Comments on Attempted 'Direct' Evaluation of Complex Constants in Multiple Equilibrium Systems by Microcalorimetric Titrations

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Abstract

The evaluation of $\log K_1$, $\log K_2$, ΔH_1 and ΔH_2 in systems involving 1:1 and 2:1 complexes by microcalorimetric titration has been described. It is demonstrated that these data are inconsistent.

Introduction

A series of papers appeared recently in which stability constants of various multidentate complexes are given [1–5]. In cases where 1:1 and 2:1 complexes occur as well a method was claimed that would allow the determination of both complex constants and all relevant thermodynamic parameters by three independent microcalorimetric titrations: two of them at high concentration of one complex partner, to determine ΔH_1 and ΔH_2 respectively directly. From this $\log K_1$ and $\log K_2$ are given with three significant figures without error estimations. Unfortunately evaluation of the data is not described in detail.

Discussion

As quoted [1] systems involving 1:1 and 2:1 complexes are determined by two equilibria

$$\mathrm{Me}^{n+} + \mathrm{L} = \mathrm{MeL}^{n+} \quad \text{with} \quad K_1 = \frac{[\mathrm{MeL}^{n+}]}{[\mathrm{Me}^{n+}][\mathrm{L}]} \tag{1}$$

$$\mathrm{MeL}^{n+} + \mathrm{L} = \mathrm{MeL_2}^{n+} \quad \text{with} \quad K_2 = \frac{[\mathrm{MeL_2}^{n+}]}{[\mathrm{MeL}^{n+}][\mathrm{L}]} \tag{6}$$

The known overall metal concentration $[\mathrm{Me}^{n+}{}_{\mathrm{tot}}]$ and the known overall ligand concentration $[\mathrm{L_{tot}}]$ are defined by the stoichiometry of the two reactions as follows (not quoted in refs. 1–5)

$$[\mathrm{Me}^{n+}{}_{\mathrm{tot}}] = [\mathrm{Me}^{n+}] + [\mathrm{MeL}^{n+}] + [\mathrm{MeL_2}^{n+}]$$

and

$$[\mathrm{L_{tot}}] = [\mathrm{L}] + [\mathrm{MeL}^{n+}] + 2[\mathrm{MeL_2}^{n+}]$$

therefore

$$K_1 = [\mathrm{Me}^{n+}\mathrm{L}]/\{([\mathrm{Me}^{n+}{}_{\mathrm{tot}}] - [\mathrm{MeL}^{n+}] - [\mathrm{MeL_2}^{n+}])([\mathrm{L_{tot}}] - [\mathrm{MeL}^{n+}] - 2[\mathrm{MeL_2}^{n+}])\} \tag{a}$$

$$K_2 = \frac{[\mathrm{MeL_2}^{n+}]}{[\mathrm{MeL}^{n+}]([\mathrm{L_{tot}}] - [\mathrm{MeL}^{n+}] - 2[\mathrm{MeL_2}^{n+}])} \tag{b}$$

Some obvious inconsistencies in refs. 1–5 are shown in the following:

(1) In ref. 2 it is stated (p. 50): 'Due to the fact that the complex formation is complete at any time of the titration...'. This assumption being used for the calculation of ΔH_1.

Table 1 shows concentrations of MeL^{n+}, $\mathrm{MeL_2}^{n+}$ and Me^{n+} as a function of added L with given parameters (Table 1 of ref. 2) calculated by solving eqns. (a) and (b) with an iterative program.

Even with the upper limit of the given salt concentration the amount of 1:1 complex does not exceed 70% of total ligand concentration; consequently the measured heat evolution of 7.9 kJ/mol cannot be considered as ΔH_1 and the given data set [2] is inconsistent with the assumption used for its derivation.

TABLE I. Composition of the Solution (%) of the Total Amount of Ligand and Molar Heat Evolution During Titration of 30 mM $\mathrm{Ba(ClO_4)_2}$ in Methanol with *cis*-Benzenetrioxide (c-BTO)[a]

Added L ($\mathrm{L_{tot}}$) [μM]	BaL^{n+}	$\mathrm{BaL_2}^{n+}$	L	Heat evolution [kJ/mol c-BTO]
10	69.4	0.0596	30.5	5.48
100	68.6	0.584	30.2	5.45
1000	62.2	4.91	28.8	5.20
2000	57.0	8.41	26.2	5.00

[a] Calculated with literature parameters [2]: $\log K_1 = 1.88$, $\log K_2 = 2.45$; $\Delta H_1 = 7.9$ kJ/mol, $\Delta H_2 = 5.9$ kJ/mol.

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TABLE 2. Composition of the Solution (%) of the Total Ba^{2+} Concentration and Molar Heat Evolution in the Titration of 90 mM c-BTO in Methanol with $Ba(ClO_4)_2$[a]

Added Ba^{2+} (Ba^{2+}_{tot}) [μM]	BaL^{2+}	BaL_2^{2+}	Ba^{2+}	Heat evolution [kJ/mol Ba^{2+}]
10	20.0	50.7	29.3	8.57
100	20.1	50.2	29.8	8.51
1000	20.4	45.4	34.1	7.88
2000	20.6	40.5	39.0	7.21

[a]Calculated with literature parameters [2] as given in Table 1.

Describing an attempt to evaluate $\Delta H_1 + \Delta H_2$ it is stated (p. 50): 'To ensure the complete formation of 2:1 complexes a salt solution (0.01–0.02 N) is titrated into a ligand solution ($7-9 \times 10^{-3}$ N).' and further: 'Thus, a complete formation of 2:1 complexes is probable.'.

The control with published parameters $\log K_1$ and $\log K_2$ shows (again with the upper limit of the given ligand concentration), that the amount of 2:1 complex does not exceed 51% and consequently the measured heat evolution of 13.8 kJ/mol cannot be considered as $\Delta H_1 + \Delta H_2$ (Table 2).

In order to have another, independent evaluation of $\Delta H_1 + \Delta H_2$ a second experiment is described (p. 50): 'A solution of the cryptand (222) (0.02–0.04 N) is titrated into a solution containing $Ba(ClO_4)_2$ ($5-6 \times 10^{-4}$ N) and a high excess of c-BTO ($2-4 \times 10^{-2}$ N). Under these experimental conditions the formation of 2:1 or X:1 complexes is complete...'.

Calculation with eqns. (a) and (b), upper and lower (in brackets) ligand concentrations and published parameters $\log K_1$ and $\log K_2$ yields the following composition relative to total Ba^{2+} content: 89.1% (76.0%) [BaL_2^{2+}], 8.13% (14.2%) [BaL^{2+}] and 2.76% (9.84%) [Ba^{2+}], heat evolution 12.9 (11.6) kJ/mol. The latter value is 50% (35%) higher than that of Table 2; in ref. 2 (Table 1) identical values are found from both methods.

NMR experiments to establish K_1 are described (p. 50): 'During these measurements the ligand ($2-12 \times 10^{-3}$ N) and salt concentration ($8-20 \times 10^{-3}$ N) are varied to ensure 1:1 complex formation'.

It can be shown that with the published parameters $\log K_1$ and $\log K_2$ and the highest given Ba^{2+} concentration 16 to 46.5% of 2:1 complexes should be present in solution (for instance with $[L_{tot}] = 12$ mM and $[Ba^{2+}_{tot}] = 20$ mM: $[Ba^{2+}] = 13.9$ mM, $[L] = 3.08$ mM, $[BaL^{2+}] = 3.26$ mM, $[BaL_2^{2+}] = 2.83$ mM).

TABLE 3. Composition (μM) of the Solution during Titration of 5 mM 15-crown-5 with $NaNO_3$[a]

L_{tot} [μM]	Added Na^+ (Na^+_{tot})	Na^+	NaL^+	NaL_2^+	L
5000	10	0.190	2.49	7.32	4982
5000	100	2.01	25.5	72.5	4829
5000	1000	36.0	322	642	3393
5000	2000	148	824	1028	2119
20000	10	0.015	0.782	9.20	19980
20000	100	0.151	7.88	92.0	19808
20000	1000	1.80	85.7	912	18089
20000	2000	4.45	189	1806	16198

[a]Calculated with literature parameters [1]: $\log K_1 = 3.42$, $\log K_2 = 2.77$.

Even if the assumption that no higher coordinated complexes exist in solution were correct (with $Ba(ClO_4)_2$ a 4:1 complex [6] precipitates from methanol solution; unfortunately only averaged ^1H NMR signals are observed in CD_3OD), all given parameters for *cis*-benzenetrioxide must be doubted.

(2) In connection with an attempt to determine K_2 it is stated in ref. 1 (p. 2752): 'As under experimental conditions the formation of the 1:1 complexes is approximately quantitative...' and further 'according to the concentration relations following simplification in eqn. (6) can be made

$$[MeL^{n+}] \approx [Me^{n+}] \tag{8}$$

In this way one obtains:

$$K_2 = \frac{[MeL_2^{n+}]}{[Me^{n+}][L]}, \tag{9}$$

(end of citation)

The concentration range of ligand is given as 5–20 mM; these two limits were chosen to calculate concentrations of MeL^{n+}, MeL_2^{n+}, Me^{n+} and L as a function of added Me^{n+} with the parameters given in Table 1 and Table 4 of ref. 1 as described above.

Analogous to the example in Table 3, it can be shown, that assumption (8) is not valid for any published pair of $\log K_1$ and $\log K_2$, the error thereby induced being somewhere in between 0.40 and 1.23 units in $\log K_2$. All given values of $\log K_2$ and consequently all thermodynamic data related to K_2 must therefore be doubted.

(3) In ref. 3 it is stated on p. 78: 'Titrating a solution containing H^+ (0.04–0.08 M) into a ligand solution (5×10^{-3} M), the concentration of the ligand is much higher when compared with the H^+ concentration in the reaction vessel. The formation of 1:1 complexes is nearly complete during titration...' and further 'The calculation of K_2 is therefore possible.'.

The concentration of the ligand is given as 5 mM; the same control as above, published values of log K_1 (2.54) and log K_2 (2.10) assumed, shows that for the given systems the concentration of 'free' protons would lie in the range of 1.7 to 26.2%, that of the 1:1 complexes from 45.3 to 95.7% of the total ligand. For the system 12-crown-4/H^+, $[H^+]$ = 100 mM the values were for instance: 45.3% $[LH^+]$, 28.5% $[L_2H^+]$ and 26.2% $[H^+]$ ($[CH_3O^+H_2]$).

(4) In connection with an attempt to evaluate $\Delta H_1 + \Delta H_2$ it is stated in ref. 4 (p. 221): 'A solution of the cryptand (222) (0.03–0.08 N) was titrated into a solution containing a salt ($6-8 \times 10^{-4}$ N) and a high excess of the ligand ($2-3 \times 10^{-2}$ N). Under these experimental conditions the formation of 2:1 complexes is complete.'.

Again with published parameters log K_1 (1.61) and log K_2 (1.90) the amount of 2:1 complexes relative to $[Me^{n+}_{tot}]$ lies between 55.7 and 96.9%, depending on the system; the values for the system 12-crown-4/Ag^+ are for instance ($[Ag^+_{tot}]$ = 0.6 mM): 55.7% $[AgL_2^+]$, 24.0% $[AgL^+]$ and 20.2% $[Ag^+]$.

(5) In ref. 5 it is stated (p. 33, 34): 'Even at seventyfold excess of the cryptand (211) over the K^+ cations, the observed reaction enthalpy ΔH_{obs} is smaller than ΔH_∞. This indicates, that the formation of 1:1 complex is not complete at this excess of ligand and no 2:1 complexes have been formed. If both complexes were present, the value of ΔH_{obs} could become smaller than that of ΔH_∞.'.

This statement is puzzling, since in the first sentence it is stated that this is already the case. In fact, 2:1 complexes cannot be excluded by these observations.

Conclusions

In systems with two equilibria a direct evaluation of ΔH_1 or ΔH_2 respectively with precision of three significant figures affords conditions where only one complex is formed with *ca.* 99% at minimum.

According to eqns. (a) and (b) log K_1 and log K_2 must then at least be 3 in solutions of <0.1 M (the highest concentration reported in refs. 1–5 is c = 0.09 M [2]) in either component. The range of accurately determinable stability constants by direct microcalorimetric titration is limited to $\log K < 4$ [7], so only if both logarithmic constants lie in between about 3 and 4 can a direct evaluation of ΔH_1 and ΔH_2 in a reasonable concentration range seem feasible; the remaining two parameters K_1 and K_2 could then be evaluated by a two-parameter error minimalisation. The only reliable method of solving thermograms with log K_1 and log K_2 values smaller than $[2 - \log c]$ is certainly an error minimalisation including all four parameters K_1, K_2, ΔH_1 and ΔH_2 [7] since they then show strong mutual correlation. A critical consideration of these problems is missing in refs. 1–5, and it seems that the inconsistencies in the data obtained there result from this shortcoming.

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