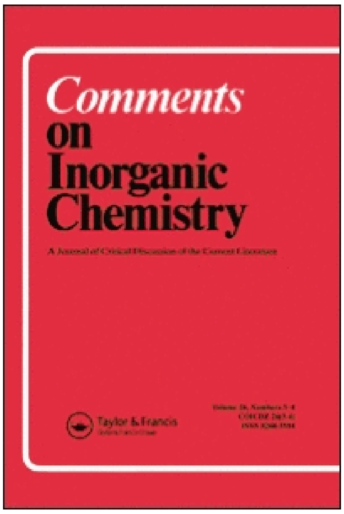

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Cooperative Metal Ion Stabilities Induced by a Reduction in Coordination Number

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Cooperative Metal Ion Stabilities Induced by a Reduction in Coordination Number

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Inversions of the usual stability constant order in which a subsequent ligand binds more strongly than a former one are described in a model in which the coordination number of the metal ion decreases. Decreasing the coordination number shortens and strengthens the metal-ligand bond. Inversions of the usual bonding order are often termed cooperative, and the model is patterned after the allosteric model used to describe cooperative oxygen binding in hemoglobin. The model is developed and applied to examples that include Al(III), Ni(II), Zn(II), Cu(I), Ag(I), and Hg(II).

Key Words: *complexes, cooperativity, coordination, metal ions, zinc*

1. INTRODUCTION

After binding the first ammonia molecule, a silver ion binds the second ammonia molecule more strongly than the first (log $K_1 = 3.2$, log $K_2 = 3.8$).[1] This inversion of the usual stability order is often termed a cooperative interaction, and it occurs in a remarkably simple system. The usual way to account for the inversion is to postulate a decrease in coordination

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number upon ligand binding. With a lesser number of ligands, metal ion to ligand bond lengths shorten, and binding becomes stronger. The suggestion of reduction in coordination number to account for augmented binding has been made many times. The allosteric treatment of Wyman, developed to describe cooperativity in protein systems such as hemoglobin,[2] offers a fruitful quantitative approach to analyzing cooperativity in metal ion systems. As with the protein systems, which are commonly treated as existing in two major conformations, we set up two channels, one for each of two coordination numbers and geometries being considered. As ligation proceeds in cooperative systems, there is a switch from the higher to the lower coordination number. This paper develops the procedure and analyzes the results for several metal ion systems that exhibit varying degrees of cooperativity. Our setup is directed toward coordination chemistry and uses a different formulation than Wyman.

The first application of the Wyman allosteric formalism to metal ion complexes was made by King.[3] His treatment is limited to two cases and is less general, he handles interaction factors in a more complicated way, and he uses a more approximate means to estimate the parameters, but he reaches some similar conclusions.

2. A SIMPLE 2 → 1 CASE

In order to gain a qualitative sense of the arguments, it is instructive to discuss the simplest case. Consider a 2 → 1 system that consists of a metal ion with two or one free coordination positions. An example is the nitrilotriacetate(NTA) complex of aluminum. Chelation of the quadridentate ligand leaves two water molecules on the hexacoordinate metal ion. The (NTA)Al$(H_2O)_2$ complex appears in a crystal structure.[4]

Two deprotonations occur from the (NTA)Al complex, the first with $pK_1 = 5.1$ and the second with $pK_2 = 8.3$ at 25°C and 0.2 M ionic strength.[5] A second study performed at 0.6 M ionic strength confirms these values.[6] The $pK_1 = 5.1$ value for water deprotonation from the complex is actually more acidic than $pK_1 = 5.5$ for deprotonation of the first water molecule in hexaaquo $Al(H_2O)_6^{3+}$.[7] We ascribe this increase in acidity in the NTA complex to a decrease in coordination number upon deprotonation.[8]

Let us consider the NTA bound Al^{3+} to be a unit and designate the hexacoordinate species with two bound waters as ^6M. Successive deprotonations from the hexacoordinate complex yields ${}^6ML$ and ${}^6ML_2$, where $L = OH^-$. Additionally, designate five-coordinate species with one bound water as ${}^5M$ and with one bound hydroxide as ${}^5ML$. These species are related as in Scheme 1, with the arrowheads indicating the direction of the equilibrium constants.

To be general, we consider addition of ligand, such as OH^-, at molar concentration [L] to define the intrinsic stability constants k_1 and k_2 according to

$$k_1 = [{}^5ML] / [{}^5M]\,[L], \quad 2k_2 = [{}^6ML] / [{}^6M]\,[L]$$

where the 2 is a statistical factor that allows for two sites for the first ligand. Binding of the second ligand molecule to ${}^6ML$ to give ${}^6ML_2$ is described by

$$k_2 f_2 / 2 = [{}^6ML_2] / [{}^6ML]\,[L]$$

where the 2 is a statistical factor that allows for two possible departing ligands in the reverse reaction, and f_2 is an interaction factor that allows for steric, electrostatic, and other non-statistical effects. If $f_2 = 1$ the binding is statistical; normally $f_2 < 1$ in metal ion complexes.

There are two channels: one that is six-coordinate and one that is five-coordinate. If there were only the six-coordinate channel, the first stability constant would be given by ${}^6K_1 = 2k_2$ and the second by ${}^6K_2 = k_2 f_2/2$. For the five-coordinate channel ${}^5K_1 = k_1$. The two channels are connected by the "isomeric" equilibrium constants designated by $I_0 = [{}^5M]/[{}^6M]$ and $I_1 = [{}^5ML]/[{}^6ML]$. (Species related by the isomeric equilibrium constants are not strictly isomers as they differ in the number of bound water molecules. However, they contain the same composition of ligands other than water and would appear as isomers in the way complexes are nor-

$$\begin{tikzcd}
{}^6M \arrow[r, "2k_2"] \arrow[d, "I_0"'] & {}^6ML \arrow[r, "k_2 f_2/2"] \arrow[d, "I_1"] & {}^6ML_2 \\
{}^5M \arrow[r, "k_1"] & {}^5ML_2 &
\end{tikzcd}$$

SCHEME 1

mally written.) There are thus five unknowns, the intrinsic equilibrium constants k_1 and k_2, the interaction constant f_2, and the isomeric equilibrium constants I_0 and I_1. Owing to the cyclic system, only four of these unknown constants are independent.

The stability constants determined by experiment are given by

$$K_1 = \frac{[^6\text{ML}] + [^5\text{ML}]}{([^6\text{M}] + [^5\text{M}])[\text{L}]} = \frac{1 + I_1}{1 + I_0} 2k_2 \,, \tag{1}$$

$$K_2 = \frac{[^6\text{ML}_2]}{([^6\text{ML}] + [^5\text{ML}])[\text{L}]} = \frac{1}{1 + I_1} k_2 f_2 / 2 \,. \tag{2}$$

With the last equalities in Eqs. (1) and (2), the product of the two experimental constants eliminates I_1,

$$K_1 K_2 = \frac{k_2{}^2 f_2}{1 + I_0} \tag{3}$$

while their ratio cancels the intrinsic constant k_6.

$$\frac{K_1}{K_2} = 4\frac{(1 + I_1)^2}{(1 + I_0) f_2} \tag{4}$$

These equations prove useful in analysis of systems.

Since the $(\text{NTA})\text{Al}(\text{H}_2\text{O})_2$ complex appears in a crystal structure,[4] this hexacoordinate form presumably predominates in solution, and $I_0 \ll 1$. With this simplification Eq. (4) becomes

$$1600 = \frac{10^{-5.1}}{10^{-8.3}} = \frac{K_1}{K_2} \simeq 4\frac{(1 + I_1)^2}{f_2}$$

If we take $f_2 = 0.2$ for a negatively charged ligand in a hexacoordinate complex (see Section 4), we find that $I_1 = 8$ for the molar ratio of pentacoordinate to hexacoordinate ML complexes. The observed acidified $\text{p}K_1 = 5.1$ value in the complex occurs because the reduction in coordination number upon the first deprotonation yields 8 times as much of the monohydroxo species ^{5}ML than ^{6}ML. Instead of $^6\text{M} \to {}^6\text{ML} \to {}^6\text{ML}_2$, the main deprotonation pathway becomes $^6\text{M} \to {}^5\text{ML} \to {}^6\text{ML}_2$.

The second equilibrium constant then refers to addition of OH^- to pentacoordinate ^5ML.

More insights may be gained by rewriting Eq. (1) as

$$K_1 = \frac{2k_2 + k_1 I_0}{1 + I_0} = \frac{^6K_1 + {}^5K_1 I_0}{1 + I_0}.$$

The first stability constants for each channel are weighted in the experimentally determined K_1 by the ratio $I_0 = [^5M]/[^6M]$. Because the lower coordination number confers a greater stability, we have $k_1 > k_2$ (or $pk_1 < pk_2$). With the results of the previous paragraph for the (NTA)Al complex, from Eqs 1, 2, and 3 we calculate that $pk_2 = 6.3$. From the cycle we know the product $k_1 I_0 = 2k_2 I_1 = 10^{-5.1}$. If $I_0 = 0.1$, we find $pk_1 = 4.1$. Thus the reduction in coordination number acidifies the water molecule by more than two log units, from $pk_2 = 6.3$ to $pk_1 = 4.1$. That $pk_1 \sim 4.1$ is reasonable, though 1.4 log units more acidic than hexaaquo $Al(H_2O)_6^{3+}$ is supported by reports from two separate groups[9,10] of $pK_1 = 4.2$ from the 2:1 picolinate (2-pyridinecarboxylate) complex of Al^{3+}. (It is possible in the picolinate case that ^5M predominates over ^6M, so that the hill of an unfavorable I_0 need not be climbed, and $pK_1 \sim pk_1$.)

Augmented stabilities and cooperativity occur in other Al(III) systems, and it has been suggested that they be accounted for by a reduction in coordination number.[8] Similar to the NTA complex, the complex of EDTA exhibits $pK_1 = 6.0$ and $pK_2 = 10.4$,[5] and a similar interpretation is suggested, but the coordination numbers are less certain. Four successive deprotonations from aqueous Al^{3+} to form $Al(OH)_4^-$ occur over a short span of only 0.7 log units while the four deprotonations from Fe^{3+} span a more normal 6.6 log units.[11] This comparison indicates high cooperativity in aqueous Al^{3+} hydrolysis and is treated below in Section 5. Augmented stabilities and cooperativity should be viewed as a general feature of Al^{3+} complexes.

3. GENERAL DESCRIPTION

It is convenient to generalize and apply the binding polynomial technique pioneered by Wyman[2] to the description of coordination chemistry. There are two kinds of binding polynomials. The experimental results of a stability constant determination are fully described by the following *experimental* binding polynomials with x referring to the molar concentration of free, basic ligand, the subscript on Q to the maximum coordination number, and the subscript on K to the successive stability constants. We also use $\beta_i = K_1K_2 \ldots K_i$.

$$\begin{aligned}
Q_1 &= 1 + K_1x, \\
Q_2 &= 1 + K_1x + K_1K_2x^2, \\
Q_3 &= 1 + K_1x + K_1K_2x^2 + K_1K_2K_3x^3, \\
Q_4 &= 1 + K_1x + K_1K_2x^2 + K_1K_2K_3x^3 + K_1K_2K_3K_4x^4, \\
Q_5 &= 1 + K_1x + \beta_2x^2 + \beta_3x^3 + \beta_4x^4 + \beta_5x^5, \\
Q_6 &= 1 + K_1x + \beta_2x^2 + \beta_3x^3 + \beta_4x^4 + \beta_5x^5 + \beta_6x^6.
\end{aligned}$$

In the literature, experimental results are usually reported as stability constants. Some references, especially the older literature, also list the average number of ligands bound per metal ion, υ, as a function of the free ligand concentration, x. The relation between υ and the experimental binding polynomial is given in Ref. 2.

$$\upsilon = \frac{x\,(dQ/dx)}{Q}. \tag{5}$$

We use Eq. (5) in several ways. When the υ versus x data are tabulated, we recalculate the stability constants by a non-linear least squares procedure[12] which gives objective and superior values with error limits. (A fractional uncertainty is taken in υ.) Since the recalculated values are derived from the same literature data but are analyzed by a more sophisticated and objective procedure, they represent a better interpretation of the data. In cases where the successive stability constants decrease in the usual manner, there is little difference between recalculated and literature values. Literature values of Cu^{2+} complexes of 4-methylimidazole[13] fall within one standard deviation of recalculated values. For imidazole complexes, the differences between recalculated and literature values for Cu^{2+} complexes are much less than those of Zn^{2+}.

On the other hand, in cases of significant cooperativity, as for zinc complexes, it is difficult to determine reliable stability constants by other than a computer driven procedure. The first four rows of Table I show results for recalculation of literature data for formation of $Zn(NH_3)_4^{2+}$

TABLE I

Parameters for Complexes of Unidentate Ligands Undergoing a 6 → 4 Transition.

	$Zn(NH_3)_4^{2+}$	Zn(4-Methyl-imidazole)$_4^{2+}$	$Zn(CN)_4^{2-}$	$Al(OH)_4^-$	$Ni(CN)_4^{2-}$
log K_1[a]	2.38(8)[b]	2.47(2)[c]	5.21(6)[d]	5.5[e]	6.6(4)[f]
log K_2	2.46(14)	2.35(13)	5.83(8)	5.8	6.6
log K_3	2.46(11)	2.75(18)	5.58(4)	6.0	9.3
log K_4	2.18(5)	2.38(12)	4.88(2)	6.2	8.5(5)
f_4	0.80(fix)	0.84	0.53	0.40(fix)	0.40(fix)
log k_6	1.55	1.66	4.20	6.2	5.8
log k_4	3.05	3.22	6.31	4.7	10.3
I_0	0.0084	0.0034	0.0082	0.0033	2×10^{-8}
I_1	0.18	0.084	0.70	0.08	3×10^{-4}
I_2	4.5	2.5	140	3.6	11
I_3	130	91	6×10^4	270	7×10^5
I_4	3200	3000	5×10^7	2.6×10^4	5×10^{10}

[a] References for the four experimental stability constants.

[b] Recalculated by non-linear least squares (one standard deviation in last digits in parentheses) from published data (last point omitted) in 2 M NH_4NO_3 at 30°C.[15] The published stability constant logs are 2.37, 2.44, 2.50, and 2.15.[1,15]

[c] Recalculated by non-linear least squares (one standard deviation in last digits in parentheses) from published data at 0.16 M ionic strength and 27°C.[13] The published stability constant logs are 2.43, 2.51, 2.62, and 2.35.

[d] Recalculated by non-linear least squares (one standard deviation in last digits in parentheses) from published data for 128 points in 3 M $NaClO_4$ at 25°C.[29] The published stability constant logs are 5.34, 5.68, 5.66, and 4.89.

[e] pK_a values from Ref. 11.

[f] Recalculated by non-linear least squares (one standard deviation in last digits in parentheses) from published data for 53 points in 3 M $NaClO_4$ at 25°C.[20] The recalculation gives log $\beta_1 = 6.6(4)$, log β_2 indeterminate, log $\beta_3 = 22.5(5)$, and log $\beta_4 = 30.96(4)$. The published values are log $\beta_1 = 7.0(2)$, log $\beta_2 < 14.0$, log $\beta_3 < 22.0$, and log $\beta_4 = 31.06(3)$. Stability constants in the table deduced from fitting and model of text.

and Zn(4-methylimidazole)$_4^{2+}$ complexes in the second and third columns, respectively. Rather than decreasing, the successive stability constants exhibit comparable values. Owing to the cooperativity and low amounts of intermediate complexes, there are relatively large standard deviations in log K_2 and log K_3. The recalculated values may be compared with the original values given in the footnotes. For Zn^{2+} complexes, there is often little difference between the recalculated and literature sum of log K_2 + log K_3 but a significant difference in the resolved values. Augmented stabilities require precise data for successful refinement by non-linear least squares. In terms of the intrinsic stability constants and interaction factors, the sub-binding polynomials or *intrinsic* binding polynomials may be written as follows with the subscript referring to the coordination number.

$$
\begin{aligned}
P_1 &= 1 + k_1 x,\\
P_2 &= 1 + 2k_2 x + f_2 k_2^2 x^2,\\
P_3 &= 1 + 3k_3 x + 3f_3 k_3^2 x^2 + f_3^3 k_3^3 x^3,\\
P_4 &= 1 + 4k_4 x + 6f_4 k_4^2 x^2 + 4f_4^3 k_4^3 x^3 + f_4^6 k_4^4 x^4,\\
P_5 &= 1 + 5k_5 x + 10 f_5 k_5^2 x^2 + 10 f_5^3 k_5^3 x^3 + 5 f_5^6 k_5^4 x^4 + f_5^{10} k_5^5 x^5,\\
P_6 &= 1 + 6k_6 x + 15 f_6 k_6^2 x^2 + 20 f_6^3 k_6^3 x^3
\end{aligned}
$$

The numerical coefficients are those of Pascal's triangle. For a four-coordinate system, for example, the addition of successive ligands proceeds through $^4M \rightarrow {}^4ML_1 \rightarrow {}^4ML_2 \rightarrow {}^4ML_3 \rightarrow {}^4ML_4$ with successive stability constants $K_1 = 4k_4 = [^4ML_1]/[^4M]x$, $K_2 = 3k_4f_4/2 = [^4ML_2]/[^4ML_1]x$, $K_3 = 2k_4f_4^2/3 = [^4ML_3]/[^4ML_2]x$, and $K_4 = k_4f_4^3/4 = [^4ML_4]/[^4ML_3]x$, where k_4 is the intrinsic stability constant and f_4 an interaction factor. To fully define the system with four unknowns requires, in addition to the intrinsic equilibrium constant k_4, three interaction factors. In modeling a tetrahedral system, one hopes that the three factors are similar enough so that a single value applies to all three. The single interaction factor in P_4 is equivalent to that given sixty years ago for a tetrahedral model of oxygen binding to hemoglobin.[14] If the interaction factor $f = 1$, the sites are independent, and the binding polynomial is factorable; e.g., $P_4 = (1 + k_4x)^4$. For metal ion complexes interaction factors are less than unity. In Wyman's treatment of allosterism, interaction factors greater than unity indicate cooperativity. For metal ion systems we handle cooperativity by the interaction between two parallel channels, one for each of two coordination numbers.

The procedure for developing a case combines the binding polynomials containing intrinsic constants according to the following sample prescription, where I_0 is the equilibrium constant between aquo ions with the ion of lesser coordination number in the numerator. To reproduce the 2 → 1 case that opened this paper we write

$$P_{21} = \frac{P_2 + P_1 I_0}{1 + I_0}.$$

Substitution of the corresponding P_2 and P_1 polynomials and rearrangement yields

$$P_{21} = 1 + \frac{2k_2 + k_1 I_0}{1 + I_0} x + \frac{k_2{}^2 f_2}{1 + I_0} x^2 .$$

From the cyclic system we have $2k_2 I_1 = k_1 I_0$. Comparison of coefficients with the experimental Q_2 polynomial yields the same set of two equations (1) and (2).

For the general m → n case we have

$$P_{mn} = \frac{P_m + P_n I_0}{1 + I_0} . \tag{6}$$

Comparison of the coefficients of the P_{mn} expression with the Q_m polynomial yields results analogous to Eqs. (1) and (2) in the cases below.

4. INTERACTION FACTORS

Interaction factors allow for reduction of second and subsequent ligand stabilities due to steric, electrostatic, and other non-statistical effects. In 2, 3, and tetrahedral systems a single interaction factor should apply to each case. In planar and 5 and 6 coordinate systems, geometric features imply that more than one interaction factor is needed in principle in each case. However, in practice only a single factor is often resolvable and is usually sufficient.

In the case of a hexacoordinate complex with a unidentate ligand, the successive stability constants expected statistically and expressed in terms of the intrinsic constant k_6 are: ${}^6K_1 = 6k_6$, ${}^6K_2 = 5k_6/2$, ${}^6K_3 = 4k_6/3$, ${}^6K_4 = 3k_6/4$, ${}^6K_5 = 2k_6/5$, and ${}^6K_6 = k_6/6$. The ratios ${}^6K_i/{}^6K_{i+1}$ expected statistically are $K_1/K_2 = 12/5 = K_5/K_6$, $K_2/K_3 = 15/8 = K_4/K_5$, and $K_3/K_4 = 16/9$. Only a few examples exist with sufficient regularity and precision that enable a test of the single interaction factor formulation.

For the case of the addition of up to six ammonia ligands to aqueous Ni^{2+}, recalculation by non-linear least squares yields the six successive log ${}^6K_i$ values: 2.79(3), 2.26(1), 1.69(2), 1.25(3), 0.71(3), and 0.05(4). (They differ only marginally from the original values obtained in 2 M NH_4NO_3 at 30°C of 2.80, 2.24, 1.73, 1.19, 0.75 and 0.03 from the classic thesis.[15]) The recalculated constants yield for the ${}^6K_i/{}^6K_{i+1}$ ratios an average deviation from the statistically expected ratios of 0.24 ± 0.07 log units. Thus a single interaction factor of $f_6 = 0.58$ describes the addition of all six ammonia molecules to within 0.1 log units in the stability constants. We may improve on this estimate by using the literature[15] tabulation of υ versus x for 14 points from $0.2 < \upsilon < 5.4$ and Eq. 5 with the P_6 polynomial to find the non-linear least squares fit of $f_6 = 0.597(5)$ with the intrinsic $\log k_6 = 2.027(5)$. (The standard deviation of the last digit in the value is given in parentheses.)

We now construct two categories of interaction factors. Since it is only in formation of a 2:1 complex that a trans interaction is possible, we assign a f_t factor to this situation and f_c to all others. Thus a f_t term appears in each term of a P polynomial that contains an interaction factor. (Note that the increasing powers of the interaction factors in the P polynomial allow for multiple (cis) interactions.) We anticipate that $f_t > f_c$.

For the case of Ni^{2+} and NH_3 we use non-linear least squares analysis of the 14 points to find $\log k_6 = 2.007(4)$, $f_{6t} = 0.72(2)$, and $f_{6c} = 0.600(3)$. Thus the two interaction factor formulation provides only a marginal improvement over the one interaction factor formulation with $f_6 = 0.60$.

For a negatively charged ligand we expect a greater interaction and hence a lesser interaction factor, and perhaps the need for the two interaction factor formulation. We examine the system of Al^{3+} plus fluoride ion.[16] Recalculation by non-linear least squares for 16 points of v versus pF results collected from $\upsilon = 0.5$ to 3.3 in 0.53 M KNO_3[17] yield $\log K_1 = 6.16(1)$, $\log K_2 = 5.04(2)$, $\log K_3 = 3.88(3)$, and $\log K_4 = 2.74(4)$. Recalculation of 19 points obtained in 0.53 M NH_4NO_3 from $\upsilon = 2.2$ to 4.7 yields $\log K_2 = 4.69(8)$, $\log K_3 = 3.80(3)$, $\log K_4 = 2.57(3)$, $\log K_5 = 1.48(5)$, and $\log K_6 = 0.5(2)$. The estimates of the original authors[17] agree better with the non-linear least squares analysis than does a proposed set of alternative values based on the same data.[18] Owing to an activity coefficient difference in solutions of the two different inert salts, the formation curves for the two kinds of solutions do not superimpose but are nearly parallel.[17] In order to convert all the values to 0.53 M KNO_3, we have taken the K_1, K_2, and K_3 values from that solution as fixed, and combined them with the points from the NH_4NO_3 solution with an adjustable parameter to be added to each v value at a given pF. The non-linear least squares results now applicable to 0.53 M KNO_3 are $\log K_4 = 2.76(4)$, $\log K_5 = 1.59(4)$, and $\Delta v = 0.130(15)$. The $\log K_4$ value falls well within one standard deviation of that at the top of the paragraph for the same salt solution. Thus the set of successive stability constant logs applicable to 0.53 M KNO_3 is 6.16, 5.04, 3.88, 2.75, 1.59, with log K_6 too uncertain to specify (highest $\upsilon = 4.7$). We now test the stability constants applicable to 0.53 M KNO_3 for the minimum number of interaction factors required in a P_6 type polynomial.

All 35 points in the Al^{3+}–F^- system were merged into one KNO_3 set by adding 0.13 to each of the 19 υ values tallied in NH_4NO_3. The non-linear least squares analysis of the P_6 polynomial with two interaction factors gives the intrinsic log $k_6 = 5.39(1)$, $f_{6t} = 0.18(1)$, and $f_{6c} = 0.147(1)$. Even for a negatively charged ligand, the two interaction factors are scarcely resolvable. The 35 points are well-fitted by a single interaction factor with log $k_6 = 5.41(1)$ and $f_6 = 0.145(1)$. Thus, even for a negatively charged ligand, the single interaction factor formulation provides a good description of the addition of successive ligands to the system. Since Al^{3+} is a small metal ion, slightly larger interaction factors may apply to other metal ions and we use $f_6 = 0.20$ for a singly negatively charged ligand in a hexacoordinate complex. In this paper we use the one interaction factor formulation except for the 3 → 2 chelate case described below where two interaction factors prove necessary.

Consistent with the above analysis, the following set of interaction factors are used in this paper for 1, 2, 3, 4, 5, and 6 fold coordination, respectively: For neutral ligands, 1.00, 0.95, 0.90, 0.80, 0.70, and 0.60, and for singly, negatively charged ligands, 1.00, 0.80, 0.60, 0.40, 0.30, and 0.20.

5. THE 6 → 4 CASE: $Zn(NH_3)_4^{2+}$, Zn(IMIDAZOLE)$_4^{2+}$, $Zn(CN)_4^{2-}$, $Al(OH)_4^-$, AND $Ni(CN)_4^{2-}$

Many zinc complexes exhibit stronger than expected successive stability constants: for example, the $Zn(NH_3)_4^{2+}$ complex where the successive stability constant logarithms are 2.38, 2.46, 2.46, and 2.18 (Table I). The second stability constant is greater than the first, and the third is as great as the second. Table I shows an even more pronounced cooperativity with $Zn(CN)_4^{2-}$. This strengthening as ligands are added is attributed to a reduction in coordination number from six for the aquo ion to four for the final complex. We need to develop the equations for the 6 → 4 case.

Scheme 2 shows the set up for the 6 → 4 case for unidentate ligands. Across the top are representations of the six equilibria for substitution of

$$\begin{tikzcd}
{}^6\mathrm{M} \arrow[r, "6k_6"] \arrow[d, swap, "I_0"] & {}^6\mathrm{ML} \arrow[r, "5k_6f_6/2"] \arrow[d, swap, "I_1"] & {}^6\mathrm{ML}_2 \arrow[r, "4k_6f_6^{2/3}"] \arrow[d, swap, "I_2"] & {}^6\mathrm{ML}_3 \arrow[r, "3k_6f_6^{3/4}"] \arrow[d, swap, "I_3"] & {}^6\mathrm{ML}_4 \arrow[r, "2k_6f_6^{4/5}"] \arrow[d, swap, "I_4"] & {}^6\mathrm{ML}_5 \arrow[r, "k_6f_6^{5/6}"] & {}^6\mathrm{ML}_6 \\
{}^4\mathrm{M} \arrow[r, "4k_4"] & {}^4\mathrm{ML} \arrow[r, "3k_4f_4/2"] & {}^4\mathrm{ML}_2 \arrow[r, "2k_4f_4^{2/3}"] & {}^4\mathrm{ML}_3 \arrow[r, "k_4f_4^{3/4}"] & {}^4\mathrm{ML}_4 & &
\end{tikzcd}$$

SCHEME 2

six ligands in a hexacoordinate complex from the aqueous hexacoordinate metal ion, ^{6}M, to the metal ion with six unidentate ligands, ${}^6\mathrm{ML}_6$. The six successive stability constants are described in terms of an intrinsic binding constant, k_6, and a single interaction factor, f_6. Across the bottom of Scheme 2 are representations for the four equilibria for tetrahedral complexes from the aqueous tetrahedral metal ion, ^{4}M, to the metal ion with four unidentate ligands, ${}^4\mathrm{ML}_4$. The four successive stability constants are characterized by an intrinsic binding constant, k_4, and a single interaction factor f_4. The two channels across the top and bottom of Scheme 2 are linked by the five isomeric equilibrium constants I_0 to I_4. There are nine unknowns, two intrinsic equilibrium constants (k_6 and k_4), two interaction factors (f_6 and f_4), and five isomeric equilibrium constants. Owing to the four cycles in the system, only five of the nine unknowns are independent so that with four known equilibrium constants we need specify only one interaction factor in order to solve for the other four parameters. Since the results are less sensitive to it, we assign only the value of f_6 as 0.60 for neutral ligands and 0.20 for singly, negatively charged ligands.

In terms of the representation in Scheme 2 the four stability constants determined by experiment may be written as follows:

$$K_1 = \frac{[{}^6\mathrm{ML}] + [{}^4\mathrm{ML}]}{([{}^6\mathrm{M}] + [{}^4\mathrm{M}])[\mathrm{L}]} = \frac{1 + I_1}{1 + I_0} 6k_6, \tag{7}$$

$$K_2 = \frac{[{}^6\mathrm{ML}_2] + [{}^4\mathrm{ML}_2]}{([{}^6\mathrm{ML}] + [{}^4\mathrm{ML}])[\mathrm{L}]} = \frac{1 + I_2}{1 + I_1} \frac{5k_6f_6}{2}, \tag{8}$$

$$K_3 = \frac{[{}^6\mathrm{ML}_3] + [{}^4\mathrm{ML}_3]}{([{}^6\mathrm{ML}_2] + [{}^4\mathrm{ML}_2])[\mathrm{L}]} = \frac{1 + I_3}{1 + I_2} \frac{4k_6f_6^2}{3}, \tag{9}$$

$$K_4 = \frac{[{}^6\mathrm{ML}_4] + [{}^4\mathrm{ML}_4]}{([{}^6\mathrm{ML}_3] + [{}^4\mathrm{ML}_3])[\mathrm{L}]} = \frac{1 + I_4}{1 + I_3} \frac{3k_6f_6^3}{4}. \tag{10}$$

The cycles in Scheme 2 allow the successive isomeric constants to be expressed in terms of I_0.

$$\begin{aligned}
&I_0 = [^4\mathrm{M}]/[^6\mathrm{M}], \quad I_1 = [^4\mathrm{ML}]/[^6\mathrm{ML}] = 2k_4I_0/3k_6,\\
&I_2 = [^4\mathrm{ML}_2]/[^6\mathrm{ML}_2] = 3k_4f_4I_1/5k_6f_6,\\
&I_3 = [^4\mathrm{ML}_3]/[^6\mathrm{ML}_3] = 2k_4f_4^2I_2/4k_6f_6^2,\\
&I_4 = [^4\mathrm{ML}_4]/[^6\mathrm{ML}_4] = k_4f_4^3I_3/3k_6f_6^3.
\end{aligned} \tag{11}$$

A non-linear least squares analysis was used to obtain the best fit of log k_6, log k_4, f_4, and I_0 to the four experimental stability constant logarithms. Table I shows the results.

The first four rows in Table I list experimental stability constants from which the other parameters were derived, either by an iterative procedure or non-linear least squares fitting of the stability constant logarithms. The interaction coefficient f_4 was sometimes fixed and sometimes treated as an adjustable parameter. Values of the three independent unknowns k_6, k_4, and I_0 were then adjusted to yield a best fit to the four experimental stability constants. The four remaining isomeric equilibrium constants I_1 to I_4 are then derived by Eq. (11). As expected, the intrinsic equilibrium constant k_4 in the 7th row of Table I is greater than that of k_6 in the 6th row.

The dimensionless isomeric equilibrium constants represent the molar ratio of lower to higher coordinate species bearing the number of ligands indicated by the subscript ($I_i = [^4\mathrm{ML}_i]/[^6\mathrm{ML}_i]$ for $i = 0$ to 4). Thus, for all the zinc complexes of Table I the higher or hexacoordinate complex is favored with zero or one ligand bound (I_0 and $I_1 < 1$), and the lower or tetrahedral complex favored with two or more bound ligands (I_2, I_3, and $I_4 > 1$). The percentage of the lower coordinate complex is given by 100 $I_i/(1 + I_i)$.

The isomeric constant I_0 is special because it refers to the molar ratio of lower to higher coordination number for the aqueous metal ion and should be independent of the ligands employed. Since by nature of the setup $I_0 \ll 1$, it cannot be found from the $1 + I_0$ expression in Eq. (1) and must be found by utilizing the cycles in Scheme 2. The I_0 value is sensitive to the values of k_4 and f_4, and it is the most uncertain of the isomeric constants, and its constancy represents a severe test for the model. For the three zinc complexes with two differently charged ligands the I_0 values in Table I span a range from 0.0034 to 0.0084, narrower than we might expect. The 2.5-fold variation in I_0 is inherent in the setup and analysis, and must be kept in mind when discussing the results. It is in the very nature of cooperative binding that low concentrations of intermediate complexes occur, and consequently there are limitations in ferreting out precise stability constants for these species. Fortunately, we are more interested in the values of the more reliable higher isomeric constants that indicate the amount of lower coordination number complexes in the presence of one or more bound ligands.

One reason for a variation in I_0 for complexes of the same metal ion with different ligands may be contributions from coordination numbers in addition to the two considered in a scheme like Scheme 2. For zinc one expects five-coordinate complexes as intermediates between six- and four-coordinate complexes, and they may become significant for some ligand occupancies. However, to add a third channel to Scheme 2 introduces three more independent parameters to be fit: an intrinsic stability constant, an interaction factor, and an isomeric equilibrium constant to link the channel to the others. Since so many constants cannot be determined with assurance, any gain from the increased latitude is more than offset by an increase in complexity. (In Section 7, however, we find cases where we need to introduce a third channel.)

In contrast to Fe^{3+} which forms successive hydroxo complexes to $Fe(OH)_4^-$ over a normal span of 6.6 log units, Al^{3+} squeezes the same set into a range of less than one log unit.[11] The four successive pK_a values for formation of $Al(OH)_4^-$ from aqueous Al^{3+} appear as the first four entries in the next to last column of Table I. The squeeze is accounted for by a reduction in coordination number from six for the aquo ion to four for tetrahedral $Al(OH)_4^-$. Table I shows the results of the analysis by the scheme of Scheme 2. For the aquo ion only 0.3% of the species are not octahedral while for $Al(OH)_4^-$ only 0.004% are not tetrahedral. Undoubtedly five-coordinate Al^{3+} species also occur in the intermediate hydroxo complexes, but the simpler Scheme 2 accommodates the principle of cooperativity of hydroxo complex formation with Al^{3+}. Curiously, with dinegatively charged catecholate ligands Al(III) binds up to three ligands and remains hexacoordinate.[19]

An example *par excellence* of a distinct two channel system is that of Ni^{2+} and cyanide that undergoes an abrupt change of spin state from a paramagnetic, green, octahedral aqueous Ni^{2+} to a diamagnetic, yellow, square planar $Ni(CN)_4^{2-}$. As a result of the highly cooperative transition some of the intermediate complexes do not appear in significant quantities, and their associated equilibrium constants are uncertain or even indeterminate. My reanalysis of 53 data points[20] by nonlinear least squares suggests that log β_1 = 6.6(4), log β_2 is indeterminate, log β_3 = 22.5(5), and log β_4 = 30.96(4). The first and last values are within two standard deviations of the published values (listed in footnote f, Table I), but the β_3 value is new and provides a crucial entry for solving the other constants in Scheme 2. The results are listed atop the last column of Table I. The intrinsic binding constant of CN to planar Ni^{2+} (k_4) is found to be $10^{4.5}$ times greater than to octahedral Ni^{2+} (k_6).

Owing to lack of evidence from ultraviolet absorption spectroscopy for $Ni(CN)^+$, it has been suggested that the potentiometric value of log K_1 = 7.0(2) is too high.[20] However, according to the successive constants of Table I the maximum amount of $Ni(CN)^+$ that appears is only 3.6%. Coupled with the fact that in the ultraviolet region the molar absorptivity of strongly absorbing square planar $Ni(CN)_4^{2-}$ is 10^4 times that of very weakly absorbing octahedral $Ni(CN)^+$, one does not expect to see spectroscopic evidence of $Ni(CN)^+$; only potentiometric analysis is able to provide evidence for this species.

It is commonly assumed that the Ni(II) complex becomes square-planar only upon binding the fourth cyanide. However, this conclusion seems to be based only on the absence of a significant amount of the 3:1 complex. According to the constants atop Table I the maximum amount of $Ni(CN)_3^-$ is 9%. With the constants listed in Table I, $I_3 = 7 \times 10^5$, indicating that the $Ni(CN)_3^-$ is overwhelmingly square planar. Indeed, with $I_2 = 11$ the results of Table I suggest that $Ni(CN)_2$ is also square planar with two bound water molecules. However, owing to the uncertainties in the stability constants in this system, another set may give $I_2 < 1$. As the maximum percentage of $Ni(CN)_2$ is only 0.2%, it is not possible to examine it directly. The triglycine complex of Ni(II) is diamagnetic with only one amino and two deprotonated amide nitrogens (though with a planar quadridentate ligand).[21–23] We conclude that the emphatic change from octahedral to planar Ni(II) complexes occurs by the binding of the third and perhaps with the second CN^-.

The tetracyano complex $Ni(CN)_4^{2-}$ adds one CN^- to give the pentacyano complex $Ni(CN)_5^{3-}$ with $K_5 = 0.20\ M^{-1}$.[24] In our model $K_5 = 2k_6f_6^4/5(1 + I_4) = 10^{-8}$, more than 10^7 times weaker than the experimental value. Thus there is not a reversion to the six-coordinate channel (Scheme 2) upon binding of the fifth cyanide. The fifth cyanide binds so as to give a pentacyano complex that is derived from the square-planar complex. Structure results suggest that the pentacyano complex is square-pyramidal.[25] The fact that no hexacyano complex forms[24] provides additional strong support that reversion to the six-coordinate channel is not energetically favored. Owing to the large I_4 term in the denominator of K_5, formation of any hexacyano complex would appear cooperative with respect to the pentacyano complex in Scheme 2.

6. THE CHELATE 6 → 4 CASE AND $Zn(en)_3{}^{2+}$

To this point we have considered only unidentate ligands. Bidentate 1,2-diaminoethane (en) forms up to a 3:1 complex with Zn^{2+} with successive stability constant logarithms at 1 M ionic strength and 25°C[1] of 5.92, 5.15, and 1.86, a notable drop-off for the last value suggesting a force from tetrahedral $Zn(en)_2{}^{2+}$ upon chelation of the third ligand to yield hexacoordinate $Zn(en_3)^{2+}$. As an alternative to tetrahedral Zn(II) for explaining the drop-off, strong favoring of *trans*-$Zn(en)_2{}^{2+}$ providing resistance to chelation of a third en is not tenable. Both Co(II) and Ni(II) add a third en with stabilities consistent with six-fold coordination throughout, and both metal ions also take up six ammonia while Zn(II) binds only four.[15]

Scheme 3 shows the setup for the 6 → 4 system with a bidentate ligand (labeled as en). Three successive equilibria for a hexacoordinate 3:1 channel across the top of Scheme 3 are connected by dimensionless isomeric equilibrium constants to the two successive equilibria for a tetracoordinate 2:1 channel at the bottom of the Scheme 3. Three different interaction factors appear, two in the 3:1 channel and one in the 2:1 channel. We define the interaction factor f_{31} for a second ligand joining a 1:1

$$\begin{tikzcd}
{}^{6}\mathrm{M} \arrow[r, "3k_3"] \arrow[d, "I_0"'] & {}^{6}\mathrm{Men} \arrow[r, "k_3f_{31}"] \arrow[d, "I_1"'] & {}^{6}\mathrm{Men}_2 \arrow[r, "k_3f_{32}{}^{2}/3"] \arrow[d, "I_2"'] & {}^{6}\mathrm{Men}_3 \\
{}^{4}\mathrm{M} \arrow[r, "2k_2"] & {}^{4}\mathrm{Men} \arrow[r, "k_2f_2/2"] & {}^{4}\mathrm{Men}_2 &
\end{tikzcd}$$

SCHEME 3

complex and f_{32} for a third ligand joining a 2:1 complex with a hexacoordinate metal ion. The three experimentally determined stability constants are given by the following equations:

$$K_1 = \frac{[^6\mathrm{Men}]+[^4\mathrm{Men}]}{([^6\mathrm{M}]+[^4\mathrm{M}])[\mathrm{en}]} = \frac{1+I_1}{1+I_0}3k_3, \tag{12}$$

$$K_2 = \frac{[^6\mathrm{Men}_2]+[^4\mathrm{Men}_2]}{([^6\mathrm{Men}]+[^4\mathrm{Men}])[\mathrm{en}]} = \frac{1+I_2}{1+I_1}k_3 f_{31}, \tag{13}$$

$$K_3 = \frac{[^6\mathrm{Men}_3]}{([^6\mathrm{Men}_2]+[^4\mathrm{Men}_2])[\mathrm{en}]} = \frac{1}{1+I_2}\frac{k_3 f_{32}{}^2}{3}. \tag{14}$$

The three isomeric equilibrium constants are defined and related by the cycles in Scheme 3 as follows.

$$\begin{aligned} I_0 &= [^4\mathrm{M}]/[^6\mathrm{M}], \quad I_1 = [^4\mathrm{Men}]/[^6\mathrm{Men}] = 2k_2 I_0/3k_3, \\ I_2 &= [^4\mathrm{Men}_2]/[^6\mathrm{Men}_2] = k_2 f_2 I_1/2k_3 f_{31}. \end{aligned} \tag{15}$$

There are three equations and five independent constants; knowledge of the third stability constant aids greatly in reducing the uncertainties in estimating the unknowns. Reference must be made to other complexes to reduce the number of unknowns from five to three.

Examination of stability constants of up to 3:1 complexes of en and glycine with hexacoordinate metal ions reveals that one interaction factor is inadequate to describe the data accurately—two are necessary. The intrinsic P_3 binding polynomial becomes

$$P_3 = 1 + 3k_3 x + 3f_{31}k_3^2 x^2 + f_{31}f_{32}^2 k_3^3 x^3. \tag{16}$$

Since the three macroscopic equilibrium constants K_1, K_2, and K_3 completely describe the system, so do the three constants in P_3. The relations between the two alternative ways to describe the system completely may be found either by comparing the P_3 and Q_3 polynomial coefficients or by manipulating Eq. (12)–(14) with the three I_i's set to zero to obtain

$$k_3 = K_1/3, \quad f_{31} = 3K_2/K_1, \quad f_{32} = 3(K_3/K_1)^{1/2}. \tag{17}$$

The ratio $f_{31}/f_{32} = K_2/(K_1K_3)^{1/2}$ compares K_2 to the geometric mean of K_1 and K_3. Since the interaction factors f_{31} and f_{32} contain the ratios of stability constants, they are valuable for comparing the internal consistency of one study to others. From many tabulated stability constants for Co^{2+} and Ni^{2+} complexes of glycine at finite ionic strength,[26] we calculate average values of $f_{31} = 0.40$ and $f_{32} = 0.21$. For complexes of 1,2-diaminoethane(en) we find for Co^{2+}, $f_{31} = 0.26$ and $f_{32} = 0.12$, while for Ni^{2+}, $f_{31} \simeq 0.21$ and $f_{32} \simeq 0.08$. (The lower values for Ni^{2+} with en may due to a fraction of $Ni(en)_2{}^{2+}$ complexes being planar.) Thus despite the negative charge on the glycinate, it suffers less hindrance to successive coordination than does en. This difference probably resides in glycine being a bidentate ligand with a carboxylate oxygen donor atom and the steric hindrance of hydrogens on the amino nitrogens of en compared to none on a carboxylate oxygen.

Solutions to several examples of bidentate chelation to zinc and cadmium are listed in Table II. For consistency and because the metal ion is similarly sized to Zn^{2+}, we have compared the stability constants of the corresponding Co^{2+} complexes to determine the interaction coefficients according to Eq. (17). Co^{2+} and Zn^{2+} share virtually identical heats and entropies of hydration. Values for the corresponding Co^{2+} stability constants are listed in the 4th to 6th rows of Table II under ${}^6K_1$, ${}^6K_2$, and ${}^6K_3$; the derived interaction coefficients f_{31} and f_{32} appear in the 7th and 8th rows. For objectivity the interaction coefficient for the tetrahedral channel is taken as $f_2 = (f_{31} + f_{32})/2$. An iterative procedure was used to solve for the remaining constants. The solution is equivalent to that obtained previously by a different procedure for the Zn-en system,[27] with the refinement here that I_0 is not taken as negligible compared to unity but is treated as an unknown to be determined.

From $\log(k_2/k_3)$ we learn that en binds 1.2 log units more strongly to tetrahedral than to hexacoordinate aquo Zn^{2+}. The percentage tetrahedral species is less than 10% for the aqueous ion, passes through 56% for $Zn(en)^{2+}$, and rises to about 90% for the $Zn(en)_2{}^{2+}$ complex. Thus the main pathway for en chelation is ${}^6M \rightarrow {}^4Men \rightarrow {}^4Men_2 \rightarrow {}^6Men_3$. The results for Zn-glycinate in the third column and Zn-serine in the fourth column of Table II show the parameters for cases where the complex remains largely hexacoordinate, becoming only about 21% tetrahedral in the $Zn(glycinate)_2$ complex.

TABLE II

Parameters for Bidentate Chelates.

	Zn-en	Zn-glycine	Zn-serine	Zn-histamine	Zn-maltol	Zn-kojic acid	Cd-en
log K_1[a]	5.92[b]	5.03[c]	4.47[d]	5.03[d]	5.56[e]	5.01[e]	5.57[f]
log K_2	5.15	4.20	3.84	4.78	4.75	4.19	4.63
log K_3	1.86	2.54	2.25	0.70[g]	2.27	2.58	2.05
log $^6K_1$[a]	5.89[h]	4.66[c]	4.20[d]	4.89[d]	5.12[e]	4.55[e]	5.89[h]
log $^6K_2$	4.83	3.85	3.36	3.54	4.07	3.70	4.83
log $^6K_3$	3.10	2.32	2.25	2.04	2.40	2.45	3.10
f_{31}	0.26	0.46	0.43	0.13	0.27	0.42	0.26
f_{32}	0.12	0.20	0.32	0.11	0.13	0.27	0.12
log k_3	5.13	4.51	3.97	4.43	4.98	4.45	4.91
log k_2	6.37	5.09	5.54	6.56	7.28	5.18	5.88
I_0	0.11	0.078	0.0020	0.0037	0.029	0.091	0.11
I_1	1.27	0.20	0.049	0.34	0.31	0.33	0.72
I_2	8.09	0.27	0.78	22	1.91	0.75	2.48
M, % 4-coord.	9.9	7.2	0.20	0.37	2.8	8.4	10.1
ML, % 4-coord.	56	16	4.6	25	24	25	42
ML_2, % 4-coord.	89	21	44	96	66	43	71

[a] References for three experimental stability constants: Zn(II), K_i; Co(II), ^6K_i; (i = 1 to 3).

[b] At 1 M ionic strength and 25°C from Ref. 1.

[c] At 0.2 M ionic strength and 25°C from Ref. 26.

[d] At 0.15 M ionic strength and 37°C from Ref. 44, and log $^6K_3$ from A. Kayali and G. Berthon, J. Chim. Phys. **77**, 333 (1980).

[e] At 2 M ionic strength and 25°C from C. Gerard and R. P. Hugel, J. Chem. Res. (S) 404 (1978).

[f] At 1 M ionic strength and 25°C from P. Paoletti, Pure and Appl. Chem. **56**, 491 (1984).

[g] See Ref. 27, Section 6.2.

[h] For the Co(II) complex at 1 M ionic strength and 30°C from Ref. 15.

Maltol (3-hydroxy-2-methyl-4-pyrone) and the related kojic acid (3-hydroxy-6-hydroxymethyl-4-pyrone) chelate through one neutral and one negatively charged oxygen. For both pyrones the K_1 and K_2 stabilities are greater for Zn(II) than Ni(II), while for K_3 the reverse sequence applies. This reversal implies formation of tetrahedral complexes with Zn(II). As with en, the reference compound in rows 4–6 is the corresponding Co(II) complex. The results in Table II indicate that the ZnL^+ species for both pyrones is only about 25% tetrahedral while for the ZnL_2 species the amount increases to an average of about 55%. That there is not better agreement in the last percentage for the two pyrones is an additional indication of the sensitivity of the numerical interpretation to small differences.

The I_0 values apply to aqueous Zn^{2+}, and should therefore be independent of ligand. For the six bidentate chelates in Table II there is a range of values demonstrating again the sensitivity of this parameter to inputs. The I_0 values in Table II are somewhat greater than those for unidentate ligands in Table I and may reflect a greater involvement of 5-coordinate complexes with the bidentate ligands. Again, however, the derived I_0 values are the most susceptible to small differences in the inputs, and are not of the most interest.

Bidentate ligands for Zn(II) may be classified into two groups: those that take up appreciable percentages of tetrahedral geometry including en, histamine, and histidine methyl ester,[27] and those that remain largely hexacoordinate, including glycinate, serine, oxalate,[27] and acetylacetone, with maltol and kojic acid intermediate (Table II). Of course, these generalizations do not exclude small amounts of the other geometry.

For the Cd(II)-en system in the last column of Table II, the corresponding Co(II) complex was again used as reference for consistency and lack of an alternative. The system becomes predominantly tetrahedral only with the $Cd(en)_2^{2+}$ complex and then only to about 71%. Use of larger interaction coefficients for the larger Cd(II) would increase the calculated amount of tetrahedral species. This example illustrates the general principle that Cd(II) systems also develop tetrahedral complexes but to a lesser extent than Zn(II). For ammonia, imidazole,[28] and cyanide[29] the first stability constant is greater for Cd(II), but all subsequent constants are greater for Zn(II). Since the successive stability constants are well spaced, there appears only a weak tendency for Cd(II) to go tetrahedral with NH_3 and imidazole. Also with glycinate Cd(II) remains hexacoordinate.

7. THE 4 → 2 CASES OF Hg(II), Ag(I), AND Cu(I)

The top of Table III illustrates a familiar pattern for complexes of Hg(II), Ag(I), and Cu(I): the first two stability constants are many powers of ten greater than the third and fourth constants. This dramatic difference has been attributed to strong linear coordination in the 2:1 complexes while the aquo ions possess a higher coordination number. Scheme 4 shows a 4 → 2 scheme which also includes an I_3 equilibrium for a trigonal intermediate that will be necessary. We may write the following experimental equilibrium constants.

$$K_1 = \frac{[{}^4\mathrm{ML}] + [{}^2\mathrm{ML}]}{([{}^4\mathrm{M}] + [{}^2\mathrm{M}])[\mathrm{L}]} = \frac{1 + I_1}{1 + I_0}\, 4k_4, \tag{18}$$

$$K_2 = \frac{[{}^4\mathrm{ML}_2] + [{}^2\mathrm{ML}_2]}{([{}^4\mathrm{ML}] + [{}^2\mathrm{ML}])[\mathrm{L}]} = \frac{1 + I_2}{1 + I_1}\, \frac{3k_4 f_4}{2}, \tag{19}$$

$$K_3 = \frac{[{}^4\mathrm{ML}_3] + [{}^2\mathrm{ML}_3]}{([{}^4\mathrm{ML}_2] + [{}^2\mathrm{ML}_2])[\mathrm{L}]} = \frac{1 + I_3}{1 + I_2}\, \frac{2k_4 f_4^2}{3}, \tag{20}$$

$$K_4 = \frac{[{}^4\mathrm{ML}_4] + [{}^2\mathrm{ML}_4]}{([{}^4\mathrm{ML}_3] + [{}^2\mathrm{ML}_3])[\mathrm{L}]} = \frac{1}{1 + I_3}\, \frac{k_4 f_4^3}{4}. \tag{21}$$

From the cycles in Scheme 4 the I_1 and I_2 isomeric constants may be expressed in terms of I_0.

$$\begin{gathered} I_0 = [{}^2\mathrm{M}]/[{}^4\mathrm{M}], \quad I_1 = [{}^2\mathrm{ML}]/[{}^4\mathrm{ML}] = k_2 I_0/2k_4, \\ I_2 = [{}^2\mathrm{ML}_2]/[{}^4\mathrm{ML}_2] = k_2 f_2 I_1/3k_4 f_4, \end{gathered} \tag{22}$$

$$\begin{tikzcd}
{}^4\mathrm{M} \arrow[r, "4k_4"] \arrow[d, "I_0"'] & {}^4\mathrm{ML} \arrow[r, "3k_4f_4/2"] \arrow[d, "I_1"'] & {}^4\mathrm{ML}_2 \arrow[r, "2k_4f_4^2/3"] \arrow[d, "I_2"'] & {}^4\mathrm{ML}_3 \arrow[r, "k_4f_4^3/4"] \arrow[d, "I_3"] & {}^4\mathrm{ML}_4 \\
{}^2\mathrm{M} \arrow[r, "2k_2"] & {}^2\mathrm{ML} \arrow[r, "k_2f_2/2"] & {}^2\mathrm{ML}_2 & {}^3\mathrm{ML}_3 &
\end{tikzcd}$$

SCHEME 4

TABLE III

Parameters for Complexes of Unidentate Ligands Undergoing a 4 → 2 Transition.

	Hg(II)-NH_3	Hg-pyridine	Hg(II)-Cl	Hg(II)-CN	Ag(I)CN	Cu(I)-CN
log K_1[a]	8.8[b]	5.1[c]	6.72[d]	18.00[e]	<9.8[f]	<10.2[f]
log K_2	8.7	4.9	6.51	16.70	>11.1	>11.5
log K_3	1.00	0.3	1.00	3.83	0.9	5.1
log K_4	0.78	0.3	0.97	2.98	<0.3	1.1
log k_4	5.00	2.84	4.44	11.02	6.1	7.6
log k_2	9.02	5.23	6.91	18.18	>11.5	>11.9
I_0	0.43	0.58	0.46	0.49[g]	<0.010	<0.010
I_1	2200	70	69	4×10^6	<1200	<100
I_2	9×10^6	6700	1380	3×10^{12}	$>2 \times 10^8$	2×10^6
I_3	2100	44	46	2×10^6	$>1.1 \times 10^4$	5×10^4

[a] References for four experimental stability constants.

[b] In up to 2 M NH_4NO_3 at 22°C from Ref. 1 and 15.

[c] At 0.5 M ionic strength and 25°C from Ref. 38.

[d] In 1 M $NaClO_4$ at 25°C from L. Ciavatta and M. Grimaldi, J. Inorg. Nucl. Chem. **30**, 197 (1968).

[e] In 0.1 M $NaNO_3$ at 20°C from G. Anderegg, Helv. Chim. Acta **40**, 1022 (1957).

[f] At 0.1 M ionic strength and 25°C from Ref. 30.

[g] This I_0 fixed at average of last three columns and find $f_2 = 0.066$; see text.

but I_3 connects a trigonal complex with the four-coordinate channel and is a separate entity that may be calculated from Eq. 20.

$$I_3 = [^3ML_3]/[^4ML_3] = 3k_3(1 + I_2)/2k_4f_4^2 - 1.$$

There are six independent unknowns and in the best cases four known stability constants. As above we set values for the two interaction factors, f_4 and f_2, and solve for the remaining parameters. Table III displays the results.

Rows 5 and 6 of Table III show that the intrinsic stability constant for the four-coordinate channel, k_4, is often many powers of ten less than that for the two-coordinate channel, k_2. Very high values for the isomeric constant I_2 indicate overwhelming digonal complexes for ML_2. Lesser but still high values for I_1 suggest that the ML complexes are already digonal, with solvent opposite the ligand in the complex. In contrast to the results in Tables I and II where $I_1 < 1$ for Zn(II) and other metal ions, all the complexes in Table III exhibit $I_1 \gg 1$; switching to the lower coordination number has already occurred at the binding of the first ligand.

The I_0 values for the first three Hg(II) complexes of Table III exhibit a narrow range from 0.43 to 0.58 with an average value of 0.49. This excellent agreement for the sensitive parameter for the aquo Hg^{2+} extends over complexes with neutral and negatively charged ligands. The relatively high values suggest that the aquo Hg^{2+} ion is an equilibrium mixture of several coordination numbers, but the limited number of inputs prevents a finer analysis.

The results in the fifth column of Table III for the Hg(II)-cyanide system illustrate a limitation of the model. When the experimental K_1/K_2 ratio is sufficiently large, it cannot be accommodated in the model with the interaction factors used for the other complexes. For this system I_0 was set to the average value for the first three complexes and the equations solved for the digonal interaction factor $f_2 = 0.066$, a value much less than assumed values of 0.80 for negatively charged ligands and 0.95 for neutral ligands. This low result is due to strong covalent interactions in the 1:1 and 2:1 Hg(II) complexes of cyanide. The Hg(II) complexes of bromide and iodide behave similarly.

The last two columns of Table III show results for the cyanide complexes of Ag(I) and Cu(I). In both cases the binding of the second CN^- is so much stronger than the first that only the experimental log K_1K_2 product may be determined.[24,30] In deriving the inequalities of Table III it is assumed that if 10% or more of ML existed it would be detectable, and this amount is equivalent to the difference log K_2 − log $K_1 > 1.3$.

Similarly, since no $Ag(CN)_4^{3-}$ was detected, a limit was placed on K_4. For both Ag(I) and Cu(I) I_0 is < 0.010, suggesting less population of lower coordination numbers in these aquo ions than in Hg(II).

By any model, if the high first and second stability constants are to be accounted for by strong linear two coordination, then the third ligand must break into this digonalization, an energetically costly process. If it does so by producing four-coordinate complexes or higher, binding of the fourth ligand should exhibit a greater stability constant than the binding of the third ligand. Equation (20) for K_3 contains a large I_2 term in the denominator. For all the complexes of Table III and others as well, the fourth stability constant is never greater than the third (a little greater would still be insufficient). Therefore, there must be a stabilization of a complex with three ligands other than solvent so that addition of the fourth ligand meets some resistance. The last row of Table III shows high to very high values of the isomeric constant, $I_3 = [^3ML_3]/[^4ML_3]$, indicating appreciable stabilization of a complex with three ligands in some cases and strong stabilization in others. The role of solvent is not determined in this analysis and probably varies in the different cases.[31,32] Texts state that three is a rare coordination number, but these examples suggest that it occurs commonly with these three metal ions.

There is support for trigonal coordination from crystal structure and other investigations. Aliphatic thiolates form trigonal complexes with Hg(II).[33,34] The $[M(NH_3)_3]NO_3$ complexes of both Ag(I) and Cu(I) display trigonal metal ions.[35] A trigonal structure also occurs in the complex $Cu_2(CN)_3^-$.[36]

Both the ammonia and imidazole complexes of Ag(I) exhibit an inversion of the usual stability order: For NH_3 log $K_1 = 3.39$ and log $K_2 = 4.15$,[37] while for imidazole log $K_1 = 3.1$ and log $K_2 = 3.8$.[28] Since there is a statistical factor of 4 or 0.60 log units favoring K_1 over K_2, the observed inversion is actually 1.3 log units or a factor of 20. Since the K_3 and K_4 constants are weak and unknown, there is insufficient information to perform the analysis of this section on this pair of complexes. A lesser inversion occurs in the Ag(I) complexes of pyridine where log $K_1 = 2.01$ and log $K_2 = 2.15$.[38]

8. COOPERATIVITY

There is a general understanding of the meaning of cooperativity in outstanding cases such as appear in Tables I and III. It is instructive to delve into the concept of cooperativity. Let us generalize a cycle in one of the schemes such as Scheme 2 with its associated equations to obtain Scheme 5 and note that the experimental stability constant for the ith ligand is given by

$$K_i = \frac{1 + I_i}{1 + I_{i-1}} \, {}^{m}K_i \tag{23}$$

where the superscript m refers to the upper or higher coordination number channel and $i = 1$ to n, where n refers to the lower coordination number channel ($m > n$). We always have $I_i > I_{i-1}$, so that the numerator in Eq. (23) is never less than the denominator. The ratio I_i/I_{i-1} is determined largely by k_n/k_m and in a minor way by statistical factors. For the cooperative cases of Tables I and III there is a point where $I_{i-1} < 1 < I_i$. There are three limiting cases to Eq. (23).

Case 1. I_{i-1}, $I_i \ll 1$ so that $K_i = {}^{m}K_i$, and complexation occurs entirely within the higher coordination number channel, ${}^{m}\mathrm{ML}_{i-1}$, $\rightarrow$ ${}^{m}\mathrm{ML}_i$. There is no cooperativity.

Case 2. $I_{i-1} \ll 1 \ll I_i$; hence $K_i = I_i \, {}^{m}K_i = I_{i-1} \, {}^{n}K_i$, and there is switch from the higher to lower coordination number channel, ${}^{m}\mathrm{ML}_{i-1} \rightarrow {}^{n}\mathrm{ML}_i$, providing cooperativity. Values in the tables for the intrinsic constants show that binding is stronger in the lower coordination number channel ($k_n > k_m$).

Case 3. $1 \ll I_{i-1}, I_i$ so that $K_i = I_i \, {}^{m}K_i/I_{i-1} = {}^{n}K_i$ and complexation occurs entirely within the lower coordination number channel, ${}^{n}\mathrm{ML}_{i-1} \rightarrow {}^{n}\mathrm{ML}_i$. As in case 1, where complexation also occurs entirely within a single channel, there is no cooperativity.

Cooperativity occurs in limiting case 2 where complexation is accompanied by a switch from a higher to a lower coordination number channel. We do not wish to impose the limiting conditions of case 2 as the criterion of cooperativity. What do we expect of a system that we call

$$\begin{tikzcd}
{}^{m}\mathrm{ML}_{i-1} \arrow[r, "{}^{m}K_i"] \arrow[d, "I_{i-1}"'] & {}^{m}\mathrm{ML}_i \arrow[d, "I_i"] \\
{}^{n}\mathrm{ML}_{i-1} \arrow[r, "{}^{n}K_i"] & {}^{n}\mathrm{ML}_i
\end{tikzcd}$$

SCHEME 5

cooperative? All the systems of Tables I and III satisfy our expectations and all have some $I_i > 1$. Probably we would not deem the Zn-glycinate system of Table II cooperative, though there is a degree of switching from six- to four-coordination, the largest $I_i = 0.27$. One reasonable criterion for cooperativity is that some $I_i > 1$, so that there is at least 50% contribution from the lower coordination number channel. Alternatively, one might require that the intrinsic constant for the lower coordination number channel, k_n, be some factor (10?) greater than that for the higher coordination number channel, k_m. By either criterion there are some close calls in Table II with the Zn(II) complexes of the closely related ligands maltol and kojic acid falling on opposite sides of the boundaries. More direct would be a criterion applicable to the experimentally determined constants, but account would have to be taken of the charge and size of the ligands. Thus, even though we have provided a scheme and analysis of cooperativity, its precise characterization for marginal cases appears to some extent arbitrary.

This article is concerned only with equilibrium constants. Greater insights into cooperativity might be obtained if the free energy could be resolved into enthalpy and entropy contributions. Such resolution requires precise work. Direct measurement of heats in a calorimeter is considered better than evaluating the temperature dependence of equilibrium constants. However, enthalpies determined from direct calorimetric measurements are often combined with free energies determined in another laboratory. In the case of cooperative interactions such as occur with Zn(II), even analysis into equilibrium constants may be difficult, and hence the enthalpies, assigned on the basis of an assumed calculated distribution of complexes in solution, similarly uncertain. With a strong interaction and $Zn(en)_2^{2+}$ 89% tetrahedral (Table II), this system should represent one of the most clear-cut cases. There is, however, a wide variation in reported entropy values for this system and even for en and Ni(II).[39] A study that reports enthalpies for en complexes of several transition metal ions combines these with free energies from other laboratories to derive entropy values.[40] At first sight the entropy values for all three en complexes of Co(II) and Zn(II) are virtually identical, suggesting that cooperativity arises in the enthalpy term. However, this conclusion based on results in 1 M KCl does not carry over to results obtained in 1 M KNO_3. Regretfully, it does not seem possible to draw firm conclusions regarding source of cooperativity in the systems discussed in this article. Equilibrium constants determined by potentiometric titrations remain the most accurately known parameters, and it seems safest at this time to base conclusions solely on the basis of free energy changes.

9. TERNARY COMPLEXES

Cooperativity may also occur when two different ligands bind to a metal ion. However, we must be careful to distinguish the often observed enhancement of binding of two different kinds of ligands that occurs without a reduction in coordination number. The binding of ammonia to $M(NTA)^-$ and of ammonia and imidazole to $M(NTA)^-$ and $M(Bic)^+$ is greater than the statistically expected value for Co(II) and Ni(II) and greater still for Zn(II) (NTA = nitrilotriacetate and Bic = bicinate = N,N-bis(2-hydroxyethyl)glycinate).[27,41] It is the latter additional enhancement alone that is attributed to a reduction in coordination number in Zn(II) and may be described as a cooperative interaction.

Consider the system where two ligands, L and Q combine with a single metal ion, M. In the higher or m coordination we have four equilibria giving rise to four equilibrium constants only three of which are independent owing to the cyclic system, ${}^mK_L{}^mK_{LQ} = {}^mK_Q{}^mK_{QL}$.

$$\begin{aligned}
&{}^m\mathrm{M} + \mathrm{L} \rightarrow {}^m\mathrm{ML}, \quad {}^mK_\mathrm{L} = [{}^m\mathrm{ML}]/[{}^m\mathrm{M}][\mathrm{L}],\\
&{}^m\mathrm{M} + \mathrm{Q} \rightarrow {}^m\mathrm{MQ}, \quad {}^mK_\mathrm{Q} = [{}^m\mathrm{MQ}]/[{}^m\mathrm{M}][\mathrm{Q}],\\
&{}^m\mathrm{MQ} + \mathrm{L} \rightarrow {}^m\mathrm{MQL}, \quad {}^mK_\mathrm{QL} = [{}^m\mathrm{MQL}]/[{}^m\mathrm{MQ}][\mathrm{L}],\\
&{}^m\mathrm{ML} + \mathrm{Q} \rightarrow {}^m\mathrm{MQL}, \quad {}^mK_\mathrm{LQ} = [{}^m\mathrm{MQL}]/[{}^m\mathrm{ML}][\mathrm{Q}].
\end{aligned}$$

Similarly, in the lower or n coordination, we have four equations with n instead of m superscripts. Figure 1 shows a cube with the m coordinated complexes at the corners of the top face connected by the four m superscripted equilibrium constants, and n coordinated complexes at the corners of the bottom face connected by four n superscripted equilibrium constants. The top and bottom faces are connected by four isomeric equilibrium constants defined as follows.

$$\begin{aligned}
&I_0 = [{}^n\mathrm{M}]/[{}^m\mathrm{M}], \quad I_\mathrm{L} = [{}^n\mathrm{ML}]/[{}^m\mathrm{ML}],\\
&I_\mathrm{Q} = [{}^n\mathrm{MQ}]/[{}^m\mathrm{MQ}], \quad I_\mathrm{QL} = [{}^n\mathrm{MQL}]/[{}^m\mathrm{MQL}].
\end{aligned}$$

We have eight species at the corners of the cube and 12 equilibrium constants on the edges. Owing to the cyclic systems, only seven of the equi-

$$\begin{tikzcd}
& {}^{m}\mathrm{MQ} \arrow[rr, "{}^{m}K_{\mathrm{QL}}"] \arrow[dd, dashed, "I_{\mathrm{Q}}"] & & {}^{m}\mathrm{MQL} \arrow[dd, "I_{\mathrm{QL}}"] \\
{}^{m}\mathrm{M} \arrow[ur, "{}^{m}K_{\mathrm{Q}}"] \arrow[rr, "{}^{m}K_{\mathrm{L}}"] \arrow[dd, "I_{0}"] & & {}^{m}\mathrm{ML} \arrow[ur, "{}^{m}K_{\mathrm{LQ}}"] \arrow[dd, "I_{\mathrm{L}}"] & \\
& {}^{n}\mathrm{MQ} \arrow[rr, dashed, "{}^{n}K_{\mathrm{QL}}"] & & {}^{n}\mathrm{MQL} \\
{}^{n}\mathrm{M} \arrow[ur, dashed, "{}^{n}K_{\mathrm{Q}}"] \arrow[rr, "{}^{n}K_{\mathrm{L}}"'] & & {}^{n}\mathrm{ML} \arrow[ur, "{}^{n}K_{\mathrm{LQ}}"] &
\end{tikzcd}$$

FIGURE 1 Ternary complex cube for binding of two ligands, L and Q, to metal ion, M, in higher, *m*, and lower, *n*, coordination numbers. Eight complex species appear at the cube corners and twelve equilibrium constants label the cube edges. Owing to the cycles on the cube faces, only seven of the equilibrium constants are independent.

librium constants are independent, and we will need to estimate some of these to solve the system. We are mainly interested in the value of I_{QL}, the isomeric constant for lower to higher coordination in the ternary complex.

For the system only with ligand L, without ligand Q, the experimental stability constant is given by

$$K_{\mathrm{L}} = \frac{[{}^{m}\mathrm{ML}] + [{}^{n}\mathrm{ML}]}{([{}^{m}\mathrm{M}] + [{}^{n}\mathrm{M}])[\mathrm{L}]} = \frac{1 + I_{\mathrm{L}}}{1 + I_{0}}\, {}^{m}K_{\mathrm{L}}$$

For the binding of ligand L in the presence of ligand Q we have the experimental stability constant

$$K_{\mathrm{QL}} = \frac{[{}^{m}\mathrm{MQL}] + [{}^{n}\mathrm{MQL}]}{([{}^{m}\mathrm{MQ}] + [{}^{n}\mathrm{MQ}])[\mathrm{L}]} = \frac{1 + I_{\mathrm{QL}}}{1 + I_{\mathrm{Q}}}\, {}^{m}K_{\mathrm{QL}}.$$

The ratio of the two experimental constants is

$$\frac{K_{\mathrm{QL}}}{K_{\mathrm{L}}} = \frac{(1 + I_{\mathrm{QL}})(1 + I_{0})}{(1 + I_{\mathrm{Q}})(1 + I_{\mathrm{L}})} \frac{{}^{m}K_{\mathrm{QL}}}{{}^{m}K_{\mathrm{L}}}. \tag{24}$$

The stability constant ratio K_{QL}/K_L expresses the tendency of ligand L to bind to a complex already containing ligand Q compared to a complex without ligand Q.

It is common practice to express the tendency for ternary complex formation in terms of the equilibrium constant for reaction of two 1:1 complexes to disproportionate to a mixed complex and the uncomplexed metal ion.[27,41,42]

$$\begin{aligned} &\mathrm{ML} + \mathrm{MQ} \rightarrow \mathrm{MLQ} + \mathrm{M}, \\ &K_d = [\mathrm{MLQ}][\mathrm{M}]/[\mathrm{ML}][\mathrm{MQ}] = K_{QL}/K_L = K_{LQ}/K_Q. \end{aligned} \tag{25}$$

For the purely statistical value we have $K_d = 1/2$. The logarithm of K_d is usually (and awkwardly) termed $\Delta\log K_M$, $\log K_d = \Delta\log K_M$, with a purely statistical value of $-\log 2 = -0.30$. Experimental values more negative than -0.30 imply steric hindrance or repulsive electrostatic interactions, while less negative or even positive values indicate a favorable interaction promoting formation of ternary complex, MLQ. Prediction of values is difficult, and we reference the experimental results for Zn(II) complexes that may undergo a reduction in coordination number against similarly sized Co(II) and Ni(II) complexes that do not. A less negative or more positive $\log K_d$ for Zn(II) suggests a reduction in coordination number. We can quantitatively express the tendency for reduction of coordination number in ternary complexes of Zn(II) (and other metal ion complexes) by the following analysis.

With both higher, m, and lower coordination number, n, complexes, we may express the disproportionation equilibrium constant in Eq. (24) as

$$\begin{aligned} K_d &= \frac{([{}^m\mathrm{MQL}] + [{}^n\mathrm{MQL}])\,([{}^m\mathrm{M}] + [{}^n\mathrm{M}])}{([{}^m\mathrm{ML}] + [{}^n\mathrm{ML}])\,([{}^m\mathrm{MQ}] + [{}^n\mathrm{MQ}])} \\ &= \frac{[{}^m\mathrm{MQL}]\,(1 + I_{QL})\,(1 + I_0)\,[{}^m\mathrm{M}]}{[{}^m\mathrm{MQ}]\,(1 + I_Q)\,(1 + I_L)\,[{}^m\mathrm{ML}]} \\ &= {}^mK_d\,\frac{(1 + I_{QL})\,(1 + I_0)}{(1 + I_Q)\,(1 + I_L)}. \end{aligned} \tag{26}$$

The last equation is identical to Eq. (24). We compare $K_d = K_{QL}/K_L$ for Zn(II) complexes with ${}^mK_d = {}^mK_{QL}/{}^mK_L$ for Co(II) or Ni(II) complexes.

For the ternary system $\mathrm{Zn(NTA)^-} + \mathrm{NH_3}$, it has been found that $\log K_d = \Delta\log K = -0.09$.[27] This value is 0.14 log units less negative than the average of -0.23 for the Co(II) and Ni(II) systems and suggests some enhancement owing to a reduction in coordination number for Zn(II). The stability constant ratio ${}^{m}K_d = {}^{m}K_{QL}/{}^{m}K_L$ is estimated to be $10^{-0.23}$ from the Co(II) and Ni(II) systems which remain hexacoordinate. We can solve for I_{QL} if we can estimate values for the three other isomeric constants on the right hand side of Eq. (24). In the previous evaluation all three of I_0, I_L and I_Q were taken as much less than one.[27] The values of $I_0 = 0.0084$ and $I_L = I_1 = 0.18$ may be taken from the $Zn(NH_3)_4^{2+}$ system of Table I. The value for I_Q, the isomeric constant for binary $Zn(NTA)^-$, presents a quandry. If the complex remains largely hexacoordinate, the value is safely much less than one. If the binary complex is mainly tetrahedral, the value is much greater than one. For Co(II) and Zn(II) the NTA[43] and glycinate[26] complexes are both marginally stronger for the latter metal ion. Since there is no special strengthening for Zn(II), we infer that all complexes remain largely hexacoordinate and use for I_Q the $I_1 = 0.20$ value for Zn-glycinate in Table II. We now solve Eq. (24) and find $I_{QL} = 0.94$, and 48% of the ternary complexes are not hexacoordinate. From the cycles around the cube it is now possible to solve for all the remaining equilibrium constants. A similar analysis for the $Zn(NTA)^-$ + imidazole system yields $I_{QL} = 1.2$, and about 54% ternary complexes are not hexacoordinate. These values are within the range previously estimated for these complexes.[27] Imidazole appears slightly more effective in reducing the coordination number of $Zn(NTA)^-$ than ammonia. Other estimates of reduction in coordination number of Zn(II) complexes of bicinate and UTP upon addition of ammonia or imidazole have been made.[27]

Results on the three ternary systems derived from two of the three ligands en, serine, and histamine in conjunction with the results of the corresponding binary systems tabulated in Table II permit estimates of the percentage of tetrahedral Zn(II). Listed first for each system is log K_d for the Zn(II) complexes followed by log ${}^{m}K_d$ from the Co(II) complexes: en-serine, –0.14, –0.46; histamine-serine, 0.17, –0.48; and histamine-en, –0.19, –0.88, all calculated from published stability constants.[44] With the values for the isomeric equilibrium constants in Table II substituted in Eq. (26) we solve for the isomeric equilibrium constant for the ternary complex, I_{QL}, and find for each system first the value for I_{QL} and second the percentage of ternary Zn(II) complex that is tetrahedral: en-serine, 3.7, 79%; histamine-serine, 6.5, 87%; histamine-en, 16, 94%. Because we have allowed for the small but non-zero values of especially I_L and I_Q in Eq. (26), these values are greater than those derived earlier,[27] and serve to reinforce the conclusions that the three ternary complexes contain mostly tetrahedral Zn(II). For each of the three ternary complexes the listed I_{QL} and tetrahedral percentage values are between the values for the corresponding binary complexes listed in Table II. The order of increasing ability to reduce the coordination number of Zn(II) is serine < en < histamine.

If both ligands are identical, L = Q in Eq. (25), and we have $K_d = K_2/K_1$, the ratio of the second to first stability constants for binding of a single kind of ligand.[45] We may use the fund of tabulated information on first and second stability constants to estimate rapidly the degree of reduction in coordination number in metal ion complexes. For identical ligands Eq. (26) becomes

$$K_d = \frac{K_2}{K_1} = \frac{(1 + I_2)(1 + I_0)}{(1 + I_1)^2} \frac{{}^mK_2}{{}^mK_1}. \tag{27}$$

Especially for unidentate ligands I_0 and I_1 are small compared to unity, and the equation may be solved for I_2 with a suitable reference for the last stability constant ratio in Eq. (27). Either statistical factors may be used or the results from suitable reference complexes that maintain their geometry. For example, for the Zn(II) complex of ammonia from Table I, $K_2/K_1 = 10^{0.08}$, and from Section 4 for the Ni(II) complex, ${}^m\mathrm{K}_2/{}^m\mathrm{K}_1 = 10^{-0.53}$. Solving Eq. (27) increases the estimated I_2 value to 4.6. These values agree well with the more comprehensively derived value of 4.5 in Table I. This kind of analysis could be extended to higher coordination number complexes; eventually steric effects would become important for larger ligands.

10. CONCLUSIONS

The allosteric formalism not only handles cooperativity in metal ion complexes successfully, but it provides valuable insights as well. There are, however, some differences of nomenclature and interpretation between the allosterism as developed by Wyman and the applications herein to metal ion complexes. Our isomeric equilibrium constants represent a much more direct and simpler presentation of these key quantities. (Our I_0 = 1/L in Wyman and our $k_m/k_n = c$ but, e.g., our $I_2 = 5Lc^2(f_6/f_4)/2$ in Wyman, and so the value of this important isomeric constant is not readily recognized.) In the strict Wyman formalism, interaction factors are unity, but metal ions are too small for successive ligand binding to be independent events. Cooperativity may be handled by interaction factors greater than unity. Our interaction factors are always less than unity; cooperativity is handled by a two channel scheme with two different coordination numbers and geometries. For metal ions Wyman and Gill support two nested parallel allosteric schemes each containing a diagonal KNF type scheme.[2] Though this format is mathematically equivalent to that presented here, it fails to provide a useful pictorial model. A thoroughly consistent KNF picture demands that parts of the coordination sphere of the same metal ion be at the same time of two different coordination numbers and geometries. On the other hand, the approach used here is ideally suited because it preserves a single coordination number throughout each channel. The advantage of this model is the presence of two parallel channels, one for each of two coordination numbers, with interaction factors within a channel less than unity. In this way not only systems with negative cooperativity, such as most metal ion ligations, but also protein interactions may be handled within a parallel formalism.

Lower coordination numbers appear commonly with many metal ions. Higher coordination numbers are often driven by large solvent excess. With expulsion of solvent, lower coordination numbers become favored, as four for Zn(II) in proteins.[27] The stronger binding resulting from reduction in coordination number yields an acidification of any bound water, as for Zn(II) in carbonic anhydrase.[46]

References

1. J. Bjerrum, Chem. Revs. **46**, 381–401 (1950).
2. J. Wyman and S. J. Gill, *Binding and Linkage* (University Science Books, Mill Valley, California, 1990).
3. E. L. King, Inorg. Chem. **20**, 2350–2352 (1981).
4. G. C. Valle, G. G. Bombi, B. Corain, M. Favarato and P. Zatta, J. Chem. Soc. Dalton Trans. 1513–1516 (1989).
5. T. R. Bhat, R. R. Das and J. Shankar, Indian J. Chem. **5**, 324–327 (1967).
6. L. Ohman, Polyhedron **9**, 199–205 (1990).
7. L. Ohman, Inorg. Chem. **27**, 2565–2570 (1988).
8. R. B. Martin, Metal Ions Biol. Syst. **24**, 1–57 (1988).
9. O. Jons and E. S. Johansen, Inorg. Chim. Acta **151**, 129–132 (1988).
10. J. A. Findlow, J. R. Duffield and D. R. Williams, Chem. Speciation Bioavail. **2**, 3–32 (1990).
11. R. B. Martin, J. Inorg. Biochem. **44**, 141–147 (1991).
12. P. R. Bevington, *Data Reduction and Error Analysis for the Physical Sciences* (McGraw-Hill, New York, 1969).

13. Y. Nozaki, F. R. N. Gurd, R. F. Chen and J. T. Edsall, J. Am. Chem. Soc. **79**, 2123–2129 (1957).
14. L. Pauling, Proc. Natl. Acad. Sci. **21**, 186–191 (1935).
15. J. Bjerrum, *Metal Ammine Formation in Aqueous Solution* (P. Haase and Son, Copenhagen, 1941).
16. R. B. Martin, Coord. Chem. Rev. **149**, 23–32 (1996).
17. C. Brosset and J. Orring, Svensk Kemisk Tidskr. **55**, 101–116 (1943).
18. E. L. King and P. K. Gallagher, J. Phys. Chem. **63**, 1073–1076 (1959).
19. T. Kiss, I. Sovago and R. B. Martin, J. Am. Chem. Soc. **111**, 3611–3614 (1989).
20. H. Persson, Acta Chem. Scand. **A28**, 885–891 (1974).
21. R. B. Martin, Metal Ions Biol. Syst. **23**, 123–164 (1988).
22. H. Sigel and R. B. Martin, Chem. Rev. **82**, 385–426 (1982).
23. R. B. Martin, M. Chamberlin and J. T. Edsall, J. Am. Chem. Soc. **82**, 495–498 (1960).
24. M. T. Beck, Pure & Appl. Chem. **59**, 1703–1720 (1987).
25. A. Terzis, K. N. Raymond and T. G. Spiro, Inorg. Chem. **9**, 2415–2420 (1970).
26. T. Kiss, I. Sovago and A. Gergely, Pure & Appl. Chem. **63**, 597–638 (1991).
27. H. Sigel and R. B. Martin, Chem. Soc. Rev. **23**, 83–91 (1994).
28. R. J. Sundberg and R. B. Martin, Chem Rev. **74**, 471–517 (1974).
29. H. Persson, Acta Chem. Scand. **25**, 543 (1971).
30. R. D. Hancock, N. P. Finkelstein and A. Evers, J. Inorg. Nucl. Chem. **34**, 3747–3751 (1972).
31. M. Sandstrom, I. Persson and S. Ahrland, Acta Chem. Scand. **A32**, 607–625 (1978).
32. S. Ahrland, Pure & Appl. Chem. **51**, 2019–2039 (1979).
33. B. V. Cheesman, A. P. Arnold and D. L. Rabenstein, J. Am. Chem. Soc. **110**, 6359–6364 (1988).
34. S. P. Watton *et al.*, J. Am. Chem. Soc. **112**, 2824–2826 (1990).
35. U. Zachwieja and H. Jacobs, Z. Anorg. Allg. Chem. **571**, 37–50 (1989).
36. D. T. Cromer, Acta Cryst. **15**, 397–403 (1962).
37. M. Maeda, G. Nakagawa and G. Biedermann, J. Phys. Chem. **87**, 121–125 (1983).
38. J. Bjerrum, Acta Chem. Scand. **26**, 2734–2742 (1972).
39. P. Paoletti, Pure & Appl. Chem. **56**, 491–522 (1984).
40. M. Ciampolini, P. Paoletti and L. Sacconi, J. Chem. Soc. 4553–4561 (1960).
41. L. Ji, N. A. Corfu and H. Sigel, Inorg. Chim. Acta **206**, 215–220 (1993).
42. D. Banerjea, T. A. Kaden and H. Sigel, Inorg. Chem. **20**, 2586–2590 (1981).
43. G. Anderegg, Pure & Appl. Chem. **54**, 2693–2758 (1982).
44. D. D. Perrin and V. S. Sharma, J. Chem. Soc. A 2060–2062 (1969).
45. R. B. Martin and R. Prados, J. Inorg. Nucl. Chem. **36**, 1665–1670 (1974).
46. R. B. Martin, Metal Ions Biol. Syst. **9**, 1–39 (1979).