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DETERMINATION OF EQUILIBRIUM CONSTANTS BY TITRATION CALORIMETRY*

PART I. INTRODUCTION TO TITRATION CALORIMETRY

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This paper is the first in a series of three written to acquaint the reader with the general usefulness of titration calorimetry for the determination of equilibrium constants (K) for reactions in solution. A general view of the method and theory involved in the determination of K values by titration calorimetry is presented in this paper together with advantages and disadvantages of the method. In the following two papers data reduction and calculation techniques (Part II, see p. 219) and the application of the method to typical systems (Part III, see p. 233) are presented and discussed.

General

In many instances, titration calorimetric data can provide sufficient information to calculate K values for proton ionization[1-4] and metal complex formation[5-9]. In addition to K values, enthalpy change (ΔH°) and entropy change (ΔS°) values can also be obtained from the calorimetric data. Titration calorimetry is often useful for the determination of K values for systems whose study is difficult by other methods, *i.e.*, non-aqueous systems, highly acidic or basic systems, and weak metal–ligand complexes.

Description of technique

Titration calorimetry is a technique where one reactant is titrated into another and the temperature of the system is measured as a function of added titrant. The temperature change may be produced by a chemical reaction or by physical interaction between the material titrated and the titrant. The resulting data in the form of temperature *vs.* volume (moles) of titrant added can be analyzed to give information on types and numbers of reactions taking place in the reaction vessel as well as to calculate the ΔH and (for incomplete reactions) K values. Titrations are usually carried out under conditions which are as nearly adiabatic as possible, the exact conditions and equipment depending on the type of information desired.

The main components of a titration calorimeter apparatus are indicated in the block diagram shown in Fig. 1. The titrant containing one of the reactants is introduced from the buret into the reaction vessel. The resulting temperature change of the reaction is sensed by the temperature sensor T, and converted to a corresponding

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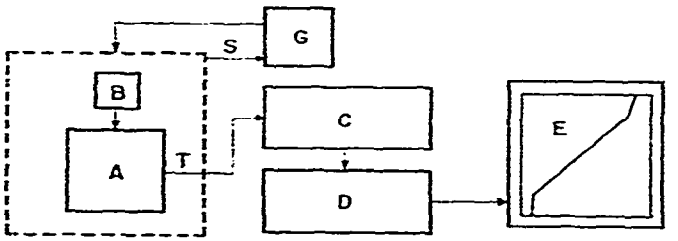


Fig. 1. Schematic of titration calorimeter apparatus: A, reaction vessel with temperature sensor; B, buret (constant rate or incremental); C, temperature measuring circuit; D, amplifier; E, data output (shown here as strip chart recorder); G, environmental control circuit.

voltage in a wheatstone bridge circuit. This voltage is amplified in the amplifying circuit and recorded on a strip chart recorder. The temperatures of the reaction vessel and the buret are measured by the sensor S, and controlled by the temperature controller. The temperatures of the titrant and titrate must be equal or their difference known very precisely.

There are two types of titration calorimeters — incremental and continuous. In the first type the titrant is added incrementally and the temperature recorded after each titrant addition. The temperature is usually readjusted to the initial temperature before each additional increment of titrant is added. This procedure has the advantage that the overall temperature change is slight for a given incremental addition of titrant and, consequently, temperature dependent corrections, *e.g.*, solution heat capacity change, etc., and heat leak corrections are kept small. Errors are introduced, however, in that a separate run has to be made for each data point obtained. Also, the number of data points obtained for the overall run is limited to the number of increments of titrant added. In continuous titration calorimetry the titrant is introduced at a constant rate during a run, and the temperature is continuously recorded. The advantage of adding the titrant continuously rather than incrementally is that a complete record is produced of the heat effects during a reaction, allowing one to choose any number of data points for calculation purposes. Calorimeters based on the continuous addition of titrant must have quick response times to temperature changes, and the systems which can be studied are limited to those where the reactions involved are rapid. One might suppose that in the continuous titration procedure larger errors would be introduced than in the incremental titration method due to (*a*) the necessity of measuring the instantaneous temperature in the reaction vessel and (*b*) the greater overall temperature changes and the resulting effects on the thermodynamic quantities being measured. This is not the case, however, if the reaction vessel and components are designed to give rapid equilibration and temperature sensing and if the experiments are designed so that the temperature change over an entire run does not exceed 0.1 °C. Errors which arise for the above reasons in continuous titration calorimetry have their counterpart in the random errors of the individual runs in incremental titration calorimetry.

The means of recording the progress of the reaction is largely a matter of

preference. The temperature change is usually sensed by a thermistor in a wheatstone bridge circuit. The unbalance of the bridge is fed into some type of indicating recording apparatus such as a strip chart recorder or into a digital voltmeter which is in turn connected to a paper tape punch or printer, a card punch, or a direct computer coupling. Both the tape punch or printer and the card punch give digital read-out which in most cases can be fed directly into a computer. Direct computer coupling eliminates much unnecessary and potentially error-producing handling of the data (*i.e.*, chart analysis, card or tape punching, etc.). The digital read-out methods and direct computer coupling are the preferred recording methods of those who are concerned with rapid data processing. The strip chart, however, supplies a readily discernable picture of the heat effects taking place in the reaction vessel and comparison of these heat changes with species distribution plots is easily accomplished. The strip chart recorder is less expensive and is the choice of those who require less exotic, classroom-type, apparatus.

Calorimeters which closely approximate isothermal conditions have recently been adapted to titration techniques[10]. Such calorimeters have the advantage that neither heat leak corrections nor heat capacity measurements need to be made.

Thermograms

A thermogram for a titration calorimetric run is a plot of temperature or heat *vs.* moles of titrant added or time of titrant delivery. The thermogram from a single continuous titration is equivalent to that constructed from data obtained from a large number of incremental titrations. For the sake of simplicity, the remainer of this paper will refer to continuous titrations unless the incremental method is specifically mentioned. It should be remembered, however, that whatever applies to the one usually applies equally to the other, with the exception that more time is required by the incremental method to get the same amount of data.

A typical thermogram for a continuous titration run for an exothermic reaction involving only one reaction is shown in Fig. 2. Region 'a' indicates the net heat gain

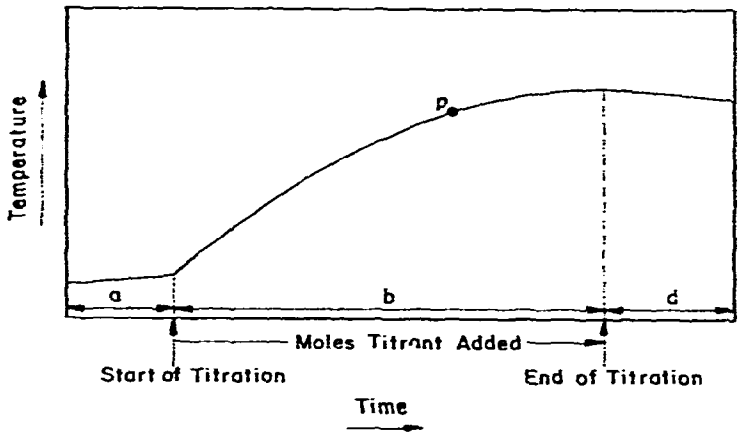


Fig. 2. Typical thermogram obtained from a continuous titration calorimeter.

of the reaction vessel and contents before the titration begins. The slope of the line is a function of heating by stirring, of resistance heating across the thermistor, and of heat leaks (heat losses by conduction, radiation, convection, and evaporation). Region 'b' indicates the heat rise due to the reaction taking place in the reaction vessel plus the heat effects resulting from (*a*) the dilution of titrant and titrate, (*b*) the temperature differential between the titrant and titrate, and (*c*) those effects mentioned for Region 'a'. Region 'c' is not represented in Fig. 2. This region would represent the portion of the curve in which the titration continues but the reaction is complete. This portion of the curve exists only for those systems in which K is too large to be determined by calorimetry. Region 'd' is generated after the titration is completed and the slope is a function of the same effects as mentioned for region 'a'. Regions 'a' and 'd' are used to make corrections for the heat loss or gain for the reaction vessel before, during, and after the titration. Other corrections must be made to allow for the effects of dilution, temperature difference of titrant and titrate, and heat capacity changes due to the addition of titrant. Methods of making the necessary heat corrections have been developed and are presented in the second paper of this series.

Analysis of a thermogram involves taking temperature readings at strategic points along the curve. The greater the complexity of the system, the greater the number of data points required. As an infinite number of points are represented on a strip chart recording, the investigator may choose as many points as the complexity of the system dictates. The temperature readings are converted into heat quantities in calories or joules and the appropriate corrections for heats of dilution, stirring, etc., are made so that each point represents the heat derived from the reaction from the beginning of the titration up to that point.

Range of applicability

The equilibrium constant for a given reaction can be determined by titration calorimetry if the magnitudes of K and ΔH for the overall reaction taking place in the reaction vessel are within certain limits. The family of curves presented in Fig. 3 shows that increased overall curvature of the thermogram is obtained with decreasing values of K (ΔH is assumed to be constant), or in other words, the shape of a given curve is a function of the K value. The curves for systems with K values greater than approximately 10^4 differ only slightly from one another; hence it is difficult to make accurate calculations of K in this region. For reactions with K values less than 0, very little reaction takes place and hence very little heat is evolved. The dependence upon ΔH is obvious in that if ΔH is small the heat change in the calorimeter is correspondingly small. It follows that in order to obtain functional thermograms the lower the K value is, the higher the ΔH must be. Fig. 4 shows a family of curves in which K is held constant and the ΔH value is varied.

The successful application of the calorimetric method of determining equilibrium constants to a given system therefore depends on [4] (*a*) the equilibrium constant being small enough ($0 < \log K < 4$) to yield a sufficiently curved thermogram and (*b*) the ΔH being concurrently large enough that a temperature change of at least 0.01°

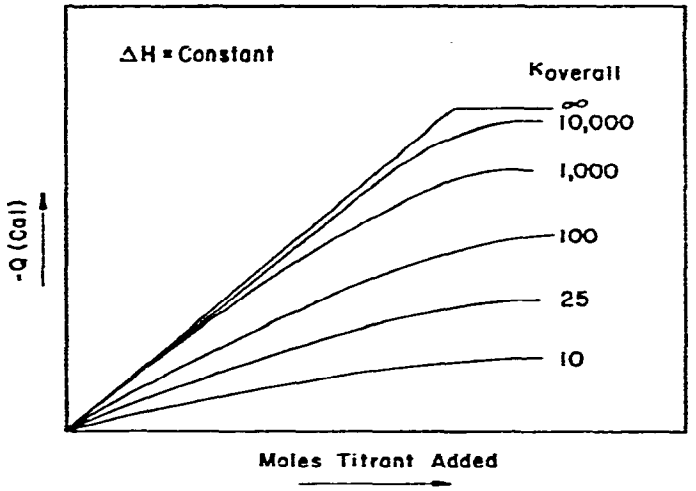


Fig. 3. Thermogram for the reaction A + B = AB, showing the effect that the value of the equilibrium constant has on the shape of the thermogram.

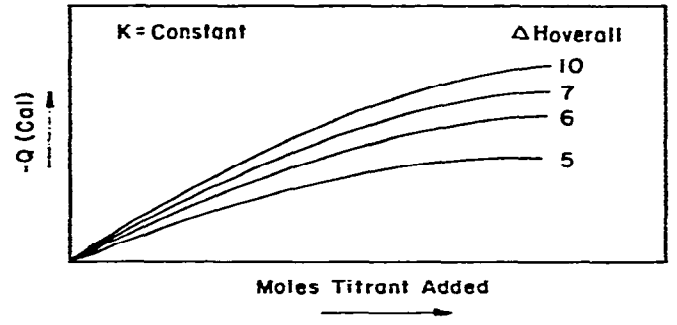


Fig. 4. Thermogram for the reaction A + B = AB, showing the effect that the value of the enthalpy has on the shape of the thermogram.

is generated by the reaction (0.01° approaches the lower limit of temperature change necessary to generate thermograms reproducible to 0.2%). These restrictions may seem severe, but they are not as limiting as they seem. It has been shown that by use of selective titrants the method can be extended to the determination of equilibrium constants for proton ionization[2] and metal–ligand interaction[11] of almost any magnitude. Further explanation of the procedures involved is given in the following sections on Proton ionization: Extension to intermediate regions: and Metal ion–ligand interaction in aqueous solution: Strong interactions.

It should be pointed out that precise evaluation of K and ΔH usually requires sophisticated titration equipment and complex analysis methods. It is possible, however, to construct simple titration calorimeters[12,13], to simplify the calculation procedures and to obtain moderately accurate results.

Calculation of equilibrium constants

The following section describes how the equilibrium constant for a simple pH

independent reaction can be calculated using titration calorimetric data. Assume the reaction producing the thermogram in Fig. 2 is for the association of A with B to yield AB. The heat corrected for all extraneous heat effects due to the reaction from the start of the titration to any point, p, on the thermogram will be $Q_{c,p}$.

$$Q_{c,p} = \Delta H(\Delta n_p) \tag{1}$$

where ΔH is the change in enthalpy for the reaction and Δn_p is the number of moles of AB formed from the start of the titration to point p. Δn_p is derived from an analysis of the concentration of each species present in the reaction vessel at point p which necessitates knowing the value of the equilibrium constant for the reaction. In this case, however, the K for the formation of AB is not known and, therefore, Δn_p is not known. If one were to approximate a value for K, a corresponding value of Δn_p can be derived. A value for ΔH can then be obtained at a given point p from Eqn. (1). This operation is carried out for each of the chosen points of the thermogram: $Q_{c,1}$, $Q_{c,2}$, $Q_{c,3}$ ... $Q_{c,n}$, using the same approximated value of K. Because ΔH is constant as is K* for a given reaction at a constant ionic strength (μ) and temperature (T) (μ and T vary only slightly during the course of reaction), it is to be expected that the calculated ΔH will be the same for each point. If such is not the case, new values of K are chosen and ΔH values are calculated until a K value is found which yields the same ΔH value at each point p throughout the run. When this occurs, the proper value for K and ΔH will have been determined. Thus both ΔH and K are determined by iterative convergence. The change in free energy (ΔG) is then determined by the relationship $\Delta G = -RT\ln K$ and the change in entropy (ΔS) by the relationship $\Delta S = (\Delta H - \Delta G)/T$.

To illustrate the above procedure, the following experimental conditions and concentrations have been assumed for the reaction A + B = AB.

A is the titrant, B is the titrate and four data points at four-minute intervals are used in the calculations. The titrant, 0.200M A, is titrated into 100.0 ml of 0.0100M B at a constant rate of 0.600 ml/min giving a total of 2.40, 4.80, 7.20, and 9.60 ml of titrant delivered respectively at the end of each interval. After analysis of the thermogram and the appropriate heat corrections are made, it is determined that the total heat of reaction at the end of each time interval is, respectively: $Q_{c,1} = 1.04$ cal, $Q_{c,2} = 1.81$ cal, $Q_{c,3} = 2.37$ cal, $Q_{c,4} = 2.77$ cal. The concentration of the various species in the calorimeter at the end of the time intervals can be calculated by using Eqns. (2–6)

$$K = [AB]_p/[A]_p[B]_p \tag{2}$$
$$[A_T]_p = [A]_p + [AB]_p \tag{3}$$
$$[B_T]_p = [B]_p + [AB]_p \tag{4}$$
$$K = [AB]_p/([A_T]_p - [AB]_p)([B_T]_p - [AB]_p) \tag{5}$$
$$K[AB]_p^2 - (K[B_T]_p + K[A_T]_p + 1)[AB]_p + K[A_T]_p[B_T]_p = 0 \tag{6}$$

*K is defined as the equilibrium constant for the reaction in question at a given ionic strength. At zero ionic strength K becomes the thermodynamic equilibrium constant.

where [A] = concentration of component A, [B] = concentration of component B, [AB] = concentration of component AB, $[A_T]$ = total concentration of A in the reaction vessel, and $[B_T]$ = total concentration of B in the reaction vessel. The initial concentrations of A_T and B_T are known and as the titration proceeds $[A_T]_p$ and $[B_T]_p$ can be calculated at the end of each time interval. For example, at the end of the first time interval 2.40 ml of titrant has been added to the reaction vessel and $[A_T]_1 = 2.40\ \text{ml} \times 0.200M/102.40\ \text{ml} = 4.69 \times 10^{-3}M$ and $[B_T]_1 = 0.0100M \times 100.0\ \text{ml}/102.40\ \text{ml} = 9.76 \times 10^{-3}M$. To calculate the concentrations of the other species at the end of each time interval, a value of K is assumed and using the appropriate values of $[A_T]_p$ and $[B_T]_p$ the values of $[AB]_p$, $[A]_p$ and $[B]_p$ are calculated from Eqns. (6), (3) and (4), respectively. In our example only the concentration of $[AB]_p$ is necessary to complete the calculations. The moles of AB formed, Δn_p, can be calculated from the relation $\Delta n_p = [AB]_p V_p$ where V_p is the volume of solution in the reaction vessel at the end of the time interval in question. ΔH is then calculated using Eqn. 1. In our example two values of K were chosen, 2×10^2 and 1×10^2 and the resulting species concentrations and ΔH values at the end of each time interval are reported in Table I. Values of ΔH were constant when K was chosen to be 1×10^2, but not when K was

TABLE I

CALCULATION OF EQUILIBRIUM CONSTANTS FROM TITRATION CALORIMETRIC DATA USING EQNS. (1)–(6)

Quantity		*Time (min)*			
		4 ($p = 1$)	*8* ($p = 2$)	*12* ($p = 3$)	*16* ($p = 4$)
$[A_T]$, moles/l		4.69×10^{-3}	9.16×10^{-3}	1.34×10^{-2}	1.75×10^{-2}
$[B_T]$, moles/l		9.76×10^{-3}	9.54×10^{-3}	9.33×10^{-3}	9.12×10^{-3}
[AB], moles/l	($K = 2 \times 10^2$)	2.74×10^{-3}	4.57×10^{-3}	5.67×10^{-3}	6.31×10^{-3}
[AB], moles/l	($K = 1 \times 10^2$)	2.04×10^{-3}	3.46×10^{-3}	4.42×10^{-3}	5.06×10^{-3}
Δn_{AB}, moles	($K = 2 \times 10^2$)	2.80×10^{-4}	4.79×10^{-4}	6.08×10^{-4}	6.92×10^{-4}
Δn_{AB}, moles	($K = 1 \times 10^2$)	2.09×10^{-4}	3.63×10^{-4}	4.74×10^{-4}	5.55×10^{-4}
Q_C, cal		1.04	1.81	2.37	2.77
ΔH, cal/mole	($K = 2 \times 10^2$)	3729	3790	3897	4011
ΔH, cal/mole	($K = 1 \times 10^2$)	5000	5000	5000	5000

Correct values of K and ΔH are 1×10^2 and 5000, respectively.

taken to be 2×10^2. Therefore for this hypothetical case, $K = 1 \times 10^2$ and $\Delta H = 5.0$ kcal/mole. An actual determination would require that activity coefficients be determined and incorporated into the calculations, that many more data points be taken from the curve, and that smaller increments be used in estimating K. [Incidentally, if K is accurately known, the ΔH of a reaction is readily determined by solving Eqn. (6) for [AB], converting [AB] to Δn, and calculating ΔH from Eqn. (1)].

The above procedure can be simplified if only approximate values of K and ΔH are desired. Combining Eqn. (5) with Eqn. (1) and using the relation $\Delta n_p = [AB]_p V_p$

gives Eqn. (7).

$$\frac{\Delta H}{K} = \frac{(V_p)[B_T]_p[A_T]_p(\Delta H)^2}{Q_{c,p}} - ([B_T]_p + [A_T]_p)\Delta H + \frac{Q_{c,p}}{V_p} \tag{7}$$

which further reduces to Eqn. (8)

$$\frac{\Delta H}{K} = X_p(\Delta H)^2 - Y_p \Delta H + Z_p \tag{8}$$

Since ΔH and K do not change for a given reaction at constant temperature and μ, $\Delta H/K$ is the same for every point on the thermogram and can be eliminated from Eqn. (8) by combining any two data points to give Eqn. (9)

$$(X_{p_2} - X_{p_1})(\Delta H)^2 - (Y_{p_2} - Y_{p_1})\Delta H + (Z_{p_2} - Z_{p_1}) = 0 \tag{9}$$

ΔH can then be obtained from Eqn. (9) and K calculated from Eqn. (8). The values of K and ΔH calculated by this method can be further refined by taking various combinations of data points and averaging the resultant values. Table II gives values

TABLE II

CALCULATION OF EQUILIBRIUM CONSTANTS FROM TITRATION CALORIMETRIC DATA USING EQNS. (1)–(9)

Quantity	*Time (min)*		
	4 ($p = 1$)		*16* ($p = 4$)
$X_p = \frac{V_p[B_T]_p[A_T]_p}{Q_{c,p}}$	4.482×10^{-6}		6.316×10^{-6}
$Y_p = [B_T]_p + [A_T]_p$	1.445×10^{-2}		2.664×10^{-2}
$Z_p = Q_{c,p}/V_p$	10.213		25.306
$X_4 - X_1$		1.834×10^{-6}	
$Y_4 - Y_1$		1.219×10^{-2}	
$Z_4 - Z_1$		15.093	
ΔH, from Eqn. (9)		5000 cal	
K, from Eqn. (8)		1×10^2	

obtained for the solution of the former example by use of this non-iterative approach using points $p_1 = 1$ (time = 4 min) and $p_2 = 4$ (time = 16 min). Although the same values for K and ΔH were obtained in this calculation as in the preceeding example, in general this will not be the case as small random errors in the values of each data point will give rise to slightly different values of K and ΔH depending on the data points used in the calculations.

It should be stressed that the non-iterative method is good only for the determination of approximate values of ΔH and K. A comprehensive review of iterative and non-iterative methods for calculating K will be given in the second paper of this series.

TABLE III

TYPICAL SYSTEMS FOR WHICH K AND ΔH FOR PROTON IONIZATION HAVE BEEN DETERMINED BY TITRATION CALORIMETRY AT 25°C AND $\mu = 0$

System		*Titration calorimetry*					*Typical values using other methods*			
		[a]*Log* $K_{overall}$	*pK*	*ΔH (kcal/mole)*	*Conditions*	*Ref.*	*pK*	*ΔH (kcal/mole)*	*Conditions*	*Ref.*
HSO_4^-	$= H^+ + SO_4^{2-}$ [b]	1.91	1.91 ± 0.01	−5.65 ± 0.08	Na_2SO_4	1	1.89–1.99	−3.9–−5.7	$\mu = 0$	16–22
		2.00	1.97 ± 0.04	−4.9 ± 0.2	$(R_4N)_2SO_4$	14				
HPO_4^{2-}	$= PO_4^{3-} + H^+$ [c]	1.61	12.39 ± 0.03	4.2–4.4		1,15	1.625			23
HPy^+	$= Py + H^+$ [d]	0.4	5.17 ± 0.02	4.98 ± 0.04	$\mu = 0.013$	2	5.17–5.18	4.72–4.80	$\mu = 0.04$–0.06	24–27
HIm^+	$= Im + H^+$ [d]	2.2	6.99 ± 0.02	8.78 ± 0.03	$\mu = 0.011$	2	6.993–6.953	8.79	$\mu = 0$	28–30
HMet	$= Met^- + H^+$ [d]	−1.0	3.76 ± 0.04	4.9 ± 0.2	$\mu = 0.016$	2	3.738	5.96	$\mu = 0$	31
HTHAM	$= THAM + H^+$ [d]	3.3	8.03 ± 0.04[e]	11.39 ± 0.04	$\mu = 0.010$	2	8.069–8.076	11.33–11.55	$\mu = 0$	32–35
$HGly^-$	$= Gly^- + H^+$ [d]	5.0	9.6 ± 0.2	10.68 ± 0.03	$\mu = 0.010$	2	9.78	10.55–10.76		36–40

[a]Log $K_{overall}$ = equilibrium constant for the overall reaction occurring in the calorimeter. [b]Strong acid titrant, $HClO_4$. [c]Strong base titrant, NaOH. [d]Weak acid titrant, acetic acid. [e]This value is incorrectly reported as 8.03 ± 0.37 in Ref. 2. Py = pyridine, Im = imidazole, Met = metanilic acid, THAM = tris-(hydroxymethyl)aminomethane, Gly = glycine.

TABLE IV

TYPICAL SYSTEMS FOR WHICH K AND ΔH VALUES FOR METAL-LIGAND INTERACTION HAVE BEEN DETERMINED BY TITRATION CALORIMETRY AT 25 °C AND $\mu = 0$

System	*Titration calorimetry*				*Typical values using other methods*		
	log β[a]	*ΔH (kcal/mole)*	*Conditions (μ)*	*Ref.*	*log β*	*Conditions (μ)*	*Ref.*
$Ag^+ + Py = AgPy^+$	2.00–2.05	−4.5–−4.83	0–0.5	5,8	2.00		41
$Ag^+ + 2Py = AgPy_2^+$	4.11	−11.21–−11.34	0–0.5	5,8	4.11–4.22		41–42
$Cu^{2+} + Py = CuPy^{2+}$	2.50 ± 0.02	−4.02 ± 0.08	0	5	2.41–2.59	0.5–1.0	
$Cu^{2+} + 2Py = CuPy_2^{2+}$	4.03 ± 0.05	−8.86 ± 0.1	0	5	4.29–4.41	0.5–1.0	42–46
$Cu^{2+} + 3Py = CuPy_3^{2+}$	5.16 ± 0.06	−16.1 ± 0.6	0	5	5.43–5.93	0.5–1.0	42–46
$Cu^{2+} + 4Py = CuPy_4^{2+}$	6.04 ± 0.1	−21.5 ± 0.5	0	5	6.04–6.54	0.5–1.0	42–46

Py = pyridine. [a] β values are for the overall reactions, *i.e.* $\beta_1 = K_1$, $\beta_2 = K_1 K_2$, etc.

Illustrative studies

Tables III, IV, V, and VI are included to illustrate the use of the titration calorimetric method in the determination of pK ($-\log K$) values for proton ionization and $\log K$ values for metal ion–ligand interactions in both aqueous and mixed solvents. A brief description of each category follows.

TABLE V

K AND ΔH VALUES DETERMINED BY TITRATION CALORIMETRY FOR THE STEPWISE INTERACTION OF Cu(II) WITH 1,10-PHENANTHROLINE IN AQUEOUS SOLUTION AT 25 °C AND $\mu = 0$

Reaction	*Titration calorimetry*[a]		*Typical values using other methods*[a]	
	Log K	*ΔH*	*Log K*	*ΔH*
$Cu^{2+} + P = CuP^{2+}$	9.14±0.06	−11.03±0.1	9.08–9.16	—
$CuP^{2+} + P = CuP_2^{2+}$	6.87±0.08	−5.42±0.1	6.42–6.96	—
$CuP_2^{2+} + P = CuP_3^{2+}$	5.42±0.1	−5.1±0.3	5.14–5.50	—

[a]Data taken from Ref. 11. P = 1,10-Phenanthroline

TABLE VI

K AND ΔH VALUES DETERMINED BY TITRATION CALORIMETRY FOR THE STEPWISE INTERACTIONS OF THIOUREA WITH $Hg(CN)_2$ IN H_2O–EtOH SOLVENT MIXTURES AT 25 °C AND $\mu = 0$[a]

Weight % EtOH	*log K_1*	*log K_2*	*ΔH_1 (kcal/mole)*	*ΔH_2 (kcal/mole)*
0.0	1.97±0.06	0.58±0.04	−1.5±0.1	−7.9±0.2
20.0	2.03±0.08	0.77±0.08	−2.4±0.1	−8.6±0.3
40.0	1.94±0.10	1.04±0.05	−4.51±0.09	−8.2±0.2
60.0	1.86±0.05	1.26±0.04	−5.93±0.04	−5.21±0.07
80.0	2.11±0.06	1.30±0.08	−5.96±0.04	−5.0±0.2
92.3	2.28±0.04	1.34±0.08	−6.16±0.03	−4.8±0.4

[a]Data taken from Ref. 6.

Proton ionization. — As previously shown, the determination of equilibrium constants by titration calorimetry is dependent upon the curvature of the thermogram. To obtain the necessary curvature the log K of the overall reaction in the calorimeter must be greater than 0 and less than 4. Strong or weak acids or bases may be used as titrants as long as the overall reaction constant meets the above criteria and the K and ΔH values of secondary reactions are accurately known. This will become more clear in the following discussion.

Acid region. — In this region the conjugate base is titrated with a strong acid, $H^+ + A^- = HA$. The results of the reaction $H^+ + SO_4^{2-} = HSO_4^-$, in which the cations present are either sodium or tetraalkylammonium ions are presented in Table III.

Basic region. — In this region weakly acidic species are titrated with strong base and proton ionization is accompanied by water formation, $HA + OH^- = A^- + H_2O$. In order to determine the pK for the ionization of HA, the measured $\log K_{overall}$ must be corrected for the formation of water, *i.e.*, $\log K_{HA} = \log K_{overall} - \log K_W$. Likewise the ΔH for the formation of water must be subtracted from the $\Delta H_{overall}$ to get ΔH_{HA}. The results in the case of the third ionization of phosphoric acid are presented in Table III. The titrant was NaOH solution and the reaction in the reaction vessel was $HPO_4^{2-} + OH^- = PO_4^{3-} + H_2O$.

Extension to intermediate regions. — In the intermediate region an acid or base is titrated with a slightly weaker or stronger acid or base such that there is competition for the proton, *i.e.*, $HA + B^- = HB + A^-$, and the difference between $\log K_{HA}$ and $\log K_{HB}$ ($\log K_{overall}$) is between 0 and 4. Log K_{HA} is determined much the same as are $\log K_{HA}$ values in the basic region, $\log K_{HB}$ is simply subtracted from $\log K_{overall}$ ($\log K_{HA} = \log K_{overall} - \log K_{HB}$).

The results of determining the pK of pyridine, imidazole, metanillic acid, protonated trishydroxylaminomethane and glycine using acetic acid as titrant are presented in Table III. The accuracy with which the pK's were determined can be correlated with how well $\log K_{overall}$ remains within the proper limits in that the best results (low standard deviation of K) were obtained when $\log K_{overall}$ was 0.4, 2.2 and 3.3 (pyridine, imidazole, and THAM respectively) and higher deviations were obtained when $\log K_{overall}$ was -1 (metanillic acid) and above 4 (glycine).

A list of possible titrants which may be used to accurately determine any $\log K_{HA}$ value less than 15 and greater than -1 is given in Table VII. The effective pK range in each case gives the range of pK values which the titrate can have for that titrant. As it is desirable to have ΔH for the reaction occurring in the calorimeter as large as possible two titrants of quite different ΔH values have been suggested for several of the ranges. Ref. 4 should be consulted for a more complete discussion of the criteria for choosing a titrant.

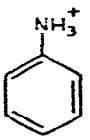
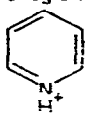
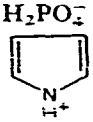
Metal ion–ligand interaction in aqueous solution

Weak interactions. — Investigation of metal ion–ligand interactions via titration calorimetry is subject to the same criteria as proton–ligand interaction, *i.e.*, $\log K_{overall}$ must have a value between 0 and 4 and sufficient heat must be released to give an accurate thermogram. The method is, therefore, extremely valuable for the determination of weak metal ion–ligand interactions. A single titration can give sufficient information to determine several $\log K$ values. Metal ion–ligand interactions are almost always complex systems in which more than one ligand associates with a given metal ion, and equilibrium constants for consecutive reactions are usually close together numerically. As expected, the precision and accuracy obtained in determining consecutive $\log K$ values is a function of the magnitude of $\log K_{overall}$. Table IV contains results of studies of silver–pyridine and copper–pyridine systems in which overall $\log K$ ($\log \beta$) values were obtained from calorimetric data.

As a matter of interest, the method also affords a somewhat qualitative check on

TABLE VII

SUGGESTED TITRANTS FOR TITRATION CALORIMETRY ($HA = A^- + H^+$)

Effective p*K range*	*Substance*	*Formula*	pK^a	ΔH° (*kcal/mole*)
<2.5	Hydrogen ion	H_3O^+	<1	0
	Hydrazinium (+2) ion	$N_2H_6^{2+}$	−0.67	8.9
1–4	Phosphoric acid	H_3PO_4	2.148	−1.88
3–6	Anilinium ion		4.60	7.28
4–7	Acetic acid	CH_3COOH	4.756	−0.01
	Pyridinium ion		5.17	4.98
6–9	Dihydrogen phosphate ion	$H_2PO_4^-$	7.198	0.90
	Imidazolinium ion		6.99	8.78
8–11	Acetylacetone	$CH_3COCH_2COCH_3$	9.02 (20°)	2.8
	Tris(hydroxymethyl)amino methane	$(CH_2OH)_3CNH_3^+$	8.069	11.33
9–12	Glycinium ion	$^+H_3NCH_2COO^-$	9.780	10.57
11–14	Monohydrogen phosphate ion	HPO_4^{2-}	12.39	4.20
	Hydroxide ion	OH^-	13.998	13.335

[a] pK and ΔH values are valid at 25 °C and $\mu = 0$ unless otherwise indicated. See Ref. 4 for a more complete discussion of the criteria for choosing a titrant.

the stoichiometry of the reactions believed to be taking place in the reaction vessel. Fig. 5 shows the titration and species distribution curves for the reaction of Ag^+ with Py. The S shape thermogram indicates that $AgPy_2^+$ is formed in a stepwise manner and further, that the heat for the formation of $AgPy_2^+$ from $AgPy^+$ is more exothermic than the heat of formation of $AgPy^+$ from Ag^+. This observation is borne out by comparing the thermogram and species distribution curves. The shape of the thermogram is thus frequently useful in interpreting data.

Strong interactions. — As in the case for proton ionization, it is possible to extend the method of calorimetrically determining equilibrium constants to any metal ion–ligand interaction. The method is the same as for acid–base reactions in that a competitive reaction between two metal ions and one ligand or between one metal ion and two ligands takes place in the reaction vessel giving rise to an overall

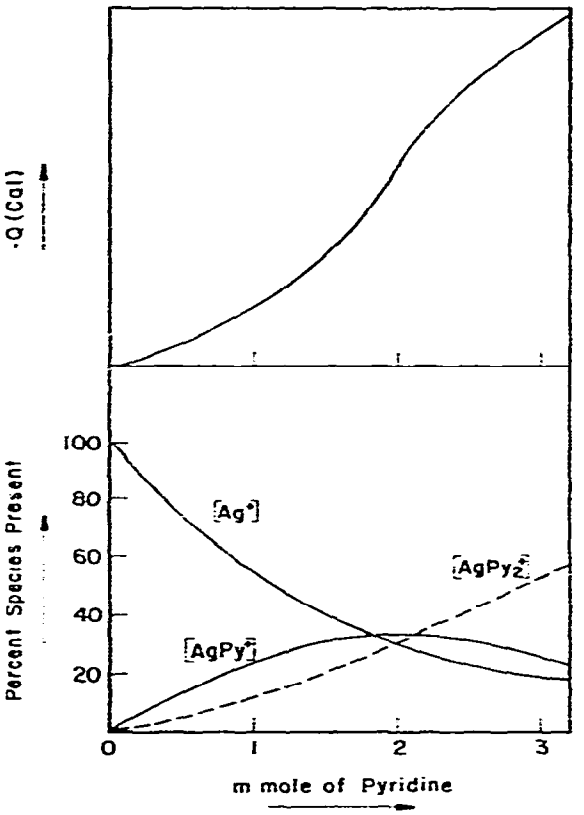


Fig. 5. Thermogram and species distribution curves for calorimetric titration of silver ion with pyridine.

reaction for which the equilibrium constant can be determined. This method is illustrated for a two metal ion–one ligand system by Eqns. (10), (11), and (12).

$$ML = M + L \qquad \log K \qquad (10)$$

$$M' + L = M'L \qquad \log K' \qquad (11)$$

$$M' + ML = M + M'L \qquad \log K_{overall} \qquad (12)$$

The equilibrium constant, K, for reaction (10) can be determined if a metal ion, M', can be found for which K' and $\Delta H'$ are known and which will complex with ligand, L [reaction (11)] so that the equilibrium constant for the reaction occurring in the reaction vessel, $\log K_{overall}$, is between 0 and 4. This method has been used to determine equilibrium constants for the interaction of scandium(III) with dipicolinate and diglycolate ions using lutetium(III) as the competing metal ion[47] and for the interaction of mercury(II) with 2-aminoethanol and copper(II) and zinc(II) with 1,10-phenanthroline using hydrogen ion as the competing ion[11]. The results of the study with copper(II) are given in Table V.

Metal ion–ligand interaction in mixed solvents

The nature of the solvent makes little or no difference in the operation of a

calorimeter, save the occasional dissolution of formerly supposedly inert inner apparatus. In non-aqueous media the equilibrium constants are determined by the same method, utilizing the same criteria as in aqueous solutions.

Among calorimetric studies involving non-aqueous and/or mixed solvents are a phenol–dimethylformamide system in isooctane and toluene solvents[7], and a $Hg(CN)_2$–thiourea system in H_2O–ethanol solvents[6]. Results of the study of $Hg(CN)_2$–thiourea in H_2O–ethanol solvents is reproduced in Table VI.

Operational limits

In spite of its versatility, titration calorimetry has operational limits beyond which the errors involved lead to unsatisfactory results. Extensive studies of error analysis have been made[4,5,48,49] and include suggestions regarding choice of solution and titrant concentration, titrant composition, and ways of reducing experimental errors.

Summary

Techniques for determining thermodynamic equilibrium constants by titration calorimetry have been developed for a wide spectrum of reactions. The method is still relatively new and improvements and extensions are foreseeable. Chief among the advantages of the method is its universality. It can be used in any solvent to determine equilibrium constants for proton ionization and metal ion–ligand interactions over a large pH range for simple and complex equilibria. It yields a good overall picture of the stoichiometry of the reaction(s) taking place and the experimentation and data analysis can be done rapidly.

The chief drawback of the method has been the initial expense of the calorimeter and the unavailability of commercial calorimeters. However, this is partially offset by the fact that commercial calorimeters are now available from LKB Instruments (Rockville, Maryland) and Tronac (Orem, Utah). Computer programs have been worked out for most types of reactions and are available in Fortran IV computer language (see Parts II and III, pp. 219–246).

Simple and inexpensive apparatus can be built for demonstration and laboratory classwork in which the equilibrium constants for simple interactions can be obtained by the solution of simultaneous equations.

REFERENCES

1 J. J. CHRISTENSEN, R. M. IZATT, L. D. HANSEN, AND J. A. PARTRIDGE, *J. Phys. Chem.*, 70 (1966) 2003.
2 J. J. CHRISTENSEN, D. P. WRATHALL, AND R. M. IZATT, *Anal. Chem.*, 40 (1968) 175.
3 R. M. IZATT, J. H. RYTTING, L. D. HANSEN, AND J. J. CHRISTENSEN, *J. Amer. Chem. Soc.*, 88 (1966) 2641.
4 J. J. CHRISTENSEN, D. P. WRATHALL, J. L. OSCARSON, AND R. M. IZATT, *Anal. Chem.*, 40 (1968) 1713.
5 R. M. IZATT, D. EATOUGH, J. J. CHRISTENSEN, AND R. L. SNOW, *J. Phys. Chem.*, 72 (1968) 1208.
6 R. M. IZATT, D. EATOUGH, AND J. J. CHRISTENSEN, *J. Phys. Chem.*, 72 (1968) 2720.
7 F. BECKER, J. BARTHEL, N. G. SCHMAHL, AND H. M. LUSCHOW, *Z. Phys. Chem. (Frankfurt)*, 37 (1963) 52.

8 P. PAOLETTI, A. VACCA, AND D. ARENARE, *J. Phys. Chem.*, 70 (1966) 193.
9 J. J. CHRISTENSEN AND R. M. IZATT, in H. A. O. HILL AND P. DAY (Eds.), *Physical Methods in Advanced Inorganic Chemistry*, Interscience, New York, 1968, p. 539.
10 J. J. CHRISTENSEN, H. D. JOHNSTON, AND R. M. IZATT, *Rev. Sci. Instrum.*, 39 (1968) 1356.
11 D. J. EATOUGH, *Anal. Chem.*, 42 (1970) 635.
12 L. D. HANSEN, R. M. IZATT, AND J. J. CHRISTENSEN, in J. JORDAN (Ed.), *Modern Titrimetry–A Treatise*, Marcel Dekker, New York, in press.
13 J. JORDAN, *J. Chem. Educ.*, 40 (1963) A5.
14 R. M. IZATT, D. EATOUGH, J. J. CHRISTENSEN, AND C. H. BARTHOLOMEW, *J. Chem. Soc., A*, (1969) 45.
15 P. PAPOFF, G. TORSI, AND P. G. ZAMBONIN, *Gazz. Chim. Ital.*, 95 (1965) 1031.
16 K. PITZER, *J. Amer. Chem. Soc.*, 59 (1937) 2365.
17 A. J. ZIELEN, *J. Amer. Chem. Soc.*, 81 (1959) 5022.
18 I. E. FLIS, *Zh. Prinkl. Khim.*, 34 (1961) 1744.
19 G. H. NANCOLLAS, *Interaction in Electrolyte Solutions*, Elsevier, New York, 1966.
20 W. L. MARSHALL AND E. V. JONES, *J. Phys. Chem.*, 70 (1966) 4028.
21 M. H. LIETZKE, R. W. STOUGHTON, AND T. F. YOUNG, *J. Phys. Chem.*, 65 (1961) 2247.
22 C. M. CRISS AND J. W. COBBLE, *J. Amer. Chem. Soc.*, 86 (1964) 5385.
23 C. E. VANDERZEE AND A. S. QUIST, *J. Phys. Chem.*, 65 (1961) 118.
24 L. SACCONI, P. PAOLETTI, AND M. CIAMPOLINI, *J. Amer. Chem. Soc.*, 82 (1960) 3831.
25 D. L. LEVI, W. S. MCEVEN, AND J. H. WOLFENDEN, *J. Chem. Soc.*, (1949) 760.
26 R. K. MURMAN AND F. BASOLO, *J. Amer. Chem. Soc.*, 77 (1955) 3484.
27 H. C. BROWN, D. H. MCDANIEL, AND O. HAFLIGER, in C. A. BRAUDE AND F. C. NACHOD (Eds.), *Determination of Organic Structure by Physical Methods*, Academic Press, New York, 1955, p. 581.
28 A. H. M. KIRBY AND A. NEWBERGER, *Biochem. J.*, 32 (1938) 1146.
29 S. P. DATTA AND A. K. GRZYBOWSKI, *J. Chem. Soc., B*, (1966) 136.
30 I. WADSO, *Acta Chem. Scand.*, 16 (1962) 479.
31 R. D. MCCOY AND D. F. SWINEHART, *J. Amer. Chem. Soc.*, 76 (1954) 4708.
32 R. G. BATES AND G. D. PINCHING, *J. Res. Nat. Bur. Stand.*, 42 (1949) 519.
33 R. G. BATES AND H. B. HETZER, *J. Phys. Chem.*, 65 (1961) 667.
34 S. P. DATTA, A. K. GRZYBOWSKI, AND B. A. WESTON, *J. Chem. Soc.*, (1963) 792.
35 B. NELANDER, *Acta Chem. Scand.*, 18 (1964) 973.
36 S. P. DATTA AND A. K. GRZYBOWSKI, *Trans. Faraday Soc.*, 54 (1958) 1179 and 1188.
37 E. J. KING, *J. Amer. Chem. Soc.*, 73 (1951) 155.
38 B. B. OWEN, *J. Amer. Chem. Soc.*, 56 (1934) 24.
39 J. A. PARTRIDGE, J. J. CHRISTENSEN, AND R. M. IZATT, *J. Amer. Chem. Soc.*, 88 (1966) 1649.
40 K. P. ANDERSON, W. O. GREENHALGH, AND R. M. IZATT, *Inorg. Chem.*, 5 (1966) 2106.
41 W. C. VOSBURGH AND S. A. COGSWELL, *J. Amer. Chem. Soc.*, 65 (1943) 2412.
42 R. J. BRUEHLMAN AND F. H. VERHOEK, *J. Amer. Chem. Soc.*, 70 (1948) 1401.
43 J. BJERRUM, *Chem. Rev.*, 46 (1950) 381.
44 J. BJERRUM, *Acta Chem. Scand.*, 18 (1964) 843.
45 D. L. LEUSSING AND R. C. HANSEN, *J. Amer. Chem. Soc.*, 79 (1957) 4270.
46 G. ATKINSON AND J. E. BAUMAN, *Inorg. Chem.*, 2 (1963) 64. The validity of the K values reported in this reference has been questioned (see correspondence from G. ANDEREGG and reply by G. ATKINSON AND J. E. BAUMAN, *Inorg. Chem.*, 2 (1963) 1082.
47 I. GRENTHE AND E. HANSSON, *Acta. Chem. Scand.*, 23 (1969) 611.
48 S. CABANI AND P. GIANNI, *J. Chem. Soc., A*, (1968) 547.
49 J. J. CHRISTENSEN, J. H. RYTTING, AND R. M. IZATT, *J. Chem. Soc. A*, (1969) 861.