Electron-Transfer Kinetics of Tris(2-(methylthioethyl))aminecopper(II/I). A Tripodal Ligand Complex Exhibiting Virtual C_{3v} Symmetry

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

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

Received September 8, 2000

The tripodal ligand TMMEA (tris(2-methylthioethyl)amine) forms a trigonal bipyramidal complex with copper(II) in which the bridgehead nitrogen occupies one axial site, a solvent molecule (or anion) occupies the opposite axial site, and the three thioether sulfurs occupy the three planar sites. Upon reduction to copper(I), the axial solvent molecule (or anion) dissociates to leave a trigonal pyramidal complex with shortened Cu−S bonds and an elongated Cu−N bond. Therefore, both oxidation states maintain virtual C_{3v} symmetry similar to that found in the type 1 blue copper protein sites. The electron-transfer cross-reaction rate constants have been determined for the $Cu^{II/I}$(TMMEA) system reacting with three reductants and three oxidants. The Marcus cross relation was then utilized to generate apparent values for the Cu(II/I) electron self-exchange rate constant (k_{11}) from the kinetic data for each of the six reactions. The median value obtained from the three reduction reactions is log $k_{11(\mathrm{Red})} = -1.5$ while the median from the three oxidation reactions is log $k_{11(\mathrm{Ox})} = +0.9$. This difference of 2.4 orders of magnitude is consistent with the dual-pathway square scheme mechanism which we have previously proposed for electron transfer in Cu(II/I) complexes. For this tripodal ligand system, however, the pathway involving a metastable $Cu^{II}L$ intermediate (pathway B) appears to be preferred over the pathway involving a metastable $Cu^{I}L$ intermediate (pathway A), which is opposite to the trend we have previously observed for a number of systems involving macrocyclic and acyclic tetrathiaethers. Both pathways exhibit relatively sluggish electron-transfer kinetics which is attributed to the rupture/formation of the strongly bound inner-sphere water molecule and the accompanying solvent reorganization.

Introduction

Many investigators have attributed the rapid electron-transfer rates exhibited by the type 1 copper site of blue copper proteins to its unusual coordination geometry. In plastocyanins[2,3] and nitrite reductases,[4] the copper atom sits in an elongated trigonal pyramidal coordination environment in which the donor atoms in the trigonal plane consist of two unsaturated nitrogens (from histidine residues) and a thiolate sulfur (from cysteine) while a thioether sulfur (from methionine) serves as the axial donor atom. In azurins,[5−7] the same coordination environment is observed with the addition of a glycine oxygen at the opposite apical site to generate a trigonal bipyramidal geometry. In both cases, the copper site maintains virtual C_{3v} symmetry in both the oxidized and reduced states.

Recently, Solomon and co-workers[8,9] have concluded that the rapid electron-transfer rates of such 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 fact that coordination geometry can play a major role in influencing the electron-transfer rates of copper(II/I) systems has recently been demonstrated in our laboratory[10] for a series of macrocyclic tetrathiaether complexes in which constrained metastable intermediate species have been shown to undergo very rapid electron-transfer kinetics. For these macrocyclic tetrathiaether systems, the donor atoms tend to occupy planar sites around copper(II) which rearrange to a tetrahedral array upon reduction to copper(I), generally requiring the inversion of two coordinated donor atoms. The intermediate species have presumably already undergone much of the change in coordination geometry, which accounts for their rapid electron transfer.

In contradistinction to the macrocyclic systems, tripodal ligands cannot place all four donor atoms into planar sites around a metal ion. Numerous crystal structures by Karlin[11,12] and others[13−15] have shown that, if all chelate rings are five-

---

* Corresponding author. E-mail: dbr@chem.wayne.edu. Fax: (313) 577−1377.

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

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

(3) 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.

(4) (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.

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

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

(7) Dodd, F. E.; Abraham, Z. H. L.; Eady, R. R.; Hasnain, S. S. *Acta Crystallogr.* **2000**, *D56*, 690−696.

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

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

(10) 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.

(11) Karlin, K. D.; Dahlstrom, P. L.; Zubieta, J. *Transition Met. Chem. (Dordrecht, Neth.)* **1981**, *6*, 314−315.

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

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

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

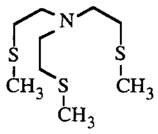
(15) Nagao, H.; Komeda, N.; Mukaida, M.; Suzuki, M.; Tanaka, K. *Inorg. Chem.* **1996**, *35*, 6809−6815.

10.1021/ic001022p CCC: \$20.00

membered, copper(II) tends to adopt a trigonal bipyramidal geometry with a solvent molecule (or anion) occupying the second axial site.[16] Upon reduction to $\mathrm{Cu^{I}L}$, the solvent molecule (or anion) tends to be lost.[17] Both oxidation states maintain virtual C_{3v} symmetry, and the overall geometric change accompanying electron transfer appears to be minor. This suggests that the reorganization energy for such C_{3v} systems could be relatively small even in the absence of the characteristic Cu−thiolate bond found in the blue copper proteins. As a result, it was surmised that the electron-transfer kinetics for such systems might be rapid.

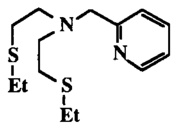
As a representative model for a tripodal ligand system, we have chosen $\mathrm{Cu^{II/I}}$(TMMEA) (TMMEA = tris(2-(methylthio-ethyl)amine) for a thorough study of its electron-transfer behavior. This system is of particular interest since, in the crystal structure for $\mathrm{[Cu^{II}(TMMEA)Br]ClO_4}$, the cation exhibits almost perfect C_{3v} symmetry with the axial position opposite to the nitrogen being occupied by the bromide ion.[13] The latter ion is presumably replaced by a solvent molecule in solution. The crystal structure for $\mathrm{[Cu^{I}(TMMEA)]ClO_4}$ shows that the axial solvent molecule (or anion) has dissociated to generate a trigonal pyramidal complex (Figure 1).[18] As shown in Table 1, some changes occur in the lengths of the remaining coordinate bonds, but the S−Cu−S and N−Cu−S bond angles remain relatively constant and the C_{3v} symmetry is maintained in both oxidation states.

TMMEA =

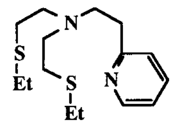


The only previous electron-transfer kinetic study involving Cu(II/I) tripodal ligand complexes is that reported by Karlin and Yandell[19] involving two ligands having an alkyl pyridine moiety and two ethylthioethyl groups attached to a nitrogen bridgehead:

PMAS =



PEAS =



The kinetic studies on these systems involved only the reduction of the $\mathrm{Cu^{II}L}$ complexes. For $\mathrm{Cu^{II}}$(PMAS), three reductants were utilized yielding calculated electron self-exchange rate constant (k_{11}) values ranging from 6 to 46 $\mathrm{M^{-1}\ s^{-1}}$. Cytochrome *c*(II) was the only reductant reacted with $\mathrm{Cu^{II}}$(PEAS) from which $k_{11} = 0.7\ \mathrm{M^{-1}\ s^{-1}}$ was calculated. These values are considerably smaller than the values obtained from reduction of most macrocyclic ligand systems.[20−24] However, it is difficult to assess the full significance of these results since no oxidation reactions were included; and numerous studies conducted in our own laboratory have indicated that the electron-transfer kinetic behavior for $\mathrm{Cu^{II/I}L}$ systems tends to differ for reduction and oxidation.[20−24]

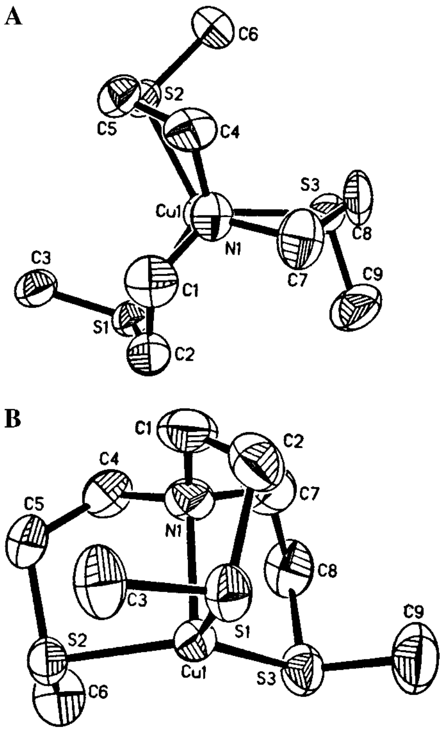


Figure 1. Crystal structure of the $\mathrm{[Cu^{I}(TMMEA)]^{+}}$ cation showing its virtual C_{3v} symmetry. (A) Top view looking down the N−Cu axis. (B) Side view from slightly underneath the $\mathrm{S_3}$ plane. The crystal structure of the $\mathrm{Cu^{II}(TMMEA)Br^{+}}$ cation is morphologically identical except for the addition of an axially coordinated bromide ion trans to the nitrogen donor atom. The latter site is presumed to be occupied by a water molecule in aqueous solution. Oxidation to Cu(II) is also accompanied by a shortening of the Cu−N bond and a lengthening of the three Cu−S bonds (Table 1).

Table 1. Average Bond Distances and Bond Angles in the Cationic Units of $\mathrm{[Cu^{I}(TMMEA)]ClO_4}$ and $\mathrm{[Cu^{II}(TMMEA)Br]ClO_4}$ (Data from Ref 18)

bond distance/angle	$\mathrm{Cu^{I}}$(TMMEA)	$\mathrm{Cu^{II}}$(TMMEA)Br
Cu−S, Å	2.26	2.38
Cu−N, Å	2.17	2.08
Cu−Br, Å		2.409
S−Cu−S, deg	120	120
N−Cu−S, deg	91.2	87
Cu displacement, Å[a]	−0.046	+0.110

[a] Displacement of the Cu atom from the $\mathrm{S_3}$ plane; a positive value represents a displacement in the direction of the apical nitrogen bridgehead donor atom.

In the current investigation, we have measured the kinetics of $\mathrm{Cu^{II/I}}$(TMMEA) electron transfer with three separate reductants ($\mathrm{A_{Red}}$) and three oxidants ($\mathrm{A_{Ox}}$):

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

The apparent $\mathrm{Cu^{II/I}L}$ self-exchange rate constant, k_{11} (eq 2), has

---

(16) If one or more six-membered chelate rings is formed, a more nearly square pyramidal geometry appears to be favored with a terminal donor of a six-membered ring occupying the axial site.

(17) Karlin, K. D.; Dahlstrom, P. L.; Stanford, M. L.; Zubieta, J. *J. Chem. Soc., Chem. Commun.* **1979**, 465−467.

(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.

(19) Karlin, K. D.; Yandell, J. K. *Inorg. Chem.* **1984**, *23*, 1184−1188.

(20) Martin, M. J.; Endicott, J. F.; Ochrymowycz, L. A.; Rorabacher, D. B. *Inorg. Chem.* **1987**, *26*, 3012−3022.

(21) Meagher, N. E.; Juntunen, K. L.; Salhi, C. A.; Ochrymowycz, L. A.; Rorabacher, D. B. *J. Am. Chem. Soc.* **1992**, *114*, 10411−10420.

(22) Leggett, G. H.; Dunn, B. C.; Vande Linde, A. M. Q.; Ochrymowycz, L. A.; Rorabacher, D. B. *Inorg. Chem.* **1993**, *32*, 5911−5918.

(23) 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.

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

been calculated from each of the experimental second-order cross-reaction rate constants. The trends in the k_{11} values are

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

consistent with our previously proposed dual-pathway square-scheme mechanism for Cu(II/I) electron transfer. However, the dominant pathway is reversed from that previously found for nearly all of the macrocyclic ligand complexes; and the k_{11} values for both pathways are surprisingly small.

Experimental Section

Reagents. The TMMEA ligand was synthesized according to the general method of Morassi and Sacconi.[25] Copper perchlorate and sodium perchlorate were prepared by adding $HClO_4$ to $CuCO_3$ and Na_2CO_3, respectively, as previously described.[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 used for all counter reagents have been previously reported.[21]

Solutions. All solutions were prepared using conductivity-grade distilled–deionized water. TMMEA was dissolved in solutions containing a large excess of $Cu(ClO_4)_2$. The concentrations of $\mathrm{Cu^{II}}$(TMMEA) complex in the solutions used for the kinetic measurements were determined spectrophotometrically using the intense S-to-Cu charge-transfer band at 374 nm ($\epsilon = 4.76 \times 10^3$ $\mathrm{M^{-1}\ cm^{-1}}$).[18] Solutions of $\mathrm{Cu^{I}}$(TMMEA) were prepared by adding copper shot to standardized $\mathrm{Cu^{II}}$(TMMEA) 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.[21] Ionic strength was maintained at 0.10 M in all solutions with $NaClO_4$, $HClO_4$, and/or $Cu(ClO_4)_2$.

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.

Results

Stability Constants, Spectra, and Formal Potential. We have recently reported the determination of several physical parameters for TMMEA and 11 closely related tripodal ligands, including (i) the ligand protonation constants, (ii) the $\mathrm{Cu^{II}L}$ stability constants, (iii) the $\mathrm{Cu^{II}L}$ visible and near-UV absorption spectra, (iv) their corresponding molar absorptivities, (v) the $\mathrm{Cu^{II/I}L}$ formal potential values, and (vi) the calculated stability constants for the corresponding $\mathrm{Cu^{I}L}$ complexes.[18,27] For the $\mathrm{Cu^{II/I}}$(TMMEA) system, the pertinent values for these parameters are as follows: (i) $K_{\mathrm{H}}{}^{\mathrm{m}} = 2.3 \times 10^8$,[28] (ii) $K_{\mathrm{Cu^{II}L}} = 1.9_5 \times 10^6$ $\mathrm{M^{-1}}$, (iii) $\lambda_{\max} = 374$ nm, (iv) $\epsilon_{\mathrm{Cu^{II}L}} = 4.76 \times 10^3$ $\mathrm{M^{-1}\ cm^{-1}}$, (v) $E^{\mathrm{f}} = 0.692$ V (vs SHE), and (vi) $K_{\mathrm{Cu^{I}L}} = 6 \times 10^{15}$ $\mathrm{M^{-1}}$.

Crystal Structures. As previously reported, the crystal structures of $[\mathrm{Cu^{I}(TMMEA)}]ClO_4$[18] and $[\mathrm{Cu^{II}(TMMEA)Br}]ClO_4$[13] indicate that both cationic units exhibit a virtual C_{3v} symmetry as illustrated in Figure 1. The average bond distances and bond angles involving the copper atom and the ligand donor atoms (Table 1) indicate that reduction of the Cu(II) ion is accompanied by a shortening of the average Cu–S bond by 0.12 Å and a lengthening of the Cu–N bond by 0.09 Å. As a result, the Cu atom moves from a position 0.11 Å above the S_3 plane (i.e., toward the apical nitrogen) in the $\mathrm{Cu^{II}}$(TMMEA)Br cation to a position 0.05 Å below the S_3 plane in $\mathrm{Cu^{I}}$(TMMEA).[18]

Reduction Kinetics. The reduction kinetics of $\mathrm{Cu^{II}}$(TMMEA) were studied using three counter reagents known to promote outer-sphere electron transfer: $\mathrm{Ru^{II}(NH_3)_4}$phen, $\mathrm{Ru^{II}(NH_3)_4}$bpy, and $\mathrm{Ru^{II}(NH_3)_5}$isn (phen = 1,10-phenanthroline; bpy = 2,2′-bipyridine; isn = isonicotinamide). Since the protonation constant for TMMEA is relatively large, the conditional stability constant for $\mathrm{Cu^{II}}$(TMMEA) decreases markedly at lower pH values. Therefore, the reaction solutions were buffered at pH 5 with PIPBS (piperazine-*N*,*N′*-bis(4-butanesulfonic acid), a buffer that has been shown not to complex with Cu(II).[29,30] Even at this pH, the conditional stability constant of $\mathrm{Cu^{II}}$(TMMEA) is calculated to be only 850 so that a large excess of Cu(II) was maintained in all $\mathrm{Cu^{II}}$(TMMEA) solutions used for reduction studies to minimize the amount of uncomplexed ligand.

The reactions were run under pseudo-first-order conditions, with $\mathrm{Cu^{II}}$(TMMEA) present in large excess. Two separate series of reactions were carried out with each reductant, the reactions being monitored by following the absorbance of the Ru(II) reagent (see Supporting Information). The integrated pseudo-first-order kinetic plots for all reduction reactions were linear, but the ratio of the pseudo-first-order rate constants (k_{obs}) to the concentration of $\mathrm{Cu^{II}}$(TMMEA) did not yield consistent values for the second-order rate constants (k_{12}), particularly in the case of the reactions with $\mathrm{Ru^{II}(NH_3)_5}$isn. This was attributed to the slow decomposition of the ruthenium reagents at pH 5, suggesting that the overall rate equation was of the form

$$-\frac{\mathrm{d[Ru^{II}]}}{\mathrm{d}t} = k_{\mathrm{obs}}[\mathrm{Ru^{II}}] \qquad (3)$$

where

$$k_{\mathrm{obs}} = k_{12}[\mathrm{Cu^{II}L}] + k_{\mathrm{d}} \qquad (4)$$

Plots of the data obtained for the reduction with $\mathrm{Ru^{II}(NH_3)_5}$isn are illustrated in Figure 2. Although the *y*-intercept values were somewhat inconsistent, such plots showed excellent linearity for all reduction reactions ($r^2 = 0.993-0.999$) yielding k_{12} as the slope. The linearity of these plots and the consistency of the k_{11} values calculated from the k_{12} values with the various Ru(II) reagents support the validity of the data treatment. The mean k_{12} value obtained in this manner with each reducing reagent is listed in Table 2.

Oxidation Kinetics. For the oxidation of $\mathrm{Cu^{I}}$(TMMEA), the reaction kinetics were studied with three oxidants including $\mathrm{Ni^{III}([14]aneN_4)(H_2O)_2}$, $\mathrm{Ru^{III}(NH_3)_2(bpy)_2}$, and $\mathrm{Fe^{III}}$(4,7-dmphen)$_3$ ([14]aneN_4 = 1,4,8,11-tetraazacyclotetradecane = cyclam; 4,7-dmphen = 4,7-dimethyl-1,10-phenanthroline). These reagents cannot be readily prepared at higher pH. However, since $\mathrm{Cu^{I}}$(TMMEA) is very stable ($K_{\mathrm{Cu^{I}L}} = 6 \times 10^{15}$),[18] the reduced complex is still fully formed at pH 1, which made it possible to study the oxidation kinetics at this low pH. The oxidation

---

(25) Morassi, R.; Sacconi, L. *Inorg. Synth.* **1976**, *16*, 174–180.

(26) Diaddario, L. L., Jr.; Ochrymowycz, L. A.; Rorabacher, D. B. *Inorg. Chem.* **1992**, *31*, 2347–2353.

(27) Although not directly related to the current work, the formation rate constants for aquated Cu(II) reacting with the unprotonated and protonated forms of TMMEA have also been determined: Ambundo, E. A.; Deydier, M.-V.; Ochrymowycz, L. A.; Rorabacher, D. B. *Inorg. Chem.* **2000**, *39*, 1171–1179.

(28) $K_{\mathrm{H}}{}^{\mathrm{m}} = [\mathrm{HL^+}]/[\mathrm{L}]a_{\mathrm{H}}$ is the mixed-mode protonation constant (where a_{H} represents hydrogen ion activity).

(29) Yu, Q.; Kandegedara, A.; Xu, Y.; Rorabacher, D. B. *Anal. Biochem.* **1997**, *253*, 50–56.

(30) Kandegedara, A.; Rorabacher, D. B. *Anal. Chem.* **1999**, *71*, 3140–3144.

Table 2. Mean Cross-Reaction Rate Constants and Calculated Self-Exchange Rate Constants for $Cu^{II/I}$(TMMEA) in Aqueous Solution at 25 °C, $\mu = 0.10$ M (ClO_4^-)

counter reagent	E^f,[a] V (vs SHE)	$10^{-7}k_{22}$, $M^{-1}\,s^{-1}$	$10^8 r$, cm	$10^{-4}k_{12}$ (or k_{21}), $M^{-1}\,s^{-1}$	calcd k_{11},[b] $M^{-1}\,s^{-1}$	log k_{11}
reductions						
$Ru^{II}(NH_3)_4$phen	0.536	0.22[c]	4.4	0.755	0.0524	−1.28
$Ru^{II}(NH_3)_4$bpy	0.535	0.22[c]	4.4	0.63	0.035	− 1.45
$Ru^{II}(NH_3)_5$isn	0.404	0.011[c]	3.8	1.03	0.0152	−1.82
oxidations						
Ni^{III}([14]aneN$_4$)$(H_2O)_2$	1.00	0.00010[d]	3.6	5.2	20.7	1.32
$Ru^{III}(NH_3)_2(bpy)_2$	0.899	8.4[c]	5.6	≈70[e]	≈2.8	≈0.45
Fe^{III}(4,7-dmphen)$_3$	0.925	33[f]	6.6	340	8.51	0.93

[a] The potential values for all counter reagents were redetermined in this work (cf. ref 21). [b] All k_{11} values were calculated from the Marcus cross relation using the following parameters for $Cu^{II/I}$(TMMEA): $E^f = 0.692$ V (vs SHE), $r = 4.4 \times 10^{-8}$ cm. [c] Brown, G. M.; Sutin, N. *J. Am. Chem. Soc.* **1979**, *101*, 883−892. The k_{22} value for $Ru^{II}(NH_3)_4$bpy is assumed to be identical to that of the corresponding 1,10-phenanthroline complex. [d] Fairbank, M. G.; Norman, P. R.; McAuley, A. *Inorg. Chem.* **1985**, *24*, 2639−2644. [e] Value listed is the approximate limiting value obtained at larger concentrations of the counter reagent. [f] The k_{22} value for Fe^{III}(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.

reaction with the Ni(III) reagent was conducted under pseudo-first-order conditions with Cu^IL in excess. Only a few kinetic runs were measured with this reagent with reasonable consistency being obtained. The reactions with the Ru(III) and Fe(III) reagents exhibited k_{21} values in the range of 10^6 $M^{-1}\,s^{-1}$ or above. These rapid reactions were run under second-order conditions with three series of kinetic runs conducted with each reagent. For the oxidation with $Ru^{III}(NH_3)_2(bpy)_2$, the k_{21} values decreased as the reagent concentration increased (see Supporting Information), but appeared to approach a limiting constant value as the counter reagent concentration was increased to 2−3 times the Cu^I(TMMEA) concentration. This behavior suggests that the concentration of the Ru(III) reagent (based on the concentration of the initial Ru(II) solution) was somewhat in error; that is, the initially prepared Ru(II) complex was incompletely oxidized. The impact of such an error on the kinetic calculations should diminish as excess Ru(III) is added, so that the limiting k_{21} value obtained at higher Ru(III) reagent concentrations is presumed to represent a reasonable approximation of the true rate constant. Nonetheless, the kinetic data obtained using $Ru^{III}(NH_3)_2(bpy)_2$ are considered to be less reliable than with the other two reagents. The mean k_{21} value obtained with each oxidizing reagent is included in Table 2.

Discussion

Electron Self-Exchange Rate Constants. The Marcus cross relation was applied to each of the individual cross-reaction rate constants to obtain an apparent value for the $Cu^{II/I}$(TMMEA) electron self-exchange rate constant, k_{11}:[20,21,31]

$$k_{11} = \frac{{k_{12}}^2}{k_{22}K_{12}f_{12}{W_{12}}^2} \quad \text{or} \quad k_{11} = \frac{{k_{21}}^2}{k_{22}K_{21}f_{21}{W_{21}}^2} \qquad (5)$$

where 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 term, and W_{12} (or W_{21}) is an electrostatic work term.[20,21,31] For the calculation of f and W, an ionic radius of 4.4 Å has been utilized for the $Cu^{II/I}$(TMMEA) complex with $E^f = 0.692$ V. The potentials, self-exchange rate constants, and ion size parameters used for all of the counter reagents are included in Table 2.[21]

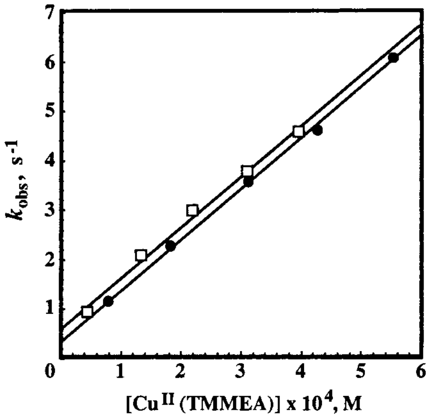


Figure 2. Plot of experimental pseudo-first-order rate constants, k_{obs}, for the reduction of Cu^{II}(TMMEA) with $Ru^{II}(NH_3)_5$isn as a function of the Cu^{II}(TMMEA) concentration. The solid circles represent data from series I ($r^2 = 0.999$) for which the slope is $k_{12} = (1.03 \pm 0.02) \times 10^4$ $M^{-1}\,s^{-1}$ while the intercept $= 0.30 \pm 0.07$ s^{-1} represents the apparent rate constant contribution due to the autodegradation of the Ru(II) reagent under the experimental conditions used (pH 5.0). The open squares represent data from series II ($r^2 = 0.995$) for which $k_{12} = (1.02 \pm 0.04) \times 10^4$ $M^{-1}\,s^{-1}$, intercept $= 0.60 \pm 0.11$ s^{-1}.

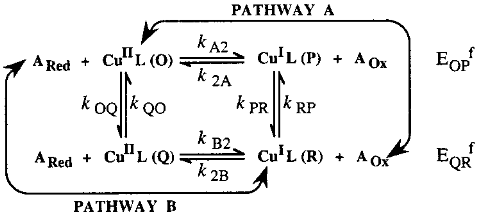
As listed in Table 2, the electron self-exchange rate constants determined for the three reduction reactions, $k_{11(Red)}$, cover a 3.5-fold range, well within the limits of experimental error considering the number of variables involved. The median value obtained is log $k_{11(Red)} = -1.5$. Similarly, the k_{11} values from the three oxidation reactions, $k_{11(Ox)}$, agree within a 7.3-fold range, with a median value of log $k_{11(Ox)} = +0.9$. Although both the reduction and oxidation reactions yield results which are internally consistent, it is evident that the median $k_{11(Red)}$ and $k_{11(Ox)}$ values differ by 2.4 orders of magnitude, well beyond the limits of experimental error. Such behavior is consistent with a dual-pathway (square-scheme) mechanism (Scheme 1)[20,21,32] of the type which we have proposed previously for the Cu(II/I)−macrocyclic ligand complexes. In this mechanism, $Cu^{II}L$(**O**) and Cu^IL(**R**) represent the thermodynamically stable forms of the two oxidation states, and $Cu^{II}L$(**Q**) and Cu^IL(**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

---

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

(32) Bernardo, M. M.; Robandt, P. V.; Schroeder, R. R.; Rorabacher, D. B. *J. Am. Chem. Soc.* **1989**, *111*, 1224−1231.

Scheme 1



geometric conformations. The relative stabilities of these two intermediates largely determine the favorability of the two mechanistic pathways, A and B.[10]

As we have noted in previous discussions of this specific mechanism,[33] the condition $k_{11(\mathrm{Red})} \ll k_{11(\mathrm{Ox})}$ implies that pathway B is the preferred reaction pathway, that is, intermediate **Q** is intrinsically more stable than intermediate **P**. For oxidation reactions, the electron-transfer step, k_{2B}, precedes the conformational change, k_{QO}, so that pathway B applies in all cases.[34] For very slow reduction reactions, the same pathway should apply as long as species $Cu^{II}L$(**O**) and $Cu^{II}L$(**Q**) are fully equilibrated. However, as the rate of reduction increases (due to an increase in driving force), conversion of $Cu^{II}L$(**O**) to $Cu^{II}L$(**Q**) could become rate-limiting, which would result in the appearance of first-order behavior, independent of the counter reagent concentration.[21] Eventually, the rate of reaction via pathway A will become dominant and the reaction will again become second order but with a different characteristic k_{11} value. All reduction reactions included in the current study appeared to be second order (i.e., first order with respect to each reactant), which implies that the latter condition pertains. Therefore, we conclude that the $k_{11(\mathrm{Red})}$ values represent pathway A while the $k_{11(\mathrm{Ox})}$ values represent the more favorable pathway B.

Effect of Chloride Anion. An earlier study conducted in our laboratory on the reduction of Cu^{II}(TMMEA) with $Ru^{II}(NH_3)_4$-phen under pseudo-first-order conditions at pH 5 yielded $k_{12} = 4.9 \times 10^3$ M^{-1} s^{-1}.[35] This value is reasonably consistent with the data from the current study. However, the corresponding study on the oxidation of excess Cu^{I}(TMMEA) with Ni^{III}([14]-aneN_4)$(H_2O)_2$ yielded $k_{21} = 5.9 \times 10^5$ M^{-1} s^{-1},[35] which is an order of magnitude larger than the k_{21} values listed for this reagent in Table 2. Examination of the conditions under which these earlier studies were conducted revealed that the TMMEA sample used at that time was the HCl salt. Since neither the inner-coordination sphere of Cu^{I}(TMMEA) nor that of the Ni(III) reagent are coordinatively saturated, it is probable that the small amount of chloride introduced with the ligand (0.05−0.4 mM) was sufficient to promote an inner-sphere pathway via chloride bridging. Copper(II/I) systems are particularly sensitive to accelerated inner-sphere electron transfer if potentially bridging ligands are available in solution since the axial inner- sphere sites on Cu(II) tend to be very labile and the inner-coordination sphere of Cu(I) can be readily expanded.[36,37]

Conclusions

In our previous Cu(II/I) electron-transfer studies involving macrocyclic tetrathiaether ligand complexes, pathway A has generally been identified as the more favorable reaction path. However, pathway B appears to be the preferred path for two recently studied Cu(II/I) complexes in which a macrocyclic tetrathiaether ligand has been constrained by peripheral substitution so that its four donor atoms are twisted out-of-plane toward a slightly tetrahedral arrangement.[10] Takagi and co-workers have also recently identified pathway B as the preferred path for several Cu(II/I) complexes with substituted phenanthrolines in which the Cu(II) complexes are distorted toward a more tetrahedral arrangement.[38−41] In the current study, the distortion of the Cu^{II}(TMMEA) complex away from a tetragonal or square pyramidal geometry is also presumed to facilitate the formation of intermediate **Q**, thereby favoring pathway B.

In the larger macrocyclic complexes, we have previously concluded that the overall electron-transfer process involves 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.[10,42] In the $Cu^{II/I}$(TMMEA) system, no donor atom inversion is required upon electron transfer. Instead, the major coordination change accompanying electron transfer appears to be the loss or gain of a tightly bound solvent molecule, a process which would be expected to occur as a concerted process with the electron-transfer step, rather than as a discrete sequential step. Therefore, the factors which bring about a change from pathway B to pathway A for the reduction reactions are unclear at this time.

For both pathways A and B, the k_{11} values determined in this work are significantly smaller than those found previously for pathway A in the electron-transfer reactions of the Cu(II/I) complexes with the previously studied macrocyclic tetrathiaether ligands.[20−24] It is likely that *for both pathways* the rupture/formation of the copper−water bond—as well as the accompanying solvent reorganization—is a significant contributor to the small k_{11} values as suggested earlier by Karlin and Yandell on the basis of their studies on $Cu^{II/I}$(PMAS) and $Cu^{II/I}$(PEAS).[19] This is consistent with our observation that Cu(II/I) systems in which the change in oxidation state is accompanied by the rupture/formation of two strongly bound water molecules exhibit even slower electron-transfer kinetics.[43] In fact, the fully aquated Cu(II/I) system has been reported by Sisley and Jordan to be exceptionally slow with $k_{11} = 5 \times 10^{-7}$ M^{-1} s^{-1}.[37] (It is worth noting that the rapidly reacting type 1 Cu sites in blue copper proteins are in a hydrophobic environment.) Even when inner-sphere solvent gain or loss is not an obvious issue, however,

---

(33) 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.

(34) See the theoretical discussions for the behavior of reactions conforming to this type of mechanism: Brunschwig, B. S.; Sutin, N. *J. Am. Chem. Soc.* **1989**, *111*, 7454−7465.

(35) Cooper, T. H. Ph.D. Dissertation, Wayne State University, 1989.

(36) Such chloride bridging is suspected to be responsible for the observation by Swaddle and co-workers that the k_{11} value for bis-(2,9-dimethyl-1,10-phenanthroline)copper(II/I) appeared to be much larger in aqueous solution than in nonaqueous solvents, since only the aqueous study involved the use of the chloride salt of Cu(II): Doine, H.; Yano, Y.; Swaddle, T. W. *Inorg. Chem.* **1989**, *28*, 2319−2322.

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

(38) Koshino, N.; Kuchiyama, Y.; Funahashi, S.; Takagi, H. D. *Chem. Phys. Lett.* **1999**, *306*, 291−296.

(39) Koshino, N.; Kuchiyama, Y.; Ozaki, H.; Funahashi, S.; Takagi, H. D. *Inorg. Chem.* **1999**, *38*, 3352−3360.

(40) Koshino, N.; Kuchiyama, Y.; Funahashi, S.; Takagi, H. D. *Can. J. Chem.* **1999**, *77*, 1498−1507.

(41) Koshino, N.; Itoh, S.; Kuchiyama, Y.; Funahashi, S.; Takagi, H. D. *Inorg. React. Mech.* **2000**, *2*, 93−99.

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

(43) The electron self-exchange rate constant for $Cu^{II/I}([9]aneS_3)(H_2O)_x$ {-[9]aneS_3 = 1,4,7-trithiacyclononane; $x = 3$ for Cu(II), $x = 1$ for Cu(I)} appears to be less than 10^{-1} M^{-1} s^{-1}: Kandegedara, A.; Krylova, K.; Nelson, T. J.; Schroeder, R. R.; Ochrymowycz; L. A.; Rorabacher, D. B., submitted for publication.

several Cu(II/I) systems involving relatively minor changes in the copper coordination sphere also exhibit surprisingly small k_{11} values, as has been reported by Stanbury, Wilson, and co-workers,[44,45] by Lappin and Peacock,[46] and by Swaddle and co-workers.[47] In combination with the current study, these observations serve to emphasize the fact that the magnitude of the reorganizational barriers involved in Cu(II/I) systems cannot be simply deduced from a gross examination of their relative morphology.

Acknowledgment. This work was supported by the National Science Foundation under Grant CHE-9817919. The authors thank Dr. Mary Jane Heeg for providing the ORTEP drawings in Figure 1.

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

IC001022P

---

(44) Xie, B.; Elder, T.; Wilson, L. J.; Stanbury, David M. *Inorg. Chem.* **1999**, *38*, 12−19. Cf.: Knapp, S.; Keenan, T. P.; Zhang, X.; Fikar, R.; Potenza, J. A.; Schugar, H. J. *J. Am. Chem. Soc.* **1990**, *112*, 3452−3464.

(45) Flanagan, S.; Dong, J.; Haller, K.; Wang, S.; Scheidt, W. R.; Scott, R. A.; Webb, T. R.; Stanbury, D. M.; Wilson, L. J. *J. Am. Chem. Soc.* **1997**, *119*, 8857−8868.

(46) Lappin, A. G.; Peacock, R. D. *Inorg. Chim. Acta* **1980**, *46*, L71-L72.

(47) Swaddle and co-workers studied the electron-transfer kinetics of $Cu(dpym)_2^{0/-}$ (Hdpym = 3,3′,5,5′-tetramethyl-4,4′-dicarbethoxydipyrromethene), which maintains tetrahedral coordination in both oxidation states. Although their reported value of $k_{11} = 5.9 \times 10^3$ M^{-1} s^{-1} is not exceptionally small, a larger value was anticipated on the basis of the minimal reorganization presumed to accompany electron transfer: Metelski, P. D.; Hinman, A. S.; Takagi, H. D.; Swaddle, T. W. *Can. J. Chem.* **1995**, *73*, 61−69.