Use of fast-scan DSC to quantify metastable forms

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Differential scanning calorimetry (DSC) has long been used for material characterization, particularly to quantify the melting behavior of polymer formulations and pharmaceutical compounds. Recently, there has been special interest in using DSC with faster heating and cooling rates to quantify the thermal characteristics of materials in metastable states. New technology allows this technique to be carried out easily and without resorting to extraordinary experimental conditions.

Use in polymer analysis

When materials are processed, they often end up in a thermodynamic state other than the most stable one. In the case of polymers, the last step in processing may be a rapid cooldown, which leaves the material with an imperfect semicrystalline structure. When such a sample is heated, it will undergo crystallization processes to achieve a more stable, low-energy form. As a result, the DSC trace reflects the net heat flow from both melting and crystallization. One well-established technique to separate these two effects is MDSC® (TA Instruments, New Castle, DE), which produces separate curves for reversible melting and nonreversible crystallization. However, this process of slow heating in either DSC or MDSC, destroys the metastable, imperfect states that in fact contribute to the properties of the material as processed, and contributes other structures that were not present in the initial material. Hence, it can be argued that slow heating destroys potentially useful structural information. If, however, the DSC scan is carried out at a sufficiently fast heating rate, then the kinetically controlled crystallization processes can be minimized. Crystallization simply does not have time to take place.

Amorphous polyethylene terephthalate (a-PET) is familiar to many thermal analysts, since its melting curve is often used in training courses. Figure 1 shows a sample of a-PET from a 2-L beverage container run at heating rates of 10, 50, 100, and 150 °C/min after shock cooling the sample from the melt. The 10 °C/min trace shows the well-known exothermic cold crystallization peak above the glass transition followed by the melting of the just-crystallized material. The 50 and 100 °C/min traces show partial crystallization followed by reduced melting. The data taken at 150 °C/min show little or no crystallization and only a small amount of melting. If there is no evidence of crystallization, any melting endotherm is due to residual crystallinity, a useful parameter to determine. While initial crystallinity can be measured by other means, this fast-rate method has the potential to be more accurate. Moreover, the fast DSC analysis is capable of giving specific heat data that are more representative of the material in its initial state.

Unlike PET, most semicrystalline polymers do not...
show extreme differences in specific heat capacity when heated at fast and slow rates. However, the small differences that are observed may provide insight into quality problems that relate to differences in processing. For example, polyolefin formulations may be characterized by the peak melting temperature, the melting onset and endpoint, and the fraction melted at a given temperature. But these parameters may be shifted by the thermal history, the cooldown history, or the formulation. The use of fast-rate DSC analysis provides data that better represent the initial crystalline morphology of the material. Figure 2 shows an example of a polypropylene sample cooled rapidly from the melt, then heated by DSC at 10 °C/min, cooled rapidly again, then heated at 100 °C/min. Notice that while the melting peak is expected to be higher at 100 °C/min because of thermal lag, it is seen to be several degrees lower because the faster rate inhibits crystallization during heating, which at 10 °C/min results in more stable, higher melting crystals. The 100 °C/min scan is thus more representative of the crystalline structures in this shock-cooled sample.

Use in pharmaceutical polymorph analysis

In pharmaceutical laboratories, the motivation for using fast heating rates is different. In documenting the physical properties of drug candidates and excipients, it is important to characterize all possible polymorphic forms. When an unstable polymorph is formed (e.g., by crystallization from a particular solvent system), it frequently reverts to a more stable form when heated. Use of a fast DSC heating rate sometimes allows the melting endotherm to be completed before the unstable material converts. This allows the thermodynamic parameters, C_p, T_m, and ΔH_m, to be determined for the metastable polymorph. These data are important to developing a phase diagram for the material and for predicting the relative stability of the polymorphs as a function of temperature. An example of this methodology can be seen in Figure 3 in the analysis of dexamethasone acetate, an anti-inflammatory agent. At 10 °C/min, the low-temperature melting polymorph exothermically converts to another form as it begins to melt, while at 150 °C/min, the low-temperature polymorph melts completely with little or no conversion to the more stable form.

Problems with fast DSC rates

There are several instrumental and procedural difficulties associated with fast-rate DSC techniques. The underlying problem is that fast scanning rates produce large temperature gradients due to thermal lag. For example, with the DSC cell and sample being held isothermally at the starting temperature, the controller commands a heating rate of 100 °C/min. Initially, the setpoint for furnace control begins heating at 100 °C/min. The furnace lags behind the setpoint temperature, the surface that supports the sample pan lags behind the furnace, the sample pan lags behind the DSC cell, and there are even temperature gradients across the sample specimen itself. Left uncorrected, these thermal lags result in grossly broadened peaks and uncertainty in temperature data. An additional concern is that the sample should achieve a constant heating rate before the data being acquired is considered to be accurate. The magnitude of these errors is roughly proportional to heating rate, sample size, pan mass, and thermal resistances in the system. To minimize errors to the point that the data are accurate enough to be useful requires correction for instrumentally caused error.
and careful sample preparation is required to minimize errors associated with specimen encapsulation. Some of the steps reported to minimize these errors are the use of foil instead of a sample pan for encapsulation, the use of grease to couple the foil to the DSC, the use of a neon purge gas mixture to enable the use of liquid nitrogen coolant over the temperature range required, and the reduction of sample mass to submilligram levels.3

Fast-rate DSC technology

For those using recent DSC technology, none of these steps is necessary to achieve heating rates up to 150 °C/min.1 Tzero™ technology (TA Instruments) provides the capability to perform fast-rate DSC analysis with a minimum of operator difficulty. The Q1000 DSC incorporates a sensor system that measures and compensates for thermal lags using a uniquely positioned, independent, null point (Tzero) thermocouple in addition to ΔT thermocouples (Figure 4). After an initial calibration of thermal characteristics of the sensor, the recorded temperature signal corresponds to the temperature of the sample pan, not to a sensor embedded in the DSC, which is normally all that is available. Moreover, the heat flow signal is compensated to minimize the smearing (peak broadening) effects caused by cell and capsule capacitance. The Q1000’s heat flow signal is the output of a four-term heat flow equation that takes into account the specific thermal characteristics of the DSC cell and capsule being used.4

The difference that this makes for fast-scan DSC can be readily seen by running the indium calibration material at high scan rates. Figure 5 shows indium scans at 50, 75, 100, and 150 °C/min using both sets of signals, those from only the ΔT output and those with the Tzero output (labeled T4P since they are the output of the four-term heat flow equation.) Tzero technology results in faster equilibration, sharper melting peaks, and better resolution. The melting point of indium, the peak onset temperature used for calibration, is essentially independent of scanning rate (heating or cooling) even at these rapid scan rates.

Summary

There has been interest lately in performing DSC analyses at faster heating rates. The ability to use fast scanning rates provides the DSC technique with an additional tool for structure elucidation and problem solving. It also increases sensitivity for the analysis of small samples and improves laboratory productivity. Fast scan rates have conventionally been associated with a major increase in errors due to sample and baseline effects. Tzero technology provides automatic compensation for thermal lag effects, which are the major source of error in fast-rate DSC. The use of the Q1000 with Tzero technology, together with careful encapsulation in a standard pan, has been shown to allow accurate data to be obtained at heating rates up to 150 °C/min, without the need to use operator-intensive foil-and-grease techniques. Experimental details and further explanation of the technique are available in the references and from TA Instruments.

References

4. Danley RL. Thermochim Acta 2003, accepted for publication.

Figure 5 Melting indium at 50, 75, 100, and 150 °C/min showing the output of the Tzero signals and the conventional DSC ΔT signals (broken lines) at an expanded scale.