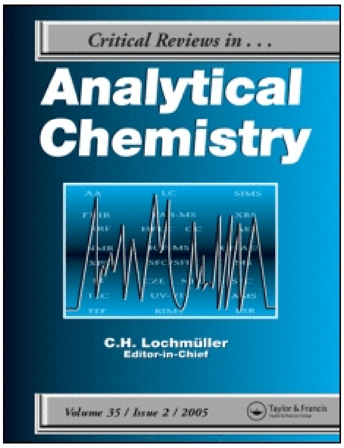

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ANALYTICAL AND MEASUREMENT ASPECTS OF THERMOMETRIC TITRIMETRY

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I. INTRODUCTION

Two distinct analytical methods based upon the measurement of temperature changes engendered by the enthalpy change accompanying solution phase have been developed during the past 2 decades. The earlier and more widely used of these 2 techniques is, in accord with an informal convention, properly termed thermometric titrimetry.[1] This method utilizes variations of temperature to indicate titration end points in precisely the same fashion as variations of conductance or limiting current are used to locate end points in conductometric and amperometric titrations. Thermometric titrimetry has been used successfully to determine acids,[2] bases,[3] redox species,[4] precipitants,[5] and complex-forming species,[6] in both ideal solutions and complex mixtures, at concentrations ranging from 1 mM to 100 mM and with a precision ranging from 0.1 to 10%. In addition to the relatively familiar reactions of inorganic analysis, the method has been applied to a number of interesting organic analytical problems including diazotization of anilides,[7] hypochlorite oxidation of sulfa drugs,[8] and organo-aluminum reactions.[9] One of the major features of thermometric methodologies is the range of problems to which they are applicable. This results from the fundamental physicochemical nature of the method. The 2 major requirements which must be met in order for thermometric titrimetry to be successfully applied are

a. The reaction enthalpy must be reasonably large. In essence, this requires that $|\Delta H^{0\prime}| > 5$ kcal/mol.

b. The reaction must be relatively fast compared to both the time scale of the analysis and the rate of heat transfer of the adiabatic system employed.

As will be discussed later, thermometric titrations are relatively immune to the equilibrium constant of the titration reactions and this is seldom a limiting feature.

A second technique, direct injection enthalpimetry, whose general practicability is of more recent vintage, has been designated as DIE by the group most responsible for its renaissance as an analytical method.[10] DIE utilizes a measurement of a net temperature change, or some related variable, as a direct measure of concentration of the sample species. Thus, DIE is related to thermometric titrimetry in the same manner as polarography and photometry are related to amperometric and photometric titrimetry. DIE differs significantly from the other direct methods such as potentiometry in that it is invariably a destructive analysis; that is, it is based upon a reaction whereas amperometry or photometry are not necessarily destructive. Consequently, DIE is always a "one-shot" analysis, unlike many other techniques where measurements may be made repeatedly on the same aliquot of unknown.

This review will deal with the principles, limitations, advantages, and other *analytical characteristics* of thermometric analysis and will contrast the technique with competitive analytical methods such as potentiometry, amperometry, and spectrophotometry. Additional discussion of the methods and the principles involved in applying thermometric analysis for the determination of thermodynamic parameters such as equilibrium constants and reaction enthalpy and the measurement of rate parameters will be included.

There are a number of thermoanalytical techniques including thermogravimetry, differential thermal analysis, and differential scanning calorimetry[11,12] which will not be reviewed here. To be sure, these (especially DTA and DSC) are allied methods in that the measured variable derives from a reaction enthalpy or a change in heat capacity. However, these methods are most frequently applied to the analysis of solid materials and to the measurement of properties of the sample over a wide range of temperature. Thermometric titrimetry and DIE are frequently carried out under almost isothermal conditions, the temperature excursion rarely exceeding a few tenths of a degree Centigrade.

No attempt will be made in this review to survey the recent literature comprehensively. The interested reader should see Zenchelsky's exhaustive review[13] of the literature through 1960. Jordan,[14] Tyrrell and Beezer,[15] and Barks and Barks[16] have reviewed the analytical literature through 1968. Reviews of the method by 3 major contributors to the field may be found in *Modern Titrimetry – A Treatise*[17] which is in press and in *Physical Methods in Advanced Inorganic Chemistry.*[18] In order to fulfill the stated purposes of these *Critical Reviews*, we will assume that the reader has at least a limited prior acquaintance with the methods described here and is familiar with the general aspects of the techniques.

A. General Discussion of the Measurement Potentialities of Thermometric Methods

Although thermometric methods are not without serious limitations, which will be discussed in detail later, they possess a variety of advantages over some of the more familiar electroanalytical and spectrochemical methods. These advantages are summarized below:

a. The nature of the solvent is virtually irrelevant.

b. The method can be applied to reactions of any type.

c. Data interpretation is generally simple.

d. The apparatus is simple and easily constructed.

Both electrochemical and spectrochemical techniques are limited by the solvent system. The mechanism by which the solvent produces this limitation depends, of course, on the technique used. As an example, most of the common solvents cannot be used in some region of the u.-v. absorption spectrum due to their intrinsic opacity.

Electrochemical methods, particularly those involving net charge transfer such as polarography, coulometry, and the familiar relaxation techniques, are not readily employed in nonaqueous solvents of low dielectric constant. This is related to the need for some inert, but conductive, electrolyte to reduce migration currents to negligible proportions and to decrease ohmic potential drops to reasonable levels. Other electrochemical methods, such as conductometry, cannot be used with any degree of precision in media containing high concentrations of inert electrolyte.

Thermometric measurements have been employed quite successfully in a wide variety of solvents including media of high and low dielectric constants (such as water and glacial acetic acid,[19,20] respectively) and in reasonably corrosive high-melting solvents such as fused salts.[21]

The only manner in which the solvent specifically affects thermometric methods is through the

TABLE 1

Heat Capacities of Some Common Organic Solvents Used in Non-aqueous Titrimetry

Solvent	Heat capacity[a] (cal/°C ml)
Acetic acid	0.52
Acetone	0.40
Acetonitrile	0.54
Benzene	0.37
Carbon tetrachloride	0.33
Chloroform	0.35
Ethanol	0.46
Ether	0.37
Pyridine	0.42

[a] At 25°C, computed from data in the *Handbook of Chemistry and Physics.*

heat capacity of the medium and through a change in the reaction enthalpy. Both of these effects are relatively trivial and never, of and by themselves, prohibit the use of the technique. In fact, thermometric titrations are frequently more easily carried out in non-aqueous organic solvents since the heat capacities (expressed in cal-deg^{-1}-l.) of these solvents are generally lower than that of water (see Table 1). Second, reaction enthalpies, particularly of acid-base reactions, are often, though not necessarily, larger in non-aqueous solvents. Both of these factors act to increase the magnitude of the temperature change and thus improve the sensitivity of the method. As the data of Tables 1 and 2 indicate, temperature changes in non-aqueous solvents are often 4 or more times as large as in aqueous solution.

Another important consideration is that of reaction type. A basic limitation of potentiometric redox titrations is that at least one of the couples must be reversible (though this can sometimes be circumvented by adding a trace of potential-mediating couple). This is, as pointed out by Meites,[22] not a serious problem in amperometric titrations since one can apply an "over" potential to force the kinetics of electron transfer. Clearly, this is not a consideration in thermometric work.

TABLE 2

Some Reaction Enthalpies in Aqueous and Non-aqueous Solvents

Reactant	Titrant	Solvent	Δ H(kcal/mol)
Ammonia	HCl	Water[a]	-12.5
	HCl	Methanol[a]	-17.7
	HBr	Acetonitrile[b]	-25.0
	HClO$_4$	Acetic Acid[b]	- 7.2
Pyridine	HCl	Water[a]	- 5.0
	Methane-sulfonic acid	Nitrobenzene[c]	-17.1
	HBr	Acetonitrile[b]	-14.4
	HClO$_4$	Acetic Acid[d]	- 8.0
Aniline	HCl	Water[a]	- 6.8
	HCl	Methanol[a]	-10.0
	HBr	Acetonitrile[b]	-14.9
	HClO$_4$	Acetic acid[d]	- 7.8

[a] Landolt, H., and Bornstein, R., *Numerical Data and Functional Relationships in Science and Technology*, 6th ed., II. Band, 4. Teil, Springer-Verlag, New York, 1961.

[b] Forman, E. J. and Hume, D. N., *J. Phys. Chem.*, 63, 1949 (1959); *Talanta*, 11, 129 (1964).

[c] Brown, H. C. and Holmes, R. R., *J. Amer. Chem. Soc.*, 77, 1727 (1955).

[d] Reference 19.

[e] Adapted from Reference 15 by permission of the copyright owner.

TABLE 3

Survey of the "Reaction Types" Used in Thermometric Titrimetry

Reaction type	Typical reaction system
1. Inorganic	
a. Acid-base (water)	Any acid with $pK_a \leqslant 9$ to 10 Any base with $pK_b \leqslant 9$ to 10
b. Precipitation	Silver precipitates (AgCl, AgBr, AgI, AgCN) Oxalates (CaC_2O_4, $Sn\,C_2O_4$, $Ba\,C_2O_4$ $Hg_2C_2O_4$, HgC_2O_4) Carbonates ($PbCO_3$, Ag_2CO_3, $ZnCO_3$, $CuCO_3$, $Al_2(CO_3)_3$) Tetraphenylborates ($K\phi_4B$, $Tl\phi_4B$, $NH_4\phi_4B$) Tetraphenylantimonium, -phosphonium and -arsonium salts (ϕ_4SbClO_4, ϕ_4PClO_4, ϕ_4AsClO_4)
c. Complexation	EDTA (Ca^{2+}, Ni^{2+}, Cu^{2+}, Cd^{2+}, Zn^{2+}, Ba^{2+}, Ag^+, Co^{3+}, Ce^{4+}, Sn^{4+}, Al^{3+}, . . .)
d. Redox	Fe(II) – MnO_4^-, UO^{++} - $Cr_2O_7^=$, Ce^{4+} - I^-, Ce^{4+} - $SO_3^=$, Ce^{4+} - $S_2O_3^=$, Ce^{4+} - Fe^{2+}, Ce^{4+} - Sn^{2+}, etc.
2. Organic	
a. Non-aqueous acid-base	"Very" weak acids and bases in appropriate solvents
b. Oximation	Aliphatic carbonyl compounds
c. Hypochlorite oxidation	Sulfonamides
d. Diazotization	Aromatic amines and sulfa drugs
e. Phenol coupling	Most mono and di substituted phenols and naphthols
f. Addition reactions	ICl-olefins, bisulfite addition to carbonyls
3. Macromolecular and Biochemical	
a. Acid-base	Proteins
b. Precipitin formation	Antigen-antibody reactions
c. Oximation	End-group determintion of free carbonyl groups of polymers

Conductometric methods generally cannot be applied to redox or chelometric reactions since such reactions are usually carried out in buffers and other high ionic strength media. Similarly photometry is difficult to apply to precipitation titrations. Table 3 summarizes a wide variety of reaction types including those of classical inorganic analysis and a number of "organic" reactions which have been used or studied by thermometric methods. The major limitations placed on thermometric measurements by the chemical reaction are

a. The reaction enthalpy and solubility of the unknown must be such as to produce an easily measured temperature change. In general, with current instrumentation, temperature changes of 0.1°C can be measured with a precision better than 0.5% under ideal circumstances. Assuming water to be the reaction medium, the temperature change may be expressed as:

$$\Delta T \cong \Delta H \cdot c \qquad (1)$$

where ΔT is in °C, ΔH is in kcal/mol and the concentration c of the substance being titrated is expressed in mol/l. Consequently, to produce an 0.1°C temperature change from an 0.01 M solution the reaction enthalpy must exceed 10 kcal/mol.

b. The added reagent (the titrant) must be about 100 times as soluble as the unknown, so that mismatch in the temperatures of the sample and titrant will cause minimal errors and also to minimize changes in heat capacity.

c. The reaction must proceed to completion in a time period which is short compared to the rate of heat loss from the calorimetric vessel and to the rate of addition of titrant. This restriction will be discussed in detail later.

d. If the process is carried out by titration, the equilibrium constant must be such that 99.9% completion is achieved with a modest (25 to 50%) excess of titrant.

Obviously the fourth restriction is common to all linear titration methods and is not restricted solely to thermometric titrimetry. Some of the more common analytical reagents which have been used in thermometric titrimetry are sodium hydroxide, hydrochloric acid, silver nitrate, sodium tetraphenylborate, sodium ethylenediaminetetraacetate (EDTA), potassium permanganate, sodium thiosulfate, potassium dichromate, and ceric sulfate. Each of these reagents is sufficiently soluble to be rather useful as a titrant. In addition, each of these reagents reacts with sufficient heat to produce large temperature changes (> 0.05°C) with 10 mM solutions of many unknowns.

A third factor of considerable importance is the ease of data reduction. Obviously thermometric titrations can be used directly to measure the enthalpy of chemical reactions. Fundamentally this is based on the magnitude of the total temperature change since the total temperature excursion is small, i.e., ΔH is evaluated under virtually isothermal conditions. One need not be concerned with the temperature coefficient of ΔH due to a difference in heat capacities of reactant and products (ΔCp). Consider Kirchoff's well-known equation:

$$\frac{\partial \Delta H}{\partial T} = \Delta C_p \qquad (2)$$

Table 4 is a compilation of the heat capacities of some common species at 10 mM and higher concentrations in water at 25°C. It is clear that the effects due to Equation 2 are extremely small.

TABLE 4

Heat Capacities of Some Dilute Solutions at 25° C

Species	Concentration (mol/kg)	Heat capacity cal-g^{-1}-deg.C^{-1}
NaCl[a]	0.00	0.99890
	0.01	0.99869
	0.10	0.99698
	1.00	0.98940
	2.50	0.99632
HCl[b]	0.01	0.99860
	0.10	0.99590
NaOH[b]	0.01	0.99871
	0.10	0.99700

[a] Experimental results of Randall, M. and Rossini, F. D., *J. Amer. Chem. Soc.*, 51, 323, (1929).

[b] Computed from the partial molal heat capacities at infinite dilution, National Bureau of Standards, Circ. 500, 1952.

When reaction enthalpies are measured via the temperature dependences of equilibrium constants through van't Hoff isochore plots (Equation 3), such factors may not be negligible.

$$\frac{d \ln K^0_{eq}}{dT} = \frac{\Delta H^0}{RT^2} \qquad (3)$$

Second, the results may be confounded by spurious effects which can cause real differences between the calorimetric approach and the temperature-coefficient method; these include, among others, the temperature coefficients of the dielectric constant, the activity coefficients, the liquid-junction potential, and the reaction enthalpy itself (see Equation 2).

Equilibrium constants, and therefore Gibbs free energy changes, may be calculated by calorimetric means based on the equation:

$$\Delta G^0 = - RT \ln K^0_{eq} \qquad (4)$$

In order to obtain K^0_{eq} it is necessary to measure the heat production as a function of the concentration of 1 or more reactants. A large number of such studies have been carried out, particularly by Izatt, Christensen, and co-workers (for a discussion of their work see References 17 and 18).

Calorimetric methods offer a reasonably simple and virtually universal approach to the measurement of small and moderately large equilibrium constants. Data interpretation is simple since one is generally dealing with a small number of reactions. The number of unknowns is equal only to the sum of the numbers of reaction enthalpies and equilibrium constants involved. This is in marked contrast to absorption measurements, wherein the number of unknowns is increased by the necessity of measuring the extinction coefficients of all of the species that may absorb light. Furthermore, if the measurements are carried out at more than 1 wavelength, these extinction coefficients must be measured at each wavelength. Similarly, equilibrium constants computed from electrode potentials are seriously encumbered by the presence of liquid-junction potentials. Conductometric methods require the measurement of the conductivities of all ionic species present.

It is entirely possible to measure the rates of chemical reactions by thermochemical means. In fact, a major application of the method has been to the measurement of the rates of biochemical processes. With conventional equipment, reactions whose half-lives are greater than 10 sec, but less than 30 min[23] are easily measured. For slower processes, more sophisticated equipment such as differential calorimeters[24,25] or highly adiabatic systems are required. Faster reactions, with half-lives as small as 50 ms, can be measured by stopped flow calorimetry.[26]

As will be shown later, the instrumentation involved in thermometric titrimetry is quite simple and is readily available or constructed. The reader is referred to the section on instrumentation for further details.

II. THEORY OF THERMAL EFFECTS

This section of the review deals with those physical and chemical phenomena which have no importance in other classical titration methods but are essential to an understanding of thermochemical methods. In order to concentrate our effort on these factors we will entirely disregard all chemical features of the technique which are not pertinent. Consequently it is assumed that the general titration reaction shown below is both complete ($K_{eq} = \infty$) and instantaneous ($k_f = \infty$).

$$A + T \underset{k_f}{\overset{k_b}{\rightleftharpoons}} A' + T' \qquad (5)$$

$$K_{eq} = \frac{C_{A'} \cdot C_{T'}}{C_A \cdot C_T} \qquad (6)$$

A. The Principal Effects and Idealized Titration Curves

The two factors that are by far the most important in thermoanalytical work are the relevant reaction enthalpies (ΔH_R, expressed henceforth for convenience in cal/mol) and the total initial effective heat capacity of the calorimetric system (C^0_p, cal/°C). C^0_p reflects contributions from the heat capacity of the analyte solution, the Dewar, and all inserts in the calorimeter.

When all innocuous and parasitic effects (see Tables 5 and 6) are absent, the entire temperature-time (or -volume) curve may be described by the following equations:

$$T = T_0 \qquad t \le 0 \qquad (7)$$

$$T = T_0 - \frac{\Delta H_R \bar{\rho} t}{C^0_p} \qquad 0 \le t \le t^* \qquad (8)$$

$$T = T_0 - \frac{\Delta H_R \bar{\rho} t^*}{C^0_p} \qquad t \ge t^* \qquad (9)$$

ΔH_R is the reaction enthalpy per mole of titrant (T). The equations are written so that an exothermic reaction ($\Delta H_R < 0$) causes an increase in temperature. The quantity $\bar{\rho}$ is the rate of titrant addition (mol/sec), t is time from the start of the buret, t* is the time at which a stoichiometrically equivalent amount of titrant is added, and T_0 is the initial temperature of the system. An idealized titration curve which follows Equations 7 to 9 is illustrated in Figure 1. It is obvious that the temperature change at the equivalence point (t*) is directly proportional to ΔH_R and inversely proportional to C°_p.

In order to simplify comparison of titration curves (T – t curves), the author has in the past found it very convenient to normalize all equations. In the present context the normalized parameters are

$$\overline{\Delta T} \equiv -\frac{(T - T_0)}{\Delta H_R \ \bar{\rho} t^*} C^0_p = \psi(T - T_0) \qquad (10)$$

$$f \equiv t/t^* \qquad (11)$$

Using the transformations implied by Equations 10 and 11 a normalized ideal thermometric titration curve is described by Equations 12 to 14.

$$\overline{\Delta T} = 0 \qquad f \le 0 \qquad (12)$$

$$\overline{\Delta T} = f \qquad 0 \le f \le 1 \qquad (13)$$

TABLE 5

Innocuous Effects on the Thermometric Titration Curve

Process	Mathematical representation of rate of heat generation	Comments
1. Mechanical or stirring	$w_1{}^a$ (a constant)	Always exothermic
2. Thermistor heating	$w_2{}^a$ (a constant)	Always exothermic
3. Evaporation	$w_3{}^a$ (a constant)	Endothermic if atmosphere is not saturated with vapor
4. Side reactions	$\Delta H_S \bar{\rho}$	Important only when titrant is on, may be either endo- or exothermic
5. Dilution	$\Delta H_D \bar{\rho}$	May be endo- or exothermic

[a] We will denote the sum of these 3 effects by w.

$$\overline{\Delta T} = 1 \qquad f \geq 1 \qquad (14)$$

The simplicity of these equations is the best demonstration of the utility of normalizing the temperature-time curve. Any deviations from ideality become quite obvious.

B. The Innocuous Effects

There are a number of factors that cause deviations from the ideal equations but do not induce non-linearity on the temperature-time curve. These innocuous effects are summarized in Table 5.

1. Stirring of the solution, which is mandated by the continuous addition of reagent and the necessity for thermal homogeneity, always acts to increase the temperature of the solution. Although this effect is constant throughout the entire titration, it has considerable nuisance value particularly in small calorimeters (1-3 ml) or when the total heat of reaction is small. It is denoted by w_1.

TABLE 6

Parasitic Effects on the Thermometric Titration Curve

Process	Mathematical representation	Comments
1. Increase in heat capacity	$\Delta C_p = c_p \dot{m} t$	Assumes additivity of heat capacity
2. Mixing of non-isothermal solutions (temperature mismatch)	$\dot{Q} = c_p \dot{m}(T - T_\tau)^a$	Exothermic when $T_\tau > T$
3. Heat transfer (poor adiabaticity)	$\dot{Q} = k(T - T_E)^b$	Exothermic when $T_E > T$

[a] T_τ is the temperature of the titrant solution.
[b] T_E is the temperature of the calorimeter's environment.

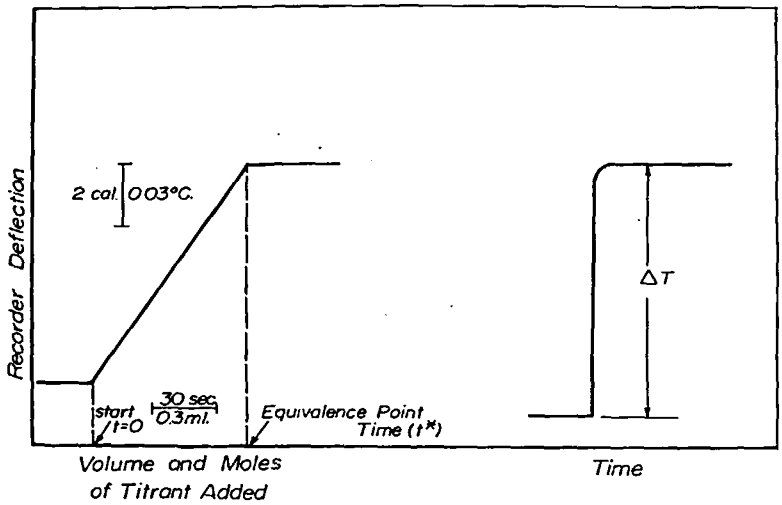


FIGURE 1. A schematic ideal thermometric titration curve indicating the basis of thermochemical analysis: (a) titrimetric analysis and (b) enthalpimetric analysis.

2. A second source of continuous heating of the solution is the thermistor used as a temperature sensor. In normal operation a thermistor is subjected to a continuous direct voltage E_T. Therefore it generates heat in accord with Equation 15.

$$\frac{d\Delta T}{dt} = \frac{1}{4.186}\frac{1}{C_p^0}\frac{E_T^2}{R_T} \qquad (15)$$

R_T is the resistance of the thermistor in the test solution. A 2,000-ohm thermistor with 1 V imposed will increase the temperature of 100 ml of solution at a rate of about 1.2×10^{-6} °C/sec. However, in a small Dewar (2 ml) the rate of increase of temperature will be 6×10^{-5} °C/sec. In a few minutes this may amount to a significant fraction of the total observed temperature change. This effect termed w_2 is generally much smaller than mechanical heating.

3. Unless the calorimeter is sealed, which is seldom the case, the solution will be cooled by continuous evaporation of the solvent. With aqueous solutions at room temperature this effect is entirely negligible; however, it can be serious with low-boiling organic solvents or even with water at high temperature. Since temperature changes are small (~0.1°C), the vapor pressure is essentially constant and, therefore, this effect is constant.

4. Another source of heat is due to the dilution of the titrant. Quite generally the titrant solution is more concentrated than 1 molar and is diluted by a factor of more than 100 over the course of the titration. To a *first approximation* the rate of heat addition may be represented by

$$\dot{Q} = \Delta H_D \bar{\rho} \qquad (16)$$

This is, however, a fiction in that the integral heat of dilution ΔH_D is a very strong function of the initial and final concentrations of the material being diluted. This effect is treated in greater detail in another section; however, the data of Table 7 may be used to *approximate* the heat generated when a 1 M solution of the indicated material is diluted to infinite dilution. It is important to note that addition of organic solvents

TABLE 7

Heat of Dilution of Some Common Aqueous Solutions from 1 M to Infinite Dilution

Solution	Heat of dilution (cal/mol)
NaOH	71[a]
HCl	405[a]
NaCl	-24.5[b]

[a] Interpolated from the data presented by Sturtevant, J. M., *J. Amer. Chem. Soc.*, 62, 584, 2276, 3265 (1940); 64, 762 (1942).

[b] Parker, V. B., Thermal Properties of Aqueous Uni-univalent Electrolytes, NSRDS – NBS2.

to aqueous solutions can produce extremely large temperature changes.

5. Side reactions of the titrant solution can supply considerable heat. For example, it is frequently necessary to prepare a titrant in an appropriate buffer, whereas the unknown is contained in a second buffer. As the titrant is added it reacts with the unknown, but the 2 buffer systems will also react to generate heat. This problem is occasionally very serious; however, in our experience one can frequently take rather straightforward measures to eliminate it. As an example, acetate buffers can be added to solutions of mineral acid with impunity, since the heat of protontion is very small (roughly +0.01 ± 0.01 kcal/mol).[27] The rate of heat generation due to side reactions (Q_S) is represented as

$$\dot{Q}_S = \Delta H_S \bar{\rho} \tag{17}$$

C. The Parasitic Effects

In addition to the above rather trivial factors, there are 3 factors which tend to cause *non-linear* deviations from the ideal situation (Equations 12 to 14).

1. The first of these processes is incomplete or poor adiabaticity. Whenever a temperature gradient exists across a boundary heat must be transferred at some finite rate. In general, heat transfer will follow Fourier's law:

$$\frac{\partial T}{\partial t} = K \Delta^2 T \tag{18}$$

Clearly, the temperature-time equation resulting from a complete analysis is quite complicated and dependent upon the geometry of the boundary. However, a Dewar flask is intentionally designed to minimize such heat transfer. Under appropriate conditions, namely when the gradient and heat transfer coefficient are both small, the overall process can be represented quite accurately by Newton's law of cooling:

$$\frac{d\Delta T}{dt} = -\frac{k}{C_p^0}(T - T_E) \tag{19}$$

The validity of this approximation rests more upon the design of the calorimeter than upon any theoretical foundation.[28] In the above equation k/C^o_p is referred to as the heat-transfer modulus, T is the internal temperature of the calorimeter, and T_E is the temperature of the environment surrounding the calorimeter. A necessary and sufficient condition for Equation 19 to hold is that k be independent of time. In general, k will show some time dependence; however, with modern equipment such as the Dewar of Christensen, Izatt, and Hansen,[29] k becomes constant within 3 sec. In actual practice rather crude calorimeters, such as ordinary thin-walled scientific Dewars or commercial thermos bottles, may be employed for analytical work provided that the duration of the experiment is restricted to a few hundred sec. The validity of Equation 19 is also dependent upon the magnitude of the thermal "head" or gradient ($T - T_E$). A more precise description of the temperature-time curve would be provided by taking higher-order terms into Equation 19, but these terms are negligible when the thermal head is small. Consequently, with poor Dewars the magnitude of the temperature change must be restricted to a few tenths degrees Centigrade. In practice, such small temperature changes are easily measured.

2. A second non-linear effect is related to the continuous addition of titrant. Assuming that the titrant acts to increase the heat capacity of the system at a rate $C_p\dot{m}$ where C_p is the heat capacity of the titrant (in cal/gm °C) and $\dot{m}$ is the mass rate of addition of titrant (g/sec), then during the period when titrant is being added the total heat capacity is given by Equation 20.

$$C_p(t) = C_p^0 + C_p\dot{m}t \tag{20}$$

This implies that the partial molar heat capacities of the 2 solutions are independent of concentration. Similarly, if the titrant and analyte solutions are not at the same temperature, it follows that the analyte temperature will change according to

$$\frac{d\Delta T}{dt} = -\frac{C_p\dot{m}(T - T_\tau)}{C_p^0 + C_p\dot{m}t} \tag{21}$$

where T_τ is the temperature of the titrant; all the other terms have been defined previously.

D. Equations of Chemical Ideal Titration Curves

Enough background material has been presented to permit the development of the complete equation for a chemically ideal titration curve. This requires that all of the above effects be appropriately superimposed.

While the computation from this point may seem very straightforward, the results in the literature are very much at odds with 1 another. One entirely rigorous approach is to write

$$\frac{dT}{dt} = -\frac{1}{C_p(t)} \sum \frac{dQ}{dt} \qquad (22)$$

where $C_p(t)$ is the time-dependent heat capacity defined in Equation 20, and $\Sigma dQ/dt$ is the rate of generation of heat (in cal/sec) due to all of the processes discussed above. The instantaneous temperature of the system is then given by integration of Equation 22 subject to an appropriate initial condition. That is:

$$T(t) - T(0) = -\int_o^t \frac{1}{C_p(t)} \sum \frac{dQ}{dt} \, dt \qquad (23)$$

It is at this point that several non-rigorous equations have appeared. For example Jordan[14] carries out the integration by tacitly assuming heat capacity to be constant. Then, after the integration is completed, the time dependence of C_p is imposed. On the other hand, Keily and Hume[30] consider that the heat generated due to titrant – sample temperature mismatch is *simply* proportional to T_0 – T_τ instead of to the instantaneous temperature difference.

We have arrived at the same equation as Christensen et al.[31] by a series of steps, some of which differ from the original derivation. From Equations 20 and 22 we may write that

$$(C_p^0 + C_p\dot{m}t) \frac{dT}{dt} = w + k\ (T_0 - T)$$
$$+ C_p\dot{m}\ (T_\tau - T) + \frac{dq_R}{dt} \qquad (24)$$

The integral of the right-hand side of Equation 24 is recognized as the total heat (Q) added to the Dewar by all heat sources:

$$Q = \int_o^t w + k\ (T_0 - T)\ dt$$
$$+ C_p\dot{m} \int_o^t (T_\tau - T)\ dt + \int_o^t \frac{dq_R}{dt}\, dt \qquad (25)$$

It should be clear that Q is also equal to the integral of the left-hand side of Equation 24, which can be shown by integration by parts to be given by

$$Q = \int_o^t (C_p^0 + C_p\dot{m}t) \frac{dT}{dt}\, dt \qquad (26)$$

$$Q = (C_p^0 + C_p\dot{m}t)\ [T - T_0] + C_p\dot{m} \int_o^t (T - T_0) \qquad (27)$$

Equating these expressions for Q yields

$$(C_p^0 + C_p\dot{m}t)\ [T - T_0] - C_p\dot{m} \int_o^t (T - T_0)\ dt$$

$$= \int_o^t w + k\ (T_0 - T)\ dt$$
$$+ C_p\dot{m} \int_o^t (T_\tau - T)\ dt + \int_o^t \frac{dq_R}{dt}\, dt \qquad (28)$$

After cancelling identical terms we arrive at

$$[C_p^0 + C_p\dot{m}t]\ (T - T_0) = \int_o^t w + k\ (T_0 - T)\ dt$$
$$+ C_p\dot{m}\ (T_\tau - T_0)\ t + \int_o^t \frac{dq_R}{dt}\, dt \qquad (29)$$

which is identical with the final equation of Christensen et al. with the exception of some differences in notation.

When the heat capacity of the system is not a linear function of time, which occurs when the partial molal heat capacities depend very strongly upon concentration, then Equation 20 and Equations 24 through 29 would have to be modified. As is indicated by the data of Table 4, however, the heat capacities of dilute (<1 M) aqueous solutions are close to the heat capacity of water, and consequently the heat capacities are to a first approximation additive.

Because of the presence of discontinuities in the titration process, such as the start of the buret and the abrupt cessation of heat generation at the equivalence point, it is convenient to divide the *titration curve into three distinct regions. It should* be noted that we are now proceeding along the lines of Barthel, Becker, and Schmahl,[32-34] who were the first authors to carry out this type of analysis; these regions will be referred to as:

1. The Fore Period
2. The Reaction Period
3. The Post Period

E. The Fore Period

This is the simplest segment of the titration curve since the only active processes are constant heating and heat transfer. Thus

$$\frac{dT}{dt} = -\frac{w + k\ (T - T_E)}{C_p^0} \qquad (30)$$

Integrating this equation with respect to time and imposing $T = T_0$ as an initial condition yields the following result:

$$T - T_0 = (T_E - T_0 - \frac{w}{k}) \left[1 - \exp - \frac{kt}{C_p^0}\right] \qquad (31)$$

In general, $kt/C^0{}_p$ is sufficiently small that the exponential function may be represented using only the first term of a Maclaurin expansion. In practice, linear base lines are observed as long as the thermal head is small (<1°C).

F. The Reaction Period

During this segment of the curve all of the aforementioned processes are operative, and the differential equation for heat generation is

$$-\frac{dT}{dt}=\frac{k(T-T_E)+C_p\dot{m}(T-T_\tau)+w+\Delta H_R\bar{\rho}+\Delta H_D\bar{\rho}}{C_p^0+C_p\dot{m}t} \qquad (32)$$

This may be integrated subject to the condition that the initial temperature is T_0 to yield

$$T-T_0=\left[\frac{kT_E+C_p\dot{m}T_\tau-w-\bar{\rho}(\Delta H_R+\Delta H_D)-T_0}{k+C_p\dot{m}}\right]$$

$$\left\{1-\left(\frac{C_p^0}{C_p^0+C_p\dot{m}t}\right)^{(1+k/C_p\dot{m})}\right\} \qquad (33)$$

There are several interesting limiting forms of Equation 33. When k approaches zero the equation becomes

$$T-T_0=\left[\frac{C_p\dot{m}T_\tau-w-\bar{\rho}(\Delta H_R+\Delta H_D)}{C_p\dot{m}}-T_0\right]$$

$$\times\left[1-\left(\frac{C_p^0}{C_p^0+C_p\dot{m}t}\right)\right] \qquad (34)$$

Clearly the temperature-time curve is not precisely linear. The limit of Equation 33 as $c_p\dot{m}$ approaches zero may be obtained by application of l'Hopital's rule; the result is

$$T-T_0=\left[\frac{kT_E-w-\bar{\rho}(\Delta H_R+\Delta H_D)}{k}-T_0\right]$$

$$\times\left(1-\exp-\frac{kt}{C_p^0}\right) \qquad (35)$$

Once again a nonlinear equation is obtained. The limiting form of Equation 35 as k approaches zero may be obtained by expanding the equation in a Maclaurin series and then letting k become small. This results in

$$T-T_0=\left[\frac{-w-\bar{\rho}(\Delta H_R+\Delta H_D)}{C_p^0}\right]t \qquad (36)$$

It should be apparent at this point that thermometric titrations would be perfectly linear if it were not for the imperfect adiabaticity of the calorimeter and the effects related to addition of the titrant.

G. The Post Period

Due to the assumption of complete reaction the heat generated by Reaction 1 stops abruptly at t = t*; however, all the other processes active in the preceding time period are still operative and consequently

$$\frac{dT}{dt}=-\frac{w+k(T-T_E)+C_p\dot{m}(T-T_\tau)+\Delta H_D\bar{\rho}}{C_p^0+C_p\dot{m}t} \qquad (37)$$

This equation may be integrated subject to the conditions that T = T* and $C_p(t) = C^*_p$ at t = t*.

$$T-T^*=\left[\frac{kT_E+C_p\dot{m}T_\tau-w-\Delta H_D\bar{\rho}}{k+C_p\dot{m}}-T^*\right]$$

$$\times\left[1-\left(\frac{C_p^*}{C_p^0+C_p\dot{m}t}\right)^{(1+k/C_p\dot{m})}\right] \qquad (38)$$

There are 3 interesting limiting forms of Equation 38. These occur when k = 0, when $C_p\dot{m}$ = 0, and when both k and $C_p\dot{m}$ are zero. These limits were obtained in the same fashion as those of Equation 33.

When k = 0 but $C_p\dot{m}$ is finite:

$$T-T^*=\left[\frac{C_p\dot{m}T_\tau-w-\Delta H_R\bar{\rho}}{C_p\dot{m}}-T^*\right]$$

$$\times\left[1-\left(\frac{C_p^*}{C_p^0+C_p\dot{m}t}\right)\right] \qquad (39)$$

When $C_p\dot{m}$ = 0, but k is finite:

$$T-T^*=\left(\frac{kT_E-w-\Delta H_D\bar{\rho}}{k}-T^*\right)$$

$$\times\left[1-\exp\left(-\frac{k(t-t^*)}{C_p^0}\right)\right] \qquad (40)$$

When both k and $C_p\dot{m}$ are zero:

$$T-T^*=-\left(\frac{w+\Delta H_D\bar{\rho}}{C_p^0}\right)(t-t^*) \qquad (41)$$

H. Normalization of the Temperature-Time Curve

Equations 30 to 41 may be normalized by use of Equations 10 and 11. The results of this process are presented in Table 8. After normalization one finds it useful to define a number of dimensionless parameters

$$\Omega=\frac{w}{\Delta H_R\bar{\rho}t^*} \qquad (42)$$

TABLE 8

Equations for Normalized Temperature-Time Curves[a]

$\overline{\Delta T}_1 = \left[(T_E - T^0)\ \psi + \frac{\Omega}{\kappa}\right]\left[1 - \exp(-\kappa f)\right]$	$f \leq 0$
$\overline{\Delta T}_2 = \left[(T_E - T_0)\ \psi + \frac{\Omega + 1 + \Delta H_D\ \psi}{\kappa + \phi}\right](1 - (1 + \phi f)^{-(1 + \kappa/\phi)})$	$0 \leq f \leq 1$
$\overline{\Delta T}_3 = (T^* - T_0)\ \psi + \left[(T_E - T_0)\ \psi + \frac{\Omega + \Delta H_D\ \psi}{\kappa + \phi}\right]\left(1 - \left(\frac{(1 + \phi f)}{(1 + \phi)}\right)^{-(1 + \kappa/\phi)}\right)$	$f \geq 1$

[a]With $T_E = T_\tau$

$$\kappa = \frac{k}{C_p^0} t^* \tag{43}$$

$$\phi = \frac{C_p \dot{m} t^*}{C_p^0} \tag{44}$$

Using the above approach normalized temperature-time curves may be computed. Figure 2 is a schematic example. The net result of an analysis of the data indicates that the dimensionless parameters ϕ and κ are responsible for errors in both calorimetric and analytical measurements unless specific correction factors are employed. Results of these computations will be presented in appropriate sections.

III. INSTRUMENTATION FOR THERMOMETRIC TITRIMETRY

A. Introduction

The essential equipment for thermometric titrimetry is relatively simple in comparison to the sophisticated apparatus encountered in electrochemical and spectrochemical analysis. The devices fall into 4 categories:

a. Temperature transducers such as thermocouples and thermistors,

b. Associated circuitry such as Wheatstone bridges and recorders,

c. Calorimetric vessels and thermostats, and

d. Ancillary equipment for calibration and automatic determination of end-point times.

Thermometric titrations can be, and are, carried out with very crude adiabatic systems. Indeed the general utility of thermometric titrimetry as an analytical method would be greatly diminished if very delicate and cumbersome calorimeters were essential. However, simple apparatus is employed only in those instances where the titration reaction is complete and rapid; more sophisticated apparatus becomes important when dealing with sluggish or highly incomplete reactions.

B. Temperature Transducers

Thermometric titrations place very stringent demands upon the nature of the temperature transducer. The earliest thermometric titration, reported by Bell and Cowell,[35] was carried out with a mercury-in-glass thermometer and by manual discontinuous addition of the titrant. Under these conditions rather large temperature changes were required in order to provide adequate precision. The time scale of such titrations was quite long and was fixed by the thermal equilibration and reading time of the thermometer. Obviously an automatic titrator requires use of a small, fast, sensitive temperature transducer of low-thermal-mass. These considerations rule out the use of many common detectors including gas, radiometric (pyrometers), and liquid-in-glass thermometers. There are 3 major types of temperature transducers which may be used: quartz thermometers, thermocouples, and resistance thermometers. Of these 3 types, it is the resistance thermometers that have been used most extensively.

The use of quartz thermometers has not yet

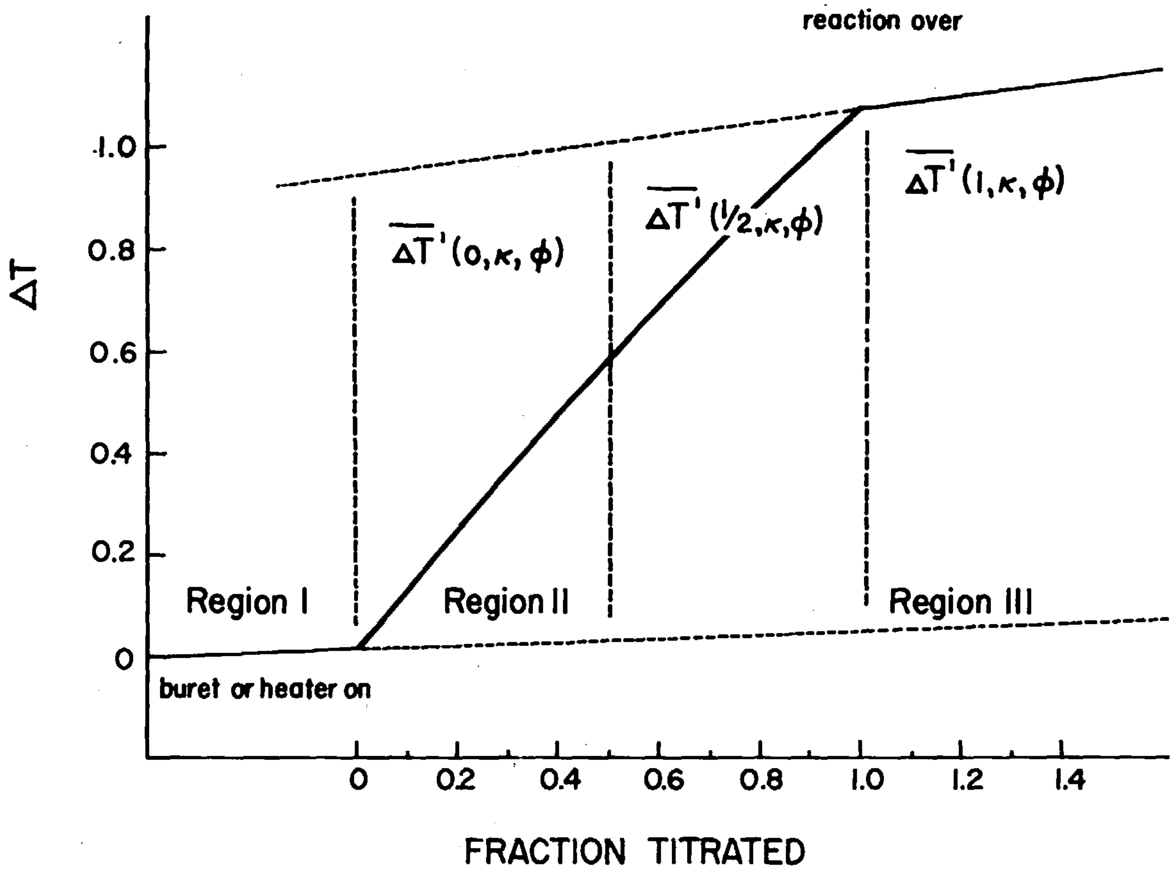


FIGURE 2. A schematic nonideal thermometric titration curve indicating the basis for heat measurement. Note the nonlinearity and inequality of fore and post slopes.

been reported in thermometric titrimetry. This transducer consists of a quartz piezoelectric resonator which is fabricated as a small ground crystal disc. Leads are attached to the crystal and an external ac signal is applied. The crystal acts as a very highly selective filter which locks the frequency of the a-c source to the natural frequency of the crystal, and it is cut in such a way that the temperature coefficient of its natural frequency is high and constant. For example, the natural frequency is 28,208 kHz, at 0°C and it increases at a rate of 1000 Hz/°C. Consequently, if a digital scaler is used to count the pulses produced in a given time period, the count rate may be calibrated in °C. According to the manufacturer's specifications probes of 0.5-g mass and heat leakage rates of 1×10^{-3} °C/sec are available. These values are sufficiently small to be useful in thermometric titrimetry. The temperature resolution is ±0.0001°C with a 10-sec counting time or ±0.001°C with a 1 sec count time. Other important specifications are listed in Table 9. The major drawback of the device is its high price.

The use of thermocouples as temperature transducers in thermometric titrimetry is limited by 2 features of such devices. One is that their intrinsic sensitivity (that is, their response to a change in temperature, which is referred to as the thermoelectric power) is quite small; the other is that measurements with thermocouples are invariably difference measurements. Consider the first of these factors. One of the most sensitive thermocouple pairs available is the Chromel P-Constantan junction. This has a sensitivity of 60 μV/°C. Thermistors commonly provide a signal of 10 mV/°C. Thus it would be necessary to prepare a 160-junction thermopile to match the intrinsic sensitivity of the thermistor. This device would generally be cumbersome, fragile, and significantly larger than a thermistor. A second possibility would be the use of a high-gain amplifier in

TABLE 9

Specifications of a Commercial Quartz Thermometer

Calibration accuracy (from factory)	±0.02°C vs. NBS platinum resistance thermometer
Linearity	Over 0 – 100°C: ±0.05°C Over any 10°C range: ±0.002°C
Stability	±0.0001°C (short-term) ±0.01°C (30 days)
Hysteresis	-80 to 250°C: ±0.05°C Over any 10°C range: 0.002°C
Sensitivity to ambient temperature changes	±0.002°C/°C room temperature
Display	Digital or analog

conjunction with a single or reasonably sized multiple-junction thermocouple. Clearly, any signal amplification could also be used in conjunction with a thermistor.

The limiting factor in any measurement is, of course, the signal-to-noise ratio. These figures are not readily available for thermocouples and will depend upon the stability of the reference junction bath. The most convenient reference temperature for work around room temperature is, of course, the ice point. The triple point of water, which is a thermodynamically invariant temperature, is reproducible to ±0.0002°C. Presumably the temperature indicated by a thermocouple would show variations at approximately this level. If the temperature of the analyte solution changed by 0.1°C the ultimate resolution would be 0.2% of the full scale change. Meites et al.[24] have shown that a temperature resolution of about 20 μ°C can be obtained with a 100,000-ohm thermistor. If an ice bath were used as the reference junction for a thermocouple, then an 0.1°C change in solution temperature would amount to an 0.4% change in the net voltage. To measure such a change with 0.5% precision would require a net resolution of 1 part in 50,000.

All modern developments in thermometric titrimetry are due entirely to the use of the thermistor as a temperature transducer. This innovation was introduced by Linde, Rogers, and Hume[37] in a classic paper published in 1953. Metallic resistance thermometers, especially the platinum resistance thermometer, have been used for years as standards for the measurement of the absolute temperature of a material. Indeed, the platinum resistance thermometer is the basis of the International Temperature Scale between 0 and 630°C. The temperature coefficients of metal thermometers are small; for example, nickel and platinum resistors have temperature coefficients of 0.68% and 0.39% per °C, respectively. Even though the stability of the absolute resistance of a platinum thermometer far exceeds that of a thermistor, the temperature coefficient of an ordinary thermistor is 4 times as large as that of a nickel resistance thermometer. Consequently the thermistor has been almost universally adopted as the standard means of temperature measurement in thermometric titrimetry, since one is generally interested in a temperature change rather than the absolute temperature of a solution.

The resistance of a thermistor can be described most accurately[38] by an equation of the form:

$$R = \exp\left(A + \frac{B}{T + C}\right) = \exp A \cdot \exp\left[\frac{B}{(T + C)}\right] \qquad (45)$$

where A, B, and C are constants for a given thermistor. Since a thermistor is essentially a semiconductor, generally a sintered mixture of oxides such as $Ni_{0.6}Mn^{2+}_{0.4}Mn^{3+}_{2}O_4$, it has a negative temperature coefficient due to the increasing population of electrons in the conduction band as the temperature rises.

The 4 most important characteristics of a thermistor are its

a. temperature coefficient (β),
b. dissipation constant (δ),
c. thermal response time, and
d. long-term stability.

The temperature coefficient defined below is not, as indicated by Equation 45, independent of temperature; the linearity of a plot of R_T vs. T as computed from Equation 45 for ranges of 0.1°C and 1°C about 25°C is indicated in Table 10.

$$\beta \equiv 100 \frac{1}{R_T} \frac{dR_T}{dT} = 100 \frac{d(\ln R_T)}{dT} \qquad (46)$$

The terms of Equation 45 were estimated from the data of Robertson et al.[39] This table indicates a maximum deviation from linearity of about 0.24% over an interval of 0.1°C and 2.4% over one of 1°C. It should be noted that β generally increases with the size (in ohms) of the thermistor.

The dissipation constant of a thermistor, δ, is defined as the power (W) required to raise the internal temperature (T_{in}) of the thermistor over the temperature (T) of the fluid in which it is immersed. It is generally assigned units of mW/°C. In practice, δ varies with the thermistor

$$\delta \equiv \frac{W}{T_{in} - T} \qquad (47)$$

type (bead, rod, washer, etc.),[40] the mounting geometry lead length, and especially the fluid in which it is immersed and its rate of motion.[41] Figure 3 illustrates the effect of stirring on δ.[41] As will be shown, the dissipation constant is quite important in fixing the signal-to-noise ratio and, therefore, the temperature resolution of thermistors. In general, δ should be as large as possible consistent with the required thermal response time.

TABLE 10

Computed Percent Change in Thermistor Resistance vs. Temperature[a]

T(°C)	Percent change	T(°C)	Percent change
25.00	0.00000	25.10	-0.50502
25.01	-0.05063	25.20	-1.00727
25.02	-0.10122	25.30	-1.50677
25.03	-0.15179	25.40	-2.00354
25.04	-0.20234	25.50	-2.49758
25.05	-0.25285	25.60	-2.98863
25.06	-0.30334	25.70	-3.47758
25.07	-0.35381	25.80	-3.96356
25.08	-0.40424	25.90	-4.44688
25.09	-0.45464	26.00	-4.92757

[a] Computed from Equation 45 with B ≈ 4639, C = 186.11°K.

The third factor, the response time, is defined as the time required for the thermistor to register 63.2% of the total resistance change upon a sharp rise in temperature.[40] The response time is difficult to predict *a priori*, but it increases as δ increases and increases as the heat capacity of the thermistor increases. If a massive thermistor is used, the response time may be so long as to cause serious errors in both analytical and thermodynamic measurements. Since most thermometric titrations for analytical purposes are carried out on a time scale of 30 to 300 sec, the response time of the thermistor should be less than 1 sec.

The long-term stability of thermistors is a topic that has been debated hotly since their development. There is no question that a "green" thermistor is subject to aging. Recognition of this factor by most manufacturers has led to their preliminary annealing at about 100 to 130°C. However, there is evidence that an excessive annealing temperature will also cause drift. A second question is whether the thermistor should be subject to continuous application of a steady current as is the contention of several groups.[14,25] Meites et al.[24] have reported on the long-term stabilities (several months) of a reasonably large number of thermistors, which were found to show rather complex behavior for several weeks: usually the resistance increased, then decreased again, and eventually settled down to a constant value. These observations were made when the thermistor was subject to a constant power of several hundredths of a mW. The most definitive and large-scale study of drift was carried out by Robertson et al.[39] of the U.S. Geologic Survey. This group compared the stability of thermistors and a platinum resistance thermometer in a series of ice baths. The first study (40 days) showed a temperature fluctuation of ±0.003°C for the thermistor, but one of only ±0.0014°C for the platinum thermometer. However, most of the fluctuation was from bath to bath despite the smaller changes shown by the metal thermometer. They concluded that over their time period the thermistor was intrinsically reproducible to several hundred microdegrees. A 10-year study of several hundred thermistors in ice baths did show a secular drift in resistance. The time dependence was linear with a mean temperature coefficient of 3.8×10^{-3}°C/month. However, the drift was seriously dependent upon the thermistor history. Generally, they conclude that most of the drift is

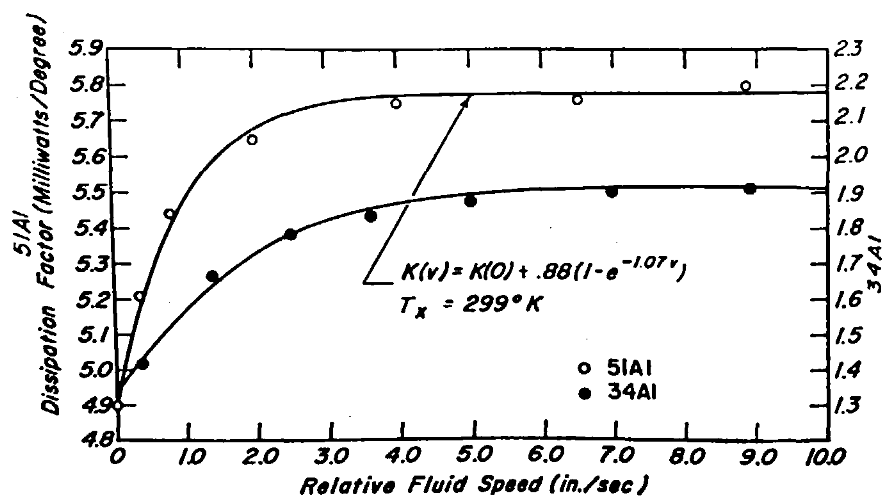


FIGURE 3. The effect of stirring on the dissipation constant of a thermistor (Reference 41, reprinted by courtesy of the copyright holder.)

due to changes in the connecting cable resistance and in the potting materials surrounding the thermistor. In contrast to the study of Meites,[24] their thermistors were not subject to the continuous passage of current. Nonetheless, it is clear that thermistors are highly reliable transducers for the measurement of absolute temperature to at least ±0.01°C over a period of several months. Indeed the remarkable long-term stability of a new constant temperature bath[43] (±0.001°C/week) indicates the reliability of the thermistor as a temperature-measuring device.

C. Adiabatic Titration Calorimeters

For many years the weakest link in the equipment used in titration calorimetry was the adiabatic flask employed. Such equipment limited the calorimetric accuracy to 1 to 2%. However, the extremely simple but carefully engineered Dewar introduced by Christensen, Izatt, and Hansen[29] has eliminated this factor as a problem. Calorimetric accuracy of 0.1 to 0.2% is possible and commensurate with the accuracy of the recording equipment. The major design goals involved in constructing an adiabatic reaction calorimeter, of which the titration calorimeter is a specific type, have been enumerated by Sunner and Wadso[28] as:

1. The reaction involved should be reasonably fast. Sunner limited his considerations to reactions which were complete within 1 hr.

2. The total heat evolved should be 50 cal or less.

3. The accuracy should be 0.1% or 0.05 cal, whichever is greater.

4. The solution volume used should be about 100 ml.

5. The device must be simple in design and easy to operate.

These factors are pertinent to vessels built for calorimetric purposes. For analytical purposes several specifications may be relaxed while others become more significant. Calorimetric accuracy of 0.1% is seldom required in thermometric titrations, and precise control of the titrant and sample solution temperatures is virtually unnecessary. In addition, analytical systems should be inexpensive, be capable of analysis times of less than ten minutes, and provide for reproducible measurement of the volume of titrant added.

Sunner and Wadso studied the characteristics of a number of designs for the calorimetric vessel. Some of these are shown in Figure 4. The crudest system (A), which strongly resembles the Dewar used by Jordan and his co-workers, consists of a silvered Dewar flask fitted with an inner thin-walled glass shield. The major disadvantages of the device were its low calorimetric accuracy (0.5%) and, most important of all, its long thermal equilibration time (see Figure 5, curve a). It is important to note that the Dewar used by Jordan et al. is capable of high analytical accuracy (0.2 to

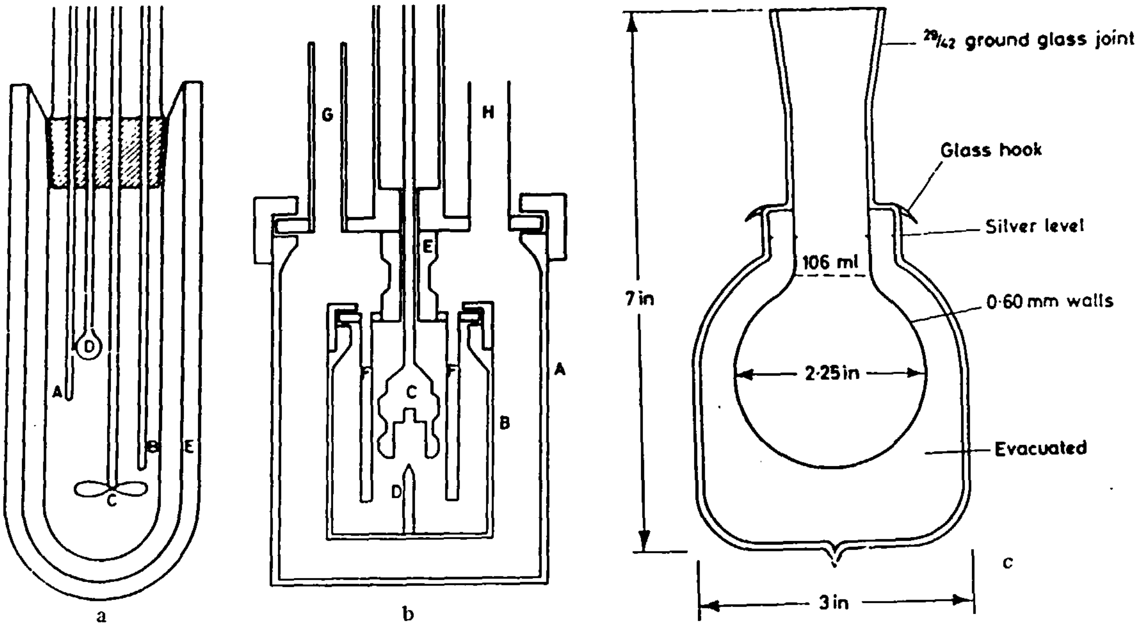


FIGURE 4. Some reaction calorimeters used in thermometric titrimetry: (a) and (b) (From Reference 28, reprinted by courtesy of the copyright holder), (c) (From Reference 29, reprinted by courtesy of the copyright holder.)

0.5%) despite its primitive adiabaticity. It is our experience that the usual thick-walled scientific Dewar is less satisfactory for rapid titrations than ordinary commercial thermos bottles which have thinner glass walls.

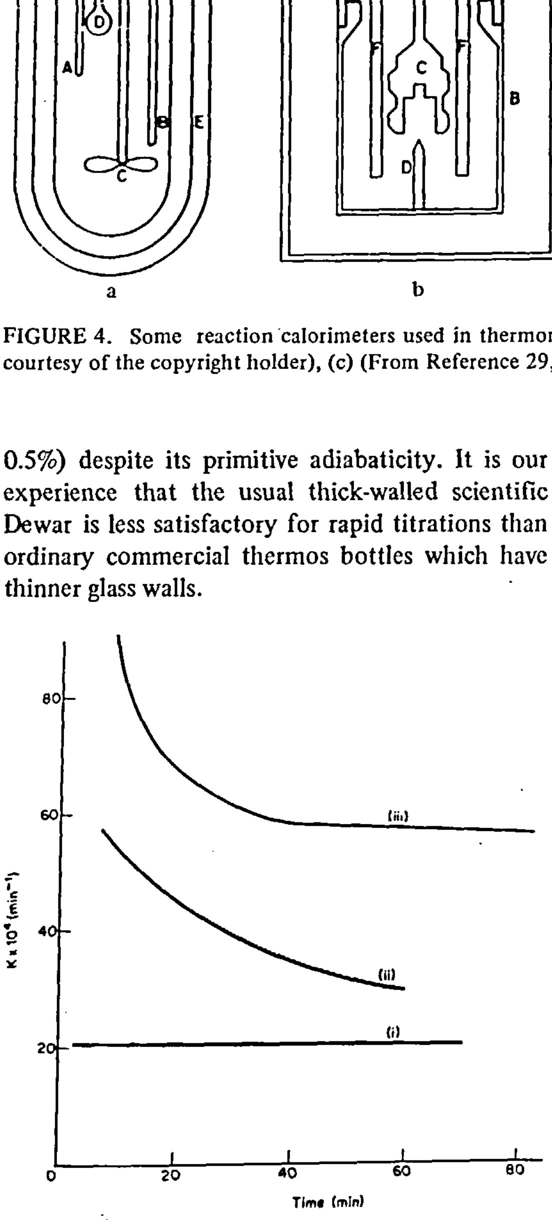


FIGURE 5. Time dependences of the heat-transfer coefficients for (i) calorimeter c (ii), calorimeter b, (iii) calorimeter a. (From Reference 15, reprinted by courtesy of Chapman and Hall.)

Sunner and Wadso found that the best Dewar is one which has a very short thermal equilibration time. Such factors as indeterminate boundaries and massive radiation shields act to introduce substantial thermal lags. The system finally adopted by them consists of a thin-walled (0.5 mm) brass can, silver-soldered to a brass lid which was chrome plated and sprayed with Teflon®. The calorimeter is fixed to a thin-walled glass tube (0.7 mm) by vacuum fittings. The space between the glass tube and the brass can is evacuated, and the entire assembly is placed in a thermostat. A system suitably modified for titration work is available from LKB Instrument Co.[42]

Most of the above criteria were adopted by Christensen et al.[29] in their novel calorimeter. It is our belief that improvement over their system will not be forthcoming for many years. Consider the following characteristics of this device. When filled with 100 cc of water, the entire system has a heat capacity of 103 cal/°C, a heat transfer modulus of 10^{-3} min^{-1}, and a thermal equilibration time of less than 3 sec. These goals were accomplished by using a spherical inner wall of very thin glass which was silvered and whose boundary with the outer wall was quite small. Due to the geometry and mass of the inner wall the ratio of volume to area is a minimum, thus providing a large heat capacity and small heat-transfer path. In addition, everything inserted into the Dewar has a low mass. This instrument is excellent in terms of both calorimetric and analytical work. This vessel and all necessary associated equipment are available from Tronac, Inc.[43]

A third commercially available titration calorimeter is the Titra Thermo Mat marketed by Aminco.[44] This is an analytical system and not a calorimeter. It is capable of reasonable analytical precision (approximately 1%), but its major virtue is its simplicity and extreme ease of operation. The author has used the instrument to carry out replicate titrations in 4 to 5 min. The adiabaticity of the system is poor (calorimetric accuracy about 5%), but the analytical characteristics suffice for many applications.

The Titra Thermo Mat has been adopted for microanalytical work. Volumes as small as 1 to 2 ml have been titrated with the device.[7] In fact, it is a major advantage of thermometric titrations that they are so much more easily scaled down to very small size than potentiometric or conductometric titrations. We have used small (about 8-ml) thin-walled cylindrical Dewars[45] which are magnetically stirred for titration purposes. Volumes as small as 2 ml are readily handled, and an analytical accuracy better than 1% can be obtained. For example, 3-ml samples of 12 mM potassium ion were titrated with tetraphenylborate. The accuracy and precision were both better than 1%, the accuracy being limited by the chemistry rather than by the thermometric system. To decrease sample sizes below 1 ml will require extensive investigation into the use of smaller thermistors as well as the development of more efficient stirring devices. As the system becomes smaller, heat losses and thermistor and mechanical warming of the solution become more important.

D. Thermostats

There are 2 schools of thought about the use of thermostats in thermometric titrimetry: the calorimetric and the analytical. There is no question that highly precise calorimetric measurements absolutely require very tight control of the titrant temperature, environment of the calorimeter, and the initial temperature of the sample solution. This is particularly true if the detailed shape of the temperature-time curve is to be used to compute equilibrium or rate constants. Measurements of reaction enthalpy by the extrapolation method (vide infra) essentially require that the temperature of the titrant and the environment remain constant during a run, but there is no need for the absolute measurement of these temperatures. Analytical measurements are readily carried out in a laboratory whose temperature is reasonably constant over the course of the titration. Rather precise analyses (0.2 to 0.5%) have been obtained by Jordan and co-workers without thermostating. There is no doubt that the use of thermostats does provide more reproducible curve shapes, but it has little effect on the end-point precision. For example, we have carried out titrations in small (8-ml) magnetically stirred Dewars which were left exposed to ambient conditions.

There appear to be 2 different approaches to the construction of thermostats for thermometric titrations. Christensen et al.[46] have constructed a water thermostat which, in conjunction with a proportional temperature controller, is capable of maintaining a thermostat at 25 ±0.003°C. This device is commercially available from Tronac. The thermostat of Sunner and Wadso also employs water as the fluid.[28]

The second approach is the use of an air bath as the controlled environment for the calorimeter. A photograph of the system used by us is shown in Figure 6. This instrument was built along the design of a system of Raffa, Stern, and Malspeis[47] and Papoff and Zambonin.[48] It employs a large fan, an air conditioner heat-transfer element for cooling, an on-off thermistor controller, and a 500-W incandescent lamp. In operation the system can control the temperature of the air to a constancy of ± 0.02 to 0.03 °C. The instrument has several advantages over water thermostats. First, samples are moved in and out of the thermostat in a matter of seconds. Second, due to the lower heat conduction of air, precise control of the thermostating fluid is not as important as with water thermostats. Third, in non-aqueous titrimetry where the presence of water is a problem, the thermostat is easily sealed and swept with dry nitrogen.

The above advantages of air thermostats are mainly analytical, not calorimetric. There is no question that the measurement of equilibrium constants and of reaction enthalpies requires very tight and reliable temperature control to at least ±0.005 to 0.01°C.

An excellent review of the design and con-

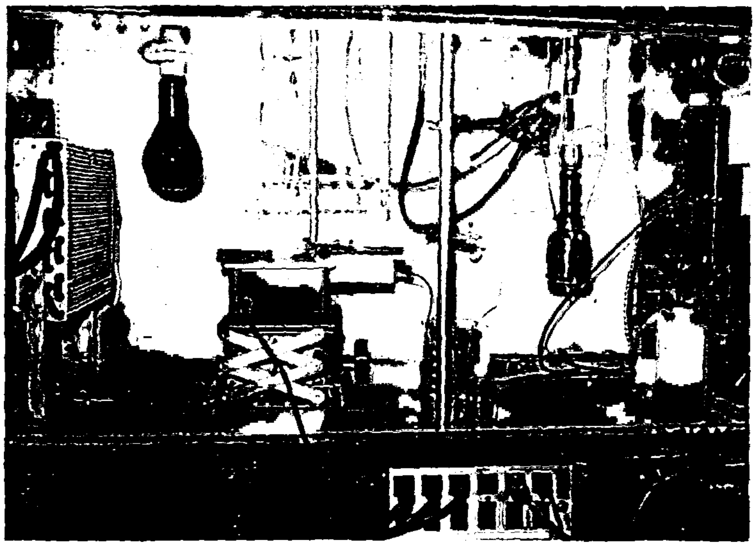


FIGURE 6. An air-bath calorimeter.

struction of thermostats has appeared recently.[49] The interested reader is referred to that source for detailed considerations of controller type, heat-transfer characteristics of the bath, thermal lag characteristics of the various elements in the bath, and other important features.

E. Ancillary Circuits and Automatic End-Point Indicators

Virtually all reaction calorimetry is directly traceable to electrical calibration and the use of the interrelationship between work and heat. The search for a suitable reference reaction continues to this day. Due to the problems involved in constructing accurate electrical calibration equipment such as heaters and leads, one should generally check out the equipment with a chemical system whose reaction enthalpy has been accurately established. For this purpose, one most commonly uses the heat of reaction of a strong acid (such as perchloric acid) with sodium hydroxide, which will be discussed in some detail in a later section of this review.[95] Fundamentally, a calorimeter is calibrated by passing a *constant current* through a standard resistor whose resistance (R_S) is known very accurately, and a resistor (R_H) immersed in the calorimeter. The voltage across each resistor is measured and the amount of heat delivered to the calorimeter is computed at

$$Q(\text{calories}) = \frac{I^2 R_H \cdot t}{4.186} = \frac{E_H \cdot E_S}{R_S \cdot 4.186} \cdot t \qquad (48)$$

where E_H and E_S are the measured voltage drops across the heater and standard resistor, respectively.

While most experimenters continue to use lead storage batteries as the power supply, we have found that a totally electronic supply is considerably more convenient since it never requires recharging, may be left on continuously, and thereby becomes very stable. A replicate of the system developed by Stern, Withnell, and Raffa[50] has been employed and found to be entirely suitable for highly precise (0.1%) calorimetric work. Both the calibration heater and power supply are shown in Figure 7. The power supply can be built in a few hours and it is well worth the effort to be able to avoid using the lead storage battery.

In conjunction with the calibration experiment, it is necessary to measure the time of heating. In order to carry out experiments in a minimum time (100 sec) and preserve experimental precision, a ±0.01-sec timer is required. We have found that the Hayden Switch Co. Model 42005 timer is a reasonably inexpensive solution to this problem.[51]

In addition to the above circuitry, it is often very convenient in analytical work to employ devices for automatic location of the end point. The most impressive apparatus for this purpose has been developed by Priestley.[52,53] The equipment has the following features:

a. The titration is very rapid, in most instances less than thirty sec.

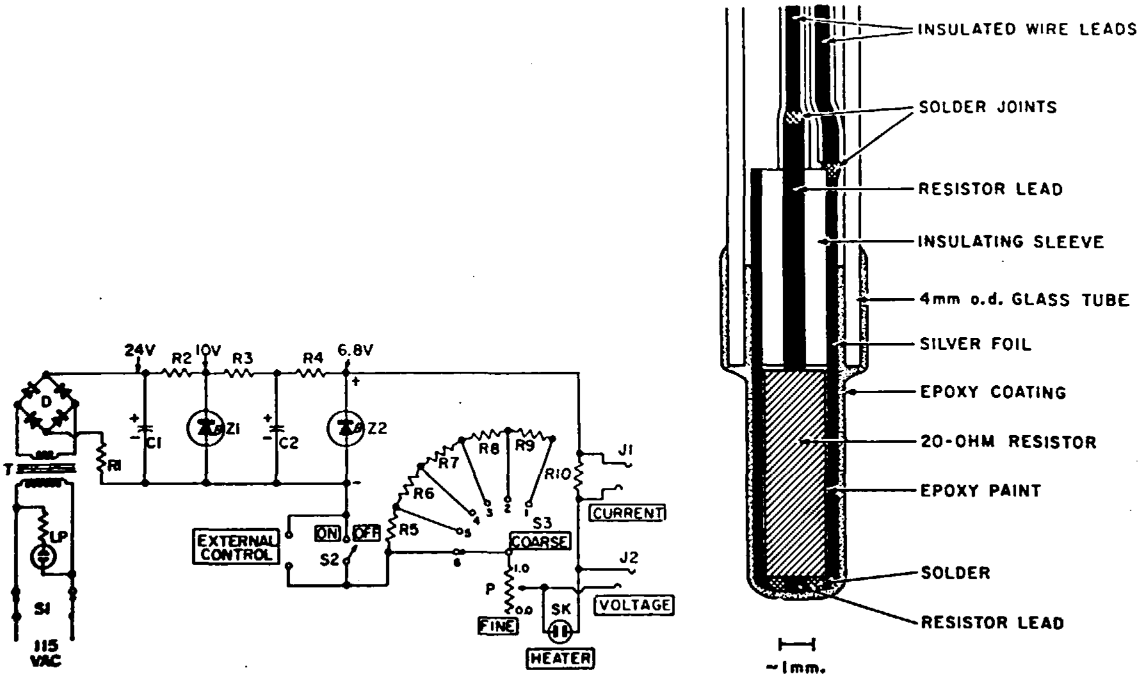


FIGURE 7. Power supply and electric calibration heater (From Reference 50, reprinted by courtesy of the copyright holder.)

b. The end point is located by differentiation of the titration curve.
c. Readout is automatic and digital.
d. The buret is refilled automatically.

In order to accomplish this degree of automation a high velocity buret and an extremely rapid mixer were developed and electronic amplification and differentiation of the temperature-time curve were implemented. A block diagram of the circuitry is shown in Figure 8, and Figure 9 is an illustration of the buret and titration vessel. As the data of Table 11 indicate, accuracy and precision better than 1% are routinely available. Since all such titrators are based upon a rapid decrease in slope as the end-point signal, they are seriously prone to premature end points whenever the reaction is appreciably incomplete in the region around the equivalence point. Thus, these instruments can only be used with high accuracy when the equilibrium constant and the rate of the chemical reaction are very high. When they are not, extrapolation of the temperature-time curve will generally yield more accurate, though not necessarily more precise, results. If automation is required it may be possible to calibrate the readout empirically by using standard solutions and relate the time measured for an unknown sample to the calibration curve.

F. Flow Calorimeters and Enthalpimetry

As has been pointed out several times in preceding sections of this review, exact matching or knowledge of the temperature of the titrant and sample solution is not necessary in thermometric titrations. Neither is it essential to provide for high calorimetric accuracy. However, in enthalpimetry where the magnitude of the temperature change is

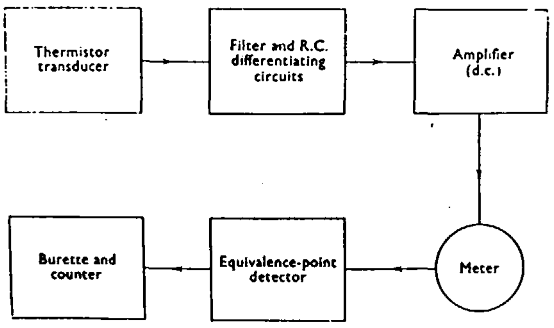


FIGURE 8. Block diagram of Priestley's automatic digital titrator. (From Reference 52, reprinted by courtesy of the copyright holder.)

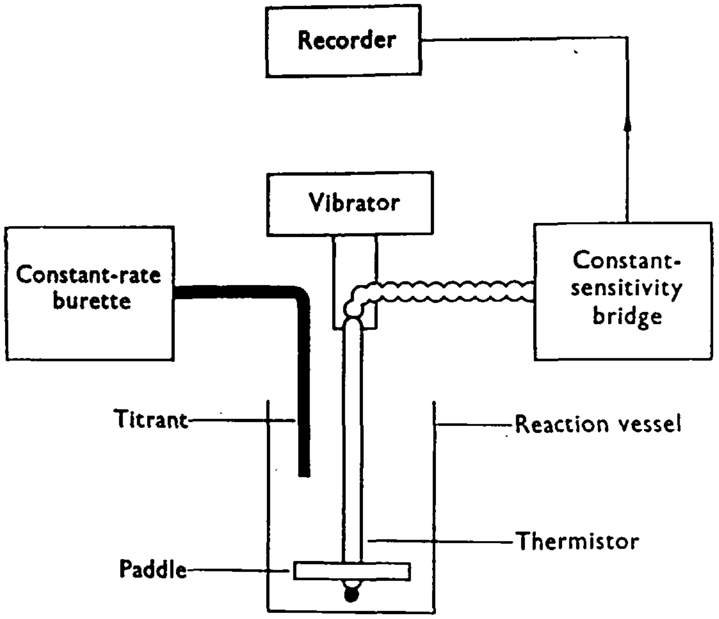


FIGURE 9. Priestley's high velocity buret and mixer for thermometric titration. (From Reference 53, reprinted by courtesy of the copyright holder.)

used to indicate a concentration, all of these factors become important. Direct injection enthalpimetry, as practiced by Wasilewski, Pei, and Jordan,[10] requires that the volume of reagent added to the unknown be so small that any temperature differential has no appreciable effect on the temperature of the mixture, that the temperature be matched, or that some means of correcting for the temperature difference be applied. This feature of the method is shown in Figure 10. It is obvious that one must know which curve to use in order to perform an analysis. In our experience, direct injection enthalpimetry requires temperature constancy of such precision as to make the technique considerably more cumbersome than titrimetric analysis when results precise and accurate to 1% are required.

TABLE 11

Precision of a Digital Thermometric Titrator[e]

Sample[a]	Titrant	Number of runs	Standard deviation, %
NaOH	HCl[b]	10	0.6
$AgNO_3$	HCl	10	0.5
NH_3	HCl	10	1.1
Na_3PO_4	HCl	10	0.6
$Ca(NO_3)_2$	EDTA[c]	8	1.0
$NiSO_4$	EDTA	11	0.6
$AgNO_3$	EDTA	4	2.0
$Mg(NO_3)_2$	EDTA	5	0.8

[a] All samples are 0.0167 M
[b] 1 Molar titrant
[c] 1 Molar titrant
[d] Poorest precision of all 50 titration reactions was 3.0%.
[e] Adapted from Reference 52 by permission of the copyright holder.

Many of these problems could be minimized by adoption of a titration technique. As will be shown, the extrapolated post-titration line yields an intercept which is *virtually* independent of the temperature mismatch, the heat of dilution of the titrant, and the increase in heat capacity. Consequently, direct enthalpimetry is most easily carried out not by injection of a sample or excess reactant but rather by adding the excess of reagent continuously and rapidly and extrapolating the temperature-time curve.

The technique described above is cumbersome in many ways and is not amenable to rapid automation of analyses of similar or even replicate samples. Priestley has described a system and termed it "continuous-flow enthalpimetry" which is capable of a high degree of automation and provides an accuracy of about ±1%.[54] The system is shown in Figure 11. In the operation 2 solutions, an unknown and an indeterminate excess of a reagent, are passed through a mixing vessel at a constant ratio of flow rates, in such a

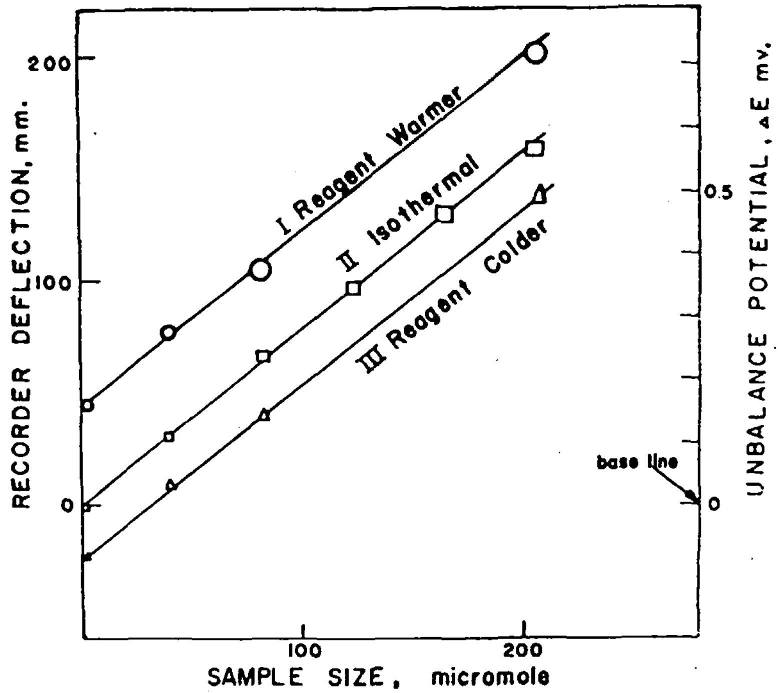


FIGURE 10. Typical calibration curves for direct injection enthalpimetry. An excess of 1M sodium hydroxide is added to the indicated amount of hydrochloric acid. (From Reference 10, reprinted by courtesy of the American Chemical Society.)

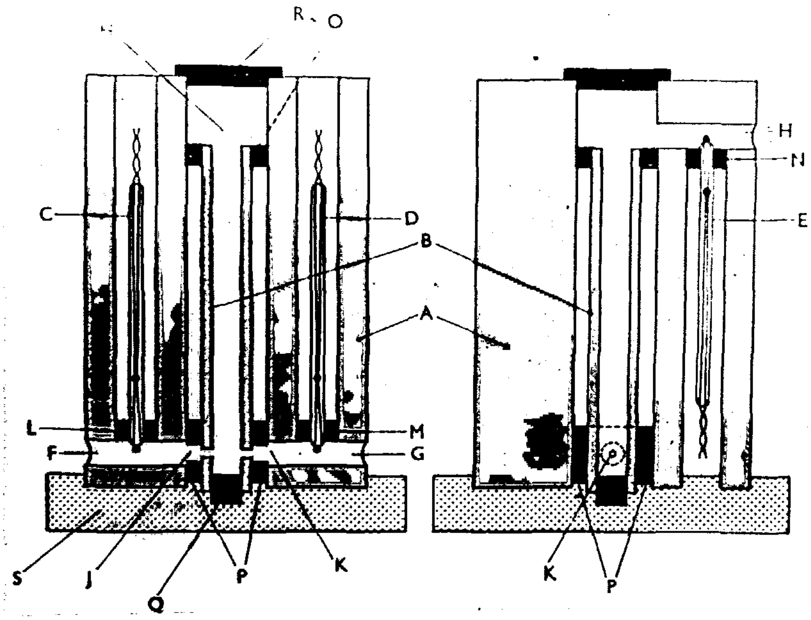


FIGURE 11. Priestley's continuous flow enthalpimeter: (a) cross section of front elevation, (b) cross section of side elevation. For complete details of lettered components see Reference 54. (Reprinted by courtesy of the copyright holder).

fashion as to insure complete mixing. The apparatus provides for this as well as for the measurement of the temperatures of the sample (T_S), the reagent (T_R), and the product solution (T_P). The results of a heat balance on the reaction vessel show that at equilibrium

$$M_S = \frac{K}{\Delta H}\left[T_p(R + 1) - T_S - RT_R\right] \tag{49}$$

where M_S is the molarity (or concentration in any desired units) of the sample, ΔH is the heat of reaction in consistent units, and K is the heat capacity per ml of the reacting and product solutions which are assumed to be equal. In practice, R, the ratio of flow rates, is fixed and $K/\Delta H$ is measured as a simple calibration factor via the use of standard solutions of the sample.

Equation 49 may be examined under 3 sets of conditions:

a. When M_S is in a range where the temperature change is easily measured, and when R is set to unity, one can rewrite Equation 49 as

$$M_S = \left[T_p - \frac{T_S + T_R}{2}\right]\frac{2K}{\Delta H} \tag{50}$$

b. When the sample is very dilute, a large value of R is unadvisable, and it is preferable to employ a concentration of reagent so high that $R << 1$ and Equation 49 becomes

$$M_S = (T_p - T_S)\frac{K}{\Delta H} \tag{51}$$

Obviously, this technique improves the sensitivity by a factor of only 2.

c. When very concentrated samples are employed, they should be diluted to produce a linear response from the thermistor bridge. Consequently when $R >> 1$ Equation 49 becomes

$$M_S = (T_p - T_R)\frac{KR}{\Delta H} \tag{52}$$

The results of Priestley's work on a number of common reactions are shown in Table 12. It is clear that the equipment is capable of quite reasonable analytical precision (±1%). Indeed, the overall precision reflects the precision of readout device and not that of the thermometric system. An obvious advantage of this system is the ease with which it handles replicate analysis and a large number of samples. In its present form the continuous flow enthalpimeter is easily incorporated into automatic analyzers including the Technicon Auto Analyzer.

G. Differential and Isothermal Calorimeters

The use of differential temperature measurements in thermoanalytical methods was introduced by Tyson, McCurdy, and Bricker.[55] In essence their system consists of 2 identical calorimeters, each containing 1 or more thermistors. In operation, a common pump is used to deliver exactly the same quantity of titrant to both calorimeters 1 of which contains only the solvent and 1 contains the solvent and a reactant. Clearly if care is used in matching heat capacities and the temperature coefficients of resistance of the transducers, such effects as stirrer and thermistor

TABLE 12

Precision and Accuracy of a Flow Enthalpimeter[a]

Reagent 0.6 M NaOH
Sample

Nominal concentration (M)		0.050	0.200	0.400
HCl	concentration found (M)	0.051	0.200	0.402
HNO_3		0.050	0.200	0.396
H_3BO_3		0.049	0.196	0.400
HOAc		0.050	0.200	0.399

Reagent 0.6 M HCl
Sample

Nominal concentration (M)		0.050	0.200	0.400
NaOH	concentation found (M)	0.050	0.200	0.400
NH_3		0.051	0.199	0.396
pyridine		0.055	0.201	0.401
Na_3PO_4		0.050	0.200	–

[a] Adapted from Reference 54 by permission of the copyright holder.

heating and heats of dilution will cancel. This technique has been used mainly for non-aqueous titrimetry wherein the heat of dilution may be so large as to obscure the heat of reaction.

Although differential calorimetry has the above advantages, it is also clear that it is subject to the 2 major problems encountered in thermodynamic measurement work. That is, it does not correct for increases in heat capacity, nor does it eliminate the adiabaticity problem. Meites et al.[24] have shown that the temperature drift problem may be virtually eliminated by this method making temperature resolution of 10 to 20 μ°C possible. However, the drift problem may also be solved by means of the device illustrated in Figure 12.

A major advance would be an adaptation of the twin calorimeter described by Sturtevant and co-workers for use in thermometric titrimetry. As described[25] this instrument consists of 2 calorimeters, each containing a resistance thermometer and a heating element. The reaction is carried out in 1 calorimeter (A), and the temperature difference between the 2 systems is fed to a servo amplifier which is designed to heat the second calorimeter (B) at such a rate as to maintain zero temperature difference. Clearly the instantaneous power dissipation in the second calorimeter is proportional to the rate of heat production in the first. Consequently, integration of the power will yield the total heat evolved in the reaction. Due to the compensation of heats the adiabaticity problem is eliminated.

A very interesting and recent innovation in titration calorimetry is the development of the true isothermal calorimeter.[46,56-58] The design of Christensen et al. is shown in Figure 13. The principle of the instrument is simple. The titration calorimeter is supplied with a highly constant source of cooling via a Peltier (thermoelectric) device. The solution temperature is monitored with the usual Wheatstone bridge arrangement, but any bridge imbalance is used to activate the output of a voltage-controlled oscillator which causes a relay to discharge a high-quality capacitor through a resistor immersed in the vessel. The discharges are counted. The rate of discharge is proportional to the degree of bridge imbalance. Thus, the system as a whole acts to maintain the temperature of the Dewar contents at the initial preset control temperature. Since each discharge delivers a known amount of heat, the total number of counts is proportional to the *heat* liberated from the start of the titration. Thus, the system is held at a temperature equal to its environment (within 0.2 m°C) and consequently there need be no concern for poor adiabaticity or heat of mixing nonisothermal solutions, and since energy rather than temperature is measured one need not correct for change in heat capacity. Using the above apparatus Christensen et al.[46] obtained a value of -13.34 ±0.03 kcal/mol for the heat of ionization of water, in excellent agreement with previous work. Clearly, this device represents a tremendous improvement in design and brings about a great simplification in evaluation of experimental data since virtually all correction factors are eliminated. A commercial model of their apparatus is available from Tronac, Inc., Orem, Utah.

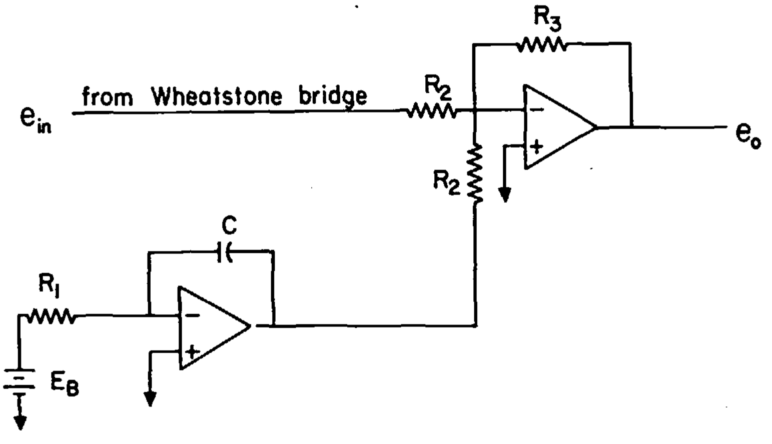


FIGURE 12. An operational-amplifier ramp generator. When R_1, C, and E_B are adjusted appropriately, e_O will be time-independent if e_{in} is a linear function of time.

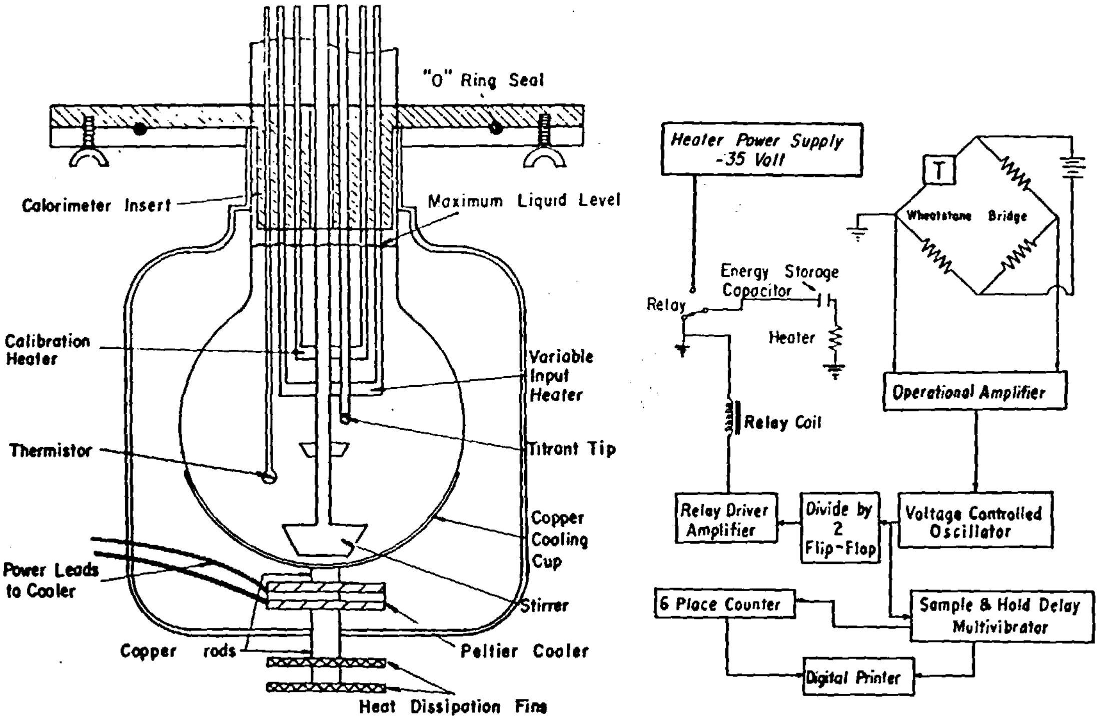


FIGURE 13. A true isothermal titration calorimeter constructed on the heat-compensation principle. (From Reference 46, reprinted by courtesy of the copyright holder.)

H. Circuitry for Measurement of Temperature Change

Since the thermistor is the most common transducer used in thermometric titrimetry, our discussion of measurement circuits will be limited to those which apply to resistance measurement. An exceedingly popular circuit for accurate measurement of absolute resistance is the well-known Wheatstone bridge illustrated in Figure 14.

In practical work the bridge proper, consisting of the elements R_1, R_2, R_3, and R_T is driven by a voltage source, E_B, which may be several 1.5 V dry cells in parallel dropped across the 10-turn potentiometer R_B. The bridge is constructed of 2 fixed resistors, R_1 and R_2, which are preferably wire-wound rather than carbon resistors so as to avoid the 1/f noise of granular circuit elements. R_3 is a variable balancing resistor which optimally is a decadic resistance substitution box. We have found that *unshielded* 5000-ohm potentiometers are extremely noisy and should be avoided, or at least thoroughly shielded. As normally constructed, the output side of the bridge should be grounded and E_B floated. Note that it is not possible to ground both E_B and e_0. The thermistor is connected at R_T, its leads should be shielded, and the shield connected to ground.

The output voltage, e_0, can be related to the bridge balance through Kirchoff's laws:

$$e_0 = i_1 \frac{R_2R_3 - R_1R_T}{R_1 + R_2 + R_3 + R_T} \tag{53}$$

where i_1 is given by

$$i_1 = \frac{\alpha E_B}{\alpha(1 - \alpha) R_B + R_{||}} \tag{54}$$

$R_{||}$ represents the series-parallel combination of the bridge elements. When $\alpha = 1$ or $R_B \ll R_{||}$, the output of the bridge is

$$e_0 = \alpha E_B \frac{R_2R_3 - R_1R_T}{(R_1 + R_2)(R_3 + R_T)} \tag{55}$$

Equations 53 to 56 have been written assuming that the recorder has infinite input impedance. When a 2000-ohm bridge is employed, this requires a recorder to have several megohms input impedance at null so that loading effects are less than 0.1%. Equation 55 implies that $e_0 = 0$ whenever

$$R_1R_T = R_2R_3 \tag{56}$$

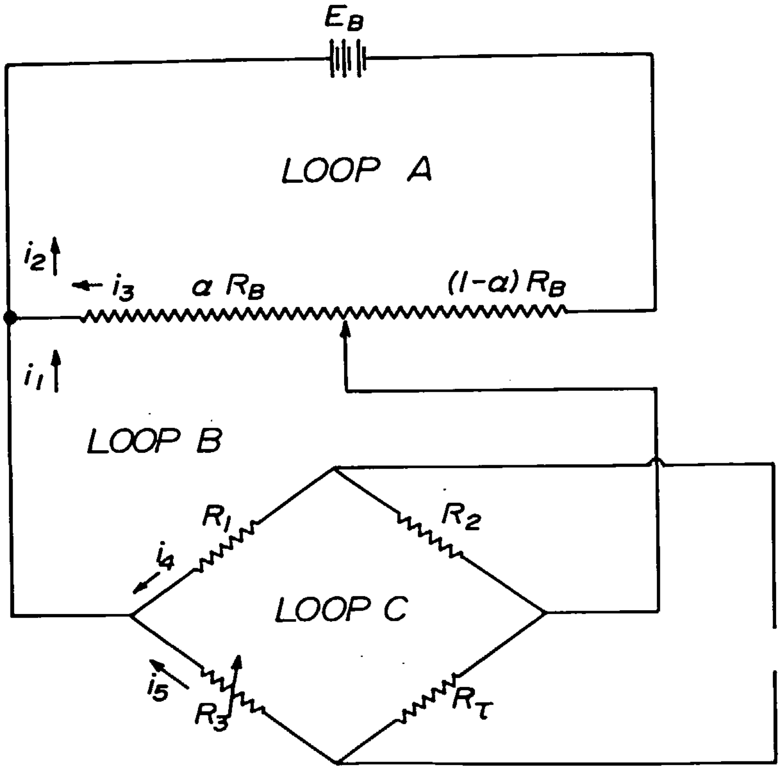


FIGURE 14. A typical Wheatstone bridge subject to the nonlinearity described by Table 13.

This is the fundamental condition of bridge balance and is independent of E_B and R_B.

Although Equation 56 is a valid description of the null condition, Equation 55 predicts that e_0 is not a perfectly linear function of a resistance change. For the moment let us suppose that

$$R_1 = R_2 = R_3 = R_T^0 \tag{57}$$

and

$$R_T = R_T^0 + \Delta R_T \tag{58}$$

then it follows that:

$$e_0 = \alpha E_B \frac{\Delta R_T}{2(2R_T^0 + \Delta R_T)} \tag{59}$$

As the temperature of a solution increases, R_T becomes smaller; therefore ΔR_T is negative and the denominator of Equation 59 decreases. Table 13 is a compilation of bridge outputs using the normalized resistance changes of Table 10, with $\alpha E_B = -1$ V. These data clearly demonstrate that the bridge response to resistance change is nonlinear and fortuitously in the opposite direction to the nonlinearity of Equation 45. Over a temperature interval of 0.1°C the net nonlinearity of the thermistor and bridge amounts to only about 0.03%; over one of 1°C it is ~ 0.3%. Thus, for the small temperature changes encountered in thermometric analysis, the overall

TABLE 13

Linearity of Bridge Output vs. Temperature for a Typical Thermistor[a]

T(°C)	e_0 (mv)	T(°C)	e_0 (mv)
25.00	0.00000	25.10	1.26570
25.01	0.12660	25.20	2.53093
25.02	0.25319	25.30	3.79554
25.03	0.37973	25.40	5.05954
25.04	0.50636	25.50	6.32293
25.05	0.63294	25.60	7.58568
25.06	0.75952	25.70	8.84779
25.07	0.88608	25.80	10.10925
25.08	1.01264	25.90	11.37002
25.09	1.13920	26.00	12.63010

[a] Computed from data of Table 10 and Equation 59.

nonlinearity is completely negligible. One should note that, as Everson[59] has pointed out, in non-aqueous titrimetry total temperature changes of several degrees centigrade are not uncommon and, therefore, substantial nonlinearity is expected. To overcome this problem, Everson[60] has designed a bridge whose output voltage is a linear function of ΔT over a temperature range of 12°C. This circuit is illustrated in Figure 15. The device indicates a maximum deviation of ±0.03°C vs. a mercury thermometer over the range of 20 to 27°C. An ordinary Wheatstone bridge would show a net nonlinearity of 2.1% over this range.

The linearity problem can be overcome in other ways. For example, a platinum resistance thermometer could be used in conjunction with an amplifier bridge (vide infra) which responds linearly to a resistance change. Additionally, selected special-purpose diodes[61] exist which produce voltage under conditions of constant current that varies linearly with temperature change over very wide ranges of temperature.

The question of the ultimate sensitivity of a thermistor and Wheatstone bridge has generally been ignored by most workers in thermometric analysis. Clearly, this issue is very significant in microcalorimetry and in highly sensitive and highly precise analysis. Since we are fundamentally interested in sensitivity toward a temperature change and thus to a percent or fractional decrement in resistance rather than to an absolute change in ohms, the sensitivity S_R will be defined as

$$S_R \equiv \frac{de_0}{dR_T/R_T} = R_T \frac{de_0}{dR_T} = \frac{de_0}{d \ln R_T} \qquad (60)$$

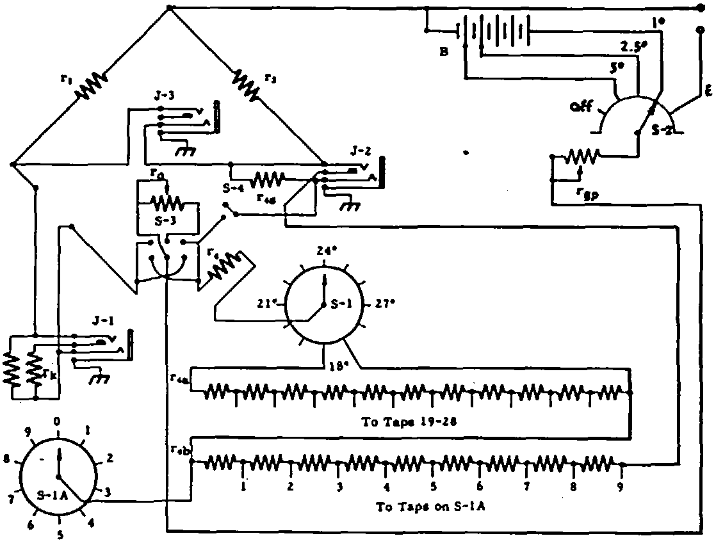
From Equation 46 the sensitivity (S_T) to a given change in temperature will be

$$S_T = S_R \cdot \frac{\beta}{100} = \frac{de_0}{dT} \qquad (61)$$

S_R may be obtained by differentiating Equation 55 with respect to R_T and multiplying the result by R_T

$$S_R = -\alpha E_B R_T \left[\frac{R_1}{(R_1 + R_T)(R_3 + R_T)} + \frac{R_2 R_3 - R_1 R_T}{(R_1 + R_2)(R_3 + R_T)^2} \right] \qquad (62)$$

Computing the sensitivity at *null* yields



S-1,S-1A = Range Switches
S-2 = Sensitivity Selector
S-3 = DPDT
S-4 = SPST
J-1 = Indicating Thermistor
J-2 = Reference Thermistor
J-3 = Output to Recorder

B = 1.34v Mercury Batteries
$r_1 - r_4$ = See Table 1
r_{sp} = Span Adjust
r_0 = Zero Adjust
r_k = Calibration Resistor

FIGURE 15. Everson's linearly compensated Wheatstone bridge for direct temperature readout. For details see Reference 60. (Reprinted by courtesy of the American Chemical Society.)

$$S_R = -\alpha E_B \frac{R_3 R_T}{(R_3 + R_T)^2} \tag{63}$$

where R_3 and R_T are subject to the constraints of Equation 56. Table 14 is a compilation of S_R as a function of the circuit elements. Under optimum conditions

$$S_R = -\frac{\alpha E_B}{4} \tag{64}$$

The voltage produced by a bridge to a given temperature change (ΔT) under the optimum conditions will be

$$e_0 = -\frac{1}{4}\alpha E_B \frac{\Delta R_T}{R_T} = \frac{1}{4}\alpha E_B \frac{\Delta T \cdot \beta}{100} \tag{65}$$

Implicit in Equation 65 is the notion that sensitivity can be increased without bound by simply increasing αE_B. Alternatively, a larger voltage can be developed by amplifying e_0 before presentation to the recorder. The ultimate limitation of both of these possibilities is the noise signal present in e_0. The noise sources present in the circuit of Figure 14 are

a. Fluctuations in E_B

b. Johnson or thermal noise in the circuit components

c. Noise pickup from stray radiation (60 cycle, switching transients from temperature controllers, etc.)

d. The pink or 1/f noise inherent in semiconductors and other granular-like materials (including, of course, the thermistor)

e. Random fluctuations in the temperature of the test solution. These might be due to thermal inhomogeneity, and particularly due to stirring and noninstantaneous mixing.

f. Random fluctuations in the internal temperature of the thermistor.

TABLE 14

Bridge Sensitivity and a Function of Circuit Elements[a]

S_R (at null)	Condition of null
0.250	$R_1 = R_2, R_3 = R_T$
0.222	$R_1 = 2R_2, R_3 = 2R_T$
0.222	$R_1 = ½R_2, R_3 = ½R_T$
0.0826	$R_1 = 3R_2, R_3 = 3R_T$
0.0826	$R_1 = 1/3R_2, R_3 = 1/3R_T$

[a]Computed according to Equation 14 with $\alpha\ E_B = -$ lv.

From Equation 47 one can see that if δ changes, then T_{int} will vary. This effect can be minimized by making δ large and stirring as uniformly as possible. Indeed we have noted that the thermistor should be placed as close to the stirrer as possible (1 mm) and fixed firmly in place. When the thermistor is some distance from the stirrer, the noise level increases. It may well be that δ decreases or undergoes greater fluctuations as it is moved away from the stirrer.

In fact, noise sources a-c are entirely negligible in a well-built circuit. Evidence for this is shown in Figure 16. Curve a was recorded with a 2,000-ohm wire-wound resistor placed in a stirred Dewar and connected to terminals R_T of Figure 14; curve b was recorded similarly with a 2,000-ohm thermistor. It is clear that there is virtually no noise present in curve a, whereas there is considerable noise in curve b. Obviously, noise sources a-c are the same in both cases and, therefore, quite small. The effect of αE_B was tested in curves b, c, and d. The results were obtained by decreasing αE_B from 5V to 1V and increasing the resolution of the recorder from 100 μV/in. to 10 μV/in. There is a dramatic decrease in noise as αE_B decreases. It is evident that this decrease must be due to noise sources e or f.

There will be 2 principal contributors to noise source e in the absence of a chemical reaction: these are the heat generated by the stirrer and heat generated by the thermistor. In most instances the stirring heat will predominate over the heater; since this was held constant in all of the measurements, we can disregard noise source e. Thus, the *major* noise source in using a thermistor is the fluctuation in its internal temperature due to changes in its dissipation constant

$$\Delta(T_{int}) = W\Delta\ \frac{1}{\delta} = \frac{\alpha^2 E_B^2\ R_T}{(R_1 + R_T)^2}\ \Delta\left(\frac{1}{\delta}\right) \tag{66}$$

where W is the power dissipated in the thermistor. Therefore, ΔT_{int} will show up at the output as the voltage-equivalent noise $e_{0,n}$

$$e_{0,n} = -\alpha E_B \frac{R_3 + R_T}{(R_3 + R_T)^2} \frac{\Delta T_{int}\ \beta}{100}\ \Delta\left(\frac{1}{\delta}\right) \tag{67}$$

Consequently, the signal-to-noise ratio will be

$$R_{S:N} = \frac{e_0}{e_{0,n}} = \frac{\Delta T_S}{\Delta T_{int}} \times \frac{(R_1 + R_T)^2}{\alpha^2 E_B^2\ \Delta\left(\frac{1}{\delta}\right) R_T} \tag{68}$$

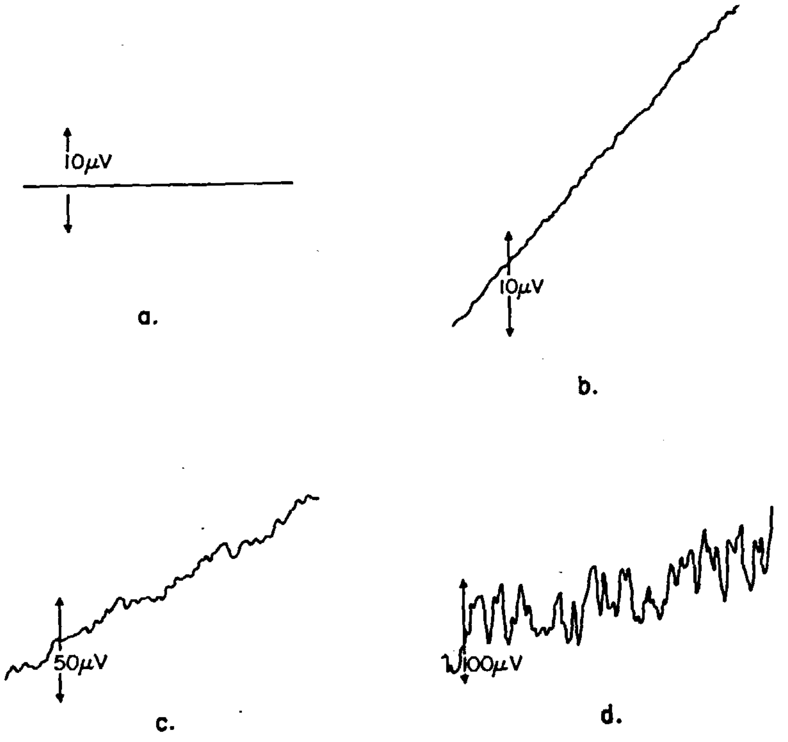


FIGURE 16. Voltage-time curves under varying experimental conditions: (a) 2,000-ohm wire = wound resistor, $E_B = 1$ V, (b) 2,000-ohm thermistor, $E_B = 1$ V, (c) 2,000-ohm thermistor, $E_B = 2.5$ V, (d) 2,000-ohm thermistor, $E_B = 5$ V.

The optimum signal-to-noise will be obtained when αE_B is quite small and when $R_1 + R_T$ is large. All of these act to decrease the power dissipated in the thermistor.

This approach explains the discrepancy between the work of Meites[24] and Jordan.[14] Meites found that a 100,000-ohm thermistor driven by a 2-V power supply produced a temperature resolution of about 10 to 20 μ°C (power dissipation about 40 μW), whereas Jordan using 2,000-ohm thermistors observed fluctuations of 10 μV or about 1,000 μ°C (power dissipation about 500 mW). It is clear that the real noise source is not the "....Heisenberg uncertainty noise inherent in the limit within which the electron distribution between conductance and valence bands of the thermistor can be localized...,"[14] rather it is a real fluctuation in the internal temperature of the thermistor.

As indicated by Equation 68 the optimum signal-to-noise ratio will be obtained with $R_1 > R_T$, since most of the power will then be dissipated in R_1 rather than R_T. This analysis is in general agreement with the results of Mitvalski.[62] However, as R_1/R_T becomes larger the net gain of the bridge decreases, in accord with the results of Table 14. Hence, as R_1 is made greater than R_T, additional. noise-free amplification will be required. Consequently, the best compromise is to keep R_1 equal to R_T but to make both as large as possible within the bounds set by the recorder impedance and the inevitable pickup and Johnson noise of large resistors. With a well-shielded bridge and a high-quality recorder one should be able to use 1-megohm bridge elements.

A fundamental difficulty in work involving measurements of high sensitivity is the temperature drift of the calorimeter and its contents due to stirring, thermistor warming, and heat transfer from the environment. In order to overcome these problems, 2 approaches are possible. The first is the use of twin differential calorimeters, the second is the use of operational-amplifier base-line correction.

I. Additional Circuits for Temperature Measurement

Because the signals measured in thermometric titrimetry are small, a totally passive bridge is generally used. However, now there are available a large variety of low-noise, inexpensive operational amplifiers which will permit the use of a number of active circuits for temperature measurement. In order to be useful such amplifiers must have a noise equivalent of less than 1 μV referred to the input. These amplifiers may then be used to recover the decrease in S_R as R_1 is made greater than R_T, or alternatively to permit the simultaneous grounding of E_B and e_0.

Bridge 2 shown in Figure 17a develops an output voltage e_0 described by the equation

$$e_0 = \frac{R_T - \frac{R_2}{R_1} R_3}{R_T + R_3} \cdot E_B \tag{69}$$

with

$$R_T = R_T^0 \left(1 + \frac{\beta\Delta T}{100}\right) \tag{70}$$

$$e_0 = \frac{\frac{\beta}{100} \frac{R_2}{R_1} \Delta T}{\frac{R_2}{R_1} \frac{\beta}{100} \Delta T + 1} \cdot E_B \tag{71}$$

When $1 \gg (R_2/R_1)\,\beta\Delta T/100$

$$e_0 = \frac{\beta(\Delta T)}{100} E_B \frac{R_2}{R_1} \tag{72}$$

From Equation 72 we see that the circuit has several advantages over the usual Wheatstone bridge:

a. With $R_1 = R_2$ its gain is 4 times as large.

b. Both the source E_B and the output e_0 are grounded, so that one can readily employ a commercial power supply rather than batteries to achieve a concomitant improvement in long-term stability.

c. Little or no current is driven through R_1 or R_2, so that they will not warm up and, therefore, drift.

d. The gain may be increased at will by making $R_2 > R_1$. This circuit is limited to low-noise amplifiers with excellent common-mode-rejection ratio due to the large common signal applied to both amplifier inputs.

Bridge 3 is shown in Figure 16b. The output of the amplifier is

$$e_0 = \left(1 + \frac{R}{R_1}\right) \frac{\frac{\beta\Delta T}{100} E_B}{4\left(1 + \frac{\beta\Delta T}{200}\right)} \cong \left(1 + \frac{R}{R_1}\right) \frac{\beta(\Delta T)\ E_B}{4} \tag{73}$$

The advantages of this circuit are

a. The gain $(1 + R/R_1)$ may be adjusted without changing the linearity. This is not true of the preceding circuit.

b. A single-ended amplifier is used. This permits the use of highly stable chopper-stabilized amplifiers, thus eliminating the drift and common-mode error of the previous circuit. Note, however, that the circuit has the same gain as the usual Wheatstone bridge and that E_B must be floated.

Bridge 4 is shown in Figure 16c. Its output follows the equation

$$e_0 = \frac{E_B}{2} \beta \frac{\Delta T}{100} \tag{74}$$

and is perfectly linear with change in resistance. Additional circuits for resistance measurement may be found in Reference 63.

As mentioned previously, under conditions of high sensitivity the voltage, e_0, increases so rapidly that the recorder is rapidly driven off scale. This problem can be eliminated through the use of a linear ramp generator and operational amplifier adder circuit which is illustrated in Figure 12. Let us assume that e_0 is some linear function of time:

$$e_0 = k \cdot t \tag{75}$$

Amplifier 1 generates a signal whose output is

$$e_0' = -\frac{1}{RC} E_B \cdot t \tag{76}$$

which is added via amplifier 2 to produce the net output

$$e_0'' = -\frac{R_2}{R_1}(e_0 + e_0') = -\frac{R_2}{R_1}\left(k - \frac{E_B}{RC}\right) t \tag{77}$$

Consequently E_B/RC may be adjusted such that e_0'' is time-independent:

IV. ANALYTICAL ASPECTS OF THERMOMETRIC TITRIMETRY

A. Introduction

In both theory and practice thermometric titrations greatly resemble other linear (or segmented) titration methods such as photometric, conductometric, and amperometric titrations. All of these techniques may be implemented by adding a titrant in either discrete or continuous aliquots to a sample solution. Some variable, such

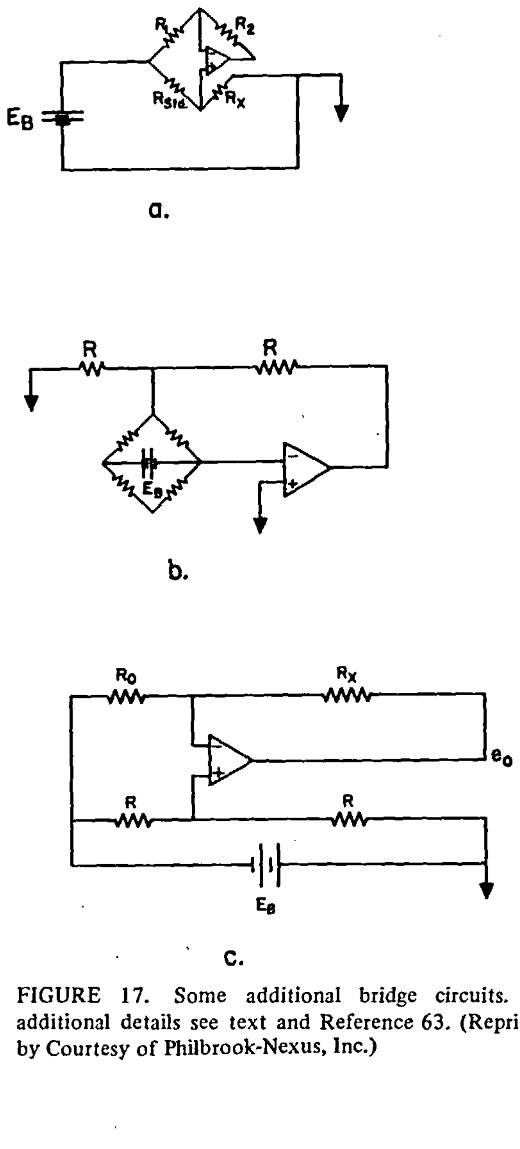


FIGURE 17. Some additional bridge circuits. For additional details see text and Reference 63. (Reprinted by Courtesy of Philbrook-Nexus, Inc.)

as the temperature change, limiting current, or reciprocal resistance, which is a linear function of concentration or change in concentration(s), is measured and plotted against the volume of titrant added. If necessary, the curve is corrected for dilution. The experimental points will frequently form 2 straight lines whose point of intersection is taken as an end point. This process and the curves to which it gives rise should be compared to the very different analytical geometry of a potentiometric titration wherein the measured variable is, in accord with the Nernst equation, a logarithmic function of concentration(s).

The end point of a potentiometric titration is located by titration to an inflection point in the potential-volume curve or to some preselected potential which is believed to be the electrode potential at the equivalence point.

The most important characteristics of an analytical method, be it a titration or a one-point direct measurement, are its accuracy, precision, sensitivity, range of application, and selectivity. This section of the review will focus on the first three of the above characteristics. However, it is important to note the already mentioned catholicity of thermometric titrimetry. This is due to the fundamental nature of the measured variable. Second, the *intrinsic selectivity of the technique* is nil. One must rely completely on the reagents employed to discriminate among the components of a complex mixture. This is, in our experience, a minor inconvenience compared to the ease and breadth of application. Chemical differentiation may be based upon thermodynamic and kinetic differences in the behavior of the sample constituents and the titrant. For example, although both calcium and magnesium precipitate in the presence of oxalate, one can titrate the mixture thermometrically under appropriate conditions since magnesium reacts much the more slowly[5] of the two. Calcium and magnesium mixtures can be titrated with EDTA; 2 distinct end points are obtained due to the differences between the formation constants and between the heats of reaction.[6] Hansen and Lewis[64] have shown that mixtures not exhibiting 2 distinct end points can be analyzed by relying solely on differences in reaction enthalpies. Because of the general nature of the detector, the development of a useful thermometric titration relies more upon the successful application of chemistry than to the use of instrumentation; it may justly be said that "more analyses are wrought by chemistry than by equipment."

The subject of this section of the review will be an analysis of the factors that affect the precision, accuracy, and sensitivity of thermochemical analysis. Such factors are examined separately. First, the measurement accuracy required to achieve a predetermined precision under ideal chemical and thermal conditions will be examined. Second, the purely thermal factors such as adiabaticity and heat-capacity increases are discussed. Third, chemical factors such as incomplete equilibria and slow reactions, which affect all automatic or constant-rate conditions, will be considered.

B. Precision and Sensitivity of Thermometric Titrations

Those factors which limit the precision and sensitivity of linear titrations were not quantitatively understood until recently. To date, the most thorough treatment of this subject in the analytical literature is the work of Rosenthal et al.,[65] upon which much of the subsequent discussion is based. In the case of a chemically ideal titration any source of random error in the measured variable ϕ, which in the case of a thermometric titration is a voltage proportional to a temperature change, will propagate itself as an uncertainty in the location of the end point which will be termed $f_{e.p.}$ Consider a perfect titration curve, which is described by the equations

$$\phi_i = m_1 f_i + b_1 \qquad f_i \leq 1 \qquad (78)$$

$$\phi_j = m_2 f_j + b_2 \qquad f_j \geq 1 \qquad (79)$$

where all observed deviations from these equations are random rather than systematic. In the above equations ϕ_i and f_i are the coordinates of points taken before the end point, while ϕ_j and f_j are those of points taken after the end point. The end point is located by extrapolating the 2 lines to a point of intersection. This is equivalent to finding the common value of f_i and f_j such that

$$\phi_i = \phi_j \qquad (80)$$

Obviously, this occurs when

$$f_i = f_j \equiv f_{e.p.} = \frac{b_2 - b_1}{m_1 - m_2} \qquad (81)$$

Any random errors in ϕ_i, ϕ_j, f_i, or f_j will be reflected in the precisions of the slopes and intercepts. In any real titration the imprecision in the fraction titrated will be so small as to be negligible in comparison to the uncertainty in ϕ_i or ϕ_j. Such uncertainty will be propagated into $f_{e.p.}$ and will be described by Equation 82

$$\sigma^2_{f_{e.p.}} = \left(\frac{\partial f_{e.p.}}{\partial m_1}\right)^2 \sigma^2_{m_1} + \left(\frac{\partial f_{e.p.}}{\partial b_1}\right)^2 \sigma^2_{b_1} + 2\left(\frac{\partial f_{e.p.}}{\partial m_1}\right)\left(\frac{\partial f_{e.p.}}{\partial b_1}\right)\sigma_{m_1}\sigma_{b_1} + \ldots \qquad (82)$$

A least-squares approach may be used to estimate m_1, b_1, m_2, and b_2 and simultaneously the uncertainty in these numbers:

$$\sigma^2_{m_1} = \sigma^2_M \, [n/n\Sigma(f_i)^2 - (\Sigma f_i)^2] \qquad (83)$$

$$\sigma^2_{b_1} = \sigma^2_M \Sigma f_i^2 / n\Sigma(f_i)^2 - (\Sigma f_i)^2 \qquad (84)$$

$$\sigma_{m_1}\sigma_{b_1} = -n\overline{f_i}\,\sigma^2_M / n\Sigma(f_i)^2 - (\Sigma f_i)^2 \qquad (85)$$

where n is the number of data points taken before the end point, $\overline{f_i}$ is the average value of f_i, and $\sigma^2{}_M$ is the variance in the measurement of ϕ_i defined below

$$\sigma^2_M = \sum_{i=1}^{n} (R_i)^2/n \qquad (86)$$

R_i refers to the residuals or deviations of the experimental points from the least-squares lines (Equations 78 and 79). Entirely analogous equations exist for the points taken after the end point. The instrumental noise level enters into Equations 83 to 85 only as R_i and thus as $\sigma^2{}_M$. All other factors are controlled by the analyst or by the chemistry of the system. Assuming that $f_{e.p.} \cong 1$ the above equations lead to the following estimate of $\sigma^2{}_{f_{e.p.}}$:

$$\sigma^2_{f_{e.p.}} = \frac{1}{(m_1 - m_2)^2}\left[\sigma^2_M \left\{\frac{n + \Sigma f_j^2 - 2n\overline{f}_i}{n\Sigma f_i^2 - (\Sigma f_i)^2}\right\} + \sigma^2_{M'}\left\{\frac{n' + \Sigma f_j^2 - 2n'\overline{f}_j}{n'\Sigma f_j^2 - (\Sigma f_j)^2}\right\}\right] \qquad (87)$$

The primed values refer to the data taken after the end point. All of the terms in Equation 87 with the exception of $m_1 - m_2$, $\sigma^2{}_M$, and $\sigma^2{}_{M'}$, are determined by the distribution of the points on the f-axis. σ_m and $\sigma_{M'}$ are determined by the noise or resolution of the instruments on the ϕ-axis, and $m_1 - m_2$ is determined by the chemistry of the system. Figure 18 shows the effect of the number of data points on the experimental precision. Obviously, increasing the number of points improves the precision. It follows from Equation 87 that the temperature of the titrant in thermometric titrimetry should not have a profound effect on the precision of the method.[66] This contradicts a number of statements in the literature of thermometric titrimetry,[67,68] and results from the fact that the mismatch has virtually identical effects on m_1 and m_2.[69] If the mismatch becomes so serious as to mandate a decrease in bridge or recorder sensitivity, then of course σ_M increases. Such changes can be avoided by using a recorder with an automatic zero reset, a very wide dynamic range device such as a digital voltmeter, or (most simply) the linear ramp generator shown in Figure 12. Figure 18 also

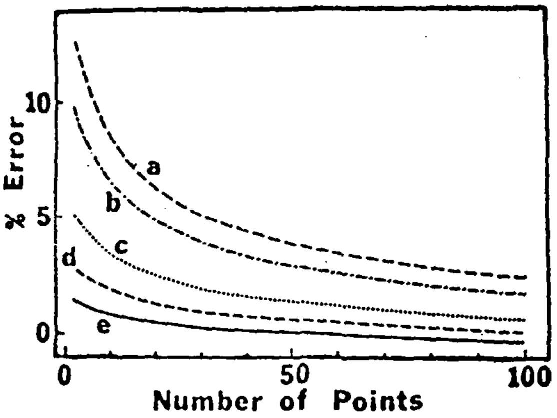


FIGURE 18. The effect of differences in extrapolation range and number of data points on percent random error. The data were computed from Equation 87 with $(m_1 - m_2)^2 = 1$ and $f_{e.p} = 1$ for the ranges (a) 0.0 to 0.2 and 2.5 to 2.7, (b) 0.0 to 0.2 and 2.0 to 2.2, (c) 0.0 to 0.4 and (d) 0.0 to 0.6 and 1.7 to 2.3 and (e) 0.0 to 0.9 and 1.1 to 2.0 (From Reference 65, reprinted by courtesy of the copyright holder.)

shows the effect of the distribution of points. Clearly the precision improves as the extrapolation becomes shorter.

Unfortunately, Rosenthal's results are not immediately applicable to the "normal" practice of thermometric titrimetry. In general, thermometric titrations are carried out by continuous automatic reagent addition along with continuous recording of the temperature change (ϕ). Consequently, the number of data points is very large. Rosenthal's equations then predict absolute certainty in locating $f_{e.p.}$ (see Equation 87). In the face of a vast amount of experimental evidence this is not a valid conclusion. This situation results from a breakdown in 1 of the assumptions of the least-squares treatment, namely the independence of data points. An exact solution has not yet been achieved due to the need for an adequate model or assumption regarding correlation or interdependence between points. In any event, the number of data points is not infinite, but is limited by the precision in the time or volume axis of the titration curve. With contemporary recorders and syringe burets this seldom if ever exceeds 0.2%. The optimum precision of thermometric titrations is generally 0.2 to 0.5%. Thus, N will be about 500. Obviously as the end-point time becomes shorter and shorter the precision in measurement along the volume axis becomes poorer. To a limited extent this can be avoided by decreasing the size of the syringe. In the remainder of the discussion we will *assume* that N is 500 and that the volumetric precision is 0.2%. Thus, the precision predicted by Equation 87 and subsequent equations will underestimate the real precision by at least 0.1 to 0.2%.

If we consider that the bases on which the end-point extrapolations are made are from N points evenly distributed in the regions

$$0 \le f_i \le f' \qquad (88)$$

and

$$f'' \le f_j \le f''' \qquad (89)$$

and N>>1 then Equation 87 may be reformulated as

$$\sigma^2_{f_{e.p.}} = \frac{\sigma^2_M}{(m_1 - m_2)^2} \frac{1}{N} \left[\frac{1 - f' + \frac{1}{3} f'^2}{f'^2/12} + \frac{1 - (f'' + f''') + f'' \cdot f''' + \frac{1}{3}(f''' - f'')^2}{(f'' \cdot f''' + (f''' - f'')^2/12)} \right] \qquad (90)$$

$$\sigma^2_{f_{e.p.}} = \frac{\sigma^2_M}{(m_1 - m_2)^2} \cdot \frac{F}{N} \qquad (91)$$

Table 15 contains some estimates of F as a function of f′ subject to the assumption that both base lines are of equal length. Clearly, the analytical precision is critically dependent upon the length of the extrapolation and the resolution of the volume axis (N). Even under optimum circumstances the resolution of the time or volume

TABLE 15

Effect of Extrapolation Base on the Precision of Continuous Linear Titrations

f′	$\%\sigma^b$	F^a
0.20	0.14	244
0.30	0.09	98
0.40	0.06	49
0.50	0.05	28
0.60	0.04	18
0.70	0.04	12
0.80	0.03	8
0.90	0.02	6
0.95	0.02	5

[a] Computed from Equation 90 with $f'' = 2\text{-}f'$, $f''' = 2$.
[b] $\Delta H_R = 10$ kcal/mol, $C^0{}_A = 10$ mM, N = 500

axis is limited by both the recorder and the titrant pump to 1 part in 500.

Equation 91 also can be used to predict the effect of concentration of the analyte on precision; that is, it can predict the sensitivity limit of thermometric titrations. We shall assume that the precision of the volume axis is constant; clearly this cannot be maintained as the concentration decreases unless the buret size or titrant concentration is decreased appropriately.

Jordan and Dumbaugh[2] have shown experimentally that as the analyte concentration *increases* the precision improves to some limit which represents the volumetric uncertainty. As Figure 19 indicates, the precision changes quite rapidly with concentration. This dependence can be estimated by assuming a temperature uncertainty, σ_M, of ± 0.0002°C. Meites et al.[24] have shown that this is a conservative estimate. We may estimate the slope m_1 as

$$m_1 = \frac{dT}{df} \cong \frac{(\Delta H_R)\ \rho t^*}{C_p} = \frac{(\Delta H_R)\ \rho t^*/V^0}{C_p^*/V^0} \tag{92}$$

and in most instances

$$m_2 \cong 0 \tag{93}$$

Note that $\rho t^*/V^0$ is equal to the analyte concentration $C^0{}_A$ (mol/l.). Thus, from Equation 91

$$\%\ f_{e.p.} \cong 100\ \frac{\sigma_M}{(\Delta H_R)\ C_A^0} \cdot 1000\ \sqrt{F/N} \cong \frac{20\ \sqrt{F/N}}{(\Delta H_R)\ C_A^0} \tag{94}$$

This equation demonstrates an inverse dependence of precision on the heat of reaction and analyte concentration. Everson[59] has shown, in agreement with this result, that extremely dilute solutions of butyllithium (< 0.01%) may be titrated with butanol due to the very high reaction enthalpy (about 53 kcal/mol). Indeed Equation 94 is a quantitative fundamental statement of the empirical "enthalpimetric sensitivity index" introduced by Jordan and Dumbaugh.[2] As pointed out previously, this equation will underestimate the experimental precision and should be reformulated as

$$\%\ f_{e.p.} \cong 0.2 + \frac{20\ \sqrt{F/N}}{(\Delta H_R)\ C_A^0} \tag{95}$$

Obviously, Equation 95 and the results presented in Table 16 are in qualitative agreement with the experimental results of Figure 19.

The precision of thermometric titrimetry can be improved when it is limited by the first term of Equation 95. In these cases the sample should be "pre-titrated" by adding a known amount of titrant from precise volumetric pipets or weight burets. The end point is then obtained by automatic titrant addition. If the "finish" is precise to ±0.2%, and there is a much smaller uncertainty in the pretitration, the overall precision will be improved in proportion to that fraction of the titration carried out in the first step. This pretitration process has been described by Brown, Issa,

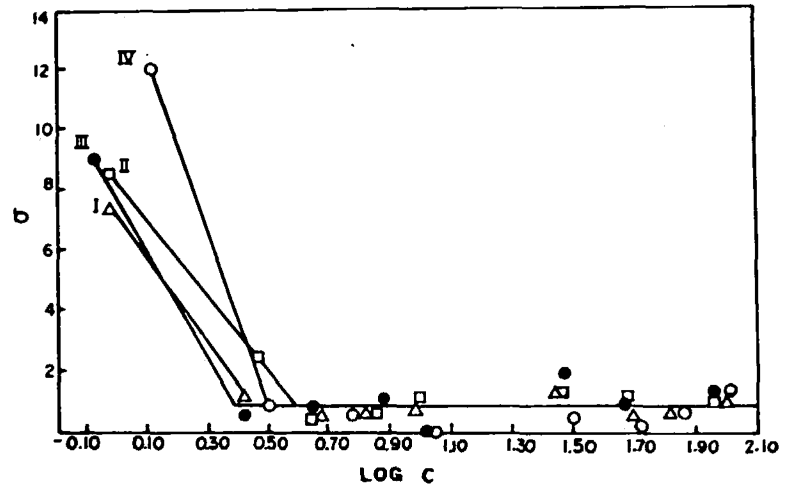


FIGURE 19. Experimentally determined precision of thermometric titrations. (I), trichloroacetic acid–sodium hydroxide, (II), monochloroacetic acid – sodium hydroxide, (III), acetic acid – sodium hydroxide, and (IV), boric acid – sodium hydroxide (From Reference 2, reprinted by courtesy of the American Chemical Society.)

TABLE 16

Effect of Analyte Concentration on Titration Precision

C^o_A(mM)	$\%\sigma_{f_{e.p.}}$
100	0.20
50	0.21
10	0.25
5	0.29
1	0.67
0.5	1.14
0.1	4.90

[a] ΔH_R = 10 kcal/mol, N = 500, f′ = 0.50

and Sinclair[70] who found it to yield results very much better than those obtained in normal practice.

The sensitivity limit of thermometric titrations may be specified as that concentration below which the precision is poorer than some arbitrarily assigned limit. If we choose the 2% level, which is quite poor precision for a titration, then the minimum concentration which may be analyzed is

$$C^0_{A(Min)} \geq \frac{20\ \sqrt{F/N}}{1.8\ (\Delta H_R)} \tag{96}$$

With reaction enthalpies not exceeding 10 kcal/mol the limit of sensitivity (at 2% precision) is somewhat less than 1 mM. Indeed, this is one of the major limitations of thermometric titrimetry – its rather poor sensitivity in comparison to other linear titration methods such as photometric and amperometric titrations. However, this limit is quite competitive with potentiometric end-point detection which is generally only useful above the millimolar concentration level.

The limit of sensitivity can be improved, assuming that N is fixed, only by decreasing σ_M, which is fixed by the inherent noise level of the thermistor, or by increasing $m_1 - m_2$. Several workers have explored this second possibility and this is discussed in the next section.

C. Chemical Techniques for Improving the Sensitivity of Thermometric Titrations – The Use of Thermometric End Point Indicating Reactions

As discussed above, thermometric titrations do not produce good precision (1%) when the analyte concentration is less than 0.5 to 1.0 mM and the reaction enthalpy is less than ±10 kcal/mol. This situation results from error propagation and the assumed values of m_1 and m_2. It is obvious that if $m_1 - m_2$ were increased, then the precision of the analysis and, therefore, the limit of sensitivity would both improve. By means of instrumentation one cannot adjust m_1 or m_2. These are set by the *chemistry of the system*. There is growing evidence in the literature that m_2 is rather easily manipulated by addition of reagents so that $m_1 - m_2$ is profoundly increased. This relies upon the addition of a so-called "thermochemical indicator species" which reacts with the titrant after the analyte has been depleted. This reagent is chosen such that its effective heat of reaction with the titrant is very different from that of the analyte.

Several different approaches have been taken, and in general the titrant need not undergo any direct chemical reaction with the indicator. These approaches are

1. Direct reaction of the titrant with the indicator species,
2. Use of the titrant as a catalyst for the indicating reaction, and
3. Exo- or endothermic dilution of the titrant in a solvent system.

A number of different indicator systems are summarized in Table 17 and several examples are discussed below.

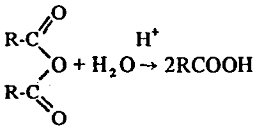
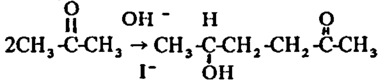
Direct titrations of salts of carboxylic acids in water are extremely imprecise when performed by thermometric titrimetry due to the very small reaction enthalpies involved. However, Hansen et al.[17] have shown that the titration is easily implemented by adding sulfate to the sample. Sulfate is a much weaker base than carboxylate salts and, therefore, it does not react until the stronger bases are consumed. It does have a much larger heat of reaction (+ 5 kcal/mol) and, therefore, serves to indicate the end point.

One of the most dramatic examples of a catalimetric thermometric end point is Vaughan and Swithenbank's work[71] on the titration of phenols in acetone with potassium hydroxide. The excess base serves as a catalyst in the well-known aldol condensation reaction of the solvent. The apparent heat of reaction is reported as 800 kcal/mol of titrant.

End point indicators are so effective that they

TABLE 17

Typical Thermometric End Point Indicator Reactions

Species titrated	Titrant	Reaction medium	Indicator reaction	Type
Ca^{2+}	EDTA	Water	$Mg^{2+} + EDTA^{4-} \rightarrow MgEDTA^{2-}$	Direct
Carboxylate salts	HCl	Water	$SO_4^{=} + H^+ \rightarrow HSO_4^-$	Direct
Weak bases	$HClO_4$	Glacial acetic acid or its anhydride	 $(RCO)_2O + H_2O \xrightarrow{H^+} 2RCOOH$	Catalytic
Weak acids	KOH	Acetone	 $2CH_3\text{-}\overset{O}{\overset{\Vert}{C}}\text{-}CH_3 \xrightarrow{OH^-} CH_3\text{-}\underset{OH}{\overset{H}{C}}\text{-}CH_2\text{-}CH_2\text{-}\overset{O}{\overset{\Vert}{C}}\text{-}CH_3$	Catalytic
Metal ions by direct titration	KI	Water	$2Ce^{4+} + As^{III} \xrightarrow{I^-} 2Ce^{3+} + As^{V}$	Catalytic
Anions by back titration	KI	Water	$2Ce^{4+} + As^{III} \xrightarrow{I^-} 2Ce^{3+} + As^{V}$	Catalytic
Metal ions	EDTA	Water	H_2O_2 + resorcinol Mn^{2+}	Catalytic
Weak bases	HCl in isopropanol	Acetone	dilution of HCl	Dilution

permit the use of coulometric reagent generation in conjunction with thermometric end-point detection. Coulometric generation of titrant has not been used extensively in thermometric titration due to the large temperature change developed by iR heating of the solution. However, Vajgand et al.[72] found that a wide variety of bases can be titrated coulometrically in acetic and propionic anhydride with a precision of 0.2 to 0.5% at the 5 to 10 μ/mol level. They utilized the extremely exothermic hydrolysis of the anhydride, which is catalyzed by protons, to indicate the titration end point. A typical titration curve is shown in Figure 20.

The results obtained by Burton and Irving[73] in direct titrations of small quantities of mercury (II) and silver (I) with iodide are shown in Table 18. The indicator process is the iodide catalysis of the cerium (IV) - arsenic (III) reaction. The fact that microgram quantities can be titrated thermometrically is indeed impressive and demonstrates the potentialities inherent in thermometric end-point indicators.

D. The Effect of Thermal Parameters on End Point Accuracy

In a previous section (Thermal Effects – II) the equations for chemically ideal, but thermometrically realistic, temperature–time curves were presented. These equations (30 through 41) may be used to determine the accuracy of the end point extrapolation procedure employed in a thermometric titration. Figure 21 shows a typical titration curve which was computed with both ϕ and κ equal to 0.1. It is immediately obvious that extrapolation of the initial slope *does not* yield an end point at f = 1.000, the stoichiometric equivalence point. However, it is also obvious that there is a discontinuity in the slopes at exactly f = 1.000. Thus, the latter segment of the titration curve may be extrapolated to yield a perfectly accurate end point whenever the reaction becomes entirely complete.

Real titration reactions invariably involve some degree of curvature in the vicinity of the equivalence point. In general, this curvature may arise from 2 sources, namely incomplete equilibria or

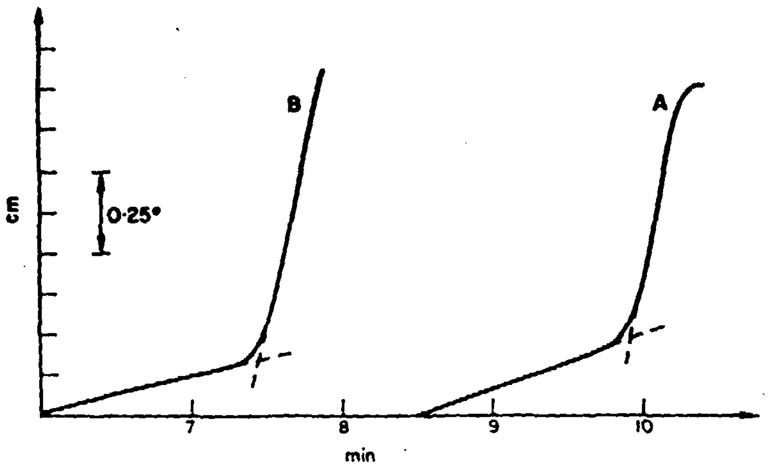


FIGURE 20. Coulometric acid-base titration using catalimetric end point location (A) 16 μ mol of potassium acetate in acetic anhydride at 2.7 mA current 2nd (B) 6.7 μ mol of benzoic acid in acetone at 1.5 mA current (From Reference 72, reprinted by courtesy of the copyright holder.)

TABLE 18

Catalimetric Thermometric Titrations of Metal Ions with Iodide

Species	Titrant	Taken (mg)	Found (mg)
Ag^+	9.883×10^{-5} M KI	2.16	2.10 ± 0.04
Ag^+	9.883×10^{-4} M KI	21.58	21.3 ± 0.4
Ag^+	9.883×10^{-3} M KI	1079	1080 ± 0.02
Hg^{2+}	9.883×10^{-5} M KI	0.200	0.198 ± 0.003
Hg^{2+}	9.883×10^{-5} M KI	1.998	2.03 ± 0.03
Hg^{2+}	9.883×10^{-5} M KI	9.991	9.97 ± 0.02

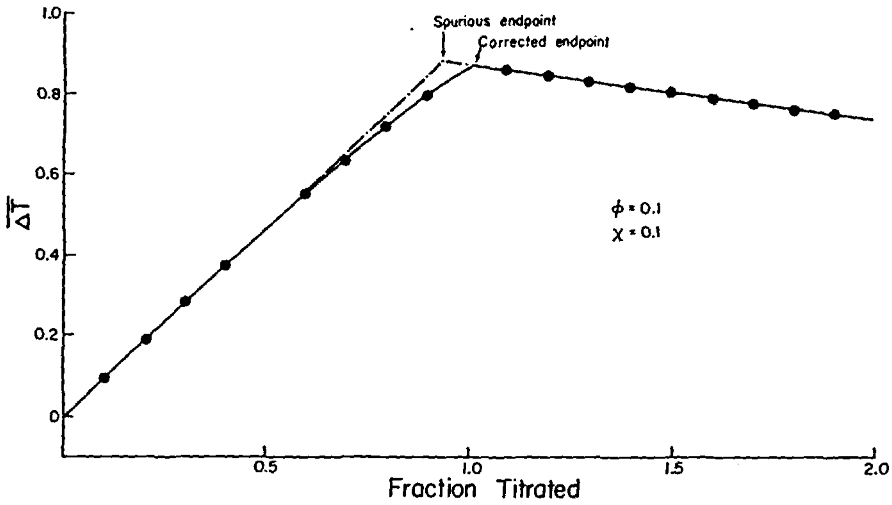


FIGURE 21. Plot of $\overline{\Delta T}$ vs. fraction titrated, indicating the effect of ϕ and κ on the end point of a thermometric titration curve; $\phi = 0.10$, $\kappa = 0.10$.

slow chemical reaction. Consequently this curvature forces the analyst to extrapolate from the beginning or initial region of the curve. This necessarily decreases the precision of the analysis and concomitantly introduces "thermal" end-point errors.

An estimate of the effect of ϕ and κ on the titration accuracy is presented in Table 19. These errors were computed by least-squares best fit of Equation 33 to the data obtained over the range from f = 0 to f = 0.5. The point of intersection with a similarly computed line (derived from Equation 38) from f = 1.5 to f = 2.0 was then evaluated algebraically from Equation 81.

E. The Effect of a Single Incomplete Chemical Equilibrium on Linear Titration Curves

A major factor in determining the utility of a chemical reaction for quantitative analysis is the magnitude of the equilibrium constant of the process. Consequently, a discussion of this problem on the accuracy and precision of thermometric titrimetry is warranted as it is in all other forms of titrimetry.

TABLE 19

Effects of Thermal Parameters on End-Point Accuracy

κ	Φ	-% Error
0.1	0.31600	14.73
0.1	0.10000	7.17
0.1	0.03160	4.34
0.1	0.01000	3.11
0.1	0.00316	2.77
0.1	0.00000	2.61
0.01	0.31600	13.08
0.01	0.10000	5.09
0.01	0.03160	1.88
0.01	0.01000	0.79
0.01	0.00316	0.43
0.01	0.00000	0.34
0.00316	0.31600	12.95
0.00316	0.10000	4.94
0.00316	0.03160	1.72
0.00316	0.01000	0.61
0.00316	0.00316	0.25
0.00316	0.00000	0.08
0	0.31600	12.89
0	0.10000	3.86
0	0.03160	1.64
0	0.01000	0.53
0	0.00316	0.17
0	0.00000	0.00

Izatt, Christensen, and their co-workers have studied the effect of equilibrium constants and reaction enthalpies on the precision and accuracy of measuring thermodynamic parameters (pK_a, ΔH^0, and ΔS^0) by thermometric titrimetry.[74,75] Tyrrell[76] has considered the effect of the equilibrium constant on the end point sharpness in thermometric titrations. Other linear titration methods such as amperometry,[22] conductometry,[77] and spectrophotometry[78] have been examined for the effect of equilibrium constants on the titration curve.

Recently Rosenthal et al.[65] presented a very general discussion of the effect of equilibrium constants on any linear titration curve. We strongly recommend reading this very valuable paper. Much of this section of the review is due to the above work.

The theory of the effect of equilibria on thermometric titration curves will be developed in terms of the following reaction

$$A + T \overset{K_f}{\rightleftharpoons} AT \tag{97}$$

where A represents the analyte species, T the titrant, and AT a product. Reaction 97 will be referred to as the titration reaction. As in preceding sections, time or the fraction titrated will be used as the independent variable. If the titrant is added via a motorized buret at a rate of $\bar{\rho}$ (mol/sec) to a volume V^0 (1.) of solution containing the analyte at an initial concentration of $C^0{}_A$ (mol/l.), then the stoichiometric equivalence point time t* (sec), will be achieved when

$$V^0 C_A^0 = \bar{\rho} t^* \tag{98}$$

The extension of all equations to a different stoichiometry (moles A per mole T) is simple (as will be shown by Table 22) and, consequently, only the case of 1:1 chemical reactions will be considered in detail. In order to simplify the presentation of results, it is convenient to normalize the concentration of all species. This normalization is carried out with respect to the initial concentration $C^0{}_A$ of analyte as the chief dependent variable:

$$\overline{C_A} \equiv C_A/C_A^0 \ ; \quad \overline{C_T} = C_T/C_A^0 \ ; \quad \overline{C_{AT}} = C_{AT}/C_A^0 \tag{99}$$

If Reaction 97 is very rapid and essentially complete, then the following results are readily generated:

$$\overline{C_A} = \frac{1 - f}{1 + rf} \qquad f \leq 1 \qquad (100)$$

$$\overline{C_T} = 0 \qquad (101)$$

and

$$\overline{C_A} = 0 \qquad f \geq 1 \qquad (102)$$

$$\overline{C_T} = \frac{f - 1}{1 + rf} \qquad (103)$$

The parameter r is included to account for the effect of dilution and is defined below. Clearly, this term is closely related to the thermal dilution parameter ϕ defined previously.

$$r = C_A^0/C_T^0 \qquad (104)$$

$C^0{}_T$ represents the concentration of T in the titrant solution. Whenever a titration reaction is perceptibly incomplete, whether due to incomplete equilibria or slow reactions, Equations 100 to 103 are invalid and must be modified accordingly.

Table 20 lists the results of a number of common titration reactions including Reaction 97, isovalent precipitation, chelate formation, 1:2 and 2:1 precipitation, and complex formation. Inspection of this table shows that all of the titration curves are defined by a plot of $\overline{C_A}$ (or any other normalized concentration) vs. the fraction titrated. See Figure 22 for titration curves describing Reaction 97. The parameter β in this table is closely related to the equilibrium constant, and it fixes the degree of completion of the reaction at any given value of the fraction titrated.

The results of Table 20 may be derived by considering the relevant mass and charge balances, dilution factors, and chemical equilibria. As an example, consider the case of Reaction 97. One can readily show that the following relationships must hold:

$$\frac{C_A^0 V^0}{V^0 + v} = (C_A + C_{AT}) \qquad (105)$$

$$\frac{\rho t}{V^0 + v} = C_T + C_{AT} \qquad (106)$$

$$K_f = \frac{C_{AT}}{C_A \cdot \overline{C_T}} \qquad (107)$$

where v is the volume of titrant added. Upon normalization, Equation 107 becomes

$$K_f \cdot C_A^0 \equiv \beta = \frac{\overline{C_{AT}}}{\overline{C_A} \cdot \overline{C_T}} \qquad (108)$$

Normalizing Equations 105 and 106 and combining with Equation 108 yields:

TABLE 20

Dimensionless Equations Describing Equilibrium Titration Curves

Chemistry	Equation	β
$A + T \leftrightharpoons AT$	$\beta\overline{C}_A^2 + (\beta(f - 1) + 1)\ \overline{C}_A - 1 = 0$	$K_{eq} \cdot C_A^0$
$A + T \leftrightharpoons A' + T'$	$(1 - \beta)\ \overline{C}_A^2 + (\beta(1 - f) - 2)\ \overline{C}_A + 1 = 0$	K_{eq}
$A + T \leftrightharpoons AT\downarrow$	$\overline{C}_A^2 + \ f - 1)\ \overline{C}_A - \beta = 0$	$K_{sp}/C_A^{0\,2}$
$A + 2T \leftrightharpoons AT_2$	$4\beta\overline{C}_A^3 + 8\beta(f - 1)\ \overline{C}_A^2 + (4\beta(f - 1)^2 + 1)\ \overline{C}_A - 1 = 0$	$K_{eq} \cdot C_A^{0\,3}$
$A + 2T \leftrightharpoons AT_2\downarrow$	$4\overline{C}_A^3 + 8(f - 1)\ \overline{C}_A^2 + 4(f - 1\ \overline{C}_A - \beta = 0$	$K_{sp}/C_A^{0\,3}$
$2A + T \leftrightharpoons A_2T$	$\beta\overline{C}_A^3 + \beta(f - 1)\ \overline{C}_A^2 + \overline{C}_A - 1 = 0$	$K_{eq} \cdot C_A^{0\,3}$
$2A + T \leftrightharpoons A_2T\downarrow$	$\overline{C}_A^3 + (f - 1)\ \overline{C}_A^2 - 2\beta = 0$	$K_{sp}/C_A^{0\,3}$

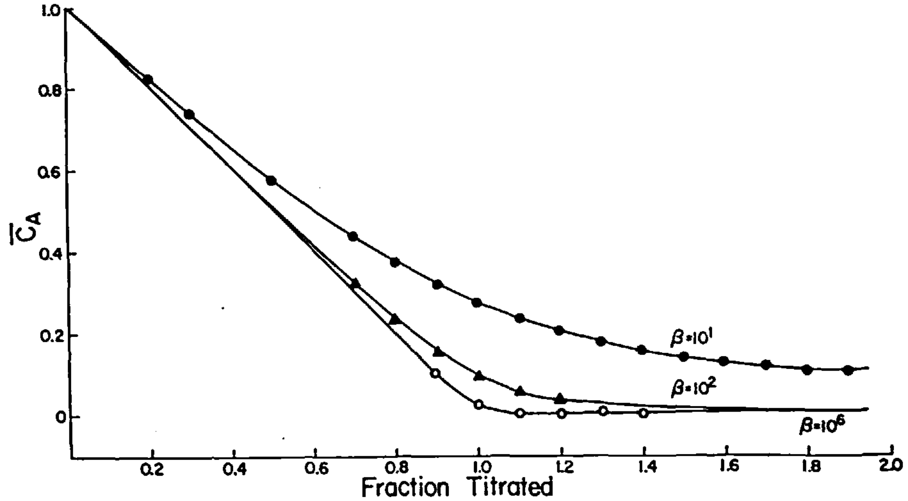


FIGURE 22. Plot of $\overline{C_A}$ vs. fraction titrated, computed from Equation 109, indicating the effect of β on end-point curvature.

$$\beta\overline{C_A}^2 + \overline{C_A}\left[\frac{\beta(f - 1)}{1 + rf}\right] + 1 - \frac{1}{1 + rf} = 0 \qquad (109)$$

Note that β is a function of both K_f and $C^0{}_A$. The degree of completion depends upon the formal free energy change ($\Delta G^{0\prime}$) and the initial concentration of analyte. The effect of β on the incompleteness of the reaction at f = 1.000 for each of a variety of reactions is shown in Figures 23 and 24. It is clear that as the analyte concentration or the free energy change increases, the reaction becomes more complete. The value of a dimensional approach to titration theory lies in the utility of the dimensionless equilibrium constant. A given value of β represents an infinite combination of equilibrium constants and initial analyte concentrations. Once a dimensionless titration curve has been computed for a given value of β it is invariant whatever the individual values of $K^0{}_{eq}$ and $C^0{}_A$ might be as long as β is held constant.

The effect of reaction incompleteness on linear and logarithmic (potentiometric) titration curves can be assessed by computing curves for Reaction 97 with the.aid of Equation 109. Linear titration curves, of which amperometric, photometric, and thermometric titrations are major examples, may be represented by plots of $\overline{C_A}$, $\overline{C_T}$, $\overline{C_{AT}}$ (and, in

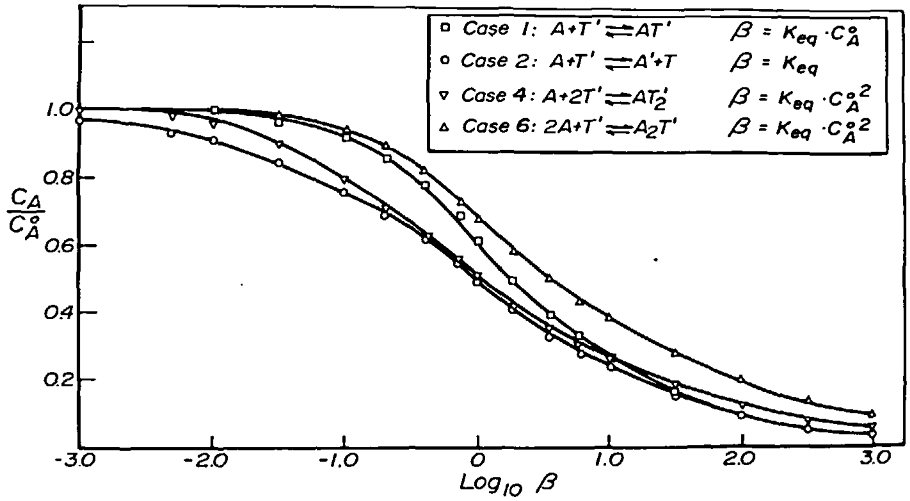


FIGURE 23. Plot of $\overline{C_A}$ vs. $\log_{10}\beta$ at f = 1.000 for reactions involving soluble products, computed from the equations of Table 20.

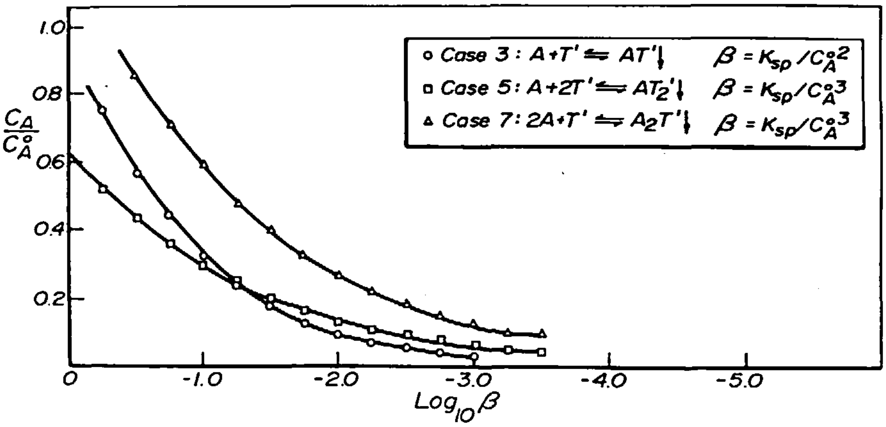


FIGURE 24. Plot of $\overline{C_A}$ vs. $\log_{10}\beta$ at f = 1.000 for reactions involving insoluble products, computed from the results of Table 20.

some instances, linear combinations of these) against the fraction titrated. Logarithmic titration curves may be expressed as plots of $p\overline{C_A}$, etc. vs. fraction titrated or as plots of an electrode potential vs. fraction titrated. If Reaction 97 were a redox process then it could be followed by a redox electrode whose potential under appropriate circumstances (electrode reversibility, etc.) would be given by the Nernst equation.

Figures 22 and 25 present a series of titration curves ($\overline{C_A}$ and $p\overline{C_A}$) for Reaction 97 with values of β ranging from 10 to 10^6. The accuracy of the linear titration curve is determined by how closely the extrapolated end point ($f_{e.p.}$) coincides with the equivalence point (f = 1.000). The end point of a potentiometric titration is most precisely, but not necessarily most accurately, determined, by locating an inflection point which corresponds to a point of maximum slope.

The literature of analytical chemistry often states that a major advantage of linear titration methods is that these techniques are highly immune to equilibrium incompleteness because one can extrapolate from regions where the reaction is

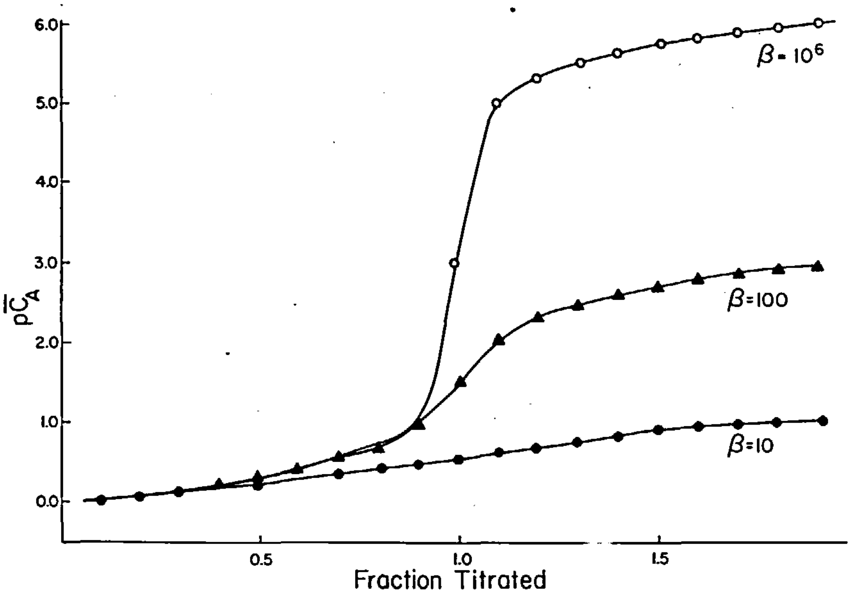


FIGURE 25. Plot of $p\overline{C_A}$ vs. fraction titrated, indicating the effect of β on end-point sharpness, computed from Equation 109.

quite complete (i.e., where 1 reagent is present in excess) and therefore carry out titrations under conditions where equilibrium constants would be impossibly small for logarithmic titrations. Under some circumstances such as Case 2 in Table 20 one can show that the slope of the titration curve at f = 0 is -1 and independent of β. Consequently extrapolation from this region to f >> 1 will invariably yield an accurate, but not necessarily a precise end point. In the present case the slope of the titration curve at f = 0, which is obtained by differentiating Equation 109 with r = 0, is

$$\left.\frac{d\bar{C}_A}{df}\right|_{f=0} \doteq -\frac{\beta}{\beta + 1} \qquad (110)$$

Thus only when $\beta >> 1$ will an accurate end point be obtained. In addition to the type of equilibrium involved, there are several other sources of error in making the extrapolation.

First, reactions having more than 1 incomplete step such as the titration of a weak acid will show very much more complex curvature, and extrapolation of the initial portion of the curve will lead to error for moderately strong acids (pK_a 1 to 3). Second, the measured variable must be accurately proportional to the concentration of only 1 concentration or concentration change. Third, precipitation processes present the annoying problem that no reaction (except for ion-pair formation, which does not involve the same enthalpy change) occurs until the solubility product is exceeded, which occurs only after some finite value of f has been reached. Last, extrapolation from the region around f = 0 to f >>1 will be very imprecise. As a consequence of 1 or more of these difficulties, one is generally forced to carry out the extrapolation over finite ranges of the fraction titrated, and this in turn will entail a determinate, although not necessarily large, error in all cases where $\beta < \infty$.

Rosenthal et al.[65] carried out a detailed analysis of the effect of β on the analytical accuracy obtained for Reaction 97. Their results are summarized in Table 21 and Figure 26. First, the extent of reaction incompletion was computed as a function of f and β. Clearly, the reaction becomes more complete as β increases. For a given value of β the reaction is *most* complete when f = 0 or f >>1 and *least* complete when f = 1.000. When the values in Table 21 and Figures 23 and 24 are compared, it is obvious that all equilibria behave qualitatively and indeed semi-quantitatively in the same way. Therefore, it is possible to generalize on the results of Rosenthal et al. for Reaction 97 and extend them to the cases described in Table 20.

A second major factor evaluated by Rosenthal is the effect of the number of data points on the titration accuracy (not precision). Over any given extrapolation range, e.g., 0 < 0.8; 1.4 < 2.2 (see Figure 26), the titration error decreases as the number of data points increases. A so called "theoretical titration error" is the intercept of Figure 26, where the number of data points is quite large. This is the situation that exists in a thermometric titration. Consequently the values in Table 22 may be used directly as estimates of the accuracy of thermometric titrations.

From their results it follows that β must exceed 1,000 to achieve an error of less than 0.1% with data obtained in the intervals $0 \leqslant f \leqslant 0.6$ and $1.7 \leqslant f \leqslant 2.3$. Considering the precision estimate discussed previously, such a titration would have a precision of 0.2% at the 10 mM level. Consequently β must be at least 500 to 1,000 for the analysis to be *precise and accurate* to better than 0.2%. Meites and Meites[79] have examined Reaction 97 for the case of potentiometric end-point location. In the absence of dilution one can show that the titration error is

$$\%\ \text{error} = -\frac{100}{\beta} \qquad (111)$$

Thus 0.1% error occurs when β = 1,000. In this instance potentiometric and linear titration methods are equally accurate and there is consequently no advantage of accuracy to be gained by using 1 technique in preference to the other. However, as will be shown in the next section, this is not always true, particularly in the case of acid-base titrations; and in addition the precisions of the 2 methods are markedly different even in this case As was stated above, a precision of the order of 0.2% can reasonably be expected in a thermometric titration for which β equals or exceeds 1,000 provided that the signal-to-noise ratio and the reaction enthalpy are not unfavorable. In the corresponding potentiometric titration, however, Meites and Meites[79] showed that in the absence of dilution the relative precision is given by

$$\%\ \text{relative precision} \cong \pm \frac{46}{\beta^{1/2}} \qquad (111a)$$

TABLE 21

PERCENT DEVIATION FROM COMPLETE REACTION FOR VARIOUS VALUES OF β[a]

Percent deviation = $100(f-[AT]/C_A^\circ)/f$

β	Fraction titrated										
	0.05	0.10	0.20	0.80	0.90	1.00	1.10	1.20	1.80	1.90	2.00
5	100	100	100	100	100	100	100	100	100	100	100
10	9.48	9.90	10.85	21.27	24.02	27.02	23.17	20.00	10.00	9.16	8.44
50	2.06	2.17	2.42	7.20	9.66	13.18	9.36	6.92	2.37	2.12	1.92
100	1.04	1.10	1.23	4.12	6.07	9.51	5.91	4.00	1.22	1.09	0.98
200	0.523	0.552	0.620	2.24	3.63	6.82	3.56	2.20	0.616	0.549	0.495
500	0.210	0.222	0.249	0.954	1.70	4.37	1.68	0.946	0.249	0.221	0.199
800	0.131	0.138	0.156	0.606	1.12	3.47	1.11	0.603	0.156	0.138	0.125
1000	0.105	0.110	0.125	0.487	0.915	3.11	0.908	0.486	0.125	0.111	0.100
5000	0.021	0.022	0.025	0.099	0.195	1.40	0.195	0.099	0.025	0.022	0.020
10000	0.010	0.012	0.012	0.049	0.098	0.991	0.098	0.049	0.012	0.011	0.010
0	0	0	0	0	0	0	0	0	0	0	0

[a] Adopted from Reference 65 with permission of the copyright owner.

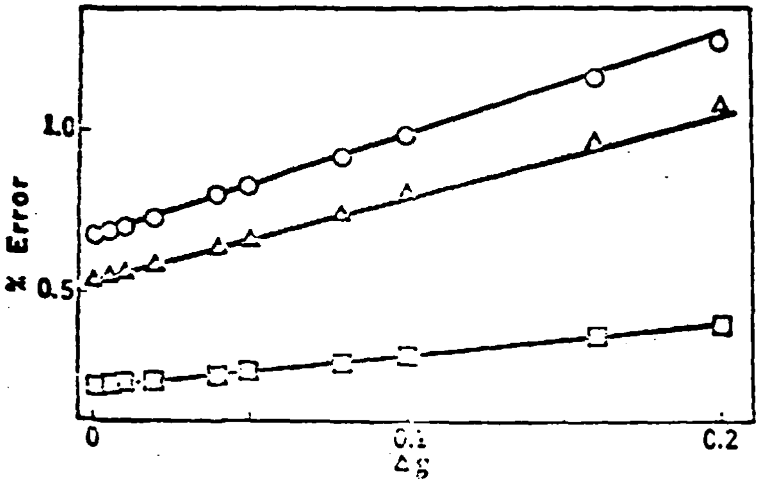


FIGURE 26. The effects of β and the number of points on the end-point errors of linear titrations. The data are computed for the ranges 0.0 to 0.8 and 1.4 to 2.2 with β = 2(O), β = 20(Δ), and β = 200 (□). (From Reference 65, reprinted by courtesy of the copyright holder.)

or about ± 1.5% if β = 1,000. In this case the linear titration method is roughly an order of magnitude more precise.

F. The Accuracy of Acid-Base Determinations by Thermometric Titrimetry

Perhaps the major application of thermometric titrimetry has been to the determinations of acids and bases. Jordan and Dumbaugh[2] demonstrated that boric acid ($pK_a = 9.2$) and hydrochloric acid have qualitatively similar titration curves. Although theoretical photometric,[78] conductometric, and potentiometric[77] weak acid-strong base titration curves have been available in the

TABLE 22

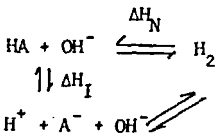
β-Values Corresponding to Particular Theoretical Titrations[a]

Ranges	Theoretical titration error (%)			
	3	1	0.1	0.01
0 – 0.2 2.5 – 2.7	11 (1.5)	42 (3.0)	458 (8.0)	4620 (154)
0 – 0.4 2.1 – 2.5	17 (1.2)	62 (2.9)	662 (19)	6670 (201)
0 – 0.6 1.7 – 2.3	31 (0.57)	111 (1.2)	1200 (2.4)	12100 (446)
0 – 0.8 1.4 – 2.2	66 (0.41)	277 (1.1)	3310 (446)	33800 (4850)
0 – 0.8 1.2 – 2.0	182 (16)	785 (79)	10400 (976)	109000 (9980)

[a] Adopted from Reference . 65 with permission of the copyright holder.

literature for some time, there are no such curves available for thermometric titrations.

The reaction of a weak acid with a strong base can be described in terms of the following reaction sequence:



$$\begin{tikzcd} HA + OH^- \arrow[r, leftrightarrow, "\Delta H_N"] \arrow[d, leftrightarrow, "\Delta H_I"] & H_2O + A^- \\ H^+ + A^- + OH^- \arrow[ur, leftrightarrow, "\Delta H_w"'] & \end{tikzcd} \qquad (112)$$

The total heat generated in a titration (Q) is the sum of the heat from ionization (Q_I) and from the formation of water (Q_W). Thus

$$Q = Q_I + Q_w \qquad (113)$$

$$Q_I = \Delta H_I \; (C_{A^-} - C^0_{A^-}) \; V^0 \qquad (114)$$

$$Q_w = \Delta H_N \; (n_{H_2O,\text{produced}}) = \Delta H_N \; (\Delta n_{H^+}) \qquad (115)$$

$$\Delta n_{H^+} = n^0_{H^+} + n_{H^+,\text{generated}} - n_{H^+} \qquad (116)$$

In the above equations C_{A^-} is the equilibrium concentration of the Bronsted base A^-, $C^0{}_{A^-}$ is the initial concentration of A^-, Δ_{nH^+} is the number of moles of hydrogen ions *consumed*, $n^0{}_{H^+}$ is the initial number of moles present, and n_{H^+} is the number of moles present at any point in the titration. The number of moles of H^+ generated during the titration is equal to the change in the number of moles of A^-, and therefore

$$Q_T = \Delta H_I V^0 \; (C_{A^-} - C^0_{A^-}) + \Delta H_w V^0 \; (C_{A^-} - C^0_{A^-} + [H^+]^0 - [H^+]) \qquad (117)$$

or

$$Q_T = (\Delta H_I + \Delta H_w) \; V^0 \; (C_{A^-} - C^0_{A^-}) + \Delta H_w V^0 \; ([H^+]^0 - [H^+]) \qquad (118)$$

Equations describing all of the concentrations in Equation 118 are readily available from the theory of equilibria in aqueous solution. Neglecting dilution, changes in ionic strength, etc., one arrives at

$$[H^+]^3 + [H^+]^2 \{K_a + f\, C^0_A\} + [H^+] \{K_a C^0_A \, (f - 1) - K_w\} - K_w K_a = 0 \qquad (119)$$

Equations 118 and 119 show that

1. At $f = 0$, $Q_T = 0$
2. With $Ka = \infty$, $C_{A^-} = C^0{}_{A^-}$ for all f
3. With $Ka = 0$, $[H^+]^0 = \sqrt{Kw}$

Theoretical thermometric titration curves were computed via these equations, and are shown in Figure 27. In each case $\Delta H_w = -13.5$ kcal/mol, $\Delta H_I = 3.5$ kcal/mol, $C^0{}_A = 10$ mM, and $K_w = 1.00 \times 10^{-14}$. As K_a becomes smaller, 3 significant features are observed: first, the *total heat* evolved decreases; second, the initial slope decreases; and third, the region around the equivalence point becomes progressively more curved when $pK_a > 7$.

The first of these points is of major calorimetric significance since it indicates that the total heat evolved may not be used as a measure of ΔH_I whenever pK_a is less than about 7 unless one corrects for the amount of acid which dissociates before the titration is begun. Thus the extrapolation procedure used by Jordan and others must be corrected appropriately.

Analytically the second and third points are significant. For moderately strong acids ($0 \leqslant pK_a \leqslant 6$) the initial part of a titration curve should not be extrapolated in locating the end point; rather it is the last 30% of the curve that should be extrapolated. Note that with pK_a-values in this range the reaction is quite complete around the end point. When $pK_a > 7$ the initial part of the curve has the correct slope because initial dissociation is negligible, and hence one may carry out accurate extrapolation in the range $7 < pK_a < 9$. For acids with $pK_a > 9$, the reaction is so incomplete that one must extrapolate from values of f so close to zero that the precision will be very poor.

These somewhat surprising thermochemical results must be viewed in the light of related linear titration methods wherein very similar phenomena are observed. In fact, curvature in titration curves for moderately strong acids ($1 < pK_a < 4$) by self-indicating photometric titrations which measure A^- is so *serious* as to render them impossible, and it seriously encumbers conductometric titrations of acids having pK_a – values around 2. Owing to our ability to perform a final extrapolation, this is not a serious problem in thermometric titrimetry. The results presented above are contingent upon the magnitude of ΔH_I and the initial concentration of weak acid. When ΔH_I is small, all acids having pK_a-values up to about 9 or 10 can be determined by initial

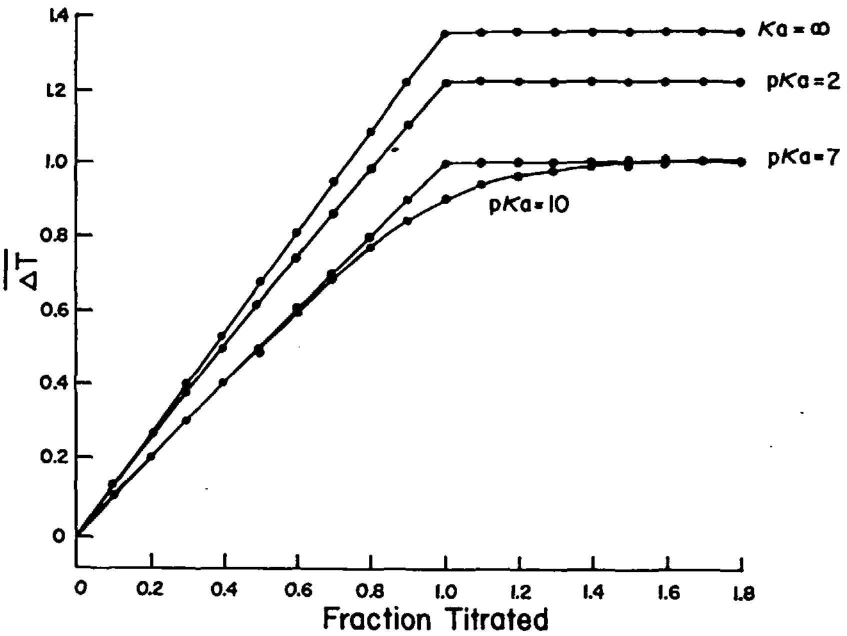


FIGURE 27. Acid-base thermometric titration curves. Plot of $\overline{\Delta T}$ vs. fraction titrated pK$_a$ of acid is indicated on the curve, initial total acidity = 10 mM, $\Delta H_I = 3.5$ kcal/mol, $\Delta H_w = -13.5$ kcal/mol, $K_w = 1.00 \times 10^{-14}$.

extrapolation. As C^0_A decreases, the upper limit in pK$_a$ will decrease with the result that the titration of a 1 mM solution of an acid with $K_a = 10^{-9}$ will be quite imprecise.

G. Analysis of Mixtures by Thermometric Titration and Direct Injection Enthalpimetry

Up to this point the detailed discussions have been limited to titrations of samples containing only 1 reactive species. Obviously, titrations can be carried out on mixtures, but the success of differentiating titrations depends strongly upon the relative free energies and reaction enthalpies. There are 4 possible cases which are enumerated in Table 23.

In 2 instances no differentiation is possible. In both of these $\Delta H_A = \Delta H_B$, so that each species has the same reaction enthalpy, and only the sum of the concentrations is accessible. However, if the 2 enthalpies are unequal differential analysis does become possible. In the simplest case, where $K_a \neq K_B$, 2 distinct end points, 1 for each species, will be observed if the equilibrium constants are significantly different ($K_A/K_B > 100$). Intuitively the analytical precision will depend principally upon the difference in reaction enthalpy when K_A/K_B is very different from unity. When the ratio of equilibrium constants becomes unity, the third case is approached as a limit.

Hansen and Lewis[64] have treated the third case both theoretically and experimentally. The analysis is based on measurements of both the total number of moles of reagent consumed (n_T) and the total heat evolved (Q_T). Assuming that both A and B react in equimolar proportions with the reagent,

$$n_T = n_A + n_B \tag{120}$$

$$Q_T = n_A \Delta H_A + n_B \Delta H_B \tag{121}$$

Solution of the 2 simultaneous equations yields values of both n_A and n_B. Through the equations of error propagation Hansen and Lewis have shown that

$$\begin{aligned}\sigma^2_{n_A} &= \left(\frac{-\Delta H_B}{\Delta H_A - \Delta H_B}\right)^2 \sigma^2_{n_T} \\ &+ \left(\frac{1}{\Delta H_A - \Delta H_B}\right)^2 \sigma^2_{Q_T} + \left(-\frac{(Q_T - \Delta H_B \cdot n_T)}{(\Delta H_A - \Delta H_B)^2}\right)^2 \sigma^2_{\Delta H_A} \\ &+ \left(\frac{Q_T - (\Delta H_\Delta \cdot n_T)}{(\Delta H_A - \Delta H_B)^2}\right)^2 \sigma^2_{\Delta H_B}\end{aligned} \tag{122}$$

TABLE 23

Differentiation of Binary Mixtures by Thermometric Titration and Kinetic Analysis

Case	Equilibrium constants	Enthalpies	Number of breaks in titration curve	Simultaneous analysis possible
1	$K_A = K_B$	$\Delta H_B = \Delta H_B$	1	no
2	$K_A \neq K_B$	$\Delta H_A = \Delta H_B$	1	no
3	$K_A = K_B$	$\Delta H_A \neq \Delta H_B$	1	yes
4	$K_A \neq K_B$	$\Delta H_A \neq \Delta H_B$	2	yes

Case	Rate constants	Enthalpies	Simultaneous analysis possible
1	$k_A = k_B$	$\Delta H_A = \Delta H_B$	no
2	$k_A = k_B$	$\Delta H_A \neq \Delta H_B$	no
3	$k_A \neq k_B$	$\Delta H_A = \Delta H_B$	yes
4	$k_A \neq k_B$	$\Delta H_A \neq \Delta H_B$	yes

Obviously, the analytical precision depends very strongly upon the difference in reaction enthalpies. The results obtained by Hansen and Lewis for mixtures of acetate plus pyridine are shown in Table 24 along with the relevant thermodynamic parameters. Their results indicate that extremely high calorimetric and analytical precisions are required in order to obtain precise analyses.

During the past decade a great amount of work was devoted to the development of kinetic analysis and particularly to kinetic differentiation of mixtures. The technique of differential kinetic analysis was initiated by Lee and Kolthoff[80] in the early 1950's, but did not become popular until Siggia and his co-workers made use of the techniques in analyzing mixtures of homologous compounds via functional group reactions. It is beyond the scope of this review to discuss the fundamentals of kinetic analysis; however, there are in essence 3 mathematically distinct procedures: the method of Roberts and Regan, proportional equations, and logarithmic extrapolation.[81] The last of these is entirely equivalent to the differential analysis of mixtures of radionuclides by differences in half-lives and has been used most extensively in thermometric analysis.

The first reported use of thermometric kinetic differentiation was that of Papoff and Zambonin.[82] This paper also contains a short but comprehensive review of the use of calorimetry to measure reaction rates. These authors used both the logarithmic extrapolation and proportional equations method to analyze mixtures of methyl and isopropyl acetate. Typical temperature-time curves and analytical results are presented in Figure 28 and Table 25. In preliminary kinetic studies on pure materials they observed precisions of ±0.5 to 3% for the measurement of rates with half-lives varying from 3.5 to 30 sec in replicate experiments. Analytical results on roughly equimolar mixtures are equally precise and accurate. In order to carry out determinations of both the more slowly and the more rapidly reacting components, it is necessary to subtract out the heat due to mixing and temperature mismatch. When mixing is completed before the first reaction proceeds to any extent, the heat of mixing can be discriminated by time resolution. Alternatively, the heat of mixing can be obtained from a blank experiment. When only the slower reacting component is of interest it may be determined from the intercept of a plot of log T vs. t (see curve b, Figure 28).

TABLE 24

Enthalpimetric Resolution of a Binary Mixture[a]

A. Thermodynamic Data

Reactant	Reaction	ΔH (kcal/mol)	pK_a
Acetate	$C_2H_3O_2^- + H^+ \rightleftharpoons C_2H_3O_2H$	0.05±0.01	4.8
Pyridine	$C_5H_5N + H^+ \rightleftharpoons C_5H_5NH^+$	–4.97±0.01	5.3

B. Analytical Data

Acetate (millimoles)		Pyridine (millimoles)		Total (millimoles)	
taken	found	taken	found	taken	found
-	-	4.97	4.97±0.04	-	-
0.52	0.63±0.02		4.95±0.04	5.49	5.57±0.02
1.56	1.67±0.03	3.98	3.95±0.03	5.54	5.62±0.02
2.62	2.75±0.03	2.49	2.45±0.02	5.11	5.20±0.03
4.19	4.21±0.08	1.49	1.52±0.02	5.68	5.74±0.07
5.24	5.32±0.13	0.50	0.52±0.03	5.74	5.85±0.02
-	5.24±0.03	-	-	-	-

[a]Reference 64

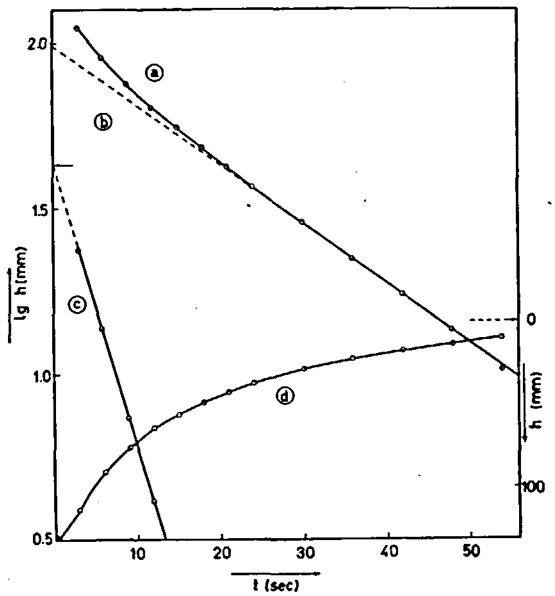


FIGURE 28. Basis for kinetic differentiation of reactants. Plot of $\log_{10}$ height vs. time, (a) log h (= log (h_{Me} + h_{isopr})) vs. t, (b) extrapolation of a to give log h^o_{isopr} vs. intercept (c) log (h – h_{isopr}) vs. t gives log h^o_{Me} vs. intercept (d) experimental h vs. t curve.

H. The Effect of Slow Chemical Reactions on Automatic Linear Titration Curves

Whenever a titrant is added continuously to an analyte solution, one must be aware that a slow chemical reaction can have profound effects on both the shape of the titration curve and the accuracy that can be secured. If the titrant is added discontinuously, as it is in manual titrations, one can wait for the process to go to equilibrium. Such is not the case in thermometric titrimetry

TABLE 25

Kinetic Resolution of a Binary Mixture[a]

Methyl Acetate		Isopropyl Acetate	
Taken (millimoles)	Found (millimoles)	Taken (millimoles)	Found (millimoles)
0.666	0.651±0.6%	0.666	0.660±1.6%
0.424	0.416±0.9%	0.848	0.845±1.3%
0.561	0.563±4.0%	0.850	0.854±2.0%

[a]Reference 82

since imperfectly adiabatic flasks are employed. For this reason thermometric analysis almost always involves slow, but continuous reagent addition.

Although the mathematics for a number of mechanistic rate laws have been developed by Cover and Meites[83] and are listed in Table 26, we shall focus on the reaction:

$$A + T \xrightarrow{k_A} \text{Prod} \qquad (123)$$

This is perhaps the most common reaction mechanism in chemistry and in our experience it

TABLE 26

Integral Rate Laws for Kinetic Titrimetry

Case[a]	Chemical system	Dimensionless rate law
1. Slow preceding reversible reaction	$\beta \underset{K}{\overset{K_{-1}}{\rightleftarrows}} A$ $A + T \xrightarrow[K_\infty]{} A' + T'$	$\overline{C_A} = \frac{1}{\beta} (\beta_2(1 - f) + \beta_3(\exp - \beta_1(f - 1))$
2. Disproportionation of a product	$A + T \xrightarrow[K_\infty]{} A' + T'$ $2A' \xrightarrow[K_D]{} A' + A''$	$\overline{C_A} = 1 - f - \sqrt{\frac{1}{4\beta}} \tanh \sqrt{4\beta}$
3. Catalytic regeneration	$A + T \xrightarrow[K_\infty]{} A' + T'$ $A' + C \longrightarrow A + C$	$\overline{C_A} = 1 - \frac{1}{\beta} (1 - \exp - \beta f)$
4. Slow first order reaction: first order in A, zeroth order in T	$A + T \xrightarrow[k_A]{} A' + T'$	$\overline{C_A} = \exp - \beta f$
5. Slow first order reaction: first order in T, zeroth order in A	$A + T \xrightarrow[k_A]{} A' + T'$	$\overline{C_A} = 1 - f - \frac{1}{\beta} \exp - \beta f$
6. Slow second order reaction: first order in A, first order in T	$A + T \xrightarrow[k_A]{} A' + T'$	$\overline{C_A} = \frac{\exp \frac{\beta}{2} \exp - \frac{\beta}{2} (f - 1)^2}{1 + \sqrt{\pi \frac{\beta}{2}} \exp \frac{\beta}{2} \left[\text{erf}\sqrt{\frac{\beta}{2}}(f-1) + \text{erf}\sqrt{\frac{\beta}{2}} \right]}$

[a] See References 83 and 84 for complete mathematical treatment

represents an extremely serious problem in the development of continuous automatic titrations of organic compounds. The overall rate can be completely defined mathematically (for the conditions that prevail in a constant-rate titration) by the following differential equations and initial conditions:

$$\frac{dC_A}{dt} = -k_A C_A C_T \qquad (124)$$

$$\frac{dC_T}{dt} = \rho - k_A C_A C_T \qquad (125)$$

$$C_A = C_A^0 \,, \quad C_T = 0 \qquad t \leq 0 \qquad (126)$$

where k_A is the relevant second–order rate constant (l./mol sec) and ρ is the *concentration* rate of titrant addition (mol/l. • sec). All other terms have been defined previously.

The unusual aspect of this set of simultaneous equations is the presence of the term ρ. Physically the parameter indicates that a titrant is being added at a constant rate; mathematically it drastically encumbers a solution of the equations.

A number of assumptions are implicit in Equations 124 to 126. First, we have assumed that the back reaction is negligible, or

$$K_{eq} = \frac{k_A}{K_{-A}} = \infty \qquad (127)$$

It is also assumed that mixing is instantaneous, and that dilution is negligibly small (i. e., that a very concentrated titrant is used). Under these conditions it is easy to show that the titrant concentration must be given by

$$C_T = \rho t + C_A - C_A^0 \qquad (128)$$

so that Equation 124 becomes

$$\frac{dC_A}{dt} = -k_A C_A (\rho t + C_A - C_A^0) \qquad (129)$$

Equation 129 is a form of Ricatti's equation. Continuing our usual practice of working with dimensionless equations, Equation 129 may be written

$$\frac{d\overline{C_A}}{df} = -\beta \overline{C_A} (f + \overline{C_A} - 1) \qquad (130)$$

where

$$\beta \equiv k_A C_A^0 t^* = k_A \rho t^{*2} = K_A C_A^0 / \rho \qquad (131)$$

Equation 130 may be solved after transformation to a linear equation with time-dependent coefficients, the result is

$$\overline{C_A} = \frac{\exp\left(\frac{\beta}{2}\right) \exp\left[-\frac{\beta}{2}(f-1)^2\right]}{1 + \sqrt{\pi \frac{\beta}{2}} \exp\left(\frac{\beta}{2}\right)\left(\operatorname{erf}\sqrt{\frac{\beta}{2}}(f-1) + \operatorname{erf}\sqrt{\frac{\beta}{2}}\right)} \qquad (132)$$

This equation was used to compute a number of simulated titration curves, which are shown in Figure 29. In reality slow kinetics have 3 principal effects on the titration curve. First, the initial slope and overall reaction rate are small. This phenomenon makes location of the start of the titration difficult and causes part of the end-point error. Physically this is due to the absence of the titrant at the start of the reaction. Second, the maximum rate of decrease in the concentration of analyte is set by ρ. In most instances ($\beta < \infty$) the slope will be less than the maximum, thereby causing erroneous extrapolation. Last, the rate of reaction (and therefore the slope) becomes small as the equivalence point is approached since the analyte is almost depleted. Analytically the first 2 effects are most serious since they lead to spurious end points.

The magnitudes of the errors are shown in Table 27 and Figure 30. End-point errors were estimated by plotting the kinetic titration curves on large sheets of graph paper such that the resolution was 0.2% in fraction titrated. The longest linear region with the greatest slope was located and extrapolated to zero on the concentration axis. The value of f at the end point could then be estimated and a theoretical error computed. Alternatively, a best straight line was calculated over that region where there are no significant deviations from linearity. The end point was taken as the value of f where $\overline{C_A} = 0.00$. The results are presented in Table 27. As Column 3 indicates, the 2 procedures are in good agreement. The direct graphical extrapolation is recommended for analytical work since it does not require much computation.

When $\beta < 7$, the linear regions of the titration curve are so short that precision is quite poor, but when $\beta > 7$, the extrapolation is simple and precise.

These results indicate that very substantial analytical errors can result even when the titration curve appears to be quite linear. It is recommended that whenever kinetic curvature is suspected one should vary C^0_A by at least a factor of 3 (which will vary β by a factor of 9). If a plot of

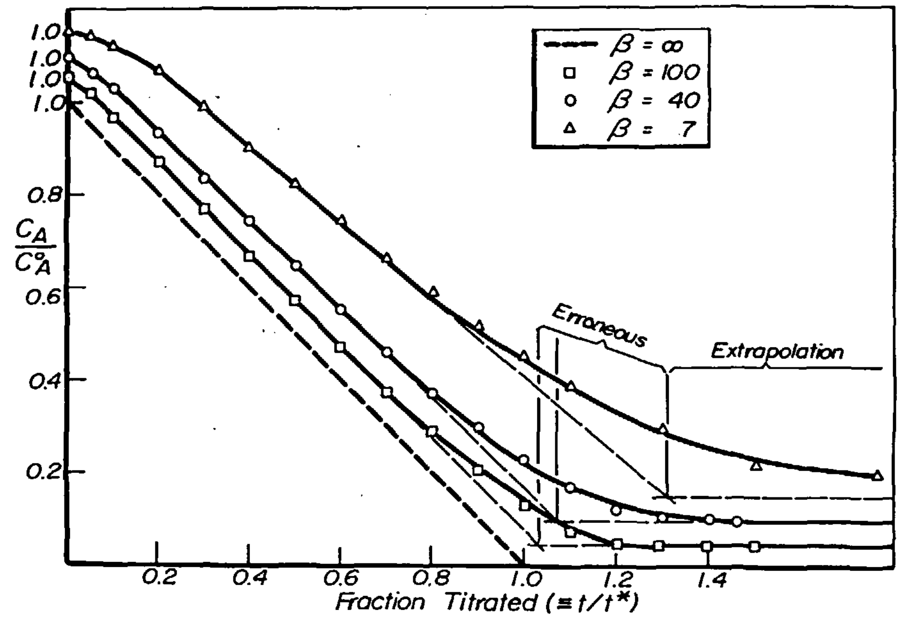


FIGURE 29. Plots of $\overline{C}_A$ vs. fraction titrated, showing the effects of β on the titration curve and analytical accuracy. All curves were computed from Equation 132.

the number of moles taken against the number found is linear, this strongly implies that the rate of titrant addition is the only slow step, and consequently kinetic errors are absent.

If kinetic errors are present then the analyst is advised to alter his reaction conditions to speed up the reaction. When this is not possible the procedures discussed below should be employed.

1. The rate of titrant addition is determined by titration of a material known to react completely with the titrant. Optimally the volume rate of addition (ml/sec) and the concentration of the titrant should be measured separately.

TABLE 27

End Point Correction Data for Kinetic Titration Curves

β	% Extrapolation error	
	Graphical	Least-Squares
7	33.5	32.9
10	25.0	24.5
25	10.5	10.5
40	7.0	6.9
75	4.5	3.9
100	3.5	3.3
175	1.5	1.5

2. The rate constant (k_A) for the species of interest is determined, e. g., by a direct injection enthalpimetric experiment. As Carr and Jordan[84] have shown, k_A may be measured by an ad hoc *titration* of a known sample.

3. The unknown sample is titrated and an end-point time, t′, is established.

A tentative estimate of β is obtained by taking t* equal to t′. A high preliminary estimate of β is invariably obtained since t′ is always greater than t*. The percent error can then be obtained from Figure 30. This will establish a new estimate of t′ since

$$\%\ \text{error} \equiv \frac{t' - t^*}{t^*} \cdot 100 \qquad (133)$$

Obviously, the entire process can be iterated graphically. In actual practice Carr and Jordan found that, with β ≈ 7, the change in t′ was within experimental error (about 0.2%) after 4 iterations. The kinetic corrections will depend very much on the rate law (see Table 26) involved. The procedure described above can be applied to any situation once a suitable working curve (such as Figure 30) has been obtained. There are a number of obvious limitations inherent in the procedure

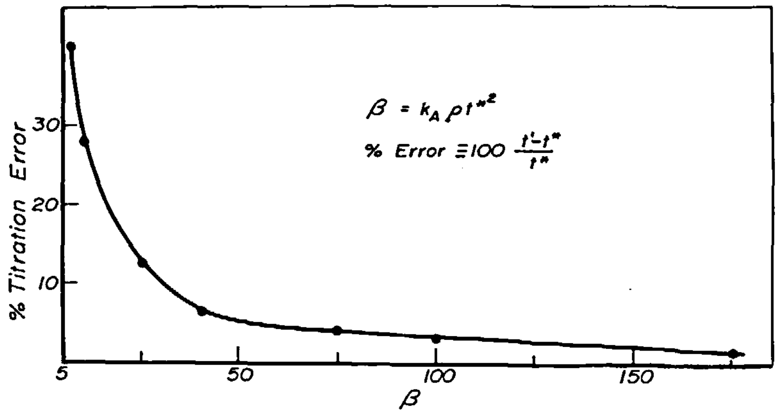


FIGURE 30. Plot of percent titration error due to slow kinetics vs. the dimensionless parameter β (= $K_A C^0{}_A t^*$).

described here. First, there is no possibility of analyzing a mixture of 2 or more slowly reacting materials. Second, one must measure the rate of reaction in order to implement an analysis. Third, it is not applicable to those cases where $\beta < 7$.

From our experience with kinetic errors in automatic titrations we must advise that, if it is at all possible, the reaction conditions (such as the pH, ionic strength, solvent, and temperature) should be changed to increase the rate. If this is not feasible, the titration should be carried out at as high an analyte concentration ($C^0{}_A$) or as low a rate of titrant addition (ρ) as possible in order to minimize the errors. Although the procedure described above is capable of good precision and accuracy (0.5%), the analysis becomes far more tedious.

It is beyond the scope of the present review to discuss the application of automatic titration to the measurement of reaction rate constants. However, it is evident from recent work that rather fast reactions can be studied by the technique.

I. Direct Injection Enthalpimetry

As was pointed out previously, direct injection enthalpimetry (DIE) is a single-point destructive method of analysis closely related to thermometric titrimetry. The technique is founded on the measurement of the heat evolved, rather than on the location of an end point, when a sample (A) is completely consumed by an excess of reagent (R). That is, Reaction 134 below is carried out under conditions where the number of equivalents of the analyte A is less than the number of equivalents of the reagent R

$$aA + rR \rightleftharpoons pP \qquad (134)$$

$$n_A < \left(\frac{r}{a}\right) n_R \qquad (135)$$

In general, a reasonably large excess of R is employed in order to drive the equilibrium of the reaction to completion and to insure that the halflife of the process is quite short in comparison to the heat transfer modulus of the calorimeter. In further discussions we will assume that the reaction is complete and so rapid that one need *not* consider heat losses.

There are 2 distinct analytical procedures for implementing the analysis. For example, the sample solution may be added to the reagent contained. in a Dewar. In this case replicate analyses are easily run. This will be referred to as Method A. The second procedure (Method B) involves addition of the excess reagent to a solution of the analyte.

No matter whether it is Method A or Method B that is employed, the chemically measured parameter is the concentration of the deficient species, A. Ignoring dilution and the mixing effect, the heat Q_R evolved due to chemical reaction is

$$Q_R = \Delta H^{0'}_A \cdot n_A \qquad (136)$$

where $\Delta H^{0'}{}_A$ is the formal enthalpy change for Reaction 134 under the experimental conditions, i. e., not an ideal state. The temperature change will be

$$\Delta T = T - T_D = \frac{Q_R}{C_D} = \frac{\Delta H^{0'}_A \cdot n_A}{C_D} \qquad (137)$$

where T_D is the initial Dewar temperature, C_D is its heat capacity, and T is the final temperature. Since the heat capacity of the Dewar reflects the volume of solution it contains, to an excellent first approximation, we can write

$$\Delta T = \frac{\Delta H^{0'}}{C_p} \cdot \frac{n_A}{V^0} = \frac{\Delta H_A^{0'}}{C_p} \cdot C_A \qquad (138)$$

where C_p is the specific heat in cal/°C· l and V^0 is the volume of solution in the Dewar. Equation 138 demonstrates that the temperature pulse is proportional to the concentration of the species A rather than to the number of moles present. This is the embodiment of the basic principle of enthalpimetric analysis: a plot of ΔT against the concentration of unknown is linear and has an intercept of zero. In practice there must be deviations from Equation 138.

In any real analysis, one must include several factors in addition to the formal reaction enthalpy. For example, the injected solution will be diluted; thus an accompanying heat of dilution will be present; second, the added volume increases the heat capacity of the Dewar; and third, the added reagent may not be at temperature T_D. In Method A we can lump the heat of reagent dilution into the formal reaction enthalpy since it will be proportional to the moles of species A. Thus, the temperature change will be

$$\Delta T = T - T_D = \frac{\Delta H_A^{0'} \cdot n_A + c_{p,A}\, v(T_A - T_D)}{C_D + c_{p,A}\, v} \qquad (139)$$

where $c_{p,A}$ is the total heat capacity (cal/°C) of reagent A and T_A is its initial temperature. In each analysis the same volume (v) of analyte must be added to maintain a linear relationship between ΔT and n_A. A plot of ΔT vs. n_A will have a zero intercept only if the second term in the numerator of Equation 139 is much less than the first. (See Figure 10 for an illustration of such a plot.) This may be arranged by matching T_A and T_D by thermostation or by the conventional calorimetric technique of breaking a thinglass vial containing species A which is pre-equilibrated by immersion in the Dewar. Each of these methods seriously compromises the major virtues of DIE, which are its speed and simplicity. The intercept can be minimized by making the second term quite small, e.g.,

$$c_{p,A}\, v(T_A - T_D) \leq 0.01\, \Delta H_R^0 n_A \qquad (140)$$

Assuming that $|\, T_A - T_D \,| \leqslant 0.5°C$; $c_{p,A} = 1$ cal/°C ml and $|\, \Delta H^\circ{}_A \,| = 10$ kcal/mol, one requires that

$$\frac{n_A}{v} \geq 0.5 \text{ M} \qquad (141)$$

This is obviously a major limitation: only rather concentrated samples can be analyzed. In this case, one is trading off sensitivity for analysis time. Obviously, one can repeatedly and rapidly inject a series of unknowns, each of which will produce a significant temperature pulse free from secondary effects, if the concentration of analyte is high.

In Method B an unknown, but constant, excess of reagent is added to the analyte contained in a Dewar. Any heat of dilution ($\Delta H^{\circ\prime}{}_{D,R}$) will not be proportional to the analyte concentration, but will represent an offset error. Thus

$$\Delta T = \frac{\Delta H_A^{0'} \cdot n_A + \Delta H_{D,R}^{0'} \cdot n_R + C_{p,R}\, v(T_R - T_D)}{C_D + C_{p,R}\, v} \qquad (142)$$

Once again linearity will occur only if a constant volume is added. In order to minimize temperature mismatch a small volume should be used. However, since this procedure is not amenable to repeated injections there is really no objection to using the reagent-in-vial technique of classical calorimetry; consequently, T_R and T_D are easily matched. If an injection technique is employed then

$$C_{p,R}\, v(T_R - T_D) \leq 0.01\, \Delta H^{0'} n_A \qquad (143)$$

The volume containing n_A is not v, but rather the volume equivalent to C_D. Thus it is possible, using concentrated solutions of the reagent R, to determine low concentrations of A without incurring much difficulty due to temperature-matching. The limit of sensitivity is then set either by the noise level (temperature resolution) or by the ratio of the heat due to reaction to the heat due to dilution. In the ideal case where $\Delta H_D = 0$ the limit of sensitivity at the 10% precision level, assuming a temperature resolution of ± 0.2 m°C, is

$$0.0002°\text{C} = \frac{\Delta H_R^{0'} \quad n_A}{C_D} \cong \frac{\Delta H_R^{0'} \cdot n_A/v}{1000 \text{ cal/°C liter}} \qquad (144)$$

$$C_A \,(\text{mole/liter}) \geq \frac{2}{\Delta H_R^{0'} \,(\text{cal/mole})} \qquad (145)$$

Consequently for a reaction involving an enthalpy change of 10 kcal/mol C_A must be equal to or exceed 0.2 mM.

Thus, Method B is much more sensitive than Method A and presents minimal problems in temperature matching. Although it is not amenable to as fast or routine use as in Method A, the overall procedure is so simple and precise that, in our opinion, Method B should be used unless a very rapid analysis at high concentration of analyte is required.

A recent paper by Zambonin and Jordan[85] illustrates some of the potentialities inherent in the use of gaseous reagents. The heat capacity per mole of gases is very much lower than that of liquids and consequently, one need have little concern in such instances for temperature matching. They explored the determination of carbon dioxide, sulfur dioxide, and nitrogen oxides by reaction enthalpimetry. The paper also reviews previous applications of gases as reagents rather than as analytes.

V. MEASUREMENT OF THERMODYNAMIC PARAMETERS BY THERMOMETRIC TITRIMETRY

A. Introduction

Implicit in the preceding discussion has been the concept that the thermodynamic parameters of a reaction may be measured by thermometric titrimetry. The simplest and most direct measurement is that of the formal enthalpy change ($\Delta H^{0\prime}$) for the titration reaction. This is derivable from the total heat evolved as measured via a temperature change. It is also possible to determine the formal equilibrium constant ($K^{0\prime}$) for the titration reaction if the temperature change is measured as a function of the amount of titrant added. In this fashion the formal free energy change ($\Delta G^{0\prime}$) and entropy change ($\Delta S^{0\prime}$) are easily derived. The term formal thermodynamic parameter, *e. g.* $\Delta G^{0\prime}$, $\Delta H^{0\prime}$ and $\Delta S^{0\prime}$, will be used throughout this discussion since experiments are rarely, if ever, carried out at infinite dilution (zero ionic strength). The true thermodynamic parameter (ΔG^0, ΔH^0, or ΔS^0) can be obtained from the formal one in 2 ways: either by correction for activity effects via an assumed model such as the Debye-Hückel limiting law (DHLL), the extended Debye-Hückel equation, or the Guggenheim-Bates equation, or by repeating, individual experiments in a series of solutions of different but high and constant ionic strengths. During the course of each titration $K^{0\prime}$ and $\Delta H^{0\prime}$ are invariant, and the data ($K^{0\prime}$, $\Delta H^{0\prime}$) are then extrapolated to infinite dilution.

It is necessary to assume that the solution is chemically and thermally homogeneous and that equilibrium is achieved very rapidly. Even if these assumptions are justified, obtaining both heats and equilibrium constants from plots of temperature vs. moles of titrant requires correction for all heat sources extraneous to the titration reaction and correction for the changes in the heat capacity of total system. Alternate heat sources include at least the heats of titrant dilution, stirring, and temperature mismatch. In this section it is assumed that such corrections, which have already been described in Section II, have been made and that a plot of Q_C (corrected heat) vs. moles of titrant has been obtained. Computer programs for this purpose are available. A discussion of the interpretation of such plots is presented in this section of the review.

B. Heats of Dilution of Electrolyte Solutions

In order to develop this discussion, which follows closely the arguments developed in the revision by Pitzer and Brewer's revision of the classical monograph of Lewis and Randall and in Harned and Owen's *Physical Chemistry of Electrolyte Solutions*[87] we will consider the following reaction

$$\mathrm{NaOH + HCl} \rightleftharpoons \mathrm{H_2O + NaCl} \qquad (146)$$

Suppose that aqueous hydrochloric acid at an ionic strength of μ_T is added to a reasonably dilute solution of aqueous sodium hydroxide having an ionic strength at μ_A. Since the hydrochloric acid is diluted from one ionic strength (μ_T) to another (μ_A), heat will be generated. This amount of heat is equal to the integral heat of dilution from μ_T to infinite dilution *less* the integral heat of dilution from μ_A to infinite dilution. At any given ionic strength the *formal* reaction enthalpy for Reaction 146 is

$$\Delta H^{0\prime} = \bar{H}_{H_2O} + \bar{H}_{NaCl} - \bar{H}_{HCl} - \bar{H}_{NaOH} \qquad (147)$$

where each $\bar{H}$ represents the partial molal heat content of the indicated species at μ_A. Note that if Reaction 146 were carried out titrimetrically the ionic strength would remain constant up to the end point (ignoring dilution) since one is in essence exchanging hydrogen ions for sodium ions. After the end point the ionic strength increases. Clearly, this fortunate situation does not always exist. It is for this reason that it is wise to take appropriate precautions to ensure that the ionic strength will remain constant during each titration: this is extremely useful, if not absolutely mandatory. The partial molal heat content of each species ($\overline{H}$) can be related to the value in the standard state via the relative heat content

$$\overline{L} = \overline{H} - \overline{H}^0 \tag{148}$$

where $\overline{L}$ is the relative molal heat content and $\overline{H}$ is the partial molal heat content. Equation 147 may now be written as:

$$\Delta H^{0\prime} = \Delta H^0 + \overline{L}_{H_2O} + \overline{L}_{NaCl} - \overline{L}_{NaOH} - \overline{L}_{HCl} \tag{149}$$

where the $\overline{L}$-values represent the difference from μ_A to infinite dilution. Obviously, $\overline{L}_{NaClO_4}$, $\overline{L}_{NaOH}$, and $\overline{L}_{HClO_4}$ are closely related to the heats of dilution from μ_A to $\mu = 0$ and most definitely are a strong function of the initial ionic strength. It should be kept in mind that a dilution process changes the heat contents of 2 species (both the solute and solvent) and therefore $\overline{L}$ is not the same as the heat of dilution.

In that range of ionic strengths where the Debye-Hückel limiting law applies, $\overline{L}_{ionic}$ may be computed from the temperature coefficient of the activity coefficient via the equations

$$\overline{L}_{ionic} = A_H \frac{\nu}{2} |z_+ z_-| \sqrt{\mu} \tag{150}$$

$$A_H = -2.303\ RT^2\ A\gamma\ 3 \left[\frac{1}{T} + \frac{\partial \ln D}{\partial T} + \frac{\alpha}{3}\right] \tag{151}$$

where $A_\gamma = 0.51$ for water at 25°C. and where D represents the dielectric constant of water. Due to uncertainties in the value of the temperature coefficient of D, A_H is not known with complete certainty (see Table 28). The term α is simply the temperature coefficient of expansion of water since we are discussing $\overline{L}$ at constant pressure. The effect of μ on $\overline{L}_{H_2O}$ may be computed by integration of the Gibbs-Duhem equation written for $\overline{L}$. This results in

$$\overline{L}_{H_2O} = \frac{-A_H\ m^{2/3}}{166.53} \tag{152}$$

for aqueous solutions at 25°C. This equation applies only to 1:1 electrolyte solutions where m is the molality of the electrolyte. This equation for $\overline{L}_{H_2O}$ is quite inaccurate in even moderately dilute solutions; however, $\overline{L}_{H_2O}$ is very much smaller than $\overline{L}_{ionic}$ since activity effects on uncharged species are small. Upon substituting the above equations for relative molal heat contents into Equation 149 we obtain

$$\Delta H^0 = \Delta H^{0\prime} - A_H \left[\frac{m^{2/3}}{166.53} + \sqrt{\mu}\right] \tag{153}$$

Since it is seldom necessary in thermometric titrimetry to titrate solutions more concentrated than 10 mM, due to the intrinsic sensitivity of the method, we will assume $\mu = 0.01$, which for a 1:1 electrolyte corresponds to m = 0.01 thus:

$$\Delta H^0 = \Delta H^{0\prime} - A_H\ [6 \times 10^{-6} + 0.1] \tag{154}$$

Obviously, $\overline{L}_{H_2O}$ is entirely negligible wherever $\mu < 0.01$. We will, therefore, assume that $\overline{L}$ is equal, but of opposite sign, to the calorimetrically determined heats of dilution denoted ΔH_D.

In the absence of a chemical reaction the heat of dilution of the titrant is given by Equation 151 written for a pair of ions, such as H^+ and ClO_4^-. While this equation provides an adequate description of the heat of dilution at low ionic strengths, it must be modified where the DHLL fails. At high to moderate ionic strengths good accuracy is provided only by calorimetric measurement of the heat of dilution. Lange[88] presents the following equation for the integral heat of dilution (ΔH_D) of a strong electrolyte from molarity M to infinite dilution:

TABLE 28

Theoretical Debye-Hückel Slopes and the Temperature Coefficient of the Dielectric Constant of Water

D	$\frac{dD}{dT}$	A_H (at constant pressure in cal-mole$^{-3/2}$-$\ell^{-1/2}$
78.25	-0.361^a	488
78.54	-0.3613^b	480
78.57	-0.3622^c	484
78.54	-0.3596^d	471
78.49	-0.363^e	491
78.30	-0.3557^f	458

[a] Latley, R. T., Gatty, O., and Davies, W. G., *Phil. Mag.*, 12, 1019 (1931).

[b] Wyman, J., *Phys. Rev.*, 35, 623 (1930).

[c] Drake, F. H., Pierce, G. W., and Dow, M. T., *Phys. Rev.*, 35, 613 (1930).

[d] Wyman, J. and Ingalls, E. N., *J. Amer. Chem. Soc.*, 60, 1182 (1938).

[e] Jones, T. T. and Davies, R. M., *Phil. Mag.*, 28, 307 (1939).

[f] Malberg, C. G. and Maryott, A. A., *J. Research Natl. Bur. Standards*, 56, 1 (1956).

[g] Adopted from Reference 88 by permission of the copyright holder.

$$\Delta H_D = \frac{\Sigma \nu_j z_j^2}{2.83} A_H M^{1/2} \qquad (155)$$

ν_j is the number of ions of a charge type in a salt and z_j is the charge. Figure 31 presents some plots of ΔH_D vs. the molarity of the solution for 1:1 charge type salts, and Table 29 presents the details of Sturtevant's data on the heat of dilution of hydrochloric acid and sodium hydroxide.

It is obvious that the Debye-Huckel equations yield useful correction factors at quite low ionic strengths ($\mu \leqslant 0.01$) for 1:1 charge type electrolytes. Although the DHLL applies to electrolytes of all charge types, it breaks down at lower *molarities* for electrolytes that are not of the 1:1 type.

Consider a conventional calorimetric experiment that involves a reaction enthalpy of 10 kcal/mol. The reaction of 100 ml of a 10 mM reagent will generate 10 cal. The dilution of 10^{-3} mol of 1M hydrochloric acid will liberate 0.4 cal., for 1 M sodium hydroxide it will liberate 0.06 cal. Under these circumstances, unless heats of dilution are corrected for, the data will only be within a few percent of the thermodynamic value.

Now consider the same reaction carried out thermometrically. For processes like Reaction 146 above there is no change in ionic strength until the equivalence point. Nonetheless, the titrant solution is diluted and generates heat. It does so continuously throughout the course of the titration and, therefore, one may extrapolate out the heat of dilution of the titrant to the initial ionic strength (μ_A) by the procedures described later. Then one need only correct for the heat of dilution from ionic strengths around 10 mM to infinite dilution. This may be evaluated from Equation 151 and the estimates of A_H from Table 28 as about 50 cal/mol for 1 millimole of material or 0.05 cal. Neglecting this correction causes an error of only 0.5%. Therefore, thermometric titrations provide a relatively rapid means of eliminating the need for high precision heats of dilution since correction need be made only for the range of ionic strength where the Debye-Hückel equation is relatively accurate.

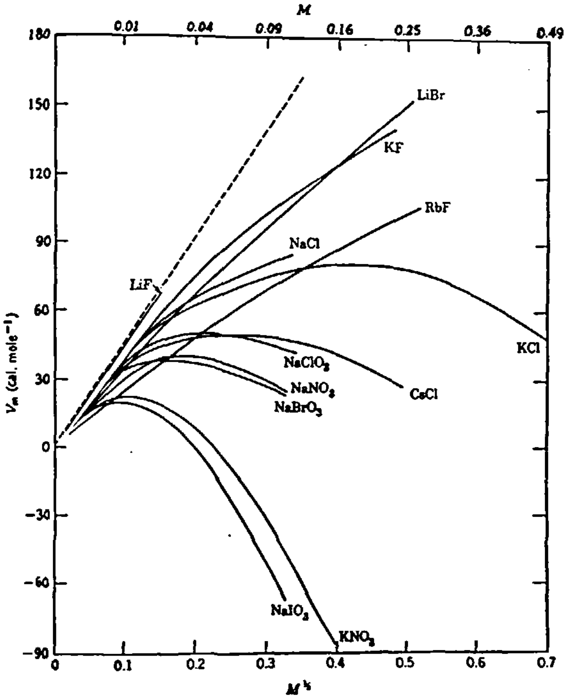


FIGURE 31. Plot of ΔH_D vs. ionic strength. (From Reference 87, reprinted by courtesy of the copyright holder.)

The validity of the approach discussed here was shown by Hale, Izatt, and Christensen[95] in their evaluation of the heat of neutralization of hydrochloric and perchloric acid by conventional (non-titrimetric) calorimetry. After classical correction for the heat of dilution of a strong acid they obtained the results presented in Table 30. Correcting the data at the indicated ionic strengths for the measured heats of dilutions of the reactants and products yields $\Delta H^\circ_N = -13.335 \pm 0.01_5$ kcal/mol; extrapolating a plot of ΔH_N vs. $\sqrt{\mu}$ to $\sqrt{\mu} = 0$ yields an intercept of -13.34 ± 0.02 kcal/mol with a slope of -430 cal/mol $\sqrt{\mu}$, in excellent agreement with the prediction of the Debye-Hückel equation.

TABLE 29

Integral Heats of Dilution of Hydrochloric Acid and Sodium Hydroxide[a]

m (molality)	ΔH_D (HCl), cal/mol	ΔH_D (NaOH), cal/mol
0.00000	0	0
0.0001110	5	5
0.001110	15	14
0.01110	48	39
0.1110	140	101
1.110	433	63

[a] Sturtevant, J. M., *J. Amer. Chem. Soc.*, 62, 584, 2276, 3265 (1940); 64, 762 (1942).

TABLE 30

Heat of Neutralization of Strong Acids with Sodium Hydroxide[a]

Acid	μ	$-\Delta H_N$, kcal/mol
HCl	0.0325	$-13.43_2 \pm 0.02_2$
HClO4	0.0325	$-13.41_3 \pm 0.02_3$
HCl	0.0162	$-13.40_3 \pm 0.01_6$
$HClO_4$	0.0162	$-13.39_2 \pm 0.01_7$
HCl	0.00472	$-13.37_5 \pm 0.02_5$
$HClO_4$	0.00472	-13.37 ± 0.03

[a] Reference 95

C. Measurement of Reaction Enthalpies of Complete Single-Step Processes or of the Overall Reaction

In this section, we will consider the measurement of reaction enthalpies in systems where the titration reactions are relatively complete. There are 2 cases, and they can be treated in precisely the same fashion. Consider for a moment the following scheme:

$$A + tT \underset{K_{f,t}}{\rightleftharpoons} AT_t \qquad (156)$$

This reaction may take place in a single step, or it may take place as a sequence of individual reactions such as

$$A + T \rightleftharpoons AT \qquad (157)$$

$$AT + T \rightleftharpoons AT_2 \qquad (158)$$

$$\vdots \qquad \vdots \qquad \vdots$$

$$AT_{t-1} + T \rightleftharpoons AT_t \qquad (159)$$

We are presently concerned only with the overall process (156) whether or not it takes place in discrete steps (157 to 159).

There are many cases in which the titration reaction is so nearly complete that there is no hope of determining its equilibrium constant with any accuracy. This situation does not preclude determining the overall heat of reaction; in fact, it simplifies the problem.

There are essentially 3 independent mathematical methods for evaluating the reaction enthalpy. Two of these are graphical: 1 involves an extrapolation and the other involves the measurement of a slope. The third method is a set of reasonably rigorous mathematical techniques which permit computation of both reaction enthalpies and equilibrium constants; this will be discussed in a subsequent section.

The initial slope procedure as developed by Keily and Hume[30] is illustrated in Figure 32. Curve 1 is a typical heater-calibration curve recorded under experimental conditions. Curve 1A is a computed curve. Initially both plots are coincident but eventually separate. This is due to heat losses from the calorimeter. Measurement of the slope of the temperature-time curve close to zero time reflects very accurately the true rate of heat generation.

In actual practice[19] it is necessary to match the titrant temperature to the initial temperature of the analyte, to correct for heats of dilution by adding the titrant to a solvent blank (or by differential calorimetry), and to measure the difference in slopes of the curve immediately before and after the start of the titration. Although Hume and co-workers have shown this to be a useful method of evaluating reaction

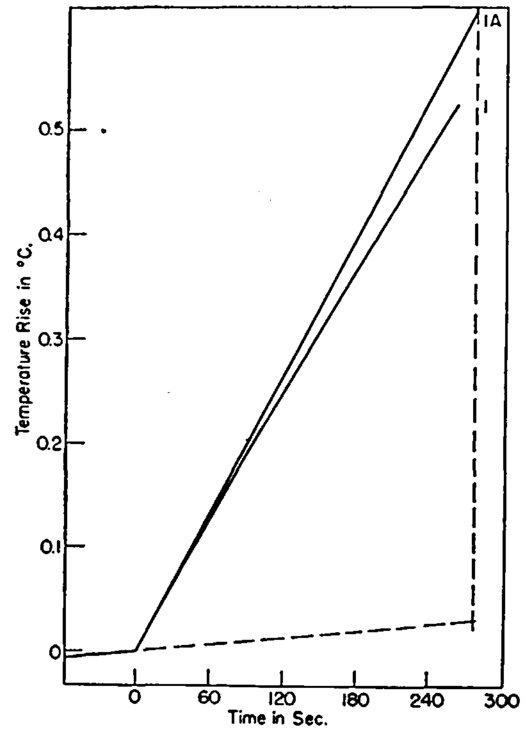


FIGURE 32. The initial-slope method for measuring reaction enthalpy: (I) theoretical heater calibration curve and (IA) actual experimental curve. (From Reference 30, reprinted by courtesy of the American Chemical Society.)

enthalpies, it is restricted to situations in which the reaction is fast and complete. In addition, it may yield spurious reaction enthalpies if the titration process is complex, for only the reaction that predominates at the start of the titration is measured. However, when the initial slope method is combined with the graphical extrapolation method used by Jordan and others one can take a very close look at the titration process.

The graphical extrapolation method is illustrated in curve b of Figure 33. Carr[89] has carried out a theoretical analysis of the procedure and found it to be surprisingly accurate under easily achieved experimental conditions. Using the equations presented in Section II a large number of titration curves were examined. If the parameter $\overline{\Delta T}'$ (f, κ, ϕ) as defined in Figure 2 is computed from the titration curve by means of least squares fits to Region 1 and 3 (see Section II), the accuracy of the method can be computed. The results of Reference 89 indicate that, when $\phi = 0$ and κ is finite, measurements should be made at the midpoint of the temperature rise. When $\kappa = 0$ and ϕ is finite, the extrapolation is made to the start of Region 2 in order to minimize errors due to temperature mismatch, heats of dilution, and changes in heat capacity. Under more realistic conditions, with both ϕ and κ finite, we have found that the true extrapolated temperature change is given quite accurately by the following approximation:

$$\overline{\Delta T}'(f,\phi,\kappa) = \overline{\Delta T}'(f,\phi,0) \cdot \overline{\Delta T}'(f,0,\kappa) \qquad (160)$$

For example, with $\phi = 0.0316$ (3.2% dilution) and $\kappa = 0.0316$, which are quite conservative estimates, the approximation is accurate to 0.2%. Consequently, the best procedure for using graphical extrapolation is to measure the recorder deflection at f = 0 for the heater calibration experiment. The real titration is also evaluated by extrapolation to f = 0. These deflections are then combined to yield

$$Q_{exp} = Q_{H.C.} \frac{\overline{\Delta T}'_{exp}}{\overline{\Delta T}'_{H.C.}} \qquad (161)$$

One may then use the correction factors ($\overline{\Delta T}'$ (ϕ, 0, f)) presented in Reference 89 to obtain $Q_{Reaction}$ as:

$$Q_{Reaction} \equiv \frac{Q_{exp}}{\overline{\Delta T}'(\phi,0,f)} \qquad (162)$$

which is a measure of the heat generated by the chemical reaction. The accuracy of this procedure is limited by that of the approximation presented in Equation 162, but this is generally quite acceptable. The major virtues of graphical extrapolation are its simplicity, lack of dependence on heats of dilution and temperature mismatch, and its independence of κ. The method can be used to measure the total heat generated in Reaction 156, but not the intervening stages. It can be applied to reactions which are incomplete at f = 1.00 if the extrapolation is made from f > 1, as in the case of end-point location. Last, it is not sensitive to the rate of reaction at f = 0 and at f ≈ 1. Its major disadvantage is that it does not provide data on equilibrium constants as do the techniques described in the next section.

D. Simultaneous Measurement of Equilibrium Constants and Reaction Enthalpies by Titration Calorimetry

The fact that one can derive equilibrium constants from potentiometric, conductometric,

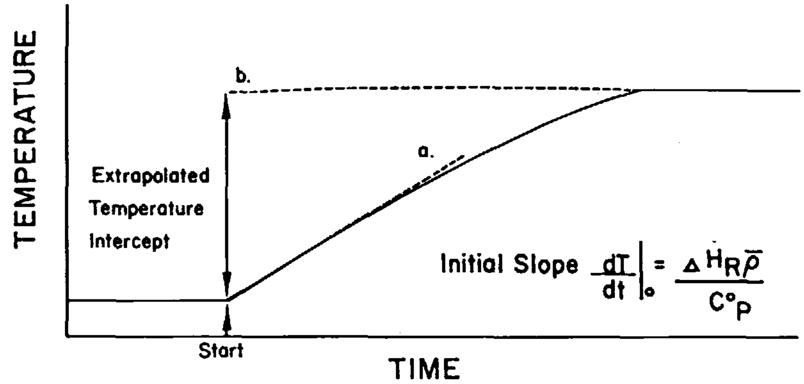


FIGURE 33. Comparison of the initial-slope and extrapolation procedures for evaluation of reaction enthalpy.

amperometric, or photometric titration curves is well accepted in the chemical literature. One simply monitors the concentraton of some species as a function of the extent of titration. Reaction enthalpies may be derived from these techniques only if the equilibrium constant is measured at 2 or more temperatures (see Equation 3). Titration calorimetry has the very significant advantage that one may, in principle, derive both $K^{0'}_{eq}$ and $\Delta H^{0'}$ from a single experiment. Thus, all of the formal thermodynamic parameters ($\Delta G^{0'}$, $\Delta H^{0'}$ and $\Delta S^{0'}$) are obtained from a consistent set of data over a very narrow range of temperatures.

To obtain an equilibrium constant and a reaction enthalpy, one must carry out a mathematical analysis of the temperature-volume curve. There are several methods for evaluating the data, and these will be discussed in roughly their chronological order of development. The most successful and practical early attempt at the interpretation of a *continuous* thermometric titration curve was that of Christensen, Izatt, Hansen, and Partridge in 1966.[31]

This group developed the method of simultaneous solution of equations (SSE) for a reaction taking place in a single step, such as

$$A + B \rightleftharpoons AB \qquad (163)$$

where the total heat generated by the reaction, previously termed Q_C, is given by

$$Q_C = \Delta H^{0'}\,[AB]\cdot V \qquad (164)$$

and

$$K^{0'} = \frac{[AB]}{[A][B]}\,\frac{\gamma_{AB}}{\gamma_A \cdot \gamma_B} = K^{0'}\,\frac{\gamma_{AB}}{\gamma_A \cdot \gamma_B} = K^{0'} \cdot \Gamma \qquad (165)$$

The terms γ_i represent the activity coefficients, and Γ is defined implicitly in Equation 165. The concentration of each species may be written as

$$[A]_{tot} = [A] + [AB] \qquad (166)$$

$$[B]_{tot} = [B] + [AB] \qquad (167)$$

Equations 164 through 167 may be manipulated to eliminate [A], [B], and [AB], yielding,

$$\frac{\Delta H^{0'}}{K^0} = \left(\frac{V[B]_{tot}\,[A]_{tot}\,\Gamma}{Q_C}\right)(\Delta H^{0'})^2 \qquad (168)$$

Note that values of $[A]_{tot}$ and $[B]_{tot}$ are experimentally available; Q_C can be derived from the temperature-volume curve after appropriate corrections; and Γ can be obtained from the Debye-Huckel equation or some other appropriate theoretical equation. Obviously Equation 168 depends very strongly on the nature of the equilibria involved in the titration process. Each multiplier of $\Delta H^{0'}$ in this equation can be estimated at every point (i) in the titration. Thus, we may write it in the formalism given below

$$\frac{\Delta H^{0'}}{K^0} = D_i\,\Delta H^{0'2} + E_i\,\Delta H^{0'} + F_i \qquad (169)$$

For any 2 points (i, j), Equation 169 can be solved for $\Delta H^{0'}$ and K^0. These data can then be averaged over each set of data points for the entire titration curve.

Wanders and Zweitung[90] have pointed out that this procedure is neither precise nor statistically efficient. In essence, if there are k data points and n unknowns (k > n), then by application of the least-squares principle a weighted average of k! | (k − n)! n! independent points should be obtained. It is now clear that the original procedure used by Christensen et al.[31] is suboptimal since it does not use the data efficiently or include appropriate weighting factors.

Wanders and Zweitung compared a least-squares approach with the SSE method. The results for a protonation of sulfate are presented in Table 31. It is obvious that their unweighted least-squares procedure did significantly improve the precisions associated with both pK_a and $\Delta H^{0'}$; thus, more efficient use is being made of the data.

Christensen and co-workers have now adopted the use of a least-squares approach. However, SSE may still be used to provide initial estimates for a least-squares procedure. The principle of this type of analysis is to minimize the sum of the squares of the difference between the experimental points and the theoretical curve which results from selection of K^0 and $\Delta H^{0'}$. Given a value of K^0 and $\Delta H^{0'}$ one may compute Q_t, a theoretical value of the heat

TABLE 31

Comparison of the Method of Simultaneous Equations and the Method of Least Squares[a]

Reaction: $HSO_4^- \rightleftharpoons H^+ + SO_4^=$

Method	pK_a^b →	$\Delta H^{o\,b}$, kcal/mol
Simultaneous equations	$1.90_2 \pm 0.04_1$	$5.63 \pm 0.2_8$
Least squares	$1.93_8 \pm 0.02_4$	$5.34 \pm 0.1_6$

[a] Reference 90
[b] Computed with 10 data points

generated at any volume of titrant added, and determine a function $U(K^0, \Delta H^{0\prime})$

$$U(K^0,\Delta H^{0\prime}) = \sum_{i=1}^{n} w_i (Q_{exp} - Q_t)^2 \qquad (170)$$

It is then possible to vary K^0 and $\Delta H^{0\prime}$ in some systematic fashion to minimize $U(K^0, \Delta H^{0\prime})$. These values of the thermodynamic parameters are taken as the best available. When a more complicated reaction (such as 1 involving 2 incomplete reactions) is involved, the function U may be represented in 5-dimensional space and must be minimized with respect to 4 variables. Clearly this is a sophisticated problem in numerical analysis.

Due to the non-linearity of the relationship among Q, $\Delta H^{0\prime}$, and K^0 it is not possible to solve an explicit equation for the desired values of the parameters as can be done in a linear least-squares problem. Thus, one is forced to use iterative procedures to find U_{min}.

There are 2 possible procedures for finding U_{Min}. One is to plot or map the entire surface, $U(K^0, \Delta H^{0\prime})$ by using assumed values of K^0 and $\Delta H^{0\prime}$ to compute Q_C and eventually U via Equation 170. Once compiled, the function can be inspected for a minimum. In this form, this is obviously an extremely laborious procedure and one that has not been employed to any extent. There is a closely related procedure in which a few values of U are computed, compared, and used to guide the choice of new values of $\Delta H^{0\prime}$ and K^0 in such a way that any desired degree of convergence may be obtained even from quite crude initial estimates,[90a] but a practical application in this area has not yet been made.

A second procedure, which has been used extensively by Sillén and his co-workers,[91] is the technique of pit mapping which has been incorporated into the program LETAGROP. Arnek[92] has described the method as applied to calorimetry in detail. Due to the iterative nature of the problem, one is forced to assume a *functional relationship* between U and the unknown parameters. In general, a quadratic relationship is assumed. Obviously, a parabolic function is the lowest degree polynomial which is capable of having a relative minimum. The error surface (U) is well represented by such a function *only* in the *immediate* vicinity of a minima; it is therefore necessary to asssume an initial value of all the sought for parameters. Obviously, the better the guess, the faster is convergence.

Izatt and co-workers[93] have developed an alternative to pit mapping which is an application of the variable metric method of minimization. In essence an explicit function is written for the gradient of U with respect to the parameter sought. The value of this parameter at which the gradient is zero is then found by iteration. In a comparison of this procedure with several others they found that it requires somewhat more computer time than pit mapping, but the area of convergence was larger, i. e., dependence of convergence on the initial guesses was not serious.

As yet, little has been said about the weighting function. In most instances a value of unity is assumed. Recently Christensen et al.[99] carried out a theoretical evaluation of the calorimetric determination of equilibrium constants in which the weighting function was given as

$$w_i = \left| Q_{exp_i} - Q_{exp_{i-1}} \right| \qquad (171)$$

This relationship implies that very little weight is given to pairs of points (i, i_1) between which there is no change in heat output. While this is very reasonable for points on the "plateau" of the thermogram, it seems most unwise for the data in the immediate vicinity of the equivalence point. As Figure 27 indicates, with acids weaker than $pK_a \approx 9$ there is considerable equilibrium curvature, and in our opinion these points *should* be weighted quite heavily in comparison to those points which simply reflect stoichiometric generation of heat. We would propose on an intuitive basis that w be taken as

$$w = \left| Q_{t,\infty} - Q_{exp} \right| \qquad (172)$$

where $Q_{t,\infty}$ is the theoretical value of the heat generated when the reaction is complete ($K^0 = \infty$ in Equation 168). This would insure that it is the points that show the greatest departure from the complete reaction line and that are most dependent on the true value of K^0, are the ones that are weighted most heavily. However, it also insures that random deviations will also be weighted heavily. Clearly more research on this procedure is required.

Christensen and co-workers[94] have carried out rather detailed calculations of the propagation of errors in the calorimetric determination of equilibrium constants. A least-squares procedure was used throughout the study. Perfect curves were computed; errors were then introduced by

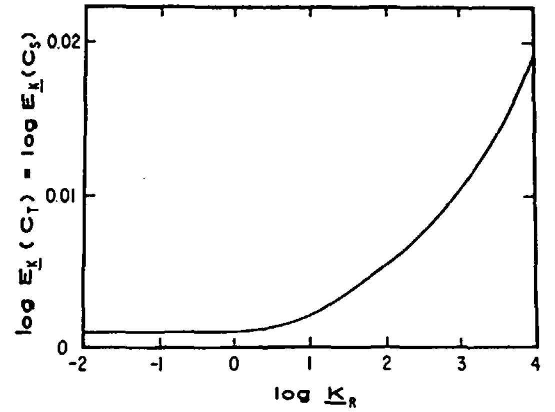


FIGURE 34. Effect of K^0 on the propagated error in pK^0 due to uncertainty in concentration. (From Reference 93, reprinted by courtesy of the American Chemical Society.)

addition of random errors to the experimental measurements (Q, C_T, and C_S). These data were then analyzed, as an experimental titration curve would be, to obtain a value of K^0 which was compared with the value used to generate the original error-free curve, and an error was computed.

They found that log $E_K(C_T)$ (which is the error in the logarithm of K^0 due to an error in the added titrant concentration C_T) is equal to log $E_K(C_S)$ and independent of C_T, C_S, or $\Delta H^{0\prime}$ as long as $\Delta H^{0\prime} > 1$ kcal/mol. However, log E_K (C) is quite dependent upon log K^0 as illustrated in Figure 34. In sharp contrast, log E_K (Q) is dependent upon $\Delta H^{0\prime}$, C_T, C_S, and K^0. A total error, log E_{total}, may be defined as:

$$\log E_{total} = \sqrt{\log^2 E_K(C_T) + \log^2 E_K(C_S) + \log^2 E_K(Q)} \qquad (173)$$

An error of 0.4% was assumed for the precision in Q. A typical error curve is presented in Figure 35. This shows that, with $|\Delta H^{0\prime}| > 1$ kcal/mol, the reaction enthalpy acts only to increase the range over which K^0 can be precisely computed but does not determine the precision at the optimum. As C_T decreases with $C_T/C_S = 20$, the value of $\Delta H^{0\prime}$ required to reach optimum precision increases.

The implication of this work is that pK° = values can be determined with a precision of ±0.01 unit if $C_T \geqslant 0.5$, $C_T/C_S \geqslant 20$ and $|\Delta H^{\circ\prime}| > 5$ kcal/mol when $-1 \leqslant \log K^\circ \leqslant 2$. In the case of

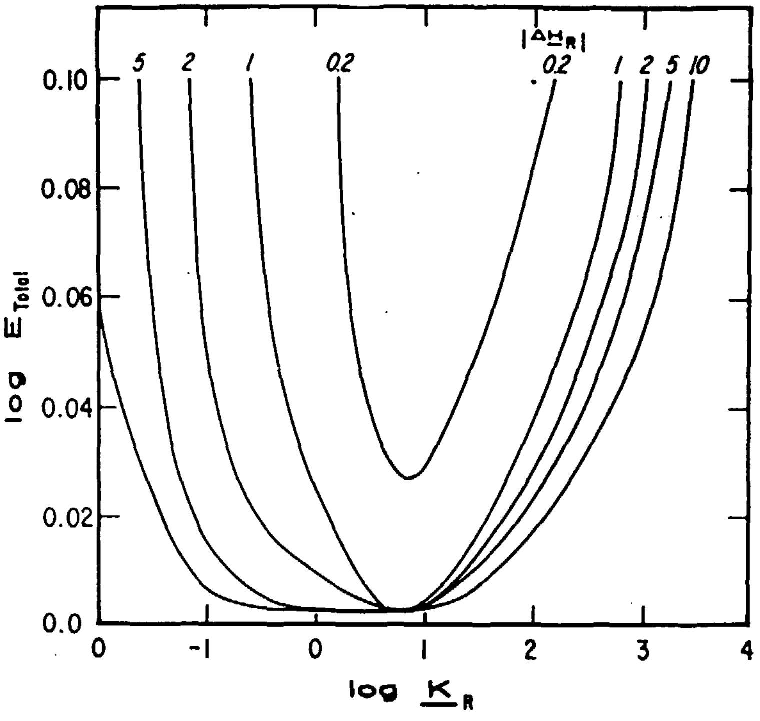


FIGURE 35. Effect of K^0 and $\Delta H^{0\prime}$ on the propagated error in pK^0 due to uncertainty in concentration and measured heat. (From Reference 93, reprinted by courtesy of the American Chemical Society.)

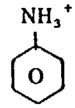
acid-base titrations, one can generally select a titrant so as to achieve these conditions.

Suggested titrants covering the entire range of acidities in aqueous solutions are shown in Table 32. These were used in experimental studies to determine the values of pK_a and ΔH_I for a number of species.

Although the above discussion has been limited to acid-base reactions, it should be apparent that the method may be generally applied to the determination of the thermodynamic parameters for a reaction of any type without any significant conceptual changes. Izatt, Christensen, and their co-workers have applied the technique to the determination of single and multiple metal ligand stability constants, an area with obvious analytical

TABLE 32

Proposed Standard Titrants for Measurement of Acid-Base Equilibrium Constants in Water[a]

Effective range	Substance	Formula	pK_a	ΔH^o, kcal/mol
<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	$H_2PO_4^-$	7.198	0.90
	Imidazolium ion		6.99	8.78
8-11	Acetylacetone	$CH_3COCH_2COCH_3$	0.02	2.8
	Tris(hydroxymethyl) aminomethane	$(CH_2OH)_3CNH_3^+$	8.069	11.33
9-12	Glycinium ion	$^+H_2NCH_2COO^-$	9.780	10.57
11-14	Monohydrogen phosphate ion	$HPO_4^=$	12.39	4.20
	Hydroxide ion	OH^-	13.998	13.335

[a] Reference 93

importance. A recent example of this work is the study of the copper (II)- and zinc (II)-1, 10-phenanthroline complexes.[95]

An extremely thorough 3-part[97-99] review of the use of titration calorimetry for the determination of thermodynamic parameters by Christensen, Izatt, and their co-workers will appear shortly in *Thermochimica Acta.* The interested reader is referred to this work for a very detailed discussion of experimental technique and theoretical evaluation of data.

VI. PROJECTED TRENDS IN THERMOMETRIC TITRIMETRY AND RELATED METHODS

As has been illustrated by early parts of this review and other reviews, thermometric methods must be counted among the most universally applicable analytical methodologies. No other analytical method, including potentiometry, amperometry, conductometry, or spectrophotometry, lends itself as readily to the measurement or study of a chemical system *without regard to the nature of the reaction or* medium in which it is carried out. Nonetheless, it is clear that the popularity of the technique is not high in comparison to the above methods. We believe that this situation is warranted by 3 paramount considerations. First, all of the above techniques may be employed in a nondestructive mode, but by their very nature thermochemical techniques require a chemical reaction to produce a measurement. Second, the sensitivity of thermochemical techniques must be considered meager in contrast to the other methods. Third, there is a lack of any real selectivity. For example, polarography can be routinely used at the 10-micromolar level in pure solutions of an electroactive species free from electroactive contaminants; with the advent of ion-selective electrodes, potentiometry can often be used at the submicromolar level. The sensitivity of photometry is highly variable, but in some cases is extremely good, as in atomic absorption, fluorescence, etc.

There are possible unexplored routes around both of the above objections. For example, with the development of insolubilized enzymes, one could conceivably coat a macroscopic thermistor with a suitable preparation and monitor surface reactions in solutions which are flowed past the electrode. The extent of the reaction would be limited to the immediate vicinity of the surface, as it is in polarography. Under these circumstances, one could avoid the destructive nature of the analysis, which is ultimately a question of degree rather than kind (consider the usual undergraduate explanation of the Heisenberg principle).

Again, in our opinion, the second objection is not fatal. As has been illustrated in this review, one can obtain very high analytical sensitivity by the use of end-point indicator reactions. These are not, however, generic solutions to the problem. As yet, no extensive use has been made of sophisticated solid-state electronics in thermometric analysis. Obviously, the limits within which a signal may be amplified are determined by the signal-to-noise ratio and the drift in the signal due to stirring, thermistor heating, and heat losses. The signal-to-noise ratio can be improved by the use of lock-in amplifiers of which several types are commercially available at quite reasonable cost (about $1,000). Assuming that a signal can be cleaned up, the drift will then become a limiting factor. We have already remarked on the availability of simple, inexpensive ramp generators which can be used, in principle, to eliminate the difficulty. There is, therefore, no reason why the limit of sensitivity of DIE and thermometric titrations cannot be reduced from a few millimolar to a few hundredths of this.

There is no ready solution to the third difficulty. We can only express the hope that work will continue in the development of analytical reagents of high selectivity including enzymes and organic functional-group reagents.

There are a number of other areas which should be discussed in this section. Although Izatt, Christensen, and their co-workers have thoroughly explored the technique as a tool for the determination of thermodynamic parameters in aqueous solutions, there exists a real need for such devices in the study of non-aqueous solvents. Jordan has been in the vanguard of such studies in fused salt media. The thermodynamic studies of Hume have also shown that valuable data can be obtained in organic media. A systematic study of the effect of solvent on acid-base thermodynamics is (with the exception of pK_a-measurements) not presently available in the literature. There is no question that calorimetric titrimetry can provide a large body of needed data. Since the National Bureau of Standards has proposed operational pH scales for methanol and D_2O, these would provide a very reasonable starting point. Glacial acetic acid and acetonitrile have been examined, but with equipment which must be considered crude by present standards; indeed, only enthalpy data were reported in the classic studies of Keily and Hume and of Forman and Hume. There is already a great deal of data on equilibrium constants in ethylenediamine and dimethyl sulfoxide, but there is also a dearth of information on reaction enthalpies. Returning to aqueous systems, it is clear that acid-base chemistry is quite well understood, but only a few of the more important redox systems have been characterized as thoroughly. A detailed study of the thermodynamics of aqueous redox systems is warranted by recent developments in theoretical chemistry such as Marcus' theory of electron transfer which relates both the rates and equilibria of such processes. Indeed, there have been very few complete thermodynamic studies, including measurements of ΔG, ΔH, and ΔS, in the light of the now well-accepted Hammett equation, of any reactions except for acid-base reactions.

The study of certain complex biochemical systems for which no other analytical tools exist will certainly grow. Calorimetric investigations of many such systems have already been carried out by Sturtevant, Izatt and Christensen, and Benzinger. It is evident that the universality of the techniques is well illustrated by recent work in Jordan's laboratory wherein thermometric titration curves of antigens with antibodies have been obtained.

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