Ring Size, Substituent, and Anion Effects on the Kinetic and Equilibrium Properties of Copper(II) Complexes with Water-Soluble Macrocyclic Tetrathia Ethers

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The complete series of alcoholic derivatives for the 13- through 16-membered macrocyclic tetrathia ethers, in which a single −OH group is attached to the central carbon of a trimethylene bridge, has now been synthesized. The derivatized ligands show a marked improvement in aqueous solubility, permitting the measurement of both the Cu(II) complex stability constants ($K_{Cu^{II}L}'$) and the corresponding formation (k_f) and dissociation (k_d) rate constants in aqueous solution at 25 °C. Insofar as possible, the $K_{Cu^{II}L}'$, k_f, and k_d values were determined from independent measurements to assess the level of consistency between them. The Cu$^{II/I}$L formal potentials for complexes of the OH-substituted ligands have also been determined, permitting the calculation of the stability constants for the Cu^{I}L complexes. Except for the potential measurements, all values were determined in the presence of both 0.10 and 1.0 M perchlorate to assess the uniformity of anion adduct effects upon the various kinetic and thermodynamic values. All values for the alcoholic derivatives are compared to the corresponding parameters determined previously for the unsubstituted macrocycles—for which, due to solubility limitations, the formation kinetic data had to be extrapolated to aqueous conditions from measurements made in methanol−water mixtures. In general, the substitution of an −OH group on the ligand backbone results in a 5−8-fold decrease in the k_f values. This decrease in complex formation rate is attributed to the influence of hydrogen bonding between the −OH group and the surrounding solvent molecules upon the preferred ligand conformation in water. The k_f values for both series of ligands are consistent with a mechanism in which the closure of the first chelate ring is the rate-determining step. The effect of −OH substitution upon the k_d values is somewhat variable but tends to be less pronounced. The OH-substituted 14-membered macrocycle appears to be somewhat unique from the standpoint that the Cu(II) complex is twice as stable as the unsubstituted analogue, whereas all other −OH derivatives show a decrease in Cu^{II}L stability. Also included in the current study are measurements on the Cu(II) complex formed with a water-soluble oxathiane derivative of the 12-membered macrocyclic tetrathia ether (oxathiane-[12]aneS$_4$).

Introduction

Ligand cyclization tends to enhance metal complex stabilities, as demonstrated by the fact that Cu^{II}([14]aneN$_4$) (i.e., Cu^{II}-(cyclam)) is 10^6 times more stable in water than the corresponding acyclic ligand complex.[2] Hinz and Margerum[3,4] attributed this macrocyclic effect to differences in ligand solvation, noting that the free macrocyclic tetraamine preferentially orients its nitrogen lone pairs into the ligand cavity[4] (a so-called *endo* conformation), making them less available for hydrogen bonding to the surrounding solvent. Thus, they proposed that the desolvation enthalpy is much smaller for metal complex formation with cyclic tetramine ligands, a hypothesis supported by later calorimetric measurements reported by Clay, Paoletti, and co-workers.[5] However, solvation interactions do not account for the entire macrocyclic effect. The Cu(II) complexes with the corresponding tetrathia ethers—for which hydrogen bonding to the solvent is minimal—exhibit a consistent macrocyclic stability increase of 10^2 in 80% methanol−20% water,[6] water,[7] and nitromethane.[8] This enhancement is almost totally due to entropy effects, the overall enthalpies of complex formation being nearly identical for Cu^{II}([14]aneS$_4$) and the corresponding acyclic ligand.[9] Moreover, DeSimone and Glick[10] were the first to note that the inherent tendency of the CC−SC torsion angles to adopt a gauche conformation predisposes uncomplexed [14]aneS$_4$ to adopt an *exo* conformation (in which the sulfur lone pairs are oriented away from the ligand cavity), an issue later emphasized by Cooper.[11] Therefore, complexation of [14]aneS$_4$ by Cu(II) involves a slight increase in internal ligand strain as the ligand converts from *exo* to *endo*.

The difference in preferred ligand conformations also appears to account for the fact that substitution of alkyl groups on the ligand backbone affects the metal complex stabilities for the [14]aneN$_4$ and -S$_4$ macrocycles in a different manner. Hinz and Margerum[4] noted that the addition of one methyl group on an α-carbon in each trimethylene bridge of [14]aneN$_4$ *decreases*

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the stability constant of the Ni(II) complex 2-fold in aqueous solution, while three methyl groups on each trimethylene bridge cause a 10^2-10^4-fold *decrease*, depending upon the specific enantiomer involved. In contrast, Gellman and co-workers[12] substituted one and two *gem*-dimethyl groups onto the central carbon of the trimethylene bridges in [14]aneS$_4$ and found that the stability constants of the Ni(II) complexes in nitromethane *increase* 7-fold for each *gem*-dimethyl group added. Crystal structures corroborated their claim that the *gem*-dimethyl groups tend to force the macrocycle toward an *endo* conformation, predisposing it for complexation.[13]

In the simplest substituent study conducted to date,[14] we found that the addition of a single −OH group on the central carbon of a trimethylene bridge in [14]aneS$_4$ causes a 2-fold *increase* in the Cu^{II}L stability constant, while an additional −OH group on the second trimethylene bridge results in a 6−37-fold *decrease* in stability (or an overall 3−17-fold reduction compared to [14]aneS$_4$), depending upon whether the two −OH groups are *syn* or *anti*. Since the steric effect of an −OH group is minimal, we surmised that the main influence might be the ability of −OH to hydrogen-bond to the surrounding water, tending to invert the macrocyclic tetrathia ether toward an *endo* conformer—although this does not explain the decrease in stability observed for the two diol compounds. We have also noted that the substitution of even a single −OH group on [14]-aneS$_4$ increases the aqueous solubility nearly 100-fold (from 4 to 350 μM) at ambient temperature. This latter observation suggested the possibility of studying the kinetic effects of macrocyclic ring size on S$_4$ complex formation directly in aqueous solution. This would circumvent our previous limitation of studying such kinetics in mixed methanol−water solvents due to the very limited aqueous solubility of the unsubstituted S$_4$ ligands.[7]

We have now prepared an entire series of macrocyclic S$_4$ ligands in which a single −OH group has been substituted on the central carbon atom of a trimethylene bridge in [13]-, [14]-, [15]-, and [16]aneS$_4$. These monoalcoholic derivatives exist as single diastereomers, thereby simplifying ligand synthesis and purification. Since the [12]aneS$_4$ macrocycle has no trimethylene bridge, a corresponding derivative could not be prepared for this ring size. However, a somewhat related oxathiane derivative has been prepared, which also exhibits enhanced aqueous solubility. All five ligands are illustrated in Figure 1.

For all compounds included in the current investigation, we have determined both the Cu^{II}L stability constants ($K_{Cu^{II}L}$) and the formation (k_f) and dissociation (k_d) rate constants directly in aqueous solution at 25 °C:

$$Cu^{II} + L \underset{k_d}{\overset{k_f}{\rightleftharpoons}} Cu^{II}L \qquad (1)$$

In view of our earlier observation that a perchlorate adduct forms with these complexes, all measurements have been conducted in the presence of both 0.10 and 1.0 M HClO$_4$. (Since these ligands do not protonate, the change in acidity is of no consequence.) We have also determined the formal Cu$^{II/I}$L potentials, which can then be used to calculate the Cu^{I}L stability constants. Since the equilibrium and kinetic data for the Cu^{II}-
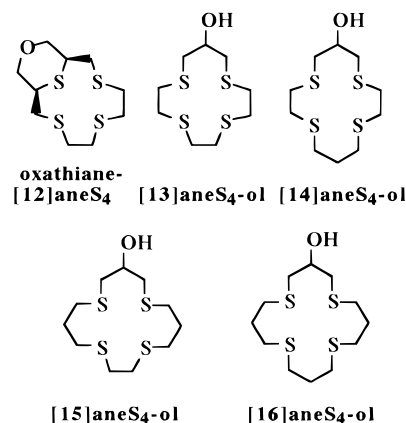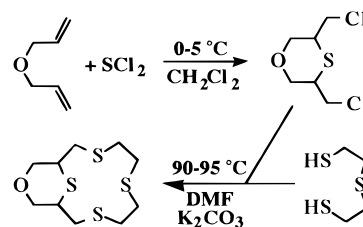

Figure 1. Ligands studied in this work.

Scheme 1

([14]aneS$_4$-ol) complex, as previously reported in 0.10 M HClO$_4$,[14] were not in satisfactory agreement, the earlier measurements on this system have been repeated in this work, along with new measurements in 1.0 M HClO$_4$.

All of the data included in this work are compared to the previous data obtained for the corresponding unsubstituted macrocyclic S$_4$ ligands. The cumulative results are examined in terms of the effects of ring size, ring substituents, and anions upon the kinetic and thermodynamic properties of these copper complexes in aqueous media.

Experimental Section

Ligand Synthetic Approaches. The general approach used for preparing the macrocyclic polythia ether alcohols has been previously described for [14]aneS$_4$-ol, in which the high-dilution condensation of 1,3-dichloro-2-propanol (Aldrich Chemical Co.) was carried out with 3,7-dithianonane-1,9-dithiol.[14] More recently, we have described an improved general method for the fine control of high-dilution conditions by addition of a single solution of the condensation reactants via a metering HPLC pump to a large diluting pool of DMF containing suspended activating carbonate base, maintained at 80−110 °C.[15] This latter modification was employed for all ligands described in the current study. We have also previously described general methods for the preparation of the dithiaalkane-ω,ω-dithiol synthons.[14,16] The preparation of the oxathiane-[12]aneS$_4$ is illustrated in Scheme 1. Preparation of the *cis*-2,5-bis(chloromethyl)-1,4-oxathiane synthon (Caution! vesicant) was by the method of Lautenschlaeger.[17] Our general separation and characterization techniques have also been previously described.[15] GC−MS data were obtained for dilute ethanol solutions. Only ^{13}C NMR data are reported, since the 400 MHz ^{1}H NMR patterns afford little *a priori* basis for distinction.

3,6,9,12-Tetrathiacyclotridecan-1-ol ([13]aneS$_4$-ol). The residue from condensation of 18.1 g (0.14 mol) of 1,3-dichloro-2-propanol and 30 g (0.14 mol) of 3,6-dithiaoctane-1,8-dithiol in 1.5 L of DMF and 45.5 g (0.33 mol) of K$_2$CO$_3$ was separated by elution chromatography

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on a 5 × 70 cm silica gel column (5/95 ethanol/toluene). The combined elution fractions containing the most mobile major component with R_f 0.35 (20/80 ethyl acetate/toluene) were recrystallized after charcoal treatment from 500 mL of 3/97 ethyl acetate/toluene to yield 10.81 g (28.6%) of colorless needles, mp 127−128 °C. ^{13}C NMR (20.15 MHz, CDCl$_3$), δ in ppm (multiplicity): 31.53 (t), 31.72 (t), 32.28 (t), 37.79 (t), 67.68 (d). FT-IR (KBr; $\bar{\nu}$ in cm^{-1} (relative intensity)): 3427 (b, s), 2938 (s), 2916 (s), 1427 (s), 1280 (m), 1270 (m), 1202 (s), 1074 (s), 581 (s). EI-MS (*m/z* (relative intensity)): 270 (M$^+$, 98), 255 (18), 122 (100), 105 (76), 92 (82), 61 (89), 59 (62). Anal. Calcd for C$_9$H$_{18}$-OS$_4$: C, 39.97; H, 6.71. Found: C, 40.14; H, 6.79.

3,7,10,14-Tetrathiacyclopentadecan-1-ol ([15]aneS$_4$-ol). The residue from condensation of 15.5 g (0.12 mol) of 1,3-dichloro-2-propanol and 29 g (0.12 mol) of 4,7-dithiadecane-1,10-dithiol in 1.5 L of DMF and 38.6 (0.28 mol) of K$_2$CO$_3$ was separated on a 5 × 60 cm silica gel column (1/99 ethanol/toluene). The combined elution fractions of the most mobile major component with R_f 0.60 (10/90 ethyl acetate/toluene) were recrystallized after charcoal treatment from 300 mL of 50/50 cyclohexane/toluene to yield 8.36 g (23.4%) of colorless needles, mp 85−86 °C. ^{13}C NMR (20.15 MHz, CDCl$_3$; δ in ppm (multiplicity)): 30.26 (t), 30.79 (t), 31.09 (t), 32.21 (t), 38.16 (t), 68.91 (d). FT-IR (KBr; $\bar{\nu}$ in cm^{-1} (relative intensity)): 3428 (b, s), 2945 (m), 2931 (s), 2850 (m), 1420 (s), 1233 (s), 1195 (m), 1060 (m), 1022 (s), 835 (w), 761 (w), 711 (w). EI-MS (*m/z* (relative intensity)): 298 M$^+$, 96), 270 (15), 197 (22), 146 (50), 133 (46), 106 (100), 73 (40), 61 (20). Anal. Calcd for C$_{11}$H$_{22}$OS$_4$: C, 44.26; H, 7.43. Found: C, 44.48; H, 7.60.

3,7,11,15-Tetrathiacyclohexadecan-1-ol ([16]aneS$_4$-ol). The residue from condensation of 12.9 g (0.1 mol) of 1,3-dichloro-2-propanol and 25.6 g (0.1 mol) of 4,8-dithiaundecane-1,11-dithiol in 1 L of DMF and 34.5 g (0.25 mol) of K$_2$CO$_3$ was separated on a 5 × 60 cm silica gel column (1/99 ethanol/toluene). The combined elution fractions of the most mobile component with R_f 0.40 (5/95 ethyl acetate/toluene) were recrystallized after charcoal treatment from 300 mL of 50/50 hexane/toluene to yield 9.98 g (32%) of colorless needles, mp 74−76 °C. ^{13}C NMR (20.15 MHz, CDCl$_3$; δ in ppm (multiplicity)): 29.27 (t), 29.55 (t), 30.63 (t), 30.73 (t), 30.79 (t), 38.02 (t), 68.76 (d). FT-IR (KBr; $\bar{\nu}$ in cm^{-1} (relative intensity)): 3430 (b, s), 2933 (s), 2912 (s), 2850 (m), 1440 (m), 1417 (s), 1295 (m), 1255 (m), 1065 (m), 1028 (s), 845 (w), 760 (w), 715 (w). EI-MS (*m/z* (relative intensity)): 312 (M$^+$, 100), 294 (14), 255 (18), 223 (12), 181 (18), 147 (28), 121 (15), 106 (65), 89 (18), 73 (30), 61 (17). Anal. Calcd for C$_{12}$H$_{24}$OS$_4$: C, 46.11; H, 7.74. Found: C, 46.50; H, 7.92.

13-Oxa-3,6,9,15-tetrathiabicyclo[9.3.1]pentadecane (oxathiane-[12]aneS$_4$). The residue from condensation of 26.7 g (0.14 mol) of *cis*-2,5-bis(chloromethyl)-1,4-oxathiane and 21.6 g (0.14 mol) of 3-thiapentane-1,5-dithiol (Aldrich Chemical Co., 2-mercaptoethyl sulfide) in 2 L of DMF and 55.2 g (0.4 mol) of K$_2$CO$_3$ was separated on a 8 × 75 cm silica gel column (5/95 ethyl acetate/cyclohexane). TLC analysis of the crude residue (10/90 ethyl acetate/cyclohexane) showed three significant components with R_f 0.65, 0.50, and 0.30. The first and third components were characterized as the intrachain cyclization byproducts 3-oxa-7,9-dithiabicyclo[3.3.1]nonane (oxathiane-[6]aneS$_2$) and 10-oxa-3,6,12-trithiabicyclo[6.3.1]dodecane (oxathiane-[9]aneS$_3$), respectively. The combined fractions of the R_f 0.50 desired component were recrystallized after charcoal treatment from 350 mL of 10/90 toluene/cyclohexane to yield 4.74 g (12%) of colorless plates, mp 102−105 °C. ^{13}C NMR (20.15 MHz, CDCl$_3$; δ in ppm (multiplicity)): 32.23 (t), 34.19 (t), 37.26 (t), 38.88 (d), 71.26 (t). FT-IR (KBr; $\bar{\nu}$ in cm^{-1} (relative intensity)): 2986 (m), 2943 (s), 2924 (s), 2895 (m), 1457 (s), 1420 (s), 1314 (m), 1270 (s), 1245 (m), 1218 (m), 1196 (m), 1115 (s), 1047 (s), 935 (m), 905 (m), 879 (s), 742 (m), 677 (m), 667 (s). EI-MS (*m/z* (relative intensity)): 282 (M$^+$, 100), 249 (27), 162 (22), 133 (29), 105 (20), 73 (33), 59 (18). Anal. Calcd for C$_{10}$H$_{18}$OS$_4$: C, 42.52; H, 6.42; S, 45.40. Found: C, 42.42; H, 6.65; S, 45.1.

Other Reagents. The preparation and purification of Cu(ClO$_4$)$_2$, used as the source of copper(II) ion, has been previously described.[14] The concentrations of the stock Cu(II) solutions were determined by titration with EDTA using murexide indicator. Stock ligand solutions were prepared by stirring a sample of the solid ligand in 0.10 M HClO$_4$ overnight and filtering off any undissolved solid. Ligand concentrations were then determined by adding a large excess of Cu(II) (ca. 0.010 M)

Table 1. Spectral and Electrochemical Properties of the Copper(II) Complexes Formed with Unsubstituted and Derivatized Macrocyclic Tetrathia Ether Ligands in Aqueous Solution at 25 °C and $\mu = 0.10$ M (HClO$_4$)

| ligand | peak max | | E^f, V^a |
	λ_1, nm (ϵ)	λ_2, nm (ϵ)	
[12]aneS$_4$	387 (6000)^b	675 (2000)^b	<0.69 (0.52?)^c
oxathiane-[12]aneS$_4$	400 (4800)	670 (1600)	0.72
[13]aneS$_4$	390 (6000)^b	625 (1800)^b	0.52^c
[13]aneS$_4$-ol	394 (6500)	616 (1860)	0.54
[14]aneS$_4$	390 (8200)^b	570 (1900)^b	0.58^c
[14]aneS$_4$-ol	390 (8800)	556 (1200)	0.49
[15]aneS$_4$	414 (8000)^b	565 (1140)^b	0.64^c
[15]aneS$_4$-ol	414 (8700)	556 (1200)	0.71
[16]aneS$_4$	440 (6100)^b	603 (800)^b	0.71^c
[16]aneS$_4$-ol	438 (6700)	586 (800)	0.73

^{a} Vs NHE. ^{b} Reference 19. ^{c} Bernardo, M. M.; Schroeder, R. R.; Rorabacher, D. B. *Inorg. Chem.* **1991**, *30*, 1241−1247.

followed by adding increments of standard Hg(II) solution and monitoring the disappearance of the Cu^{II}L absorbance in the vicinity of 400 nm, thus providing a displacement mole ratio plot. Reagent grade HClO$_4$ was obtained from G. F. Smith Chemical Co. Distilled−deionized water was used in the preparation of all solutions.

Instrumentation. All absorbance measurements were carried out using a Cary 17-D double-beam recording spectrophotometer equipped with a thermostated cell holder. Stopped-flow kinetic measurements were made using a Durrum Model D-110 stopped-flow spectrophotometer equipped with glass and Kel-F fittings and gastight syringes. For both instruments, temperature was controlled at 25.0 ± 0.2 °C using a circulating water bath. The formal potentials of the Cu$^{II/I}$L complex systems in 0.10 M HClO$_4$ were determined at room temperature with slow-scan cyclic voltammetry using a BAS 100 electrochemical analyzer (Bioanalytical Systems, Lafayette, IN). A typical three-electrode cell was utilized with a glassy-carbon working electrode (3 mm diameter), a Ag/AgCl reference electrode (0.197 V vs NHE), and a platinum-wire auxiliary electrode (BAS, Lafayette, IN).

Results

Formal Potentials. The formal potentials for all Cu$^{II/I}$L species included in this work were determined in 0.10 M HClO$_4$ at scan rates ranging from 0.1 to 2.5 V s^{-1}, as defined by the half-reaction

$$\text{Cu}^{II}\text{L}' + e^- \rightleftharpoons \text{Cu}^{I}\text{L}' \qquad (2)$$
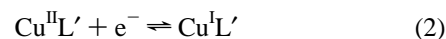
The primes denote all species of complexed copper in these specific oxidation states, including any perchlorate adducts of the type previously detected for the Cu(II) complexes with the unsubstituted macrocyclic tetrathia ethers:[9,18]

$$[\text{Cu}^{II}\text{L}'] = [\text{CuL}^{2+}] + [\text{CuL}(\text{ClO}_4)^+] + [\text{CuL}(\text{ClO}_4)_2] \qquad (3)$$
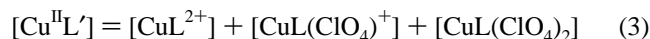
The cyclic voltammograms were well-behaved in all cases, except for the oxathiane-[12]aneS$_4$ system, which showed evidence of adsorption of the Cu^{I}L species on the electrode surface. The potentials obtained are tabulated in Table 1, all values being referenced to the normal hydrogen electrode.

Spectra and Stability Constants. As with the corresponding unsubstituted tetrathia ether complexes,[19] all of the Cu^{II}L complexes included in the current study exhibit strong charge-transfer bands in the vicinity of 400 and 600 nm. The former peak exhibits the larger molar absorptivity constant and was used to monitor the reactions. Since the copper(II) complexes

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Table 2. Formation and Dissociation Rate Constants and Conditional Stability Constants for Copper(II) Ion Reacting with both Unsubstituted and Derivatized Macrocyclic Tetrathia Ether Ligands in Aqueous Solution at 25 °C, $\mu = 0.10$ M, and 1.0 M HClO$_4$[a]

ligand	[HClO$_4$], M	$10^{-4} k_f$, M^{-1} s^{-1} [b]	k_d, s^{-1} [b]	$10^{-3} K_{Cu^{II}L}'$(kinetic), M^{-1} [c]	$10^{-3} K_{Cu^{II}L}'$(equil), M^{-1} [b,d]	$10^{-12} K_{Cu^{I}L}'$, M^{-1} [e]
[12]aneS$_4$	0.10	0.65[f]	4.8[g,h]	1.4	2.47,[i] 3.01[j]	1
	1.0	1.3[c]	0.6[g,h]		21.9[j]	
oxathiane-[12]aneS$_4$	0.10	0.223(4), 0.15(1)	1.95(5), 2.2(4)	1.1$_4$, 0.68	1.049(3)	1.$_0$
	1.0	0.43(1)	0.3(2)	14	6.09(7)	
[13]aneS$_4$	0.10	7.4[f]	56[g,h]	1.3	2.77,[i] 2.59[j]	0.01$_0$
	1.0	25[c]	14.1[g,h]		17.7[j]	
[13]aneS$_4$-ol	0.10	2.1(9), 1.81(3)	25(1), 27.5(1)	0.84, 0.66	1.48(5), 0.94(1)	0.05
	1.0	5.5(3)	6.1(1)	9.0	8.8(1)	
[14]aneS$_4$	0.10	13[f]	9[g,h,k]	14	21.8[i]	0.8$_8$
	1.0	45[c]	2.4[g,h]		187[i]	
[14]aneS$_4$-ol	0.10	3.98(5)[l]	0.549(2)[g,l]	72	39.0(5)[l]	0.04$_7$
	1.0	9.5(6)	0.179(3)[g]	530	201(13)	
[15]aneS$_4$	0.10	23.5[m]	100[m]	2.4	1.5[i]	0.6$_3$
[15]aneS$_4$-ol	0.10	3.7[c]	[2.0(2)] × 10^2 [g]		0.19(3)	1.$_2$
	1.0	13(2)	205(9)	0.63	0.69(2)	
[16]aneS$_4$	0.10	17[f]	1.06 × 10^3 [c]		0.16[i,j]	1.$_0$
	1.0				1.41[j]	
[16]aneS$_4$-ol	0.10	0.64[c]	~2 × 10^2 (est)[g,n]		0.032(3)	0.4$_4$
	1.0	2.2[c]	[2.0(3)] × 10^2 [g]		0.109(3)	

[a] All values for unsubstituted ligands are from previous studies as noted; data for [15]- and [16]aneS$_4$ were primarily available only for 0.10 M HClO$_4$. [b] Values in parentheses represent standard deviations relative to the last digit shown: e.g., 0.223(4) represents 0.223 ± 0.004. [c] Values in italics were calculated from data in other columns using eq 8. [d] Determined directly using the McConnell–Davidson method. [e] Stability constants for Cu^{I}L complexes were calculated from $K_{Cu^{II}L}$ and E^f values using eq 9 (see text). [f] Extrapolated to aqueous solution from studies in methanol–water mixtures. [g] Obtained experimentally from mercury displacement kinetics in aqueous solution. [h] Reference 21. [i] Reference 9. [j] Reference 18. [k] A value of $k_d = 11$ s^{-1} was determined independently for Cu^{II}([14]aneS$_4$) from dissociation following rapid oxidation of the Cu^{I}L complex: Martin, M. J.; Rorabacher, D. B. Unpublished results as cited in ref 7. [l] Values originally reported for Cu^{II}([14]aneS$_4$-ol) in aqueous solution at 25 °C and 0.10 M HClO$_4$ were as follows: $k_f = 1.38 \times 10^4$ M^{-1} s^{-1}, $k_d = 2.6$ s^{-1}, $K_{Cu^{II}L}' = 4.9 \times 10^4$ M^{-1}.[14] These values were internally inconsistent and were re-determined in the current work. [m] Direct determination in aqueous solution[7]. [n] The dissociation rate constant for Cu^{II}([16]aneS$_4$-ol) in 0.10 M HClO$_4$ was imprecise due to the very small amount of complex formed.

are relatively weak, the stability constants and molar absorptivity values were determined simultaneously by the method of McConnell and Davidson,[20] as previously described.[9,18] All stabilities are reported as conditional stability constants based on the total Cu^{II}L complex formed in the presence of both 0.10 and 1.0 M HClO$_4$:

$$K_{Cu^{II}L}' = \frac{[Cu^{II}L']}{[Cu^{2+}][L]} \tag{4}$$

A tabulation of the visible wavelengths associated with the absorption peak maxima and the corresponding molar absorptivity values are given for all Cu(II) unsubstituted and monoalcoholic macrocyclic tetrathia ether complexes in Table 1. The conditional stability constants are listed in Table 2 as $K_{Cu^{II}L}'$(equil).

Formation and Dissociation Rate Constants. The formation rate constants for the Cu^{II}L complexes, as represented in reaction 1, were determined at 25 °C in both 0.10 and 1.0 M HClO$_4$ under pseudo-first-order conditions using a large excess of Cu(II) ion. The complex formation reactions did not proceed to completion, so that the resultant pseudo-first-order rate constant, k_{obs}, includes the contribution of the dissociation reaction

$$k_{obs} = k_f[Cu^{II}] + k_d \tag{5}$$

A typical plot of k_{obs} vs [Cu^{II}] is shown in Figure 2 for the data involving oxathiane-[12]aneS$_4$ in 0.10 M HClO$_4$, from which k_f is obtained as the slope and k_d as the intercept. For both the oxathiane-[12]aneS$_4$ and [13]aneS$_4$-ol systems at 0.10 M HClO$_4$, two sets of k_f and k_d values are entered in Table 2, representing

(20) McConnell, H.; Davidson, N. *J. Am. Chem. Soc.* **1950**, *72*, 3164–3167. Cf.: Benesi, H. A.; Hildebrand, J. H. *J. Am. Chem. Soc.* **1949**, *71*, 2703–2707.
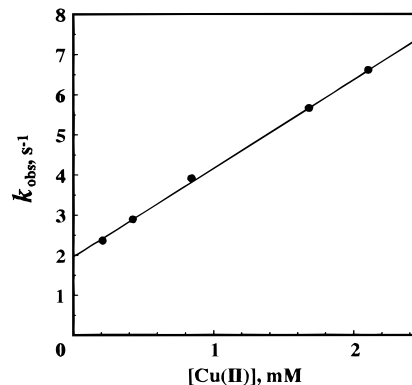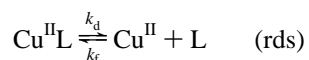

Figure 2. Plot of eq 5 for the experimental pseudo-first-order formation kinetic data for Cu^{II}(oxathiane-[12]aneS$_4$) at 25 °C in 0.10 M HClO$_4$. The slope yields $k_f = (2.23 \pm 0.04) \times 10^3$ M^{-1} s^{-1}, while a value of $k_d = 1.95 \pm 0.05$ s^{-1} is obtained from the intercept. For these measurements, the total ligand concentration is 2.5×10^{-5} M.

results obtained by two separate investigators. The Cu^{II}([14]aneS$_4$-ol) complex was too stable to provide a reliable k_d value from the formation kinetic studies. Therefore, the k_d value for this system was determined independently from mercury displacement kinetic studies as described below.

Direct kinetic measurements on the formation of Cu^{II}([15]aneS$_4$-ol) in 0.10 M HClO$_4$ and of Cu^{II}([16]aneS$_4$-ol) at both HClO$_4$ concentrations did not yield reliable data. Due to the small stability constants, a very large excess of Cu(II) was required to force the reaction to the right, which then increased k_{obs} to unmeasurable levels. For the former system, the use of 1.0 M HClO$_4$ increased the conditional stability constant (due to the formation of an adduct between perchlorate ion and the Cu^{II}L complex)[9,18] sufficiently to permit the direct evaluation of the formation kinetics. However, the Cu^{II}([16]aneS$_4$-ol) complex was too weak to yield measurable kinetic data even at this high perchlorate concentration.

For the 14−16-membered ligands, the dissociation rate constants were determined independently from kinetic measurements on the Hg(II) exchange reaction with the $Cu^{II}L$ complex in a manner identical with that used previously for the Cu(II) complexes with the unsubstituted 12−14-membered cyclic tetrathia ethers in aqueous solution:[21]
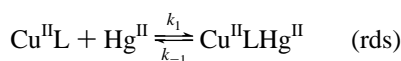
$$Hg^{II} + Cu^{II}L \rightarrow Hg^{II}L + Cu^{II} \qquad (6)$$
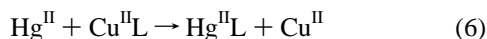
In this procedure, a large concentration of Cu(II) was added to the ligand solution to force a significant amount of the $Cu^{II}L$ complex to form. This $Cu^{II}L$ solution was then mixed with Hg(II) and the disappearance of $Cu^{II}L$ was monitored. The much higher stability constant of the $Hg^{II}L$ complexes ($K_{Hg^{II}L} \approx 10^{10}$)[22] compared to the $Cu^{II}L$ species forced the exchange reactions to proceed to completion despite the excess Cu(II) present.

As we have noted earlier,[21] the Hg(II) displacement reaction can proceed by two pathways, one involving the simple scavenging of the ligand after the $Cu^{II}L$ complex has dissociated (pathway 1) and the other involving the attack of the Hg(II) ion on the $Cu^{II}L$ complex to generate a mixed binuclear intermediate, $Hg^{II}LCu^{II}$ (pathway 2):

pathway 1

$$Cu^{II}L \underset{k_f}{\overset{k_d}{\rightleftharpoons}} Cu^{II} + L \qquad (rds)$$

$$Hg^{II} + L \rightleftharpoons Hg^{II}L \qquad (fast)$$

pathway 2

$$Cu^{II}L + Hg^{II} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} Cu^{II}LHg^{II} \qquad (rds)$$

$$Cu^{II}LHg^{II} \rightleftharpoons Hg^{II}L + Cu^{II} \qquad (fast)$$

where rds = rate-determining step. Both processes may contribute to the observed kinetics, leading to the overall reaction rate expression

$$-\frac{d[Cu^{II}L']}{dt} = k_1[Hg^{2+}][Cu^{II}L'] + k_d[Cu^{II}L'] \qquad (7a)$$

If Hg(II) is maintained in large excess over the total ligand, the apparent pseudo-first-order rate constant, k_{app}, can then be expressed as

$$k_{app} = k_d + k_1[Hg^{II}] \qquad (7b)$$

A plot of k_{app} against [Hg^{II}] for a series of successive measurements on the [14]aneS$_4$-ol system yielded k_1 as the slope and k_d as the intercept. In the case of the [15]- and [16]aneS$_4$-ol systems, the $Cu^{II}L'$ complex was not fully formed at the time the reaction was initiated. Under these circumstances, the free ligand reacts immediately with Hg(II) but has no effect upon the observed dissociation kinetics, since it does not affect the rate of disappearance of $Cu^{II}L'$. For both the [15]- and [16]-aneS$_4$-ol systems, plots of eq 7b yielded horizontal lines, indicating that only the dissociation pathway (pathway 1) was contributing significantly to the observed exchange kinetics (see Figure 3). Although the k_d values are very large for these two
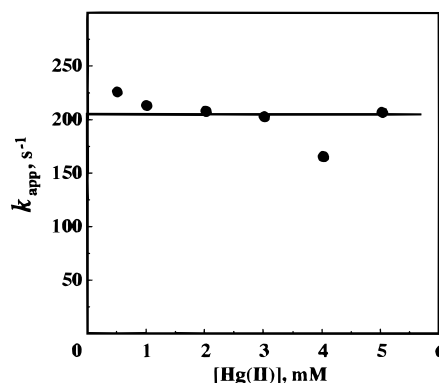
(21) Diaddario, L. L., Jr.; Ochrymowycz, L. A.; Rorabacher, D. B. *Inorg. Chem.* **1992**, *31*, 2347−2353.
(22) Jones, T. E.; Sokol, L. S. W. L.; Rorabacher, D. B.; Glick, M. D. *J. Chem. Soc., Chem. Commun.* **1979**, 140−141.

Figure 3. Plot of eq 7b for the experimental pseudo-first-order kinetic data for the exchange of mercury(II) with $Cu^{II}([15]aneS_4$-ol) at 25 °C in 0.10 M HClO$_4$. The lack of a positive slope in this plot indicates that this reaction is proceeding entirely by pathway 1, in which the mercury ion is serving as a scavenger for the ligand following the unaided dissociation of the $Cu^{II}L$ complex. Therefore, the value of k_d for the Cu(II) complex was obtained as the mean k_{app} value. For these measurements, initial concentrations are [Cu(II)] = 1.62×10^{-3} M and [L] = 4.32×10^{-5} M.

systems, reasonable accuracy was achieved except in the case of the [16]aneS$_4$-ol system in 0.10 M HClO$_4$, where the Cu(II) complex was too weak to provide accurate dissociation rate data.

The experimentally determined formation and dissociation rate constant values for all five systems included in the current study are listed in Table 2. The corresponding values for the Cu(II) complexes with the unsubstituted ligands are included for comparison. The ratio of the formation and dissociation rate constants for each system was used to generate an independent value of the complex stability constant, designated as $K_{Cu^{II}L}'$(kinetic) (eq 8),

$$K_{Cu^{II}L}' = k_f/k_d \qquad (8)$$

for comparison to the values obtained directly from equilibrium measurements, $K_{Cu^{II}L}'$(equil) (see Table 2). Since k_f values could not be measured directly for $Cu^{II}([15]aneS_4$-ol) in 0.10 M HClO$_4$ or for $Cu^{II}([16]aneS_4$-ol) in either 0.10 or 1.0 M HClO$_4$, no $K_{Cu^{II}L}'$(kinetic) values are entered for these systems under these conditions. In these last cases, values of k_f were calculated from $K_{Cu^{II}L}'$(equil) and k_d using eq 8. These calculated k_f values are included in Table 2.

Discussion

The hydroxy group on the polythia ether ligands included in this study is an extremely weak base, as are the thia ether sulfur donor atoms. Thus, as noted in the Introduction, these ligands are effectively devoid of protonation phenomena so that their metal complexes are insensitive to pH, as demonstrated in our earlier study on the alcoholic derivatives of [14]aneS$_4$.[14] As a result, differences in the HClO$_4$ concentration are presumed to have no effect on our data other than the influence of ionic strength and perchlorate concentration.

Stability Constants. Given the experimental difficulties encountered, the $K_{Cu^{II}L}'$(kinetic) and $K_{Cu^{II}L}'$(equil) values in Table 2 are considered to be reasonably consistent in all cases for which both values could be obtained independently. This observed level of agreement provides an indication of the level of confidence to be placed in the experimental data.

For all systems, the $Cu^{II/I}L$ formal potentials and the $K_{Cu^{II}L}'$(equil) values were inserted into the Nernst equation to permit calculation of the stability constants for the reduced complexes, K_{Cu^IL}', at 0.10 M HClO$_4$ as previously described:[15]

$$E_{Cu^{II/I}L}{}^f = E_{Cu^{II/I}solv}{}^f - \frac{2.303RT}{F}\log\frac{K_{Cu^{II}L}'}{K_{Cu^{I}L}'} \qquad (9)$$

For these calculations, a value of 0.13 V was utilized for the formal potential of the aquated redox couple, $E_{Cu^{II/I}solv}{}^f$, at 25 °C, and $\mu = 0.10$.[15] The values of $K_{Cu^{II}L}'$ calculated in this manner are listed in the last column of Table 2.

Stability Constant Trends. For most of the macrocycles included in Table 2, the $K_{Cu^{II}L}'$(equil) values in 1.0 M perchlorate are about 5−8 times larger than in 0.10 M. The exceptions are the [15]- and [16]aneS$_4$-ol complexes, for which a 3.6-fold increase is noted. The data are sufficiently precise to suggest that this difference in the magnitude of the perchlorate effect may be a real one. However, an 8.8-fold increase in $K_{Cu^{II}L}'$ was found for Cu^{II}([16]aneS$_4$)[18] on increasing HClO$_4$ from 0.10 to 1.0 M (see Table 2), indicating that the perchlorate dependence is not necessarily a function of ring size. Izatt, Gellman, and co-workers have previously observed differences in the magnitude of the perchlorate effect on Cu(II) complexes with *gem*-dimethyl-substituted [14]aneS$_4$ macrocycles in 80% methanol which were dependent upon the extent of ring substitution.[23] However, ring size was not varied in their study.

The general trend in the apparent Cu^{II}L stability constant as a function of perchlorate concentration has previously been ascribed to the formation of an adduct with the perchlorate ion:[9,18]

$$CuL^{2+} + ClO_4^- \rightleftharpoons CuL(ClO_4)^+ \qquad K_{1X} \qquad (10)$$

On the basis of an earlier thorough study on the [12]-, [13]-, and [14]aneS$_4$ complexes, involving wider variations in the perchlorate ion concentration, we estimated that $K_{1X}{}^0 \approx 24\ M^{-1}$ (extrapolated to zero ionic strength) regardless of the macrocyclic ring size.[18] Since the CuL^{2+} and CuL(ClO$_4$)$^+$ species appear to be spectrally identical,[8,18] our measurements of [Cu^{II}L$'$] always include the sum of both species:

$$K_{Cu^{II}L}' = \frac{[Cu^{II}L']}{[Cu'][L]} = \frac{[CuL^{2+}] + [CuL(ClO_4)^+]}{[Cu^{2+}][L]} =$$
$$\frac{[CuL^{2+}](1 + K_{1X}[ClO_4^-])}{[Cu^{2+}][L]}$$

or

$$K_{Cu^{II}L}' = K_{Cu^{II}L}(1 + K_{1X}[ClO_4^-]) \qquad (11)$$

If the value of K_{1X} were to remain at 24 M^{-1} over the range of ionic strengths studied, the term in parentheses (i.e., $(1 + K_{1X}[ClO_4^-])$) should have values of 3.4 and 25 in the presence of 0.10 and 1.0 M perchlorate ion, respectively. This would result in an apparent stability constant increase of about 7.4-fold over this range. Within the limits of our experimental error and in acknowledgment of the fact that ionic strength should influence the magnitude of K_{1X}, the majority of the current data appear to be consistent with this prediction, suggesting that perchlorate adduct formation occurs with nearly equal facility for most of the complexes studied.

The trends in the stability constants as a function of ring size are illustrated in Figure 4 for the data obtained in 0.10 M perchlorate ion. For the Cu(II) complexes, the previous observation that the stability reaches a distinct maximum for the 14-membered ring among the unsubstituted S$_4$ macrocycles
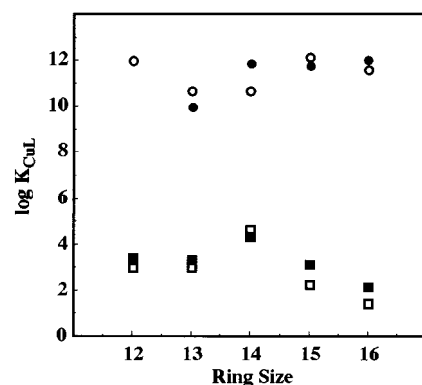

Figure 4. Trends in the logarithmic stability constants for the Cu^{I}L (circles) and Cu^{II}L stability constants (squares) as a function of ring size. The solid symbols represent data for the unsubstituted ligand complexes, while the open symbols represent the OH-derivatized complexes (or, in the case of the 12-membered macrocycle, the oxathiane derivative). No K_{Cu^IL}' value was calculated for the [12]aneS$_4$ complex due to the uncertainty in E^f for this system.

(solid squares) is confirmed by the same trend in the alcoholic derivatives (open squares). Crystal structures have shown that the cavity size for the 14-membered S$_4$ macrocycle provides the optimum cavity size to accommodate Cu(II).[24] As noted in the Introduction, larger ring sizes result in elongated Cu−S bonds and/or greater internal ring strain, while the 12- and 13-membered macrocycles require the copper to sit atop the plane of the four sulfurs with an apical solvent molecule (or anion) completing a square-pyramidal coordination sphere.[24] With regard to the current study, the most notable feature among these data is that [14]aneS$_4$-ol has the unique feature of being the only −OH derivative which exhibits a larger stability constant with Cu(II) than does the unsubstituted compound. This surprising anomaly in the overall trend has caused us to recheck this result carefully, but the difference appears to be a real one.

The K_{Cu^IL}' data (circles) are not considered to be sufficiently accurate to permit firm conclusions to be drawn, although it does appear that the 13-membered macrocycles form somewhat less stable Cu(I) complexes than do the larger rings. As noted above, the cavity of the 13-membered macrocycle is too small to accommodate the copper ion. Since Cu(I) prefers a tetrahedral coordination sphere, it is presumed that Cu^I([13]aneS$_4$) and Cu^I([13]aneS$_4$-ol) (as well as the corresponding complexes with the 12-membered macrocycles) consist of three coordinated sulfur atoms and a coordinated solvent molecule, resulting in a distorted-tetrahedral geometry similar to that found in an early crystal structure of Cu^I([14]aneS$_4$).[25]

Formation and Dissociation Rate Constants. Of the eight systems for which k_f values are available for both 0.10 and 1.0 M perchlorate ion concentrations, the value of k_f is observed to increase by a remarkably consistent factor of about 3−3.5 (with the 12-membered macrocycles showing a slightly smaller increase, possibly attributable to experimental error). The values of the dissociation rate constants decrease significantly with increasing levels of perchlorate. Although this effect appears to diminish as the ring size increases, this may simply reflect the uncertainty in the k_d values for the [15]- and [16]aneS$_4$-ol

(23) Nazarenko, A. Y.; Izatt, R. M.; Lamb, J. D.; Desper, J. M.; Matysik, B. E.; Gellman, S. H. *Inorg. Chem.* **1992**, *31*, 3990−3993.

(24) Pett, V. B.; Diaddario, L. L., Jr.; Dockal, E. R.; Corfield, P. W. R.; Ceccarelli, C.; Glick, M. D.; Ochrymowycz, L. A.; Rorabacher, D. B. *Inorg. Chem.* **1983**, *22*, 3661−3670.

(25) Dockal, E. R.; Diaddario, L. L.; Glick, M. D.; Rorabacher, D. B. *J. Am. Chem. Soc.* **1977**, *99*, 4530−4532. In contrast, see the distorted-tetrahedral structure obtained for the closely related Cu^I([14]aneNS$_3$) complex: Bernardo, M. M.; Heeg, M. J.; Schroeder, R. R.; Ochrymowycz, L. A.; Rorabacher, D. B. *Inorg. Chem.* **1992**, *31*, 191−198.
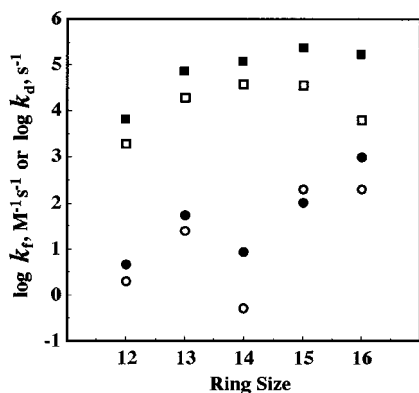
Figure 5. Trends in the logarithmic values of the formation rate constants (squares) and dissociation rate constants (circles) for the $Cu^{II}L$ complexes as a function of ring size. The solid symbols represent data for the unsubstituted ligand complexes, while the open symbols represent the OH-derivatized complexes (or, in the case of the 12-membered macrocycle, the oxathiane derivative).

complexes, since these values are pushing the limit of the stopped-flow method.

Rate Constant Trends. The rate constants obtained in 0.10 M $HClO_4$ are plotted in logarithmic form in Figure 5 for both the alcoholic (and oxathiane) derivatives (open symbols) and the corresponding unsubstituted macrocycles (solid symbols). The $Cu^{II}L$ formation rate constant data (squares) clearly exhibit parallel trends for both series of ligands. The 13–15-membered macrocycles show little dependence of k_f upon ring size (particularly for the unsubstituted macrocycles), whereas the 12-membered macrocyclic complexes are essentially one order of magnitude slower to form. This latter feature is attributed to the greater rigidity of the 12-membered macrocycles which hinders the conformational rearrangements necessary for sequential coordinate bond formation. The much larger spread between the k_f values for the two 16-membered macrocycles is considered to be relatively meaningless since the k_f value for $Cu^{II}([16]aneS_4-ol)$ was calculated rather than measured and is dependent on a very approximate estimate of the k_d value.

The k_d values for both series of ligands tend to increase with increasing ring size, except for a marked dip at the 14-membered macrocycle. For both the 12- and 13-membered macrocycles, the copper sits above the S_4 plane so that the mechanism for complex dissociation must be somewhat different, with the 12-membered ligands being slower to alter conformation in the successive dissociative steps. The nearly perfect fit of the 14-membered macrocycle to the copper(II) ion is presumed to account for the smaller dissociation constant for this ring size, as elaborated in the next section.

The seemingly constant k_d value for the two largest alcoholic macrocycles is again dependent on a very approximate value for the $[16]aneS_4-ol$ system. The most notable feature among the alcoholic derivatives is the marked decrease in the k_d value for $Cu^{II}([14]aneS_4-ol)$. In fact, it is this decrease which accounts for the fact that this specific complex is the only alcoholic derivative which forms a more stable $Cu^{II}L$ complex than its unsubstituted counterpart.

Mechanistic Inferences. From an analysis of our earlier kinetic data on the reaction of solvated Cu(II) with the unsubstituted tetrathia ethers,[7] we concluded that the formation rate constants were consistent with a mechanism involving a stepwise substitution process in which the second bond formation (i.e., closure of the first chelate ring) with the macrocyclic ligand represents the rate-determining step. The underlying arguments given at that time are presumed to be applicable to the current studies as well.

In more recent work[26] we have analyzed the complex formation mechanism in greater detail, including a consideration of the conformational changes which must accompany each step of the substitution process. A schematic of the resultant step-by-step mechanism is illustrated in Figure 6 for the reaction of hexaaquacopper(II) ion with $[14]aneS_4-ol$. In this figure, species A represents the two reaction partners after they have diffused together to become nearest neighbors (outer-sphere complex). The formation of the first coordinate bond, designated by rate constant k_1, is governed by the rate constant for a $Cu-OH_2$ bond rupture[7,27] followed by the rapid insertion of a sulfur donor atom into the vacated inner-sphere site. The specific position and conformation of the ligand will determine the fraction of such sequences in which a donor atom will be positioned to enter a vacated inner-sphere site in competition with the surrounding bulk solvent molecules.

The rate of formation of the second coordinate bond, identified by rate constant k_2, is governed by the rate constant for the rupture of a second $Cu-OH_2$ bond *cis* to the first coordinate bond and the probability that a proximal sulfur donor atom is positioned to enter this site (in competition with surrounding solvent molecules) to complete the first chelate ring.[28] For the 14-membered macrocycle, two intermediate species can be generated at this point, depending upon whether the first chelate ring involves an ethylene bridge (C-I) or a trimethylene bridge (C-II). Thus, k_2, k_{-3}, etc. are likely to be composite values.

In the current study, hydrogen bonding between the $-OH$ group and the surrounding solvent will presumably cause the $-OH$ group to be *exo* to the ring cavity, thereby forcing the two sulfur atoms proximal to the hydroxy group into *endo* orientations. Initial bond formation to one of the two distal sulfurs—to generate intermediate B in Figure 6—may be relatively unaffected by the hydroxy substituent. However, the reduction in the steric availability of the two proximal sulfurs could reduce the rate of first-bond formation by up to a factor of 2. If the first bond formation does involve a distal sulfur, there is at least a 50/50 chance that the second bonding step—to close the first chelate ring—will involve a sulfur proximal to the hydroxy group. Depending upon the relative orientations of the proximal and distal sulfurs, this could reduce the formation rate constant by as much as an additional factor of 2. (In the case of $[14]aneS_4-ol$, the chances that a proximal donor atom is involved in chelate ring closure may be more than 50% since, as noted above, the favored closure of a five-membered chelate ring must involve one proximal sulfur atom.) On the basis of the foregoing rationale, a single $-OH$ substituent could reduce the formation rate constant by a factor of 4 or more. For the 13- and 14-membered macrocycles, the actual observed decrease in k_f for the OH-derivatized ligands is in the range of 3–4-fold. The foregoing analysis may be overly simplified, since larger decreases are apparent upon $-OH$ substitution for the 15- and 16-membered macrocycles. However, as noted earlier for these larger macrocycles, the formation rate constants for the hydroxy-substituted ligands are admittedly less accurate since they were not measured directly.

It might be noted that the initial coordinate bond formation could involve the alcoholic oxygen atom in the case of the OH-

(26) Aronne, L.; Yu, Q.; Ochrymowycz, L. A.; Rorabacher, D. B. *Inorg. Chem.* **1995**, *34*, 1844−1851.

(27) For a discussion of the rate constant characteristic of $Cu^{II}-OH_2$ bond rupture in $Cu(H_2O)_6{}^{2+}$, see: Sokol, L. S. W. L.; Fink, T. D.; Rorabacher, D. B. *Inorg. Chem.* **1980**, *19*, 1263−1266 and ref 29 therein.

(28) Moss, D. B.; Lin, C.-T.; Rorabacher, D. B. *J. Am. Chem. Soc.* **1973**, *95*, 5179−5185.
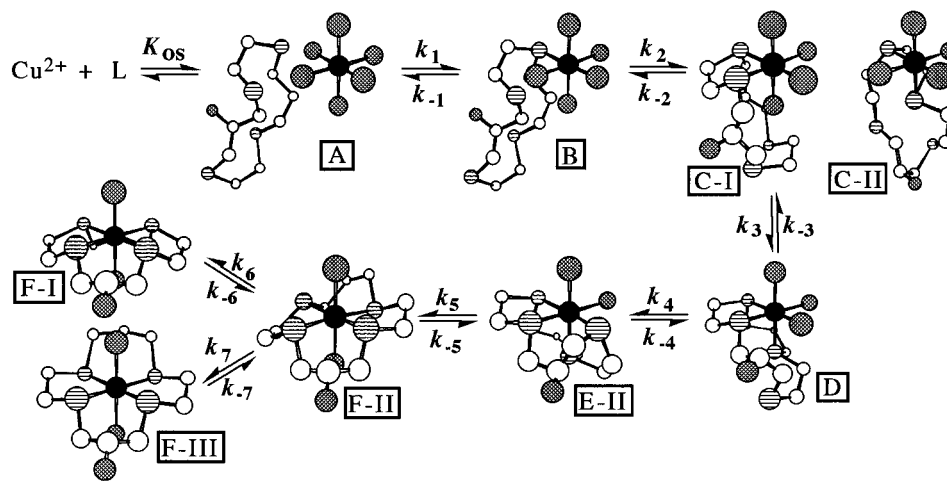
Figure 6. Proposed stepwise mechanism for the formation and dissociation of $Cu^{II}([14]aneS_4-ol)$. The copper is represented as a solid circle, oxygens are cross-hatched, sulfurs are striped, and the open circles are carbons; hydrogens are omitted for clarity. The sulfur atom involved in forming the first coordinate bond (species B) is shown here as one of the sulfurs distal from the hydroxy substituent. The formation of the second bond (step k_2) to complete the first chelate ring (species C) represents the rate-determining step. For [14]aneS_4-ol, this may involve either a five-membered ring (C-I) or six-membered ring (C-II). The former species must necessarily involve a sulfur proximal to the hydroxy group on the ligand backbone.

derivatized ligands. Although alcoholic oxygens form only weak bonds to Cu(II),[28] it is not clear that they are significantly weaker than the thia ether sulfur donor atoms. However, if a Cu−O bond forms initially and is followed by the formation of a Cu−S bond to complete the first chelate ring, the Cu−O bond will ultimately have to rupture prior to complete complexation with the macrocycle. Therefore, this alternative mechanism is presumed not to contribute significantly to the observed kinetics.

The influence of the hydroxy groups upon the k_d values are of smaller magnitude and appear to be less uniform in nature. For the 14- through 16-membered macrocycles, the fully formed complex must first involve the inversion of one sulfur donor atom, represented by rate constant k_{-6} or k_{-7} (depending upon which of the stable conformers is involved, F-I or F-III),[26] followed by conversion to a cis conformation, E-II. Only at this point can the three coordinate bonds in the remaining S_3 plane begin to rupture in the sequence designated by rate constants k_{-4}, k_{-3}, and k_{-2} (the last step being rate-determining). At least two of the bond ruptures must be proximal to the −OH group. The influence of the −OH group should again hinder the rotation of the sulfurs toward *exo* conformations, as required to effect bond rupture. This influence presumably accounts for the noted decrease in k_d values upon the addition of an −OH group.

If our analysis of the stepwise mechanism is correct, the notably smaller k_d value for the complexes formed with the 14-membered macrocycles must arise either (i) from more unfavorable equilibria in rearranging the ligand conformation to achieve one or more of the successive intermediates and/or (ii) in a reduction of the rate constant for opening the last chelate ring. Six-membered chelate rings are more easily rearranged and more

easily ruptured than five-membered rings. Therefore, the increase in k_d as the ring size progresses from 14 through 16 is readily rationalized. The magnified effect of −OH substitution upon the k_d value of $Cu^{II}([14]aneS_4-ol)$ complex would appear to imply that the interaction of the −OH group with the surrounding solvent is particularly effective in restraining the rearrangement of adjacent five-membered chelate rings.

The data obtained for the oxathiane-[12]aneS_4 ligand are worthy of special comment. The small [12]aneS_4 macrocycle is more rigid than for the larger macrocycles, and the ligand cavity has been shown to be too small to accommodate the Cu(II) ion (as is the 13-membered macrocycle as well).[24] As a result, Cu(II) sits atop the S_4 plane with an anion or solvent molecule coordinated at an apical position to complete a square-pyramidal complex. The sulfur atom incorporated into the oxathiane ring has a strong tendency to adopt an *endo* conformation relative to the macrocyclic ring, as demonstrated both by a crystallographic structure of the free ligand[29] and by molecular mechanics calculations. This ligand also appears to be more rigid than the unsubstituted [12]aneS_4 ligand. Interestingly, however, the effects of the fused oxathiane ring upon the rate constant data are similar to the effects of a single −OH group in the alcoholic derivatives. This somewhat surprising result may reflect the unique coordination geometries associated with small macrocycles. This possibility will be pursued in a future study.

(29) Salhi, C. A. Ph.D. Dissertation, Wayne State University, 1993.