Thermochimica Acta, 70 (1983) 257–268
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

COMPARISON OF THE DETECTION LIMITS OF MICROCALORIMETERS *

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(Received 26 May 1983)

ABSTRACT

Different calorimetric methods are compared with regard to the minimum detectable total heat effect that can be measured. This heat effect is shown to be dependent on: (a) the peak-to-peak uncertainty in the primary measurement which should be expressed in either degrees Kelvin or watts depending on whether the primary measurement is of temperature or power, (b) the time constant of the calorimeter system, and (c) the total energy equivalent of the reaction vessel and contents if the primary measurement is temperature.

INTRODUCTION

The choice of a solution microcalorimeter for measuring enthalpy changes for reactions in which reactants are of limited availability is not a simple matter. The general problem is to maximize the amount of information obtained per unit of material. One of the objectives of this paper is to develop ways in which different calorimeters may be compared with regard to this criterion. The physical and chemical properties of the material to be studied (e.g. viscosity, rate of reaction) may also dictate the choice of method, but that must be considered specifically for each chemical system and will not be considered here. A second objective is to carefully define the specification parameters necessary to establish the detection limit of a given calorimeter. No unified scheme for reporting detection limits or time constants currently exists in the literature on calorimetry. Calorimetric detection limits and time constants have been given in several significantly different ways in the literature [1–8].

Calorimeters suitable for microcalorimetric measurements may be divided into three types according to the way the heat measurement is made, and further into three subtypes depending on the way the reactants are mixed.

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* Contribution No. 318 from The Thermochemical Institute.

0040-6031/83/$03.00

The three types of calorimeters together with the method of measuring the heat effect are: (a) isoperibol and adiabatic, temperature change; (b) isothermal calorimeters, power to a heater; and (c) heat conduction, electrical output from a thermoelectric device. The three fundamentally different ways of mixing reactants in a calorimeter are: (a) all at once, (b) continuous titration of one reactant, and (c) continuous flow of both reactants.

A calorimeter in which the primary measurement is the change in temperature may be either an isoperibol or adiabatic calorimeter depending respectively on whether the surrounding temperature is held constant or the same as the reaction vessel contents. In isothermal calorimeters, the temperature of the reaction vessel is actively controlled to be constant. Those calorimeters in which the primary measurement is the voltage output of a Seebeck device or thermopile between the sample and a constant temperature heat sink are heat conduction calorimeters.

Calorimeters in which the total volumes of the two reactants are mixed all at once will be referred to as batch calorimeters. For the purposes of this paper, titration calorimeters will refer to those instruments in which the total volume of one reactant is present in the reaction vessel throughout the experiment, while the other reactant is added at a known, usually constant, rate and measurements are made continuously or at periodic short intervals during the titration. Calorimetric experiments in which the titrant is added in increments rather than continuously have also been called titration calorimetry by other workers, but in the context of this paper such an experiment will be labelled as a series of batch experiments. Flow calorimeters are defined to be those in which both reactants flow into a reaction zone and the product stream flows from the reaction zone.

THEORY

Making direct comparisons among the various types of calorimeters is not simple because the primary measurements are of different quantities and the amount of reactant used per experiment is time-dependent in some cases and not in others. It is the purpose of this section to define ways in which meaningful comparisons of different calorimeters can be made. It is not our purpose to make comparisons of commercially available instruments since such comparisons would have only a short-term validity. However, we shall use data comparable to the best current technology for illustrative purposes.

Figures 1–4 show the form of the data collected by the various types of calorimeters. The uncertainties and time constants associated with the measurements are also defined in Figs. 1–4. In each of these figures, the vertical, double-ended arrow indicates the peak-to-peak noise observed in the recorded signal. The length of this arrow includes 99% of the data in a continuous trace of the output signal from the calorimeter.

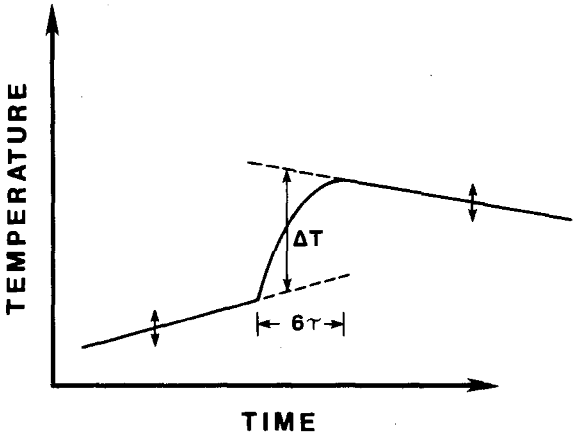

Fig. 1. Form of data ouput from isoperibol or adiabatic batch calorimeters.

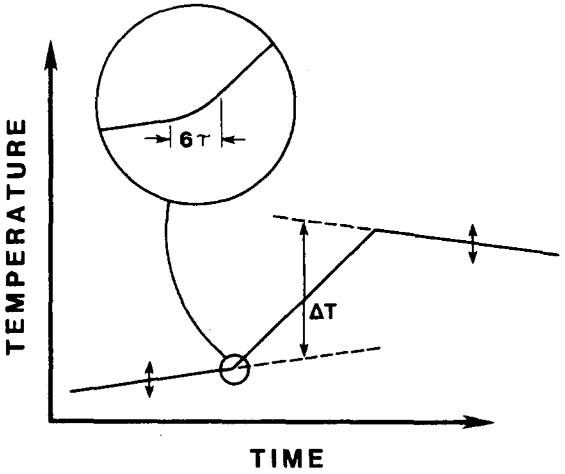

Fig. 2. Form of data output from isoperibol or adiabatic titration calorimeters.

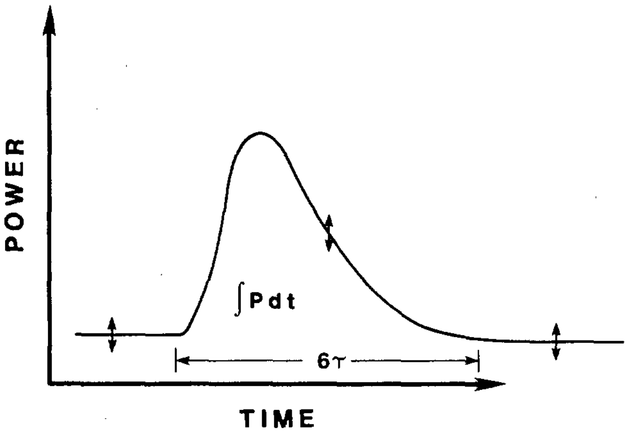

Fig. 3. Form of data output from isothermal and heat conduction batch calorimeters.

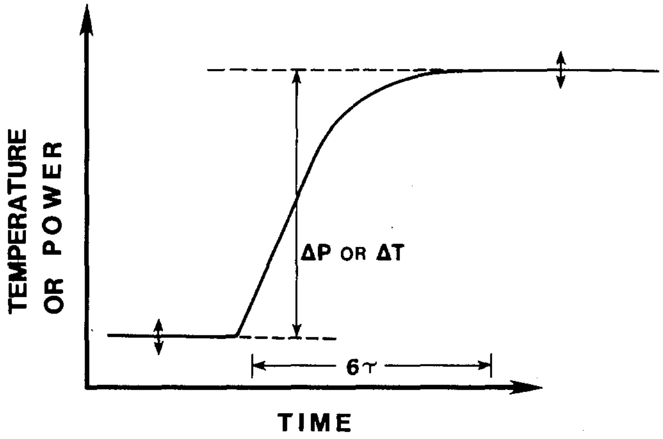

Fig. 4. Form of data output from isoperibol or adiabatic flow, isothermal flow and titration, and heat conduction flow and titration calorimeters. The trail period is not shown.

There are two quantities necessary to calculate the minimum total heat detectable by any type of calorimeter: (a) the standard deviation in the primary measurement, σ, and (b) the time constant of the calorimeter system, τ. The standard deviation in the measurement, σ, is approximately equal to one fifth of the peak-to-peak noise in the output signal [9] (see Figs. 1–4). The peak-to-peak noise is statistically equivalent to the 99% confidence interval (which equals 5.152σ) and is the most easily measured noise parameter. The standard deviation defined in this way is also equal to the root-mean-square noise. We shall assume that the output signal of the calorimeter has a constant peak-to-peak noise throughout all the measurement periods including the base line and reaction periods. Also, as shown in Fig. 3, we assume that the base lines are at the same value in the lead and trail regions for an isothermal or a heat conduction calorimeter. The time constant is defined to be one sixth of the settling time, where the settling time is the time required to reach 99.75% of the final steady state after an instantaneous step or pulse input of heat. The size of the step or pulse should be small enough so that the time constant is independent of the size of the step or pulse. In addition to the standard deviation and time constant, the thermal equivalent is required for the calculation for isoperibol or adiabatic calorimeters.

The specification parameters that should always be reported for any calorimeter are: (a) the peak-to-peak noise (in degrees Kelvin for isoperibol and adiabatic calorimeters and in watts for all other types of calorimeters), (b) the time constant of the instrument as it is actually used, and (c) the pertinent volumes and flow rates of liquids in the reaction vessel. Since the measured peak-to-peak noise depends on the time constant, the noise and the time constant must both be measured under identical instrument conditions. If the detector used to measure peak-to-peak noise is different from the detector normally used, it must have a much shorter time constant and measurement period than the frequency of the noise so that it does not inadvertently act as a noise filter.

EXPERIMENTAL

Table 1 gives the necessary "state of the art" specifications which we have chosen to represent each microcalorimetric method.

Specification of measurement uncertainty, time constant and reaction vessel volumes and flow rates for the isoperibol batch and titration, the isothermal batch, titration and flow, and the heat conduction batch calorimeters have all been measured in our laboratory or are typical of the appropriate Tronac instrument. The isoperibol calorimeter used to obtain the data in Table 1 for the batch and titration calorimeters was a Tronac model 450 with a 1.5 ml water-filled Dewar flask [10,11]. We found that the temperature measurement uncertainty is determined by the thermal inhomogeneities in the water in the Dewar flask and not by the temperature resolution of the thermistor or the bridge. This is generally the case because the heat of stirring is by far the largest non-chemical heat effect in the reaction vessel, often exceeding the measured heat effect by an order of magnitude or more [10]. The bridge in this instrument was found to have a peak-to-peak noise of less than 1 μK when the thermistor was inserted in an insulated Al block suspended in a water bath thermostatically controlled to ± 0.2 mK. Other workers have reported similar values for temperature measurement uncertainties in other stirred solution calorimeters [9,12–15]. The response time was determined by measuring the time required to establish a constant rate of temperature rise after the calibration heater was switched on. Thus the response time includes the response time of the heater. The time constant was set equal to one sixth of this value [16].

For the case of isoperibol or adiabatic flow calorimeters, the temperature noise might be reduced because the temperature sensor is not placed directly in a vigorously stirred liquid. However, since there are not enough data in the literature to establish a better value, for comparison purposes we have chosen to keep the temperature uncertainty parameter the same for the flow isoperibol or adiabatic calorimeter as we have used for the titration and batch calorimeters of this type. The response time of a flow isoperibol or adiabatic calorimeter depends on the linear flow rate of the fluid and the distance between the point of reaction and the temperature sensor as well as the time constant of the sensor. We have chosen this time to be six seconds [17]. Flow isoperibol or adiabatic calorimeters are currently marketed by Microscal and Techneurop and similar flow calorimeters designed for determination of heat capacity or chemical analyses have been described [7,8,17–20].

TABLE 1

Microcalorimeter specifications and resulting capabilities

Calorimeter type	Peak-to-peak noise[a]		Time constant, τ (s)	V[b] (ml)	dV/dt[b] (ml min^{-1})	Detection limit[c] (μJ)	Volume/data point[d] (μl)	Rel. conc.[e]
	(μK)	(μW)						
Isoperibol or adiabatic batch (Fig. 1)	25		0.5	1.5		90[f]		
Isoperibol or adiabatic titration (Fig. 2)	25	50	0.5	1.5	0.01	50[f]	0.5	833
Isoperibol or adiabatic flow (Fig. 4)	25	0.3	1		0.2[g]	1.2[h]	10	1
Isothermal batch (Fig. 3)		30	30[i]	3.0		3000		
Isothermal titration (Fig. 4)		30	30[i]	3.0	0.01	3000	30	833
Isothermal flow (Fig. 4)		15	15[i]		0.2[g]	750	150	42
Heat conduction batch (Fig. 3)		0.1	200	0.1		70		
Heat conduction titration (Fig. 4)		10	20	0.5	0.01	780	20	325
Heat conduction flow (Fig. 4)		1	200		0.2[g]	780	2000	3

[a] Equal to 5σ.

[b] V = reaction vessel volume; dV/dt = flow rate.

[c] Minimum detectable total heat effect.

[d] Volume of reactant solution delivered in 6τ.

[e] Relative concentration of reactant required to obtain the minimum detectable total heat effect in 6τ. Normalized to lowest value = 1.

[f] Directly proportional to reaction vessel volume.

[g] Total flow for both reactant lines, i.e. the flow rate is 0.1 ml min^{-1} in each line.

[h] Directly proportional to flow rate.

[i] An actively controlled system actually has a minimum of three time constants. We have chosen to simplify this by using only the time constant which describes a critically damped system, i.e. one sixth of the settling time.

Tronac model 550 isothermal calorimeters with either 4 ml water-filled reaction vessels or flow cells as described in previous publications from this laboratory [1–4] were used to obtain the values given in Table 1 for isothermal calorimeters. The time constant for the isothermal calorimeters was set equal to one sixth of the settling time for these instruments. There are three significant time constants (i.e. those of the sensor, controller and heater) which determine the form of the output signal in these actively controlled instruments. Because of these three time constants, the output approximates to the sum of a damped sine wave and an exponential decay function applied to the input signal, but the settling time is approximately the same as that of a critically damped system [21]. The settling time was defined to be the time required to reach a constant value of the output signal after the calibration heater was switched on.

The data given in Table 1 for the heat conduction batch calorimeter were obtained with a Tronac model 351RA heat conduction calorimeter [22]. This calorimeter is very similar in design to the LKB heat conduction calorimeter [5]. The time constant for this type of calorimeter is usually determined by filters in the output circuitry. Increasing the time constant beyond 200 s, however, did not further decrease the measurement uncertainty for the particular instrument used in this study. Similar measurement specifications have been reported for a modified LKB batch heat conduction calorimeter [23]. Calvet-type heat conduction microcalorimeters, marketed by Setaram, also have measurement specifications very similar to those given in Table 1 for the heat conduction batch calorimeter [24].

The value of the measurement uncertainty for the heat conduction flow calorimeter was obtained from data in the literature [6].

The combination of heat conduction calorimetry and continuous titration of one reactant has been reported recently [25], but no details were given so we have simply estimated the best set of specifications that we believe could be achieved. This involved decreasing the time constant and increasing the measurement uncertainty proportionally. The measurement uncertainty was based on that established for the heat conduction flow calorimeter since titration also involves flow of liquid across the calorimeter boundary. The time constant given, 20 s, is probably the minimum obtainable with foreseeable Seebeck devices.

All data on the peak-to-peak measurement uncertainties determined in this laboratory were obtained by measurement of the width of the band of ink produced on a strip chart recorder (Hewlett-Packard model 7100B, full scale response time = 0.5 s) running at a chart speed much slower than the frequency of the noise being measured.

Instrument manufacturers and research workers who have constructed calorimeters may take issue with some of the specific values in Table 1. However, published descriptions of calorimeters rarely contain enough well-defined data to make the comparisons we are making in this paper. In order to make such comparisons possible, future descriptions of calorimeters should contain (a) the peak-to-peak noise in the primary measurement, given in units of degrees Kelvin or watts, (b) the time constant of the calorimeter including any filtering in output circuits that are normally used and (c) the volumes and/or flow rates that are typical of the instrument. Instrument manufacturers may also wish to give the best, average, and worst acceptable values for σ and τ.

CALCULATIONS

One quantity which can be calculated for all types of calorimeters from the data in Table 1 is the minimum detectable total heat effect.

The minimum detectable total heat effect is proportional to the smallest observable shift in the base-line temperature or power for the isoperibol or adiabatic batch and flow, isothermal titration and flow, and heat conduction titration and flow calorimeters (see Figs. 1 and 4). Neglecting the effect of the extrapolation of the non-zero and changing slope over the 6τ seconds in the case of the isoperibol or adiabatic batch calorimeter, the standard deviation of any difference on the measurement axis is given by

$$\sigma_{\text{base-line diff}} = 2^{0.5}\sigma \tag{1}$$

Equation 1 is simply the combination of the errors in the positions of the lead and trail. The units for $\sigma_{\text{base-line diff}}$ are μK for the isoperibol or adiabatic batch and flow calorimeters and μW for the isothermal titration and flow and the heat conduction flow and titration calorimeters. In the case of the isoperibol or adiabatic batch calorimeter, multiplying $\sigma_{\text{base-line diff}}$ by the thermal equivalent, ~ 6.3 J K^{-1} for a water-filled 1.5 ml reaction vessel, converts the result to μJ. The results for the other calorimeters must be multiplied by 6τ, the minimum time in which a measurement could be made in order to obtain the result in μJ. The results of these calculations are given in Table 1.

The problem is different for isoperibol or adiabatic titration calorimeters in that it is the change in slope that must be detected instead of a base-line shift (see Fig. 2). The uncertainty in the slope in the lead region can be made very small because the number of data points, N, can be made very large. Thus, the uncertainty in the change in slope at the juncture of the lead and reaction regions can be expressed solely as the uncertainty in the reaction region slope as given by

$$\sigma_{\text{slope}} = \left\{ \frac{N\sigma^2}{\tau^2\left[N\Sigma i^2 - (\Sigma i)^2\right]} \right\}^{0.5} \tag{2}$$

if data points are taken at τ intervals [26]. Because the minimum time over which a meaningful measurement could be made is 6τ, we chose $N = 6$ and obtained $\sigma_{\text{slope}} = 8 \mu\text{K s}^{-1}$. Multiplying by the thermal equivalent, ~ 6.3 J K^{-1}, and 6τ gives the value of the minimum detectable total heat effect given in Table 1.

Calculation of the minimum detectable total heat effect for isothermal and heat conduction batch calorimeters is a different problem since the calculation of a total heat effect requires integration of the measurement signal (see Fig. 3). The desired result is given by the uncertainty in the area under the curve which must be at least 6τ in length. The areal uncertainty for small signals is approximated by

$$\sigma_{\text{area}} = 2^{0.5} 6 \tau \sigma \qquad (3)$$

The results are shown in Table 1.

The measurement uncertainty for isoperibol or adiabatic titration and flow calorimeters can also be expressed in terms of power for these instruments. The uncertainty in power is calculated by multiplying the uncertainty in the temperature slope calculated above ($8 \mu\text{K s}^{-1}$) by the reaction vessel energy equivalent ($6.3\ \mu\text{J}\ \mu\text{K}^{-1}$) in the case of the titration calorimeter. For the flow calorimeter, the power uncertainty is obtained by multiplying the temperature measurement uncertainty by the total flow rate and the fluid heat capacity. The results of these calculations assuming water as the fluid are given in Table 1. Note that the power measurement uncertainties in these cases are directly proportional to the reaction vessel volume and flow rate, respectively.

The minimum relative concentration of reactants that are required by the various flow and titration calorimeters to obtain the minimum detectable total heat effect in 6τ are given in the last column of Table 1. These values were calculated by dividing the minimum detectable total heat effect by the volume of titrant or by one half the total flow delivered in 6τ and normalizing all the values so that the lowest value is 1.

DISCUSSION

The results given in Table 1 on the minimum detectable total heat effect predict that a measurement with an isoperibol or adiabatic flow calorimeter may have a detection limit forty times smaller than any other calorimeter. However, this result still requires experimental proof. The batch and titration isoperibol or adiabatic, and batch heat conduction calorimeter designs all have about the same detection limit. The isothermal flow and heat conduction titration and flow calorimeters all have similar detection limits. The isothermal batch and titration calorimeters have the largest detection limits.

It is of interest that the heat conduction flow method, which is an order of magnitude poorer than four of the other methods according to the criterion used here, i.e. minimum detectable total heat effect, has been one of the most commonly used calorimetric techniques in biochemical studies. The choice of an instrument in this case has apparently been made on the basis of ease of operation and simplicity of data analysis. Operation and data analysis are considerably more complex for isoperibol or adiabatic titration calorimetry than for any of the other methods and this is probably the reason that these methods are used in only a few laboratories.

Under some conditions, solution concentration as well as the minimum detectable heat is an important criterion of choice since the maximum solution concentration may be limited by solubility or other factors. The last column of Table 1 gives a relative comparison of the solution concentration required in order to measure the minimum detectable total heat effect in 6τ for a given flow or titration calorimetric method. By this concentration criterion, the isoperibol or adiabatic flow and heat conduction flow calorimeters are all comparable. The next best choice is the isothermal flow calorimeter which requires an order of magnitude increase in concentration. The other types of calorimeters require another one or two orders of magnitude increase in concentration of titrant to achieve an optimum use of the instrument. Thus, when the heat effect to be measured is concentration limited rather than total material limited, the calorimeter with the lowest power measurement capability will have the best figure of merit.

Another criterion which must be considered in planning a calorimetric measurement is the time span of the reaction. Depending on the kinetics of the reaction for which the heat is to be measured, times of a few seconds to several days must be considered. The isoperibol or adiabatic batch and titration methods are useful only for experiments lasting less than about an hour. All of the other methods are capable of following reactions which continue indefinitely. The maximum heat effect expected is also of importance since certain designs will not operate well above certain maxima. An excellent example of the differences in operation and application of isothermal and heat conduction calorimeters has been published [27]. In that study, a heat conduction calorimeter was used to determine the metabolic rate of a bacterial culture at low substrate concentrations where the heat rates were well below the detection limit of isothermal calorimetry. An isothermal calorimeter was used to determine the metabolic rate at high substrate concentrations where the culture had to be stirred and heat rates were too large to be measured accurately with the heat conduction calorimeter. Many of the specific considerations needed for choosing a solution calorimeter for biological chemistry applications have been discussed previously by Langerman and Biltonen [28].

The calculation methods and calorimeter classification scheme developed in this paper can be readily extended to differential scanning calorimeters (DSC). Differential thermal analysis is comparable to isoperibol calorimetry, heat compensating instruments such as the Perkin-Elmer DSC are comparable to isothermal calorimeters, and DSC instruments such as the Tronac or Hart Scientific units are very similar in design to heat conduction solution calorimeters.

In conclusion, the choice of a calorimetric method must be based on several criteria. This paper shows how the various forms of data output from different methods may be organized and the results compared for different instruments. We have also shown that the least explored calorimetric method, isoperibol or adiabatic flow, has the best potential detection limit of any method. In this paper we have stressed the lower limits on the detection of a total heat effect and hence on the amount of material required for a solution calorimetry measurement. Other criteria will be of more significance in choosing a calorimeter for determinations where large amounts of heat and materials are available.

ACKNOWLEDGEMENT

We wish to thank R. Hart for many helpful discussions in developing the ideas in this paper.

REFERENCES

1 D.J. Eatough, J.J. Christensen and R.M. Izatt, J. Chem. Thermodyn., 7 (1975) 417.
2 J.J. Christensen, J.W. Gardner, D.J. Eatough, R.M. Izatt, P.J. Watts and R.M. Hart, Rev. Sci. Instrum., 44 (1973) 481.
3 J.J. Christensen, L.D. Hansen, D.J. Eatough and R.M. Izatt, Rev. Sci. Instrum., 47 (1976) 730.
4 J.J. Christensen, L.D. Hansen, R.M. Izatt, D.J. Eatough and R.M. Hart, Rev. Sci. Instrum., 52 (1981) 1226.
5 I. Wadso, Acta Chem. Scand., 22 (1968) 927.
6 P. Monk and I. Wadso, Acta Chem. Scand., 22 (1968) 1842.
7 P. Picker, C. Jolicoeur and J.E. Desnoyers, J. Chem. Thermodyn., 1 (1969) 469.
8 P. Picker, P.-A. Leduc, P.R. Philip and J. Desnoyers, J. Chem. Thermodyn., 3 (1971) 631.
9 L.D. Bowers and P.W. Carr, Thermochim. Acta, 10 (1974) 129.
10 L.D. Hansen, T.E. Jensen, S. Mayne, D.J. Eatough, R.M. Izatt and J.J. Christensen, J. Chem. Thermodyn., 7 (1975) 919.
11 L.D. Hansen, R.M. Izatt, D.J. Eatough, T.E. Jensen and J.J. Christensen, in R.S. Porter and J.F. Johnson (Eds.), Analytical Calorimetry, Vol. 3, Plenum Press, New York, 1974, pp. 7-16.
12 R.L. Berger, W.S. Friauf and H.E. Cascio, Clin. Chem. (Winston-Salem, NC), 20 (1974) 1009.
13 B.H. Vassos and R.A. Rodriguez, Anal. Chem., 53 (1981) 135.
14 E.B. Smith, C.S. Barnes and P.W. Carr, Anal. Chem., 44 (1972) 1663.
15 A.E. Van Til and D.C. Johnson, Thermochim. Acta, 23 (1978) 1.
16 J.J. Christensen, R.M. Izatt and L.D. Hansen, Rev. Sci. Instrum., 36 (1965) 779.
17 P. Picker, Can. Res. Dev., (1974) 11.

18 Microscal Ltd., 79 Southern Row, London W10 5AL, Gt. Britain; 95 Lerida Ct., Portola Valley, CA 94025, U.S.A.
19 R.S. Schifreen, C.S. Miller and P.W. Carr, Anal. Chem., 51 (1979) 278.
20 D. Smith-Magowan and R.H. Wood, J. Chem. Thermodyn., 13 (1981) 1047.
21 G.W. Ewing, J. Chem. Educ., 53 (1976) A372.
22 L.D. Hansen and R.M. Hart, J. Electrochem. Soc., 125 (1978) 842.
23 I. Wadso, Plenary Lecture, IUPAC Conference on Chemical Thermodynamics, London, 1982.
24 Calorimeters, Calvet Microcalorimeters, −206 to +1500°C, Setaram, 69451 Lyon, France, p. 5.
25 P. Paoletti, Gazz. Chim. Ital., 112 (1982) 135.
26 P.R. Bevington, Data Reduction and Error Analysis for the Physical Sciences, McGraw Hill, New York, 1969, pp. 92–118.
27 A.S. Gordon, F.J. Millero and S.M. Gerchakov, Appl. Environ. Microbiol., 44 (1982) 1102.
28 N. Langerman and R.L. Biltonen, Methods Enzymol., 61 (1979) 261.