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A Structural Strategy for Generating Rapid Electron-Transfer Kinetics in Copper(II/I) Systems

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Electron-transfer in low molecular weight copper(II/I) systems is generally accompanied by a large reorganization of the inner-coordination sphere. On the basis of recent kinetic studies involving Cu(II/I)-macrocyclic polythiaether complexes, it was hypothesized that forcing Cu(II) out of the macrocyclic cavity (i) decreases the changes in bond angles upon reduction and (ii) obviates any need for donor atom inversion. This should diminish the reorganizational barrier and, thereby, increase the electron self-exchange rate. This hypothesis has now been tested utilizing a somewhat soluble 12-membered macrocyclic tetrathiaether, oxathiane[12]aneS$_4$ (L). Crystal structures of the Cu^{II}L and Cu^{I}L complexes confirm that, whereas one Cu−S bond dissociates upon reduction, the remaining bond lengths and angles change only minimally. The free ligand, oxathiane[12]aneS$_4$, $C_{10}H_{18}OS_4$, crystallizes in the orthorhombic space group *Pbca* with $Z = 8$, $a = 15.211(2)$ Å, $b = 8.5113(9)$ Å, $c = 20.548(3)$ Å. The Cu^{II}L complex crystallizes as a 5-coordinate monomer with water as the apical ligand: $[CuL(OH_2)](ClO_4)_2 \cdot H_2O$, $C_{10}H_{22}O_{11}S_4Cl_2Cu$, monoclinic $P2(1)/c$, $Z = 4$, $a = 15.774(2)$ Å, $b = 8.485(5)$ Å, $c = 16.508(9)$ Å, $\beta = 112.11(6)°$. The Cu^{I}L complex crystallizes as a binuclear species: $[(CuL)_2NCCH_3](ClO_4)_2 \cdot NCCH_3$, $C_{24}H_{42}N_2O_{10}S_8Cl_2Cu_2$, in the triclinic space group $P\bar{1}$ with $Z = 4$, $a = 12.5917(2)$ Å, $b = 13.0020(3)$ Å, $c = 14.9285(3)$ Å, $\alpha = 68.356(1)°$, $\beta = 84.298(1)°$, $\gamma = 61.129(1)°$. The kinetics of Cu$^{II/I}$(oxathiane[12]aneS$_4$) reacting with four selected counter reagents—two oxidants and two reductants—yield exceptionally large cross-reaction rate constants. Application of the Marcus cross relation yields calculated self-exchange rate constants ranging from 4×10^5 to 8×10^5 M^{-1} s^{-1} (median: 6×10^5 M^{-1} s^{-1}) for this Cu$^{II/I}$L redox system at 25 °C, $\mu = 0.10$. A comparable result of $k_{11} = (8.4 \pm 0.8) \times 10^5$ M^{-1} s^{-1} has been obtained by NMR line-broadening measurements (at 25 °C, corrected to $\mu = 0.10$). This is the largest self-exchange rate constant ever reported for a low molecular weight Cu(II/I) system. Thus, elimination of donor atom inversion coupled with a constrained inner sphere appears to represent a feasible approach for accelerating electron transfer in Cu(II/I) macrocyclic systems.

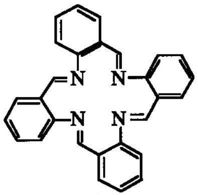
Introduction

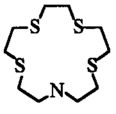
Much attention has been devoted in the literature to the relationship between the geometry of the copper site in redox-active enzymes and their resultant rate of electron transfer. Among the largest reliable Cu(II/I) self-exchange rate constant values which have been reported are those for azurins and related type 1 blue copper proteins for which $k_{11} = 10^5$−10^6 M^{-1} s^{-1}.[2−6]

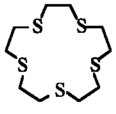
$$^{*}Cu^{I}L + Cu^{II}L \overset{k_{11}}{\rightleftharpoons} {}^{*}Cu^{II}L + Cu^{I}L$$

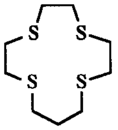
The copper sites in this class of enzymes are essentially either trigonal pyramidal (plastocyanins) or trigonal bipyramidal (azurins)[7] and their rapid electron-transfer kinetics have been attributed to the effects of this distorted geometry. However, efforts to generate low molecular weight copper complexes with similar geometries have not only failed to yield large k_{11} values, but have often resulted in very small values.[8−10]

Although k_{11} values for low molecular weight Cu(II/I) complexes are reported to span twelve orders of magnitude,[11] only four complexes have been reported with reliable values of $k_{11} \geq 10^5$ M^{-1} s^{-1} at 25 °C. These include a porphyrin-like complex first reported by Pulliam and McMillin, Cu$^{II/I}$(TAAB),[12]


TAAB


[15]aneNS$_4$


[15]aneS$_5$


[13]aneS$_4$

for which $k_{11} = 5 \times 10^5$ M^{-1} s^{-1} (in methanol); and three systems studied in our own laboratory, Cu$^{II/I}$([15]aneNS$_4$),

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

(2) (a) Groeneveld, C. M.; Ouwerling, M. C.; Erkelens, C.; Canters, G. W. *J. Mol. Biol.* **1988**, *200*, 189−199 ($k_{11} = 4 \times 10^5$ M^{-1} s^{-1} for *Pseudomonas aeruginosa* azurin). (b) Groeneveld, C. M.; Dahlin, S.; Reinhammar, B.; Canters, G. W. *J. Am. Chem. Soc.* **1987**, *109*, 3247−3250 ($k_{11} = 2 \times 10^6$ M^{-1} s^{-1} for *P. aeruginosa* azurin).

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10.1021/ic990365o CCC: $18.00

Cu$^{II/I}$([15]aneS$_5$), and Cu$^{II/I}$([13]aneS$_4$), for which the k_{11} values are 1×10^5, 2×10^5, and 3×10^5 M^{-1} s^{-1}, respectively (in water).[13−15] Of these four systems, the structures of the Cu(II) complexes have been determined crystallographically for [15]aneS$_5$[16] and [13]aneS$_4$;[17] but only in the former case is the structure of the corresponding Cu(I) complex also available.[16] In the [15]aneS$_5$ system, the Cu(II) complex is distorted square pyramidal and, upon reduction, one of the equatorial Cu−S bonds breaks to generate a distorted tetrahedral Cu(I) complex—with a minimal change in the remaining bond lengths and angles as illustrated in Figure 1B.[16] The geometric changes accompanying electron transfer for the other three systems can be inferred by reference to crystal structures for related systems[18−21] aided by molecular mechanical calculations.[22]

Coordination invariance is not presumed to be achieved with any of these four rapidly reacting complexes. In the Cu$^{II/I}$(TAAB) system (Figure 1A), two Cu−solvent bonds are believed to rupture upon reduction[12] while a Cu−S bond apparently ruptures for each of the other three systems (Figure 1B and C).[16,17] Thus, we conclude that simple coordinate bond rupture is not an overriding contributor to the overall reorganizational barrier in these Cu(II/I) systems. However, a unique feature shared by all four systems is that *the donor atoms do not invert* upon changing the oxidation state of copper. This behavior contrasts to that for [14]aneS$_4$ and other saturated quadridentate N- and S-donor macrocycles in which the copper atom fits into the macrocyclic cavity and donor atom inversion accompanies electron transfer[23] (Figure 1D). This difference in behavior—which has not been previously noted—is particularly relevant since we have recently concluded that donor atom inversion of nitrogen and/or sulfur donors may be the major factor leading to conformational control in the electron-transfer kinetics of many copper systems.[23]

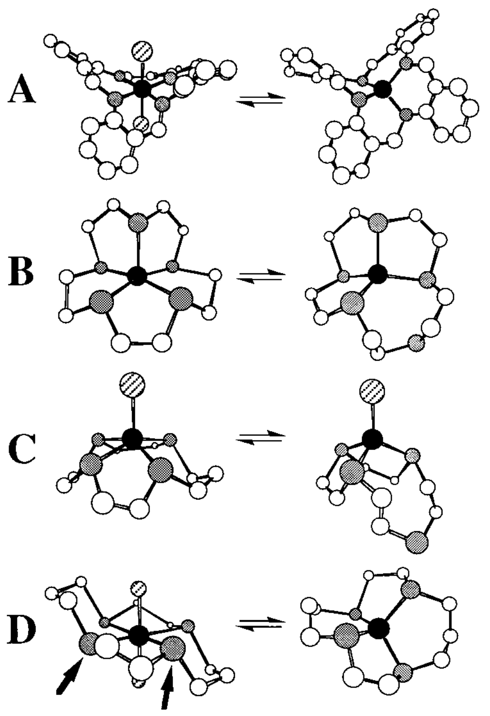
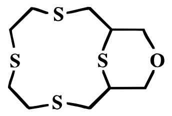


Figure 1. Schematic representation of the structural changes presumed to accompany electron transfer for the four low molecular weight Cu(II/I) systems which exhibit electron self-exchange rate constants of $k_{11} \geq 10^5$ M^{-1} s^{-1}: (A) Cu$^{II/I}$(TAAB), (B) Cu$^{II/I}$([15]aneS$_5$) and Cu$^{II/I}$([15]aneNS$_4$), and (C) Cu$^{II/I}$([13]aneS$_4$). None of these systems require the donor atoms to undergo inversion upon Cu^{II}L reduction. By contrast, Cu^{II}([14]aneS$_4$) (D) requires inversion of two donor atoms (designated by heavy arrows) to produce the stable tetrahedral conformation preferred by the Cu(I) complex.[23] Structures shown are based on molecular mechanical calculations supported by crystal structures for Cu^{II}- and Cu^{I}([15]aneS$_5$),[16] Cu^{II}([14]aneS$_4$),[18] Cu^{II}([13]aneS$_4$),[17] and related Cu(I) complexes.[19−21] Atom designations are as follows: solid = copper; shaded = nitrogen or sulfur; diagonally striped = solvent donor atom; open = carbon. Hydrogens are omitted for clarity. In all cases, Cu^{II}L and Cu^{I}L species are in the left and right columns, respectively.

On the basis of the foregoing considerations, we hypothesized that a square pyramidal Cu(II) complex, in which the copper atom is forced further out of plane, might exhibit an even larger k_{11} value since the strained S−Cu^{II}−S bond angles would more nearly approximate the tetrahedral angles exhibited by Cu^{I}−polythiaether complexes when the copper ion is not constrained to remain within a macrocyclic cavity.[20,24] It was recognized that an excellent candidate for investigating this issue would be the Cu$^{II/I}$([12]aneS$_4$) system; however, previous electron-transfer studies on this system have been hampered by the very limited solubility of the Cu^{I}L species.[25,26]

As recently demonstrated in our laboratory,[27] the Cu^{I}L insolubility problem can be ameliorated to some degree by incorporating an oxathiane ring into the [12]aneS$_4$ structure:

oxathiane-[12]aneS$_4$ =


With the availability of this latter ligand, we have now investigated the electron-transfer kinetics of Cu$^{II/I}$(oxathiane-[12]aneS$_4$) to test the hypothesis that such a system might exhibit

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greater electron-transfer reactivity than any of the other macrocyclic polythiaether complexes studied to date—including the $Cu^{II/I}$([13]aneS_4) system—due to (i) the greater displacement of the Cu atom from the 12-membered macrocyclic cavity and (ii) the presumed avoidance of accompanying donor atom inversion. It is also noteworthy that the Cu(II/I) formal potential for this system is 0.73 V (vs SHE),[27] one of the higher values known for copper.[28]

Experimental Section

Reagents. The synthesis of the oxathiane[12]aneS_4 ligand has been reported.[27] Copper(II) perchlorate and sodium perchlorate were prepared as previously described.[29] The preparation of all counter reagents were based on literature methods as cited earlier.[30]

Structural Determinations. Crystals of the free ligand were obtained by evaporation from 80% methanol−20% water (w/w). A colorless rod ($0.38 \times 0.35 \times 0.23$ mm^3) of L was mounted on a Siemens/Bruker P3 diffractometer equipped with Ni-filtered Cu Kα radiation and the manufacturer's XSCANS software. A total of 2020 reflections were collected in the 2θ range 6−110° for the octant $+h$, $+k$, $+l$. Absorption corrections were applied on the basis of psi scans and resulted in transmission coefficients between 0.20 and 0.06. The structure was solved and refined on F^2 with the programs SHELXS and SHELXL-93.[31] Hydrogen atoms were placed in observed positions and refined; all other atoms were anisotropically described.

Crystals of the $Cu^{II}L$ complex were obtained by mixing $Cu(ClO_4)_2$ and the ligand in 80% methanol and permitting the solution to evaporate slowly to yield dark green tablet-shaped crystals of $[Cu^{II}L(OH_2)](ClO_4)_2\cdot H_2O$. A crystal $0.22 \times 0.16 \times 0.12$ mm^3 was mounted on a Siemens/Bruker P3 diffractometer equipped with monochromated Mo Kα radiation and the manufacturer's XSCANS software. A total of 4250 reflections were collected by scanning over $\theta/2\theta$ in the 2θ range 5−50° for the quadrant $+h$, $+k$, $\pm l$. Absorption corrections were applied on the basis of psi scans and resulted in transmission coefficients between 0.79 and 0.75. The structure was solved and refined on F^2 with the programs SHELXS and SHELXL-93.[31] Hydrogen atoms on the macrocycle were placed in observed positions and refined isotropically; some hydrogen atoms associated with the water molecules were assigned. All other atoms were anisotropically described. The asymmetric unit contains one cation (with a coordinated water molecule), two perchlorate anions and a water of hydration. The perchlorate oxygen atoms exhibit their typical disorder as evidenced by high thermal parameters.

To obtain crystals of the $Cu^{I}L$ complex, $Cu(CH_3CN)_4ClO_4$ (prepared by the method of Hathaway et al.)[32] was mixed with the ligand in acetonitrile and a layer of methylene chloride was carefully introduced above it. Crystals of dimeric $[(CuL)_2NCCH_3](ClO_4)_2\cdot CH_3CN$ formed as colorless irregular fragments. A large crystal $0.45 \times 0.4 \times 0.4$ mm^3 was mounted on a Siemens/Bruker P4/CCD diffractometer equipped with monochromated Mo Kα radiation and the manufacturer's SMART collection software and SAINT processing software. A hemisphere of data was collected at 10 s/frame with 0.3° between each frame out to a resolution of 0.75 Å. A total of 11 883 reflections were integrated from the 1500 frames collected. Absorption corrections were applied with the program SADABS[31] and 7849 reflections were obtained after averaging ($R_{int} = 0.029$). The structure was solved and refined on F^2 with the programs of SHELXS and SHELXL-93.[31] Hydrogen atoms were placed in calculated or observed positions. All non-hydrogen atoms were anisotropically described. The asymmetric unit contains one binuclear dication (including a coordinated acetonitrile), two perchlorate anions and a noncoordinated acetonitrile solvent molecule.

Instrumentation. A BAS 100 electrochemical analyzer (Bioanalytical Systems, Lafayette, IN) was used for routine cyclic voltammetric measurements at ambient temperature. Low-temperature and rapid-scan voltammograms were conducted with a custom-designed instrument constructed in our laboratory.[23] In all cases, a typical three-electrode cell was utilized with a glassy carbon working electrode (3 mm dia), a small Ag/AgCl (3 M NaCl) reference electrode (No. RE-5B, 6 mm dia) and a platinum wire auxiliary electrode (all electrodes from BAS). A ferroin solution in 0.05 M KCl ($E^f = 1.112$ V)[25,33] was used as an external reference.[28] UV−visible spectra were obtained with a Hewlett-Packard model 8453 diode array spectrophotometer. A Cary model 17D double-beam spectrophotometer was used for making precise absorbance measurements in determining solution concentrations. A Varian Unity 500 NMR spectrometer was used for line-broadening measurements.

Kinetic Measurements. All reactions were studied in aqueous solution at 25 °C using a Durrum D-110 stopped-flow spectrophotometer whose mixing and filling parameters have been fully characterized.[34] The ionic strength of all solutions used in cross-reaction kinetic studies was maintained at 0.10 with $HClO_4$ (since this system is independent of pH). Distilled−deionized water was utilized for the preparation of all solutions. The data for the three fastest reactions (involving ruthenium counter reagents) were analyzed using the approximation that the solution within the observation cell is homogeneous—while making appropriate adjustments to the apparent reactant and product concentrations at the selected time zero—as recently described and demonstrated in our laboratory.[34]

Results and Discussion

Crystal Structures. The parameters for the crystallographic structural determinations of the oxathiane[12]aneS_4 ligand and its Cu(II) and Cu(I) complexes are listed in Table 1. The bond lengths of primary interest are given in Table 2. The principal bond angles of interest for the two copper complexes are given in Table 3.

DeSimone and Glick[35] were the first to observe that the sulfur donor atoms in free macrocyclic polythiaethers tend to have their lone electron pairs oriented away from the macrocyclic cavity (the so-called "exo" conformer), an orientation which Cooper has subsequently attributed to the slight predisposition of C−S−C−C segments to adopt gauche arrangements coupled with the strong preference of S−C−C−S segments to adopt anti arrangements.[36,37] As illustrated in Figure 2, all four sulfur atoms in the free oxathiane[12]aneS_4 ligand adopt the "exo" conformation with the oxathiane ring in a chair conformation so that the oxygen atom is under the ligand cavity. Upon complexation to Cu(II), all four sulfur donor atoms coordinate to the copper atom and become nearly "endo", although their degree of reorientation is limited by the fact that Cu(II) is situated 0.55 Å above the best S_4 plane (Figure 3), analogous to the structure of the Cu^{II}([12]aneS_4) complex previously reported.[17] The oxathiane ring maintains a chair conformation with the oxygen now swung away so that it is no longer situated under the macrocyclic cavity.

Upon reduction, the bond between the copper atom and the oxathiane-S atom dissociates to generate a tetrahedral $Cu^{I}L$ complex (Figure 4). The latter complex actually crystallized as

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Table 1. Crystal Parameters and Experimental Data for X-ray Diffraction Measurements on L, $[Cu^{II}L(OH_2)](ClO_4)_2\cdot H_2O$, and $[(Cu^{I}L)_2NCCH_3](ClO_4)_2\cdot CH_3CN$ (L = Oxathiane[12]aneS$_4$)

parameter	L	$[Cu^{II}L(OH_2)](ClO_4)_2\cdot H_2O$	$[(Cu^{I}L)_2NCCH_3](ClO_4)_2\cdot CH_3CN$
empirical formula	$C_{10}H_{18}OS_3$	$CuC_{10}H_{22}O_{11}S_4Cl_2$	$Cu_2C_{24}H_{42}N_2O_{10}S_8Cl_2$
formula weight	282.48	580.96	973.06
space group	*Pbca*	*P*2(1)/*c*	$P\bar{1}$
a, Å	15.211(2)	15.774(2)	12.5917(2)
b, Å	8.5113(9)	8.485(5)	13.0020(3)
c, Å	20.548(3)	16.508(9)	14.9285(3)
α, deg			68.356(1)
β, deg		112.11(6)	84.298(1)
γ, deg			61.129(1)
V, Å^3	2660.3(6)	2047(2)	1980.05(7)
Z	8	4	2
T, °C	23	23	23
λ, Å	1.541 78	0.710 73	0.710 73
ρ_{calcd}, g cm^{-3}	1.411	1.885	1.632
μ, mm^{-1}	6.344	1.885	1.681
$R(F)^{a}$	0.047 [0.053]	0.052 [0.090]	0.065 [0.083]
$R_w(F^2)^{b}$	0.130 [0.144]	0.100 [0.111]	0.183 [0.199]

[a] $R(F) = |F_c||/\sum|F_o|$ for $2\sigma(I)$ reflections; $R(F)$ for all data is given in brackets. [b] $R_w(F^2) = [\sum(F_o^2 - F_c^2)^2/\sum w(F_o^2)^2]^{1/2}$ for $2\sigma(I)$ reflections; $R_w(F^2)$ values for all data are given in brackets.

Table 2. Average Crystallographic Bond Lengths in the Uncomplexed Ligand, L, and in the Cationic Units of $[Cu^{II}L(OH_2)](ClO_4)_2\cdot H_2O$ and $[(Cu^{I}L)_2NCCH_3](ClO_4)_2\cdot CH_3CN$ (All Values in Å)

	L	$Cu^{II}L(OH_2)$	$Cu^{I}L$−subunit A	$Cu^{I}L$−subunit B
Cu−O		2.092(7)		
Cu−N			1.965(5)	
Cu−S(1)		2.358(2)		2.2495(12)
Cu−S(2), Cu−S(8)		2.330(2)	2.368(2)	2.292(2)
Cu−S(3), Cu−S(7)		2.312(2)	2.372(2)	2.353(2)
Cu−S(4), Cu−S(6)		2.319(2)	2.361(2)	2.352(2)
S(1)−C(1), S(5)−C(11)	1.838(4)	1.848(7)	1.827(5)	1.820(6)
S(1)−C(8), S(5)−C(18)	1.844(4)	1.836(7)	1.821(5)	1.821(6)
S(2)−C(2), S(6)−C(12)	1.811(4)	1.806(7)	1.825(6)	1.810(5)
S(2)−C(3), S(6)−C(13)	1.824(5)	1.801(7)	1.802(9)	1.809(6)
S(3)−C(4), S(7)−C(14)	1.817(5)	1.817(7)	1.857(9)	1.809(6)
S(3)−C(5), S(7)−C(15)	1.847(6)	1.809(6)	1.919(13)	1.761(8)
S(4)−C(6), S(8)−C(16)	1.852(7)	1.818(7)	1.754(14)	1.846(9)
S(4)−C(7), S(8)−C(17)	1.823(4)	1.809(7)	1.811(5)	1.809(6)

Table 3. Average Crystallographic Bond Angles in the Cationic Units of $[Cu^{II}L(OH_2)](ClO_4)_2\cdot H_2O$ and $[(Cu^{I}L)_2NCCH_3](ClO_4)_2\cdot CH_3CN$ (All Values in Deg)

	$Cu^{II}L(OH_2)$	$Cu^{I}L$−subunit A	$Cu^{I}L$−subunit B
O(2)−Cu−S(1)	94.7(2)		
O(2)−Cu−S(2), N(1)−Cu(1)−S(4), S(1)−Cu(2)−S(6)	107.8(2)	108.9(2)	109.06(5)
O(2)−Cu−S(3), N(1)−Cu(1)−S(3), S(1)−Cu(2)−S(7)	101.2(2)	127.4(2)	122.46(5)
O(2)−Cu−S(4), N(1)−Cu(1)−S(2), S(1)−Cu(2)−S(8)	111.6(2)	114.0(2)	116.22(5)
S(1)−Cu−S(2)	86.55(8)		
S(2)−Cu−S(3), S(8)−Cu−S(7)	86.95(8)	91.25(8)	93.26(6)
S(3)−Cu−S(4), S(7)−Cu−S(6)	88.72(7)	89.23(8)	89.05(5)
S(1)−Cu−S(4)	87.03(8)		
S(1)−Cu−S(3)	164.04(7)		
S(2)−Cu−S(4), S(6)−Cu(2)−S(8)	140.42(7)	124.70(6)	123.78(5)

a dimer in which the Cu(I) in subunit A (at left in Figure 4) is coordinated to three ligand donor atoms and a solvent molecule (in this case CH_3CN since this was the solvent used for crystallization); and the Cu(I) in subunit B (at right in Figure 4) is coordinated to the corresponding three sulfurs from the second ligand while bridging to the oxathiane sulfur from the first ligand to complete its inner coordination sphere. The distance from the Cu atom in subunit A to the dissociated S(1) atom is 3.096 Å, indicating that the latter sulfur has moved 0.73 Å away from the Cu upon reduction. Similarly, the Cu−S(5) distance in subunit B is 3.091 Å. These Cu−S distances are less than for the noncoordinated Cu−S in Cu^{I}([15]aneS$_5$) (see Figure 1), presumably due to the constraints imposed by the oxathiane ring. Surprisingly, this Cu^{I}−S distance is the same whether the dissociated oxathiane sulfur is bonded to a second Cu or completely noncoordinated. Despite the differences in the apical donors for the two Cu(I) atoms in the dimer, all other bond lengths and angles for the two subunits are very similar (see Tables 2 and 3); and the bond distances remain nearly unchanged after the copper is reduced—except for the dissociation of one Cu−S bond.

An examination of the bond angles in Table 3 reveals that, upon reduction of Cu(II) to Cu(I), two basic conformational changes accompany the dissociation of the oxathiane-S to Cu bond. The first is that the bond angle formed by the apically coordinated atom, the Cu atom and the sulfur opposite the dissociated sulfur (i.e., angle N(1)−Cu(1)−S(3) in subunit A and S(1)−Cu(2)−S(7) in subunit B) increases by more than 20° (from 101° to 122° or 127°) as the apical atom moves to a more central position over the three remaining coordinated

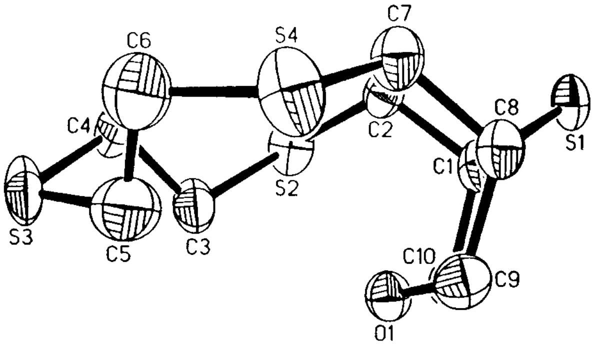

Figure 2. ORTEP drawing of the uncomplexed oxathiane[12]aneS$_4$ ligand showing the atom labeling scheme. Hydrogen atoms are omitted for clarity. Note that all sulfur atoms have their lone pairs pointed away from the macrocyclic cavity to generate an “exo” conformation.

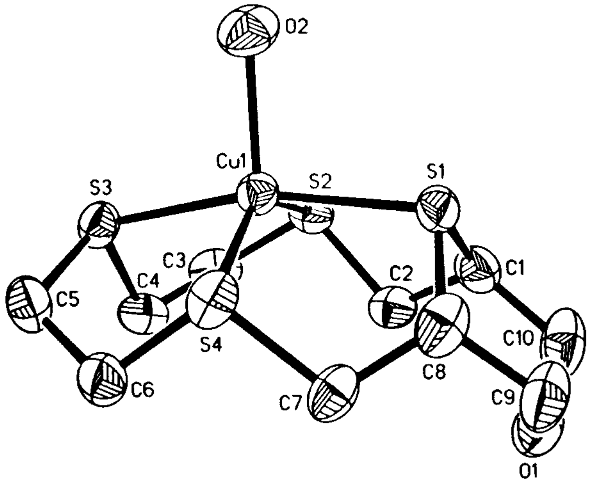

Figure 3. ORTEP drawing of the cationic unit in the crystal structure of [Cu^{II}(oxathiane[12]aneS$_4$)(OH$_2$)](ClO$_4$)$_2$·H$_2$O showing the atom labeling scheme. The apical oxygen is from a coordinated water molecule. The copper atom is positioned 0.55 Å above the average plane of the four sulfur donor atoms.

sulfurs. The second change is that the S(2)−Cu(1)−S(4) (or S(6)−Cu(2)−S(8)) bond angle, involving the two sulfurs adjacent to the oxathiane ring, decreases by about 16° (from approximately 140° to 124°) as these two sulfurs attempt to approach more closely to regular tetrahedral angles. Although these changes are significant, they are relatively small compared to the changes which normally accompany copper reduction in the majority of complexes.

Potential Determination. Slow-scan cyclic voltammograms ($v = 10{-}50$ mV s^{-1}) for Cu$^{II/I}$(oxathiane[12]aneS$_4$) were nearly reversible with $E_{1/2} = 0.734$ V (vs SHE) at ambient temperature. The formal potential of this redox couple was also determined by a potentiostatic-spectrophotometric method[26] in which the potential applied to a Cu$^{II/I}$(oxathiane[12]aneS$_4$) solution was stepped in 0.02 V increments every half hour and the concentration of the Cu(II) complex at each potential determined spectrophotometrically at 400 nm ($\epsilon = 4830$).[27] These latter measurements yielded an average potential of 0.72 V (vs SHE). A value of 0.73 V was utilized in all subsequent calculations.

Evidence for Monomeric Cu^{I}L in Solution. Although the crystal structure of the Cu^{I}L complex revealed the presence of a dimer, entropic considerations alone suggest that this species is more likely to exist as a monomer at the low concentrations used for the solution studies (1−60 μM). Extensive cyclic voltammetric measurements in 80% methanol-20% water (w/w) at temperatures down to −77 °C and scan rates up to 5 kV s^{-1} revealed a single cathodic and anodic peak under all conditions with the peak-to-peak separation approaching 59 mV at the slowest scan rates. This behavior is consistent with monomeric Cu^{I}L (and also indicates the absence of metastable intermediates under these conditions of the type noted for Cu$^{II/I}$([14]aneS$_4$) and related systems).[23,26] Rapid equilibration with dimeric Cu^{I}L cannot be ruled out, but the reactive behavior of the Cu(I) complex is indistinguishable from a solution in which only a monomer exists and the data may be adequately treated by considering only the monomer. This conclusion is further supported by the first-order dependence on each reactant in the electron-transfer kinetic measurements.[38]

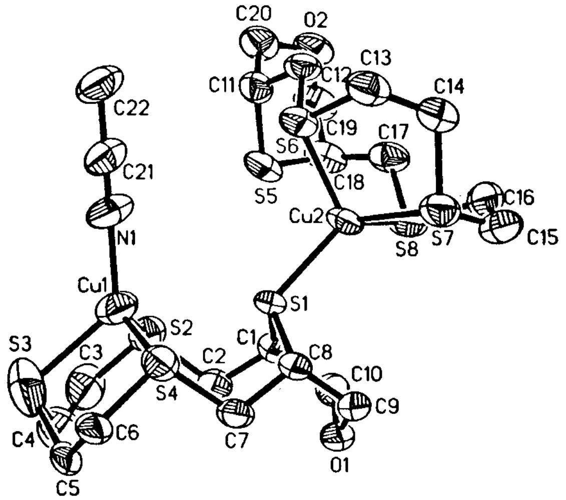

Figure 4. ORTEP drawing of the cationic dimer in the crystal structure of [{Cu^{I}(oxathiane[12]aneS$_4$)}$_2$(NCCH$_3$)](ClO$_4$)$_2$·CH$_3$CN showing the atom labeling scheme. As shown by the data in Tables 2 and 3, the bond lengths and bond angles in subunit A (at left) and subunit B (at right) are similar despite the different donor atoms occupying the apical site. For both subunits, the Cu bond to the sulfur of the oxathiane ring has been ruptured. The crystal was grown in acetonitrile which accounts for the apically coordinated CH$_3$CN molecule in the left subunit.

Kinetics of Electron-Transfer Cross Reactions. The cross-reaction kinetics for both the oxidation and reduction of the Cu$^{II/I}$L system were studied by stopped-flow spectrophotometry using Ru^{II}(NH$_3$)$_5$isn and Ru^{II}(NH$_3$)$_4$bpy as reductants (A_{Red}) and Ru^{III}(NH$_3$)$_2$(bpy)$_2$ and Ni^{III}([14]aneN$_4$)(H$_2$O)$_2$ as oxidants (A_{Ox}) {isn = isonicotinamide, bpy = 2,2′-bipyridine, and [14]aneN$_4$ = 1,4,8,11-tetraazacyclotetradecane (i.e., cyclam)}:

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

The second-order reactions tended to be exceptionally fast with the three reactions involving ruthenium reagents exhibiting cross-reaction rate constants, k_{12} and k_{21}, exceeding 4×10^7 M^{-1} s^{-1} (see Table 4). The mean rate constant value calculated for each of the four cross reactions is included in Table 4. Evaluation of these large rate constants was made possible only by our recent development and demonstration of a reliable approach for handling second-order stopped-flow data which

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(38) All cross reactions appeared to be first order with respect to each reactant. In the specific case of Cu^{I}L reacting with excess Ni^{III}([14]aneN$_4$), the pseudo-first-order rate constant was observed to parallel the Ni(III) concentration over the 6-fold concentration range tested. This rules out the possibility of a stable Cu$^{I}_2$L$_2$ dimer acting as a two-electron donor prior to dissociation and is consistent with the hypothesis that Cu^{I}L reacts solely as a monomer in dilute solution. The agreement between the electron-transfer kinetics observed for both reduction and oxidation is also consistent with the contention that only monomeric Cu^{I}L is of importance in solution.

Table 4. Electron-Transfer Rate Constants for $Cu^{II/I}$(oxathiane[12]aneS_4) Reacting with Four Counter-Reagents in Aqueous Solution at 25 °C, $\mu = 0.10$ M (ClO_4^-)

counter-reagent[a,b]	k_{12} or $k_{21} \times 10^{-7}$, M^{-1} s^{-1}	log k_{11} (M^{-1} s^{-1}) calcd[c]
NMR line-broadening		5.92 ± 0.04^{d}
$Ru^{II}(NH_3)_5$isn	$9._{7}^{e}$	5.8 ± 0.8
$Ru^{II}(NH_3)_4$bpy	$4._{3}^{e}$	5.7 ± 0.4
$Ru^{III}(NH_3)_2(bpy)_2$	13^{e}	5.9 ± 0.3
Ni^{III}([14]aneN_4)$(H_2O)_2$	0.32(2), 0.31(5), 0.32(6) [f]	5.6 ± 0.1^{g}

[a] Ligand abbreviations: bpy = 2,2′-bipyridine, isn = isonicotinamide, [14]aneN_4 = 1,4,8,11-tetraazacyclotetradecane (cyclam). [b] For the potentials, self-exchange rate constants, and ion size parameters utilized for all counter-reagents, see ref 30 (except as noted). [c] Based on $E^{f} = 0.73$ V (vs SHE) for $Cu^{II/I}$(oxathiane[12]aneS_4) as determined in this work using ferroin as an external standard for which a formal potential of $E^{f} = 1.112$ V was assumed (ref 33). [d] Value determined at $\mu = 0.044$ was $k_{11} = (7.1 \pm 0.7) \times 10^5$ M^{-1} s^{-1}; correction to $\mu = 0.10$ with the extended Debye−Hückel equation yields $k_{11} = (8.4 \pm 0.8) \times 10^5$ M^{-1} s^{-1} (based on a center-to-center distance of closest approach of 8.8×10^{-8} cm). [e] Median value. [f] Mean values (standard deviations for last digit in parentheses) based on three separate studies run under pseudo-first-order conditions where each reactant, in turn, was held in excess. [g] Based on $E^{f} = 1.00$ V for $Ni^{III/II}$([14]aneN_4)$(H_2O)_2$; a calculated value of log $k_{11} = 6.1$ is obtained if a potential of 0.95 V is applied for this counter-reagent as utilized in previous studies (see refs 15, 21, 30, 39, and 42).

involve inhomogenieties within the observation cell.[34] For the reaction involving $Ru^{II}(NH_3)_5$isn, the resolved second-order rate constants varied widely in repetitive experiments since, at the lowest observable reactant concentrations, the signal-to-noise ratio for the observable portion of the reaction was very small. Nonetheless, the fact that we have been able to achieve reproducible results for four different cross-reactions with such large rate constants represents the first independent demonstration of the efficacy of the approach used.

No evidence of limiting first-order (i.e., "gated") behavior[15,21,30,39] was observed with any of the reagents under any of the conditions utilized. Since three of these reactions have pushed our improved data resolution techniques to the limit, this failure to observe gated behavior implies that any conformational changes accompanying electron transfer are rapid for the $Cu^{II/I}$(oxathiane[12]aneS_4) system relative to the time domain accessible by the stopped-flow method. This conclusion is consistent with our low temperature and rapid-scan cyclic voltammetric studies.

The self-exchange rate constant for the $Cu^{II/I}$(oxathiane-[12]aneS_4) redox couple was calculated by application of the Marcus cross relation[40] as previously described[25] for each individual stopped-flow experiment. The parameters applied for the four counter reagents were identical to those previously reported[30] with the exception that, based on extensive recent measurements in our laboratory,[41] a corrected potential of $E^{f} = 1.00$ V was utilized for $Ni^{III/II}$([14]aneN_4) (as compared to $E^{f} = 0.95$ V which we have used previously).[15,21,30,39,42] Despite the inaccuracies inherent in evaluating the rate constants for these very rapid reactions, all four reactions yielded consistent $Cu^{II/I}L$ k_{11} values as illustrated in Table 4. The median value from the four individual reactions is $k_{11} = 6 \times 10^5$ M^{-1} s^{-1}.

Electron Self-Exchange Rate Constant by NMR Line Broadening. The electron self-exchange rate constant for $Cu^{II/I}$(oxathiane[12]aneS_4) was also obtained directly from NMR line-broadening measurements in the same manner as previously described for several related $Cu^{II/I}$−polythiaether systems.[13−15,21,30,39] Although the solubility limitations for $Cu^{I}L$ resulted in peaks which were not well resolved in D_2O—even with a 500 MHz spectrometer—a ^1H peak at 3.17 ppm (relative to the solvent peak at 4.66 ppm), assigned to the bridgehead carbons, was sufficiently well-defined to permit viable line-broadening measurements. In preliminary experiments with nonoptimal conditions, we obtained k_{11} values of $(10 \pm 4) \times 10^5$ and $(7.3 \pm 1.2) \times 10^5$ M^{-1} s^{-1}, respectively, at 25 °C, $\mu \approx 0.05$. For the final measurements, the following conditions were utilized: [$Cu^{I}L$] = 0.49 mM; [Cu^{II}] = 14.7 mM (to force the $Cu^{II}L$ species to remain fully formed); [$Cu^{II}L$] = 0.012−0.15 mM. (By utilizing a constant concentration of Cu^{2+}, any paramagnetic ion effects were constant.) Following completion of the NMR measurements, the solution absorbance at $\lambda = 400$ nm (using a small volume 1-cm cell) was measured to determine the actual concentration of $Cu^{II}L$ in each tube. The final k_{11} value calculated for $Cu^{II/I}$(oxathiane[12]aneS_4) was $(7.1 \pm 0.7) \times 10^5$ M^{-1} s^{-1} at 25 °C, $\mu = 0.044$. Correction to $\mu = 0.10$ M, using the extended Debye−Hückel equation, yields $k_{11} = (8.4 \pm 0.8) \times 10^5$ M^{-1} s^{-1}.

The foregoing results are in reasonable agreement with an early study of ours on Cu^{II}([12]aneS_4) reduction for which we obtained $k_{11(Red)}$ values of 3.1×10^5 and 4.9×10^5 M^{-1} s^{-1} with two different reducing reagents.[25] However, in the earlier study we also reported $k_{11(Ox)} = 1.0 \times 10^{-2}$ M^{-1} s^{-1} for the oxidation of Cu^{I}([12]aneS_4). The latter value now appears to be erroneous, presumably because the actual cross-reaction rate was too rapid for us to evaluate at that time—although the difficulties caused by the insolubility of the Cu(I) complex also played a role. The discrepancy in the original k_{11} values obtained from the reduction and oxidation kinetics of the $Cu^{II/I}$([12]aneS_4) system was attributed to a switch in the reaction pathway—a phenomenon since shown to be common to many Cu(II/I) reactions.[15,21,30,39] Our current study shows no evidence of such a switch for the oxidation kinetics of Cu^{I}(oxathiane[12]aneS_4) even under the most severe conditions which can be accessed experimentally.

Conclusion

Previous studies have shown that, for the $Cu^{II/I}$([14]aneS_4)[30] and -([15]aneS_4)[15] complexes, the k_{11} values are approximately 10^4 M^{-1} s^{-1} for the most favorable reaction pathway. In both systems, electron transfer is believed to require the inversion of two donor atoms.[23] Substituted [14]aneS_4 complexes, in which donor atom inversion is impeded, exhibit k_{11} values of only 10^2−10^3 M^{-1} s^{-1}.[43] By contrast, the calculated k_{11} value for $Cu^{II/I}$(oxathiane[12]aneS_4) exceeds 10^5 M^{-1} s^{-1}, a property which it shares in common with other macrocyclic tetrathiaether and pentathiaether complexes of copper which do not require donor atom inversion.

In the Cu(II) complexes with oxathiane[12]aneS_4 and [13]-aneS_4, the Cu atom sits 0.55 and 0.38 Å, respectively, above the average S_4 plane.[17] Extrusion of the Cu atom further out of the donor atom plane appears to reduce the inner-sphere

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reorganization which accompanies electron transfer, a feature which is presumed to be largely responsible for the 2-fold increase in the k_{11} value obtained for the smaller macrocyclic system.

As noted in the foregoing discussion, the cross-reaction kinetics yield a median value of $k_{11} = 6 \times 10^5$ M^{-1} s^{-1} for Cu$^{II/I}$(oxathiane[12]aneS$_4$). In combination with the value determined by NMR line-broadening (8.4×10^5 M^{-1} s^{-1}), we conclude that $k_{11} = 7 \times 10^5$ M^{-1} s^{-1} represents the most representative value for this system. Thus, the Cu$^{II/I}$(oxathiane[12]aneS$_4$) system appears to slightly exceed the Cu$^{II/I}$(TAAB) system ($k_{11} = 5 \times 10^5$ M^{-1} s^{-1})[12] as *the most reactive low molecular weight Cu(II/I) system yet reported*. Efforts to design complexes which avoid inversion of donor atoms upon electron transfer would appear to represent a relevant approach for generating rapidly reacting macrocyclic Cu(II/I) systems.

In reaching the foregoing conclusion, it should be noted that a few complexes which involve neither a change in coordination number nor donor atom inversion have been found to exhibit relatively slow electron-transfer kinetics. These include systems in which the coordination number appears to remain invariant at either four[44] or five[45] during the electron-transfer process. For such Cu(II/I) systems, it appears that factors other than coordinate bond rupture and donor atom inversion are contributing significantly to the reorganizational barriers.

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Supporting Information Available: Three X-ray crystallographic files, in CIF format, are available free of charge via the Internet only at http://pubs.acs.org.

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