The Chelate Effect: a Simple Quantitative Approach

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Equations are constructed which accurately predict the stability constants of metal complexes of polydentate ligands from the stability constants of the complexes of the unidentate analogues. The factors considered are the asymmetry of the standard state, and the reduction of steric hindrance and mutual electrostatic repulsion in the complexes of the polydentate as compared with the unidentate ligands. The equations have been applied successfully to complexes of polyamine ligands and of ligands containing alkylamine and carboxylate functional groups. The same equations can be used to calculate formation constants of complexes containing unidentate ligands which are unstable in aqueous solution from the stability constants of stable complexes of polydentate ligands. Thus, log K_1 4.3 has been calculated for the complex $[Fe(NH_3)]^{3+}$.

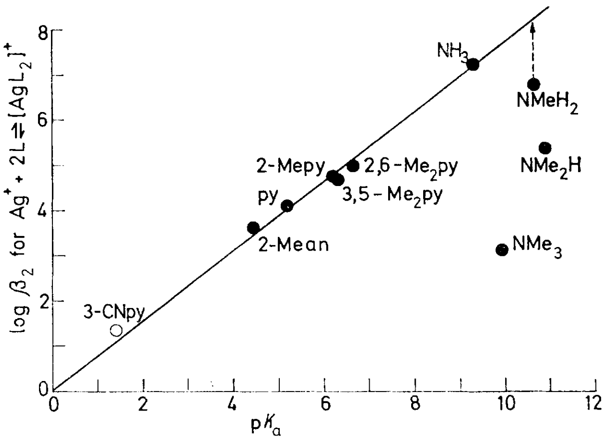
ADAMSON'S proposal [1] that the chelate effect is largely a consequence of the asymmetry of the standard reference state has the mathematical consequence (1) for the

$$\log K_1(\text{polydentate}) = \log \beta_n(\text{unidentate}) + (n - 1) \log 55.5 \quad (1)$$

complexes of an n-dentate polydentate ligand and its unidentate analogues.† If there is no extra stabilization over and above that predicted by equation (1), this equation should be able to predict the stability constants of, say, the complexes of a series of polyamines from the stabilities of the analogous ammonia complexes. However, equation (1) always underestimates the stability constants, as for the nickel(II) complexes of $H(NHCH_2CH_2)_yNH_2$ (y = 1—4).

y =	1	2	3	4
log $\beta(y + 1)$ (NH_3)	5.1	6.7	8.0	8.7
log K_1 (calc.)	6.8	10.2	13.2	15.7
(obs.)	7.6	10.8	14.3	17.5

The usual choice of ammonia for comparison with the polyamines is understandable, since the stability constants of the primary alkylamines, which would, from an electronic point of view, be a more logical choice, are similar to those of the ammonia complexes. However, a linear free-energy relation (l.f.e.r.) of log β_2 for silver(I) complexes against ligand pK_a for amine ligands (Figure) shows that pyridines and ammonia fall on one line, and that alkylamines lie below the line, indicating relatively greater affinity for the proton. This type of effect is commonly attributed to steric hindrance, since the proton is supposedly too small to be sterically hindered. It may seem somewhat surprising that primary amines are sterically hindered in their complexes, but space-filling models show that this is so, with clashes occurring between the alkyl substituent and adjacent ligands or co-ordinated water molecules. In contrast, models show that the ethylene bridge of the ring in the analogous polydentate ligands is fairly rigid, so that steric hindrance is not possible. In support of this, it has been found [2] that N-alkyl substituents lower the value of the ligand-field-splitting energy, 10Dq, in ethylenediamine (en) complexes, a fact that has been attributed to steric hindrance. We have found a corresponding decrease in 10Dq in ethylamine complexes [3] compared with the analogous en complexes, which it seems reasonable to attribute to steric hindrance as well.



Linear free-energy relation of log β_2 for the formation of silver(I) amine complexes against pK_a of the ligand. The arrow indicates the expected position of the hypothetical primary alkylamine which does not suffer from steric hindrance. (●), From ref. 5. (○), from ref. 6; py = Pyridine, an = aniline

It therefore seems that ammonia is not an appropriate unidentate analogue for comparison with the polyamines. What is required for this comparison is a hypothetical non-sterically hindered alkylamine. We could read the stability constant of our hypothetical complex off an l.f.e.r. such as that in the Figure. Since such l.f.e.r.s always go very nearly through the origin, the required constant of the hypothetical alkylamine can be generated more simply from equation (2). The pK_a values of

$$\log \beta_n(\text{alkylamine}) = \log \beta_n(NH_3) \,.\, pK_a(\text{alkylamine})/pK_a(NH_3) \quad (2)$$

alkylamines are *ca.* 10.6 and that of ammonia is 9.2, a factor of 1.152, so that equation (1) should be corrected to give (3). Equation (3) predicts more closely the

$$\log K_1(\text{polyamine}) = 1.152 \log \beta_n(NH_3) + (n - 1) \log 55.5 \quad (3)$$

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† Throughout this paper the symbol K_1 refers to the stepwise stability constant for the formation of the first complex [ML], and β_n refers to the cumulative stability constant for the formation of subsequent complexes, $[ML_n]$

[1] A. W. Adamson, *J. Amer. Chem. Soc.*, 1954, **76**, 1578.

[2] S. F. Pavkovic and D. W. Meek, *Inorg. Chem.*, 1965, **4**, 20.

[3] R. D. Hancock and G. McDougall, unpublished work.

stability constants of polyamine complexes for several metal ions.

$y =$	1	2	3	4
(*a*) Copper(II)				
$\log K_1$ calc.	10.8	16.0	20.2	21.4
$\log K_1$ obs.	10.8	16.0	20.5	22.8
(*b*) Nickel(II)				
$\log K_1$ calc.	7.6	11.2	14.4	17.0
$\log K_1$ obs.	7.6	10.8	14.3	17.5
(*c*) Cobalt(II)				
$\log K_1$ calc.	6.0	8.9	11.6	13.6
$\log K_1$ obs.	6.0	8.3	11.1	14.2

In calculating the above constants, constants reported by Bjerrum [4] for ammonia were used wherever possible, although data selection is not critical. The remaining constants were taken from ref. 5. Similar results can be obtained for other metal ions, such as Mn^{II}, Fe^{II}, Co^{III}, and $[Tl(OH)_2]^+$. Having corrected the constants for asymmetry of the standard state, and chosen appropriate unidentate analogues, *i.e.* the hypothetical non-sterically hindered alkylamines, it can be seen that for the polyamines there is very little unaccounted-for stabilization associated with the chelate effect.

For heterodentate ligands containing charged groups, such as the carboxylate group, a new consideration arises. The large stepwise decrease in the value of the successive stability constants, *i.e.* $\log K_n - \log K_{(n+1)}$ which we shall call λ, found in charged ligands is commonly believed to be due to mutual electrostatic repulsion. However, when the charged groups are joined together by carbon–carbon bonds, as in oxalate or ethylenediaminetetra-acetate (edta), this consideration is no longer of such importance. A new value of λ will now be appropriate. If we assume that λ is the same for addition of the first carboxylate to a metal ion having an alkylamine already bonded to it as for subsequent additions of carboxylate, we can predict the stability constants of complexes of, for example, nitrilotriacetate (nta) by use of equation (4). The quantity 6λ is derived

$$\log K_1(\text{nta}) = 1.152 \log K_1(\text{NH}_3) + 3 \log K_1(\text{MeCO}_2^-) - 6\lambda + 3 \log 55.5 \quad (4)$$

from the assumption that the decrease in $\log K_1(\text{MeCO}_2^-)$ on adding the first acetate to the alkylaminemetal part of the complex will be λ, on adding the second 2λ, and for the third 3λ, giving a total decrease of 6λ; λ will of course only be useful if it is the same for several ligands, such as the series glycine (Gly), iminodiacetate (ida), and nta. If we assume λ is the same whether we have one or two alkylamine groups, as in nta and edta respectively, we then have a general equation (5) for a ligand containing n alkylamine and m carboxylate groups. Equation (5) should now apply to complexes of Gly, ida, nta, edta, and ethylenediamine-*NN*- and -*NN'*-diacetate (edda and edda'). Making the assumption that λ has the same magnitude for the addition of the second carboxylate in oxalate as for the above ligands we obtain equation (6).

$$\log K_1(\text{polydentate}) = 1.152 \log \beta_n(\text{NH}_3) + m \log K_1(\text{MeCO}_2^-) - \left(\sum_{i=1}^{m} i\right)(\lambda) + (n + m - 1) \log 55.5 \quad (5)$$

$$\log K_1(\text{C}_2\text{O}_4^{2-}) = 2[\log K_1(\text{MeCO}_2^-)] - \lambda + \log 55.5 \quad (6)$$

A large number of perhaps theoretically unjustifiable simplifying assumptions has been made. The test of these assumptions lies in the predictive powers of the equations. For example, we may calculate from $\log K_1$ 18.6 for the edta complex of Ni^{II} that $\lambda = 0.316$. Using this value of λ and equations (5) and (6) we calculate the following values of $\log K_1$ for Ni^{II}:

	$C_2O_4^{2-}$	Gly	ida	nta	edda	edda'	edta
calc.	5.05	6.45	9.36	11.95	13.63	13.63	(18.60)
obs.	5.18	6.18	8.19	11.54	13.73	13.50	18.60

Making one more simplifying assumption, that λ is proportional to $\log K_1$ for acetate, we obtain equation (7) from the results for Ni^{II}. We are now able to calculate

$$\lambda = 0.175 \log K_1(\text{MeCO}_2^-) \quad (7)$$

the constants for other metal ions, bearing in mind that for acetate, a charged ligand and therefore very sensitive to ionic strength, data selection is critical. All the data for acetate have to be at infinite dilution, since the constants in the model refer to the constant for nickel(II) acetate at infinite dilution. For Co^{II} and Fe^{II}, for example, we obtain the following values of $\log K_1$:

	$MeCO_2^-$	$C_2O_4^{2-}$	Gly	ida	nta	edda	edda'	edta
Co^{II} calc.		4.51	5.52	8.25	10.71	11.84	11.84	16.50
Co^{II} obs.	1.52	4.70	5.10	6.95	10.81	11.78	11.2	16.55
Fe^{II} calc.		4.30	4.51	7.15	9.56	9.81	9.81	14.20
Fe^{II} obs.	1.4		4.30	5.8	8.84	9.81		14.33

Apart from ida, for which the calculated stability is always too high, the equation as it stands, with perhaps the maximum number of simplifying assumptions, has considerable predictive power. If $\log K_1$ values at infinite dilution are used, it is found that equations (5)—(7) apply reasonably well to all other systems for which sufficient data are available.

Uncharged ligands such as the polyamines previously discussed have dipoles, which in the unidentate analogues must repel each other in a manner analogous to that considered for charged ligands. Equation (3) can therefore be modified, with λ as an adjustable parameter appropriate to the polyamines rather than to experimentally derived values from ammonia complexes [equation (8)]. Adjusting λ to give a best fit, we obtain

$$\log K_1(\text{polyamine}) = 1.152\left[n \log K_1(\text{NH}_3) - \left(\sum_{i=1}^{n-1} i\right)\lambda\right] + (n - 1) \log 55.5 \quad (8)$$

$\lambda = 0.50$ for the nickel(II) polyamine complexes, which

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[4] J. Bjerrum, 'Metal Ammine Formation in Aqueous Solution,' Thesis, 1941, reprinted by P. Haase and Son, Copenhagen, 1957.

[5] 'Stability Constants of Metal-Ion Complexes,' Special Publ., Nos. 17 and 25, The Chemical Society, London, 1964 and 1971.

is very close to $\lambda = 0.55$ for the ammonia complexes, in accordance with the small effect which dipole–dipole repulsion effects are expected to have. Using $\lambda = 0.50$ has very little effect on the lower homologues, but greatly improves the accuracy of prediction for large polyamine ligands such as *NNN'N'*-tetra(2-aminoethyl)-ethylenediamine, where the value calculated from equation (3), log K_1 18.76, increases to log K_1 19.41 as compared with the observed value of 19.30.

Using the assumptions made here regarding the asymmetry of the standard state, the steric hindrance, and the mutual electrostatic repulsion, whether between dipoles or between charged groups, the reader, by suitable application of equation (5) or an extension thereof, can predict the stabilities of almost any polydentate ligand system for which sufficient data are available. Satisfactory calculations were made for ligands containing different combinations of alkylamine, carboxylate, pyridine, phenolic, and imidazole groups. A very high dipole–dipole interaction was found for pyridine groups. This might be thought to be due to electronic delocalization over the carbon–carbon bond joining the two pyridine groups in bipyridyl, but the same constants apply for 2-aminomethylpyridine complexes, where such delocalization cannot occur.

It is obvious from the many simplifications made that sophistication of the equations will improve their predictive power. One such improvement is differentiating between primary, secondary, and tertiary amines. For example, use of the actual pK_a of the nitrogen-donor atom in the series of ligands from Gly to edta in place of the pK_a of a primary amine in deriving our steric-hindrance reduction factor greatly improves predictive powers, and largely removes the discrepancy observed for ida complexes. One might consider the possibility of steric hindrance in carboxylate groups in a manner analogous to the polyamines. Another approximation which could be improved is that used in equation (7), since it was found that for unidentate ligands λ is better approximated by equations of the form $\lambda = f \log K_1 + c$.

However, the present equations already have a useful accurate power of prediction. An interesting use to which they can be put is in calculating stability constants for unidentate ligands whose complexes do not exist in aqueous solution. For example, the ammonia complexes of Fe^{III} are completely hydrolysed in water. However, many complexes of Fe^{III} exist which contain an alkylamine group as part of a polydentate ligand. If we estimate log $K_1 = 4.3$ for the ammonia complex of Fe^{III}, we are able to predict quite well the log K_1 values for several iron(III) chelate complexes, indicating the reliability of the estimate:

	$MeCO_2^-$	Gly	nta	edta	$[NH_2{\cdot}(CH_2)_2{\cdot}NH{\cdot}CH_2{\cdot}]_2$
calc.		9.5	16.7	25.5	21.6
obs.	3.38	10.0	16.3	25.2	21.9

Other estimated log K_1 values of possible interest are for the ammonia complexes of $[UO_2]^{2+}$ (3.1), Pb^{II} (1.6), and La^{III} (0).

One area in which the preceding equations break down is where the polydentate ligand is unable to assume the same co-ordination geometry as the unidentate analogue. An obvious example of this is linearly co-ordinated Hg^{II}, or, less obviously, tetrahedrally co-ordinated Cd^{II} and Zn^{II}, in which there is considerable strain in forming a five-membered ring. In these cases, one may estimate constants for the hypothetical octahedrally co-ordinated complexes of Zn^{II} or Cd^{II} with unidentate ligands in the same way as was done for the ammonia complex of Fe^{III}. These constants can then be used to give satisfactory sets of constants for polydentate ligands. The equations also do not apply in their simplest forms to the complexes of tetragonally distorted ions such as Cu^{II}, $[VO]^{2+}$, or $[UO_2]^{2+}$. and have to be modified in order to reproduce the stability constants of the complexes of these ions.

All the discussion has been centred on complexes with five-membered rings. The stabilities of complexes having larger rings are invariably lower than predicted. If stereoscopic models are made of, for example, propylene-1,3-diamine complexes, it is found that the methylene groups of the ring sterically hinder co-ordination at the axial co-ordination site of the metal ion. We suggest that this is a major factor in the decrease in stability of complexes with increasing ring size. By empirically altering the steric-hindrance reduction factor in equations (3) or (5), good agreement may be achieved between calculated and observed stability constants for complexes of six-membered and larger rings. An interesting point is that, for complexes of tropolone containing a five-membered ring and pentane-2,4-dionate complexes containing a six-membered ring, stability constants for the same metal ion are almost identical. The ligands appear to be very similar electronically,[7] so that one must assume that the planarity has prevented steric hindrance at the axial co-ordination site and therefore has removed the usual difference in stability found in complexes of different ring size.

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[6] R. D. Hancock and F. Marsicano, unpublished work.

[7] L. G. Hulett and D. A. Thornton, *Spectrochim. Acta*, 1971, **A27**, 2089.