Quantitative Analysis of Solid-State Processes Studied With Isothermal Microcalorimetry

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Quantitative analysis of solid-state processes from isothermal microcalorimetric data is straightforward if data for the total process have been recorded and problematic (in the more likely case) when they have not. Data are usually plotted as a function of fraction reacted (α); for calorimetric data, this requires knowledge of the total heat change (Q) upon completion of the process. Determination of Q is difficult in cases where the process is fast (initial data missing) or slow (final data missing). Here we introduce several mathematical methods that allow the direct calculation of Q by selection of data points when only partial data are present, based on analysis with the Pérez-Maqueda model. All methods in addition allow direct determination of the reaction mechanism descriptors m and n and from this the rate constant, k. The validity of the methods is tested with the use of simulated calorimetric data, and we introduce a graphical method for generating solid-state power−time data. The methods are then applied to the crystallization of indomethacin from a glass. All methods correctly recovered the total reaction enthalpy (16.6 J) and suggested that the crystallization followed an Avrami model. The rate constants for crystallization were determined to be 3.98×10^{-6}, 4.13×10^{-6}, and 3.98×10^{-6} s^{-1} with methods 1, 2, and 3, respectively.

Introduction

Isothermal microcalorimetry is a particularly useful technique for studying solid-state processes, because invariably such events will progress with a change in enthalpy. In addition, the physical form of the sample has no bearing on the operation of the instrument, and it is easy to control environmental variables, such as temperature and relative humidity. Data analysis can present a challenge, however, especially if the reaction has not progressed to completion or multiple processes are occurring.

The kinetics of solid-state processes are usually described by expressions cast in terms of fraction of progression (α). Hence, if the temporal axis of data for a given solid-state process can be presented in terms of α, analysis is straightforward using any of the multitude of models available in the literature. From the perspective of calorimetric data, conversion of data to α is easy if the total enthalpy of the process (Q) is known;

$$\alpha = \frac{q_t}{Q} \tag{1}$$

where q_t is the heat output to time t. We have discussed previously the analysis of solid-state calorimetric data where Q is available[1,2] and various methods for the determination of reaction mechanism for processes occurring in solution.[3−5] However, while calorimetry is extremely suited to the study of solid-state processes, it is highly likely that only partial data will be available. If the process is reasonably fast, the initial data will be missing (a consequence of the time required to prepare and load the sample in an ampule, external to the calorimeter), and if the process is very slow, data may not have returned to baseline within an acceptable time period. (Processes that occur in the calorimeter on a time-scale on the order of the instrument's time constant (ca. 2 min) can be considered very fast, and the data would need correction to account for the delay in capture: this is typically the case for titration experiments. Here it is assumed that reasonably fast crystallization would still be on the order of hours, otherwise no data would be recorded, and hence dynamic correction is not needed.) In either case it is not possible to determine the value of Q by simple integration of the data, and hence conversion to α is impossible.

An alternative approach is to fit the data to a suitable model, using least-squares minimization, to determine the values of any reaction parameters, including Q. This is an approach that we have used in most of our previous work,[1−5] but it is only possible in the case where the fitting model can be integrated with respect to time. Most solid-state models that describe crystallization, including that used in this work, cannot be integrated with respect to time and hence cannot be cast in a form that describes power−time data.

Consideration of these issues has led to a mathematical treatment that allows direct determination of Q when only partial data have been recorded. Knowledge of this value allows conversion of the time axis of the data to α and thus straightforward analysis. In addition, the methods allow direct determination of the reaction mechanism descriptors m and n (see eq 2 for definitions), which reduces the burden on the fitting process, leaving the rate constant as the only unknown parameter and for which can be directly solved. The methods are in principle easier to use than a model fitting approach, requiring the analyst only to select a few data points and plug them into the equations presented. The validity of the approaches is demonstrated with reference to simulated data, and a graphical method for the generation of simulated solid-state power-time data is presented. Application to real data is demonstrated, using

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the crystallization of indomethacin from a glass as a model solid-state process.

Experimental Methods

Crystalline indomethacin (>99%) was purchased from Molekula Ltd. Amorphous indomethacin was prepared by melt-cooling. Amorphous indomethacin was prepared by melting crystalline indomethacin in aluminum foil on a hot plate. The melted drug was then quench-cooled in liquid nitrogen before being stored in a desiccator over P_2O_5 for 1 h. The dried sample was then ground gently using a mortar and pestle and then passed through a 90 μm sieve. The sieved sample was further dried over P_2O_5 and then stored at −80 °C until further use.

Calorimetric measurements were conducted with a 2277 thermal activity monitor (TAM, TA Instruments Ltd.) at 35 °C. Ampules were left in the equilibration position for 30 min before being lowered to the measuring position. Data capture was subsequently initiated with the dedicated software package Digitam 4.1. The time axis was corrected before analysis to account for the 30 min delay in data capture. The instrument was calibrated prior to use with the electrical substitution method and operated on an amplifier range of 100 μW.

Data Analysis. There are many equations in the literature that describe solid-state processes. The methods described here are applicable to most of them, but we select as our base model the equation of Pérez-Maqueda et al.,[6] which is itself a derivative of the Ng equation;[7]

$$\frac{d\alpha}{dt} = k\alpha^m(1 - \alpha)^n \tag{2}$$

The indices m and n are the mechanism descriptors; by selecting various combinations of these values, eq 2 can be made essentially to conform to many of the models proposed in the literature (comprehensive examples are provided in Cai and Liu[8]). Several derivatives of eq 2 have been discussed in the literature,[7,8] some of which include additional parameters that essentially account for deviations from ideal Avrami crystallization behavior. These correction factors have not been included here, but it is possible to follow the methods described below starting from any of the alternative expressions. Substitution of eq 1 into eq 2 and rearrangement gives a calorimetric form of the kinetic expression;

$$\frac{dq}{dt} = \Phi = kQ(\alpha)^m(1 - \alpha)^n \tag{3}$$

Both heat-conduction and power-compensation calorimeters measure dq/dt (given the symbol Φ) directly. Data that conform to eq 3 will progress through a maximum (assuming the values of m and n are greater than 0), the position of that maximum with respect to the α-axis being dependent upon the values of m and n. It is assumed for the purpose of the mathematical treatments that not all of the data have been recorded by the calorimeter, and hence analysis methodologies are presented appropriate for instances where the following occurs.

(i) The initial data are missing, but the process has progressed to completion.

(ii) The initial data are captured, but the process has not progressed to completion.

(iii) Neither the initial nor final data are captured, but the data have progressed through the maximum.

Method 1. Starting with condition (i), it is evident that the time at which the power signal returns to zero denotes the end of reaction or the point at which $\alpha = 1$. Selection of any earlier time (t_1) and corresponding power (Φ_1) allows a partial area (q_1) to be determined. Substitution of these values into eqs 1 and 3 yields;

$$\Phi_1 = kQ\left(\frac{Q - q_1}{Q}\right)^m\left(1 - \frac{Q - q_1}{Q}\right)^n \tag{4}$$

Similar equations can be constructed for three other randomly selected time points;

$$\Phi_2 = kQ\left(\frac{Q - q_2}{Q}\right)^m\left(1 - \frac{Q - q_2}{Q}\right)^n \tag{5}$$

$$\Phi_3 = kQ\left(\frac{Q - q_3}{Q}\right)^m\left(1 - \frac{Q - q_3}{Q}\right)^n \tag{6}$$

$$\Phi_4 = kQ\left(\frac{Q - q_4}{Q}\right)^m\left(1 - \frac{Q - q_4}{Q}\right)^n \tag{7}$$

If the following are defined for clarity;

$$\log\frac{\Phi_1}{\Phi_2} = \log R_1 \tag{8}$$

$$\log\frac{\Phi_1}{\Phi_3} = \log R_2 \tag{9}$$

$$\log\frac{\Phi_1}{\Phi_4} = \log R_3 \tag{10}$$

Then there are three equations and three unknown variables. By substitution and rearrangement of eqs 8, 9, and 10;

$$\frac{\log R_2 \log\left(\frac{q_1}{q_2}\right) - \log R_1 \log\left(\frac{q_1}{q_3}\right)}{\log\left(\frac{q_1}{q_2}\right)\log\left(\frac{Q - q_1}{Q - q_3}\right) - \log\left(\frac{q_1}{q_3}\right)\log\left(\frac{Q - q_1}{Q - q_2}\right)} - \frac{\log R_3 \log\left(\frac{q_1}{q_2}\right) - \log R_1 \log\left(\frac{q_1}{q_4}\right)}{\log\left(\frac{q_1}{q_2}\right)\log\left(\frac{Q - q_1}{Q - q_4}\right) - \log\left(\frac{q_1}{q_4}\right)\log\left(\frac{Q - q_1}{Q - q_2}\right)} = 0 \tag{11}$$

The value of Q can thus be determined from eq 11. Once Q is known, the values of m and n are also easily calculable;

$$m = \frac{\log R_3 \log\left(\frac{q_1}{q_2}\right) - \log R_1 \log\left(\frac{q_1}{q_4}\right)}{\log\left(\frac{q_1}{q_2}\right)\log\left(\frac{Q - q_1}{Q - q_4}\right) - \log\left(\frac{q_1}{q_4}\right)\log\left(\frac{Q - q_1}{Q - q_2}\right)} \tag{12}$$

$$n = \frac{\log R_2 - m\log\left(\frac{Q - q_1}{Q - q_3}\right)}{\log\left(\frac{q_1}{q_3}\right)} \tag{13}$$

Method 2. It is possible to follow the same logical argument presented above to deal with condition (ii), but an alternative approach starts with the differential form of eq 3;

$$\frac{d^2q}{dt\,d\alpha} = kQ(\alpha)^m(1 - \alpha)^n\left[\frac{m}{\alpha} + \frac{-n}{(1 - \alpha)}\right] \tag{14}$$

$$\frac{d^2q}{dt\,d\alpha} = \frac{dq}{dt}\left[\frac{m}{\alpha} + \frac{-n}{(1 - \alpha)}\right] \tag{15}$$

Thus;

$$\frac{d^2q}{dt} = \frac{dq\frac{dq}{Q}}{dt}\left[\frac{m}{\alpha} + \frac{-n}{(1 - \alpha)}\right] \tag{16}$$

$$\frac{d^2q}{dt\,dt} = \frac{dq\,dq}{dt\,dt}\left[\frac{\frac{m}{\alpha} + \frac{-n}{(1 - \alpha)}}{Q}\right] \tag{17}$$

$$\frac{d^2q}{dt^2} = \left(\frac{dq}{dt}\right)^2\left[\frac{\frac{m}{\alpha} + \frac{-n}{(1 - \alpha)}}{Q}\right] \tag{18}$$

$$\frac{d^2q}{dt^2} = \left(\frac{dq}{dt}\right)^2\left[\frac{\frac{mQ}{q} + \frac{-nQ}{(Q - q)}}{Q}\right] \tag{19}$$

$$\frac{d^2q}{dt^2} = \left(\frac{dq}{dt}\right)^2\left[\frac{m}{q} + \frac{-n}{Q - q}\right] \tag{20}$$

If three power−time points are selected with three corresponding tangents, then;

$$\frac{d^2q_1}{dt_1^2} = \left(\frac{dq_1}{dt_1}\right)^2\left[\frac{m}{q_1} + \frac{-n}{Q - q_1}\right] \tag{21}$$

$$\frac{d^2q_2}{dt_2^2} = \left(\frac{dq_2}{dt_2}\right)^2\left[\frac{m}{q_2} + \frac{-n}{Q - q_2}\right] \tag{22}$$

$$\frac{d^2q_3}{dt_3^2} = \left(\frac{dq_3}{dt_3}\right)^2\left[\frac{m}{q_3} + \frac{-n}{Q - q_3}\right] \tag{23}$$

Letting;

$$A = \frac{d^2q_1}{(dt_1)^2} \tag{24}$$

$$B = \left(\frac{dq_1}{dt_1}\right)^2 \tag{25}$$

$$C = \frac{d^2q_2}{(dt_2)^2} \tag{26}$$

$$D = \left(\frac{dq_2}{dt_2}\right)^2 \tag{27}$$

$$E = \frac{d^2q_3}{(dt_3)^2} \tag{28}$$

$$F = \left(\frac{dq_3}{dt_3}\right)^2 \tag{29}$$

By substitution and rearrangement of eqs 21, 22, and 23, it is possible to solve for Q directly;

$$Q = \frac{\frac{AF}{B}(q_1^2q_2 - q_1^2q_3) + \frac{CF}{D}(q_2^2q_3 - q_2^2q_1) + E(q_3^2q_1 - q_3^2q_2)}{\frac{AF}{B}(q_1q_2 - q_1q_3) + \frac{CF}{D}(q_2q_3 - q_2q_1) + E(q_3q_1 - q_3q_2)} \tag{30}$$

Once the value of Q is known, the values of m and n may be calculated;

$$m = \frac{\frac{A}{B}q_1q_2 - \frac{A}{BQ}q_1^2q_2 + \frac{C}{DQ}q_2^2q_1 - \frac{C}{D}q_1q_2}{q_2 - q_1} \tag{31}$$

$$n = \frac{\frac{A}{B}(q_1Q - q_1^2 - q_1q_2) + \frac{C}{D}(q_2Q - q_2^2 - q_1q_2) + \frac{A}{BQ}q_1^2q_2 - \frac{C}{DQ}q_2^2q_1}{q_2 - q_1} \tag{32}$$

Method 3. For condition (iii), it is assumed that neither the initial nor final data have been captured, but that the reaction has progressed through a maximum. Proceeding in the manner introduced for method 2, selecting an additional power value and corresponding tangent;

$$\frac{d^2q_4}{dt_4^2} = \left(\frac{dq_4}{dt_4}\right)^2\left[\frac{m}{q_4} + \frac{-n}{Q - q_4}\right] \tag{33}$$

As before, letting;

$$G = \frac{d^2q_4}{(dt_4)^2} \tag{34}$$

$$I = \left(\frac{dq_4}{dt_4}\right)^2 \tag{35}$$

Then by substitution and rearrangement of eqs 21, 22, 23, and 33;

$$Q = \frac{\frac{AI}{B}(q_1^2q_2 - q_1^2q_4) + \frac{CI}{D}(q_2^2q_4 - q_2^2q_1) + G(q_4^2q_1 - q_4^2q_2)}{\frac{AI}{B}(q_1q_2 - q_1q_4) + \frac{CI}{D}(q_2q_4 - q_2q_1) + G(q_4q_1 - q_4q_2)} \tag{36}$$

Noting here that;

(i) The right-hand side of eq 30 minus the right-hand side of eq 36 must equal zero.

(ii) Although the absolute values of q_1, q_2, q_3, and q_4 cannot be known, since the initial data are missing, it is possible to define the additional area between q_1 and the larger q values thus;

$$q_2 = q_1 + a \tag{37}$$

$$q_3 = q_1 + b \tag{38}$$

$$q_4 = q_1 + c \tag{39}$$

It is then possible to write;

$$\frac{\frac{AF}{B}q_1^2(a-b) + \frac{CF}{D}(q_1+a)^2b + E(q_1+b)^2(-a)}{\frac{AF}{B}q_1(a-b) + \frac{CF}{D}(q_1+a)b + E(q_1+b)(-a)} - \frac{\frac{AI}{B}q_1^2(a-c) + \frac{CI}{D}(q_1+a)^2c + G(q_1+c)^2(-a)}{\frac{AI}{B}q_1(a-c) + \frac{CI}{D}(q_1+a)c + E(q_1+c)(-a)} = 0 \tag{40}$$

By iteration, the value of q_1 can be determined. The value of Q may then be calculated from eq 36.

Method 4. An alternative method of analysis is available, but this approach gives only information on the mechanism descriptors: it is possible to extend this method to allow the calculation of Q, but the equations are not directly solvable, and so for clarity their derivation is omitted. Since it is required here that the data have progressed through a maximum, at the maximum eq 15 must be equal to zero. Hence;

$$\alpha_{peak} = \frac{m}{m+n} = \frac{q_{peak}}{Q} \tag{41}$$

where α_{peak} is the extent of reaction at the maximum and q_{peak} is the cumulative heat released at the maximum. Equation 41 implies that, if the data are plotted as power versus α, then the value of α at the maximum is dependent only upon the ratio $m/(m + n)$. Since the values of m and n are defined in the literature for various reaction mechanisms, it is possible to calculate the appropriate ratios for these mechanisms, and hence, use of eq 41 provides a rapid and convenient check of the reaction mechanism followed by the study process. Table 1 lists the appropriate values for several mechanisms.

TABLE 1: Values of *m* and *n* for Various Nucleation and Growth Models

nucleation and growth mechanism[a]	*m*	*n*	*m*/*m* + *n*
A1.5	0.338	0.856	0.283
A2	0.511	0.794	0.392
A2.5	0.616	0.757	0.449
A3	0.686	0.733	0.483
A4	0.775	0.703	0.524

[a] Data from Cai and Liu (2009), assuming their fitting constant, q, is equal to 1.

Results and Discussion

Testing with Simulated Data. We have long advocated the use of simulated data for testing calorimetric models because they are free from random noise and other errors and the values of the variables describing the process are known absolutely. However, generation of power−time data from the Ng equation, or derivatives of it, has proved impossible to date because the function cannot be directly integrated, and so previously we have tested models by applying them to simulated power−heat data. Here a graphical method is introduced that allows generation of the time axis so that power−time data for solid-state processes can be generated directly. Noting that;

$$\frac{dt}{dq} = \frac{1}{kQ(\alpha)^m(1-\alpha)^n} \tag{42}$$

$$\int \frac{dt}{dq}dq = \int \frac{1}{kQ\left(\frac{q}{Q}\right)^m\left(1-\frac{q}{Q}\right)^n}dq \tag{43}$$

$$t = \int \frac{1}{kQ\left(\frac{q}{Q}\right)^m\left(1-\frac{q}{Q}\right)^n}dq \tag{44}$$

Integration of a plot of 1/power versus heat will thus generate the time points associated with each power data point.

A set of model data were thus simulated using the graphical method noted above with the following values for the reaction variables; $Q = 1 \times 10^9$ μJ, $k = 3 \times 10^{-7}$ s^{-1}, $m = 0.75$, $n = 0.625$. The data, shown graphically in Figure 1, were then analyzed with the four methods introduced.

Method 1. Data points were selected at random covering various percentages of the data set (20, 40, and 60%), and the values of Q, m, and n calculated (Table 2). It is apparent that the method consistently returned the correct values, irrespective of the percentage of data used.

Method 2. Various data points were selected from the derivative data and the values of Q, m, and n calculated (Table 3). In this case it is not true that any selection of points will return the correct values of the reaction variables; it appears that it is a requirement that one of the points selected must be that at which the derivative power is zero.

Method 3. The method requires calculation of q_1 before determination of Q. Four points were selected at random and used to determine the value of q_1. Points were selected either all before or before and after the maximum (Table 4). In either case, excellent agreement with the correct q_1 value was seen.

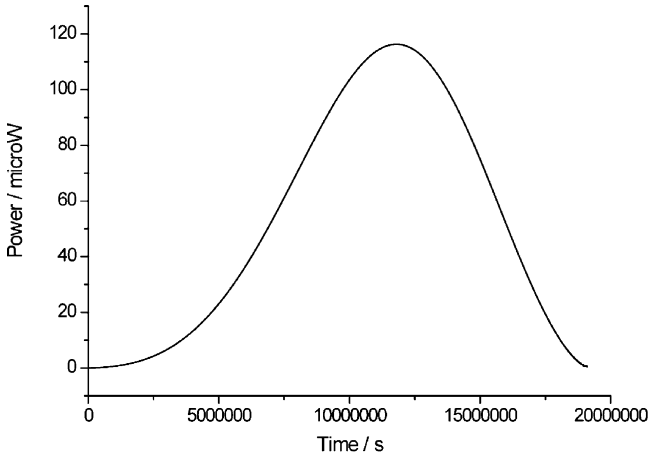

Figure 1. Simulated power−time data ($Q = 1 \times 10^9$ μJ, $k = 3 \times 10^{-7}$ s^{-1}, $m = 0.75$, $n = 0.625$) used for testing the analysis methodologies.

TABLE 2: Calculated Values for the Reaction Variables Using Method 1

% data used	Q/μJ	m	n
20%	1×10^9	0.75	0.625
40%	1×10^9	0.75	0.625
60%	1×10^9	0.75	0.625

TABLE 3: Calculated Values for the Reaction Variables Using Method 2

data points selected	Q/μJ	m	n
maximum derivative; minimum derivative; zero derivative	1×10^9	0.75	0.625
maximum derivative; minimum derivative; random point between them	1×10^9	0.75	1.306
one point before maximum power; one after the maximum power; one near maximum power	1×10^9	0.75	1.071
three points before maximum power	9.8×10^8	0.75	5.419
three points after maximum power	1×10^9	0.75	–12.849
one random point before and after the maximum; zero derivative	1×10^9	0.75	0.625

TABLE 4: Calculated q_1 Values Compared with Actual q_1 Values Using Method 3

data points selected	q_1(calculated) (J)	q_1(actual) (J)
four points before maximum	0.133	0.133
two points before and two points after the maximum	0.884	0.880

Method 4. Method 3 allows simple determination of the value of the ratio $m/m + n$ from knowledge of the α value at the turnover point, in this case 0.54538. The expected ratio is 0.54545.

Testing with Real Data. One obvious drawback of the methods outlined here is that, in selecting only a few data points from a large data set, much of the information in the recorded data is not used. Mathematically this does not matter if, as in the case of the simulated data, there is no noise. In the case of real data, the presence of noise in the selection of a few data points could be problematic, especially with method 2, since it utilizes a derivative signal. Hence, the methods were applied to real (i.e., noisy) data to determine their utility.

An indomethacin glass was allowed to crystallize with time in the TAM at 35 °C; progression to the crystalline state was seen as an exothermic peak, Figure 2. Because the process progressed to completion, it was possible to integrate the data

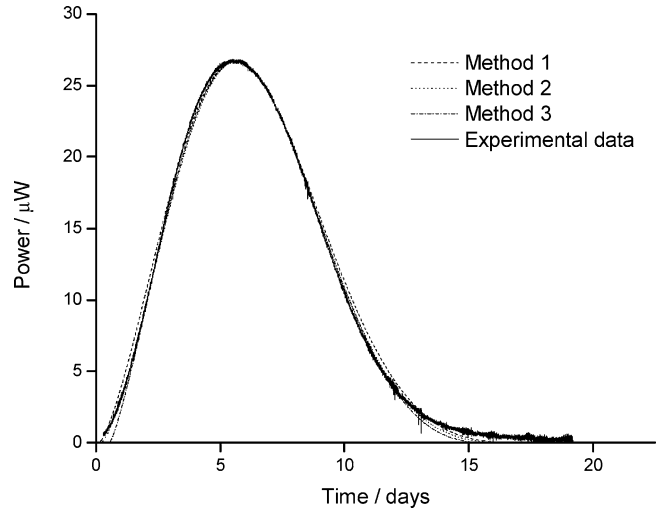

Figure 2. Calorimetric data for the crystallization of amorphous indomethacin from a glass at 35 °C (solid line) and the fit fine obtained using analysis methods 1, 2, and 3. Residual values (areas under experimental curve − area under each fit curve; method 1, −0.217 J (1.31%); method 2, 0.267 J (1.61%); method 3, 0.402 J (2.42%)).

to obtain Q directly (16.62 J); this provided a reference value to check the validity of the analysis methods, but we note that progression to completion is not a requirement for our analyses.

Data were analyzed with methods 1, 2, and 3 as described above. The calculated values are shown in Tables 5 (method 1), 6 (method 2), and 7 (method 3). Considering method 1 first, it is evident that the robustness of the technique is not so good with real data compared with simulated data: this could be a function of noise or of the fact that the data are taken primarily from the region in which the crystallization process is finishing; it is well-known that Avrami models begin to fail at high (>0.8) α values because they do not account for impingement of individually growing crystals.[9] If the total data set (which rather negates the point of the exercise), or power−time points selected in close pairs before and after the maximum, are used, the method returns excellent values (indicated by the values of Q close to 16.62 J). Equations of the form of those of Ng and Pérez-Maqueda contain two terms representing growth and decay; selecting data pairs on either side of the maximum ensures that in one region growth predominates and in the other decay predominates. This probably provides sufficient information in the data for correct analysis. Using the values determined by selecting data pairs, the rate constant was calculated (from eq 3) to be 3.98×10^{-6} s^{-1}. The fit line to the data is given in Figure 2.

The issue of noise is important, because the method requires selection of just a few data points from a large set of data: obviously, random fluctuations may then adversely affect the calculated reaction parameters (this is especially true when differential data are used). Here the data were smoothed (using the appropriate function in Origin) prior to analysis.

The reaction variables calculated with method 2 are also in excellent agreement with those calculated with method 1 (Table 6). The calculated rate constant in this case is 4.13×10^{-6} s^{-1}. The fit line to the data is given in Figure 2.

Using method 3 also gave excellent results, listed in Table 7. The total area was calculated to equal 16.215 J, and m and n were 0.556 and 0.736, respectively. These values gave a rate constant of 3.98×10^{-6} s^{-1}. The fit line to the data is given in Figure 2.

Once Q is known, it is easy to plot the data as power versus α (Figure 3) and hence to determine the value of α at the

TABLE 5: Calculated Values for the Reaction Variables for Indomethacin Crystallizing from a Glass at 35 °C Using Method 1

% data used	Q (J)	m	n
20%	could not calculate	could not calculate	could not calculate
40%	128.8	12.005	1.013
60%	33.2	2.299	0.940
80%	19.7	1.016	0.905
90%	14.8	0.186	0.390
100%	16.5	0.527	0.745
two close points before maximum Φ and two close points after maximum Φ	16.8	0.580	0.766

TABLE 6: Calculated Values for the Reaction Variables for Indomethacin Crystallizing from a Glass at 35 °C Using Method 2

data points selected	Q (J)	m	n
one random point before and after the maximum; zero derivative	16.351	0.589	0.767

TABLE 7: Calculated Values for the Reaction Variables for Indomethacin Crystallizing from a Glass at 35 °C Using Method 3

data points selected	Q (J)	m	n
two random points before and one after the maximum; maximum	16.215	0.556	0.736

maximum, in this case 0.4225. Method 1 gave an expected ratio of 0.431, method 2 a ratio of 0.429, and method 3 a ratio of 0.430. The excellent agreement in these values highlights the utility of the method 4 as a rapid check of the mechanism type and comparison with the data in Table 1 suggests that the data follow Avrami model A2.5.

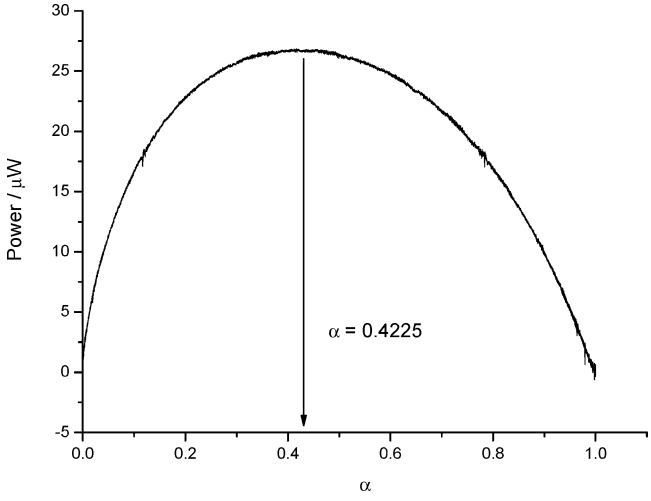

Figure 3. Crystallization of indomethacin from a glass at 35 °C showing power versus α and the value of α at the maximum.

Summary

Consideration of the analysis of partial calorimetric data led to the development of three methods that allow the direct determination of the total heat change of the process, Q. The value of Q cannot in this case be determined by fitting the data to a solid-state model with least-squares minimization because the model cannot be integrated with respect to time. Once Q is known, the data are easily converted to power versus α and analyzed in the usual way. However, our methods in addition allow direct determination of the mechanism descriptors, m and n and, hence, the rate constant, k. In testing the models we developed a graphical method for simulating power−time data, something that has always proved impossible in the past, and showed that the methods are valid, although method 2 requires that one data point is that where derivative power is zero. Testing the models with real data for the crystallization of indomethacin showed that all three gave consistent results. The methods are easy to apply, requiring the user to select a few data points and plug them into the appropriate equations.

References and Notes

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