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Cryptand Conformational Analysis and Its Mechanistic Implications. Molecular Mechanics Calculations on Cryptands [111] and [222][1]

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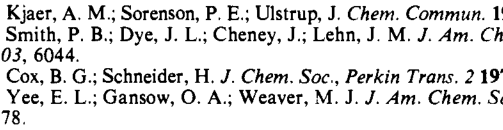
Abstract: The conformational analysis of the [111] and [222] cryptands has been carried out by molecular mechanics calculations on the free molecules. Semiempirical CNDO2 calculations were performed on the optimized structures resulting from the molecular mechanics strain energy minimization. Agreement in all cases is excellent. [111] is found to be a relatively rigid molecule for which the endo–endo conformation is by far the most stable. [222] is a fairly flexible molecule which is capable of facile exo–endo interconversion. There are four conformations of [222] of similar strain energy which differ from one another in cavity size and shape. The conformations are endo–endo (I), endo–endo (II), endo–exo, and exo–exo. A surprising structural result is that the most elongated cryptand conformation is endo–endo (I). Nitrogen inversion produces exo conformations which have *shorter* nitrogen–nitrogen distances, the cryptand being more spherical. Endo–endo (II) is similar in cavity size and shape to exo–endo and exo–exo. Thermodynamic, structural, and kinetic implications of these results are presented.

Cryptands are macrobicyclic ligands which are capable of forming inclusion complexes[3,4] with metal ions. The [222] cryptand, $N(CH_2CH_2OCH_2CH_2OCH_2CH_2)_3N$, contains a total of six ether oxygen donor atoms in the three linkages between the two bridgehead nitrogens. The ligand with one less $(-CH_2CH_2O-)$ group is known as [221] with other similar ligands being named in the same way. Many cryptands and cryptand analogues have now been synthesized which vary considerably in cavity size, flexibility, number and type of donor atom, and ligand topology.[5] The idea is to enhance metal ion specificity by selective variation of structural and chemical characteristics of the ligands. It is, of course, the selectivity of the metal cryptation process which is primarily responsible for the continuing high interest in these ligands. Although the best fit of metal ion to ligand cavity is a prime structural requisite for cryptate stability, a complicated interaction of enthalpic and entropic contributions is involved in determining ligand specificity with no obvious thermodynamic generalization being apparent.[6]

The dynamics of cryptate formation are characterized by rate constants[7-11] which are in general considerably less than those which are calculated based on a simple dissociative interchange (I_d) mechanism. Possible interpretations of this result are either that the conformational equilibrium of the cryptand itself favors an unreactive form[12] or that the ligand imposes constraints on the entry of the metal ion into the cavity. These interpretations are not mutually exclusive and the latter, in particular, is supported by results of kinetic studies of proton-transfer reactions of cryptands[13-17] and the observation[18] that the difference in the rates of complexation of the various metal ions is much greater than the variation in water exchange rates of the ions.

One of the important factors upon which a better understanding of the reaction thermodynamics and kinetics depends is a knowledge of cryptand conformational equilibria. Although there are conformational problems associated with the strands between the bridgehead nitrogens, the principal conformational question concerns the orientation of the lone pairs of electrons on the nitrogens. Each lone pair may be oriented either into the ligand cavity (an endo conformation) or away from the ligand cavity (an exo conformation). One can, therefore, easily envision a minimum[19] of three possible conformations for the nitrogens; exo–exo, exo–endo, and endo–endo (**1**). Although the structures of un-



(1)

complexed [222][20] and $[2_B2_B2]$[21] in the solid state are endo–endo, results of NMR experiments[22] on the larger cryptands and on

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(1) Preliminary results of this work were presented at the 181st American Chemical Society National Meeting, Atlanta, GA, April, 1981 (Pizer, R.; Geue, R. INOR 150).

(2) (a) Australian National University. (b) Molecular Design Ltd. (c) Brooklyn College.

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(19) A structure of a macrobicyclic diamine cryptand analogue shows planar (sp^2) bridgehead nitrogen atoms. (Newkome, G. R.; Majestic, V.; Fronczek, F.; Atwood, J. L. *J. Am. Chem. Soc.* **1979**, *101*, 1047). A recent paper which reports molecular mechanics calculations on complexes of encapsulated Co^{2+} and Co^{3+} also discusses this point (Bond, A. M.; Hambley, T. W.; Snow, M. R. *Inorg. Chem.* **1985**, *24*, 1920).

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structurally similar macrobicyclic diamines indicate that the inversion frequency of the bridgehead nitrogens is high. Similarly, although crystal structures of metal cryptates[23] invariably show the ligand to be endo–endo, Lehn has suggested[4] that, in solution, inclusive cryptate complexes may exist in an equilibrium involving all three ligand conformations.

There have been several experimental approaches to the conformation problem. We studied proton-transfer reactions of [222] by the temperature-jump relaxation method[13] in part to elucidate the nature of the conformational equilibria. The results of the study were that at least two conformations are in rapid equilibrium and that nitrogens in both exo and endo conformations could be protonated. A more recent study of [222] by ultrasonic absorption[24] was interpreted in terms of three ligand conformations in rapid equilibrium and it was noted that the conformational rearrangements would not appear to be rate-limiting steps for cryptate formation. However, more extensive studies[14,17] of proton-transfer reactions of [222] and other cryptands have been interpreted in terms of a predominant endo–endo conformation. While there is some disagreement in the literature concerning the conformation of [222], the situation with respect to [111] is much clearer. An early, remarkable result of Lehn[25] was that deprotonation of diprotonated [111] occurs only slowly in concentrated base. This was interpreted in terms of inclusive protonation, the ligand being endo–endo. A subsequent detailed NMR study[16] of the proton-transfer reactions of [111] is discussed in terms of a complex mechanism in which unprotonated nitrogens are exclusively endo.

In this paper we examine the conformational behavior of cryptands theoretically. A molecular mechanics scheme is used for the determination of cryptand structural features and conformation energetics. The method is described in the next section. In order to understand the effect of ring size on cryptand flexibility, we studied both [111] and [222]. The results not only provide insight into questions of cryptand conformation but also permit a consistent interpretation to be made of a wide range of experimental results.

Methodology

Molecular Mechanics Calculations. Molecular mechanics is a useful method for determination of molecular geometry and energetics. The method has been successfully applied to many kinds of problems, including systems as complex as proteins.[26] Molecular mechanics treats molecular strain energy by using a classical model in which the strain energy is expressed as a sum of energies associated with particular molecular deformations. Equilibrium values of bond lengths and angles and the force constants for various molecular deformations can be determined experimentally. For example, it is possible to obtain a force field which relates the strain energy of a molecule to its geometry by normal-coordinate analysis of molecular vibrations.[27]

The force field used in this study[28] was originally developed to reproduce accurately the geometry of hydrocarbons and related molecules. The method is, therefore, suitable for the study of cryptands. The force field is consistent with chemical intuition in that the total strain energy, U_T, is given as a sum of stretching energies, U_S; bending energies, U_B; energy due to stretch-bend

$$U_T = U_S + U_B + U_{SB} + U_{NB} + U_1 + U_d \tag{2}$$

deformations, U_{SB}; energies from nonbonded interactions, U_{NB}; torsional energies, U_1; and dipole interaction energies, U_d. Electrostatic effects are treated empirically in the dipole interaction terms.[28] The functional form of each contribution is shown in eq 3. The summations in eq 3 are over all possible interactions for a particular structure. The symbols in eq 3 are defined in the Appendix.

$$\begin{gathered} U_S = \sum K_S(l - l_0)^2 \\ U_B = \sum K_B(\theta - \theta_0)^2 \\ U_{SB} = \sum K_{SB}(\theta - \theta_0)[(l - l_0)_a + (l - l_0)_b] \\ U_{NB} = \sum K_{NB} \exp(-12.5/P) - 2.25P^6 \\ P = r_{ij}/R_{vdw} \\ U_1 = \sum V_1(1 + \cos\omega) + V_2(1 - \cos 2\omega) + V_3(1 + \cos 3\omega) \\ U_d = \sum K_d \mu_A \mu_B(\cos X - 3\cos\alpha\cos\beta)/\epsilon R^3 \end{gathered} \tag{3}$$

Equations 2 and 3 provide a method for determination of the strain energy as a function of molecular geometry. In order to determine the equilibrium configuration, the atomic coordinates are varied via an iterative Newton–Raphson procedure to minimize the strain energy. What this procedure does is to find the nearest local minimum, not a global minimum. Therefore, one must consider a large number of starting points for the optimizations as described below. These molecular mechanics calculations are contained in the MM2 program.[29]

Modeling Schemes. The modeling schemes discussed below were facilitated with use of CHEMLAB,[29] an integrated molecular modeling system containing molecular graphics, molecular energetics, and several quantum chemistry routines including CNDO2.

[111]. Various starting coordinates were entered with use of a computer graphics drawing tablet. Initial structures were easily drawn in exo–exo, exo–endo, and endo–endo conformations. These structures were then transformed to optimized three-dimensional structures by using molecular mechanics. A large number of starting points with different nitrogen–nitrogen distances and different ring conformations in the ether linkages were considered. In addition to full molecular mechanics minimizations, the various starting conformations were also minimized with the coordinates of the nitrogens being kept fixed. The minimum energy structures and corresponding strain energies are reported in the next section.

A quantum mechanical CNDO2 calculation[30] was performed on the minimum energy structures. This calculation treats electronic effects explicitly. The conformational energy as calculated by CNDO2 is included for comparison with molecular mechanics results. Agreement between the two calculations verifies the parameters used in the molecular mechanics calculations.

[222]. Conformational analysis of [222] was carried out by utilizing a modeling scheme similar to that for [111]. However, the crystal structures of [222][20] and many cryptate complexes[23] are known. Thus, the atomic coordinates of the ligand as determined by X-ray analysis were used as starting points. Although the reported structures are endo–endo, exo–endo and exo–exo starting conformations can be generated by flipping the nitrogens out of the cryptand cavity. In addition, the crystal structure[20] of the bis borane adduct of [222] has been determined and the ligand conformation used as an exo–exo starting point. Many other starting points were considered and several calculations were done with the nitrogens being held fixed. CNDO2 calculations were then performed on the minimum energy conformations.

It should be noted that the strain energies reported are not free energies since effects due to entropy are not included. Furthermore, although it is possible in more detailed calculations to include

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(23) For example: Moras, D.; Weiss, R. *Acta Crystallogr., Sect. B* **1973**, *B29*, 396. Metz, B.; Moras, D.; Weiss, R. *Acta Crystallogr., Sect. B* **1973**, *B29*, 1377. Metz, B.; Moras, D.; Weiss, R. *Acta Crystallogr., Sect. B* **1973**, *B29*, 1382.

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(29) Computer programs available from Molecular Design, Ltd., 2132 Farallon Dr., San Leandro, CA 94577. The MM2 force field contains all necessary parameters for cryptands including the NCCO fragment which is not included in ref 28.

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Table I. Strain Energy (kcal mol^{-1}) of [111] Calculated by MM2

	endo–endo	exo–exo
compression	3.0	3.4
bending	12.9	32.0
stretch–bend	1.3	2.3
nonbonded interaction	17.9	23.2
torsion	20.4	19.9
dipole	3.6	0.6
total strain energy	59.1	81.4

Table II. Relative Strain Energies (kcal mol^{-1}) and Geometries of [111] Cryptand Conformations

			strain energy	
	R_N (Å)	R_{CP} (Å)	MM2	CNDO2
endo–endo	3.67	4.46	0	0
exo–exo	4.74	4.22	22.3	19.5

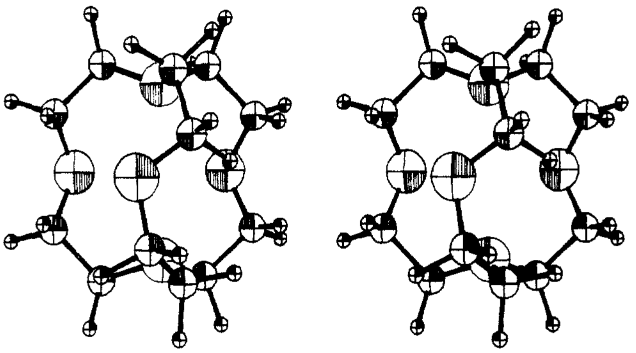

Figure 1. [111] endo–endo conformation.

the influence of solvent,[31] the calculations here are done on the free molecules. Because of this, no estimate of the conformational equilibrium constants can be made from the calculations.

Results

[111]. Energy minimization of any endo–endo starting configuration results in the same endo–endo conformation. Starting with initial structures which are exo–endo also results in the endo–endo structure. Although a very high energy exo–endo structure can be obtained if the positions of the nitrogens are held fixed, all attempts from several different starting points to find an exo–endo conformation with unconstrained minimization produce the endo–endo conformation. Energy minimization of exo–exo starting configurations results in an exo–exo conformation. The strain energy of the optimized exo–exo conformation is considerably higher (22.3 kcal mol^{-1}) than that of endo–endo (Table I). A comparison of the relative strain energies for the optimized endo–endo and exo–exo conformations as calculated by molecular mechanics and semiempirical CNDO2 is given in Table II. Agreement is excellent, confirming the results of the molecular mechanics calculations.

Comparison of the individual components of the strain energy (Table I) indicates that the added strain in the exo–exo conformation is primarily due to bond angle deformation. For example, while the average C–N–C bridgehead angle in the endo–endo conformation is relatively large, 113.1°, in the exo–exo conformation it is even larger, 115.2°. The exo–exo conformation is both more planar[19] and more highly strained about the bridgehead than is the endo–endo conformation.

Stereoviews of the exo–exo and endo–endo conformations are shown in Figures 1 and 2 with relevant geometric data being given in Table II. A useful way of seeing the differences between the two conformations with respect to cavity geometry is to compare the distances between the planes of the three carbon atoms bonded to the bridgehead nitrogens. This distance, R_{CP}, has an unambiguous meaning only if the two planes are parallel. Since this is not the case in general, R_{CP} is calculated here by taking the distance between the bridgehead nitrogens, R_N, and subtracting (for exo nitrogens) or adding (for endo nitrogens) the distance from each bridgehead nitrogen to the center of the carbon plane. The utility of this parameter is that a small value of R_{CP} requires that the cryptand cavity be more spherical; a large value requires that the cavity be more elongated. The distance between the bridgehead nitrogens, R_N, does not define cavity geometry in this way. This is shown by the results for [111] as presented in Table II. R_N in the exo–exo conformation is considerably greater than R_N in the endo–endo conformation, yet R_{CP} is slightly *less* in the exo–exo conformation. The difference in R_{CP} is not large and the cavities are comparable in size and shape.

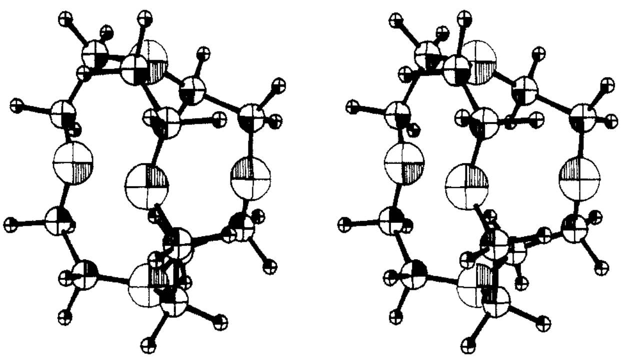

Figure 2. [111] exo–exo conformation.

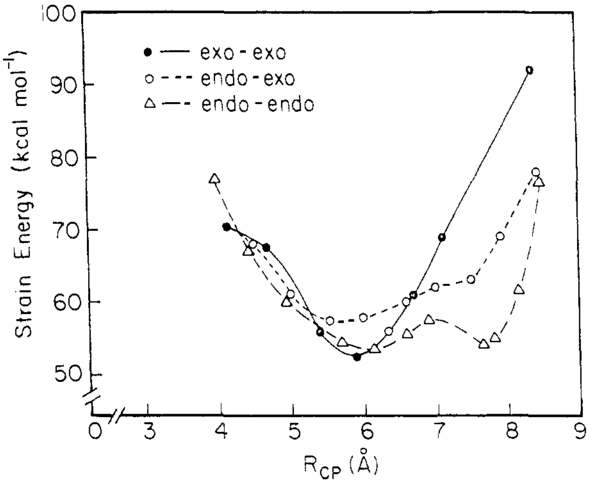

Figure 3. [222] strain energy as a function of R_{CP} for various conformations.

Even though the high strain energy associated with exo nitrogens indicates that [111] is a fairly rigid molecule, there is a small degree of flexibility associated with the endo–endo conformation. When R_N in the endo–endo configuration is decreased by 1 Å and held fixed, the strain energy increases by 6.5 kcal mol^{-1}.

[222]. Starting with X-ray data[20] for [222], the calculation produces an optimized endo–endo conformation with R_N = 6.77 Å and R_{CP} = 7.64 Å, this result not being greatly different from the starting coordinates. Crystal structures[23] of cryptates were also used to provide some starting points for endo–endo ligand conformations. The calculations yielded only endo–endo conformations of higher strain energy. Generating other starting points yields three other conformations (exo–exo, exo–endo, and a second endo–endo) of similar energy at much lower values of R_{CP}. Once the local minima were found, the determination of the strain energy as a function of R_{CP} for each conformation was carried out by changing R_N and holding it fixed during the molecular mechanics calculation. The results are shown in Figure 3. It should be noted that Figure 3 does not necessarily represent the energy barrier for conformational transitions because at each point the nitrogens were held fixed with all other atoms being allowed to relax to their minimum energy configuration. However,

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(31) The study of medium effects on conformational equilibria by molecular dynamics calculations has recently been reviewed. Jorgensen, W. L. *J. Phys. Chem.* **1983**, *87*, 5304.

Table III. Relative Strain Energies (kcal mol^{-1}) and Geometries of [222] Cryptand Conformations

	R_N (Å)	R_{CP} (Å)	strain energy MM2	strain energy CNDO2
endo–endo (I)	6.77	7.64	0	0
endo–endo (II)	5.27	6.17	−0.4	−2.6
endo–exo	5.50	5.54	3.6	1.7
exo–exo	6.71	5.89	−1.2	0.2

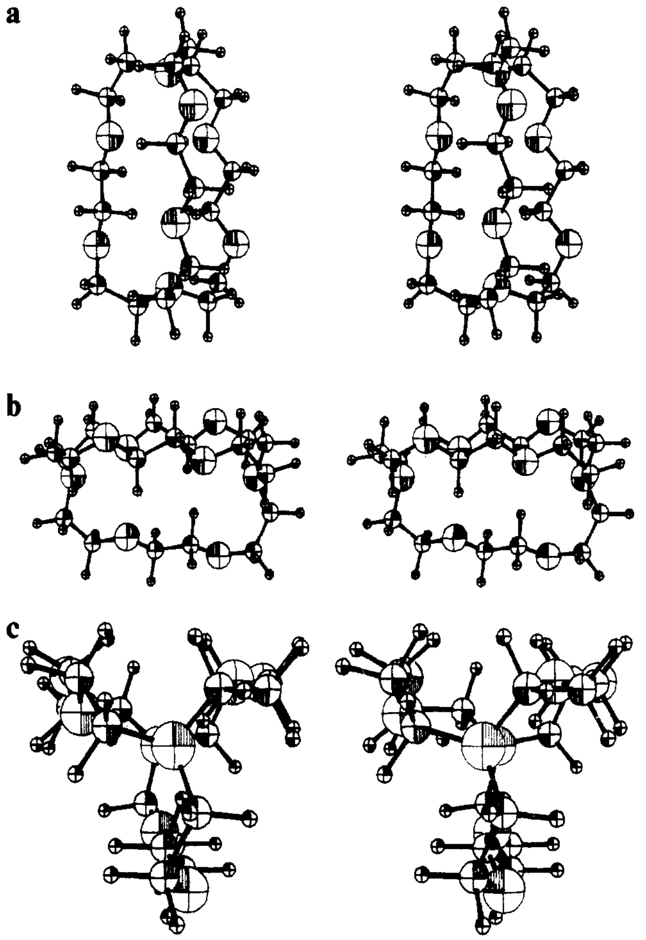

Figure 4. (a) [222] endo–endo (I) conformation. (b) [222] endo–endo (I) conformation, alternative view. (c) [222] endo–endo (I) conformation, alternative view.

the result that several conformations are similar in energy, coupled with the fairly shallow minima in Figure 3 (particularly for the endo–endo and endo–exo conformations), clearly indicates that [222] is much more flexible than [111]. Further, the fact that the three conformations at similar, low values of R_{CP} are close in energy, differing structurally from one another principally via nitrogen inversion, suggests the possibility of facile exo–endo interconversion.

Relevant geometric data and a comparison of molecular mechanics and CNDO2 calculations are given in Table III. The two calculations are in substantial agreement in showing that the various conformations are quite similar in energy.

The structures of the various conformations are presented in Figures 4–7. A view along the N–N axis (Figure 4c) shows approximate threefold symmetry. However, given the flexibility of the molecule (Figure 3), perfect symmetry is not expected. The structure that results from minimization of the X-ray coordinates (endo–endo (I)) has a much larger value of R_{CP} than either endo–endo (II), exo–endo, or exo–exo. The ligand cavities of the latter three conformations are compressed by about 1.5 to 2.0 Å compared with endo–endo (I), and, as a result, they are considerably more spherical. This can be further demonstrated by comparing the average distances between the centers of mass and the ether oxygens in endo–endo (I) and endo–endo (II). In endo–endo (I) this distance is 3.02 Å while in endo–endo (II) it is 3.26 Å.

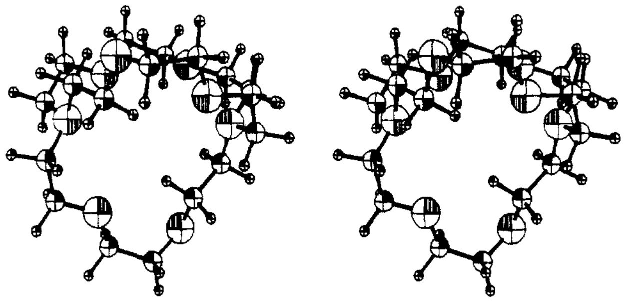

Figure 5. [222] endo–endo (II) conformation.

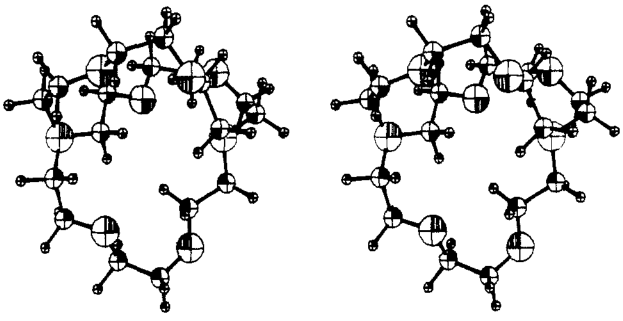

Figure 6. [222] endo–exo conformation.

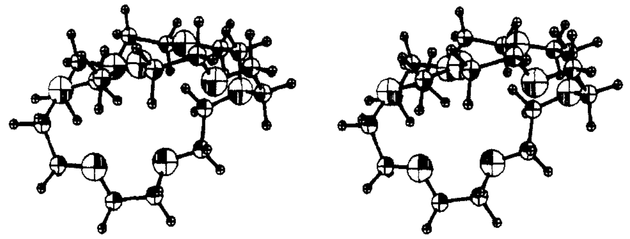

Figure 7. [222] exo–exo conformation.

One surprising result of this calculation is that the most elongated structure of [222] is endo–endo (I). R_N for exo–exo is actually *less* by 0.06 Å than R_N for endo–endo (I). Since endo → exo nitrogen inversion might logically be expected to increase R_N (as in [111], for example), the fact that R_N for exo–exo is unexpectedly shorter than R_N in endo–endo (I) emphasizes the importance of conformational changes in the strands between the nitrogens in determining cryptand geometry.

Discussion

[111]. The results for [111] show a fairly rigid molecule in which the endo–endo conformation is much lower in energy than the exo–exo. Although exo conformations can result from external binding of the bridgehead nitrogens either to protons[16,25] or to borane,[16] experimental evidence concerning the conformation of the free ligand is unequivocal in demonstrating that it is predominantly endo–endo. These experiments include an analysis[32] of the IR spectrum of [111] in DCCl$_3$, NMR studies[16] of proton transfer reactions, and analyses[16,32] of pK_a data.

With respect to the very large difference in strain energy for the two conformations, such a difference is not without precedent. Although 1-azabicyclo[4.4.4]tetradecane is not a precise cryptand analogue, it is a bicyclic amine in which the one bridgehead nitrogen is endo and which has a cavity only slightly smaller than [111]. It is estimated[33] that "there must be an energy penalty of 15–20 kcal mol^{-1} in strain energy associated with outward pyramidalisation of the nitrogen".

[222]. The major differences between the molecular mechanics results for [111] and [222] are that [222] is considerably more

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(32) Cheney, J.; Kintzinger, J. P.; Lehn, J. M. *Nouv. J. Chim.* **1978**, *2*, 411.

(33) Alder, R. W.; Arrowsmith, R. J. *J. Chem. Res.* (*S*) **1980**, 163.

flexible and that facile exo–endo interconversion is possible for [222]. There is ample experimental support for each of these conclusions.

The flexibility of [222] is demonstrated in several ways. For example, measurements[34] of the standard molar volumes of complexation of [222] with alkali metal ions indicate that the size of the ligand internal cavity depends upon the metal ion with which it is complexed. It is even possible for [222] to form an inclusion complex with Cs^+, an ion whose radius is larger than that of the cavity of the uncomplexed cryptand.[35,36] Crystal structures of lanthanide cryptates[37–39] show the close approach of small anions to the 3+ metal center which results in considerable distortion of the complexed ligand as compared with free [222].[20] The occurrence of similar distortions in solution is supported by the facts that lanthanide cryptates interact with small anions in solution[18,40] and that the single ion assumption fails to describe[41] the enthalpies of transfer of cryptates from one solvent to another. It has also been pointed out[42] that crystal structure determinations of metal cryptates are often characterized by relatively high R values which may be due to disorder in some of the ethylene groups of the five-membered chelate rings.

A facile exo–endo interconversion is indicated by many kinetic experiments. Temperature-jump studies of [222] proton-transfer reactions,[13] sound absorption studies,[24] and NMR experiments[22,35,43] have all been interpreted in terms of rapid conformational exchange. By contrast, another study[14] of proton-transfer reactions has been interpreted in terms of a mechanism in which the endo–endo conformation is predominant and exclusive protonation does not occur. However, the availability of exo nitrogen for participation in chemical reactions has since been shown in several experiments. Exclusive complexation of [222] has been demonstrated in solution for UO_2^{2+} cryptates,[44] Pb^{2+} cryptates,[45] and binuclear Cu^{2+} cryptates.[46] But most striking is the very interesting result that the dissociation of metal cryptates is often acid catalyzed.[9,11,18,47–49] One very reasonable suggestion[9] by Cox and Schneider which accounts for this observation is that the endo–endo inclusion complex is in equilibrium with an exo–endo inclusion complex. Protonation of the exo nitrogen followed by dissociation of the complex accounts for the observed hydrogen ion dependence.

It should be pointed out that despite the large amount of experimental work concerning cryptand conformational analysis, no determination of conformational equilibrium constants has ever been made. However, the understanding of conformational geometries as provided by the molecular mechanics calculations permits interesting and significant interpretations to be offered for a wide range of experimental results. The major conclusion about the conformational geometries from the calculations is that endo–endo (I) is considerably elongated with respect to any of the other conformers. This is a surprising result and it is supported by a comparison of the X-ray structures[20] of [222] and its bis borane adduct. Although [222] is endo–endo and $[222]\cdot 2BH_3$ is constrained to be exo–exo, R_N in $[222]\cdot 2BH_3$ is less than R_N in [222] by ~ 0.1 Å in excellent agreement with the molecular mechanics results (Table III).

The conformations of [222] with low R_{CP} (Table III) are more spherical than endo–endo (I). We propose that these conformations are kinetically reactive because they are more open, and this facilitates metal ion entry into and exit from the ligand cavity. However, the conformation of [222] in a complex is more elongated. This is indicated by the experimental result that R_N in cryptates[23,37–39,42] is intermediate between the calculated values of R_N in endo–endo (I) and endo–endo (II). Although the encapsulated ion prevents the adoption of the endo–endo (I) conformation, the conformation of [222] in complexes is elongated with respect to the kinetically reactive conformations of low R_{CP}. This is consistent with the idea that metal ion entry into the ligand cavity is followed by a conformational change to produce a relatively elongated endo–endo cryptate complex. Since the average metal–oxygen distance in cryptates is less than the average metal–nitrogen distance,[23,37–39,42] the primary interaction of the metal ion is with the oxygens. The conformational change which occurs on metal ion entry brings the oxygens closer to the metal ion; the nitrogens actually move further away. It is a curious result that the endo–endo conformation is favored for cryptates not because it enhances the metal ion–nitrogen interaction but because it brings the *oxygens* in closer proximity to the metal ion.

The major results of kinetic experiments on cryptate formation and dissociation are that the rate of cryptate formation is considerably slower than a dissociative interchange mechanism predicts[7–11] and that cryptate dissociation is often acid catalyzed.[9,11,18,47–49] Considering the acid-catalyzed dissociation first, the question is why acid catalysis occurs at all. If an endo → exo conformational change precedes metal ion exit from the cavity, protonation of the exo nitrogen maintains the open conformation which facilitates metal ion exit from the cavity. It has also been pointed out[11] that proton attack could involve protonation of the endo–endo conformation directly for complexes of small cations. This could possibly involve a conformational change from a relatively elongated cryptate to a state in which the ligand conformation is similar to that of the kinetically reactive endo–endo (II).

The fact that rate constants for cryptate formation are low compared with the predictions of an I_d mechanism can be interpreted in terms of steric hindrance imposed by the ligand on metal ion entry into the cavity and/or the fact that the cryptand conformational equilibrium may favor an unreactive form. The latter possibility is supported by the geometries of [222] (Figures 4–7) on the basis of which we propose that only conformations of low R_{CP} are kinetically reactive. If the conformational equilibrium favors the unreactive endo–endo (I), then significantly low rates of cryptate formation will be observed. In addition to low values of R_{CP}, another requirement for reactivity is that the ether oxygens be accessible to interaction with the incoming metal ion. It has been pointed out[11] that the initial interaction of metal ion with [222] is likely to be with one or more of the ether oxygens, not the bridgehead nitrogen. This additional orientational factor also contributes to observed low values of forward rate constants. Figures 5–7 which are of the kinetically reactive conformations of [222] are pictured in orientations which emphasize the availability of the ether oxygens and the accessibility of the ligand cavity. Although a knowledge of cryptand conformational geometries permits an argument to be made concerning the reactive conformations of [222], the extent to which the ligand inhibits metal ion entry into the cavity cannot be made on the basis of these results.[50]

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The thermodynamic specificity of cryptands principally resides in the dissociation rate constant, the most stable cryptate of a particular metal ion generally having the smallest value of the dissociation rate constant.[7,8,11] Such an easy generalization is complicated by the fact that there are also considerable differences in the formation rate constants. The trends in acid-catalyzed dissociation have also been discussed extensively,[9,11,18] but again, no broad generalizations are yet apparent. The present results offer general explanations for the kinetic results in terms of the conformations of the free ligands. An additional, important factor is the effect of metal ion on ligand conformation both in cryptates[51] and in the transition state. When structural evidence is available, unusual thermodynamic[6] and kinetic[11] results are often explained in terms of specific conformational effects. The specific influence of metal ions on conformational equilibria and energetics in undoubtedly one reason for the many exceptions to whatever broad thermodynamic and kinetic generalizations have been made about cryptates. This problem will be investigated in future studies.[52]

Conclusions

[111] is a relatively rigid molecule in which the lowest energy state is clearly endo–endo.

[222] is a flexible molecule characterized by facile exo–endo interconversion. Four conformations of similar strain energy exist, two endo–endo, an endo–exo, and an exo–exo. A number of conclusions can be made about cryptate formation based on the geometries of these various conformations:

(1) Cryptate complexes are endo–endo because this conformation brings the oxygens closest to the metal ion center.

A number of conclusions can be made about cryptate formation based on the geometries of these various conformations: (1) Cryptate complexes are endo–endo because this conformation brings the oxygens closest to the metal ion center. A number of conclusions can be made about cryptate formation based on the geometries of these various conformations.

(2) Acid-catalyzed dissociation occurs because protonation maintains relatively open, kinetically reactive ligand conformations.

(3) Cryptate formation is relatively slow compared with an I_d mechanism in part because not all conformations of [222] are kinetically reactive.

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Appendix. Definition of Terms Used in (3)

K_s	force constant for bond length deformation
l	bond length
l_0	equilibrium bond length
K_B	force constant for bond angle deformations
θ	bond angle
θ_0	equilibrium bond angle
K_{SB}	force constant for stretch–bend deformations
K_{NB}	coefficient for nonbonded interactions
r_{ij}	distance between atoms *i* and *j*
R_{vdw}	sum of van der Waal's radii for atoms *i* and *j*
V_1, V_2, V_3	barriers for torsional motion
ω	torsional angle
K_d	coefficient for dipole–dipole interactions
μ_A	dipole moment of bond A
μ_B	dipole moment of bond B
X	angle between the dipoles
α, β	angles between the dipole axes along R
R	line between midpoints of the bonds
ϵ	dielectric constant, taken to be 1.5

Registry No. Cryptand 111, 37095-49-1; cryptand 222, 23978-09-8.

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(51) A molecular mechanics calculation on [222] and alkali metal cryptate complexes appeared while this paper was in review (Wipff, G.; Kollman, P. *Nouv. J. Chim.* **1985**, *9*, 457). An excellent account is given therein of the structural aspects of various metal cryptates and the relationship between the complexed and uncomplexed ligand. Our calculations based on crystal structure data as starting points are in substantial agreement with the same calculations in this work in showing that the lowest energy conformation among this set is an elongated endo–endo with the conformations derived from the ligand structures of the sodium cryptate and calcium cryptate being higher in energy by 3.4 and 11.1 kcal, respectively. We disagree only in finding that the optimized conformation beginning with the ligand structure found in the barium cryptate is just slightly higher in energy (0.7 kcal) than endo–endo (I). No conformation lower in relative strain energy than those presented here is reported.

(52) **Note Added in Proof**: The crystal structure of [111] has just been determined (Brügge, H.-J.; Carboo, D.; von Deuten, K.; Knöchel, A.; Kopf, J.; Dreissig, W. *J. Am. Chem. Soc.* **1986**, *108*, 107).

Gouterman's "Four-Orbital" Model and the MCD Spectra of High-Symmetry Metalloporphyrins

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Abstract: This paper offers a description of the magnetooptical properties of highly symmetric metalloporphyrins within the framework of the Gouterman "four-orbital" model. Expressions are derived for the Faraday parameters of the Q and B (Soret) transitions of the porphyrin system as a function of the energy and intensity parameters and of the angular momenta of the relevant excited states. A discussion of these results highlights the distinct roles of two competing mechanisms, which procure the Q band intensity. On the one hand this transition may steal intensity from the Soret band as a result of interstate interactions. On the other hand the zeroth order Q^0 state may also carry a non-zero transition dipole moment as a consequence of the tetragonal symmetry of the porphyrin skeleton. The latter feature is a typical characteristic of the Gouterman model and does not occur in the algebraic solution of the perimeter model for cyclic π-electron systems. In a final section MCD spectra are reported for meso- and exo-substituted zinc porphyrins and the corresponding cyanide and pyridine complexes. From these data Faraday parameters were extracted by using a Gaussian fitting procedure. Parameter shifts caused by a change of the axial ligand are shown to follow the theoretical predictions.

Gouterman's "four-orbital" model of the π–π^* transitions in porphyrins is firmly established as a simple unifying theory of porphyrin spectra.[1-4] It provides parametric expressions for the frequencies and intensities of the α–β (Q) and Soret (B) bands