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Review

A review of analytical applications of calorimetry

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1. Introduction

This review is an attempt to present some of the more important applications of calorimetric instrumentation and methods to analytical problem solving. As such, this paper has a decided industrial orientation to the topics covered, but is certainly not limited to industrial applications. This review is not intended to be comprehensive, but informative regarding key analytical applications.

In each section of this paper, the significance of the calorimetric method is discussed along with guidance on use of the methods and instrumentation, interpretation of the results, accuracy and precision estimates and common pitfalls. Detailed description of instrumentation is avoided. The reader is urged to refer to other literature sources for additional information on instrumentation.

2. Characterization of materials

2.1. Thermometric titrimetry

Thermometric titrimetry is a technique well suited to both analytical and thermo-chemical problem solving. Its strength as an analytical tool for quantitating species in solution include the ease of quantitating single species even in complex solution matrices and the ability to frequently carry out simultaneous quantitation of multiple species, or impurities in a single experiment. As a general problem-solving tool, the breadth of applications to which it has been applied demonstrates the versatility of thermometric titrimetry. Measurements may be done on liquid–liquid or heterogeneous liquid–solid systems to quantitate heats of reaction, metal-ligand interaction, adduct formation, proton ionization, micellization, dissolution or dilution. Measurements may also quantitate equilibrium constants, or enable sequential determination of multiple pK_a values.

2.1.1. Methodology

Several calorimetric techniques may be considered under the general heading of thermometric titrimetry. They are usually based on the measurement of temperature change in a constant temperature environment. Different methods may be used to initiate the desired reaction, e.g. batch injection or continuous titration of the reactant. Earlier literature referred to these techniques as direct injection enthalpimetry (DIE), catalytic thermometric titrimetry (CTT) and thermometric titration (TET), but due to potential confusion with those terms they will not be used in this review. A typical apparatus for thermometric titrimetry consists of a buret, preferably motor-driven, a titration vessel, and a temperature-measuring device. These are incorporated into a system designed to maximize the observable temperature changes resulting from desired reactions, and to minimize the effects

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of variation in the temperature of the immediate environment. There are several general references the reader may consult [1–5]. A laboratory manual [6], out of print, provides another resource to acquaint the reader with the general usefulness of the techniques of thermometric titrimetry and titration calorimetry.

Direct injection and titration are both designed to follow the mixing of reagents and subsequent reactions. The mode of reagent introduction differentiates the two techniques. In a direct injection experiment, excess reagent is rapidly combined with sample by an instantaneous injection of one into the other, with the experimental readout consisting of a plot of temperature versus time. Titration, on the other hand, is where a reagent is added gradually, usually continuously, at a constant rate, but sometimes discontinuously in discrete injections, to obtain a volumetric endpoint that corresponds to a stoichiometric equivalence point for the titration reaction. Temperature is plotted versus the volume (amount, moles, etc.) of the titrant, with the titration endpoint indicated by a change in slope of the plot. Information obtained can include both the volumetric endpoint and the overall magnitude of the heat effect.

Catalytic titration is similar to titration but uses a thermometric indicator. When the first excess of titrant is present, an exothermic indicator reaction is initiated and the accompanying rise in temperature denotes the end-point.

Thermometric titration may use temperature-rise, power-compensation, or heat conduction calorimetric detection and, a portion of the subsequent discussion focuses on the particular advantages and limitations inherent in these three basic types of calorimeters. Regardless of the calorimetric design, the ultimate experimental desire is to quantitate the amount of reactant and/or heat evolved or consumed in the reaction vessel.

The heat effect q_r is a quantitative measure of the amount of product formed, n_p, because $q_r = n_p \Delta_R H$. Measurement of q_r is simple, versatile and nearly universal. Wide applicability is inherent because nearly every reaction has a non-zero enthalpy of reaction, $\Delta_R H$, or can be coupled to a secondary reaction to aid in detection. Quantitation of q_r is ultimately accomplished by temperature measurement. The advantage in such a measurement is that it is relatively unaffected by non-reacting impurities and heterogeneous matrices. An accompanying disadvantage, however, is that of poor selectivity. Because side reactions will yield an interfering heat effect, selectivity is therefore dependent on chemical rather than instrumental factors.

In the experimental design for direct injection, titration or catalytic titration, relatively small volume changes throughout the course of the experiment are recommended. In titration, the titrant should normally be 50 times as concentrated as the sample solution. Solubility of the reagent thus imposes a limit. Sample size is typically 4–50 cc.

In addition to the discrete techniques of direct injection, titration and catalytic titration, continuous-flow techniques are increasingly used and are particularly suitable for routine analysis. Two procedures are typically employed: (a) continuous mixing of sample and titrant, and (b) injection of the sample in pulses to a continuous-flow of titrant. In both methods, the temperature rise is related to the sample concentration so the methods can be considered an extension of direct injection.

Direct injection, titration, catalytic titration and continuous-flow methods are all suitable for the analysis of pure compounds, formulations and complex mixtures provided that a selective reaction or appropriate indicator reagent is available. Selectivity cannot be achieved instrumentally when the response is measured thermometrically, unless the kinetics of the desired reactions are very different from those of interfering reactions.

2.1.2. Thermodynamic and kinetic considerations in direct injection, titration and catalytic titration

A titration experiment is conceptually equivalent to a series of incremental direct injection experiments using increasing reagent/sample ratios. As the equilibrium constant controlling the reaction of interest becomes smaller, the breakpoint in the slope of the titration temperature versus volume curve becomes less sharp. This increasing degree of curvature at the endpoint degrades the precision of the endpoint.

Kinetic considerations, on the other hand, pose a greater problem than thermodynamic factors in a titration experiment; reactions having sluggish kinetics can cause misleading results in most titration techniques. This problem, in part, may be overcome by the adding titrant discontinuously, and allow sufficient time between titrant addition intervals for the

reaction mixture to reach chemical equilibrium. Thermometric titrations, however, generally use continuous addition of titrant at a constant rate. If the rate of titrant addition is of comparable magnitude to the rate of the chemical reaction, the experimental endpoint will display curvature and will lag behind the equivalence point. A definitive treatment of kinetic effects in linear titration methods with continuous titrant addition has been reported [7].

There are two kinetic considerations with direct methods. For relatively fast reactions, one must be aware of the time constant of the calorimeter being used. For very slow reactions, non-chemical effects and heat losses introduce large errors when a temperature-rise calorimeter is used to collect data beyond approximately 30 min. Use of power-compensation or heat conduction calorimetry allows much longer data collection times.

2.1.3. Considerations regarding selection of temperature-rise or power compensation calorimetry

Power compensation or isothermal calorimetry is a technique in which the temperature of the system is kept constant and the heat flow through the system required to maintain this constant temperature is measured as a function of time or of titrant added. Heat flow from the system results in an instrumental time constant on the order of a few minutes. The temperature of the calorimeter reaction vessel, the contents and the surroundings are maintained at the same temperature, so that radiation heat losses are eliminated and all changes in heat flow out of the system are due only to chemical or physical changes occurring inside the calorimeter reaction vessel. These fundamental operating principles of isothermal calorimetry illustrate why it is particularly useful for processes involving slow reactions such as microbial growth and metabolism, processes in which large amounts of heat are produced, such as reactions occurring in concentrated aqueous solutions and mixing of organic liquids, and systems involving large changes in heat capacities during the titration, such as mixing of liquids, reactions in concentrated solution and reactions involving two liquid phases.

Temperature-rise calorimetry is a technique in which the temperature of the sample varies. The temperature of the surroundings may be held constant, isoperibol, or at the same temperature as the sample, adiabatic. With such an experimental design, all heat contributions to the system must be accounted for to extract the correct heats for the reactions of interest in the system. Background heat effects may include stirring and heating by the temperature sensor (both always exothermic), condensation or sorption of water from the air, solvent evaporation (always endothermic) and heat transfer between the sample and the surroundings (either exothermic or endothermic), which may be time and volume dependent. These effects can readily be accounted for by collection of baseline data and calibration with heat pulses both before and after the experiment of interest, thus directly measuring the effects of changes in the physical properties of the system during and after reagent addition. Depending on the rate of reagent addition for a particular experiment, the pre and post-experiment baselines may be used in different ways. For a direct injection experiment, because the entire reagent is rapidly added at the beginning of the experiment, changes in physical properties occur near the onset of the experiment. Because of this, the baseline best suited for use with such experimental data is that collected post-experimentally. More appropriate for continuous titration is a time weighted-average of the pre and post-baselines because the sample composition and physical properties change continually through the course of the titration. Additional sources of heat input and output that can be corrected, include temperature mismatch of titrant, heat of titrant and titrate dilution and change in heat capacity of the system.

2.1.4. Direct injection: precision and accuracy

As a rule-of-thumb, precision and accuracy of 3–5% can be attained at millimolar concentrations in direct injection experiments. The magnitude of the analytical signal, ΔT, depends on both $\Delta_R H$ and sample concentration. The ultimate precision attainable depends on the noise in ΔT, which can be as low as is about 50 μC. This limiting value reflects thermal inhomogeneities in the solution.

The accuracy of a determination depends on knowing the actual degree of completion of the reaction, which may be readily calculated from the equilibrium constant and relevant concentrations. Reaction kinetics can also indirectly affect accuracy. Slow reactions require a longer measurement time during which extraneous thermal effects (heat effects primarily from

stirring, sensor heating, evaporation and heat transfer) become proportionately larger and thereby degrade the accuracy of the ΔT signal. Other thermal effects can be significant in both fast and slow reactions, e.g. temperature mismatch between sample and reagent solution and heats of dilution. These limitations are discussed in more detail elsewhere [7].

2.1.5. Titration: precision and accuracy

Typically, the precision and accuracy in titration experiments are limited by the titrant delivery system to about 0.2–0.5%. The precision of the endpoint, being located by extrapolation of straight-line segments, depends on the magnitude of the change in the slope and on sharpness of the endpoint. Thus, the heat of reaction must not be small compared with the heat of dilution. The sharpness of the endpoint depends largely on the equilibrium constant and kinetics of the titration reaction. The precision and accuracy of the endpoint are directly related to the equilibrium constant; for K_{eq} greater than approximately 10^5, precision and accuracy of approximately 0.5% or better is expected. Contributions from stirring, sensor heating, evaporation and heat of titrant dilution do not seriously detract from the analytical utility of the titration curve. On the contrary, heat transfer, temperature mismatch of titrant and a change in the heat capacity may cause non-linear deviations, which make endpoint determination less precise and less accurate. These processes must be minimized by the use of relatively concentrated titrants and optimum titration times and/or corrected for by appropriate data reduction.

2.1.6. Catalytic titration: precision and accuracy

The precision and accuracy using catalytic titration are typically on the same order of magnitude as for direct injection, when titrants of the same concentration are used. Catalytic titration offers the advantage of being applicable to the determination of much smaller sample concentrations, typically in the ppm range, because the response of the indicator reagent is not influenced by analyte concentration.

2.1.7. Overview comparison between direct injection, titration, catalytic titration and continuous-flow methods

Catalytic titration is the thermometric method of choice on the grounds of sensitivity, simplicity, convenience and low cost. Its scope, however, is limited by the availability of suitable thermometric indicators. Both direct injection and titration have a wide range of applications, with direct injection or continuous-flow methods being chosen for rapid analyses, and also multiple analyses by successive injections of several discrete samples into one lot of reagent. Titration is generally the method of choice for the determination of several constituents or reactive functionalities in the same sample and offers better accuracy and precision than direct injection.

2.1.8. Applications — general

The following discussion cites example literature applications of direct injection, catalytic titration, titration and continuous-flow techniques and highlights specific experimental enhancement techniques.

2.1.9. Applications — direct injection

The analytical, kinetic and calorimetric possibilities of direct injection, especially the reaction rate range in which direct injection can be efficiently used for kinetic measurements, are made apparent by the use of well-known saponification reaction of methyl acetate and ethyl acetate by sodium hydroxide [8].

The reader may also refer to discussions of water determination by direct injection [9].

The direct calorimetric determination of most serum enzymes is precluded by sensitivity limitations. But a method for quantitation of serum cholinesterase via direct injection, for example, is made feasible through 'chemical amplification' of the hydrolysis reaction of interest. The heat change produced by the enzymatic hydrolysis of a substrate such as butyrylcholine ($+1.3$ kJ mol^{-1}) can be amplified by the enthalpy change associated with the concurrent protonation of Tris buffer (-47.7 kJ mol^{-1}). The utility of calorimetric methods, for this enzymatic determination and numerous other applications [10], is based on the facility to measure the primary enzymatic event without recourse to coupling reactions in order to produce a measurable entity as is done in spectrophotometric determinations. Thus, determinations of enzymes in biological specimens can be done with a minimum of sample pretreatment and the propagation errors inherent in these procedures avoided.

Determination of serum glucose levels has been the subject of several reports. A conventional calorimetric

method [11] quantitates glucose by the heat of phosphorylation by $Mg(ATP)_2$. This work, along with others, led to glucose determinations in serum [12]. In an excellent illustration of the ability of enthalpimetry to tolerate the presence of unreactive matrix ingredients without a significant loss in precision, McGlothlin and Jordan extended their procedure to the determination of glucose in plasma and whole blood. This direct injection procedure is quantitative over more than a thirty-fold glucose concentration range, a much greater range than for spectrophotometric procedures.

2.1.10. Applications — titration

The equilibrium constant (K) for some reactions can be determined directly by either continuous or stepwise titration calorimetry if the magnitudes of K and ΔH for the overall reaction taking place in the reaction vessel are within certain limits. The curvature of a plot of q versus volume of titrant is a function of K_{eq}. The curves for the systems with K values greater than approximately 10^4 differ only slightly from one another [2,13].

Titration determinations enable selective, consecutive determination of several components in a mixture. An example of a calorimetric study involving non-enzymatic protein chemistry [14] shows that the carboxyl, imidazole and amino groups of egg albumin can be delineated by means of titration with sodium hydroxide solution. This is in contrast to a classical potentiometric titration, which can only determine the carboxylic acid groups.

Additional applications of titration methods have been reviewed [10,15] and include determination of total serum protein through the use of anionic precipitants serial determination of calcium and magnesium in human serum using EDTA, by taking advantage of differences in the relative formation constants and reaction enthalpies. A titration method has also been used to for the study micelle formation in the interaction of block polypeptides with surfactants [16].

A discussion of calorimetric monitoring of industrial chemical processes [17] focus both on chemical analysis and process control. On-line methods may be applied to concentration analysis, to safety monitoring and to the control of reaction progress. There may be a hesitation to apply flow calorimeters because plugging may be a major problem with small, undiluted process streams. Therefore, batch injection might prove the method of choice, where a sample is separated from the main process stream and then analyzed. The areas of calorimetric safety monitoring and process control are covered in greater detail later in this paper.

2.1.11. Applications — flow calorimetry

Flow calorimetry for the determination of heats of mixing was pioneered by Wadso and Picker in the late sixties and has evolved into determinations at elevated temperatures and pressures [18].

Calorimetric measurements with a microcalorimetry operated in a continuous flow mode have been conducted on immobilized enzyme inhibitors. A rapid, reproducible method is available [19] for the determination of the relative inhibitory strengths of a series of reversible cholinesterase inhibitors. The technique continuously monitors the activity of glass-immobilized cholinesterase's that can be rapidly and quantitatively reactivated simply by removal of the inhibitors. For particularly effective inhibitors, quantities as low as 5 nmol can be detected. For analyses to determine relative inhibitor strengths, the use of immobilized enzymes enables circumvention of some of the problems of the more standard approach with soluble enzymes. The latter is less quantitative, necessitates more equilibration time, encounters difficulties in obtaining exactly the same activity of enzyme per run and incurs the expense of using the non-recovered soluble enzyme.

2.1.12. General applications in biochemical systems

There is growing use of microcalorimetric analyses in the field of pharmaceuticals. Several reviews of the application of calorimetry to biochemical systems are available [10,20–26].

Many diverse applications of thermometric titrimetry, primarily in the support of the pharmaceutical industry, have been reviewed [27]. Pertinent determinations may be thought of as applying to either pharmaceutical substances or formulations, or to clinical and biochemical analyses. Clinical samples are complex mixtures and determination of specific constituents by the thermometric method usually requires use of specific or highly selective reagents. Enzyme-substrate reactions, as well as antibody-antigen reactions are examples of specific reactions [28].

Biochemical and clinical analyses by calorimetric measurements address characterization of non-enzymatic proteins, enzyme activities and substrate quantitation [10].

2.2. Application of calorimetry to pore size determination

A novel application of changes in the observed melting point of various substances is the determination of pore size and pore size distributions in various substrates, a method referred to as thermoporimetry. Pore size and pore size distributions are critical characteristics for materials ranging from membranes to filters to molecular sieves to chromatographic column packing. Current methods for characterizing pore size and distribution include microscopy, nitrogen adsorption and mercury intrusion. Thermoporimetry provides a simple calorimetric method for determining pore size and distributions.

The basis for thermoporimetry can be understood by consideration of the free energy of a liquid in a pore [29]. As the surface to volume ratio changes for a small pore, the effect of surface tension on the system changes, being manifested as a change in the melting point for a liquid in the pore. Brun and co-workers [29] have given a detailed derivation of this phenomena. They point out that crystallization and melting curves will be slightly different, the difference being related to the pore geometry. The general form of the equation relating the change in melting point/crystallization temperature is:

$$R = \frac{A}{\Delta T + B} \tag{1}$$

where R is the pore radius, A and B are constants which can be derived theoretically. Sufficient surface tension data exists only for water and benzene to allow for the calculation to be made, this last point potentially limiting the application of the method.

Because Eq. (1) relates ΔT to the pore radius, if a distribution of ΔT exists, a distribution of pore radii can be determined. The change in the melting point of water trapped in small pores is represented in Fig. 1. In this figure, the data points are for water in porous glass beads and the line is the theoretically derived equation.

In addition to determining the pore size, the number of pores of each size can be determined from the total heat, that is the quantity of material melting over any temperature range is a direct indication of the number of pores in that size range. In determining the total number or fraction of pores, the heat of fusion must be corrected for the depressed melting point of the probe molecule, as ΔT of 40 K can be observed, making a significant change in the heat of fusion from that of the normal melting point.

Commercially available differential scanning calorimeters (DSC) used for thermoporimetry have been reported in the literature [30–33]. A portion of the material to be studied, after being equilibrated with the appropriate probe material, is sealed into a DSC container. The sample is then scanned at a slow rate, 2–60 K h^{-1}, in both cooling and heating modes.

Thermoporimetry has been applied to the study of membrane systems [29,30,32] with water as the probe molecule. In one application, this method was used to study ultrafiltration membranes [33] where a distribution of pore radii ranging from 3 to 10 nm were observed with water as the probe liquid. This work also points out that one must be cautious in using thermoporimetry to obtain the equilibrium melting conditions if one is to calculate accurate pore radii and volume fractions. These works point out that pores with a radius of much less than 2 nm cannot be studied, at least using water as the probe molecule, because theoretical derivations of the relationship between ΔT and pore size does not give high resolution at smaller pore radii. In the literature, theoretical derivations have only been developed for water and benzene. This limitation can be overcome by characterizing inert materials, such as porous glass beads, with water as the probe molecule and then determining the freezing point depression for a new probe molecule and fitting these data to the appropriate equation [29,30].

2.3. Oxidation of materials by calorimetry

Studies relating to the oxidative stability of nearly all organic materials, e.g. foods, fuels, lubricants and polymers, are critical for determining long-term stability at the temperature of use. Calorimetric methods are often used to study the oxidative stability of materials. The oxidation of organic materials is exothermic by approximately 350 kJ mol^{-1} of oxygen reacted if $H_2O(g)$ is a product and 455 kJ mol^{-1} if

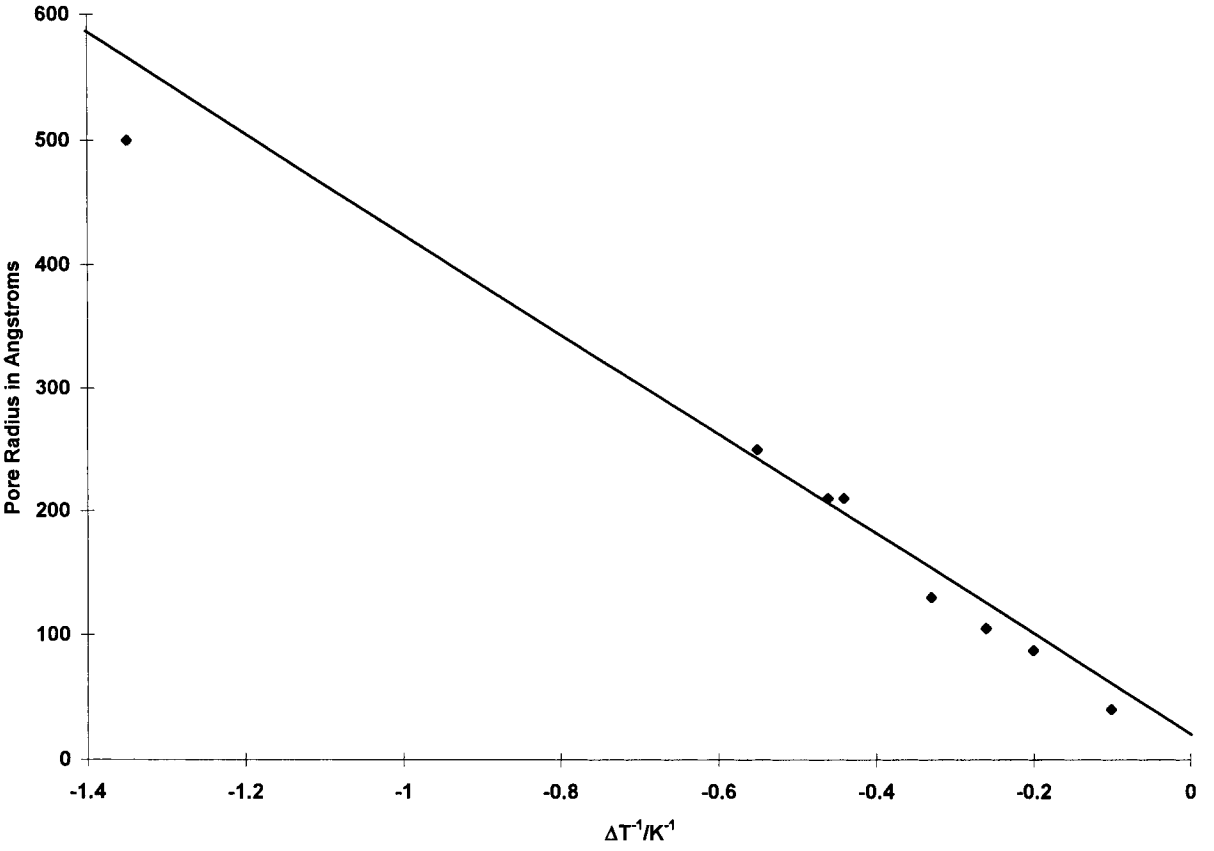

Fig. 1. Pore size vs. inverse freezing point ΔT for water. The change in the inverse of the freezing point (ΔT^{-1}) for water in pores of various radii. The line is a theoretical curve. The points are data for water in the pores of silica column packings with known pore radii.

H_2O(l) is a product [34]. With this large heat evolution it is convenient to detect the rate of oxidation processes calorimetrically.

While virtually all organic materials exhibit some rate of oxidation even at room temperature, the rate of oxidation increases several fold at elevated temperatures. Thus, the application of calorimetry at elevated temperatures to study these processes is an ideal analytical application for determining the relative stability of systems of interest. Calorimetry can be used to answer three questions relating to high temperature oxidative stability of materials. (1) At what temperature does the oxidation process begin to occur at a significant rate? (2) What is the rate of oxidation? (3) What is the relative efficiency of antioxidants added to a material and how much should be added?

The oxidation of lubricating oils in oxidative atmospheres have been studied using DSC [35] with an air atmosphere either at ambient or high pressure. Scanning experiments were performed to determine the onset temperature of the various oils studied. In addition, isothermal experiments were performed at elevated temperatures and varying air pressures to determine the effect of increased oxygen content on the onset of oxidation. The effects of adding various materials to the oil, such as stabilizers, were also studied. At a given temperature, the induction time for the onset of rapid oxidation may be linear over a range of useful concentrations. The concentration of stabilizer in the oil can be determined from induction time measurements. Samples with known concentrations of stabilizers can be used to obtain a calibration curve of stabilizer concentration versus oxidation induction time. In another study of the oxidation of lubricating oils, the effectiveness of various antioxidants was determined from the induction time for

the onset of rapid oxidation. Arrhenius plots were used to determine the activation energy [36]. Similar methods have been used to study the oxidative stability of elastomers [37], vegetable oils [38] and fuel oils [39].

As with most calorimetric techniques, this method for studying oxidative stability is nonspecific and, therefore, can be affected by impurities in the system.

3. Thermodynamics and phase behavior

3.1. Use of calorimetry to study crystallinity and crystallization processes

3.1.1. Crystallization and crystallinity

For many materials, the extent to which the material is crystalline can have a significant effect on properties ranging from tensile strength to elongation to rate of dissolution. Thus, it is important to know to what extent a material has crystallized. Crystallinity, melting point and the heat of fusion for some materials can be related to sample purity and in some cases, the 'crystalline form' (polymorph). These topics are covered in separate sections.

If the extent of crystallization is important for the performance of a material, then the rate of crystallization is also important since one needs to know if, during processing, the sample will attain the desired level of crystallinity. Calorimetry is an ideal tool for studying the crystallinity of organic, inorganic and polymeric materials. The application of calorimetry to the quantitative determination of crystalline components is discussed in the section on compositional determination. However, sometimes a material does not fully crystallize, and calorimetry can also be used to study the extent of crystallization. This application is particularly important for polymers, which do not fully crystallize. Various authors have pointed out that the extent of crystallinity, X_c, can be determined from knowledge of the heat of fusion, $\Delta_{Fus}H^0$, and the heat of fusion for a fully crystalline material, $\Delta_{Fus}H^0$ [40,41].

$$X_c = \frac{\Delta_{Fus}H}{\Delta_{Fus}H^0} \quad (2)$$

From this simple relationship the level of crystallinity for a sample can be determined.

One difficulty in applying Eq. (2) is knowledge of the heat of fusion for fully crystalline material. $\Delta_{Fus}H^0$ can be determined from a combination of calorimetric measurements and X-ray diffraction (XRD) data, where XRD data are used to determine the level of crystallinity and calorimetry the heat of fusion for that sample. The heat of fusion for a fully crystalline sample is then calculated from these data. Several samples are usually run to determine an average value for the heat of fusion. Another method has been described by Karasz et al. [42]. When a polymer is below its glass transition temperature (T_g), then, for a semi-crystalline system, it can be assumed that all of the polymer chains exist either in the amorphous or crystalline phase. At the glass transition, a shift in the specific heat capacity of the sample occurs in going from the glassy to liquid state. This heat capacity shift has a constant value for a given polymer, so the magnitude of the heat capacity change at T_g is a direct quantitation of the fraction of polymer in the amorphous phase. Since the heat of fusion is a direct measure of the crystallinity of the material, a plot of the heat capacity change at T_g versus the observed heat fusion will give a line where the intercepts represent the heat capacity change at T_g for the fully amorphous polymer and the heat of fusion for fully crystalline material. This procedure has been applied to the study of syndiotactic polystyrene [43]. The extent of crystallization can also be obtained from the heats of solution and from the heat of crystallization. These methods are particularly useful in the pharmaceutical industry.

Crystallization rate can also be followed calorimetrically [40,41]. When held isothermally at conditions where the material will crystallize, either from a melt or from a solution, the heat rate during crystallization can be followed, and from these data and a determination of the heat of fusion after the crystallization process, the crystallization rate can be determined.

3.1.2. Crystallization process development and optimization

3.1.2.1. Areas of application. Crystallization is a key unit operation in the chemical industry, particularly for the manufacture of speciality chemicals and pharmaceuticals. Reliable control of crystallization

is essential to consistently make product with the desired properties, both to maximize efficiency in downstream unit operations and to meet product quality specifications. For example, crystal properties such as crystal size, shape and purity, and the amount of solvent included within the crystal matrix all impact efficacy of the subsequent solid–liquid separation and drying operations. If the crystalline product is an active ingredient in a drug, these crystal properties can also influence the product formulation process and the drug's efficacy.

The driving force for a material to crystallize is proportional to the amount of supersaturation which can be determined from solubility measurements provided the amount of material dissolved in the liquid is known or can be measured. To control crystallization, one must control the rate of nucleation and the rate at which material crystallizes (the crystallization profile as a function of time). The progress of a crystallization event is typically followed via turbidity and temperature measurements. Turbidity measurement is a convenient tool for determining the onset of crystallization [44], however, it loses sensitivity with increasing slurry opacity. Temperature measurements can also, in some cases, be used to detect the onset of crystallization, but they give only qualitative information about the crystallization progress. A convenient, quantitative, means of obtaining the compete crystallization profile is to perform an energy balance on the crystallizer. An energy balance yields the heat release rate from the crystallization process, from which the crystallization profile is directly obtained provided the heat of crystallization is known). On a production scale, performing this energy balance involves turning the production process equipment into a larger calorimeter. On a laboratory scale, heat flow or power compensation calorimeters can be used. Reaction calorimeters have been found to be a particularly convenient tool for the study of crystallization. Key advantages include adequate agitation and the ease of carrying out temperature ramps and continuous additions.

3.1.2.2. Examples. Albino [45] used reaction calorimetry to optimize crystallization of a pharmaceutical from solution. Heat flow was used to monitor the onset of crystallization. Optimization of the amount of seeding and the cooling curve resulted in a significant reduction in manufacturing costs by eliminating two downstream particle-sizing steps.

Borghese [46] used reaction calorimetry to better understand the crystallization of milacemide out of acetone–water. The crystallization, induced by a combination of the addition of acetone and cooling, had occasionally produced a coagulated, jelly-like, reaction mass. Calorimetric analysis showed this to be the result of a crystallization event following by a 'coagulation'. Based upon this work, processing conditions were refined to avoid coagulation and to enable the production of products with two different crystal morphologies.

Tavana and Bayat [47] demonstrated the use of a turbidity photometer in conjunction with reaction calorimetry to study the crystallization of an organic salt via batch evaporative crystallization.

Velich and co-workers describe an isoperibol reaction twin (IRT) calorimeter for studying the precipitation of barium sulphate and calcium oxalate [48,49]. The progress of these crystallizations was followed via heat flow measurement, with the integral heat giving the total enthalpy of the process.

3.2. Phase equilibria

Knowledge of equilibrium phase boundaries is useful in a wide variety of applications. The simplest example, the solid–liquid phase boundary (the melting point) for a substance, allows determination of the temperature requirements for processing and storage. Also, the properties of substance may change in fundamental ways, depending on the particular phase of the material. For example, a pharmaceutical or an agricultural chemical may exist in one or more crystalline forms (polymorphic forms) yet only one of these forms may be permitted for the intended use.

A number of techniques have been developed to determine temperature–phase relationships. For pure substances (and less accurately for mixtures), the melting point can be easily determined by visual observation of the sample while heating. For solid–solid transitions, visible light microscopy and XRD have been used. In the latter case, samples must be prepared and tested under equilibrium conditions or quench-cooled to 'freeze-in' a higher temperature phase. Although not a calorimetric technique,

thermogravimetry (TG) has found wide application in studying gas–solid phase equilibria [50].

Calorimetry has a number of advantages over other techniques for determining phase boundaries. First, phase transitions such as crystalline-liquid or crystalline–crystalline are accompanied by the liberation or consumption of energy. This energy is usually of sufficient magnitude and rate to be easily detected. Second, many calorimetric techniques, especially the temperature scanning instruments, e.g. DSC, require vary small sizes (ca. 0.5–5 mg). Sometimes even the sign of the energy release can give one insight into the processes taking place. For example, if during heating of a sample, an endotherm is followed by an exotherm, this may represent an endothermic phase transition (melt) followed by an exothermic recrystallization into another crystal phase. Another advantage of calorimetry is the fact that the energy for the transition can sometimes be used to extrapolate the phase relationships to other temperature conditions.

Using standard, commercially available DSCs, the temperature range available for study is typically −100 to 600°C. For studying materials (such as ceramics and inorganics) at higher temperatures, DSCs and differential thermal analyzers (DTAs) are commercially available which can go to 2400°C. In a typical experiment, a 1–500 mg sample is heated in the DSC at a rate of 1–10°C min^{-1}.

The determination of solid–liquid phase diagrams using scanning calorimetric techniques is a widely used and generally accurate technique. Several good reviews of the general techniques and concepts involved in these determinations have been published [51–55]. The concept is straightforward as the temperature of a sample changes (heating or cooling), a heat signal is observed as a phase diagram boundary is passed.

The simplest example is a pure crystalline material at a temperature below its melting point. As the sample is heated in the calorimeter, an endothermic event is observed as the melting point is traversed. Thus, for this simple pure system, the solid–liquid phase boundary can be defined.

For binary systems in which one component is considered the 'solvent', the determination of the phase diagram in the manner presented here is equivalent to the determination of solubility. Normally, solubilities are thought of in terms of approaching or crossing the phase boundary at constant temperature with increasing concentration of the solute in the solvent, but the concepts are, in fact, equivalent.

For a binary mixture that exhibits a simple eutectic, DSC (or DTA) traces will generally show the behavior illustrated in Fig. 2. For every composition other than the eutectic, two endothermic peaks are observed on heating. The first peak is due to the melting of the eutectic composition. Once all of the eutectic has melted, the DSC signal does not return to baseline as the sample continues to be heated further. This is due to the fact that the remaining solid becomes increasingly enriched in component *A* and the melting point of the remaining solid increases as governed by the phase diagram. The second peak is due to the end of melting of the system, i.e. the last solid melts, which at this point must be bulk composition.

3.2.1. Considerations and pitfalls

3.2.1.1. Sample preparation. It is important in this type of work to make sure that the materials are prepared and sampled so that they are representative of the desired composition and that they are true representations of the equilibrium composition. For example, if a solid mixture is prepared by allowing the liquid to cool and crystallize, the first crystals to appear will be of different composition than the last crystals to appear. This non-homogeneity makes it difficult to obtain representative samples. One should consider thorough blending of the sample (where practical) after solidification. Grinding can, in some cases, induce polymorphic changes in the sample.

Also, under rapid cooling conditions, there is always the possibility of crystallizing the sample into a metastable phase. If this occurs, the DSC scan may exhibit an exothermic event on heating due to the transformation from the metastable phase to the stable phase. These effects can lead to interpretation problems.

Many times the ambiguities which arise in interpretation of DSC curves can be resolved using XRD and visible microscopy, particularly, hot-stage microscopy.

3.2.1.2. Difficult samples. For samples, which have very low melting points, crystallization temperatures

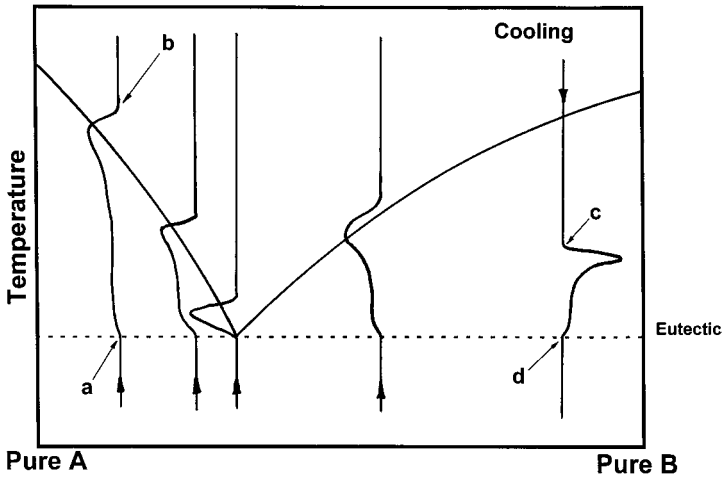

Fig. 2. A hypothetical binary phase diagram with superimposed DSC signal. In the case illustrated, the DSC signals are for the solid being heated (arrows pointing up) and melting occurs endothermically. In one DSC trace labelled 'cooling' (arrow pointing down), the experiment illustrates the liquid being sub-cooled and crystallizing exothermically well below the equilibrium freezing-point. Point 'a' in the figure corresponds to the onset temperature of melting where the first solid to melt is the eutectic composition. Point 'b' is the temperature at which the final solid melts. Note that this temperature may be higher than the actual phase diagram boundary of the endotherm. Point 'c' is the onset of crystallization for the sub-cooled liquid. Point 'd' is the temperature where the last liquid crystallizes with the composition of the eutectic.

can be difficult to measure since the samples may be very difficult to get to solidify in the crystalline state. This generally occurs in viscous systems in which molecular mobility is restricted and the tendency to form the highly ordered crystalline phase is reduced. For some particularly 'stubborn' samples, crystallization may never be achieved. In such cases, however, one may resort to other estimation techniques to predict the freezing point of the sample [56].

3.2.1.3. Heating versus cooling. One might initially think that cooling a liquid in a DSC cell and recording the onset temperature of crystallization is the best way to perform experiments of this type. Unfortunately, the kinetic barrier to the formation of the new crystalline phase is inversely proportional to sample size. Thus, while it may be easy to crystallize a sample in 'bulk', say at 5–10 g scale, it may not occur easily at the 0.001–0.010 g scale typical of most DSC samples. What may occur (and is actually quite common for organic materials and even some metals) is supercooling of the liquid. Thus, there is always the question of whether the observed exothermic crystallization is occurring at the equilibrium phase boundary or at some lower temperature. A hypothetical case where sub-cooling is observed is illustrated in Fig. 2. This effect does not occur upon heating a solid however, and thus, heating is the preferred procedure.

3.2.1.4. Accurate determination of the phase boundary temperature. The DSC instruments are normally calibrated using melting point standards, and the accepted procedure is to take, as the melting temperature, the extrapolated onset of the melting endotherm. In the determination of phase diagram boundaries, the situation is slightly different. Since the melting of the eutectic represents a congruent phenomenon, the extrapolated onset is the appropriate temperature. As the sample is heated further, the liquid–solid boundary is traversed and the DSC signal returns to baseline. In this case, the peak temperature is nearer the boundary since this temperature is closest to the temperature at which the last solid melts. The return to baseline after melting is governed by the characteristic time constant for the instrument. Also note that melting of the eutectic may not always be observed because sample compositions 'far away' from the eutectic contain too little eutectic for the DSC to detect. A good example may be found in the $KNO_3/NaNO_3$ phase diagram work in reference [57].

In the case illustrated in Fig. 2, all but one of the DSC signals are for a solid being heated. The DSC trace labelled 'cooling' illustrates a liquid being super-cooled below the equilibrium freezing point.

3.2.2. Selected examples from the literature

Most published work on the use of scanning calorimetry for the study of phase diagrams has been in the inorganic/metals/ceramic area. Some selected references are [58–66]. In the organic/pharmaceutical field, some selected references include [67–69].

3.3. Polymorphism

The ability of a substance to exist in more than one crystalline phase is called polymorphism and each distinct phase is a polymorph. Polymorphism is an important consideration in pharmaceutical and agricultural chemical industries because a particular material may be polymorphic but only one of polymorphs may be active.

Polymorphic transitions are easily detected with temperature scanning calorimetry in an analogous manner to the solid–liquid transitions discussed above. When heating or cooling a solid, a distinct peak is observed in the calorimeter signal as the transition boundary is traversed. In binary systems, horizontal lines in the phase diagram indicate solid–solid transitions.

3.3.1. Considerations and pitfalls

One of the most common problems in using scanning calorimetric techniques for the determination of polymorphic behavior is maintaining phase equilibrium in the sample during the test. For example, it is relatively common for a polymorph to melt to a metastable liquid that then recrystallizes to the stable polymorph which itself eventually melts. This recrystallization may never occur in the DSC cell due to the small sample size, and thus the existence of another polymorph is not determined. The complementary techniques of XRD and hot-stage microscopy can often help to sort out confusing calorimetric results.

3.3.2. Selected examples from the literature

A good source of solid–solid phase transition data for pure organic materials is a compilation in [70]. Other examples of polymorphic studies of organic systems can be found in [71–74].

3.4. Purity by calorimetry

Determination of the purity of compounds by calorimetric methods has proven important for both organics and inorganics from the research stage to full scale manufacturing. The calorimetric methods of purity determination generally apply to any compound containing low levels of impurities. At first, methods were based on adiabatic calorimetry, but became more widely used with the advent of rapid and convenient differential scanning calorimetry in the 1960s. One of the critical needs driving the use of these methods is the requirement for purity characterization of industrial standards and compounds submitted for governmental registration [75,76].

The calorimetric approach affords several advantages over conventional chromatographic or spectroscopic methods. First, a high purity standard of material of interest is not required for the method. Second, precision of better than 0.2 mol% is attainable at purity levels greater than 98 % [77]. Third, in many cases only a few milligrams of sample are needed for analysis by DSC.

The method is based on the Van't Hoff relationship that relates the melting point depression of an impure material to the mole fraction of the impurity [78]:

$$T = T_0 - \left(\frac{RT_0^2}{\Delta_{\mathrm{Fus}}H}\right)\frac{X_2}{F} \tag{3}$$

where T is the melting temperature of the impure material, T_0 the melting point of pure material, Δ_{Fus} the molar heat of fusion, R the gas constant, F the fraction of solid melted at the temperature T and X_2 is the mole fraction impurity. The mole fraction of the impurity in the melt changes during the calorimetric experiment since crystalline material continues to melt as the temperature is increased. In the application of the method, the mole fraction melted at any point during the experiment is calculated from the fraction of the heat of fusion liberated at that temperature. The slope of a plot of observed temperature versus reciprocal fraction melted yields the mole fraction impurity.

Eq. (3) is a simplified form of a thermodynamic relationship describing the equilibrium between a

liquid containing impurities and a pure solid [79]. Several assumptions apply to the working equation above. Firstly, the system must behave ideally, namely that the impurity is completely soluble in the melt and that no solid solutions form. Secondly, equilibrium must be achieved in the melt–solid system. Thirdly, the mole fraction of impurity must be small, less than 1.5 mol%, due to a mathematical approximation in the derivation. In addition to the restriction of the working equation, a number of other assumptions are applicable in purity determination by calorimetry. These have been summarized in [80].

3.4.1. Instrumentation

Although most purity determinations are now done with DSC instrumentation, some of the more accurate and precise measurements have been accomplished using adiabatic calorimetry and commonly referred to as a cryoscopic method [79]. In general, sample size is large, on the order of 50–100 g, and the measurement period is long to achieve equilibrium, on the order of many hours for each fraction melted. The heat of fusion of the pure material is measured in a separate experiment while the triple point is obtained from the Van't Hoff relationship. Heat capacity corrections for the phase present and pre-melting effects must be incorporated in the calculations. If the heat of fusion and triple points are known, a single measurement of fraction melted yields a purity value.

The DSC method requires only small amounts of sample, usually less than 5 mg, but depends upon the specific instrumentation used. In contrast to the adiabatic calorimetry approach, DSC affords relatively rapid analyses, often less than 1 h because it is a dynamic heating method. But, a number of experimental parameters must be carefully selected and controlled to achieve accurate results [77,80]. Recommended heating rates are less than 2.5 K min^{-1}. The choice of scan rate and sample size is critical to accurate purity measurements by dynamic methods. Sample encapsulation is also important. Vaporization of the sample must be minimized during analysis by use of hermetically sealed containers with small headspace. Sample movement must be avoided during the scan and intimate thermal contact between the sample and the container must be assured. This may be accomplished by melting the sample once prior to the measurement if pre-melting of the sample does not alter the crystalline form or cause decomposition. Finely divided materials may be handled by premelting.

As with the adiabatic calorimetry method, corrections to the data for heat capacities of container and sample and pre-melting effects, along with the determination of the heat of fusion, are critical to accurate determinations. In addition, DSC data must be corrected for thermal lag due to thermal resistance between the sample and detector. In current commercial instrumentation, computerized data acquisition, correction and reduction are readily available which greatly reduces analysis time. However, the analyst should be aware that the details of the calculational methods are not usually available from the instrument manufacturers and one must assume that the calculations are correct or carry out the calculations by hand. Confirmation of the accuracy of the calculations may be partially addressed by analyzing samples of known purity prior to analysis of an unknown material. Such samples are available from The National Institute of Standards and Technology (NIST). Due to the complexities of phase behavior of impure compounds, it is advisable to prepare purity standards of the compounds and impurities of interest whenever possible. It is also strongly recommended that purity determinations by calorimetric methods be validated by other analytical methods.

3.4.2. Examples

Furakawa et al. [79] demonstrated the ability to determine very low levels of impurities using the cryoscopic method on benzene samples containing *n*-heptane from 0.001 to 1.168 mol% with high accuracy in the middle concentration range. Although the precision of the measurements was high for all specimens, the accuracy decreased at the highest and lowest impurity levels studies [79].

Grady et al. [81] studied over 100 pharmaceuticals using DSC and compared the data to those obtained by chromatographic methods [81]. Many compounds could not be analyzed by DSC due to decomposition upon heating.

Habash et al. [82] used DSC techniques to examine menadione and phenacetin containing varying levels of different impurities, some similar to the major constituent and others quite dissimilar in chemical structure. They concluded that the nature of the

impurity could affect the accuracy of the determination. Thus, in general one cannot assume ideal behavior and corroboration with other analytical methods is advisable.

3.4.3. Pitfalls

In addition to the potential pitfalls mentioned above, there are several general areas of concern in purity determinations. First, calorimetric methods are not applicable to materials that decompose at or near the melting point. Materials must also be non-reactive towards the sample container and the atmosphere surrounding the sample. Visual examination of the sample after measurement helps to identify unwanted reaction or decomposition.

Contamination of the sample during preparation must be avoided and is of special concern with the very small sample size employed in the DSC method. Also, samples which contain a contaminant, such as finely divided silica, which is not soluble in the melt phase will give incorrect values for the purity.

Materials that readily convert from one polymorphic form to another during the measurement may not yield useful purity results by calorimetry. This behavior is often identified by melting curves that have unusual shapes, e.g. double peaks or exothermic events. In some cases of decomposition or polymorphic inter-conversion, the early portion of the melting curve may be used to obtain approximate values of the purity providing that an accurate heat of fusion is known.

It is generally accepted that calorimetric purity determinations can only be used with samples with purity levels exceeding 98 mol% [80]. Below this level, the accuracy of the analytical method decreases rapidly. However, DSC can be used to reliably demonstrate that a compound is less than 98 mol% pure without quantifying the purity level.

The calculational approach to calorimetric determination of purity usually accounts for some small fraction of the sample, which has melted prior to the temperature region of the measurement. This fraction of 'pre-melted' sample is treated as a fitting parameter that is varied until the Van't Hoff plot becomes linear. Large values of this parameter, i.e. greater than 5–10% fraction melted for high purity materials, suggests that the method is ill suited for the sample. The considerable discussion surrounding the issue of 'pre-melted' sample has recently been reviewed [80].

3.5. Mechanical effects on materials

The properties and performance of solid materials such as metals and engineering polymers often depend upon the nature of their response to mechanical stresses and thermomechanical history. When a force is applied to a solid system, it will respond by deforming. Deformation calorimetry is used to study the work and heat involved during the deformation process.

Conventional studies on the deformation of solids consider only the work done. However, a more in-depth understanding of the process is gained by using a thermodynamic approach that considers thermodynamic potentials that involve both heat and work. The thermodynamic approach, based upon the first law of thermodynamics, allows study of both reversible and irreversible processes in the same framework. In a simplified form applicable to elongation, the first law may be written as:

$$\mathrm{d}U = \mathrm{d}Q + f\,\mathrm{d}x \tag{4}$$

where $\mathrm{d}Q$ is the change in heat, $f\,\mathrm{d}x$ the work associated with elongation or compression due to applying a force f through a distance $\mathrm{d}x$ and $\mathrm{d}U$ is the resultant change in internal energy. A fundamental understanding of material response to deformation can be gained by measuring and comparing the elastic response, $f\,\mathrm{d}x$, to the entropic response, $\mathrm{d}Q$, and to the stored energy $\mathrm{d}U$, all of which are obtained via deformation calorimetry.

Due to its general nature, deformation calorimetry can be applied to materials such as polymers, metals, ceramics, and films, although much of the effort has focused on polymer behavior. The information acquired via deformation calorimetry has proved useful in studying inter and intra-chain effects, stress softening, and reinforcement by fillers in rubbery solids. The behavior at low deformation (reversible), thermo-elastic effect (Kelvin effect), cycling and fatigue, inversion of internal energy and thermal expansion coefficient, strain-induced crystallization and filler effects in glassy, semi-crystalline and liquid crystalline materials have also been studied. Deformation calorimetry principles, instrumentation and

applications have recently been reviewed by Godovsky [83].

There are indirect experimental alternatives to deformation calorimetry. After deformation of a glassy material below its glass transition temperature (T_g), the internal energy, or 'stored' energy may be measured via DSC. During heating of the strained material, the 'stored' energy is released as heat near T_g as the material relaxes. This heat appears as an exothermic event on the DSC curve as compared to the DSC curve of unstrained material. This experimental approach is limited to glassy or crystalline polymers.

Alternatively, the 'stored' energy may be determined via heat of solution measurements. In this method the strained and unstrained materials are dissolved in separate experiments in a suitable solvent. The difference in the heats of solution represent the 'stored' energy, or change in internal energy, because the final solution state of the materials are the same. This approach is not applicable to rubbery materials and is dependent upon finding a suitable solvent.

Although a considerable amount of work exists in the area, temperature measurements of polymers during deformation (which use thermocouples, infrared cameras, or other thermometric devices) will not be addressed here because they are rarely applied in a calorimetric mode [84,85].

3.5.1. Instrumentation and methods

3.5.1.1. Deformation calorimetry. The majority of deformation calorimetry studies are carried out at, or near, room temperature and atmospheric pressure with either temperature-rise calorimeters or heat flow calorimeters. In principle, these calorimeters are capable of isothermal measurements over wide temperature ranges. In a few cases, the temperature dependencies of the thermo-mechanical response of polymers have been explored to near glass transition temperature.

'Gas calorimeters' are temperature-change calorimeters that operate essentially as a gas thermometer and were the first method used to perform deformation calorimetry [86]. Temperature changes in the polymer during deformation cause the temperature of the surrounding gas to increase. This temperature increase results in a gas pressure increase that can be related quantitatively to the heat produced during the deformation [87]. Specimens, typically 0.1 mm×3 mm×3 cm in dimension, are deformed at rates of approximately 0.1–30 cm min^{-1} which produce a total heat effect of 0.01–1 with a precision of about ±3%. There are some questions about quantitative measurements on endothermic processes with this calorimeter style. The relatively small time constant of the calorimeter, less than 10 s is an advantage for higher deformation rates. Although gas calorimeters are simple in principle, they are complex to build and operate. No commercial instruments are available at this time.

The heat flow principle is also commonly used in deformation calorimetry measurements. The calorimeters of this type are modifications of early Tian–Calvet devices to accommodate the specimen and the mechanical assembly for deformation [83] in the calorimeter. Linear deformation rates range from 0.01 to 2 mm s^{-1} for specimens of approximate dimensions 0.2 mm×3 mm×7 cm. Typical detection limits for heat flow are mW with a time constant of approximately 30 s. The precision of the total heat measurements is 3%. Although commercial calorimeters of the Calvet style are available, their sensitivity, time constant and cell construction are not viewed as adequate for most deformation studies.

Both the heat flow calorimeter and the 'gas calorimeter' approaches to deformation calorimetry rely upon electrical calibration. A calibration heater is attached directly to the specimen while mounted in the mechanical deformation assembly to assure that the heat flow calibration is reliable for the device as used. Other experimental methods have been developed which focuses on deformation and stored energy of cold worked metals [88].

3.5.1.2. Post-deformation calorimetry. The energy state, or 'stored energy', of a previously deformed polymer may be assessed using DSC [83] and solution calorimetry [89] methods. These methods are based upon causing the stored energy to be released during the calorimetric experiment.

The DSC method applies only to glassy or semicrystalline materials that may be heated through the glass transition region in which the mobility of the material becomes high enough to release the 'stored energy' as heat. This heat is identified as a deviation from the normal DSC curve of the unstrained speci-

men that is conveniently measured during a second scan of the specimen. The difference between the curves is integrated to yield the heat value. The 'stored energy' may be observed over a fairly broad temperature range starting from well below the glass transition temperature and is related to the temperature of the specimen during the initial deformation process. The DSC method required small amounts of specimen, typically 10–20 mg, (which must be prepared without affecting the deformed state of the sample) and must be encapsulated so that contraction of the sample during heating does not adversely affect the measurement. Heating rates for the experiment are those typical for heat capacity measurements, 5–20 K min^{-1}. The expected precision of the measurement is approximately 10% for highly deformed samples.

The heat of solution method also applies only to glassy or semi-crystalline materials that contain 'stored energy' of deformation. The 'stored energy' is determined by dissolution of the material in a suitable solvent in a calorimeter. The 'stored energy' may be obtained, in the simplest approach, by difference between the heat of solution of the deformed and the undeformed specimen under identical experimental conditions. When this is not possible, the individual contributions to the heat of solution must be determined, i.e. heat of fusion of the crystalline component, excess enthalpy of the glassy state and heat of dilution of the sample in the selected solvent. The measured heats of solution are usually large, up to 200 J g^{-1}, compared to the typical values for 'stored energy' of deformation, often in the range of 0.5–10 J g^{-1} or larger. Hence, the precision of the measurement must be less than 0.2 J g^{-1}. High precision commercial calorimeters capable of handling solid samples are suitable for this application. Sample sizes are selected to give final concentrations of only a few percent to facilitate mixing and dissolution of polymeric specimens. The experimental method may be tedious due to the long time necessary for equilibration and dissolution of some samples. In addition, the measurement may be complicated by a change in crystallinity of the material during the deformation process that requires additional measurements.

3.5.1.3. Examples. The thermo-elasticity of rubber-like materials has been studied from a thermodynamic point of view for many years. Deformation calorimetry has played a major role in gaining a better understanding of the energetic and entropic components of the deformation of polymer networks. Godovsky [90] studied many different rubbery polymers and developed equations to describe intra-molecular energy contribution to elongation based on the inversion of heat and energy.

For polymers that may crystallize during orientation, a common event during industrial processing of plastics, crystallization may be induced by deformation. Andrianova et al. [91] have utilized deformation calorimetry to study the crystallization of poly(ethylene terephthalate, PET) under varying conditions of strain and temperature. Their work defined the temperature envelope for strain-induced crystallization of PET.

4. Engineering applications of reaction calorimetry

Chemical processes, particularly for speciality chemicals, frequently involve complex reactions, multiple phases, continuous additions and/or reactive chemical hazards. The engineering challenge is to obtain the critical process design information to enable safe and efficient process development and optimization. Process safety must be considered early in the development of a new product, during the initial process development. This is particularly important in the pharmaceutical industry, where the choice of the production process is made early in the development as a result of regulatory requirements; subsequent changes to the process are both difficult and costly. To further complicate matters, achieving the desired positioning of the product in the marketplace demands the rapid development of processes.

4.1. Areas of application

To meet this challenge, it is critical that reliable and scaleable data be obtained in an efficient manner. Reaction calorimeters are often the instruments of choice. They are relatively small, lab-scale tools that are large enough to be able to provide design data and, if required, simulate the proposed full-scale process. Areas of application include reactive chemicals

screening, process development and optimization and scale-up and plant design. The specific information that can be obtained from reaction calorimetry includes heat of transformation, heat evolution rate, adiabatic temperature rise (under controlled conditions), heat transfer coefficients, specific heat of the reaction mass, required cooling capacity, influence of mixing on mass and heat transfer and crystallization behavior. Reaction calorimetry, thus, provides both process design information and process safety information.

In order to evaluate the thermal hazard, it is of key importance to obtain thermodynamic and kinetic information concerning the desired reaction under the conditions of the manufacturing plant. Reaction calorimetry can provide this information. Note, however, that in many cases, some or all of this information can be determined without reaction calorimetry. Methods used include any combination of (1) theoretical calculation, (2) classic synthetic chemistry in the lab and (3) more routine reactive chemical tools, such as DSC. Situations in which reaction calorimetry has proven to be particularly useful, even critical, include those involving multi-phase reactions, cases in which mass transfer rates affect the observed rate of reaction, and reactions where other analytical methods are inapplicable.

4.2. Instrumentation and methods

Reaction calorimeters are heat flow calorimeters of sufficient scale such that production plant conditions (such as reagent addition and agitation) can be mimicked. Several types of reaction calorimeters are available commercially (Table 1).

Operating principles vary. Heat flow from the process is determined with Mettler–Toledo's RC1 reaction calorimeter by performing a heat balance. This heat balance must account for heat flow arising from reagent additions, heat accumulation in the reaction mass, heat exchange with the environment, heat exchange with the jacket, etc. The jacket heat flow is calculated as an overall jacket heat transfer coefficient, UA, multiplied by the temperature difference across the jacket. The UA is determined via the change in the temperature difference across the jacket upon

Table 1
Commercially available reaction calorimeters

Calorimeter[a]	Sensitivity W[b]	Principle[c]	Size (l)	Temperature range (°C)	Temperature ramps?	Pressure range (bar g)
RC1/AP01	0.2	HB/UA	0.5–2	−60 to 200	Yes	−0.95 to 1 (glass)
RC1/MP10	0.2	HB/UA	0.4–1	−60 to 200	Yes	−1 to 10 (glass)
RC1/HP60	0.2	HB/UA	0.5–1.5	−60 to 300	Yes	−1 to 60 (metal)
RC1/SV01	0.2	HB/UA	0.1–0.8	−20 to 200	Yes	−0.95 to 0 (glass)
CPA	0.01	HF/TP	0.04–0.18	−50 to 200	Yes	−1 to 20 (glass)
RM/2S	0.05	HB/F&UA	to 0.25	−20 to 200	No	−1 to 20 (glass) −1 to 100 (metal)
RM/2L	0.2	HB/H&UA	0.2–2	−20 to 200	No	−1 to 0.5 (glass) −1 to 25 (metal)
Simular	0.25	HF/PC	0.25–20	−80 to 500	No[d]	−1 to 400 (metal) −1 to 1 (glass)
Auto-MATE	0.05	HF/PC	0.025–0.1	−80 to 500	No[d]	−1 to 200

[a] The RC1 systems are manufactured by Mettler Instrument Co. For information, contact Mettler–Toledo, Attn. Tom Basalik, 1-800-METTLER Ext. 1-8877#, 69 Princeton-Hightstown Rd, Box 71, Hightstown, NJ 08520 or Mettler–Toledo, GmbH; Attn: Urs Groth, Sonnenbergstrasse 74, P.O. Box CH 8603 Schwerzenbach, Switzerland. The CPA and RM systems are available from Allied Chemical Technologies, Attn. Nick Chacos, 1-301-931-3210, 6860 Distribution Drive, Beltsville, MD 20705 or from ChemiSens AB, int. +46-46-18-40-43, Porfyrvagen 11, 224 78 Lund, Sweden. The Simular and the auto-MATE systems are manufactured by Hazard Evaluation Lab (HEL). For information, contact HEL, Attn. Avtar Bhatoey, 1-732-329-3090, 1 Deer Park Drive Suite L, Monmouth Junction, NJ 08852.

[b] Sensitivities as reported by the manufacturer.

[c] See text for description of various operating principles; higher temperature and pressure special-order reactors are available, currently up to 300°C and 200 bar g.

[d] Temperature ramps can be performed, but not while doing calorimetry.

introduction of a calibration heat pulse. With this heat balance via UA (or HB/UA) method, the major error in determination of jacket heat flow resides in determining an accurate UA.

In an effort to minimize this problem, ChemiSens has developed the RM2S and RM2L calorimeters using a combination of the HB/UA method with measurement of the enthalpy difference $(C_p(T_1)\times T_1 - C_p(T_2)\times T_2$, in units of J g^{-1}) between the inlet to the outlet of the jacket (heat balance via jacket flow and UA or HB/*F* and UA method). Unlike Mettler–Toledo's RC1, ChemiSens reaction calorimeter vessels only transfer heat via a flat bottom plate. This method insures that the heat transfer area is constant, but sacrifices some in simulation of plant vessel agitation. The entire calorimeter is enclosed in an air chamber to minimize exchange of heat between the vessel and the environment. This improves baseline determination but makes access to the vessel more difficult. The calorimeters based on the HB/*F* and US method are only for isothermal operations.

The second type of reaction calorimeter provided by ChemiSens, the CPA, both measures heat flow and exchanges heat via a thermopile (heat flow via a thermopile or HF/TP) in the bottom plate. This is a much smaller reaction calorimeter, but provides enhanced sensitivity (see Table 1). The heat flow through the bottom plate can also be measured via power compensation (HF/PC), as is done with the auto-MATE mini-reactor and calorimeter offered by Hazard Evaluation Laboratory (HEL). The auto-MATE, unlike the CPA, is not immersed in a temperature bath. This makes determination of the baseline heat flow (and hence instrument accuracy) lower, however, the unit is more accessible. The second reaction calorimeter offered by HEL also uses power compensation, but in this case, the jacket is kept at a constant temperature and the reaction heat determined from the amount of heat required to be input via an electrical heater.

Table 2 presents some relative advantages and disadvantages for some commercially available reaction calorimeters.

4.3. Example applications

4.3.1. Secondary amine synthesis from an amine plus acrylonitrile

Stoessel [92] used data from a reaction calorimeter in a model to determine optimum temperature, continuous addition rate for the acrylonitrile and the best choice of reactor size for optimal productivity while maintaining process safety. Data obtained included heat flow versus time, heat of reaction, heat capacity and the internal film heat transfer coefficient (from data on overall heat transfer coefficient versus agitation speed).

4.3.2. Sulphonation of a nitro-aromatic

Stoessel's goal, as in the above example, was to maximize productivity while maintaining a safe process [92]. Adjustable process variables were the rate of addition of SO_3 and the initial temperature. Kinetic parameters were determined from batch experiments in a reaction calorimeter by following conversion thermally and chemically at different initial concentrations and reaction temperatures. Reaction calorimetry of the semi-batch process was used to obtain the heat of reaction, the heat capacity of the reaction mixture, and the heat flow profile versus time (from which the reactor potential energy profile could be calculated). From the potential energy, the final temperature of the system in the event of a runaway (e.g. loss of cooling) was determined. It was known that

Table 2
Relative advantages and disadvantages for some commercially available reaction calorimeters

Calorimeter	RC1	RM-2S	RM-2L	CPA	Simular	Auto-MATE
Simulation of plant jacket performance	+	−	−	0	+	+
Simulation of larger-scale vessel mixing	+	−	0	−	+	−
Easy access for reagent additions–distillation apparatus	+	−	+	−	+	+
Visibility of reactor contents	+	0	+	0	+	0
Sensitivity	−	0	−	+	−	−
Measurement of baseline heat flow	−	0	0	+	−	−
Smaller volumes — can be safer and easier to construct	−	+	−	+	−	+

above some maximum temperature, the rate of decomposition was sufficiently fast to cause an explosion; therefore, process optimization demand that this final temperature be below this threshold maximum temperature. Based upon this information, a model was constructed to optimize the reaction simultaneously for safety and for productivity.

4.3.3. On-line monitoring and control of biological processes

Marison [93], used reaction calorimetry to monitor and control both microbial and animal cell cultures. Reaction calorimetry offers advantages in that the cultures can be operated as a standard bio-reactor, including agitation, pH control and reagent addition. Heat flow versus time data gives a direct measure of the amount of cells and of product formed (provided the stoichiometric coefficient relating heat generation to cell mass or product formation is known). On-line heat flow data can be used directly in the control strategy for the process, for instance to control the rate at which a carbon source is fed.

4.3.4. Polymerizations

Jansson and co-workers [94] used reaction calorimetry to study the decomposition kinetics of a rapid redox initiator system for the initiation of the emulsion polymerization of vinyl chloride. A heat flow reaction calorimeter based upon a Peltier device (HF/TP) provided calorimetric data from which the rate of polymerization could be obtained directly.

Varela-de la Rosa co-workers [95] obtained details of the kinetics for emulsion polymerization of styrene as a function of the amount of emulsifier, the reactor pressure and the agitation speed. Heat flow data from reaction calorimetry experiments were used to obtain a continuous profile of fractional conversion versus time and the total heat for the polymerization.

4.3.5. Manufacturing plant-scale calorimetry

The heat evolving from a production process can be monitored on-line. This required a heat balance be performed around the production vessel; thus treating it as a large-scale reaction calorimeter. There must be sufficient instrumentation and process data to allow mass and heat balances to be made. This information can be used in several applications, for example, (1) the determination of the extent of reaction (and determine if the reaction is proceeding as expected), (2) the development of a model for use in a model-predictive control scheme for improved process control, and (3) the actuation of alarms if certain undesired situations arise.

References

[1] J.M. Sturtevant, in: C.H.W. Hirs (Ed.), Methods in Enzymology, Vol. 26, Part C, Academic Press, New York, 1972, pp. 227–53.

[2] D.J. Eatough, R.M. Izatt, J.J. Christensen, in: G. Svehla (Ed.), Titration and Flow Calorimetry: Instrumentation and Data Calculation, Compr. Anal. Chem., Vol. 12(B), Elsevier, Amsterdam, The Netherlands, 1982, Chapter 2, pp. 3–38.

[3] W. Hemminger, G. Hoehne, Calorimetry: Fundamentals and Practice, Verlag Chemie, 1984.

[4] J. Jordan, J.W. Stahl, in: J.K. Grime (Ed.), Fundamentals of Analytical Solution Calorimetry, Chem. Anal. (New York), 79 (Anal. Solution Calorim.), 1985, Chapter 2, pp. 17–56.

[5] J.K. Grime, in: J.K. Grime (Ed.), General Analytical Applications of Solution Calorimetry, Chem. Anal. (New York), 79 (Anal. Solution Calorim.), 1985, Chapter 6, pp. 163–298.

[6] D.J. Eatough, J.J. Christensen, R.M. Izatt, Experiments in Thermometric Titrimetry and Titration Calorimetry, Brigham Young University Press, 1974.

[7] P.W. Carr, J. Jordan, Anal. Chem. 45 (1973) 634.

[8] P. Boudeville, J.L. Burgot, Direct injection enthalpimetry and differential kinetic analysis- analytical and calorimetric possibilities, Thermochim. Acta 204 (1) (1992) 89–97.

[9] P. Marik-Korda, in: H.G. Wiedmann (Ed.), Proceedings of the International Conference on Thermal Analytical Water Determination by DIE Method, Thermal Anal., 6th Edition, Vol. 1, Theory, Instrumentation, Applied Sciences, Industrial Applications, Birkhaeuser, Basel, Switzerland, 1980, pp. 529–534.

[10] J.K. Grime, Biochemical and clinical analysis by enthalpimetric measurements — a reaslistic alternative approach? Anal. Chim. Acta 118 (2) (1980) 191–225.

[11] C.D. McGlothlin, J. Jordan, Anal. Chem. 47 (1975) 786.

[12] C.D. McGlothlin, J. Jordan, Clin. Chem. 21 (1975) 741.

[13] D.J. Eatough, E.A. Lewis, L.D. Hansen, in: J.K. Grime (Ed.), Determination of ΔH_r and K_{eq} Values, Chem. Anal. (New York), 79 (Anal. Solution Calorim.) 1985, Chapter 5, pp. 137–162.

[14] N.D. Jesperson, J. Jordan, Anal. Lett. 3 (1970) 323.

[15] L.D. Hansen, R.M. Izatt, J.J. Christensen, Applications of thermometric titrimetry to analytical chemistry, Treatise Titrimetry 2 (1974) 1–89.

[16] K.M. Kate, L. Vielle, G.C. Kresheck, G. Vanderkooi, Biopolymers 18 (1979) 1889.

[17] W. Regenass, Calorimetric monitoring of industrail chemical processes, Thermochim. Acta 95 (2) (1985) 351–368.

[18] J.P.E. Grolier, Solution calorimetry at high temperatures and elevated pressures, Pure Appl. Chem. 62 (11) (1990) 2115–2120.
[19] M.J. Trewhella, R.K. Owusu, A. Finch, Enthalpimetric measurements of the strengths of immobilized cholinesterase inhibitors, Thermochim. Acta 90 (1985) 305–312.
[20] R.L. Biltonen, N. Langerman, Methods Enzymol. 61 (1979) 287–318.
[21] N. Langerman, R.L. Biltonen, Methods Enzymol. 61 (1979) 261–286.
[22] L.D. Hansen, T.E. Jensen, D.J. Eatough, in: A.E. Beezer (Ed.), Biological Microcalorimetry, Academic Press, New York, 1980, pp. 453–476.
[23] D.J. Eatough, S.J. Rehfeld, R.M. Izatt, J.J. Christensen, in: G. Svehla (Ed.), Titration and Flow Calorimetry: Application to Proteins and Lipids, Compr. Anal. Chem., Vol. 12(b), Elsevier, Amsterdam, The Netherlands, 1982, Chapter 7, pp. 112–135.
[24] B. Mattiasson, B. Danielsson, Calorimetric analysis of sugars and sugar derivatives with aid of an enzyme thermistor, Carbohydr. Res. 102 (1) (1982) 273–282.
[25] P. Schuler, J. Herrnsdorf, in: H.U. Bergmeyer (Ed.), Enthalpimetry, Methods of Enzyme Analysis, 3rd Edition, Vol. 1, Verlag Chemie, 1983, Weinheim, Federal Republic Germany, pp. 417–424.
[26] J.K. Grime (Ed.), Application of Solution Calorimetry to Biochemical and Clinical Analyses, Chem. Anal. (New York), 79 (Anal. Solution Calorim.) 1985, Chapter 7, pp. 299–390.
[27] B.Z. Chowdhry, A.E. Beezer, E.J. Greenhow, Analysis of drugs by microcalorimetry — isothermal power-conduction calorimetry and thermometric titrimetry, Talanta 30 (4) (1983) 209–243.
[28] J.K. Grime, in: G. Svehla, Enzymatic Enthalpimetry, Compr. Anal. Chem., Vol. 12(B), 1982, Elsevier, Amsterdam, The Netherlands, Chapter 8, pp. 136–175.
[29] M. Brun, A. Lallemand, J. Quinson, C. Eyraud, Thermochim. Acta 21 (1977) 59–88.
[30] D. Bargemna, E. Vugteven, J. Te Hennepe, J. Van't Hof, C. Smolders, in: J. Kahovec (Ed.), Proceedings of the 29th Conference on Synthetic Polymeric Membranes, Prague, 1987, pp. 637–644.
[31] M. Brun, J. Quinson, L. Benois, Thermochim. Acta 49 (1981) 49–52.
[32] L. Zeman, G. Tkacik, P. Le Parlouer, J. Membr. Sci. 32 (1987) 329–337.
[33] C. Jallu, J. Lenoir, C. Bardot, C. Eyruad, J. Membr. Sci. 68 (1992) 271–282.
[34] P.C. Bowes, Self-Heating Evaluating and Controlling the Hazards, Elsevier, Amsterdam, 1984, p. 292.
[35] J.A. Walker, W. Tsang, Society of Automotive Engineers (SAE), Technical Paper Series, Paper 801383 (1980).
[36] J. Griffiths, P. Laye, D. Rose, N. Taylor, IMechE Seminar 8 (1991) 97–108.
[37] G. Balazs, S. Doszlop, O. Biro, L. Palotas, J. Thermal Anal. 36 (1990) 1861–1865.
[38] B. Kowalski, Thermochim. Acta 156 (1989) 347–358.
[39] J.A. Ayala, M.E. Rincon, Prepr. Papers- Am. Chem. Soc., Div. Fuel Chem. 3 (1981) 120–130.
[40] M.J. Richardson, Polym. Testing 4 (1984) 101–115.
[41] J.N. Hay, Anal. Proc. (London) 17 (1980) 240–245.
[42] F.E. Karasz, H.E. Bair, J.M. O'Reilly, J. Phys. Chem. 69 (1963) 2657–2667.
[43] A.J. Pasztor Jr., B.G. Landes, P.J. Karjala, Thermochim. Acta 177 (1991) 187–195.
[44] R.W. Chrisman, R.D. McLachlan, R.S. Harner, U.S. Patent No. 4,672,218 (1987).
[45] N.M. Albino, Proceedings of the 3rd RC User Forum USA, Part No. 21985, Mettler Instrument Co., Highstown, NJ.
[46] A. Borghese, Proceedings of the 4th RC User Forum, Europe, Montreux, Switzerland, Mettler Instrument Co., Hightstown, NJ.
[47] A. Tavana, B. Vayat, Proceedings of the 4th RC User Forum, USA, New Orleans, LA, Part 110536, Mettler Instrument Co., Highstown, NJ.
[48] V. Velich, O. Sohnel, A. Costa-Bauza, M. Kroupa, Crystal Res. Technol. 27 (1992) 1133–1139.
[49] O. Sohnel, A. Costa-Bauza, V. Velich, J. Crystal Growth 126 (1993) 493–498.
[50] D. Dollimore, C. Keattch, An Introduction to Thermogravimetry, 2nd Edition, Heyen, London, 1975.
[51] J. Sestak, Thermophysical properties of solids, in: Wilson and Wilson's Comprehensive Analytical Chemistry, Vol. 12, Part D, Elsevier, New York, 1984, pp. 121–134.
[52] T. Daniels, Thermal Analysis, Wiley, New York, 1973, p.119.
[53] M.E. Brown, An Introduction to Thermal Analysis, Chapman and Hall, London, 1988, pp. 41–43.
[54] B. Wunderlich, in: E.A. Turi (Ed.), Thermal Characterization of Polymeric Materials, Academic Press, New York, 1981, pp. 194–208.
[55] B. Wunderlich, Thermal Analysis, Academic Press, New York, 1990, pp. 171–177.
[56] R.C. Reid, J.M. Prausnitz, B.E. Poling, The Properties of Gases and Liquids, 4th Edition, McGraw-Hill, New York, 1987, pp. 25–26.
[57] W. Perron, G. Bayer, H.G. Wiedemann, Thermal analysis, in: H.G. Wiedemann (Ed.), Proceedings of the 6th International Conference on Thermal Analysis, Vol. 1, 1980, pp. 279–291.
[58] J. Sestak, J. Thermal Anal. 36 (1990) 1639–1650.
[59] R.E. Mills, C.R. Thomas, Thermochim. Acta 124 (1988) 65–77.
[60] R.E. Mills, C.R. Thomas, Thermochim. Acta 124 (1988) 799–888.
[61] R.E. Mills, C.R. Thomas, Thermochim. Acta 124 (1988) 89–98.
[62] R.D. Shull, Thermal Anal. Metall. (1992) 95–119.
[63] J.K. Gibson, R.G. Haire, Thermochim. Acta 207 (1992) 65–78.
[64] M. Freisel, B. Baranowski, L. Bogdan, A. Lunden, J. Phys. Chem. 94 (1990) 1113–1117.
[65] H.J. Seifert, Thermochim. Acta 114 (1987) 67–74.
[66] H.J. Seifert, G. Theil, Thermochim. Acta 100 (1986) 81–107.
[67] M. Radomska, R. Radomski, J. Thermal Anal. 37 (1991) 693–704.

[68] H. Shibuya, Y. Suzuki, Y. Yasuo, K. Yamaguchi, A. Katsunobo, K. Arai, S. Saito, Fluid Phase Equilib. 82 (1993) 397–405.
[69] R. Ozawa, M. Matsuoka, J. Crystal Growth 98 (1989) 411–419.
[70] E.S. Domalski, W.H. Evans, E.D. Hearing, Heat Capacities and Entropies of Organic Compounds, J. Phys. Chem. Ref. Data, 13 (Suppl. 1) 1984.
[71] R. Duclos, J.M. Saiter, J. Grenet, A.M. Orecchioni, J. Thermal Anal. 37 (1991) 1869–1875.
[72] D. Lourdin, A.H. Roux, J.P.E. Grolier, J.M. Buisine, Thermochim. Acta 204 (1992) 99–110.
[73] A. Gonthier-Vassal, H. Scwarc, F. Romain, Thermochim. Acta 202 (1992) 87–96.
[74] K. Takamizawa, Y. Nagao, D. Irii, Y. Urabe, Thermochim. Acta 88 (1985) 205–210.
[75] A.A. Van Dooren, B.W. Muller, Thermochim. Acta 66 (1983) 161–186.
[76] J.R. Donnelly, L.A. Drewes, R.L. Johnson, W.D. Munslow, K.K. Knapp, G.W. Sovocool, Thermochim. Acta 167 (1990) 155–187.
[77] J.E. Hunter, R.L. Blaine, in: R.L. Blaine, C.K. Schoff (Eds.), Purity Determinations By Thermal Methods, ASTM Special Technical Publications 838, American Society for Testing Materials, 1984, pp. 29–38.
[78] E.E. Marti, Thermochim. Acta 5 (1972) 173–220.
[79] G.T. Furukawa, J.H. Piccirelli, M.L. Reilly, in: R.L. Blaine, C.K. Schoff (Eds.), Purity Determinations By Thermal Methods, ASTM Special Technical Publication 838, American Society for Testing Materials, 1984, pp. 90–106.
[80] J.L. Ford, P. Timmins, Pharmaceutical Thermal Analysis, Wiley, New York, 1989, pp. 108–135.
[81] L.T. Grady, S.E. Hays, R.H. King, H.R. Klein, W.J. Mader, D.K. Wyatt, R.O. Zimmerer, J. Pharm. Sci. 62 (1973) 456–464.
[82] T.F. Habash, J.J. Houser, P.D. Garn, J. Thermal Anal. 25 (1982) 271–277.
[83] Y.K. Godovsky, Thermophysical Properties of Polymers, Springer, New York, 1992, pp. 125–296.
[84] A. Cross, R.N. Haward, J. Polym. Sci., Polym. Phys. Ed. 11 (1973) 2423–2439.
[85] S. Matsuoka, H.E. Bair, J. Appl. Phys. 48 (1977) 4058–4062.
[86] Von F.H. Muller, Ad. Engelter Rheologica Acta 1 (1958) 39–53.
[87] R.E. Lyon, R.J. Farris, Rev. Sci. Instrum. 57 (1986) 1640.
[88] J.G. Byrne, Recovery, Recrystallization and Grain Growth, MacMillan, New York, 1965, pp. 17–22.
[89] J.L. DeRudder, F.E. Filisko, J. Appl. Phys. 48 (1977) 4026–4031.
[90] Y.K. Godovsky, Polymer 22 (1981) 75–86.
[91] G.P. Andrianova, B.A. Arutyunov, Y.V. Popov, J. Polym. Sci., Polym. Phys. Ed. 6 (1978) 1139–1154.
[92] F. Stoessel, Chemical Plants and Processing, 1991, p. 8.
[93] I.W. Marison, Performance Chem. 7 (1992) 3.
[94] L. Jansson, H. Nilsson, C. Silvergren, B. Tornell, Thermochim. Acta 118 (1987) 97–105.
[95] Varela-de la Rosa, E.D. Sudol, A. Klein, M.S. El-Aasser, Proceedings of the 5th RC User Forum USA, Part 110566, October 1992, San Antonio, TX, Mettler Instrument Co., Hightstwon, NJ.