Effect of Macrocyclic Ligand Constraints upon the Kinetics of Complex Formation and Dissociation and Metal Ion Exchange. Copper(II) Complexes with Cyclohexanediyl Derivatives of the Cyclic Tetrathiaether [14]aneS_4 in 80% Methanol

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Complex formation kinetics have been measured for solvated Cu(II) reacting with an entire series of cyclohexanediyl derivatives of the 14-membered cyclic tetrathiaether [14]aneS_4 (1,4,8,11-tetrathiacyclotetradecane) using stopped-flow spectrophotometry. In this ligand series, *cis*- or *trans*-1,2-cyclohexanediyl has been substituted for one or both of the ethylene bridges in [14]aneS_4 resulting in two monocyclohexanediyl and five dicyclohexanediyl derivatives. The complex formation rate constants in 80% methanol–20% water (by weight) for the reaction of Cu(II) with the parent [14]aneS_4 ligand and all seven cyclohexanediyl-substituted derivatives at 25.0 ± 0.2 °C, $\mu = 0.10$ M ($HClO_4$), are found to lie within the narrow range of $(2-5) \times 10^4$ M^{-1} s^{-1}. The consistency in these values implies that the introduction of cyclohexanediyl substituents does not induce significant steric effects relative to the first two bond formation steps. Using solvated Hg(II) ion as a ligand scavenger, the first-order dissociation rate constants have been measured independently under the same conditions and are found to vary over a range of 10^4. The ratios of the formation and dissociation rate constants are shown to agree closely with the previously determined stability constants, thereby establishing the fact that the kinetically observed products are the thermodynamically stable species. Strain optimization calculations indicate that one of the ligand conformational changes, which must precede the first Cu–S bond rupture, represents the most unfavorable step in the dissociation process. The rate constants for direct mercury(II) exchange provide additional insight into the dissociation behavior of the Cu(II) complexes.

Introduction

The enhanced stability of macrocyclic ligand complexes relative to similar acyclic analogues (the so-called "macrocyclic effect")[2,3] is well recognized from a thermodynamic perspective. The implications of this phenomenon have also led to a number of correlated kinetic studies, principally involving polyamine ligands.[3–5] Unfortunately, the very high basicity of macrocyclic polyamines generally makes it impossible to resolve the specific rate constant terms for unprotonated ligand species in aqueous solution.[6] For the protonated species, the tendency toward strong intramolecular hydrogen bonding generates relatively unreactive ligand conformers which can lead to erroneous interpretations of the kinetic results.[7]

Several investigators have circumvented the problems associated with polyamine protonation using either of two possible approaches: (i) by operating in highly basic aqueous media[7–10] or (ii) by utilizing aprotic coordinating solvents such as acetonitrile,[11] dimethyl sulfoxide (DMSO),[12] or dimethylformamide (DMF).[12–14] We have earlier pointed out that studies on the macrocyclic polythiaethers represent an additional alternative since these latter ligands, being completely devoid of protonation phenomena, yield rate constants that are always representative of the unprotonated ligand species.[15]

One of the most valuable conclusions derived from kinetic studies with both unprotonated polyamines and polythiaethers is that metal complex formation rate constants are virtually identical for unsubstituted cyclic and acyclic ligand analogues.[7,11,12,15] Since the rate-determining step in these reactions tends to be at the point of either first- or second-bond formation (*vide infra*), this equivalency in kinetic behavior implies that the formation of the first one or two coordinate bonds is unaffected by simple ligand cyclization. Thus, the large increases in the stability constants for the macrocyclic ligands must be attributed to the later stages of complexation.

For the cyclic ligands themselves, an issue of continuing interest is the impact of ring substituents upon both the

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thermodynamics and kinetics of metal complexation. In an early study on Cu(II) complexation kinetics with cyclic polyamines in highly basic aqueous media, we found that the addition of two or six methyl substituents on the trimethylene bridges of [14]aneN$_4$ (cyclam)—to generate *meso*-Me$_2$[14]aneN$_4$ and *meso*-Me$_6$[14]aneN$_4$ (tet-a)—decreased the complex formation rate constant by 5- and 300-fold, respectively.[7] In studying a large number of substituted analogues of [14]aneN$_4$, Röper and Elias[14] reported rate constant decreases of 8- and 40-fold, respectively, for the complexation of Ni(II) by these same two ligands in dimethylformamide (DMF). However, Hay and Norman[11] reported finding almost no change in formation rate constants for Ni(II) reacting with these ligands in acetonitrile. Although each of these studies was conducted in a different solvent, the discrepancies in the behavior are difficult to rationalize.

In the only kinetic study reported to date on substituted macrocyclic polythiaethers, we observed that the addition of one or two hydroxy groups to the trimethylene bridges of [14]aneS$_4$ resulted in decreases in the Cu(II) complex formation rate constant of 10-, 100-, and 35-fold, respectively, for [14]aneS$_4$-ol and *syn*- and *anti*-[14]aneS$_4$-diol.[16] Since uncomplexed [14]aneS$_4$ is known to prefer an exodentate ligand conformation[17] —in which the lone electron pairs on the sulfur donor atoms are oriented away from the ligand cavity—it has been presumed that the donor atoms are readily accessible for initial bond formation with the approaching metal ion. Therefore, the observed sluggishness in the complexation reactions of the mono- and dialcoholic derivatives was postulated to result from a switch to a more endodentate conformation in which the donor atoms are significantly less accessible for initial coordinate bond formation.[16]

In attempting to extend our understanding of the effect of macrocyclic ring substituents upon complexation phenomena, we recently synthesized an entire series of ligands in which one or both of the ethylene bridging groups in [14]aneS$_4$ were replaced by 1,2-phenylene or *cis*- or *trans*-1,2-cyclohexanediyl.[18] These latter substituents are presumed to (i) decrease the flexibility of the macrocyclic ring and (ii) force the donor atoms to adopt a conformation which is more endodentate in character and, therefore, better organized to accommodate metal ion complexation from a thermodynamic standpoint. Although the Cu(II) complexes formed with the phenylene derivatives have proved to be of low thermodynamic stability (presumably due to the strong negative inductive effects of the benzene rings), the cyclohexanediyl-substituted ligands exhibit stability constant increases of approximately 50-fold for each cyclohexanediyl substituent in both 80% methanol and in acetonitrile.[18] In the former solvent, this enhancement has been shown to correlate to a decrease in enthalpy amounting to about 8 kJ mol^{-1} per cyclohexanediyl group,[18] consistent with predictions arising from the concept of ligand preorganization.

From a kinetic standpoint, if the cyclohexanediyl-substituted ligands adopt a more endodentate conformation, as inferred from the stability constant data, a *decrease* in the rate of first-coordinate-bond formation might be anticipated. In addition, any decrease in ligand flexibility might be expected to hinder the closure of the first chelate ring. On the basis of this logic, it was anticipated that an examination of the complex formation and dissociation kinetics of the cyclohexanediyl-substituted derivatives might yield additional insight into the influence of substituents upon the flexibility and preferred conformation of these ligands.

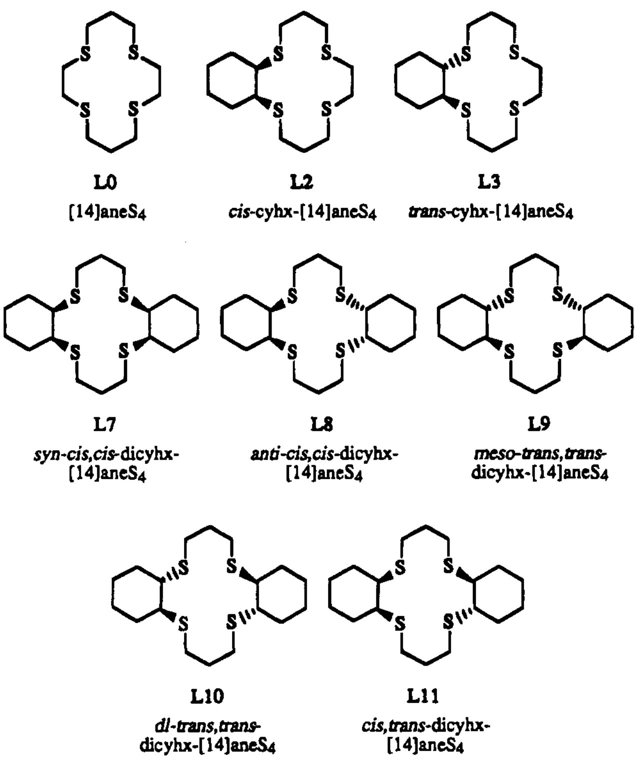

Figure 1. Cyclohexanediyl derivatives of [14]aneS$_4$ included in the current study. Ligand number designations are assigned to be consistent with ref 18, which also included corresponding phenylene derivatives.

In the current work, we have investigated the kinetics of Cu(II) reacting with all seven cyclohexanediyl derivatives of [14]aneS$_4$ illustrated in Figure 1. Since the uncomplexed ligands are only sparingly soluble in water, the current kinetic measurements have been carried out in 80% methanol−20% water (by weight).[19] Formation rate constants have been determined by following the formation of the Cu^{II}L complex. Dissociation rate constants were determined independently using solvated Hg(II) ion as a ligand scavenger. Strain optimization calculations of the various proposed intermediates have been made in an attempt to understand the influence of the cyclohexanediyl substituents upon the individual steps in the reaction mechanism.

Experimental Section

Reagents. The synthetic procedures used to prepare all of the ligands included in this work have been previously described.[18] Similarly, all other reagents utilized were prepared by procedures outlined elsewhere.[18,20] Solutions of Cu(ClO$_4$)$_2$ and Hg(ClO$_4$)$_2$ in 80% methanol were standardized by titration against aqueous EDTA, which, in turn, had been standardized against primary standard Cu(NO$_3$)$_2$ prepared by the dissolution of clean 99.99% pure copper wire (Fisher Scientific) in a minimum amount of HNO$_3$. Concentrations of the individual ligand solutions in 80% methanol were determined spectrophotometrically as the Cu^{II}L complexes using the molar absorptivity values previously determined.[18] For each solution, a large excess of Cu(II) was added in the presence of 0.10 M HClO$_4$ to ensure complete complex formation and the absorbance measurements were made using a Cary 17-D double-beam recording spectrophotometer. All solutions were prepared with

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distilled, deionized water and methanol from one of the following two sources: GR grade from EM Science or HPLC grade from Fisher Scientific.

Kinetic Measurements. All kinetic measurements were made using a Durrum D-110 stopped-flow spectrophotometer equipped with glass and Kel-F fittings. This instrument was interfaced to an Eltech Turbo XT computer equipped with a Metrabyte 12-bit A/D board. Ionic strength and constant perchlorate concentration were maintained by adding 0.10 M $HClO_4$. Temperature was controlled at 25.0 ± 0.2 °C using a Forma-Temp 1095 water bath, which provided circulation around the cell block and syringes. Reactions were monitored using the large $Cu^{II}L$ absorbance peak in the region 382–390 nm.[18]

Strain Optimization Calculations. For determining the probable geometries and strain energies of various reaction intermediates, we have utilized the molecular mechanical software package included with Chem3D Plus (Cambridge Scientific Computing, Inc.). Several simplifications have been invoked. The values of force constants for Cu(II)–S bonds were left undefined (since these values have not been determined). As a result, structures were minimized in terms of the "root-mean-squared" error rather than in absolute energy units. To ensure that the structure corresponding to minimum bond strain was obtained in each case, the results of a large number of bond manipulations were explored in searching for the global minimum. In trials on species for which crystal structures already exist,[21] this approach led to close agreement between calculated and observed structures. Although Cu(II) complexes are known to exhibit Jahn–Teller distortion, no attempt was made to define an elongated axis in the intermediate species since Jahn–Teller inversion is a rapid dynamic process[22] and inner-sphere distortions should be of decreased significance in the absence of uniform ligand fields. Errors introduced by this omission should affect comparisons between folded and planar intermediates but should not have a significant effect upon comparisons of one planar conformer with another.

Results

In mixed methanol–water solvents, the Cu(II) ion exists as an equilibrated mixture of seven different solvated species ranging from $Cu(H_2O)_6^{2+}$ through $Cu(CH_3OH)_6^{2+}$.[15] For simplicity, [Cu(II)′] is used throughout this document to represent the total concentration of all uncomplexed Cu(II) species in 80% methanol:[23]

$$[\mathrm{Cu(II)'}] = [\mathrm{Cu(H_2O)_6}^{2+}] + [\mathrm{Cu(H_2O)_5(CH_3OH)}^{2+}] + [\mathrm{Cu(H_2O)_4(CH_3OH)_2}^{2+}] + \ldots \quad (1)$$

The complex formed between Cu(II) and the macrocyclic ligand also includes coordination of the copper ion to one or two water or methanol molecules, and as shown in our previous studies,[24,25] it is apparent that ClO_4^- (used for ionic strength control) can form adducts with the Cu(II)–polythiaether complexes. Thus, for simplicity, the total concentration of copper complex is designated as $[Cu^{II}L']$:

$$[\mathrm{Cu^{II}L'}] = [\mathrm{CuL(H_2O)}_x{}^{2+}] + [\mathrm{CuL(H_2O)}_{x-1}\mathrm{(CH_3OH)}^{2+}] + [\mathrm{CuL(H_2O)}_{x-1}\mathrm{(ClO_4)}^{+}] + [\mathrm{CuL(CH_3OH)}_{x-1}\mathrm{(ClO_4)}^{2+}] + \ldots \quad (2)$$

where $x = 1$ or 2 depending upon the specific complex involved.

Formation Kinetics. For a constant solvent composition of 80% methanol and in the presence of 0.10 M $HClO_4$, the relative mole fractions of all species in eqs 1 and 2 will be constant. Thus, the overall reaction kinetics, representing the sum of the individual contributions of all relevant species in solution, may be treated as a single system as represented in reaction 3,

$$\mathrm{Cu(II)'} + \mathrm{L} \underset{k_d}{\overset{k_f}{\rightleftharpoons}} \mathrm{Cu^{II}L'} \quad (3)$$

where k_f represents the second-order conditional rate constant for complex formation and k_d represents the corresponding first-order conditional rate constant for complex dissociation. The differential expression for the complexation kinetics can then be represented as

$$d[\mathrm{Cu^{II}L'}]/dt = k_f[\mathrm{Cu(II)'}][\mathrm{L}] - k_d[\mathrm{Cu^{II}L'}] \quad (4)$$

For all complex formation kinetic measurements conducted during this investigation, pseudo-first-order conditions were maintained in which the total concentration of Cu(II)′ was in large excess over the total concentration of ligand. Under these conditions the integrated expression becomes

$$\ln\{[\mathrm{Cu^{II}L'}]_e/([\mathrm{Cu^{II}L'}]_e - [\mathrm{Cu^{II}L'}])\} = k_{obsd}t = (k_f[\mathrm{Cu(II)'}] + k_d)t \quad (5)$$

where $[Cu^{II}L']_e$ and $[Cu^{II}L']$ represent the molar concentrations of $Cu^{II}L'$ at equilibrium and at any time, *t*, respectively.

For all complex formation studies, the ligand concentrations were in the range 10–60 μM while five different concentrations of excess Cu(II)′ were utilized spanning a 10- to 20-fold concentration range. From a plot of k_{obsd} against [Cu(II)′], k_f was obtained as the slope (eq 5). Only in the case of the parent ligand, [14]aneS_4, did the least-squares regression line yield a significant intercept from which the value of k_d could be evaluated. For all other systems, reaction 3 proceeded nearly to completion so that the contribution of the dissociation reaction did not differ statistically from zero. All experimental k_f values are listed in Table 1.

Dissociation Kinetics and Mercury(II) Exchange. For each Cu(II) complex, the dissociation rate constant was determined from an independent series of kinetic measurements in which solvated Hg(II) was utilized as a scavenger for the ligand:

$$\mathrm{Cu^{II}L'} + \mathrm{Hg(II)} \rightleftharpoons \mathrm{Cu(II)'} + \mathrm{Hg^{II}L} \quad (6)$$

This reaction is quantitative in 80% methanol since the Hg(II) ion forms much stronger complexes with the polythiaether ligands than does Cu(II).[26] From our previous studies utilizing this approach,[20] two reaction pathways are operative including a direct dissociation pathway

$$\mathrm{Cu^{II}L'} \underset{k_f}{\overset{k_d}{\rightleftharpoons}} \mathrm{Cu(II)'} + \mathrm{L} \quad \text{(slow)} \quad (3')$$

$$\mathrm{Hg(II)} + \mathrm{L} \xrightarrow{k_{Hg}{}^{L}} \mathrm{Hg^{II}L} \quad \text{(rapid)} \quad (7)$$

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Table 1. Formation, Dissociation, and Mercury(II) Exchange Rate Constants and Stability Constants for the Complexes of Solvated Copper(II) Ion with the Cyclohexanediyl Derivatives of [14]aneS$_4$ in 80% Methanol at 25.0 °C, $\mu = 0.10$ M (HClO$_4$)[a]

complexed ligand	$10^{-4}k_f$, $M^{-1}\,s^{-1}$	k_d,[b] s^{-1}	k_A,[c] $M^{-1}\,s^{-1}$	$10^{-6}K_{Cu^{II}L}'$(kinetic),[d] M^{-1}	$10^{-6}K_{Cu^{II}L}'$(equil),[e] M^{-1}	k_A/k_d M^{-1}
[14]aneS$_4$ (L0)	2.25(7) 2.6(2)[g]	7.6(8),[f] 12.3(3) 8.6(5)[g]	821(82)	0.0030, 0.0019 0.0030[g]	0.00300(2) 0.0032[h]	110, 70
cis-cyhx-[14]aneS$_4$ (L2)	3.02(6)	0.178(7)	52(2)	0.17_0	0.161(2)	290
trans-cyhx-[14]aneS$_4$ (L3)	3.0(5)	0.50(3)	43(9)	0.060	0.112(1)	86
syn-cis,cis-dicyhx-[14]aneS$_4$ (L7)	5.1(8)	0.0023(1)	0.27(4)	22	55(2)	110
anti-cis,cis-dicyhx-[14]aneS$_4$ (L8)	2.5(3)	0.502(8)	19(2)	0.050	0.0501(3)	40
meso-trans,trans-dicyhx-[14]aneS$_4$ (L9)	3.9(9)	0.0066(5)	3.0(1)	5.9	7.2(2)	460
dl-trans,trans-dicyhx-[14]aneS$_4$ (L10)	4(1)	≈0.01−0.02		≈2−4	5.0(3)	
cis,trans-dicyhx-[14]aneS$_4$ (L11)	4.5(7)	0.0111(5)	2.8(2)	4.1	7.4(5)	250

[a] Unless otherwise indicated, all rate constants are from this work; standard deviations are given in parentheses and refer to the last digit listed (e.g., 2.25(7) represents 2.25 ± 0.07). [b] Except as noted, the dissociation rate constants were determined from the Hg(II) exchange intercepts by utilizing eq 12. [c] The k_A values, representing the rate constants for direct mercury exchange, were obtained as the slopes from plots of eq 12. [d] The $K_{Cu^{II}L}'$(kinetic) values represent the ratio of the experimental formation and dissociation rate constants. [e] The $K_{Cu^{II}L}'$(equil) values were determined from equilibrium measurements.[18] [f] Dissociation rate constant obtained from the formation rate constant study as the intercept from a plot of k_{obsd} versus [Cu′] (eq 5). [g] Values from previous measurements carried out in 80% methanol under identical conditions.[15] [h] Room-temperature value reported in: Desper, J. M.; Gellman, S. H. *J. Am. Chem. Soc.* **1991**, *113*, 704−706.

and a pathway involving mercury attack to form a binuclear intermediate

$$\mathrm{Cu^{II}L'} + \mathrm{Hg(II)} \underset{k_{-A}}{\overset{k_A}{\rightleftharpoons}} \mathrm{Cu^{II}LHg^{II}} \quad \text{(slow)} \qquad (8)$$

$$\mathrm{Cu^{II}LHg^{II}} \xrightarrow{k_B} \mathrm{Cu(II)'} + \mathrm{Hg^{II}L} \quad \text{(rapid)} \qquad (9)$$

If both pathways contribute to the observed kinetics, the kinetic expression is of the form[20]

$$-\mathrm{d}[\mathrm{Cu^{II}L'}]/\mathrm{d}t = \{k_d + k_A[\mathrm{Hg(II)}]\}[\mathrm{Cu^{II}L'}] \qquad (10)$$

For the conditions used in the current study, [Hg(II)] ≫ [Cu^{II}L′], yielding a simplified pseudo-first-order relationship

$$-\mathrm{d}[\mathrm{Cu^{II}L'}]/\mathrm{d}t = k_{app}[\mathrm{Cu^{II}L'}] \qquad (11)$$

where

$$k_{app} = k_d + k_A[\mathrm{Hg(II)}] \qquad (12)$$

For nearly all Cu(II) complexes included in this work, plots of k_{app} against [Hg(II)] yielded both intercepts and slopes which were statistically significant, indicating that both pathways contributed to the overall kinetics. In the case of the *dl-trans,trans*-dicyhx-[14]aneS$_4$ system, the first-order plots of eq 11 appeared to be sigmoidal in the early part of the reaction, indicative of a slight induction period which is not easily explicable. This behavior led to considerable uncertainty in the intercepts for eq 12 and inconsistent slopes. The resolved values of k_d and k_A for all systems are included in Table 1.

Discussion

Proposed Stepwise Mechanism. The reaction of solvated transition metal ions with multidentate ligands generally occurs in a stepwise manner in which coordinated solvent molecules are sequentially replaced by bonds to the ligand donor atoms.[27] Such a mechanism is illustrated in Figure 2 using the reaction of Cu(II) with *meso-trans,trans*-dicyhx-[14]aneS$_4$ as an example. This figure serves to define the various stepwise processes and rate constants considered in the ensuing discussion. The other ligands in this study should react by a similar series of steps, with slight differences in geometry for some of the intermediate species.

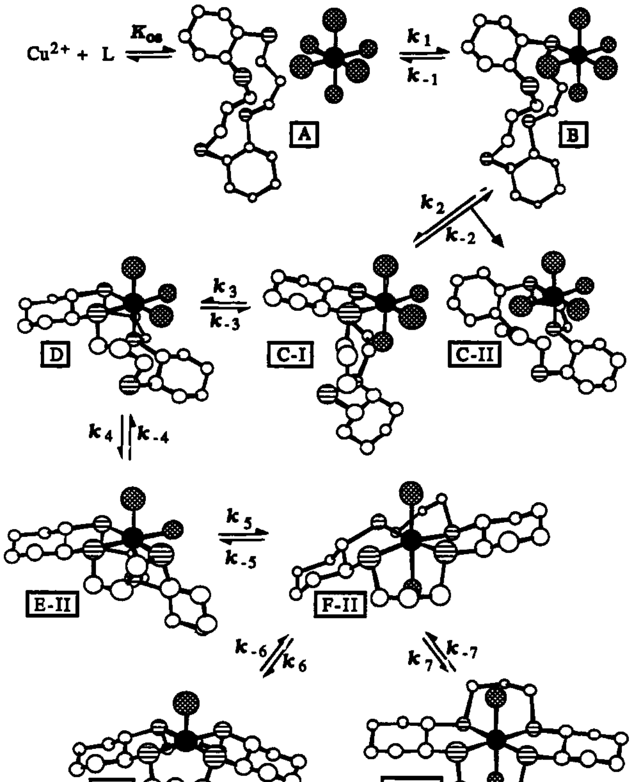

Figure 2. Schematic representation of the proposed primary complexation pathway for Cu(II) reacting with *meso-trans,trans*-dicyhx-[14]aneS$_4$. Conformations with minimum internal strain, as shown for each of the intermediate species, were generated from strain optimization calculations using Chem 3D-Plus (see text). Species C-I and C-II represent alternative configurations, both of which are reasonably unstrained. Alternative coordination geometries are also possible for intermediate D but are much more highly strained and are not included in this scheme. Species F-I is represented as a five-coordinate complex on the basis of related crystal structures. In each species, the solid atom represents copper(II), the horizontally striped atoms are sulfurs, and the cross-hatched atoms represent coordinated solvent donor atoms (or perchlorate anions); all others are carbons. Hydrogens are omitted for clarity.

For a quadridentate macrocyclic ligand such as [14]aneS$_4$ or [14]aneN$_4$, either the fully coordinated ligand may be folded, so that one of the donor atoms is apical to the plane of the

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Table 2. Relative Strain Energies for Conformations of the Fully Coordinated Copper(II) Complexes with [14]aneS$_4$ and Its Dicyclohexanediyl Derivatives

donor chirality (lone pair orientn)[b]	conformer designation	representation in Figures 2 and 3	calculated rms values[a]					
			L0	L7 (*syn*)	L8 (*anti*)	L9 (*meso*)	L10 (*dl*)	L11 (*cis,trans*)
			Folded Conformations					
RSRS (+ + + +)	*cis*-I	(not shown)	1.6	5.1	4.4	5.1	2.4	5.1
RRRS (+ + − +)	*cis*-II	E-II	1.8	3.0	3.0	2.8	4.0	3.2
RRRR (+ − + −)	*cis*-V	E-V	1.2	1.4	1.4	4.5	2.0	1.7
			Planar Conformations					
RSRS (+ + + +)	*trans*-I	F-I	2.9	4.3	4.3	5.3	5.3	5.0
RRRS (+ − + +)	*trans*-II	F-II	9.1	12.7	10.1	12.8	10.7	12.7
RRSS (+ − − +)	*trans*-III	F-III	5.3	5.6	5.6	5.8	14.8	5.6
RSSR (+ + − −)	*trans*-IV	(not shown)	10.8	14.5	15.0	16.3	16.8	15.6
RRRR (+ − + −)	*trans*-V	F-V	25.2	25.4	25.9	39.7	25.5	25.5

[a] rms represents the minimized "root-mean-squared" error as calculated using Chem3D Plus (see text). [b] See text for description of conformers.

other three (a so-called *cis* conformation) or all four donor atoms may lie within the same plane (a *trans* conformation).[28] With few exceptions, *cis* conformers are not the thermodynamically stable products; that is, the final product is generally in a *trans* conformation.[29] Five different conformations of the ligand have been identified in which the four donor atoms lie in essentially the same plane.[28,30,31] These differ in the relative chirality of the donor atoms (also defined in terms of the orientations of the hydrogens on the amine nitrogens—or the nonbonded lone electron pairs on the thiaether sulfurs) and have been designated as follows:[28,30,32] *trans*-I (RSRS or + + + +), *trans*-II (RRRS or + − + +), *trans*-III (RRSS or + − − +), *trans*-IV (RSSR or + + − −), *trans*-V (RRRR or + − + −).[33] For the folded intermediate preceding the isomerization to a planar arrangement of the donor atoms, three conformers have been identified which are analogues of *trans*-I, *trans*-II, and *trans*-V: *viz.*,[28,30,34] *cis*-I (RSRS or + + + +), *cis*-II (RRRS or + − + +), and *cis*-V (RRRR or + − + −).

The relative strain energies associated with the various *cis* and *trans* conformers have been calculated for each of the Cu(II) complexes included in the current study using the program Chem3D Plus as described in the Experimental Section. The residual "root-mean-squared" (rms) errors for the presumed global minima are tabulated in Table 2 for the [14]aneS$_4$ complex and each of the dicyclohexanediyl-substituted analogues. Whereas the rms values are presumed to provide reasonable comparisons of strain energies among the various *cis* conformers and among the *trans* conformers, comparisons between *cis* and *trans* conformers are presumed to be unreliable due to (i) our failure to account for Cu(II) Jahn−Teller distortion and (ii) differences in solvation interactions for the two conformer types. Thus, the fact that the *cis* conformers have smaller rms values than do the *trans* conformers is probably not a reliable indicator of their relative stabilities.

The rms calculations indicate that, of the *cis* conformers, the *cis*-V species is generally the most stable, in agreement with the conclusions of previous workers. However, the *cis*-II conformation is not significantly strained and both species appear to be energetically competitive in our systems. If we presume that the transformation from a folded to a planar conformation occurs without donor atom inversion (i.e., unfolding and inversion occur sequentially rather than concertedly), the *cis*-V intermediate would yield a *trans*-V successor intermediate which tends to be exceptionally strained (see Table 2). Therefore, in formulating the mechanism in Figure 2, we have represented the *cis*-II species as intermediate E-II followed by the *trans*-II conformer as species F-II. Although much less strained than the *trans*-V species, the *trans*-II conformer is still relatively unstable and would be expected to relax to either the *trans*-I or *trans*-III conformation, represented as F-I or F-III, respectively, in Figure 2.[35] For purposes of comparison, we have represented the alternate sequence of intermediates in Figure 3 for the case in which a *cis*-V intermediate (E-V) is succeeded by a *trans*-V (F-V) intermediate. Inversion of one donor atom in the F-V intermediate produces the *trans*-II (F-II) intermediate which can then continue with the inversion of a second donor atom to produce F-I or F-III as in Figure 2.

For unsubstituted [14]aneS$_4$ and [14]aneN$_4$, it has generally been assumed that the *trans*-III conformer (F-III) is the most thermodynamically stable species on the basis of both crystal structure determinations[36] and earlier molecular mechanical calculations.[37] Our calculations indicate that the *trans*-I conformer (F-I) appears to be of slightly lower energy than the *trans*-III conformer, and in some cases, this appears to be corroborated by recently obtained crystal structures.[38] However, the small differences in the calculated rms errors for these two conformers coupled with the omission of solvation energies in

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(28) Bosnich, B.; Poon, C. K.; Tobe, M. L. *Inorg. Chem.* **1965**, *4*, 1102−1108.

(29) In the case of some sterically restricted ligands, such as tet-b, the folded complex may be reasonably stable: Clay, R.; Murray-Rust, J.; Murray-Rust, P. *J. Chem. Soc., Dalton Trans.* **1979**, 1135−1139.

(30) Wagner, F.; Mocella, M. T.; D'Aniello, M. J., Jr.; Wang, A. H.-J.; Barefield, E. K. *J. Am. Chem. Soc.* **1974**, *96*, 2625−2627.

(31) Barefield, E. K.; Bianchi, A.; Billo, E. J.; Connolly, P. J.; Paoletti, P.; Summers, J. S.; Van Derveer, D. G. *Inorg. Chem.* **1986**, *25*, 4197−4202.

(32) Curtis, N. F.; Swann, D. A.; Waters, T. N. *J. Chem. Soc., Dalton Trans.* **1973**, 1963−1974.

(33) The *trans* designation refers to the fact that, if, in addition to the quadridentate ligand, a fifth and a sixth donor atom are coordinated to the central metal ion, the latter will lie *trans* to each other. The *R* and *S* designations in parentheses define the chirality of the coordinated donor atoms whereas the "+" and "−" designations define the direction of the hydrogens (in the case of amine nitrogens) or nonbonding lone pairs (in the case of thiaether sulfur atoms) relative to the plane of the four coordinated macrocyclic donor atoms. For each species in Figures 2 and 3, the chirality is always cited by beginning with the donor atom in the left foreground and proceeding clockwise around the macrocyclic ring.

(34) Whimp, P. O.; Bailey, M. F.; Curtis, N. F. *J. Chem. Soc. A* **1970**, 1956−1963.

(35) We have specifically represented species F-I as a five-coordinate square pyramidal complex since all crystal structures for Cu(II)−macrocyclic S$_4$ complexes for which this structure has been observed have been found to be five-coordinate (see refs 21, 38).

(36) (a) Bosnich, B.; Mason, R.; Pauling, P. J.; Robertson, G. B.; Tobe, M. L. *Chem. Commun.* **1965**, 97−98. (b) Davis, P. H.; White, L. K.; Belford, R. L. *Inorg. Chem.* **1975**, *14*, 1753−1757. (c) Glick, M. D.; Gavel, D. P.; Diaddario, L. L.; Rorabacher, D. B. *Inorg. Chem.* **1976**, *15*, 1190−1193.

(37) Brubaker, G. R.; Johnson, D. W. *Inorg. Chem.* **1984**, *23*, 1591−1595.

(38) Crystal structures of both $\mathrm{Cu^{II}}$(*cis*-cyhx-[14]aneS$_4$) and $\mathrm{Cu^{II}}$(*trans*-cyhx-[14]aneS$_4$) show the ligands to be in a *trans*-I ("boat") conformation: Salhi, C. A.; Heeg, M. J.; Juntunen, K. L.; Ochrymowycz, L. A.; Rorabacher, D. B. Manuscript in preparation.

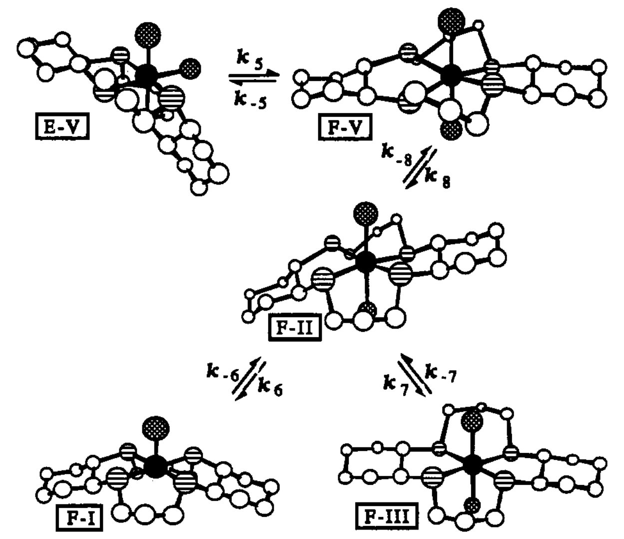

Figure 3. Schematic representation of an alternate reaction pathway in the later stages of Cu(II) complexation with *meso-trans,trans*-dicyhx-[14]aneS$_4$. The initial intermediates (A–D) are identical to those in Figure 2 and are not reproduced here.

making these calculations suggest that considerable caution should be used in drawing specific conclusions in this regard.

Literature Data on Intermediate Interconversions. For macrocyclic tetraamines, ample evidence exists in the literature for slow transformations among the species designated as E-II (or E-V), F-I, F-II, and F-III. From the time of the earliest kinetic studies on the reactions of Ni(II) and Cu(II) with cyclic tetraamines, investigators have reported observing a slow succeeding reaction following the initial rapid formation of a complex.[6b,8,9,11–13,39] This slow step has generally been interpreted to represent a conformational change of the initially formed planar complex (often presumed to be analogous to species F-I) to a more stable species, presumed to be F-III. In fact, Hay and Norman[11] reported observing as many as three distinct kinetic steps for some Ni(II) reactions with macrocyclic tetraamines in acetonitrile. Moore and co-workers[40] prepared the "boat" or *trans*-I conformer (F-I) of the Ni(II) complex with tetra-*N*-methyl-substituted [14]aneN$_4$ and were able to follow the isomerization kinetics to the "chair" or *trans*-III conformation (F-III) in DMSO using NMR as a monitor. On the basis of the NMR spectra, they also suggested that a third "twisted" or *trans*-II conformer was present; shortly thereafter, this was confirmed in correlated studies by Lincoln.[41] In addition, Chung and co-workers have conducted detailed studies on the isomerization kinetics of Cu(II) complexes of both *meso*- (tet-a)[42] and *rac*-Me$_6$[14]aneN$_4$ (tet-b)[43] from a folded to a planar conformation and have noted that these isomerizations are catalyzed by base. Similar observations have been made by Billo in studying the kinetics of folded-to-planar conformational interconversions for Ni^{II}([14]aneN$_4$).[44] This base dependency is consistent with donor atom inversion in which a hydrogen ion must be abstracted from an amine nitrogen before inversion can occur.

Additional detailed kinetic studies on the overall complexation reactions were recently reported by Elias and co-workers, who determined the formation rate constants for the reaction of Ni(II) and Cu(II) with a variety of derivatized [14]aneN$_4$ ligands.[13,14,45] They reported the resolution of two[14] or, in some cases, three[45] successive rate constants in DMF. Using rapid-scan stopped-flow spectrophotometry, these investigators were able to characterize the spectra of the intermediate species and concluded that all three species involved in the latter two steps contain a planar array of coordinated donor atoms. Although the specific transformations responsible for the observed rate constants were not identified by these investigators, the three successive planar species may be F-II, F-I, and F-III—or F-V, F-II, and F-III (or F-I)—if the alternate pathway represented in Figure 3 is predominant.

Consideration of Intermediate Buildup for the Polythiaethers. For the systems included in the current investigation, only a single reaction was observed during the measurements on the complex formation kinetics. However, a succeeding slow reaction could remain unobserved if (i) the pertinent conformational transformations generate only small changes in absorbance at the single wavelength monitored in this work or (ii) the extreme sluggishness of a succeeding reaction prevents its observation during the time interval over which the reaction is monitored. Our independent measurements on the dissociation kinetics were carried out specifically for the purpose of determining the internal consistency of the kinetic behavior. To ensure that the thermodynamically stable conformer was fully attained, the Cu^{II}L solutions were allowed to equilibrate for at least 24 h prior to initiating the reactions with Hg(II).

As noted in Table 1, the ratio of the experimentally obtained k_f and k_d values for all ligand systems are within a factor of 2 of our recently measured equilibrium constants.[18] This level of agreement is considered to be within our experimental error, particularly in view of the uncertainties in the equilibrium constant values for some of the very strong complexes. Therefore, we conclude that there is no evidence of intermediate buildup in any of our studies on the polythiaether complexes, and only a single formation reaction is kinetically discernible.

Assignment of the Rate-Determining Step. Of the complexation reactions examined to date involving solvated Cu(II), the vast majority have been consistent with a mechanism in which either first- or second-bond formation represents the rate-determining step.[46] If this step is at the point of first-bond formation, the experimentally observed formation rate constant can be formulated as[7]

$$k_f = K_{os}k_1 \qquad (13)$$

In this expression, K_{os} represents the equilibrium constant for the formation of the outer-sphere complex (i.e., a contact pair) designated as species A in Figure 2. There is ample evidence that the first bond formation step for solvated Cu(II) is dissociative in nature (i.e., independent of the nucleophilicity of the incoming donor atom) and, therefore, k_1 can be represented as[27,47]

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(41) Lincoln, S. F.; Coates, J. H.; Hadi, D. A. *Inorg. Chim. Acta* **1984**, *81*, L9–L10.

(42) Liang, B.-F.; Chung, C.-S. *Inorg. Chem.* **1981**, *20* , 2152–2155.

(43) Lee, C.-S.; Wang, G.-T.; Chung, C.-S. *J. Chem. Soc., Dalton Trans.* **1984**, 109–114.

(44) Billo, E. J. *Inorg. Chem.* **1981**, *20*, 4019–4121. Additional studies on similar Ni(II) complexes have been reported by Hay and Pujari: Hay, R. W.; Pujari, M. P. *J. Chem. Soc., Dalton Trans.* **1986**, 1485–1489.

(45) Elias, H.; Sanzenbacher, R. XIXth International Symposium on Macrocyclic Chemistry, University of Kansas, June 12–17, 1994; Abstract ST-54.

(46) Moss, D. B.; Lin, C.-T.; Rorabacher, D. B. *J. Am. Chem. Soc.* **1973**, *95*, 5179–5185 and references therein.

(47) Eigen, M.; Wilkins, R. G. *Mechanisms of Inorganic Reactions*; Advances in Chemistry Series 49; American Chemical Society: Washington, DC, 1965; Chapter 3.

$$k_1 = k^{\mathrm{Cu-solv}}/p \tag{14}$$

where $k^{\mathrm{Cu-solv}}$ represents the rate constant for Cu(II)−solvent bond rupture[22] and p represents the steric factor encountered in forming a bond with a donor atom which is attached to groups with significant steric bulk.[48] Equations 13 and 14 have been shown to apply for macrocycles having at least one strongly bonding donor atom. For example, $\mathrm{Cu^{II}([14]aneNS_3)}$ exhibits a k_f value of 3.2×10^6 $\mathrm{M^{-1}\ s^{-1}}$ in aqueous solution.[49] Since $K_{os} = 0.15$ $\mathrm{M^{-1}}$ [46,50,51] and $k^{\mathrm{Cu-solv}} = 2 \times 10^8$ $\mathrm{s^{-1}}$,[22] eqs 13 and 14 yield $p \approx 10$, which is actually slightly smaller than steric factors obtained for Ni(II) reacting with similar mono- and diamines.[52,53] Thus, the first-bond formation must represent the rate-determining step in the reaction of Cu(II) with $\mathrm{[14]aneNS_3}$.

On the basis of earlier measurements on the rate of Cu(II) complexation with $\mathrm{NH_3}$ as a function of solvent composition in methanol-water mixtures,[15,54] we have found that the rate constant for the first-coordinate-bond formation parallels the mole fraction of the hexaaquacopper(II) species present.[55] It has been estimated[54] that about one-tenth of the total solvated Cu(II) exists in the form of $\mathrm{Cu(H_2O)_6^{2+}}$ in 80% methanol. Thus, although the kinetics for Cu(II) reacting with $\mathrm{[14]aneNS_3}$ have not been measured directly in 80% methanol, the predicted formation rate constant is $k_f \approx 3.2 \times 10^5$ $\mathrm{M^{-1}\ s^{-1}}$. The k_f value determined in this work for Cu(II) reacting with $\mathrm{[14]aneS_4}$ in 80% methanol is 2.3×10^4 $\mathrm{M^{-1}\ s^{-1}}$ (Table 1). This large decrease in reactivity relative to $\mathrm{[14]aneNS_3}$ cannot be attributed to steric effects and must imply that the rate-determining step lies at the point of second-bond formation (or possibly beyond) when sulfur forms the initial bond. Thus, we conclude that the formation rate constant can probably be represented as

$$k_f = K_{os}k_1k_2/k_{-1} \tag{15}$$

More detailed arguments have previously been applied in concluding that eq 15 applies to the reactions of the hexaaquacopper(II) ion with several other ligands including acyclic species such as branched polyamino alcohols[46] and polyamino thiaethers.[56] In these cases, the first coordinate bond formed must involve an alcoholic oxygen or thiaether donor atom, either of which is very weak. The considerations covered in those studies are equally relevant to the current work.

Comparison of Formation Rate Constants for Various Cyclohexanediyl Derivatives. As noted in Table 1, the k_f values for Cu(II) reacting with all ligands studied in the current work are consistent within a factor of about 2. From this it is apparent that the cyclohexanediyl groups do not hinder the complex formation process prior to the point of the rate-determining step. If we may safely assume that the rate-determining step in the formation of $\mathrm{Cu^{II}([14]aneS_4)}$ is at the point of second-bond formation as argued above, the same conclusion must apply to all other ligands included in this investigation. It is apparent, therefore, that the cyclohexanediyl groups do not affect the formation of either of the first two coordinate bonds in the complex formation process to a significant extent. This leads to the conclusion that the cyclohexanediyl-substituted ligands must not be completely endodentate in their orientation and that all ligands are sufficiently flexible to rotate readily into a conformation suitable for chelate ring closure.

Dissociation Rate Constants. The independently measured k_d values listed in Table 1 vary over a range of 10^4. As noted above, the agreement between the experimental ratios for k_f/k_d and the independently measured stability constants (Table 1) implies that the products formed in the study of the complex formation kinetics represent the thermodynamically stable conformations of the Cu(II) complexes. If k_2 represents the rate-determining step in the formation reaction, k_{-2} must be the rate-determining step for dissociation. Assuming that the stepwise mechanism conforms to that shown in Figure 2, the case in which species F-III is the most stable product leads to the following expression for k_d:

$$k_d = K_{-7}K_{-5}K_{-4}K_{-3}k_{-2} \tag{16}$$

where K_{-7}, K_{-5}, K_{-4} and K_{-3} represent the equilibrium constants for the conversions F-III → F-II, F-II → E-II, E-II → D, and D → C-I, respectively. Equation 16 states that, in the absence of intermediate buildup, the specific energy barriers between these intermediates are of no consequence. Only the equilibrium constants for adjacent species are of interest in examining the overall dissociation kinetics. These equilibria, in turn, should depend on the relative stabilities of species C-I, D, E-II, etc. in Figure 2; and a major factor influencing the stabilities should be the internal strain energies.

Correlation of Strain Energies to the Reaction Rates. In the generation of the geometries of the most stable conformations of each of the intermediate species, strain optimization calculations were carried out as described above. In all cases, the geometry exhibiting the minimum "root-mean-squared" (rms) error is represented for each intermediate in Figures 2 and 3. Only in the case of species C have two different coordination modes been included since both alternatives are comparatively strain free.

Relative to the similarities in the formation rate constant data which we have observed, it is interesting to note that the two sulfur donor atoms bridged by a single *trans*-cyclohexanediyl group in the outer-sphere complex (species A in Figure 2) have their lone electron pairs oriented in the same direction in a manner which requires little rearrangement for chelate ring closure. In fact, *the conformation of the ligand remains nearly unchanged in species A, B, and C-I.* The same relative constancy in ligand conformation for these three intermediate species is noted with most of the other cyclohexanediyl-substituted ligands included in this work and presumably accounts for the similarity in the experimental k_f values.

Although a considerable rearrangement of the ligand backbone is involved in the interconversions among E-II, F-I, F-II,

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(48) (a) Lin, C.-T.; Rorabacher, D. B. *Inorg. Chem.* **1973**, *12*, 2402−2410. (b) Taylor, R. W.; Stepien, H. K.; Rorabacher, D. B. *Inorg. Chem.* **1974**, *13*, 1282−1289.

(49) Westerby, B. C.; Juntunen, K. L.; Leggett, G. H.; Pett, V. B.; Koenigbauer, M. J.; Purgett, M. D.; Taschner, M. J.; Ochrymowycz, L. A.; Rorabacher, D. B. *Inorg. Chem.* **1991**, *30*, 2109−2120.

(50) Rorabacher, D. B. *Inorg. Chem.* **1966**, *5*, 1891−1899.

(51) In calculating a value of $K_{os} = 0.15$, we have utilized a center-to-center contact distance of 4 Å in treating the $\mathrm{[14]aneNS_3}$ ligand as a "nitrogen donor atom attached to a tail." In taking this approach, we have ignored the contribution to the overall reaction kinetics in which one of the sulfur donor atoms forms the initial coordinate bond. The error introduced by ignoring the latter contribution is less than 5% of the overall reaction rate.

(52) Rorabacher, D. B.; Melendez-Cepeda, C. A. *J. Am. Chem. Soc.* **1971**, *93*, 6071−6076.

(53) Turan, T. S.; Rorabacher, D. B. *Inorg. Chem.* **1972**, *11*, 288−295.

(54) Jambor, L. G. Ph.D. Dissertation, Wayne State University, 1975.

(55) This implies that the value of $k^{\mathrm{Cu-H_2O}}$ for $\mathrm{Cu(H_2O)_6^{2+}}$ is much larger than either $k^{\mathrm{Cu-H_2O}}$ or $k^{\mathrm{Cu-CH_3OH}}$ for $\mathrm{Cu(H_2O)_5(CH_3OH)^{2+}}$ (or any of the other mixed solvated species present), a conclusion which is entirely consistent with the concept of Jahn−Teller distortion in Cu(II) complexes. (Note that K_{os} should be unaffected by the change in dielectric constant in going from water to 80% methanol since the unprotonated ligand has no charge.)

(56) Cooper, T. H.; Mayer, M. J.; Leung, K.-H.; Ochrymowycz, L. A.; Rorabacher, D. B. *Inorg. Chem.* **1992**, *31*, 3796−3804.

and F-III, the accompanying donor atom inversions are much more facile for thiaether sulfurs than for amine nitrogens since hydrogen ion abstraction is not involved. This is presumed to account for the fact that, in our complexation reactions, we do not observe intermediate buildup of the type reported in reactions with corresponding macrocyclic polyamines. As noted earlier, prior to nitrogen atom inversion, a hydrogen ion must be abstracted from an amine nitrogen, a relatively unfavorable process. Such abstraction is easily accomplished for polyamines only in highly basic media, where no successive reactions have been observed.[7-10] The behavior of the polythiaethers may, therefore, be equated to that of the polyamines at higher pH.

In the absence of intermediate buildup, the activation barrier involved in each stepwise rearrangement of the ligand backbone is of no consequence in our analysis. Only the absolute differences in energy of species F-I and F-II or F-III and F-II affect the values of the K_{-7} or K_{-6} equilibrium constants. Our strain optimization calculations (Table 2) indicate that *species F-II is significantly strained* relative to species F-I and F-III (except for the *dl-trans,trans* derivative for which F-III is particularly strained since the innate "twist" given to the sulfur donor atoms by the two *trans*-cyclohexanediyl groups makes it difficult for the ligand to adapt to this conformation). Therefore, for the dissociation reaction, we suggest that K_{-7} (or K_{-6}) is a very unfavorable equilibrium constant in eq 16. The remaining intermediates depicted in Figure 2, including species E-II, are relatively strain free for all of the ligands studied. On the basis of this analysis, we conclude that the transformation of F-I or F-III to F-II is likely to be the most significant factor in determining the dissociation rate for these Cu(II) complexes. In this regard, it is interesting to note that the difference in rms values for the F-I and F-III conformers relative to the F-II conformer is smaller for the *anti-cis,cis* derivative than for any other dicyclohexanediyl-substituted system. This is consistent with the fact that the *anti-cis,cis* complex exhibits the largest dissociation rate constant of any of the dicyclohexanediyl derivatives. For the other ligand systems, the trend in the k_d values also roughly parallels the trend in the differences in the calculated rms values for the F-II and the F-I or F-III conformers. However, these trends are not large, and we suggest that additional considerations, such as solvation effects, probably play a significant role in influencing the overall parameters.

For the mercury exchange pathway (represented by k_A), at least one and perhaps two Cu−S bonds must rupture before Hg(II) can begin to coordinate with the ligand. Thus, Hg(II) attack must occur with intermediate C or D in Figure 2. This implies that the $Cu^{II}L$ complex will already have traversed the strained intermediate F-II (as well as E-II) prior to the point where Hg(II) begins to influence the reaction rate. Since we have concluded that this intermediate species has the greatest influence on the overall dissociation rate constant, it might be expected that the values of k_A and k_d should be parallel. As indicated in the last column in Table 1, the *anti-cis,cis*-dicyhx-[14]aneS_4 complex exhibits a ratio which is about 2-fold smaller than that for Cu^{II}([14]aneS_4) while those for the *cis*-cyhx-, *cis,trans*-dicyhx-, and *meso-trans,trans*-dicyhx-[14]aneS_4 complexes are $2^1/_2$−$4^1/_2$ times larger. Although these variations in ratio may be significant, they are minor compared to the 10^4-fold range in the observed k_A and k_d values themselves. To the extent that the variations in the k_A values do not parallel the k_d values, the former values must reflect small differences in the other terms in eq 16 as well as steric effects in the ability of Hg(II) to attach itself to intermediate D or C.

Correlated Literature Calculations. Brubaker and Johnson[37] have previously applied molecular mechanical calculations to a series of Cu(II)−macrocyclic tetrathiaether complexes. In all cases, the most stable conformations which they derived for the fully complexed species were either F-I (for small cavity sizes) or F-III, and all were in close agreement with our earlier crystal structure data.[21] In attempting to examine the differences in dissociation kinetic behavior, Canales and Zimmer have made similar calculations on the relative strain energies for conformations corresponding to intermediates E-V and F-II for Cu^{II}(tet-a) and Cu^{II}(tet-b).[57] Their calculations indicated that intermediate E-V was very strained for the tet-a complex but not for tet-b; and while both systems exhibited even larger strains in F-II, the tet-b complex was the more strained of the two systems. Our conclusions regarding the relative strain in the successive equilibrium steps during the dissociation process appear to be in qualitative agreement with Canales and Zimmer's results.

Conclusions. Our analysis of the stepwise mechanism in Figure 2 appears to provide an adequate explanation for both the similarities in formation kinetics and the differences in dissociation kinetics observed for the current series of ligands. In all cases, it appears that intermediate F-II represents a very strained conformation. It is pertinent that an intermediate of this conformation is not required in the dissociation of acyclic ligands. Thus, we infer that the K_{-7} (or K_{-6}) equilibrium constants in eq 16 largely account for the small k_d values encountered with the macrocyclic ligand species.

In view of the uniformity of the formation rate constants in the current study, the much smaller formation rate constants observed previously for the [14]aneS_4-diol ligands,[16] as mentioned in the Introduction, cannot be explained by the influences considered in this work. Even full-blown molecular mechanical calculations do not account for ligand−solvent interactions, and we presume that it is the hydrogen bonding between the ligand −OH groups and the surrounding water molecules that accounts for the observed diol behavior in aqueous solution. In fact, the dissociation rate constants for the −OH-substituted [14]aneS_4 systems are much more similar than the formation rate constants. This latter observation is consistent with strain optimization calculations which indicate that intermediates E-II and F-II are relatively unaffected by the presence of the −OH substituents.

Molecular mechanical calculations also cannot explain the differing behaviors noted in the Introduction for Ni(II) and/or Cu(II) reacting with the *C*-methyl-substituted N_4 ligands. The differing formation rate constant trends observed for the reactions of these ligands with Ni(II) in acetonitrile[11] and DMF[14] strongly point to a solvent-dependent role. Parallel data on complex formation reactions with ligands of this type will doubtless need to be gathered in a variety of solvents before a complete understanding of macrocyclic ligand complexation behavior can be generated. In the meantime, attempts to formulate broad generalizations regarding macrocyclic complexation behavior, without taking ligand−solvent interactions into account, should be undertaken only with great caution.

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(57) Canales, C. R.; Zimmer, M. *J. Mol. Struct.* **1991**, *245*, 341−347. These authors have attempted to distinguish between two purportedly different reaction schemes for Cu(II) complexation with a cyclic quadridentate ligand. However, both schemes appear to be congruent if one recognizes that Jahn−Teller inversion is virtually instantaneous.