Direct Evidence for a Geometrically Constrained “Entatic State” Effect on Copper(II/I) Electron-Transfer Kinetics As Manifested in Metastable Intermediates

Qiuyue Yu,[1a] Cynthia A. Salhi,[1a] Edna A. Ambundo,[1a] Mary Jane Heeg,[1a] L. A. Ochrymowycz,[1b] and D. B. Rorabacher*,[1a]

Contribution from the Departments of Chemistry, Wayne State University, Detroit, Michigan 48202, and the University of Wisconsin−Eau Claire, Eau Clarie, Wisconsin 54701

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Abstract: The absolute magnitude of an “entatic” (constrained) state effect has never been quantitatively demonstrated. In the current study, we have examined the electron-transfer kinetics for five closely related copper(II/I) complexes formed with all possible diastereomers of [14]aneS_4 (1,4,8,11-tetrathiacyclotetradecane) in which both ethylene bridges have been replaced by *cis*- or *trans*-1,2-cyclohexane. The crystal structures of all five Cu(II) complexes and a representative Cu(I) complex have been established by X-ray diffraction. For each complex, the cross-reaction rate constants have been determined with six different oxidants and reductants in aqueous solution at 25 °C, $\mu = 0.10$ M. The value of the electron self-exchange rate constant (k_{11}) has then been calculated from each cross reaction rate constant using the Marcus cross relation. All five Cu(II/I) systems show evidence of a dual-pathway square scheme mechanism for which the two individual k_{11} values have been evaluated. In combination with similar values previously determined for the parent complex, $Cu^{II/I}$([14]aneS_4), and corresponding complexes with the two related monocyclohexanediyl derivatives, we now have evaluated a total of 16 self-exchange rate constants which span nearly 6 orders of magnitude for these 8 closely related Cu(II/I) systems. Application of the stability constants for the formation of the corresponding 16 metastable intermediates—as previously determined by rapid-scan cyclic voltammetry—makes it possible to calculate the specific electron self-exchange rate constants representing the reaction of each of the strained intermediate species exchanging electrons with their stable redox partners—the first time that calculations of this type have been possible. All but three of these 16 specific self-exchange rate constants fall within—or very close to—the range of 10^5−10^6 M^{-1} s^{-1}, values which are characteristic of the most labile Cu(II/I) systems previously reported, including the blue copper proteins. The results of the current investigation provide the first unequivocal demonstration of the efficacy of the entatic state concept as applied to Cu(II/I) systems.

Introduction

The “entatic” (or “strained”) state hypothesis was first proposed by Vallee and Williams[2] as a rationale to account for the high level of reactivity observed for enzymes, in general, and for metalloenzymes, in particular. These authors suggested that the active site in an enzyme is constrained by the surrounding protein matrix to adopt a geometry similar to that of the transition state that would exist in a similar unconstrained system, thereby reducing the reorganizational energy. In expanding on this theme, Williams[3,4] subsequently focused on redox-active copper enzymes as one of the prime examples in which the entatic state might be expected to be operative since the coordination geometries preferred by copper(I) and copper(II) are distinctly different, the former generally preferring a 4-coordinate (tetrahedral) geometry and the latter a 6-coordinate (distorted octahedral) or 5-coordinate (square pyramidal or trigonal bipyramidal) geometry.[5]

Extensive structural studies have shown that the type 1 sites in blue copper proteins are unusual involving an elongated trigonal pyramidal (4-coordinate) geometry (as found in both plastocyanins[6,7] and copper-containing nitrite reductases)[8−12] or a similar trigonal bipyramidal geometry (as found in azurins).[13−15]

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* Address correspondence to this author. E-mail: dbr@chem.wayne.edu

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In both plastocyanins and azurins, the structural change that accompanies electron transfer appears to be minimal.[14,16] The unusual geometry of the type 1 copper site has been used to justify the fact that the self-exchange rate constants (k_{11}) for

$$^*\mathrm{Cu(II)} + \mathrm{Cu(I)} \xrightleftharpoons{k_{11}} {}^*\mathrm{Cu(I)} + \mathrm{Cu(II)} \qquad (1)$$

many blue copper proteins are 10^5−10^6 $\mathrm{M^{-1}\ s^{-1}}$,[17−26] a range which is 1 to 6 orders of magnitude larger than the values exhibited by most low molecular weight Cu(II/I) complexes.[27]

Recently, Solomon and co-workers have proposed that the properties of the blue copper sites in plastocyanins and azurins arise principally from the unusually short Cu−S(cys) bond that is highly covalent in nature.[28−34] They have concluded that the only significant entatic effect imposed by the protein matrix is in the elongation of the Cu−S(met) axial bond.[35−38] Ryde and co-workers have come to similar conclusions based on high-level quantum mechanical calculations[39,40] and combined density functional and molecular mechanical methods.[41] These latter workers claim that, in a low molecular weight analogue, cysteine thiolate and methionine thioether groups lower the reorganizational energy accompanying Cu(II/I) electron transfer by flattening the potential surfaces and stabilizing a nearly tetrahedral structure for the oxidized state. Thus, they have concluded that the blue copper site is virtually strain free.[42,43] Both Solomon's and Ryde's results indicate that the entatic state in these proteins may be expressed as an enhanced electronic state rather than a geometrically strained state. Nonetheless, the fact that geometric constraints can also be significant in copper(II/I) electron-transfer reactivity has recently been demonstrated by the *decreased* k_{11} values obtained for mutants of amicyanin (a closely related blue copper protein) in which the coordination geometry is distorted away from the preferred configuration.[44]

Although the term entatic state concept has been utilized in various ways, in the current study this term is used to refer to the imposition of steric constraints on the coordination geometry of Cu(II/I) centers in such a way as to lower the Franck−Condon barrier accompanying electron transfer and, thereby, increase the overall electron-transfer rate. Several attempts have been made to generate low molecular weight copper complexes with induced geometric constraints such that the coordination geometries either approximate that of the type 1 active site[45−50] or maintain a constant coordination number of 4 or 5 in both the Cu(I) and Cu(II) oxidation states.[51−56] All have failed to generate k_{11} values which approach the magnitude of the rapidly reacting copper proteins. By contrast, five inorganic Cu(II/I) complexes have been demonstrated to exhibit k_{11} values exceeding 10^5 $\mathrm{M^{-1}\ s^{-1}}$, all of which involve a change in coordination number during electron transfer.[57−61] In these latter cases, however, the overall changes in bond angles and distances are relatively small and, in contrast to the systems included in

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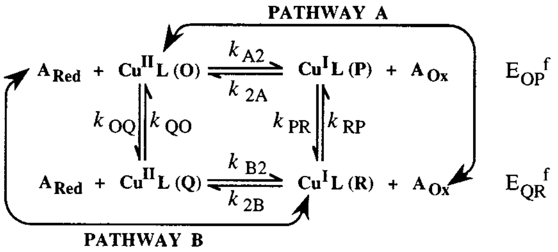
Scheme 1



the current work, no donor atom inversion accompanies the overall electron-transfer process (vide infra).

Prior studies carried out in our laboratory on the Cu(II/I) electron-transfer kinetics of complexes formed with a broad range of macrocyclic polythiaether ligands have demonstrated that the observed behavior is consistent with a dual-pathway (square scheme) mechanism (Scheme 1)[62,63] in which the reaction of counter reagents A_{Red} and A_{Ox} with the thermodynamically stable oxidized and reduced complexes of copper, $Cu^{II}L$(**O**) and $Cu^{I}L$(**R**), involves the formation of metastable intermediates ($Cu^{II}L$(**Q**) and/or $Cu^{I}L$(**P**)). These intermediates are presumed to differ in their coordination geometry from the ground state species in such a way as to more closely resemble the transition state. In this sense, they represent true entatic states.

In the current work we have carried out extensive cross-reaction kinetic measurements for the Cu(II/I) complexes formed with the dicyclohexanediyl derivatives of 1,4,8,11-tetrathiacyclotetradecane ([14]aneS_4), designated as L7 through L11 in Figure 1. These ligands were selected on the basis of a number of favorable properties. The use of ligands containing soft sulfur donor atoms results in strong S→Cu(II) charge-transfer bands in the visible region[64] (similar to those exhibited by the type 1 "blue" copper site) which are useful for monitoring purposes. At the same time, the sulfur donors promote high Cu(II/I) redox potentials[65,66] and lower reorganizational barriers.[67,68] The use of macrocyclic ligands stabilizes the Cu(II) complexes which are otherwise relatively weak with tetrathiaether ligands.[69] The use of the several diastereomers included in the current study ensures the presence of uniform inductive effects. Moreover, molecular models and simple molecular mechanical calculations,[70] supported by $Cu^{II}L$ crystal structures (vide infra), indicate that the cis and trans orientations of the substituent cyclohexane moieties influence the preferred orientation of the four sulfur donor atoms in the ground state, resulting in differing amounts of internal strain for the various conformers of the respective $Cu^{II}L$ complexes and, possibly, the $Cu^{I}L$ complexes as well. Therefore, the effect of the differing combinations of *cis*- and *trans*-cyclohexane moieties in the various diastereomers should produce slight distortions corresponding to partial "entatic" or "rack" states.[4,71]

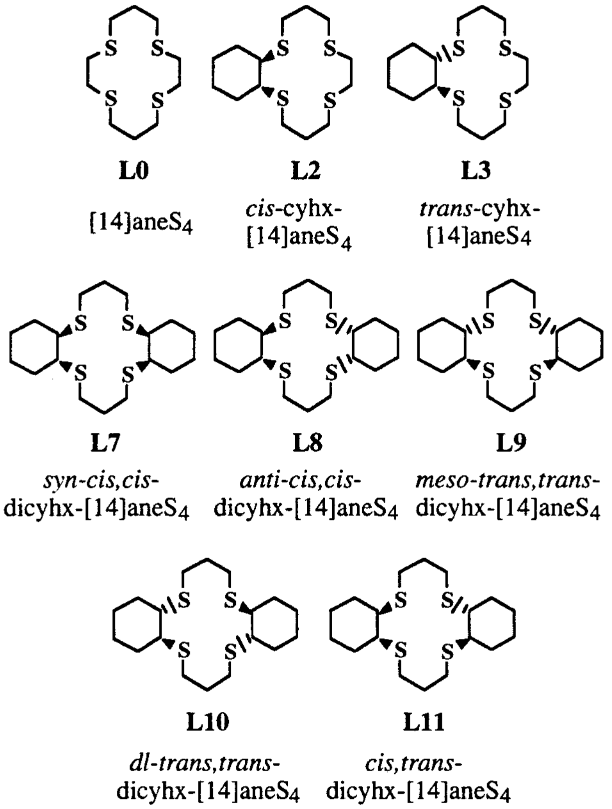


Figure 1. Ligands discussed in this work. The numbering of the ligands is consistent with designations used previously (refs 70, 73, 76, and 97).

Each of the five dicyclohexanediyl-[14]aneS_4 complexes of copper (L7−L11) have been reacted with three oxidants and three reductants which have been selected to promote outer-sphere electron transfer while varying the driving force of the reactions.[72] Along with earlier studies on the Cu(II/I) complexes formed with ligands L0, L2, and L3,[73] we have now generated k_{11} values representative of both Pathway A and Pathway B for all eight systems. When combined with previous data from exhaustive rapid-scan electrochemical measurements for these same eight Cu(II/I) systems,[70] the specific electron self-exchange rate constants characteristic of the metastable intermediates **Q** and **P** can now be estimated. *The latter values provide the first quantitative evaluation of variations in Cu(II/I) electron-transfer kinetics resulting from the entatic effect.*

Experimental Section

Crystallographic Determinations. For each of the six X-ray crystal structure determinations, the crystal was mounted on a Siemens/Bruker R3/CCD diffractometer equipped with monochromated Mo Kα radiation and the manufacturer's SMART collection software and SAINT processing software. In each case a hemisphere of data was collected at 10 s/frame with 0.3° between each frame for a total of 1650 frames. Absorption corrections were applied with the program SADABS.[74] The number of reflections initially observed and those obtained after

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[72] The term "driving force", as used in this context, is defined as the product of the cross reaction equilbrium constant (K_{12} or K_{21}) multiplied by the electron self-exchange rate constant for the counter reagent utilized (k_{22}) (see ref 75).

[73] Ligands designated L1, L4, L5, and L6 are analogous to L2, L7, and L8 with a benzene ring substituted for one or both *cis*-cyclohexane rings. These four phenyl derivatives were not included in the current study since they are virtually insoluble in water and form very weak complexes with Cu(II) even in acetonitrile (see refs 76 and 97).

Table 1. Physical Parameters for Copper(II) Complexes with [14]aneS_4 and Its Cyclohexanediyl Derivatives in Aqueous Solution at 25 °C, $\mu = 0.10$ M (ClO_4^-)

complexed ligand	E^f, V vs SHE	λ_{max}, nm[a]	$\epsilon_{Cu^{II}L} \times 10^3$ [a]
L0	0.58[b]	390	8.0
L2	0.54[c]	390	7.4
L3	0.60[c]	388	8.9
L7	0.492[d]	392	8.6
L8	0.566[d]	396	9.1
L9	0.518[d]	388	9.6
L10	0.640[d]	390	4.6
L11	0.558[d]	390	8.1

[a] Reference 76. [b] Reference 66. [c] Reference 81. [d] Aqueous potential values re-determined in this work using ferrocene ($E^f = 0.400$ V vs SHE) as an internal or external reference (see text).

averaging (R_{int}) were as follows: $[Cu^{II}(L7)(H_2O)](ClO_4)_2$ 9259, 5868 (0.025); $[Cu^{II}(L8)(H_2O)_2](ClO_4)_2$ 18537, 3712 (0.025); $[Cu^{II}(L9)(H_2O)_2](ClO_4)_2$ 18559, 6884 (0.038); $[Cu^{II}(L10)(ClO_4)]ClO_4$ 35495, 6864 (0.094); $[Cu^{II}(L11)(H_2O)](ClO_4)_2$ 19056, 6664 (0.029); $[Cu^{I}(L10)]ClO_4$ 16434, 5317 (0.022). The structures were solved and refined on F^2 with the programs of Sheldrick.[74] Hydrogens were placed in observed or calculated positions. Hydrogen atoms on the solvent water molecules could not be located in all cases. The perchlorate anions were typically disordered.

Reagent Preparation and Properties. Synthetic procedures and solution preparation of all counter reagents used in this work have been presented earlier.[62,75] The syntheses of the five dicyclohexanediyl derivatives of [14]aneS_4 (i.e., L7−L11 in Figure 1) have been previously described.[76] The Cu(II) complexes formed with all eight ligands depicted in Figure 1 exhibit a strong S→Cu charge-transfer peak in the region of 390 nm for which the molar absorptivity values have also been reported[76] as listed in Table 1. As part of the current study, improved $Cu^{II/I}L$ potentials were determined from slow scan (10−100 mV s^{-1}) cyclic voltammograms using ferrocene as an internal or external reference standard to correct for errors in the potential value of the Ag/AgCl reference electrodes obtained from Bioanalytical Systems (BAS, Lafayette, IN). These Ag/AgCl reference electrodes, purportedly containing a 3 M NaCl filling solution, are expected to have a potential value of about 0.208 V vs the standard hydrogen electrode (SHE). However, extensive measurements with different Ag/AgCl (3 M NaCl) electrodes against ferrocene and several other redox couples have shown that the potential of these reference electrodes in aqueous solution is 0.232 ± 0.005 V vs SHE.[77]

Solutions and Instrumentation. Solutions of the Cu(II) complexes were prepared by dissolving each ligand in water containing a large excess of purified $Cu(ClO_4)_2$. The resultant solutions were then standardized spectrophotometrically by Hg(II) displacement by monitoring the absorbance in the region of 390 nm as previously described.[76] Solutions of the Cu(I) complexes were prepared by placing the $Cu^{II}L$ solutions over copper shot under argon. For the cross-reaction kinetic measurements, the ionic strength was controlled using 0.10 M $HClO_4$. Deionized−distilled water was used for the preparation of all solutions. All studies were conducted at 25.0 ± 0.2 °C using a circulating water bath. All kinetic measurements were obtained using a Durrum D-110 stopped-flow spectrophotometer interfaced to a personal computer with a Metrabyte A/D board. The physical mixing and flow characteristics of the latter instrument have been carefully determined and approaches have been developed and tested for determining the kinetics of second-order reactions with rate constants as large as 10^8 M^{-1} s^{-1} using this instrument.[61,78,79]

Results

Potential Values. As noted in the foregoing section, the potential values of the five dicyclohexanediyl-substituted $Cu^{II/I}L$ systems previously reported in aqueous solution[76] were found to be in error due to an erroneous potential for the reference electrode used at that time.[77] Since accurate potential values are essential to resolve the $Cu^{II/I}L$ electron self-exchange rate constants from the experimental cross-reaction rate constants, these potentials were carefully re-determined by slow scan cyclic voltammetry using ferrocene as an internal or external reference. The resulting E^f values were taken as the average $E_{1/2}$ value based on several single scans and are listed in Table 1 along with corresponding potentials for $Cu^{II/I}(L0)$, $Cu^{II/I}(L2)$, and $Cu^{II/I}(L3)$. In referencing the E^f values to the standard hydrogen electrode (SHE), the aqueous E^f value for ferrocene was assumed to be 0.400 V vs SHE.[80] (These new values are uniformly about 0.10 V lower than the E^f values previously obtained for these same systems in 80% methanol.)[70]

Crystal Structures of Cu(II) Complexes. The structures of the perchlorate salts of the Cu(II) complexes formed with all five dicyclohexanediyl derivatives of [14]aneS_4 (i.e., L7−L11) were determined by X-ray crystallography. The crystal parameters and related experimental data for these five compounds are listed in Table 2 and ORTEP drawings of the cationic units (50% probability, hydrogens omitted for clarity) are provided in Figure 2. The crystal parameters for the perchlorate salt of the reduced complex, $Cu^I(L10)$, are also listed in Table 2 and the ORTEP drawing is illustrated in Figure 3. Since the structure of this latter complex is unremarkable and very similar to the structures previously reported for $Cu^I(L3)$[81] and two other closely related Cu(I) macrocyclic ligand complexes,[82,83] no concerted effort was made to determine the crystal structures for the other Cu(I) complexes included in this work. The principal bond lengths and bond angles of interest for the cationic units in all six crystal structures are listed in Table 3. (A more complete listing of the structural parameters is available—see Supporting Information.)

Copper(II/I) Cross-Reaction Kinetics. In the current work, both the kinetics for $Cu^{II}L$ reduction and $Cu^{I}L$ oxidation were studied:

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

For each of the five $Cu^{II}L$ complexes, the reduction kinetics were determined using three counter reagents: $Ru^{II}(NH_3)_4bpy$, $Ru^{II}(NH_3)_5isn$, and $Ru^{II}(NH_3)_5py$ {bpy = 2,2′-bipyridine; isn = isonicotinamide; py = pyridine}. Three counter reagents were also used for the corresponding $Cu^{I}L$ oxidation kinetic studies: $Ru^{III}(NH_3)_4bpy$, $Ru^{III}(NH_3)_2(bpy)_2$, and $Ni^{III}([14]aneN_4)(H_2O)_2$ {[14]aneN_4 = 1,4,8,11-tetraazacyclotetradecane = cyclam}. The

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Table 2. Crystal Parameters and Experimental Data for X-ray Diffraction Measurements on the Copper(II) Complexes Formed with All Five Dicyclohexanediyl-[14]aneS$_4$ Ligands and the Copper(I) Complex with *dl-trans,trans*-Dicyclohexanediyl-[14]aneS$_4$ (X = ClO$_4$)[a]

parameter	[Cu^{II}(L7)(H$_2$O)]X$_2$	[Cu^{II}(L8)(H$_2$O)$_2$]X$_2$	[Cu^{II}(L9)(H$_2$O)$_2$]X$_2$	[Cu^{II}(L10)X]X	[Cu^{II}(L11)(H$_2$O)]X$_2$	[Cu^{I}(L10)]X
emperical formula	CuC$_{18}$H$_{34}$S$_4$Cl$_2$O$_9$	CuC$_{18}$H$_{36}$S$_4$Cl$_2$O$_{10}$	CuC$_{18}$H$_{36}$S$_4$Cl$_2$O$_{10}$	CuC$_{18}$H$_{32}$S$_4$Cl$_2$O$_8$	CuC$_{18}$H$_{34}$S$_4$Cl$_2$O$_9$	CuC$_{18}$H$_{32}$S$_4$ClO$_4$
fw	657.13	675.15	675.15	639.12	657.13	539.67
space group	$P\bar{1}$	*Pbca*	$P2_1/n$	*Pbca*	$P2_1/n$	monoclinic
a, Å	10.2133(8)	10.8358(5)	20.0273(13)	13.0498(7)	11.5370(6)	10.916(2)
b, Å	10.3016(8)	14.8072(7)	6.9960(4)	16.9827(8)	13.7475(7)	15.602(3)
c, Å	14.8454(12)	17.2021(8)	20.2965(13)	23.5634(11)	17.7187(9)	13.660(3)
α, deg	96.025(1)	90	90	90	90	90
β, deg	99.552(1)	90	101.536(1)	90	101.785(1)	91.87(3)
γ, deg	117.543(2)	90	90	90	90	90
V, Å^3	1336.1(2)	2760.0(2)	2786.3(3)	5222.1(4)	2751.0(2)	2325.4(8)
Z	2	4	4	8	4	4
T, K	295(2)	295(2)	295(2)	295(2)	295(2)	295(2)
ρ_{calcd}, g cm^{-1}	1.633	1.625	1.609	1.626	1.587	1.541
μ, mm^{-1}	1.375	1.336	multiscan	1.402	1.335	1.435
$R(F)^b$	0.0479	0.0559	0.0739	0.0960	0.0529	0.0374
$R_w(F^2)^c$	0.1052	0.1647	0.2070	0.2730	0.1471	0.1035

[a] $\lambda = 0.71703$ Å. [b] $R(F) = \sum||F_o| - |F_c||/\sum|F_o|$ for $2\sigma(I)$ reflections. [c] $R_w(F^2) = [\sum w(F_o^2 - F_c^2)^2/\sum w(F_0^2)^2]^{1/2}$ for $2\sigma(I)$ reflections.

properties for all counter reagents used in this work have been tabulated previously.[75]

All cross reactions involving Cu^{II}L reduction were assumed to be first-order with respect to each reactant based on our previous studies with a large number of closely related complexes.[60−62,75,81,83] For the reactions of Ru$^{III/II}$(NH$_3$)$_4$bpy with the Cu$^{II/I}$(L10) system, $\Delta G^0 \approx 0$. Moreover, the oxidations of the Cu(I) complexes of L8, L11, and, particularly, L10 as well as the reduction of Cu^{II}(L7), were thermodynamically uphill with this counter reagent so that the reactions did not proceed to completion. As a result, these reactions were treated as reversible systems.

With the exception of Cu^{I}(L9), all reactions with Ru^{III}(NH$_3$)$_2$(bpy)$_2$ exhibited second-order rate constants exceeding 10^7 M^{-1} s^{-1}, which resulted in the generation of a significant concentration gradient down the length of the observation cell. The kinetic data for the latter reactions required the use of a modified treatment developed and tested in our laboratories[79] that has recently been demonstrated to yield viable rate constant resolution for rate constants up to 10^8 M^{-1} s^{-1} when compared with corresponding data from NMR line-broadening studies.[61] The individual cross-reaction rate constants are provided in the Supporting Information. Summaries of the second-order rate constants obtained for all 30 reactions studied in the current investigation are listed in Table 4.

Discussion

Ligand Conformations in Crystal Structures. As illustrated in Figure 3, the crystal structure for Cu^{I}(L10) shows that the ligand is in conformer **V**[70] in which the orientation of the lone electron pairs on the sulfur donor atoms alternate relative to the macrocyclic ring (designated as + − + −). This conformation, which has been previously observed for Cu^{I}(L3),[81] Cu^{I}([14]aneNS$_3$),[82] and Cu^{I}(*trans*-cypt-[14]aneS$_4$),[83] is believed to be the predominant conformer in solution for all Cu(I) complexes included in this study as indicated by molecular mechanical calculations.[70,83]

Three distinct conformations of the macrocyclic ligand are found in the resolved structures of the five Cu(II) complexes as noted on the first line of Table 3. The complexes with L7 and L11 are in conformer **I**[70] (Figure 2A,E) in which the unshared lone electron pairs on all four sulfur donor atoms are oriented in the same direction relative to the macrocylic ring (+ + + +), while the fifth (apical) coordination site is occupied by a water molecule. Such square pyramidal complexes of Cu(II) were previously found for Cu^{II}(L2) and Cu^{II}(L3)[81] as well as for the two corresponding monocyclopentanediyl derivatives of [14]aneS$_4$.[83] By contrast, both Cu^{II}(L8) and Cu^{II}(L9), like Cu^{II}(L0),[84] are in the more commonly encountered conformer **III**[70] (Figure 2B,C) in which the lone electron pairs on the sulfur atoms connected by one trimethylene bridge are oriented above the macrocyclic plane and the lone pairs on the other two sulfurs are oriented below this plane (+ − − +). The two apical sites in these latter two complexes are also occupied by water molecules. Conformers **I** and **III** are generally recognized to be the most stable conformations for simple quadridentate, 14-membered-macrocyclic ligands in forming octahedral or square planar complexes with Cu(II),[81,85] Ni(II),[68,86−89] and other metal ions.[90−95] By contrast, however, the Cu^{II}(L10) complex is in conformer **II**[70] (Figure 2D) in which the lone electron pairs on three sulfurs are oriented above the macrocyclic plane while the lone pair on the fourth sulfur is oriented below the plane (+ + − +). An apical perchlorate anion completes the inner-coordination sphere of the Cu(II), which is presumably replaced by a coordinated water molecule in aqueous solution. This latter conformational geometry is rare for similar macrocyclic ligand complexes[96] and is presumed to result from the twist exerted

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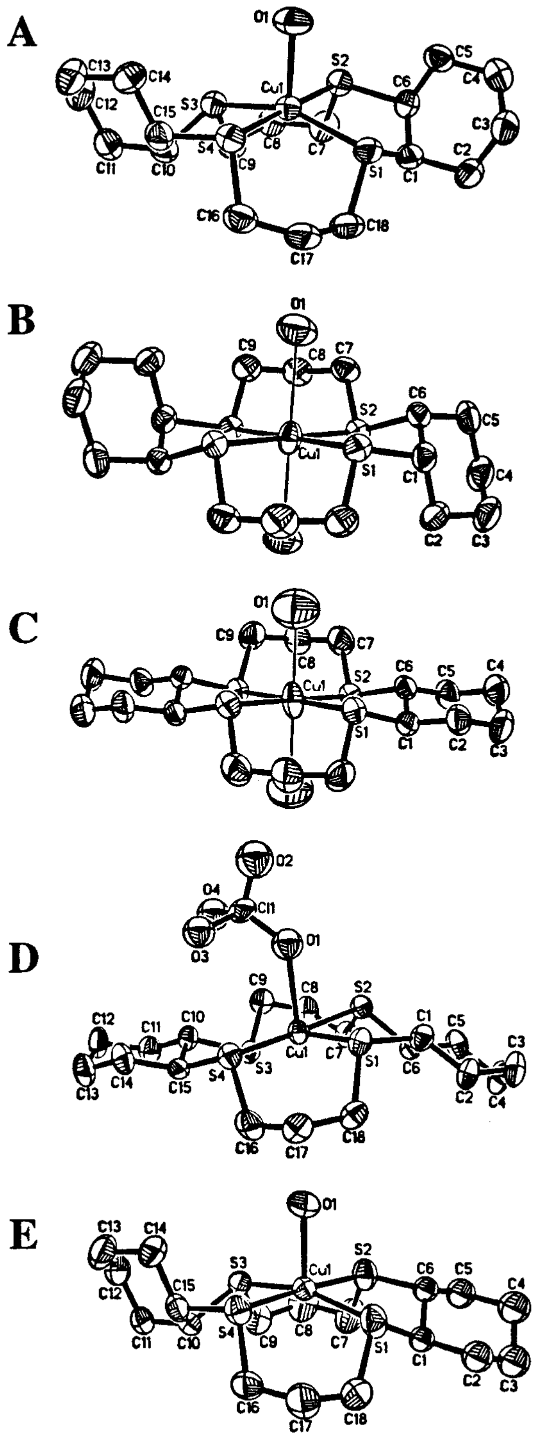

Figure 2. ORTEP drawings of the cationic units of the five Cu(II) complexes with (A) $Cu^{II}(L7)(H_2O)$, (B) $Cu^{II}(L8)(H_2O)_2$, (C) $Cu^{II}(L9)(H_2O)_2$, (D) $Cu^{II}(L10)(ClO_4)$, and (E) $Cu^{II}(L11)(H_2O)$. In both the L7 (A) and L11 (E) complexes, all lone electron pairs on the coordinated sulfur donor atoms are oriented in the same direction relative to the macrocyclic ring (+ + + +) to generate Conformer **I**. For the L8 (B) and L9 (C) complexes, the lone electron pairs on the coordinated sulfur donor atoms connected by a single trimethylene bridge are oriented in the same direction while those connected by the other trimethylene bridge are oriented in the opposite direction (+ − − +) to generate Conformer **III**. In the L10 (D) complex, the lone electron pairs on three of the coordinated sulfur donor atoms are oriented in the same direction relative to the macrocyclic ring while that of the fourth sulfur is oriented in the opposite direction (+ + − +) to generate Conformer **II**—a conformer rarely obtained in crystal structures. In all structures, hydrogens have been omitted for clarity.

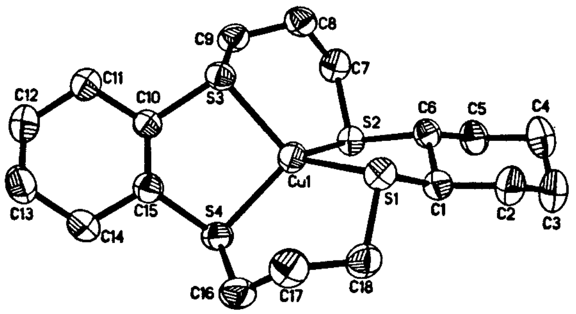

Figure 3. ORTEP drawing of the cationic unit of $Cu^{I}(L10)$ showing the alternating pattern of the lone electron pairs on the sulfur donor atoms (+ − + −) in conformer **V**.

on the four sulfur donor atoms by the opposing trans conformations of the two cyclohexane moieties.

Electron Self-Exchange Rate Constants. Our recent extensive rapid-scan cyclic voltammetric study on the Cu(II/I) complexes with all eight ligands yielded behavior that was shown to be consistent with the mechanism illustrated in Scheme 1.[70] As discussed in that work, the intermediates designated as **P** and **Q** are presumed to be conformationally altered species, more nearly resembling the geometry of their stable redox conjugates, **O** and **R**, respectively.[63,75] Although some coordination changes doubtless accompany the electron-transfer step itself, the major conformational change is assumed to take place in forming the intermediate species, that is, in the steps **O** → **Q** or **R** → **P**.[70] Therefore, in a very real sense, intermediates **P** and **Q** should approximate "entatic" state species.

The $Cu^{II/I}(L0)$ system and several other closely related complexes have previously been shown to exhibit cross-reaction electron-transfer kinetic behavior that conforms to this dual-pathway mechanism.[60,62,75,79,81,83,97] Application of the steady-state approximation to the proposed metastable intermediates, **Q** and **P**, yields the following differential expressions which describe the kinetic behavior to be expected under all conditions:[98]

Reduction of $Cu^{II}L$

$$-\frac{d[Cu^{II}L]}{dt} = \left(\frac{k_{A2}k_{PR}}{k_{2A}[A_{Ox}] + k_{PR}} + \frac{k_{B2}k_{OQ}}{k_{B2}[A_{Red}] + k_{QO}}\right)[O][A_{Red}] \quad (3)$$

Oxidation of $Cu^{I}L$

$$-\frac{d[Cu^{I}L]}{dt} = \left(\frac{k_{2A}k_{RP}}{k_{2A}[A_{Ox}] + k_{PR}} + \frac{k_{2B}k_{QO}}{k_{B2}[A_{Red}] + k_{QO}}\right)[R][A_{Ox}] \quad (4)$$

where [O], [R], $[A_{Ox}]$, and $[A_{Red}]$ represent the molar concentrations of the stable conformers of $Cu^{II}L$ and $Cu^{I}L$ and the

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(96) A similar conformation has been indicated for the blue form of Cu^{II}-(C-*meso*-5,5,7,12,12,14-hexamethyl-1,4,8,11-tetraazacyclotetradecane), although the crystal structure was not satisfactorily resolved: Clay, R.; Murray-Rust, J.; Murray-Rust, P. *J. Chem. Soc., Dalton Trans.* **1979**, 1135−1139.

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Table 3. Comparison of Structural Parameters of Principal Interest in the Cationic Units of the Copper(II) Complexes Formed with All Five Dicyclohexanediyl-[14]aneS$_4$ Ligands and the Copper(I) Complex Formed with *dl-trans,trans*-Dicyclohexanediyl-[14]aneS$_4$

conformer	$Cu^{II}(L7)(H_2O)$ **I**	$Cu^{II}(L8)(H_2O)_2$[a] **III**	$Cu^{II}(L9)(H_2O)_2$[a,b] **III**	$Cu^{II}(L10)(ClO_4)$ **II**	$Cu^{II}(L11)(H_2O)$ **I**	$Cu^{I}(L10)$ **V**
			bond lengths, Å			
Cu−S(1)	2.315(1)	2.2819(9)	2.280(1)	2.315(2)	2.314(1)	2.2670(9)
Cu−S(2)	2.323(1)	2.2904(9)	2.288(1)	2.306(2)	2.306(1)	2.2656(9)
Cu−S(3)	2.323(1)			2.315(2)	2.310(1)	2.2619(9)
Cu−S(4)	2.316(1)			2.294(2)	2.320(1)	2.2680(8)
Cu−O(1)	2.199(4)	2.652(1)	2.510(2)	2.36(2)	2.215(3)	
			bond angles, deg			
S(1)−Cu−S(2)	89.29(4))	89.92(3)	90.01(5)	88.40(7)	88.71(4)	94.89(3)
S(2)−Cu−S(3)	90.66(4)	90.08(3)	89.99(5)	93.34(7)	92.22(4)	111.92(4)
S(3)−Cu−S(4)	89.24(4)			88.29(7)	89.06(3)	94.71(3)
S(4)−Cu−S(1)	90.44(4)			90.56(8)	89.17(4)	112.51(3)
S(1)−Cu−S(3)	155.43(4)	180.0	180.0	159.20(9)	163.55(4)	120.99(3)
S(2)−Cu−S(4)	179.10(4)			177.88(8)	176.58(4)	124.09(3)
S(1)−Cu−O(1)	101.8(1)	80.2(1)	87.2(1)	89.4(4)	98.4(1)	
S(2)−Cu−O(1)	91.1(2)	95.2(1)	93.7(1)	87.7(4)	92.62(9)	
S(3)−Cu−O(1)	101.8(1)			111.4(4)	98.0(1)	
S(4)−Cu−O(1)	89.8(2)			90.5(4)	90.35(9)	
			distortions from S$_4$ plane			
Cu displacemnt, Å[c]	0.26	0	0	0.19	0.20	
S$_4$ deviation, Å[d]	±0.24	0	0	±0.22	±0.13	
dihedral angle (deg)[e]	24.6	0	0	20.9	16.6	81.6

[a] Only the unique bond distances and bond angles are listed for $Cu^{II}(L8)(H_2O)_2$ and $Cu^{II}(L9)(H_2O)_2$. [b] Two independent half molecules, with very similar structural parameters, exist in the unit cell for $Cu^{II}(L9)(H_2O)_2$; the parameters for only one molecule are listed here. [c] Cu atom displacement from the average S$_4$ plane (in Å). [d] Deviation of the sulfur donor atoms from the average S$_4$ plane. [e] Dihedral angle between the S(1)−Cu−S(2) and S(3)−Cu−S(4) planes (in deg).

Table 4. Mean Experimental Cross-Reaction Rate Constants for Cu(II/I)-Dicyclohexanediyl-[14]aneS$_4$ Complexes Reacting with Various Counter Reagents in Aqueous Solution at 25 °C, $\mu = 0.10$ M (ClO_4^-)

	k_{12} or k_{21} ($M^{-1}\ s^{-1}$)[a]				
counter reagent	$Cu^{II/I}(L7)$	$Cu^{II/I}(L8)$	$Cu^{II/I}(L9)$	$Cu^{II/I}(L10)$	$Cu^{II/I}(L11)$
reductants					
$Ru^{II}(NH_3)_4bpy$	$9(1) \times 10^4$	$3.8(3) \times 10^4$	$1.8(2) \times 10^4$ [b]	$3(1) \times 10^{5}$[a]	$7(2) \times 10^4$
$Ru^{II}(NH_3)_5isn$	$5.6(8) \times 10^5$	$2.4(3) \times 10^5$	$1.8(6) \times 10^5$ [b,c]	$8.8(5) \times 10^5$	$5.1(8) \times 10^5$
$Ru^{II}(NH_3)_5py$	$1.0(2) \times 10^6$	$4.6(7) \times 10^5$	$2.4(7) \times 10^5$ [b]	$2.3(8) \times 10^6$	$1.0(1) \times 10^5$
oxidants					
$Ru^{III}(NH_3)_4bpy$	$3.0(3) \times 10^5$	$2.0(1) \times 10^4$	3.0(1) x 10^4	$6(1) \times 10^3$	$2.6(1) \times 10^4$
$Ni^{III}([14]aneN_4)(H_2O)_2$	$1.4(4) \times 10^6$	$1.3(3) \times 10^6$	$1.1(3) \times 10^5$ [d]	$5(1) \times 10^5$	$1.2(1) \times 10^6$
$Ru^{III}(NH_3)_2)(bpy)_2$	$2.0(7) \times 10^7$	$5(2) \times 10^7$	$1.7(4) \times 10^6$ [b]	4×10^7	$4(2) \times 10^7$

[a] Values in parentheses represent the weighted standard deviation in terms of the last digit listed (e.g., $5.6(8) \times 10^5$ represents $(5.6 \pm 0.8) \times 10^5$. [b] Under second-order conditions, the resolved k_{12} or k_{21} values appeared to decrease with increasing reactant concentrations; this indicates the existence of a slight error in either the reactant concentrations or the molar absorptivity values utilized for data analysis. [c] A value of 0.6×10^5 M^{-1} s^{-1} was obtained in an independent study of this reaction. [d] A decrease in k_{21} was noted with increasing Ni(III) when the latter reagent was held in large excess, indicating the possible onset of "gated" behavior.

oxidized and reduced forms of the counter reagent, respectively. The parenthetical coefficients are equivalent to the experimentally observed second-order rate constant (k_{12} for eq 3 or k_{21} for eq 4) with the first parenthetical term in each equation representing the kinetic contribution of Pathway A and the second term representing the contribution of Pathway B. In their theoretical treatment of dual-pathway mechanisms related to systems of the type shown in Scheme 1, Brunschwig and Sutin[99] have noted that conformational changes following the electron-transfer step should not become rate-limiting for thermodynamically favorable reactions. As a result, eqs 3 and 4 can be simplified to the forms:

$$-\frac{d[Cu^{II}L]}{dt} = \left(k_{A2} + \frac{k_{B2}k_{OQ}}{k_{B2}[A_{Red}] + k_{QO}}\right)[O][A_{Red}] \quad (3')$$

$$-\frac{d[Cu^{I}L]}{dt} = \left(\frac{k_{2A}k_{RP}}{k_{2A}[A_{Ox}] + k_{PR}} + k_{2B}\right)[R][A_{Ox}] \quad (4')$$

The relative magnitude of the parenthetical terms in eqs 3′ and 4′ determines which of several limiting conditions may apply:

Reduction of Cu^{II}L

Pathway A dominant: $$k_{A2} \gg \left(\frac{k_{B2}k_{OQ}}{k_{B2}[A_{Red}] + k_{QO}}\right)$$

$$\text{that is, } k_{12(obs)} = k_{A2} \quad (3a)$$

Pathway B dominant: $$k_{A2} \ll \left(\frac{k_{B2}k_{OQ}}{k_{B2}[A_{Red}] + k_{QO}}\right)$$

$$\text{If } k_{B2}\ [A_{Red}] \ll k_{QO}: \qquad k_{12(obs)} = K_{OQ}\, k_{B2} \quad (3b)$$

$$\text{If } k_{B2}\ [A_{Red}] \gg k_{QO}: \qquad k_{12(obs)} = \frac{k_{OQ}}{[A_{Red}]} \quad (3c)$$

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Table 5. Summary of Electron Self-Exchange Rate Constants for the Copper(II/I) Complexes with Eight Related Macrocyclic Tetrathiaether Ligands As Calculated by Applying the Marcus Relationship to the Cross-Reaction Rate Constants with a Variety of Counter Reagents in Aqueous Solution at 25 °C, $\mu = 0.10$ M (ClO_4^-)

	log k_{11} (M^{-1} s^{-1}) for complexed ligands							
	L0	L2	L3	L7	L8	L9	L10	L11
NMR relaxation	3.88[a]	4.7[b]	≤ 3[b]					
reductants:								
$Ru^{II}(NH_3)_4bpy$	3.79[a]	4.60[b]	3.20[b]	4.0	1.9	2.1	2.6, 1.2[c]	2.6
$Ru^{II}(NH_3)_4phen$		4.4[b]	3.2[b]					
$Ru^{II}(NH_3)_5isn$	4.02[a]	4.19[b]	3.33[b]	3.7	1.9	2.0	2.0	2.7
$Ru^{II}(NH_3)_5py$	3.89[a]	4.13[b]	2.80[b]	4.0	2.2	2.3	2.6	3.0
$Co^{II}(bpy)_3$		4.8[b]	3.1[b]					
oxidants:								
$Ru^{III}(NH_3)_4bpy$	2.58[a]			3.9	2.8	2.3	3.0	2.8
$Ni^{III}([14]aneN_4)$	2.44[a]	4 (A)[b] 1.6 (B)[b]	2.6 (A)[b] 1.8 (B)[b]	2.2	3.2	2.3 (A) −0.32 (B)	3.3	3.0
$Ru^{III}(NH_3)_2(bpy)_2$	0.1[a]	0.9[b]	1.0[b]	0.9	2.7	−1.1	3.5	2.4
$Fe^{III}(4,7\text{-}Me_2phen)_3$	−0.17[a]	1.0[b]	0.8[b]					

[a] Reference 75. [b] Reference 81. [c] The two log k_{11} values shown were obtained from two series of runs, the smaller k_{11} value having been determined using larger concentrations of the $Ru^{II}(NH_3)_4bpy$ reagent.

Oxidation of Cu^IL

Pathway A dominant:

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

$$\text{If } k_{2A}\,[A_{Ox}] \ll k_{PR}: \qquad k_{21(obs)} = K_{RP}k_{2A} \tag{4a}$$

$$\text{If } k_{2A}\,[A_{Ox}] \gg k_{PR}: \qquad k_{21(obs)} = \frac{k_{RP}}{[A_{Ox}]} \tag{4b}$$

Pathway B dominant:

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

$$\text{that is, } k_{21(obs)} = k_{2B} \tag{4c}$$

Equations 3c and 4b represent conditions under which a conformational change preceding electron transfer becomes the rate-limiting step and the reaction becomes independent of the concentration of the counter reagent. This results in the condition known as "gated" electron transfer.[100] Behavior corresponding to eq 4b has been observed for the oxidation of several Cu^IL systems studied previously in our laboratory from which we have been able to evaluate k_{RP}.[60,62,75,81,83] Due to the magnitude of the current investigation, however, we have not attempted to carry out the detailed experimental studies required to evaluate the onset of gated behavior, but, instead, have focused our efforts on obtaining the second-order rate-limiting behavior for both Pathways A and B as represented by eqs 3a, 3b, 4a, and 4c.

For each of the reactions studied in this work, the apparent electron self-exchange rate constant, k_{11}, has been calculated from each k_{12} or k_{21} cross-reaction rate constant by application of the Marcus cross relation.[62,75,101] The resultant logarithmic k_{11} values are tabulated in Table 5 (listed in order of increased driving force)[72] along with the corresponding values reported previously for the Cu(II/I) complexes with L0, L2, and L3. For each specific complex, the k_{11} values obtained for $Cu^{II}L$ reduction reactions ($k_{11(red)}$) are seen to be internally consistent within experimental error. By contrast, the values obtained from the oxidation studies ($k_{11(ox)}$) on the Cu^IL complexes involving L0, L2, L3, L7, and L9 decrease for the reactions exhibiting the largest driving force, the lower limiting $k_{11(ox)}$ values being significantly smaller than the $k_{11(red)}$ values. As discussed in earlier papers,[60,62,75,81,83,98] this pattern of behavior is consistent with the mechanism in Scheme 1 under conditions where Pathway A is preferred (i.e., intermediate **P** is more stable than intermediate **Q**). Under such circumstances, Pathway B is accessed only in the case of those oxidation reactions in which the rate of the **R** → **P** conformational change has been exceeded, representing a switch in behavior from eq 4a to eq 4c. This implies that the values of $k_{11(red)}$ represent the self-exchange rate constants via Pathway A ($k_{11(A)}$) while the *lower limiting* values of $k_{11(ox)}$ represent the self-exchange rate constants for Pathway B ($k_{11(B)}$).[75,98]

In the case of $Cu^{II/I}$(L8) and $Cu^{II/I}$(L10), it is to be noted that $k_{11(red)} < k_{11(ox)}$. Assuming that these differences are beyond experimental error, this pattern of behavior implies that, for these systems, Pathway B is preferred (i.e., intermediate **Q** is intrinsically more stable than intermediate **P**), the first time that such behavior has been observed among the Cu(II/I)-polythiaether systems (although similar behavior has recently been observed by Takagi and co-workers for Cu(II/I)-bisbipyridyl and -bisphenanthroline complexes).[102−104] For all $Cu^{II}L$ reduction reactions studied with these two systems, it would appear that the rate of the conformational change **O** → **Q** has been exceeded so that the reaction mechanism has switched to Pathway A.

For the $Cu^{II/I}$(L11) system, the values for $k_{11(red)}$ and $k_{11(ox)}$ are equivalent. This implies that the same mechanistic pathway is followed for all reactions studied,[61] but the absence of a behavioral change makes it impossible to determine which specific pathway is involved based solely on the data obtained in this study. However, in an earlier electron-transfer kinetic study on the $Cu^{II/I}$(L11) system in acetonitrile,[97] a decrease in $k_{11(ox)}$ was observed for the oxidation reaction with Fe^{III}(4,7-dimethyl-1,10-phenanthroline)$_3$ which has an exceptionally large driving force, leading to the conclusion that this latter reaction involves a shift to Pathway B while all of the reactions of this Cu(II/I) system in the current study represent Pathway A. Since earlier electron-transfer studies on $Cu^{II/I}$(L0) in water[75] and

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Table 6. Electron Self-Exchange Rate Constants for Pathways A and B and Specific Self-Exchange Rate Constants ($k_{11(OP)}$ and $k_{11(QR)}$) 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, $\mu = 0.10$ M

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

[a] The log $k_{11(B)}$ value listed is based on the limiting $k_{11(ox)}$ value obtained for Cu^{I}(L11) reacting with Fe^{III}(4,7-Me_2phen)$_3$ in acetonitrile (ref 97); this value, in turn, was used to calculate the value of log $k_{11(QR)}$. [b] In ref 70, the values of K_{RP} and K_{OQ} were inadvertently listed with the incorrect sign on the exponents. [c] The extreme values obtained for log $k_{11(OP)}$ and log $k_{11(QR)}$ for $Cu^{II/I}$(L8) suggest the possibility of experimental error in one or more parameters.

acetonitrile[105] resulted in very similar k_{11} values in both solvents, we assume that the value of $k_{11(B)}$ obtained for $Cu^{II/I}$(L11) in acetonitrile approximates the aqueous value.[106]

For the eight $Cu^{II/I}$L systems considered, we have now generated a total of 16 k_{11} values from which the following conclusions can be drawn: (1) All $k_{11(red)}$ values represent $k_{11(A)}$. (2) With the exception of the $Cu^{II/I}$(L11) system, the $k_{11(ox)}$ values (or the *limiting lower* values if a trend exists) represent $k_{11(B)}$.

The median values of $k_{11(A)}$ and $k_{11(B)}$ for all systems, as implied by the experimental data, are tabulated in Table 6.

Electron Self-Exchange Rate Constants Representative of Intermediate States. On the basis of Scheme 1, the following specific self-exchange rate constants may be defined for the metastable intermediates **P** and **Q** reacting with their stable redox partners:

$$^{*}\mathbf{O} + \mathbf{P} \xrightleftharpoons{k_{11(OP)}} {}^{*}\mathbf{P} + \mathbf{O} \tag{5}$$

$$^{*}\mathbf{Q} + \mathbf{R} \xrightleftharpoons{k_{11(QR)}} {}^{*}\mathbf{R} + \mathbf{Q} \tag{6}$$

Under conditions where the metastable intermediates **P** and **Q** are equilibrated with **R** and **O**, respectively, the values of $k_{11(OP)}$ and $k_{11(QR)}$ must be related to $k_{11(A)}$ and $k_{11(B)}$ as follows:

$$k_{11(A)} = K_{RP}k_{11(OP)} \tag{7}$$

$$k_{11(B)} = K_{OQ}k_{11(QR)} \tag{8}$$

where $K_{RP} = [\mathbf{P}]/[\mathbf{R}]$ and $K_{OQ} = [\mathbf{Q}]/[\mathbf{O}]$.

On the basis of our extensive investigation of rapid-scan cyclic voltammetric behavior combined with computer simulations for the eight $Cu^{II/I}$L systems considered here, the approximate values of K_{RP} and K_{OQ} for all eight systems are listed in Table 6.[70,107] Thus, for the first time we are now in a position to utilize eqs 7 and 8 to estimate the values for the specific self-exchange rate constants $k_{11(OP)}$ and $k_{11(QR)}$ as given in the last two rows of Table 6. It should be noted that the individual $k_{11(A)}$ and $k_{11(B)}$ values in this table cover a range of nearly 6 orders of magnitude. However, 13 of the 16 estimates of $k_{11(OP)}$ and $k_{11(QR)}$ lie within a factor of 2 of the narrow range of 10^5−10^6 M^{-1} s^{-1}.

Entatic States. As noted earlier, the Cu(II) complexes formed with 14-membered macrocyclic ligands such as [14]aneS_4, [14]aneN_4 (cyclam), and their derivatives tend to preferentially involve conformer **I** or **III** as illustrated in Figure 4. By contrast, the corresponding Cu(I) complexes with these same ligands tend to prefer conformer **V**. These conformational preferences indicate that, in most cases, electron transfer must be accompanied by the inversion of two coordinated donor atoms, a conclusion that is supported by molecular mechanical calculations.[70] Although inversion of coordinated sulfur donor atoms is relatively facile,[68] we have previously proposed that the intermediate species **P** and **Q** represent conformers in which one or two sulfur donor atoms are inverted relative to the stable ground-state species and that the electron-transfer step itself occurs without simultaneous donor atom inversion.

In the process of reorganizing from conformer **I** or **III** to conformer **V**, the ligand must always adopt conformer **II** as an intermediate state.[70] This is illustrated in Figure 4 where the arrows indicate the sulfur donor atom which needs to invert in converting from each individual conformer to conformer **II**.[108] As stated earlier, the crystal structure obtained for Cu^{II}(L10) shows that this ligand has, in fact, adopted conformer **II** in the stable Cu(II) complex, presumably as a result of the twist imposed on the four sulfur donor atoms by the opposed orientations of the two *trans*-cyclohexane rings. This suggests that the ground-state species, Cu^{II}(L10)(**O**), more nearly approximates the geometry of the corresponding Cu^{II}(L10)(**Q**) intermediate than is the case for any of the other seven complexes included in the current comparison. Such a hypothesis is strongly supported by the fact that the log K_{OQ} value for the $Cu^{II/I}$(L10) system (Table 6) is significantly larger than that for any other system considered in this work. It is also noted that this same system exhibits the largest $k_{11(B)}$ value that has been observed for any system in which we have been able to unequivocally determine a separate electron self-exchange rate constant for this pathway.[60,62,75,81,83,97,109,110]

Conclusions. For the five low molecular weight Cu(II/I) complexes previously reported to exhibit electron self-exchange rate constants in the range of 10^5−10^6 M^{-1} s^{-1}, four were macrocyclic polythiaether complexes in which the geometry precluded donor atom inversion upon electron transfer.[61] The fact that nearly all of the $k_{11(OP)}$ and $k_{11(QR)}$ rate constants evaluated in the current study lie within this same range suggests that the electron-transfer processes, $\mathbf{O} \rightleftharpoons \mathbf{P}$ and $\mathbf{Q} \rightleftharpoons \mathbf{R}$, in the current systems are free from significant donor atom inversion barriers. This is consistent with our earlier hypothesis that the major Franck−Condon barrier presumably occurs during the vertical processes in Scheme 1: $\mathbf{O} \rightarrow \mathbf{Q}$ and $\mathbf{R} \rightarrow \mathbf{P}$.[70]

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(106) Takagi and co-workers have recently observed nearly identical electron self-exchange rate constants in water and acetonitrile for a number of metal complexes of the type M([9]aneS_3)$_2^{3+/2+}$ ([9]aneS_3 = 1,4,7-trithiacyclononane): Matsumoto, M.; Itoh, M.; Funahashi, S.; Takagi, H. D. *Can. J. Chem.* **1999**, *77*, 1638−1647.

(107) The estimated K_{OQ} and K_{RP} values reported here were determined using 80% CH_3OH/20% H_2O (w/w). An earlier study on the electron self-exchange kinetics of $Cu^{II/I}$([15]aneS_5) yielded identical values for k_{11} in both D_2O and 80% CD_3OD/20% D_2O (ref 58). Therefore, we assume that the values of K_{OQ} and K_{RP} are very similar in both water and 80% methanol.

(108) The fifth possible conformation, designated as Conformer **IV**, has the two pairs of donor atoms bridged by ethylenes (or cyclohexanes) oriented in opposite directions relative to the plane of the macrocyclic ring (+ + − −). This conformation tends to be highly strained and is considered to be a "dead-end" in electron-transfer reactions (see ref 70).

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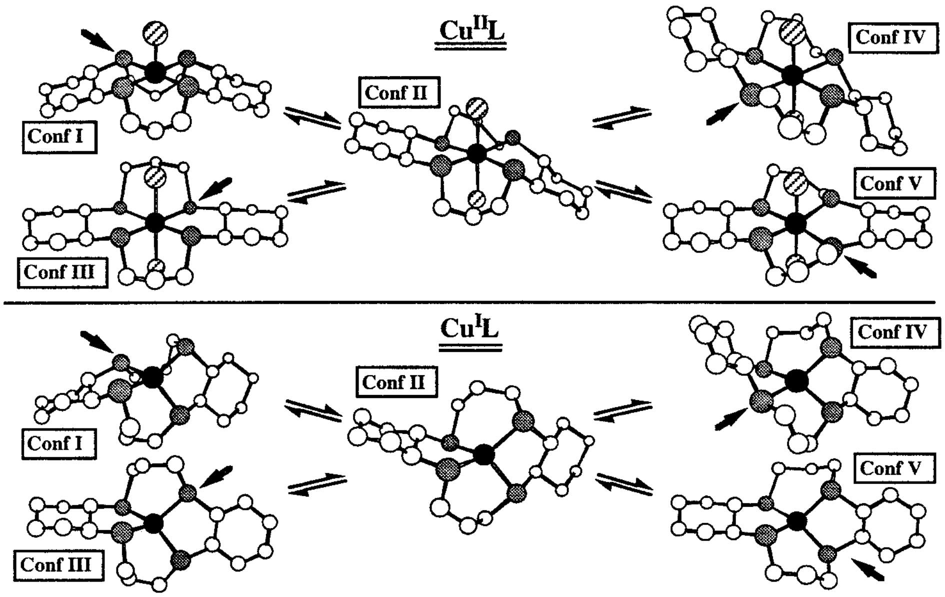

Figure 4. Schematic representations of the five conformers possible for Cu^{II}L (top) and Cu^{I}L (bottom) complexes with [14]aneS$_4$ and its derivatives. The *meso-trans,trans*-dicyhx-[14]aneS$_4$ is utilized in these representations. The solid circles represent the central copper atom, shaded circles represent the sulfur donor atoms, diagonally striped circles are coordinated solvent molecules, and the open circles are the carbon atoms. (Hydrogens have been omitted for clarity.) Conformers **I**, **III**, **IV**, and **V** can convert to conformer **II** by inverting the sulfur donor atom indicated by the arrow. Conformer **I** for Cu^{II}L is represented as a five-coordinate species with a single coordinated solvent molecule based on known crystal structures with this conformation as in Figure 2A,D. Electron transfer can occur between Cu^{II}L and Cu^{I}L species having the same conformation. (Figure reprinted from ref 70.)

We have previously suggested that Cu^{I}L(**P**) and Cu^{II}L(**Q**) may represent conformers **II** and **V**, respectively.[70] Whatever the specific geometric configurations of the **P** and **Q** intermediates may be, however, they are, by their very reactivity, much closer in energy to the reaction transition state than are the ground-state complexes **O** and **R**. As such, they may be considered to represent true "entatic states" for the reduced and oxidized species. Thus, *the data presented in this study provide the first extensive example of the effect of entatic state species upon the rate of electron transfer in Cu(II/I) systems*. It is apparent that, if the geometries adopted by intermediates **P** and **Q** could be stabilized by appropriate modifications on the ligand structures, more rapid overall electron-transfer kinetics should be achieved.[111]

Although the $k_{11(OP)}$ and $k_{11(QR)}$ values obtained in this work and the k_{11} values reported for the most rapidly reacting blue copper proteins are in the same range (10^5−10^6 M^{-1} s^{-1}), the agreement may be fortuitous. Using the two-sphere model,[112] we estimate that solvent reorganization contributions should result in a limiting value of $k_{11} \approx 2 \times 10^8$ M^{-1} s^{-1} for our complexes, 2 orders of magnitude larger than our $k_{11(OP)}$ and $k_{11(QR)}$ values. Thus, it is likely that an appreciable, though reduced, Franck−Condon barrier still accompanies the actual electron-transfer step itself in the current systems.

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Supporting Information Available: Tables of experimental cross-reaction rate constants for 30 electron-transfer reactions (PDF) and 6 X-ray crystallographic files (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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