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Anion Binding in Macrobicyclic Metal Cryptate Complexes: Copper(II)-BISTREN

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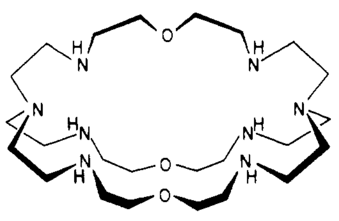
From a comparison of pH (−log [H^+]) profiles of various ratios of copper(II) to the cryptand BISTREN (7,19,30-trioxa-1,4,10,13,16,22,27,33-octaazabicyclo[11.11.11]pentatriacontane) measured in 0.100 M sodium perchlorate and sodium chloride media, the binding constants of the complexes of this macrobicyclic polyamine ligand were determined for chloride and hydroxide anions. The cagelike structure of the cryptand favors "cascade" type anion binding to coordinated metal ions or to a combination of a metal ion and protonated amino groups in the ligand. The suggested coordination scheme shows chloride or hydroxide ion bridging the Cu(II) ions in the binuclear cryptates. For the mononuclear structures it is suggested that these anions are coordinated to Cu(II) at one end of the cage and hydrogen bonded to symmetrically distributed protonated amino groups at the other end. Equilibrium constants of relevant reactions are reported and discussed.

Introduction

Recently it has been shown that the protonated forms of BISTREN, 7,19,30-trioxa-1,4,10,13,16,22,27,33-octaazabicyclo[11.11.11]pentatriacontane (1), form stable inclusion complexes with several anions.[1] Subsequent measurements by potentiometric methods[2] showed that anion complexes of considerable stability form between chloride and nitrate anions and hexaprotonated BISTREN, H_6L^{6+}, as well as with H_5L^{5+} and H_4L^{4+}. However, H_3L^{3+} and less protonated species showed much weaker binding. Furthermore, the cryptates containing metal ions were stabilized by coordination of μ-hydroxo groups and, in the case of Co(II), by the formation of (μ-hydroxo)(μ-peroxo)-bridged species.[2] On the basis of these observations, it was postulated that it should be possible to form stable metal cryptate species in solutions containing anionic ligands such as Cl^-, Br^-, I^-, F^-, etc., bound in a "cascade" fashion.[3] ("Cascade" is a term employed[3] to indicate a situation whereby a primary ligand binds one or more metal ions in such a way as to induce secondary binding between the metal ion(s) and other donor molecules or ions.) The determination of binding constants in aqueous solution had not been carried out, and there appears to be no precedent in the literature for the approach described in this paper, which consists of a potentiometric determination of the stability constants of the Cu(II)-BISTREN cryptate complexes in the presence of high concentrations of the anions under investigation. Because of the limitations on the availability of the cryptand BISTREN, the initial potentiometric study of this type of complex was carried out only for the copper(II)-BISTREN system in the presence of coordinating chloride and hydroxide ions.



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Experimental Section

Details of the potentiometric method have been described in a previous paper.

Both 1:1 and 2:1 molar ratios of Cu(II) to BISTREN hexahydroperchlorate were measured in both sodium perchlorate and in sodium chloride media. In each case 0.050 mmol of BISTREN was taken and the entire pH profile was determined experimentally with over 80 data points per run. Because of limitations in the supply of cryptand, the solution with perchlorate supporting electrolyte was quantitatively transformed to chloride medium by passing the final solution obtained after the potentiometric determinations in perchlorate through fine-mesh Dowex-1 (Sigma) anion-exchange resin in the chloride form and subsequent removal of Cu(II) by treatment with H_2S. The final volume was adjusted so that the final ionic strength was exactly 0.100 M, with KCl as supporting electrolyte.

Table I. Overall Stability Constants (log β Values) for the Cu-BISTREN System (μ = 0.100 M, t = 25.0 °C)

	log of overall stability const	
quotient[a]	perchlorate medium	chloride medium
[ML]/[M][L]	17.36	16.54
[M(OH)L][H]/[M][L]	6.92	6.17
[MHL]/[M][H][L]	25.50	24.98
$[MH_2L]/[M][H]^2[L]$	33.01	33.10
$[MH_3L]/[M][H]^3[L]$	38.36	40.09
$[M_2L]/[M]^2[L]$	27.32	29.05
$[M_2(OH)L][H^+]/[M]^2[L]$	25.07	23.63

[a] Charges omitted for clarity in equilibrium quotients; H = H^+, OH = OH^-, M = Cu^{2+}, H_3L = H_3L^{3+}, ML = CuL^{2+}, M(OH)L = $Cu(OH)L^+$, MHL = $CuHL^{3+}$, MH_2L = CuH_2L^{4+}, MH_3L = CuH_3L^{5+}, M_2L = Cu_2L^{4+}, $M_2(OH)L$ = $Cu_2(OH)L^{3+}$.

The computations were carried out with the Fortran program BEST[4] on the VAX-11/780 computer. In the preparation of the chloride medium solution, some material (~4.5%) was inevitably lost in the manipulations. The amount of the ligand lost, and the free protons present in these solutions, was determined by using the same computer program by iteration of the calculations with these quantities as variables.

Experiments were performed on 2,2′,2″-triaminotriethylamine (TREN) to investigate the extent of Cl^- binding to Cu^{2+} in the absence of the organic ligand. Since the computed equilibrium constants for both ClO_4^- and Cl^- media were identical with experimental error, it was concluded that the aquo Cu(II) ion is not bound sufficiently to Cl^- under our reaction conditions to affect the computation of the calculated constants for BISTREN.

Results

Two sets of macroscopic stability constants were determined for the interaction of the copper(II) ion with BISTREN. These are listed in Table I as computed from representative data shown in Figure 1. The large differences in the profiles of the Cl^- vs. ClO_4^- curves at low pH values and at pH values above 7 are reflected in the substantial differences in the equilibrium constants presented in Tables I and II.

The conventional formation constants have been computed for each medium and are tabulated in Table II, together with

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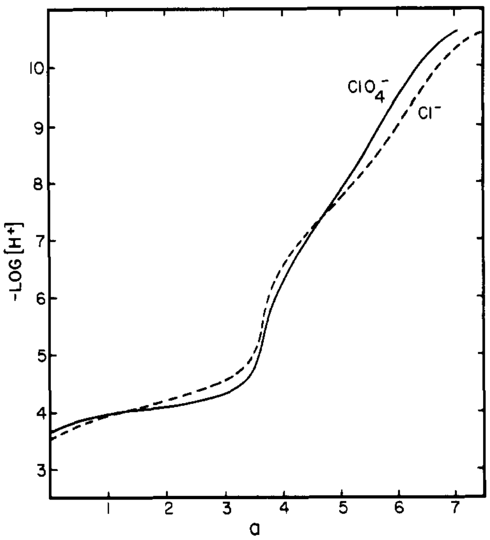


Figure 1. Comparison of the potentiometric curves for chloride and perchlorate BISTREN–Cu(II) 1:1 systems (a = mol of base/mol of ligand).

Table II. Logarithms of the Stability Constants for the Cu(II)-BISTREN Complexes ($\mu = 0.100$ M, $t = 25.0$ °C)

	log Q		
log quotient, Q	perchlorate medium	chloride medium	Δ-(log Q)[a]
$K_{ML} = [ML]/[M][L]$	17.36	16.54	0.82
$K^{-H}{}_{MOHL} = [MOHL][H^+]/[ML]$	−10.44	−10.38	0.06
$K^{H}{}_{MHL} = [MHL]/[ML][H]$	8.13	8.43	0.30
$K^{H}{}_{MH_2L} = [MH_2L]/[MHL][H^+]$	7.51	8.12	0.61
$K^{H}{}_{MH_3L} = [MH_3L]/[MH_2L][H^+]$	5.36	6.99	1.63
$K^{H}{}_{M_2L} = [M_2L]/[ML][M]$	9.96	12.51	2.55
$K^{-H}{}_{M_2(OH)L} = [M_2OHL][H^+]/[M_2L]$	−2.24	−5.43	−3.19

[a] $\Delta(\log Q) = \log Q_{Cl^-} - \log Q_{ClO_4^-}$.

the differences on going from one medium to the other. Equations 1–7 define the overall chemical equilibria that apply throughout the entire pH range studied for this system. (The formulas used in these equations are defined in the footnote of Table I.)

$$M + L \rightleftharpoons ML \quad (1)$$

$$ML \rightleftharpoons MLOH + H^+ \quad (2)$$

$$ML + H \rightleftharpoons MHL \quad (3)$$

$$MHL + H \rightleftharpoons MH_2L \quad (4)$$

$$MH_2L + H \rightleftharpoons MH_3L \quad (5)$$

$$ML + M \rightleftharpoons M_2L \quad (6)$$

$$M_2L \rightleftharpoons M_2(OH)L + H^+ \quad (7)$$

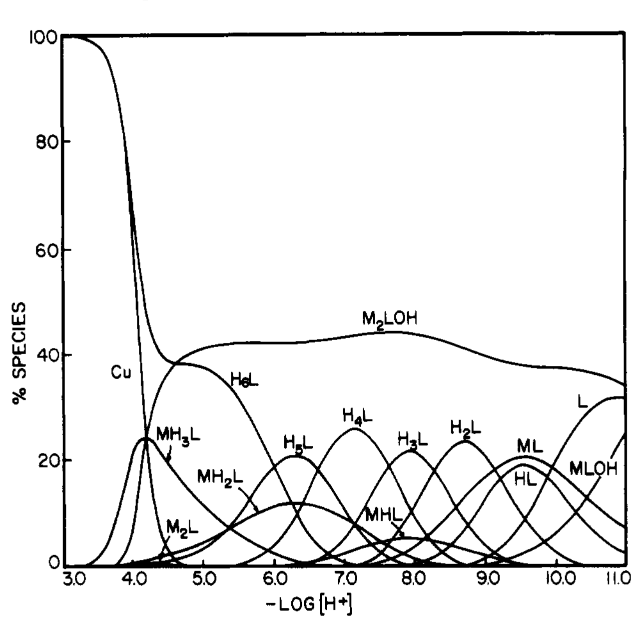


Figure 2. Macroscopic species distribution diagram for a 1:1 copper–BISTREN solution ($T_L = T_M = 0.00100$ M) as a function of $-\log [H^+]$ measured in 0.100 M $NaClO_4$.

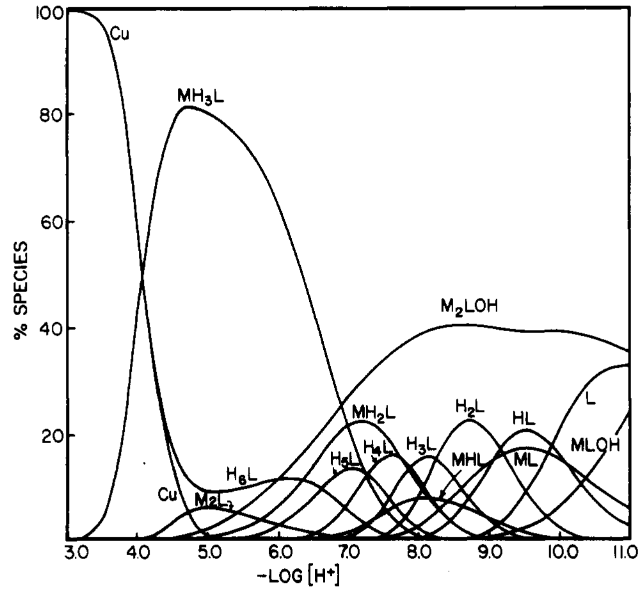


Figure 3. Macroscopic species distribution diagram for a 1:1 copper–BISTREN solution ($T_L = T_M = 0.00100$ M) as a function of $-\log [H^+]$ measured in 0.100 M chloride medium.

While some differences exist for all the cryptates studied, it is particularly noteworthy that the formation constants for M_2L, MH_3L, and M_2OHL differ by more than 1 full log unit between the two media. These differences in speciation can be better visualized by comparing the species distribution curves for the perchlorate (Figure 2) and chloride (Figure 3) media. Figure 2 (for a 1:1 molar ratio of metal ion to ligand) shows a maximum concentration of MH_3L at pH 4.2 of 25% in the perchlorate medium. However, when chloride is present, this value goes up dramatically to 81%, as seen from Figure 3. Furthermore this gain in stability is reflected in the repression of the formation of M_2OHL when going from perchlorate to chloride. Finally, is is seen that, in perchlorate (Figure 2), the M_2L species is essentially absent, while in chloride solution it forms to the extent of 6.5% at pH 4.8. The relative distributions of the 2:1 species are more dramatic in the species distribution curves of the system containing 2 mol of metal ion per ligand (not shown) but follow the same general pattern illustrated for the 1:1 systems. In addition, similar visual comparisons can be made on the basis of the data in Table II for the species whose formation constants show smaller differences on going from one medium to the other.

Cascade Anion Binding

Since perchlorate is probably not appreciably bound in hexaprotonated BISTREN[2] it is reasonable to assume that measurements in perchlorate reflect a situation whereby ClO_4^-

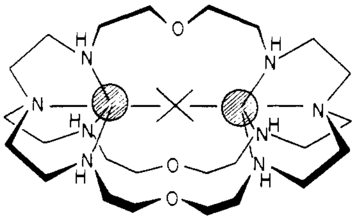
Table III. Anion Binding Constants for Polycationic Species of BISTREN ($\mu = 0.100$ M, $t = 25$ °C)

quotient,[a] Q	log Q	quotient, Q	log Q
$[M_2LCl]/[M_2L][Cl^-]$	3.55	$[M_2LOH]/[M_2L][OH]$	11.56
$[MH_3LCl^-]/[MH_3L][Cl^-]$	2.62	$[MLOH]/[ML][OH]$	3.36
$[MH_2LCl]/[MH_2L][Cl^-]$	1.48	$[H_6LCl]/[H_6L][Cl^-]$	2.36[2]
$[MHLCl]/[MHL][Cl^-]$	0	$[H_5LCl]/[H_5L][Cl]$	1.71[2]
		$[H_4LCl]/[H_4L][Cl^-]$	0.62[2]

[a] The chloro complexes reported here represent the minimum number of species needed to account for the potentiometric data. The binding constant of unity for the monoprotonated mononuclear complex, however, makes only a minor contribution.

binding does not occur to an appreciable extent with the metal complexes. Although it is quite possible that the perchlorate ion may be weakly bound inside the cryptand, for the purpose of this paper it is assumed that there is no such binding. In any case, because of its size, the perchlorate anion should form weaker inclusion complexes with metal cryptates than with protonated cryptands. The latter binding was assumed to be zero in the previous publication.[2] With respect to ClO_4^- binding, a rough estimate was given in footnote 18 of ref 1.

Thus, the M_2L formulation has two alternative interpretations depending on whether one considers reactions occurring in a ClO_4^- medium or Cl^- medium. The former is chosen as the reference state that involves an uncomplexed "ML" species. In the latter there is the assumption that a chloride inclusion complex forms, so that "M_2L" and "M_2LCl" species are both present. In the cascade chloro complex, the chloride ion is expected to be strongly coordinated between two closely spaced Cu(II) ions, which are held apart at a favorable distance by the basic nitrogen donors of the two TREN subunits of the cryptand, as represented schematically by structure **2**. The equilibrium relationships that apply to chloride indicate that



2, X = Cl⁻ or OH⁻

$$[M_2L]_T = [M_2L] + [M_2LCl] \qquad (8)$$

If one defines $K^{Cl} = [M_2LCl]/[M_2L][Cl^-]$, then eq 8 becomes

$$[M_2L]_T = [M_2L](1 + K^{Cl}[Cl^-]) \qquad (9)$$

Since neither M nor ML binds Cl^- to any appreciable extent under the experimental conditions employed, K^{Cl} may be calculated by eq 10.

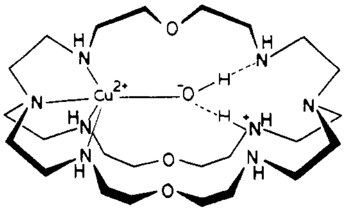
$$K^{Cl^-}{}_{M_2L}/K^{ClO_4^-}{}_{M_2L} = 1 + K^{Cl}[Cl^-] \qquad (10)$$

Table III lists the relevant *Cl^- binding constants* obtained from the application of this approach, as represented by eq 10 and the above discussion, to the binuclear and to the protonated mononuclear species formed in these systems. The analogous hydroxo constants are also presented. From the data in Table III, it appears that the bis(dicationic) cavity of Cu_2L^{4+} has an unusually large formation constant ($10^{3.55}$) for the coordination of Cl^- to form the Cu_2LCl^{3+} species. The strength of the chloride interaction is somewhat lower for the pentapositive species CuH_3L^{5+} by a factor of 10, even though the charge is higher, probably because of the larger size of the cavity and the fact that the hydrogen bonds involving the Cl^- ion are generally relatively weak. Apparently the fit of the Cl^- ion between the two Cu(II) ions and the known affinity between Cl^- and Cu^{2+} favor stronger bonding. Although MH_2L^{4+} has the same charge as M_2L^{4+}, the change in cavity size, as well as other electrostatic interactions of the secondary ammonium groups, results in somewhat lower affitnity for the bridging chloride ion. The binding constant for $CuHLCl^{2+}$ calculated for this system is approximately unity (log $K \sim 0$), indicating relatively very weak binding. For comparison, the chloro complexes of the penta- and tetraprotonated forms of the cryptand ligand are also listed. It seems that the binding strengths of the chloro complexes are increased by substitution of the Cu(II) ion in place of the coordinated protons.

The relatively strong binding of the chloride ion in the binuclear and mononuclear Cu(II) cryptates may be considered to be due in large measure to the contributions of Cu(II)–Cl^- coordinate bonds. In the case of the protonated metal-free chloride complexes of BISTREN,[2] binding of chloride was found to be relatively weak, with a maximum value of $\sim 10^3$ for the hexaprotonated form of the ligand. In fact, the binding constant of chloride to the hexaprotonated ligand was found to be a factor of 5 lower than that of nitrate, which is itself an extremely weak coordinating anion when it is a free ion in aqueous solution.

The *binding of the hydroxo group* to the bimetallic center of the M_2L chelate is considerably larger at $10^{11.56}$ than that of the chloride ion, probably an indication of much stronger coordinate bonding and perhaps more favorable steric factors for hydroxide binding. The exceptionally high affinity for hydroxide ion is further indicated by the fact that almost the entire distribution curve (Figure 2) is dominated by this species in perchlorate and above pH 7 in chloride media. It is possible that additional bonding to an ether oxygen assists in the stabilization of the hydroxo complex. The logarithm of the chloride binding constant of the binuclear Cu(II) cryptate is ~ 3.5 units higher than that of the free aquo ion, and log $K \sim 5.3$ log units higher for the binuclear cryptate than for the free aquo Cu(II) ion,[5] indicating an increment of over 2 log units that may be due to a better fit of the hydroxide ion, as suggested above. This question warrants further investigation.

The unusual stability of the binuclear hydroxo complex may be appreciated by comparison with the hydroxo binding constant of the mononuclear cryptate ML^{2+}, $10^{3.36}$, which is 8 orders of magnitude lower. The latter value is below normal, as it is almost 10^3 smaller than the aquo Cu(II) ion hydroxylation constant at $10^{6.5}$.[5] In this case there may be an "inverse" cryptate effect that inhibits the hydrolysis of the mononuclear chelate. This effect may be explained in terms of formation of a more stable hydroxo complex of the monoprotonated mononuclear cryptate complex, $CuHL^{3+}$, illustrated by **3**. The totally deprotonated hydroxo mononuclear chelate would be expected to be considerably less stable. Complex **3** is of course indistinguishable from the aquo species with respect to thermodynamic acid–base measurements.



3, $Cu^{2+}\cdot H_2O$ or $Cu(OH)HL^{2+}$

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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 ($\epsilon = 6\text{-}10 \times 10^3$ 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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