Inorg. Chem. **2003**, *42*, 5267–5273

Inorganic Chemistry

Article

Electron-Transfer Kinetics of Copper(II/I) Tripodal Ligand Complexes

Edna A. Ambundo,[1a] Qiuyue Yu,[1a] L. A. Ochrymowycz,[1b] and D. B. Rorabacher*,[1a]

Departments of Chemistry, Wayne State University, Detroit, Michigan 48202, and
University of Wisconsin—Eau Claire, Eau Claire, Wisconsin 54701

Received June 2, 2003

The electron-transfer kinetics for each of three copper(II/I) tripodal ligand complexes reacting with multiple reducing and oxidizing counter reagents have been examined in aqueous solution at 25 °C, $\mu = 0.10$ M. For all of the ligands studied, an amine nitrogen serves as the bridgehead atom. Two of the ligands (PMMEA and PEMEA) contain two thioether sulfurs and one pyridyl nitrogen as donor atoms on the appended legs while the third ligand (BPEMEA) has two pyridyl nitrogens and one thioether sulfur. Very limited kinetic studies were also conducted on two additional closely related tripodal ligand complexes. The results are compared to our previous kinetic study on a Cu(II/I) system involving a tripodal ligand (TMMEA) with thioether sulfur donor atoms on all three legs. In all systems, the Cu(II/I) electron self-exchange rate constants (k_{11}) are surprisingly small, ranging approximately 0.03–50 M^{-1} s^{-1}. The results are consistent with earlier studies reported by Yandell involving the reduction of Cu(II) complexes with four similar tripodal ligand systems, and it is concluded that the dominant reaction pathway involves a metastable $Cu^{II}L$ intermediate species (designated as pathway B). Since crystal structures suggest that the ligand reorganization accompanying electron transfer is relatively small compared to our earlier studies on macrocyclic ligand complexes of Cu(II/I), it is unclear why the k_{11} values for the tripodal ligand systems are of such small magnitude.

Introduction

The type 1 copper site in blue copper proteins has been the focus of intensive research for more than three decades.[2,3] This site is characterized by an unusual coordination geometry—which is essentially either trigonal pyramidal or trigonal bipyramidal[4−8] and it is known to undergo rapid electron transfer.[9] Although the kinetic behavior of type 1 copper sites has often been attributed to this unusual geometry, Solomon and co-workers[10,11] have recently concluded that the rapid electron-transfer rates of blue copper proteins are primarily the result of the strong copper—thiolate (cysteine) bond, which results in a "poised" electronic state, and that this, in turn, dictates the unusual geometry. Nonetheless, the specific influence of a trigonal pyramidal or bipyramidal geometry upon the electron-transfer kinetics of copper(II/I) systems remains a matter of prime interest as noted below.

In relatively unconstrained complexes, Cu(II) generally adopts a 6-coordinate tetragonal or a 5-coordinate square pyramidal geometry while Cu(I) is commonly in a 4-coordinate tetrahedral geometry. As a result, the reorganizational barrier is presumed to be relatively large for many Cu(II/I)

---

* To whom correspondence should be addressed. E-mail: dbr@chem.wayne.edu. Fax: (313) 577-1377.

(1) (a) Wayne State University. (b) University of Wisconsin—Eau Claire.

(2) Gray, H. B.; Malmstrom, B. G.; Williams, R. J. P. *J. Biol. Inorg. Chem.* **2000**, *5*, 551−559.

(3) Guss, J. M.; Freeman, H. C. *J. Mol. Biol.* **1983**, *169*, 521−563.

(4) Shibata, N.; Inoue, T.; Nagano, C.; Nishio, N.; Kohzuma, T.; Onodera, K.; Yoshizaki, F.; Sugimura, Y.; Kai, Y. *J. Biol. Chem.* **1999**, *274*, 4225−4230.

(5) (a) Inoue, T.; Gotowda, M.; Deligeer; Kataoka, K.; Yamaguchi, K.; Suzuki, S.; Watanabe, H.; Gohow, M.; Kai, Y. *J. Biochem.* **1998**, *124*, 876−879. (b) Suzuki, S.; Kataoka, K.; Yamaguchi, K.; Inoue, T.; Kai, Y. *Coord. Chem. Rev.* **1999**, *192*, 245−265.

(6) Adman, E. T. *Adv. Protein Chem.* **1991**, *42*, 145−197.

(7) Shepard, W. E. B.; Anderson, B. F.; Lewandoski, D. A.; Norris, G. E.; Baker, E. N. *J. Am. Chem. Soc.* **1990**, *112*, 7817−7819.

(8) Dodd, F. E.; Abraham, Z. H. L.; Eady, R. R.; Hasnain, S. S. *Acta Crystallogr., Sect. D* **2000**, *56*, 690−696.

(9) (a) Groeneveld, C. M.; Canters, G. W. *J. Biol. Chem.* **1988**, *263*, 167−173. (b) Groeneveld, C. M.; Ouwerling, M. C.; Erkelens, C.; Canters, G. W.; *J. Mol. Biol.* **1988**, *200*, 189−199. (c) Groeneveld, C. M.; Dahlin, S.; Reinhammer, B.; Canters, G. W. *J. Am. Chem. Soc.* **1987**, *109*, 3247−3250. (d) Canters, G. W.; Hill, H. A. O.; Kitchen, N. A.; Adman, E. T. *J. Magn. Res.* **1984**, *57*, 1−23. (e) Dahlin, S.; Reinhammer, B.; Wilson, M. T. *Biochem. J.* **1984**, *218*, 609−614. (f) Kyritsis, P.; Dennison, C.; Ingeldew, W. J.; McFarlane, W.; Sykes, A. G. *Inorg. Chem.* **1995**, *34*, 5370−5374.

(10) Solomon, E. I.; LaCroix, L. B.; Randall, D. W. *Pure Appl. Chem.* **1998**, *70*, 799−808.

(11) Randall, D. W.; Gamelin, D. R.; LaCroix, L. B.; Solomon, E. I. *J. Biol. Inorg. Chem.* **2000**, *5*, 16−29.

10.1021/ic030176c CCC: $25.00

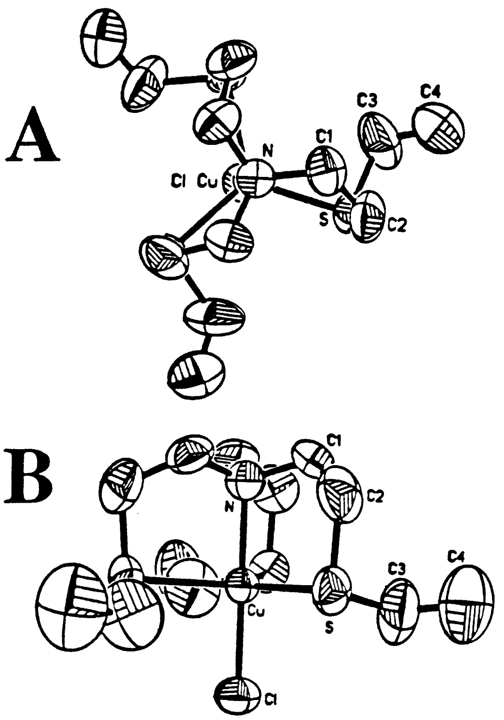
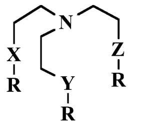


Figure 1. Typical structure of a copper−tripodal ligand complex having C_{3v} symmetry. The example shown is for the cationic unit of [Cu^{II}(TEMEA)Cl], where TEMEA is the ethyl analogue of TMMEA (the latter of which is missing the C4 atoms). View A illustrates the C_{3v} symmetry as viewed down the N−Cu−Cl axis; view B illustrates the side view. In aqueous solution, the axial Cl ion is presumed to be replaced by a coordinated water molecule. In the cationic unit of the corresponding reduced complex, [Cu^{I}(TEMEA)], the Cl atom is removed, but the structural morphology is otherwise virtually identical to that of the Cu(II) complex shown here.[18]

systems. We have recently demonstrated that macrocyclic Cu(II/I) systems which undergo minimal ligand reorganization can result in electron self-exchange rate constants which are within the same order of magnitude as the blue copper proteins—even though the coordination number changes.[12] Trigonal pyramidal or bipyramidal complexes should also minimize the geometric changes occurring in conjunction with electron transfer and, therefore, might be expected to minimize the overall reorganizational barrier. However, very few Cu(II) complexes with this geometry are known.

The best known examples of low molecular weight trigonal bipyramidal complexes with Cu(II) are those formed with tripodal ligands in which each of the three legs contains a donor atom (X, Y, or Z) that is connected to the nitrogen bridgehead by a two carbon atom bridge to form three five-membered chelate rings.[13−17]



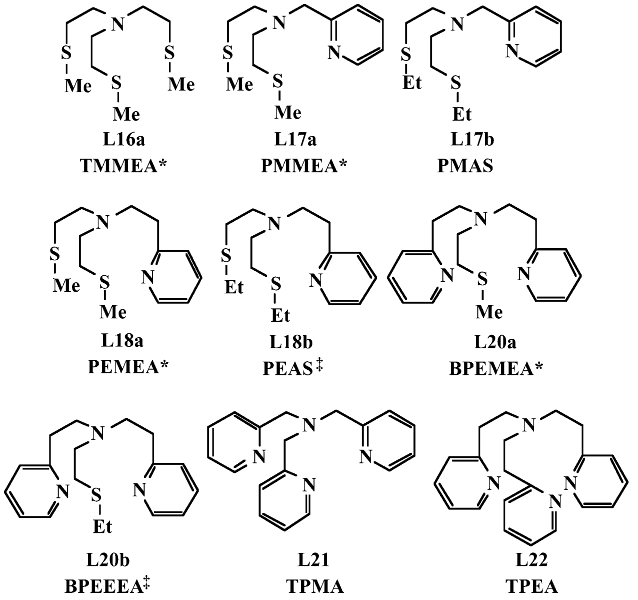


Figure 2. Ligands discussed in this work. The number designations correspond to those used in previous work.[18] Ligands marked by an asterisk designate those for which the electron-transfer kinetics of their Cu(II/I) complexes have been thoroughly studied in the current work or in a related previous study.[21] Limited kinetic studies were conducted on the electron-transfer kinetics of the Cu(II/I) complexes with the two ligands marked with a double dagger. Earlier kinetic studies were conducted by Yandell on the Cu(II/I) complexes with PMAS, PEAS, TPMA. and TPEA.[19,20]

A fifth coordination site, opposite to the bridgehead atom, is occupied by a solvent molecule or anion to generate virtual C_{3v} symmetry (Figure 1).[18] Reduction generally results in the loss of the axial solvent molecule (or anion) so that the Cu(I) complexes are trigonal pyramidal (Figure 1).[18] For tripodal ligands in which one or more legs form a six-membered chelate ring with the bridgehead nitrogen, the Cu(II) complexes tend to lose their virtual C_{3v} symmetry and adopt a square pyramidal geometry in which the donor atom in the longer leg occupies the axial site, while the four planar sites are occupied by the bridgehead nitrogen, the donor atoms on the other two legs, and a solvent molecule or anion.[14] No previous study has been made to compare the effects, if any, of this coordination change upon the resulting electron-transfer kinetic behavior.

It was originally anticipated that rapid electron-transfer kinetics might be exhibited for Cu(II/I)−tripodal ligand complexes since the changes in coordination geometry accompanying oxidation and reduction appear to be relatively small. However, in kinetic studies on the reduction of four closely related Cu(II)−tripodal ligand complexes (L = PMAS, PEAS, TPMA, TPEA—see Figure 2) with cytochrome *c* (A_{Red}), Yandell[19,20] calculated Cu$^{II/I}$L electron self-exchange rate constants (k_{11}) which were within the narrow range of 46−71 M^{-1} s^{-1} for three of these systems, while

---

(12) Krylova, K.; Kulatilleke, C. P.; Heeg, M. J.; Salhi, C. A.; Ochrymowycz, L. A.; Rorabacher, D. B. *Inorg. Chem.* **1999**, *38*, 4322−4328.

(13) Karlin, K. D.; Dahlstrom, P. L.; Zubieta, J. *Transition Met. Chem. (Weinheim, Ger.)* **1981**, *6*, 314−315.

(14) Karlin, K. D.; Hayes, J. C.; Juen, S.; Hutchinson, J. P.; Zubieta, J. *Inorg. Chem.* **1982**, *21*, 4106−4108.

(15) Nishida, Y.; Takahashi, K. *Mem. Faculty Sci., Kyushu Univ., Ser. C* **1982**, *13*, 335−342.

(16) Nishida, Y.; Takahashi, K. *Inorg. Chem.* **1988**, *27*, 1406−1410.

(17) Nagao, H.; Komeda, N.; Mukaida, M.; Suzuki, M.; Tanaka, K. *Inorg. Chem.* **1996**, *35*, 6809−6815.

(18) Ambundo, E. A.; Deydier, M.-V.; Grall, A. J.; Aguera-Vega, N.; Dressel, L. T.; Cooper, T. H.; Heeg, M. J.; Ochrymowycz, L. A.; Rorabacher, D. B. *Inorg. Chem.* **1999**, *38*, 4233−4242.

k_{11} for the fourth system (L = PEAS) was 100-fold smaller at 0.7 M^{-1} s^{-1}.

$$\mathrm{Cu^{II}L} + \mathrm{A_{Red}} \underset{k_{21}}{\overset{k_{12}}{\rightleftharpoons}} \mathrm{Cu^{I}L} + \mathrm{A_{Ox}} \tag{1}$$

$$\mathrm{{}^{*}Cu^{II}L} + \mathrm{Cu^{I}L} \overset{k_{11}}{\rightleftharpoons} \mathrm{{}^{*}Cu^{I}L} + \mathrm{Cu^{II}L} \tag{2}$$

In a recent thorough study on both the reduction and oxidation kinetics of $Cu^{II/I}$(TMMEA) (Figure 2) with a number of counter reagents,[21] we obtained an even smaller self-exchange rate constant on the basis of reduction reactions ($k_{11} \approx 0.04$ M^{-1} s^{-1}), but the corresponding value obtained from oxidation reactions was 2.5 orders of magnitude larger. The differing behavior for reduction and oxidation was considered to arise from the dual-pathway mechanism which we have previously proposed for Cu(II/I) macrocyclic ligand complexes,[22−25] although the relative k_{11} values for the two pathways were reversed in the case of the $Cu^{II/I}$(TMMEA) system. These intriguing results indicated that studies on additional Cu(II/I) tripodal ligand complexes, including those with and without virtual C_{3v} symmetry, were merited.

In this work, we have examined both the reduction and oxidation kinetics of the Cu(II/I) complexes with the methyl analogues of PMAS and PEAS—designated as PMMEA and PEMEA. We have also included a dipyridyl analogue of the latter ligand, designated as BPEMEA (Figure 2). To provide an internal check on the consistency of the resulting calculated k_{11} values, each system was reacted with three reducing and two or three oxidizing reagents known to promote outer-sphere electron transfer. A limited reduction kinetic study and a single oxidation study were also conducted on $Cu^{II/I}$(PEAS) for comparison to Yandell's earlier data (which involved reduction only), and a single reduction study was also carried out on the ethyl analogue of Cu^{II}(BPEMEA), namely, Cu^{II}(BPEEEA) (Figure 2).

Experimental Section

Reagents. The syntheses of all tripodal ligands discussed in this work have been previously described.[18] Copper perchlorate and sodium perchlorate were prepared by adding $HClO_4$ to $CuCO_3$ and Na_2CO_3, respectively, followed by recrystallization.[26] (*Warning! Perchlorate salts are potentially explosive and should be handled with care in small quantities. They should never be heated to dryness!*) The preparative methods utilized for all counter reagents have been previously reported.[23] For studies in which pH was controlled in the region of pH 4.5−5.5, PIPBS (piperazine-*N*,*N*′-bis(4-butanesulfonic acid) (GFS Chemical Co., Powell, OH) was used as a buffer since this compound has been demonstrated not to complex with Cu(II) ion.[27,28] Preliminary studies were also conducted using borate−mannitol mixtures and MES (2-morpholinoethanesulfonic acid—also obtained from GFS Chemical Co.) as buffer systems.

Table 1. Physical Parameters for the Tripodal Ligands Discussed in This Work and Their Copper(II/I) Complexes in Aqueous Solution at 25 °C and $\mu = 0.10$ ($NaClO_4$) (Data from Ref 21)

ligand	E^f (vs SHE)[a]	log K_{H1}^{m} [b]	log K_{H2}^{m} [b]	log $K_{Cu^{II}L}$	log $K_{Cu^{I}L}$
TMMEA (L16a)	0.692	8.36	NA	6.29	15.80
PMMEA (L17a)	0.384	6.53	<2	11.06	15.36
PMAS (L17b)	0.397	6.56	<2	10.48	15.00
PEMEA (L18a))	0.595	7.33	3.26	7.89	15.76
PEAS (L18b)	0.607	7.35	3.21	7.87	15.94
BPEMEA (L20a)	0.457	7.66	3.74[c]	9.10	14.63
BPEEEA (L20b)	0.471	7.78	3.81[d]	9.20	14.97
TPMA (L21)	−0.147[e]	6.24	4.41[f]	17.59	12.9
TPEA (L22)	0.51	8.21	3.94[g]	9.35	15.8

[a] All potentials (V) were experimentally referenced against ferroin (0.05 M KCl) as an external standard and corrected to SHE on the basis of a ferroin potential value of $E^f = 1.112$ V.[22] [b] The K_{H1}^{m} and K_{H2}^{m} values represent the stepwise ligand mixed-mode protonation constants: e.g., $K_{H1}^{m} = [HL^{+}]/(a_{H+}[L])$, where a_{H^+} is the activity of hydrogen ion in solution. [c] For BPEMEA, log $K_{H3}^{m} = 2.38$. [d] For BPEEEA, log $K_{H3}^{m} = 2.58$. [e] Baek, H.; Holwerda, R. A. *Inorg. Chem.* **1983**, *22*, 3452−3456. [f] For TPMA, log $K_{H3}^{m} = 2.57$, log $k_{H4}^{m} = <2$. [g] For TPEA, log $K_{H3}^{m} = 3.51$, log $K_{H4}^{m} = <2$.

Solutions. All solutions were prepared using conductivity-grade distilled−deionized water. The concentration of the tripodal ligand solutions were determined by potentiometric titration against $Hg(ClO_4)_2$ solutions using a mercury pool indicating electrode. For the kinetic studies, excess $Cu(ClO_4)_2$ was added to the ligand to ensure complete complexation. Solutions of $Cu^{I}L$ were prepared by adding copper shot to standardized $Cu^{II}L$ solutions and letting them sit under a nitrogen atmosphere with stirring for approximately 2 h. The concentrations of all counter reagent solutions were determined spectrophotometrically as described previously.[23] Ionic strength was maintained at 0.10 M with either $HClO_4$ or $NaClO_4$.

Kinetic Measurements. All kinetic measurements were made using a Durrum D-110 stopped-flow spectrophotometer interfaced to a personal computer. The temperature of the solutions was maintained at 25.0 ± 0.2 °C using a circulating water bath. The kinetic data were analyzed using software developed in house, designed specifically to treat reactions which did not proceed to completion.[29]

Results

Electron-Transfer Kinetic Studies. For all tripodal ligands discussed in this study, the ligand protonation constants, $Cu^{II}L$ stability constants, $Cu^{II/I}L$ formal potential values, and calculated $Cu^{I}L$ stability constants were determined in a previous study[18] and are listed in Table 1. In all cases, the ligands exhibit at least a 10^6-fold preference for Cu(I) relative to H^+ so that the reduced complexes are fully formed even at pH 1.0. However, the $Cu^{II}L$ stability constants indicate that most of the oxidized species are not fully

---

(19) Karlin, K. D.; Yandell, J. K. *Inorg. Chem.* **1984**, *23*, 1184−1188.
(20) Yandell, J. K. In *Copper Coordination Chemistry: Biochemical and Inorganic Perspectives*; Karlin, K. D., Zubieta, J., Eds.; Adenine: Guilderland, NY, 1983; pp 157−165.
(21) Ambundo, E. A.; Ochrymowycz, L. A.; Rorabacher, D. B. *Inorg. Chem.* **2001**, *40*, 5133−5138.
(22) Martin, M. J.; Endicott, J. F.; Ochrymowycz, L. A.; Rorabacher, D. B. *Inorg. Chem.* **1987**, *26*, 3012−3022.
(23) Meagher, N. E.; Juntunen, K. L.; Salhi, C. A.; Ochrymowycz, L. A.; Rorabacher, D. B. *J. Am. Chem. Soc.* **1992**, *114*, 10411−10420.
(24) Bernardo, M. M.; Robandt, P. V.; Schroeder, R. R.; Rorabacher, D. B. *J. Am. Chem. Soc.* **1989**, *111*, 1224−1231.
(25) Rorabacher, D. B.; Meagher, N. E.; Juntunen, K. L.; Robandt, P. V.; Leggett, G. H.; Salhi, C. A.; Dunn, B. C.; Schroeder, R. R.; Ochrymowycz, L. A. *Pure Appl. Chem.* **1993**, *65*, 573−578.
(26) Diaddario, L. L., Jr.; Ochrymowycz, L. A.; Rorabacher, D. B. *Inorg. Chem.* **1992**, *31*, 2347−2353.
(27) Yu, Q.; Kandegedara, A.; Xu, Y.; Rorabacher, D. B. *Anal. Biochem.* **1997**, *253*, 50−56.
(28) Kandegedara, A.; Rorabacher, D. B. *Anal. Chem.* **1999**, *71*, 3140−3144.
(29) Leggett, G. H.; Dunn, B. C.; Vande Linde, A. M. Q.; Ochrymowycz, L. A.; Rorabacher, D. B. *Inorg. Chem.* **1993**, *32*, 5911−5918.

Table 2. Potentials, Self-Exchange Rate Constants, and Ion Size Parameters for Counter Reagents Used in This Work (Aqueous Solution at 25 °C, $\mu = 0.10$ M)

redox couple	E^{f},[a] V (vs SHE)	$10^{-7}k_{22}$, M^{-1} s^{-1}	$10^{8}r$, cm
Ru$^{III/II}$(NH$_3$)$_5$isn	0.404	0.011[b]	3.8
Ru$^{III/II}$(NH$_3$)$_4$bpy	0.535	0.22[b]	4.4
Ru$^{III/II}$(NH$_3$)$_4$phen	0.536	0.22[b]	4.4
Ru$^{III/II}$(NH$_3$)$_2$(bpy)$_2$	0.899	8.4[b]	5.6
Fe$^{III/II}$(4,7-dmphen)$_3$	0.925	33[c]	6.6

[a] The potential values for all counter reagents were redetermined as part of this work (cf., ref 23). [b] Brown, G. M.; Sutin, N. *J. Am. Chem. Soc.* **1979**, *101*, 883−892. The k_{22} value for Ru$^{III/II}$(NH$_3$)$_4$bpy is assumed to be identical to that of the corresponding 1,10-phenanthroline complex. [c] The k_{22} value for Fe$^{III/II}$(4,7-dmphen)$_3$ is assumed to be identical to that of the corresponding 1,10-phenanthroline complex: Ruff, I.; Zimonyi, M. *Electrochim. Acta* **1973**, *18*, 515−516.

complexed at low pH values. Extensive preliminary studies were conducted on the reduction kinetics of Cu^{II}(PMMEA) and Cu^{II}(BPEMEA) to determine the potential effect of pH control on the subsequent electron-transfer kinetics. Consistent results were obtained for solutions buffered at pH 4.5−5.5 with MES, PIPBS, or borate−mannitol mixtures as well as for unbuffered solutions in which both reactant solutions were initially at pH 5. For most subsequent reduction studies, both the Cu^{II}L and counter reagent solutions were prepared at pH 4.5 or 5.0 with PIPBS buffer using 0.10 M NaClO$_4$ to control the ionic strength. In all cases, an excess of Cu(II) (≈1 mM) was also added to the Cu^{II}L solutions to ensure that the tripodal ligand was fully complexed. In the absence of counter reagents that are capable of forming inner-sphere bridged species, the excess aquated Cu(II) ion does not contribute to the observed electron-transfer kinetics[30] due to the exceptionally small self-exchange rate constant for the aquated Cu(II/I) couple.[31]

The reduction kinetics of Cu^{II}(PMMEA), Cu^{II}(PEMEA), and Cu^{II}(BPEMEA) were each studied using three counter reagents known to promote outer-sphere electron transfer: Ru^{II}(NH$_3$)$_4$phen, Ru^{II}(NH$_3$)$_4$bpy, and Ru^{II}(NH$_3$)$_5$isn (phen = 1,10-phenanthroline; bpy = 2,2′-bipyridine; isn = isonicotinamide). As shown by the reagent potentials listed in Table 2, the reactions with Cu^{II}(PMMEA) and, to a lesser extent, with Cu^{II}(BPEMEA), tended to be thermodynamically uphill so that a large excess of one reactant was added to drive the reactions toward completion. At least two separate series of kinetic runs were conducted with each reagent under these pseudo-first-order conditions, each series involving an average of five different reactant concentrations. The specific pseudo-first-order rate constants obtained experimentally (based on 8−10 duplicate runs for each set of concentrations) are provided as Supporting Information. The mean k_{12} value obtained for each individual study is listed in Table 3.

The very large stability constants for the Cu^{I}L complexes made it possible to carry out the oxidation kinetics at low pH. For these studies, the counter reagents were generally prepared in 0.10 M HClO$_4$ (or, in the case of Fe^{III}(dmphen)$_3$ and Ru^{III}(NH$_3$)$_5$isn, in 0.10 M HNO$_3$). For the preparation of the Cu^{I}L solutions, the corresponding Cu^{II}L complexes were prepared in 0.10 M NaClO$_4$ at pH 5.0 (PIPBS buffer) and reduced to Cu^{I}L over copper shot. When the two reactant solutions were mixed in the stopped-flow spectrophotometer, the acid in the counter reagent solution overwhelmed the buffer so that the final pH at which the electron-transfer kinetics were conducted was approximately 1.3. This approach excluded the possibility of monitoring the reactions by following the appearance of Cu^{II}L since the latter complexes tend to dissociate at this low pH value. For comparative purposes, the oxidation reactions of Cu^{I}(BPEMEA) with Ru^{III}(NH$_3$)$_4$phen and Ru^{III}(NH$_3$)$_5$isn were carried out under conditions where both reactant solutions were prepared at pH 5.0. No significant difference was observed in the results.

The oxidation studies on Cu^{I}(PMMEA) and Cu^{I}(BPEMEA) were conducted using the oxidized counterparts of the reagents used for the reduction studies, that is, Ru^{III}(NH$_3$)$_5$isn, Ru^{III}(NH$_3$)$_4$bpy, and Ru^{III}(NH$_3$)$_4$phen. All studies with these reagents were conducted under pseudo-first-order conditions—generally with the Cu^{I}L complex in large excess. Due to the small driving force, many of the oxidation and reduction reactions with these two Cu(II/I) systems did not proceed to completion as reflected in the positive intercepts obtained when plotting the pseudo-first-order rate constants against the Cu^{I}L concentration. When using the same redox couple as counter reagent for both Cu^{II}L reduction and Cu^{I}L oxidation, the ratio of the second-order rate constants should

Table 3. Median Cross-Reaction Rate Constants Calculated for Cu(II/I) Tripodal Ligand Complexes Reacting with Selected Counter Reagents in Aqueous Solution at 25 °C and $\mu = 0.10$ M (ClO$_4^-$)

	$10^{-3}k_{12}$ or k_{21}, M^{-1} s^{-1} [a]				
counter reagent[b]	Cu$^{II/I}$(PMMEA)	Cu$^{II/I}$(PEMEA)	Cu$^{II/I}$(PEAS)	Cu$^{II/I}$(BPEMEA)	Cu$^{II/I}$(BPEEEA)
		Reductions			
Ru^{II}(NH$_3$)$_4$phen	0.99(3), 0.93(4)	1.79(4), 1.74(2)		0.394(7), 0.386(7)	
Ru^{II}(NH$_3$)$_4$bpy	0.54(2), 0.43(2)	1.76(10), 1.45(7)		0.221(2), 0.208(4)	
Ru^{II}(NH$_3$)$_5$isn	2.09(6), 2.51(8)	12.0(1), 9.2(8), 10.5(4)	10.8(3)	0.817(5), 0.72(2)	1.05(4)
		Oxidations			
Ru^{III}(NH$_3$)$_5$isn	3.0(2), 2.7(1)			1.6(4), 1.4(1)	
Ru^{III}(NH$_3$)$_4$bpy	59(1), 60(2)			32(2)	
Ru^{III}(NH$_3$)$_4$phen	150(5), 134(11)			26(4), 23(1)	
Ru^{III}(NH$_3$)$_2$(bpy)$_2$		2.7(3) × 10^3	3.2(1) × 10^3		
Fe^{III}(4,7-dmphen)$_3$		3.4(2) × 10^3, 3.1(4) × 10^3			

[a] The number in parentheses following each rate constant value represents the standard deviation in terms of the last digit(s) shown; e.g., 0.99(4) and 1.76(10) represent 0.99 ± 0.04 and 1.76 ± 0.10, respectively. Multiple values represent the results of two or more indpendent studies. [b] For all reactions, the absorbance of the counter reagent (either the reactant or product species) was monitored using the following wavelengths and molar absorptivity values, respectively: Ru^{II}(NH$_3$)$_4$phen, 471 nm, 7570 M^{-1} cm^{-1}; Ru^{II}(NH$_3$)$_4$bpy, 522 nm, 2980 M^{-1} cm^{-1}; Ru^{II}(NH$_3$)$_5$isn, 478 nm, 11 900 M^{-1} cm^{-1}; Ru^{III}(NH$_3$)$_2$(bpy)$_2$, 488 nm, 9390 M^{-1} cm^{-1}; Fe^{II}(4,7-dmphen)$_3$, 512 nm, 14 000 M^{-1} cm^{-1}.

Table 4. Electron Self-Exchange Rate Constants Calculated from the Cross Reactions of Cu(II/I) Tripodal Ligand Complexes with Selected Counter Reagents in Aqueous Solution at 25 °C and $\mu = 0.10$ M (ClO_4^-)

counter reagent	$Cu^{II/I}$(TMMEA)[a]	$Cu^{II/I}$(PMMEA)	$Cu^{II/I}$(PEMEA)	$Cu^{II/I}$(PEAS)	$Cu^{II/I}$(BPEMEA)	$Cu^{II/I}$(BPEEEA)
	log k_{11}, M^{-1} s^{-1}					
			Reductions			
$Ru^{II}(NH_3)_4$phen	−1.28	2.15, 2.10	−1.00, −1.02		0.02, 0.01	
$Ru^{II}(NH_3)_4$bpy	−1.45	1.60, 1.40	−1.03, −1.20		−0.50, −0.55	
$Ru^{II}(NH_3)_5$isn	−1.82	1.63, 1.78	−0.23, −0.46, −0.35	- 0.51	−0.40, −0.51	−0.41
			Oxidations			
$Ru^{II}(NH_3)_5$isn		1.27, 1.15			1.96, 1.85	
$Ru^{II}(NH_3)_4$bpy		0.60, 0.61			1.21	
$Ru^{II}(NH_3)_4$phen		1.40, 1.30			1.01, 0.90	
$Ni^{III}([14]aneN_4)(H_2O)_2$	1.32					
$Ru^{III}(NH_3)_2(bpy)_2$	1.27		0.27	0.60		
Fe^{III}(4,7-dmphen)$_3$	0.93		−0.45, −0.53			

[a] Values for $Cu^{II/I}$(TMMEA) are from ref 21.

reflect the equilibrium constant for the overall reaction. In the case of the reactions involving $Cu^{II/I}$(BPEMEA) and $Ru^{III/II}(NH_3)_5$isn, however, particularly poor agreement was noted which appears to reflect a significant error in the rate constant for Cu^IL oxidation with this reagent.

Due to the higher potential of Cu^I(PEMEA), $Ru^{III}(NH_3)_2(bpy)_2$ and Fe^{III}(4,7-dmphen)$_3$ (4,7-dmphen = 4,7-dimethyl-1,10-phenanthroline) were selected as the counter reagents. The resulting reactions were carried out under second-order conditions (i.e., with both reactant concentrations within the same order of magnitude). The resulting second-order rate constants exceeded 10^6 M^{-1} s^{-1} but were well within the time domain accessible with our instrument.[32] The mean k_{21} values obtained with all oxidizing reagents are included in Table 3.

Discussion

Electron Self-Exchange Rate Constants. The Marcus cross relation was applied to each of the individual cross-reaction rate constants in Table 3 to obtain an apparent value for the $Cu^{II/I}L$ electron self-exchange rate constant, k_{11}:[22,23,33]

$$k_{11} = \frac{{k_{12}}^2}{k_{22}K_{12}f_{12}{W_{12}}^2} \quad k_{11} = \frac{{k_{21}}^2}{k_{22}K_{21}f_{21}{W_{21}}^2} \tag{3}$$

Here k_{22} represents the self-exchange rate constant for the counter reagent used, K_{12} (or K_{21}) represents the equilibrium constant for the cross reaction, f_{12} (or f_{21}) is a nonlinear correction term, and W_{12} (or W_{21}) is an electrostatic work term.[22,23,33] For the calculation of f and W, an ionic radius of 4.4 Å has been utilized for all $Cu^{II/I}L$ complexes. The self-exchange rate constants and ion size parameters used for the counter reagents are included in Table 2.[23]

From eq 3 it is evident that errors in the experimental k_{12} or k_{21} values become squared in the calculated k_{11} values. The k_{11} values are further affected by several experimental uncertainties including the folowing: (i) the reagent self-exchange rate constant, k_{22}; (ii) the potentials for both the $Cu^{II/I}L$ complexes and the counter reagents which are used in calculating K_{12} and K_{21}; (iii) the ion size parameters which are used in computing W_{12} and W_{21}. The use of multiple counter reagents provides a more thorough picture of the magnitude of k_{11} for each $Cu^{II/I}L$ system studied.

Table 5. Summary of Median Electron Self-Exchange Rate Constants Determined for Copper(II/I) Complexes with Tripodal Ligands on the Basis of Reduction and Oxidation Kinetic Studies in Aqueous Solution at 25 °C and $\mu = 0.10$ M[a]

complexed ligand	log $k_{11(Red)}$, M^{-1} s^{-1} [b]	log $k_{11(Ox)}$, M^{-1} s^{-1} [b]	ref
TMMEA (L16a)	−1.5	1.3	c
PMMEA (L17a)	1.7	1.2	this work
PMAS (L17b)	[1.6]		*d*, *e*
PEMEA (L18a)	−1.0	−0.1	this work
PEAS (L18b)	−0.5, [−0.2]	≈0.6	this work, *d*, *e*
BPEMEA (L20a)	−0.5	1.2	this work
BPEEEA (L20b)	−0.4		this work
TPMA (L21)	[1.8]		e
TPEA (L22)	[1.8]		e

[a] Values in brackets were determined by Yandell as referenced. [b] Values listed are the median values. [c] Reference 18. [d] Reference 19. [e] Reference 20.

Table 4 lists all the logarithmic k_{11} values calculated from the reduction and oxidation studies in this investigation. The general trends in these values are more readily envisioned by comparing the median logarithmic $k_{11(Red)}$ and $k_{11(Ox)}$ values obtained for each Cu(II/I) system as listed in Table 5. This table also includes the $k_{11(Red)}$ values previously reported by Yandell. It is apparent that, for a single Cu complex species, the calculated $k_{11(Red)}$ or $k_{11(Ox)}$ values are within one order of magnitude which is generally accepted as the range of experimental error.[34]

The nine ligands in Table 5 include three pairs which differ only in the size of the terminal alkyl groups attached to the thioether sulfur atoms, viz., (i) PMMEA and PMAS, (ii) PEMEA and PEAS, and (iii) BPEMEA and BPEEEA. The $k_{11(Red)}$ values for the systems with Cu^{II}(PMMEA) and Cu^{II}(PMAS), each of which was based on kinetic data for the reactions with three separate counter reagents, are in excellent

---

(30) Koenigbauer, M. J. Ph.D. Dissertation, Wayne State University, 1983.

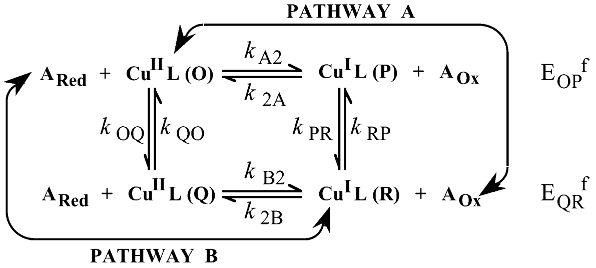
(31) Sisley, M. J.; Jordan, R. B. *Inorg. Chem.* **1992**, *31*, 2880−2884.

(32) Dunn, B. C.; Meagher, N. E.; Rorabacher, D. B. *J. Phys. Chem.* **1996**, *100*, 16925−16933.

(33) Marcus, R. A.; Sutin, N. *Biochim. Biophys. Acta* **1985**, *811*, 265−322.

(34) In a thorough analysis of a wide variety of cross reactions, it was found that most metal complexes, other than aquated and cyano complexes, yielded values within a 10-fold range of the values predicted by the Marcus relationship: Chou, M.; Creutz, C.; Sutin, N. *J. Am. Chem. Soc.* **1977**, *99*, 5615−5623.

Scheme 1



agreement. By contrast, our $k_{11(Red)}$ value for Cu^{II}(PEMEA) differed from Yandell's value for Cu^{II}(PEAS) by a factor of six. Since the latter value was based solely on the reaction with a single counter reagent (cytochrome *c*), we undertook an additional kinetic study on the reduction of Cu^{II}(PEAS) with $Ru^{II}(NH_3)_5$isn which yielded a value intermediate between the other two. All three, however, are within the accepted experimental error. The $k_{11(Red)}$ values for Cu^{II}(BPEMEA) are also in good agreement with the lone value determined for Cu^{II}(BPEEEA). On the basis of these cumulative results, we conclude that the size of the terminal group on the thioether sulfur atoms has no significant bearing on the rate of electron transfer in these $Cu^{II/I}$L complexes.

Although consistency is observed for the reduction kinetics obtained for systems involving pairs of similar ligands, large discrepancies exist among different ligand types. In particular, it is noted that the $k_{11(Red)}$ values for Cu^{II}(PMMEA), Cu^{II}(PMAS), Cu^{II}(TPMA), and Cu^{II}(TPEA) in Table 5 are nearly 100 M^{-1} s^{-1} whereas the corresponding values for the other five systems are less than unity. The difference in these self-exchange rate constants cannot be attributed to differences in coordination geometry since three of the Cu^{II}L complexes (PMMEA, PMAS, and TPMA) with larger $k_{11(Red)}$ values are trigonal bipyramidal while the fourth (TPEA) is not.[14] Moreover, Cu^{II}(TMMEA) is also trigonal bipyramidal and it exhibits the smallest $k_{11(Red)}$ value obtained in this series.

Of the more limited $k_{11(Ox)}$ data, three Cu^{I}L complexes (TMMEA, PMMEA, and BPEMEEA) yielded virtually identical values, and the $k_{11(Ox)}$ value for Cu^{I}(PEAS) agrees within experimental error, particularly considering the fact that the latter value was based on reaction with a single reagent. The smaller $k_{11(Ox)}$ value obtained for Cu^{I}(PEMEA) may be significant, but the oxidation studies on this system were generally more difficult to resolve. (Moreover, attempts to generate additional data using $Ru^{III}(NH_3)_4$bpy as the counter oxidant yielded rate constants which increased with increasing reactant concentrations, and the independent data obtained by two separate investigators were in such poor agreement that they were considered unreliable.)

In our earlier study on the $Cu^{II/I}$(TMMEA) system, we noted that the median value of $k_{11(Red)}$ was nearly three orders of magnitude smaller than the median $k_{11(Ox)}$ value. A similar, though smaller, discrepancy is apparent in the current data for $Cu^{II/ I}$(BPEMEA). This behavior is consistent with a dual-pathway (square scheme) mechanism (Scheme 1) of the type which we have proposed previously for Cu(II/I)−macrocyclic ligand complexes.[22−24] In this mechanism, Cu^{II}L(**O**) and Cu^{I}L(**R**) represent the thermodynamically stable forms of the two oxidation states and Cu^{II}L(**Q**) and Cu^{I}L(**P**) are metastable intermediates. The rate constants for the vertical reactions, k_{OQ}, k_{QO}, k_{PR}, and k_{RP}, are presumed to represent conformational changes since the intermediate species are perceived to differ from the stable species in terms of their geometric conformations. The relative stabilities of these two intermediates largely determines the favorability of the two mechanistic pathways, A and B.[35]

In nearly all of our previous studies on Cu(II/I) complexes with macrocyclic polythiaether ligands,[22−24,29,35−37] we have observed that the $k_{11(Red)}$ values for a particular system were either equal to or significantly larger than the corresponding $k_{11(Ox)}$ values. We have shown that this behavior is consistent with a situation in which intermediate **P** is more stable than **Q** so that pathway A is generally preferred. For reaction conditions in which the oxidation rate becomes more rapid than the **R** to **P** conformational change, the observed rate constant first becomes independent of the counter reagent concentration (being solely dependent on k_{RP}) and then switches to pathway B as the driving force of the reaction is increased. On the basis of these same considerations, the condition $k_{11(Red)} \ll k_{11(Ox)}$ implies that pathway B is the preferred reaction pathway; that is, intermediate **Q** is intrinsically more stable than intermediate **P**. The smaller values for $k_{11(Red)}$ are then attributable to the fact that the reduction rate has exceeded k_{OQ} and the reduction reaction has switched to pathway A. This situation is most obvious for the $Cu^{II/I}$(TMMEA) system; but it also appears to apply for the $Cu^{II/I}$(BPEMEA) for which the median $k_{11(Red)}$ and $k_{11(Ox)}$ values differ by nearly 2 orders of magnitude.

For the other tripodal ligand systems, we hypothesize that the electron-transfer rate for the reduction reactions never exceeded the rate of conformational change (i.e., k_{OQ}). Therefore, for these systems, both the $k_{11(Red)}$ and $k_{11(Ox)}$ values represent self-exchange by the same pathway—which, by analogy to the other tripodal ligand systems, is expected to be pathway B. In view of the relatively large $k_{11(Red)}$ values which Yandell reported for Cu^{II}(TPMA) and Cu^{II}(TPEA), it is presumed that these values also represent the more favorable pathway B.

Identification of pathway B as the more favorable reaction pathway has been observed previously by Takagi and coworkers[38] in Cu(II/I) systems involving bis complexes of substituted phenanthroline or bipyridyl ligands. In these complexes, the four ligand donor atoms are twisted out of

---

(35) Yu, Q.; Salhi, C. A.; Ambundo, E. A.; Heeg, M. J.; Ochrymowycz, L. A.; Rorabacher, D. B. *J. Am. Chem. Soc.* **2001**, *123*, 5720−5729.

(36) Salhi, C. A.; Yu, Q.; Heeg, M. J.; Villeneuve, N. M.; Juntunen, K. L.; Schroeder, R. R.; Ochrymowycz, L. A.; Rorabacher, D. B. *Inorg. Chem.* **1995**, *34*, 6053−6064.

(37) Wijetunge, P.; Kulatilleke, C. P.; Dressel, L. T.; Heeg, M. J.; Ochrymowycz, L. A.; Rorabacher, D. B. *Inorg. Chem.* **2000**, *39*, 2897−2905.

(38) (a) Koshino, N.; Kuchiyama, Y.; Funahashi, S.; Takagi, H. D. *Can. J. Chem.* **1999**, *77*, 1498−1507. (b) Koshino, N.; Kuchiyama, Y.; Ozaki, H.; Funahashi, S.; Takagi, H. D. *Inorg. Chem.* **1999**, *38*, 3352−3360. (c) Koshino, N.; Kuchiyama, Y.; Funahashi, S.; Takagi, H. D. *Chem. Phys. Lett.* **1999**, *306*, 291−296. (d) Koshino, N.; Itoh, S.; Kuchiyama, Y.; Funahashi, S.; Takagi, H. D. *Inorg. React. Mech.* **2000**, *2*, 93−99. (e) Itoh, S.; Funahashi, S.; Koshino, N.; Takagi, H. D. *Inorg. Chim. Acta* **2001**, *324*, 252−265.

plane so that they are predisposed to move into a tetrahedral geometry upon reduction to Cu(I). In the Cu^{II}(TMMEA) complex, the four ligand donor atoms also occupy sites approximating a tetrahedral arrangement. We assume that it is this prearrangement of the Cu(II) coordination sphere which facilitates the formation of intermediate **Q**, thereby favoring pathway B.

The k_{11} values representative of pathway A, as determined in this work, are consistently smaller than corresponding values determined previously for Cu(II/I) complexes with macrocyclic ligands[22−24,29,35−37] despite the fact that the change in coordination geometry appears to be relatively small for the tripodal ligand systems. In the larger macrocyclic complexes, we have concluded that electron transfer is accompanied by the inversion of two donor atoms and we have proposed that one or both donor atom inversions are involved in the formation of the metastable intermediates.[35,39] Since no donor atom inversion is required upon electron transfer in the tripodal ligand complexes, the slow electron-transfer kinetics must be attributed to other reorganizational factors. As we have noted in our previous study on $Cu^{II/I}$(TMMEA),[21] the dominant reorganizational contribution accompanying electron transfer in complexes with C_{3v} symmetry is postulated to be the loss or gain of the solvent molecule at the axial site opposite the nitrogen bridgehead. Those Cu(II) tripodal ligand complexes which exhibit square pyramidal geometries also have a coordinated water molecule, although it is within the plane.[40] We have previously hypothesized[21] that it is the rupture/formation of this $Cu-OH_2$ bond— and the accompanying solvent reorganization— which is a major contributor to the small k_{11} values, a suggestion made earlier by Karlin and Yandell on the basis of their more limited studies on $Cu^{II/I}$(PMAS) and $Cu^{II/I}$(PEAS).[19] However, in a recent study on Cu^{II}(TPMA)(H_2O), van Eldik and co-workers have reported that the axially coordinated water is exchanged very rapidly with solvent (k_{ex} = (8.6 × 10^6 s^{-1})—an observation which implies that this cannot represent a significant barrier to the electron-transfer process.[41] Takagi and co-workers have suggested that, instead, electronic factors may represent the dominant energy barrier in Cu(II/I) electron-transfer reactions of such species.[38e] It is not apparent why such factors should be larger in the case of the tripodal ligand complexes than in previous Cu(II/I) systems which exhibit much larger self-exchange rate constants.

It should be noted that unusually slow electron-transfer kinetics have been reported for other Cu(II/I) complexes. Stanbury and co-workers have recently reported two Cu(II/I) systems which exhibit exceptionally small k_{11} values (0.16 and 0.01 M^{-1} s^{-1})[42,43] despite the fact that both complexes were also expected to undergo very small changes in coordination geometry. At least one (and perhaps both) of the Cu(II) complexes was presumed by the authors to involve no inner-sphere solvent molecules. Thus, at this juncture, it must be acknowledged that the reorganizational barriers governing Cu(II/I) electron transfer are still imperfectly understood.

Acknowledgment. This work was supported by the National Science Foundation under Grant CHE-9817919.

Supporting Information Available: Tables of experimental rate constants for all electron-transfer cross reactions. This material is available free of charge via the Internet at http://pubs.acs.org.

IC030176C

---

(39) Villeneuve, N. M.; Schroeder, R. R.; Ochrymowycz, L. A.; Rorabacher, D. B. *Inorg. Chem.* **1997**, *36*, 4475−4483.

(40) Alilou, E. H.; Hallaoui, A. E.; Ghadraoui, E. H. E.; Giorgi, M.; Pierrot, M.; Reglier, M. *Acta Crystallogr., Sect. C* **1997**, *53*, 559−562.

(41) Neubrand, A.; Thaler, F.; Körner, M.; Zahl, A.; Hubbard, C. D.; van Eldik, R. *J. Chem. Soc., Dalton Trans.* **2002**, 957−961.

(42) Xie, B.; Elder, T.; Wilson, L. J.; Stanbury, D. M. *Inorg. Chem.* **1999**, *38*, 12−19.

(43) Xie, B. P.; Wilson, L. J.; Stanbury, D. M. *Inorg. Chem.* **2001**, *40*, 3606−3614.