The large difference $\Delta(\log Q)$ for $M_2(OH)L$ formation (Table II) is easily understood on the basis of competition reaction with other species. The equilibrium constants determined in perchlorate and chloride media can be expressed as the logarithms of the hydroxylation constants 11.56 and 8.36, respectively. This difference of -3.19, an apparent destabilization, largely disappears when one considers that the term in the denominator of the quotient $[M_2L]$ consists primarily of $[M_2LCl]$ in the chloride medium, as is seen from the $10^{2.55}$:1 ratio of $[M_2LCl]$ to $[M_2L]$ for the 0.100 M chloride medium, as indicated in Table III. Similarly, the -0.82 value of $\Delta(\log Q)$ for ML can be rationalized by considering the competition for the ligand in chloride medium by chloride complexation and stabilization of the highly protonated forms of the ligand H_6L, H_5L, and H_4L.

Further investigations of anion cascade type complexes of mononuclear and dinuclear metal cryptates will be carried out on BISTREN and on other macrobicyclic ligands that have become available by the recent development of a synthetic method based on a (tripode + tripode) coupling process.[6]

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Registry No. Cl^-, 16887-00-6; OH^-, 14280-30-9.

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Quantitative Estimates of Steric Effects. Intramolecular Strain-Energy Effects on the Stability and Dissociation Rate Constants of Polythia Ether Macrocycle Complexes of Copper(II)[1]

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Intramolecular strain energies for a homologous series of copper(II) polythia ether macrocycle complexes have been calculated and compared with experimentally determined stability constants, dissociation rates, and free energies of formation. For the complexes with the tetrathia macrocycles 1,4,7,10-tetrathiacyclododecane ([12]-ane-S_4), 1,4,7,10-tetrathiacyclotridecane ([13]-ane-S_4), 1,4,8,11-tetrathiacyclotetradecane ([14]-ane-S_4), 1,4,8,12-tetrathiacyclopentadecane ([15]-ane-S_4), and 1,5,9,13-tetrathiacyclohexadecane ([16]-ane-S_4), stability constants and dissociation rate constants decrease with increasing intramolecular strain. The free energy of formation within this series is inversely proportional to intramolecular strain, yielding a "strain-free" free energy of formation of -8.65 (0.66) kcal mol^{-1} for tetrathia ether macrocycle complexes of copper(II). The anomalous behavior of the pentathia ether ligand 1,4,7,10,13-pentathiacyclopentadecane ([15]-ane-S_5) is ascribed to entropic terms. The observed agreement with experimentally determined parameters indicates that, while there is no evidence for systematic variations in intramolecular strain with the number of atoms or interactions in a chosen force field model, molecular-mechanics techniques are readily adapted to systems with a variety of nuclei.

Introduction

Conformational analysis, long a familiar concept among organic chemists,[2] has been applied to problems in coordination chemistry since Bailar and Corey published a classic paper on nonbonded interactions in diamine chelates.[3] Over the last 10 years, conformational analysis (or, more generally, strain-energy minimization) calculations have been applied to increasingly diverse problems in coordination stereochemistry.[4] With few exceptions,[5,6] strain-energy minimization calculations have been limited to Werner-type complexes of cobalt(III).

The overall success (measured in terms of agreement between calculations and experimental observation) of strain-energy minimization calculations, the widespread availability of an efficient computer program for strain-energy minimization calculations, and increased experience with potential energy functions and interaction constants suggested to us that we could successfully apply the method to other coordination environments. In this paper, we report the first systematic study that correlates intramolecular strain with experimentally measured stability constants for a homologous series of copper(II) complexes.

The complexes of interest in this study are copper(II) complexes with polythia macrocycle ligands which have been extensively studied by Rorabacher and co-workers.[7] These complexes are characterized by high molar absorptivity in the visible spectrum ($\epsilon = 6-10 \times 10^3$ at 530-625 nm) and reduction potentials in the range +590 to +800 mV. These spectroscopic and redox characteristics have been compared with those of type I or "blue" copper centers in proteins.[8]

In the present study we have focused on the relationship between the strain-energy potential field and the vibrational

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Table I. Comparison of Selected Observed and Calculated Bond Distances (Å)[a] and Angles (deg) for Some Polythia Ether Macrocycle Copper(II) Complexes

	[12]-ane-S_4		[13]-ane-S_4		[14]-ane-S_4		[15]-ane-S_4		[16]-ane-S_4		[15]-ane-S_5	
dist or angle	X-ray	calcd	X-ray	calcd	X-ray	calcd	X-ray	calcd	X-ray	calcd	X-ray	calcd
Cu-S(1)	2.34	2.34	2.334	2.34	2.308	2.29	2.323	2.32	2.331	2.34	2.33	2.34
Cu-S(2)	2.30	2.35	2.333	2.34	2.297	2.29	2.323	2.32	2.387	2.38	2.31	2.33
Cu-S(3)	2.37	2.37	2.310	2.34	2.308	2.29	2.313	2.32	2.331	2.34	2.38	2.36
Cu-S(4)	2.32	2.35	2.330	2.34	2.297	2.29	2.313	2.31	2.387	2.38	2.34	2.35
Cu-O(1)	2.11		2.14			2.13		2.13		2.14	2.39	2.36
Cu-O(2)						2.13		2.13		2.14		
S(1)-C	1.84	1.83	1.84	1.82	1.831	1.83	1.82	1.82	1.82	1.82	1.81	1.82
S(1)-C	1.80	1.83	1.81	1.83	1.828	1.82	1.80	1.82	1.82	1.82	1.82	1.82
S(2)-C	1.85	1.83	1.80	1.82	1.829	1.83	1.81	1.82	1.82	1.82	1.81	1.82
S(2)-C	1.89	1.84	1.81	1.83	1.825	1.83	1.83	1.82	1.82	1.82	1.81	1.82
S(3)-C	1.74	1.82	1.79	1.82	1.831	1.83	1.82	1.82	1.83	1.83	1.81	1.82
S(3)-C	1.91	1.84	1.87	1.83	1.828	1.82	1.80	1.82	1.82	1.82	1.80	1.82
S(4)-C	1.73	1.82	1.75	1.82	1.829	1.83	1.81	1.82	1.82	1.82	1.81	1.82
S(4)-C	1.84	1.83	1.87	1.83	1.825	1.82	1.83	1.82	1.83	1.83	1.81	1.82
S-Cu-S	94.1	90.7	90.9	89.9	90.1	90.9	90.3	90.9	90.37	90.4	88.5	88.3
S-Cu-S	86.5	83.8	89.6	89.5	89.9	89.1	89.7	89.1	89.63	89.6	91.6	90.8
S-Cu-S	81.4	81.8	86.0	84.0	90.1	90.6	90.3	90.7	90.37	90.2	91.7	90.9
S-Cu-S	85.8	82.4	87.7	88.7	89.9	89.4	89.7	89.3	89.63	89.8	92.3	93.2
S-Cu-O(1)	107.4	109.7	98.7	103.3	87.0	87.5	93.0	94.0	91.7	92.4	91.4	91.6
S-Cu-O(2)					93.0	92.2	87.0	86.0	88.3	88.0		
Cu-S-C	91	94	103.3	105.7	100.8	99.5	102.5	103.0	110.7	110.9	101	102
Cu-S-C	101	106	102.1	105.7	99.1	99.5	102.5	103.3	104.7	106.4	100	102
Cu-S-C	101	106	106.0	106.6	104.2	106.2	103.9	104.3	110.5	111.9	100	102
Cu-S-C	99	100	100.1	100.9	104.7	107.0	101.3	102.1	103.0	105.6	101	103
Cu-S-C	96	102	100.1	101.3	100.8	99.8	101.3	102.1	110.7	110.8	101	103
Cu-S-C	100	104	94.5	104.2	99.1	99.5	108.2	109.3	104.7	106.4	103	104
Cu-S-C	106	107	105.0	106.0	104.2	106.0	102.0	105.3	110.5	110.3	99	101
Cu-S-C	95	101	98.9	101.0	104.7	106.1	103.9	105.8	103.0	105.4	100	105
S-C-C	117	110	112.4	113	107.9	109.0	110.6	111	113.0	113.4	109	108
S-C-C	111	111	116	113	107.7	109.3	109	108	110.1	110.6	108	109
S-C-C	103	105	114	111	112.0	112.0	108.0	108	112.5	112.8	117	113
S-C-C	117	113	115	112	109.3	110.2	103	106	110.5	109.9	115	113
S-C-C	113	111	109	109	107.9	108.5	108	107	113.0	113.4	108	107
S-C-C	103	104	111	110	107.7	108.3	103	107	110.1	110.6	109	108
S-C-C	117	113	113	111	112.0	110.9	108	104	112.5	113.0	116	114
S-C-C	108	109	105	107	109.3	110.0	103	107	110.5	111.0	117	116
C-C-C			115	114	114.9	114.8	116	114	114.0	114		
C-C-C					114.9	114.6	117	115	115.0	114		
C-C-C							116	115	114.0	114		
C-C-C									115.0	114		

[a] The number of significant figures given in this table is governed by the number of digits given in the crystal structure.[15]

spectrum of these complexes and on the relationship between intramolecular strain and the stability of these complexes in aqueous solution. Our results may be compared with a study of the relationship between aquation rates and strain energy for a closely related series of tetraaza macrocycle complexes of cobalt(III).[9]

Methods

Strain-Energy Minimization. A locally modified version of Boyd's program MOLBD[10] executed on a PR1ME 400 computer (32-bit internal precision) was used for all calculations. The program, calculational method, and assumptions implicit in the force field model as it is applied to transition-metal complexes have been discussed in detail elsewhere.[5,11-13]

Interaction Constants. To the best of our knowledge, this is the first report of a strain-energy minimization calculation that includes the copper(II) ion and divalent sulfur in addition to the common first-row elements. Intraligand C–C bond and angle deformation constants, torsion potentials, and C–H and H–H nonbonded repulsions were adopted from earlier calculations[11-13] and, as usual, are assumed to be relatively insensitive to metal coordination. Carbon–sulfur and S–H nonbonded repulsions were adapted from the corresponding Cl–C and Cl–H interactions of DeHayes and Busch.[11] Initial Cu(II)–S force constants were derived from the vibrational spectra of Woodruff et al.[14] Initial C–S force constants were estimated from group frequency tables for similar bonds. We have taken the unstrained C–S–C angle to be 100°, consistent with the observation that valence angles around divalent sulfur are normally smaller than the 109° predicted from simple electron-repulsion concepts. The C–S–C deformation force constant was initially taken as one-tenth of the C–S stretching force constant, consistent with previous experience.[5,12,13] Interaction constants used in this study are published elsewhere;[4c] the same interaction set was, of course, used for all calculations.

Trial Coordinates. Initial coordinates were taken from the crystallographic results of Rorabacher et al.[15] Though crystallographic coordinates are available for each of the compounds reported herein, as a matter of convenience we chose to begin only with the coordinates of $[Cu([13]\text{-ane-}S_4)]^{2+}$, $[Cu([15]\text{-ane-}S_5)]^{2+}$, and $[([16]\text{-ane-}S_4)]^{2+}$, for which hydrogen positions were reported. The remaining complexes, $[Cu([15]\text{-ane-}S_4)]^{2+}$, $[Cu([14]\text{-ane-}S_4)]^{2+}$, and $[Cu([12]\text{-ane-}S_4)]^{2+}$, were derived from $[Cu([16]\text{-ane-}S_4)]^{2+}$ by successive deletion of methylene groups. For simplicity in calculation, water molecules were substituted for perchlorate ions in axial sites, as required. A comparison of selected crystallographic and energy-minimized bond distances and angles is given in Table I. Except for the substitution

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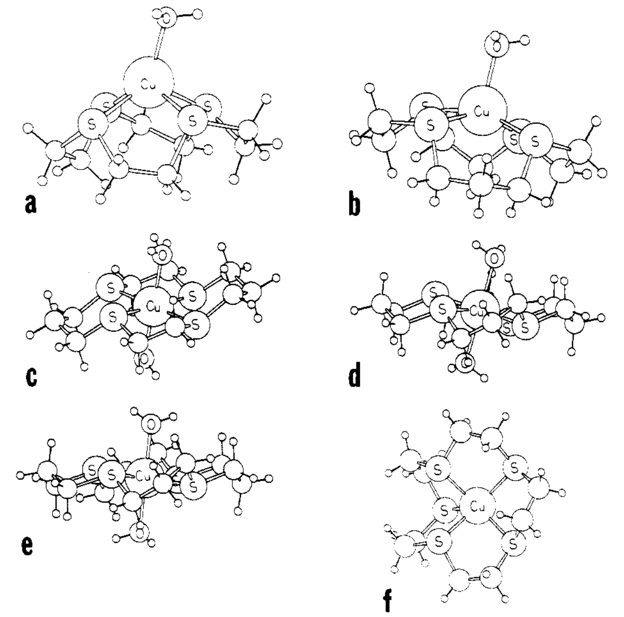

Figure 1. Strain-energy-minimized structures: (a) $[Cu([12]\text{-ane-}S_4)]^{2+}$; (b) $[Cu([13]\text{-ane-}S_4)]^{2+}$; (c) $[Cu([14]\text{-ane-}S_4)]^{2+}$; (d) $[Cu([15]\text{-ane-}S_4]^{2+}$; (e) $[Cu([16]\text{-ane-}S_4)]^{2+}$; (f) $[Cu([15]\text{-ane-}S_5)]^{2+}$.

of water for coordinated perchlorate, strain-energy-minimized structures are essentially identical with the crystallographic structures (Figure 1).

Results

The calculated structures rapidly converged to an rms coordinate shift of 0.01 Å with nuclear positions close to the input crystallographic parameters.[15] Minor differences found around the coordinated sulfur atoms early in the calculation were corrected by adjusting the sulfur angle deformation potential parameters. No other parameters were adjusted.

We have used a feature of Boyd's program that calculates vibrational frequencies for strain-energy-minimized structures to confirm our choice of interaction constants. Measured Cu–S stretching frequencies lie in the range 247–281 cm^{-1}.[14] Using simulated isotopic substitution, in which we calculate vibrational frequencies based both on a normal distribution of isotopic masses and for hypothetical copper(II) isotopes (e.g., ^{73}Cu), we have identified the calculated Cu–S stretch within the range 239–284 cm^{-1}. Within this range, the lowest frequency corresponds to $[Cu([16]\text{-ane-}S_4)]^{2+}$, in agreement with experiment[14] ($\nu_{obsd} = 247$ cm^{-1}; $\nu_{calcd} = 239$ cm^{-1} (^{63}Cu), 243 cm^{-1} (^{53}Cu), 237 cm^{-1} (^{73}Cu)). We believe that the differences between the calculated and observed frequencies (ca. 5%) arise from minor errors in all of the force constants involved in nuclear displacements at the metal-donor bond. It is clear from our simulated isotopic substitution that the vibrational frequency calculations also reflect coupling among various vibrational modes (albeit informally, since no coupling constants are employed in the calculation).

In these copper complexes, the distribution of the strain energy varies with ring size (Table I). We have not found any atom to make an unusual contribution to the strain energy, nor have we found evidence for a systematic dependence on the number of atoms or interactions (i.e., no simple, additive "methylene group" contribution to the overall intramolecular strain energy is apparent). The total strain energy we calculate for these complexes is surprisingly small. We find a range of 2.9_9–5.5_2 kcal mol^{-1}, in contrast with the range of 19.7–35.6 kcal mol^{-1} calculated for the complexes $[Co([13]\text{-ane-}N_4)Cl_2]^+$ through $[Co([16]\text{-ane-}N_4)Cl_2]^+$ by Hung and Busch.[9]

The nonbonded contribution to the strain energy in each of these structures is dominated by small long-range attractive terms (Table II). Similar dominance of nonbonded energies by long-range attractive terms was observed by DeHayes and Busch[13] in their studies of diamine chelate rings and is not surprising in essentially planar complexes with macrocyclic ligands. Furthermore, intra-ring nonbonded distances are greater in the polythia ether macrocycle complexes because carbon–sulfur distances (1.82 Å) are greater than carbon–nitrogen distances (1.45–1.48 Å). In addition, the sulfur donors, in contrast with the nitrogen donor in the corresponding saturated tetraaza macrocycle complexes, do not bear protons; the N–H protons in amine complexes are frequently the source of the largest nonbonded repulsions.[5,12,16]

Table II. Calculated Intramolecular Strain Energies for Some Polythia Ether Macrocycle Copper(II) Complexes

complex	A/I^a	R_{ij}	θ_{ijk}	ϕ_{ijkl}	NB	total
$[Cu([12]\text{-ane-}S_4)]^{2+}$	32/279	0.3	3.4	3.3	−3.3	3.7
$[Cu([13]\text{-ane-}S_4)]^{2+}$	35/320	2.3	5.5	1.5	−5.9	3.5
$[Cu([14]\text{-ane-}S_4)]^{2+}$	41/390	2.1	5.0	1.4	−5.5	3.0
$[Cu([15]\text{-ane-}S_4)]^{2+}$	44/419	0.9	5.0	2.9	−4.7	4.1
$[Cu([16]\text{-ane-}S_4)]^{2+}$	47/455	0.9	5.4	3.7	−4.5	5.5
$[Cu([15]\text{-ane-}S_5)]^{2+}$	36/332	0.6	7.7	5.8	−2.9	11.2

^{a} Atoms/interactions.

We have calculated the intramolecular strain for the hypothetical copper(II) complexes $[Cu(1,2\text{-ethanedithiolato})Cl_4]^{2-}$ ($[Cu(es)Cl_4]^{2-}$) and $[Cu(1,3\text{-propanedithiolato})Cl_4]^{2-}$ ($[Cu(ts)Cl_4]^{2-}$) for the purpose of comparing the strain energies of single-ring diamine and dithiolate complexes. As expected, the overall strain energy of the dithiolate chelates is less than that of the diamine chelates (ethylenediamine = 0.58, es = −0.77 kcal mol^{-1}; 1,3-diaminopropane = 3.55, ts = −0.43 kcal mol^{-1}) and is dominated by small attractive terms.

Discussion

The principal objective of the present work is a test of the *quantitative* estimate of steric effects derived from semi-empirical molecular-mechanics calculations. Energies estimated from atomic coordinates and one or more key vibrational frequencies are compared with experimentally measured thermodynamic parameters. Previous attempts have met with variable success.[5,6,9,17] In the course of this exercise, both atomic coordinates and vibrational frequencies have been calculated for comparison with experimental values[14,15] to demonstrate that the high information density of a vibrational spectrum may be used to refine the empirical force field.

The system chosen for study has been thoroughly characterized experimentally;[7] crystal structures, stability constants, enthalpies, entropies and free energies of formation, rates of complexation, dissociation and electron transfer, vibrational spectra, and electronic spectra have been reported for an homologous series of closely related complexes. In this[7] and related works,[9] systematic variations in reactivity have been ascribed to the size of the macrocyclic ligand or, more generally, to steric effects.

Since the variations in steric demands among the ligands derive from changes in the number of methylene groups within the macrocycle, the compounds considered in this study have variable numbers of atoms and interactions (Table II); since the computational method simply accumulates the individual contributions to intramolecular strain, it is particularly interesting to note that there is no simple monotonic increase in intramolecular strain with increasing numbers of atoms and interactions.

Sokol et al.[18] in their discussion of macrocyclic and ring-size effects on the equilibrium constants and thermodynamic pa-

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Table III. Observed and "Strain-Free" Thermodynamic Parameters for Some Polythia Ether Macrocycle Copper(II) Complexes[a]

complex	ΔH_{obsd}	ΔS_{obsd}	ΔG_{obsd}	H_{stn}	ΔH_{int}	ΔG_{int}
$[Cu([12]\text{-ane-}S_4)]^{2+}$	+0.11	15.9	−4.63	3.7	−3.5	−8.3
$[Cu([13]\text{-ane-}S_4)]^{2+}$	−2.37	7.8	−4.69	3.5	−5.8	−8.1
$[Cu([14]\text{-ane-}S_4)]^{2+}$	−4.22	5.6	−5.92	3.0	−7.2	−8.8
$[Cu([15]\text{-ane-}S_4)]^{2+}$	−3.28	3.6	−4.33	4.1	−7.3	−8.4
$[Cu([16]\text{-ane-}S_4)]^{2+}$	−1.43	5.3	−3.00	5.5	−6.9	−8.5
$[Cu([15]\text{-ane-}S_5)]^{2+}$	−3.02	9.0	−5.70	11.2	−14.2	−16.9

[a] ΔH and ΔG in kcal mol^{-1}; ΔS in eu; obsd = observed (ref 17); stn = strain (Table II); int = intrinsic (or strain free).

rameters of copper(II) polythia ether macrocycle complexes suggest that the entropies of formation for these complexes (Table III) are dominated by competing effects of desolvation of the aquocopper ion and stereorestriction of the macrocycle. The former contribution is largest the complexes with the ligand [15]-ane-S_5, which displaces all of the coordinated water, smallest for complexes with the 14-, 15-, and 16-membered macrocycles, which displace four coordinated water molecules, and intermediate for complexes with the 12- and 13-membered macrocycles, which displace five water molecules. The contribution from stereorestriction of the macrocycle evidently is largest for the larger, more flexible macrocycles.[18] The effects of solvation of these moderately hydrophobic ligands were shown to be minor.[19]

In the ensuing discussion, the enthalpy of formation will be considered to be the sum of any number of energy terms analogous to those that comprise the strain energy:

$$\Delta H_{obsd} = \Delta H_{intrinsic} + \Delta H_{strain} + \Delta H_{outer\ sphere} + \ldots + \ldots$$

Of these, we are particularly interested in the term that reflects the energy difference between the $Cu^{2+}{}_{aq}$ ion and a hypothetical strain-free Cu(II) cyclic polythia ether complex ($\Delta H_{intrinsic}$) and that which reflects the intramolecular strain energy in the ligands (ΔH_{strain}).[19] Succeeding terms such as those ascribable to outer-sphere reorganization etc. are not resolvable at the present level of approximation.

In Table III we show that $\Delta H_{intrinsic} = \Delta H_{obsd} - \Delta H_{strain}$ is approximately constant at 7.2 kcal mol^{-1} for copper(II) complexes with [14]-ane-S_4, [15]-ane-S_4, and [16]-ane-S_4 within the 10% error in ΔH_{obsd}[18] and our estimated 10% error in ΔH_{strain} (estimated from vibrational spectra vide supra), consistent with the interpretation of Sokol et al. The free energy of formation calculated from $\Delta H_{intrinsic}$ and the experimentally determined entropy of formation[18] are approximately constant at 8.5 kcal mol^{-1} for the same complexes (Table III).

We also find a correlation between the experimentally determined free energy of formation of tetrathia ether macrocycle copper(II) complexes and the strain energy (Figure 2); linear least-squares analysis of five points resulted in a slope of −1.04 (0.16) with an intercept of −8.65 (0.66) kcal mol^{-1} (correlation coefficient 0.97) corresponding to the free energy of formation of the hypothetical strain-free structure. Though we cannot explain the linear relationship between intramolecular strain and the free energy of formation outside the three tetragonal complexes, it is interesting to note that the same strain-free enthalpy of formation, $\Delta H_{intrinsic}$, is found in either approach.

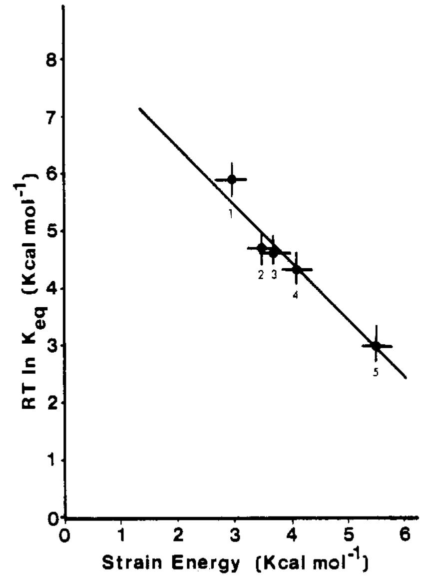

Figure 2. $RT \ln K_{eq}$ for the reaction $Cu^{2+}{}_{aq} + L \rightleftarrows [CuL]^{2+}{}_{aq}$ as a function of intramolecular strain energy in complexes with the tetrathia ether ligands (L): (1) [14]-ane-S_4; (2) [13]-ane-S_4; (3) [12]-ane-S_4; (4) [15]-ane-S_4; (5) [16]-ane-S_4. See the text for error estimates and the linear least-squares analysis.

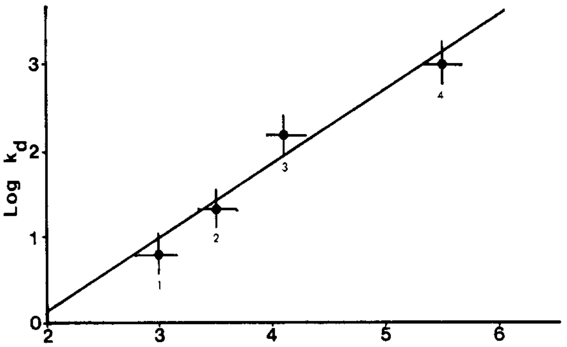

Figure 3. ln k_d for the reaction $[CuL]^{2+}{}_{aq} \rightarrow Cu^{2+}{}_{aq} + L$ as a function of the intramolecular strain energy in complexes with the tetrathia ether ligands (L): (1) [14]-ane-S_4; (2) [13]-ane-S_4; (3) [15]-ane-S_4; (4) [16]-ane-S_4. See the text for error estimates and the linear least-squares analysis.

Similarly, we find a remarkable correlation between ground-state strain energy and dissociation rate constants, k_d, in 0.1 M aqueous perchlorate[20] for this series of tetrathia ether complexes (Figure 3) (correlation coefficient 0.98). It is not surprising to find that intramolecular strain contributes to the activation energy for ligand dissociation in a manner analogous to its contribution to the free energy of formation. Unfortunately, activation parameters have not been estimated for all of the complexes under study, so we cannot make a direct

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(19) In these calculations, the intramolecular strain in the free ligand is ignored. We have attempted to estimate the strain in the metal-free ligand by deleting the metal ion from the [14]-ane-S_4 complex and the related interactions from the input file. We find that the energy-minimized coordinates and the strain energy of this ligand conformer are essentially those of the coordinated ligand, indicating a local minimum probably due to carefully balanced nonbonded repulsions in the coordinated ligand. In contrast, when we initialized the free ligand calculation using crystal coordinates (DeSimone, R. E.; Glick, M. D. *J. Am. Chem. Soc.* **1976**, *98*, 762) the energy-minimization calculation converged on the crystal coordinates as an essentially strain-free structure. This, we believe, is evidence for a low strain energy in the free ligand as well as evidence for a multiplicity of conformations with low and/or closely spaced intramolecular strain energies.

(20) Diaddario, L. L.; Zimmer, L. L.; Jones, T. E.; Sokol, L. S. W. L.; Cruz, R. B.; Yee, E. L.; Ochrymowycz, L. A.; Rorabacher, D. B. *J. Am. Chem. Soc.* **1979**, *101*, 3511.

comparison as we have done with equilibrium constants.

The complex $[Cu([15]\text{-ane-}S_5)]^{2+}$ is more stable[18] and dissociates more slowly[20] than expected on the basis of the calculated strain energy (Table III). This finding is consistent with the premise[18] that the pentacoordinate ligand enjoys an additional entropic contribution to the complex stability in addition to the enthalpic contribution of the fifth Cu–S bond.

We find, in these calculations that are based on axial coordination by water (vide supra), no basis in molecular strain for the observed anion effects[18] in solution. Indeed, the differences in formation constants within this series can be ascribed to strain-energy differences, alone, at constant anion concentrations, consistent with the proposed outer-sphere or "tight ion pair" interpretation.[18]

There is no obvious correlation between ground-state strain energy for the copper(II) complexes and rates of complex formation, k_f. In the proposed mechanism,[20] the rate-determining step is the closure of the first chelate ring (i.e., attachment of the second sulfur donor). It has been proposed that this step is dependent on the conformation of the unicoordinated ligand. We do not believe that we have a reliable model for the ligand in this state.[19] We note, however, that, for the odd ligands ($[13]\text{-ane-}S_4$ and $[15]\text{-ane-}S_4$), there are two different kinds of sulfur donors. For the former ligand, these join two five-membered rings or a five- and a six-membered ring; for the latter, they join two six-membered rings or a five- and a six-membered ring. If the rate of complex formation is strongly influenced by the rate of chelate-ring closure, we would expect the complexation rates for these ligands to reflect some selectivity (e.g., selection of the five-membered in preference to the six-membered chelate ring). We cannot find any correlation with either the ring size or the ground-state strain energy of the copper(II) complexes indicative of this selectivity.

At this point, however, we are wary of overinterpreting the available data. The magnitudes of both the experimental and calculated quantities are small, with the stability constant in the range $10^{2.2}$–$10^{4.3}$ and strain energy in the range 3–4 kcal mol^{-1}. Thus, the formation rate constants vary only by a factor of 36 throughout the series of tetrathia ether macrocycle complexes, while the uncertainties in some rate constants are as much as a factor of 2.[20] Similarly, we believe that the uncertainties in the calculated strain energies (which completely ignore environmental effects) are at least 10% (estimated from vibrational frequencies). Given the small range and large uncertainties in all of these quantities, we do not believe that the effects of small conformational differences among partially coordinated ligands can be inferred.

Conclusions

1. Molecular-mechanics methods are readily adapted to any collection of atoms for which some reliable structural data and molecular spectra are available. Within a controlled series of structurally related compounds, steric contributions to enthalpies of formation may be quantitatively estimated. In the present model, subtraction of calculated strain energies from experimentally determined enthalpies of formation resulted in a constant "intrinsic" or strain-free enthalpy of formation. The latter quantity is, itself, a composite of contributions from the differences in enthalpies of formation of the aquo ion and CuS_4 coordination center, crystal field effects, outer-sphere coordination, etc., which are not resolvable either by experiment or in the calculational model employed here.

2. While molecular vibrations can be identified by looking at atomic displacements derived from the calculated eigenvectors associated with each frequency, computer-simulated isotopic substitution in a molecular-mechanics calculation may provide a quick and accurate means for identifying selected molecular vibrations. The molecular spectroscopy of particular classes of compounds can be used to refine a force field model, lending credence to the calculated strain enthalpies.

3. There is no evidence for simple additive steric effects within this series of structurally related compounds.

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Registry No. $[Cu([12]\text{-ane-}S_4)]^{2+}$, 57673-84-4; $[Cu([13]\text{-ane-}S_4)]^{2+}$, 57673-85-5; $[Cu([14]\text{-ane-}S_4)]^{2+}$, 57673-86-6; $[Cu([15]\text{-ane-}S_4)]^{2+}$, 57673-87-7; $[Cu([16]\text{-ane-}S_4)]^{2+}$, 57673-88-8; $[Cu([15]\text{-ane-}S_5)]^{2+}$, 60165-93-7; $[Cu(es)Cl_4]^{2-}$, 89746-89-4; $[Cu(ts)Cl_4]^{2-}$, 89746-90-7.