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Thermochimica Acta 380 (2001) 205–208

thermochimica acta

www.elsevier.com/locate/tca

An outline of new calculation methods for the determination of both thermodynamic and kinetic parameters from isothermal heat conduction microcalorimetry

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Abstract

An outline of equations allowing calculation, from calorimetric data, of both thermodynamic and kinetic parameters for reactions which proceed to completion is given. In addition equilibrium constants are calculable for reactions which proceed to an equilibrium position. Advantages of the methods for solid state kinetic and stability studies are briefly discussed.

Keywords: Calorimetry; Thermodynamics; Kinetics; Equilibrium

1. Introduction

Willson et al. [1] introduced methods for the determination, from isothermal heat conduction microcalorimetry, of order of reaction, n, reaction rate constant, k, and reaction enthalpy change, $\Delta_R H$ (hereafter referred to as H for simplicity). The basis of the method was to develop a ''calorimetric'' equation from a simple, conventional chemical kinetic equation. An equation for a simple process such as

$$A + B \Rightarrow P, \tag{1}$$

has, as its kinetic expression,

$$\text{rate} = \frac{dx}{dt} = k(A - x)^m(B - x)^n. \tag{2}$$

Conventionally the rate expression is expressed in the dimensions of mol dm^{-3} s^{-1} with A, B and x expressed in terms of mol dm^{-3}. The reaction rate constant then takes the dimensions required by order of reaction and the dimensional homogeneity of the equation. Here, then, x is the concentration of reagent that has reacted to time t, m and n the orders of reaction with respect to reagents A and B. the overall reaction order is $(m + n)$.

Calorimetric output is of thermal power (dq/dt; W) as a function of time (t; s) and consequently the integral of this data to time t is equal to q (J). However, note that H is a per mole parameter and hence the above equation, for use in analysis of calorimetric data, must be converted to quantity terms (mole, g).

If we regard this equation as being cast in quantity terms then it is possible to develop a ''calorimetric'' form of the equation. Of course, it is simple to convert concentration terms to the required quantity terms by appropriate incorporation of the volume of solution used in the calorimetric experiment. For simplicity of presentation the quantity related terms are retained in this outline. Thus, assigning the enthalpy change for

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0040-6031/01/$ – see front matter
PII: S0040-6031(01)00673-6

the reaction as H allows x to be set equal to q/H. Therefore, the rate of reaction can be expressed in terms of the thermal power:

$$\frac{dx}{dt} = \left(\frac{1}{H}\right)\frac{dq}{dt}. \quad (3)$$

Incorporating these calorimetric forms into a chemical kinetic equation (now simplified further for ease of development only) such as A ⇒ P yields the following equation:

$$\frac{dq}{dt} = kH\left(A - \frac{q}{H}\right)^m. \quad (4)$$

Note here A is also defined in terms of a quantity (number of moles) as is necessary since H is a per mole quantity. The consequence of this definition is that the rate constant in the above equation has, for all orders, the dimensions of $\text{mol}^{(1-m)}\ \text{s}^{-1}$. It is simple [2] to convert the equation to a form which incorporates concentration and volume and in which, therefore, the rate constant will take the dimensions appropriate to the reaction order (e.g. for $n = 2$ the rate constant, k, has the dimensions $\text{mol}^{-1}\ \text{dm}^{-3}\ \text{s}^{-1}$). The use of concentrations allows comparison of calorimetric rate constant data with that determined from conventional chemical kinetic studies. Many examples of the calorimetric form of equation have been developed [1–4]. For example, solid state reactions, autocatalysis reactions, enzyme catalysed reactions, coagulation reactions and complex sequential and parallel reactions.

The fact that calorimetry is a non-invasive, non-destructive method has encouraged the application of the methods of data analysis for the determination of k and H to a range of stability related studies. Prominent amongst these has been the application to long-term stability and compatibility determinations for pharmaceutically related systems. For example there are reports of the stability of ascorbic acid in both the solution [5] and the solid [6] states and to the analysis of complex, sequential reaction systems [7]. For all these reactions both rate constants and enthalpies were determined. The analysis of the experimental data [5–7] relied upon iteration of calorimetric data through an equation of the form of (4) via some suitable graphics package (Microcal, Amherst, MA, USA) for values of k and H. Note that for the complex reaction system (the hydrolysis of a triaminesulphonate which corresponds to a reaction scheme of the A → B → C → D type) it was possible to determine values of k and H for the three separate reaction steps in the process.

More recently this method has been applied to the solid state degradation of benzoyl peroxide [8] and to its formulated products [9]. This latter study involved an investigation of excipients in formulated products of different strengths and their rôle in influencing the stability of that product.

However, a limitation in this method was the required assumption that all the material loaded into the calorimeter would react. This is obviously a severe constraint on the application of the procedure — as is the requirement to iterate.

More recently new procedures have been developed that permit the direct calculation of these parameters for reactions that go to completion. For those reactions which do not proceed to completion, i.e. that proceed to a defined equilibrium state, it is possible to calculate directly all these parameters free of assumptions.

The method developed for the analysis of calorimetric data is outlined below. For the first time it is shown that calculation is now possible rather than iteration for reactions that go to completion. For reactions that achieve an equilibrium state more detail can be found in [10].

2. Reactions that go to completion

It is possible to evaluate Q, the total number of joules that would be recorded if a reaction studied in a microcalorimeter were allowed to proceed to an end, i.e. to completion or to its final equilibrium position, without the need to follow the reaction of the whole of its lifetime [10,11]. Furthermore, it is possible to write, for calorimetric studies over a range of initial loads, A, that the signal at time $t = 0$ is given by

$$\left(\frac{dq}{dt}\right)_0 = kHA^n. \quad (5)$$

Thus, a plot of $\ln(dq/dt)_0$ versus $\ln A$ will have a slope of n, the reaction order and an intercept value of $\ln kH$. At any time t the signal from the calorimeter can be expressed [1] as

$$\frac{dq}{dt} = kH^{1-n}(Q - q). \quad (6)$$

Substituting from the intercept as $Z = kH$ into Eq. (6) produces

$$\frac{dq}{dt} = ZH^{-n}(Q - q)^n. \quad (7)$$

And, as all the terms other than H in this equation are known, then H may be calculated directly — and hence so can k. The requirement here is clearly that the values of A are known and that all the A loaded into the calorimeter reacts to completion.

3. Reactions that proceed to a position of equilibrium

Consider a reaction (again only for simplicity are such systems described — as noted in [10] any reaction system which can be described through an equilibrium constant expression can be treated) such as

$$A \Leftrightarrow B \quad (8)$$

The value of n can be determined as described above but now it is possible to use not A but A the total quantity loaded into the calorimeter of which quantity A can react under the prevailing conditions of temperature, relative humidity, partial pressure of oxygen, etc. By making measurements of Q as a function of temperature (most usefully at temperatures close to ambient/storage conditions) it is possible to calculate [10], through simple application of the van't Hoff isochore, a value for Q_0. This is the notional number of joules that would be recorded if all the sample loaded into the calorimeter reacted — this, therefore, is a theoretical quantity and A_0 is now expressed as Q_0/H. The equilibrium constant for this simple process can be expressed as

$$K = \frac{[A]}{[A_0] - [A]}. \quad (9)$$

Here the square brackets only imply equilibrium conditions not concentrations (although note again that it is trivial to incorporate concentration terms into the equation). It is, therefore, simple to convert this expression into its equivalent calorimetric form:

$$K = \frac{Q}{Q_0 - Q}.$$

The terms in which K is expressed are directly accessible from the experimental data. They require no assumption about an extent of reaction and require no ancillary data. Thus, not only are values of n, k and H now available free of assumption but also without the need for iteration again. Furthermore values for K can be calculated and hence so can those of G (through $G = -RT \ln K$) and S. The availability of k as a function of temperature allows E_a, the activation energy, to be determined from an Arrhenius plot.

Of course an appropriate test for the existence of an equilibrium position is to determine Q as function of temperature. Constancy of Q indicates a reaction that proceeds to completion and variation in Q indicates a reaction that proceeds to an equilibrium position.

Now that microcalorimeters are capable, as this outline indicates, of allowing calculation of both thermochemical and kinetic parameters it would be extremely useful to have a test reaction available. An important requirement of a reaction that is to be used as a validating test reaction for isothermal heat conduction microcalorimeters is that it should be reproducible, robust, simple to operate and widely applicable. A further requirement is that the test reaction should proceed to completion and show no sensitive dependence upon environmental variables. The imidazole catalysed hydrolysis of triacetin has now been proposed [12] as this test reaction following intra- and inter-laboratory trials. It has been shown, by the tests outlined above, to be appropriate in all the criteria proposed. These include the demonstration that the reaction proceeds to completion and not to an equilibrium position.

4. Conclusion

This paper has outlined the calculation of important thermodynamic and kinetic parameters from isothermal heat conduction microcalorimetric data without the need for any prior assumptions. The methods are applicable [11] to the analysis of simple and complex reaction schemes. Indeed it is not necessary, for reactions which proceed to an equilibrium position, to be able to specify the sample other than to know the total mass of sample loaded into the calorimeter. Even in this circumstance it is possible to calculate values for Q and for Q_0. This means that, as a value for H is also determinable, then it is possible to know the

number of moles of reaction that take place in the sample and, in addition, the total quantity of potentially reactable material present in the sample. Of course, there is no information available on the identities of the reacting compounds only their respective mass presence in the sample.

To date these more recent equations have only been examined through simulated data [2,3,4,10] and the impact of the experimental uncertainty on the outcomes is, as yet, unknown. However given the capacity of microcalorimeters to accept reacting systems of any physical form (solid, liquid, gas or any combination) then their potential is great.

Studies of solid state systems may present challenges, particularly as the understanding of solid state kinetics is currently quite modest [13]. Indeed there will be systems involving simultaneous physical processes, for example crystallisation, solvation/desolvation that will require careful deconvolution of data. Note that if such deconvolution is possible the derived thermodynamic and kinetic data will not, of itself, indicate the nature of the process — this must be found from other experiments. However direct, non-invasive, non-destructive methods of study of such complex reaction systems may prove useful.

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