185,186}

For a wide variety of cupredoxins, self-exchange rate constants have been determined by NMR line broadening or related spectroscopic techniques. These values may be slower than the electron-transfer reactions with their substrates since the proteins are generally charged at the reactive patch, and thus, the oxidized and reduced forms of the protein tend to repel each other in a self-exchange reaction. Sato, Kohzuma, and Dennison¹⁸⁷ have recently noted that, whereas the acidic patch on higher plant plastocyanins may result in electron self-exchange rate constants as small as $10^3 M^{-1} s^{-1}$, removal of some of the acidic residues at this site increases the self-exchange rate constant to $\sim 10^4 M^{-1} s^{-1}$, while complete removal leads to rate constants in the range of 10^5 – $10^6 M^{-1} s^{-1}$.

A number of representative cupredoxins are listed in Table 14, along with their reported electron self-exchange rate constants, most of which were determined by NMR line broadening.^{188–198} As noted above, the largest self-exchange rate constants for these copper proteins are in the range of 10^5 – $10^6 M^{-1} s^{-1}$. This is equivalent to the largest values determined for inorganic copper complexes in Table 12 and is also in the same range as the rate constants calculated for the electron-transfer process between stable $Cu^{II}L$ and $Cu^I L$ complexes with their corresponding metastable intermediate species after correction for the conformational changes (Table 8).¹³⁷ The similarity in the maximum k_{11} values for both the cupredoxins and the inorganic $Cu(II/I)$ systems suggests that further investigation of the influence of specific structural changes upon electron-transfer rates in inorganic systems may lend insight into the factors that govern corresponding biological systems.

The most interesting kinetic feature shared by copper proteins and inorganic copper systems is that of conformational gating in the overall electron-transfer process. Brunori et al.¹⁹⁹ noted as early as 1975 that azurin appears to undergo conformational changes upon electron transfer. In the first kinetic study on rusticyanin, Lappin and co-workers²⁰⁰ observed limiting kinetic behavior for the protein oxidation, which they attributed to a rate-limiting conformational change. More recently, Sigfridsson²⁰¹ observed conformationally gated electron transfer in

plastocyanin, and Malmström and co-workers²⁰² observed gated electron transfer in reactions of cytochrome-*c* oxidase in which the rate-limiting step was a proton-dependent conformational change. Additional examples of gated behavior continue to appear in the literature for both copper-containing proteins and other biological systems of which recent studies by Kostic and co-workers^{203–206} and by Davidson^{207–209} would appear to be particularly noteworthy.

Crystal structures show that electron transfer is accompanied by only minimal changes in the copper coordination site of plastocyanins¹² and azurins.²¹⁰ However, the water molecules within the protein are usually not well defined in the crystal structures and changes in their orientation could contribute significantly to the overall reorganization barrier.

8. Conclusions

Observation of Scheme 1 Behavior. Theoretical considerations in conjunction with the available electron-transfer kinetic data suggest that Scheme 1 may represent a general mechanism for all $Cu(II/I)$ electron-transfer reactions. However, if the rate of equilibration of the “preferred” metastable intermediate (**P** or **Q**) with its corresponding stable conformer (**R** or **O**) is rapid relative to the rate of the electron-transfer step, the onset of “gated” electron transfer, the switch to the less preferred pathway, or both may never become apparent. Since the majority of electron-transfer cross-reactions have been studied by stopped-flow spectrophotometry, this generally limits the reaction rates that can be monitored successfully to half-lives of about 0.5 ms or longer. Thus, for reactions for which pathway A is preferred, conformational gating will become a dominant process only if $k_{PR} \leq 200 s^{-1}$, and the same limitation applies to k_{OQ} for those reactions that prefer pathway B. *If the onset of “gating” (or a complete switch to the less preferred pathway) is not observed experimentally, it will be impossible to confirm that two discrete steps are involved and the electron-transfer reactions will appear to proceed by a classic single-step process following the formation of an outer-sphere complex even if Scheme 1 applies.* To demonstrate the existence of Scheme 1 for more rapidly equilibrating systems, faster techniques would need to be utilized such as pulse radiolysis or flash-induced electron transfer.

To date, two classes of ligands have provided direct experimental evidence for the operation of a dual pathway mechanism of the type illustrated in Scheme 1. The most definitive data arise from the studies on the macrocyclic tetrathiaether complexes, particularly those involving various substitutions on [14]aneS₄, for which a very large number of cross-reactions have been studied involving both reduction and oxidation with multiple counterreagents. These systems tend to exhibit consistent values among the calculated self-exchange rate constants from various reduction reactions, $k_{11(Red)}$, that are in very good agreement with $k_{11(NMR)}$ values determined directly from NMR line broadening for the several systems where the latter values have also been determined. For those tetrathiaether systems for which multiple oxidation kinetic studies are

available, the resolved $k_{11(\text{Ox})}$ values are also similar to the $k_{11(\text{Red})}$ and $k_{11(\text{NMR})}$ values when the cross-reactions involve a small driving force. However, such values tend to decrease markedly for reactions in which large driving forces are involved. For a variety of such Cu(II/I) systems, first-order “gated” behavior has been observed with one or two reagents that provide intermediate driving forces. The k_{RP} values determined for such systems are typically in the range of 30–200 s^{-1} . All of the data on these polythiaether complexes are consistent with the behavior predicted by the Scheme 1 mechanism in which pathway A is preferred.

For the Cu(II/I) systems with *dl-trans,trans*-dicyhex-[14]aneS₄ and *dl-trans,trans*-dicypt-[14]aneS₄, in which ligand substituents tend to force the coordinated sulfur donor atoms to distort toward a flattened tetrahedral geometry even with Cu(II), the preferred pathway appears to switch to pathway B. The preference for this latter pathway is even more pronounced for polypyridyl complexes. In fact, the Cu(II/I) systems exhibiting the strongest evidence for pathway B as the preferred mechanistic pathway are substituted bipyridine and phenanthroline ligands in which methyl groups are attached to the carbons α to the nitrogen donor atoms. This is seen by the fact that the reduction reactions can become gated, as has been most convincingly demonstrated for the reactions of Cu^{II}(dpmp)₂ and Cu^{II}(6,6'-Me₂bpy)₂ with ferrocene and decamethylferrocene.^{113,119} As the driving force is increased further, the reduction kinetics for these systems resume second-order behavior with a smaller resolved rate constant value, the latter behavior being demonstrated in the case of Cu^I(6,6'-Me₂bpy)₂⁺ reacting with Co^{III}(bpy)₃³⁺.¹¹⁹ A few pieces of data do not fit this overall pattern, most notably the oxidation study of Cu^I(6,6'-Me₂bpy)₂⁺ reacting with Ru^{III}(hfac)¹¹⁵ for which a smaller self-exchange rate constant was generated. If pathway B is preferred for this system as expected, all $k_{11(\text{Ox})}$ values should be identical within experimental error. It is possible that the anomalous $k_{11(\text{Ox})}$ value obtained for this system reacting with Ru^{III}(hfac) represents an experimental error arising from the fact that this specific reaction was thermodynamically unfavorable. However, other explanations are currently being explored by Takagi and co-workers.

Two of the tripodal ligand complexes, TMMEA and PMMEA, also show behavior that is indicative of a dual-pathway mechanism in which pathway B is preferred. It is noteworthy that these complexes, like the polypyridyls, result in unfavorable coordination geometries for the Cu(II) complexes which, presumably, lower the reorganizational energy barrier for forming the Cu^{II}L(Q) intermediate.

More intricate behavior than that depicted in Scheme 1 may be involved in a number of systems. Analysis of the structural changes that accompany electron transfer in the Cu(II/I) complexes with macrocyclic tetrathiaether complexes, such as [14]aneS₄, indicate that two distinct conformational changes must occur involving the inversion of two of the four coordinated donor atoms.⁵¹ This suggests that a “stepladder scheme” may be involved such as

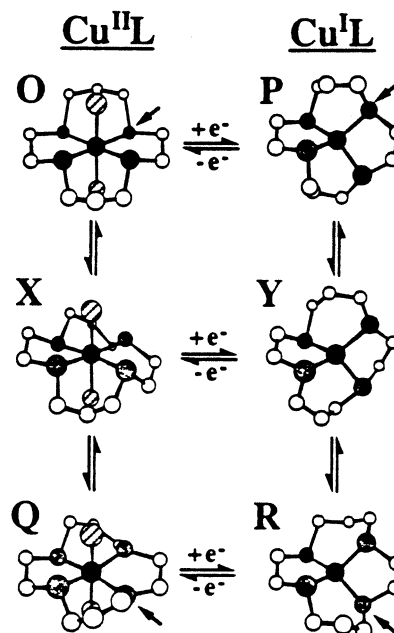


Figure 16. Proposed “stepladder scheme” for a system involving four metastable intermediates, Cu^{II}L(X), Cu^{II}L(Q), Cu^IL(Y), and Cu^IL(R) (adapted from ref 51). Of the three possible reaction pathways, it is unlikely that more than two will ever be experimentally accessible. Thus, this mechanism is presumed to be indistinguishable from Scheme 1.

that shown schematically for Cu^{II/I}([14]aneS₄) in Figure 16. It is doubtful, however, that all three pathways (i.e., O → P → Y → R, O → X → Y → R, and O → X → Q → R) will ever be independently observable. However, if the middle pathway (O → X → Y → R) were preferred, it is conceivable that a system could exhibit gated electron transfer in both directions, that is, k_{RY} could be rate-limiting for specific oxidation reactions and k_{OX} could become rate-limiting for reduction. In this manner, all three pathways could ultimately be sampled.

Applicability of the Marcus Relationship to Copper(II/I) Systems. The huge differences in resolved k_{11} values reported by Yandell and Holwerda for the Cu^{II/I}(bpy)₂^{2+/+} and Cu^{II/I}(phen)₂^{2+/+} systems, based on limited reduction reactions by the former group and a single oxidation study by the latter, originally generated considerable controversy regarding the applicability of the Marcus cross-relationship to Cu(II/I) systems (see section 4.3). As noted in this review, however, the $k_{11(\text{Ox})}$ values reported by Munakata and Endicott and a “preliminary” $k_{11(\text{Ox})}$ value reported by Davies strongly suggest that the data obtained by Holwerda and co-workers were the result of an inner-sphere mechanism. If that interpretation is correct, the attempt to apply the Marcus relationship to their data for the purpose of obtaining a resolved k_{11} value was misleading. *This revelation emphasizes the need to utilize multiple oxidizing and reducing counterreagents in characterizing the kinetic behavior of Cu(II/I) systems.*

For those systems in which NMR relaxation measurements have been reported, the k_{11} values determined by this approach are generally in excellent agreement with either the $k_{11(\text{Red})}$ or $k_{11(\text{Ox})}$ values

calculated from cross-reactions as noted above. Since the NMR data do not depend on the Marcus relationship, this agreement amply demonstrates that eq 14 is valid for these Cu(II/I) systems. The formation of a metastable intermediate simply involves a prior equilibrium step that is incorporated into the overall calculated k_{11} value. Since this equilibrium constant also affects the electrochemical potential of the Cu^{II/I}L system, the application of the Marcus approach provides consistent results. It should be reemphasized, however, that when gated (limiting first-order) behavior is encountered, the reaction rate constant is not dependent upon the electron-transfer process and the Marcus relationship no longer applies.

Factors Affecting the Magnitude of the Copper(II/I) Self-Exchange Rate Constants. Of the Cu(II/I) systems that have come under scrutiny to date, the most perplexing results are those obtained for systems that are purported to be coordination invariant. Although some of these systems exhibit k_{11} values in the range of $(1-3) \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$, such as Stanbury and Wilson's (imidH)₂DAP and (5-Meimid)₂DAP systems and Garner's bimdpk complex (Table 10), none of these rate constants are as large as might be anticipated if the reorganizational barrier were truly minimized. In fact, the studies on Cu^{II/I}(bite) and Cu^{II/I}(bib)₂, which purportedly retain a coordination number of four for both oxidation states, have yielded the smallest k_{11} values yet seen for multidentate ligand complexes. As Stanbury has noted,¹⁴² the reorganizational energies of these latter systems may still readily account for their sluggishness despite one's predisposition to presume that reorganization should be minimal in such cases.

The combined studies of Villeneuve et al.⁵¹ and Yu et al.¹³⁷ have demonstrated that the equilibrium constants for conformational change, occurring as a sequential process to the electron-transfer step, can be independently evaluated by rapid-scan cyclic voltammetry under appropriate circumstances. The availability of such values then makes it possible to evaluate the rate constant for the electron-transfer step itself. For the eight Cu(II/I) systems for which the latter calculations have been made (Table 8),¹³⁷ it has been shown that the self-exchange rate constant is about $10^5-10^6 \text{ M}^{-1} \text{ s}^{-1}$ once the conformationally strained intermediate species has been formed. The k_{11} value for the Cu^{II/I}([9]aneS₃)₂ redox couple (both species existing as the 1:2 complex) is also about $10^5 \text{ M}^{-1} \text{ s}^{-1}$ as are the overall k_{11} values for the fastest reacting inorganic complexes in Table 12. These observations indicate that it should be possible to generate Cu(II/I) systems in which the coordination geometry is held sufficiently rigid to achieve overall k_{11} values approaching (or even exceeding) $10^6 \text{ M}^{-1} \text{ s}^{-1}$. Such systems could then provide copper catalysts that are superior to any currently known.

Upon examination of all of the available data for general trends in the Cu(II/I) self-exchange rate constants, it is noted that the fully aquated (or predominantly aquated) systems are extremely sluggish to undergo electron transfer and systems that have no more than three nonsolvent donor atoms

coordinated to the Cu (such as in the 1:1 complexes with [9]aneS₃, phen, and terpy) appear to exhibit very small k_{11} values. By contrast, all of the Cu^{II/I}L systems that exhibit self-exchange rate constants $\geq 10^5 \text{ M}^{-1} \text{ s}^{-1}$ appear to avoid the dissociation or formation of a strongly bound water molecule in conjunction with electron transfer. This observation may reflect the fact that a strong Cu-OH₂ bond causes the coordinated water molecule to form stronger hydrogen bonds to the surrounding solvent matrix. Dissociation or insertion of such a strongly bound inner-sphere water molecule may significantly increase the solvent reorganizational contributions to the overall reaction energetics.

Implications of Gated Electron Transfer. The onset of gated electron-transfer has been predicted to exist for other systems, particularly biological processes, where the rate of conformational change may provide absolute control for the rate of electron-transfer reactions. The Cu(II/I) systems included in this review provide direct evidence for the various behavioral aspects that have been predicted for this phenomenon. Several copper proteins have shown similar behavior indicative of conformational gating. This implies that inorganic Cu(II/I) systems can provide relevant information to enhance our understanding of the more complex proteins. In this sense, the inorganic Cu(II/I) systems can be said to be truly biomimetic.

9. Acknowledgments

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