APPENDIX

Theory of the Calorimetric Purity Method
(Standard Method of Calculation)

The determination of the purity of an organic compound by differential scanning calorimetry (DSC) is based upon the well known fact that the presence of even minute amounts of an impurity in a material broadens its melting range and lowers the final melting point of the material from T_o, the melting temperature of an infinitely pure material, to a lesser temperature, T_m.

As the DSC theory predicts, as the impurity content increases, the melting point decreases and the range of melting broadens. Even minute differences in the impurity content of the samples result in distinct differences in the DSC melting peak shape and final melting temperature.

The quantitative assessment of the purity of an organic material requires the knowledge of three important sample parameters:

- melting point
- heat of fusion (ΔH_f) (also referred to as the heat of melting, ΔH_m)
- analysis of the DSC melting peak shape

Power-compensated differential scanning calorimeters provide both accurate temperature measurements and true calorimetric measurements, thus permitting the simple determination of each of these three important sample parameters from a single dynamic (i.e., non-isothermal) DSC experiment.

A true DSC measures directly the amount of energy absorbed or emitted by a sample, dq/dt, which can be expressed by the following simplified equation (Eq. 1):

$$\frac{dq}{dt} = \frac{dT_S}{dt} \times \frac{dq}{dT_S} \qquad (1)$$

where:

$\frac{dT_S}{dt}$ = scanning (heating) rate (°C / min)

$\frac{dq}{dT_S}$ = heat capacity of the sample or the energy required to accomplish a transition (J / °C)

The heat capacity term, dq/dT_S, in this equation (1) provides important information about the shape of a melting peak and, therefore, is the most important term here. From the Van't Hoff equation, which describes the rate of melting of a compound as a function of sample temperature, we can obtain relationships describing the heat flow to or from a sample and the melting point depression of a sample due to the presence of an impurity. These relationships (Eqs. 2 and 3) are as follows:

$$\frac{dq}{dT_s} = \frac{\Delta q\,(T_o - T_m)}{(T_o - T_s)^2} \qquad (2)$$

where:

Δq = total heat of fusion of the sample (J)

T_o = melting point of a 100 % pure material

T_m = melting point of the sample

$(T_o - T_m)$ = melting point depression due to the impurity

T_s = sample temperature

The melting point depression due to an impurity $(T_o - T_m)$ can be expressed as:

$$(T_o - T_m) = \frac{R\,T_o^2\,X_2}{\Delta H_f} \qquad (3)$$

where:

R = molar gas constant, 8.314 J/mol K

X_2 = mole fraction of the impurity

ΔH_f = molar heat of fusion (J/mol)

From these two basic Van't Hoff relationships (Eqs. 2 and 3), the theory of the determination of the purity of a sample by DSC can now be derived. To do this, we must first integrate Eq. 2. This results in an expression which describes the fraction of material reacted (i.e., melted in the case of a purity analysis) at any sample temperature on the melting curve (Eqs. 4 and 5):

$$F = \frac{T_o - T_m}{T_o - T_s} \tag{4}$$

Rearranging this equations gives:

$$T_s = T_o - \frac{T_o - T_m}{F} \tag{5}$$

where:

F = fraction of sample which has melted

T_s = sample temperature

The theoretical discussion is now nearly complete. By substituting Eq. 3, which defines the melting point depression due to an impurity, into Eq. 5, we can obtain the now familiar linear equation used for the determination of purity by DSC (Eq. 6):

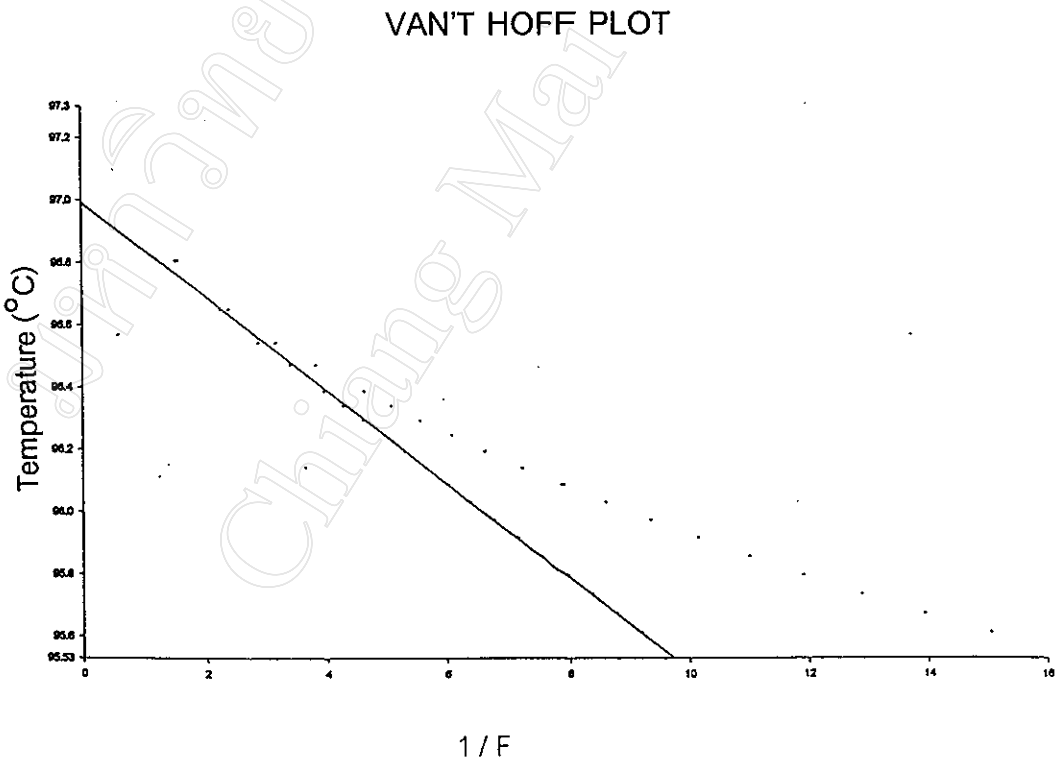
$$T_s = T_o - \frac{R\,T_o^2\,X_2}{\Delta H_f} \cdot \frac{1}{F} \tag{6}$$

Since Eq. 6 is a linear equation, a plot of the sample temperature (T_s) versus the reciprocal of the fraction of material melted at that temperature (1/F) should give a straight line with a negative slope equal in the magnitude to the melting point depression and an intercept on the T_s axis of T_o.

i.e., $$\text{slope} = -\frac{R\,T_o^2\,X_2}{\Delta H_f}$$

$$\text{Intercept (at } 1/F = 0) = T_o$$

This linear plot is referred to as a Van't Hoff plot, an example of which is shown in the figure below. The fraction of material melted (F) at any sample temperature (T_S) is determined directly from the dynamic DSC scan and is proportional to the peak area under the curve up to that temperature. By generating this Van't Hoff plot from a series of sample temperature and fraction melted results, in the range from approximately 5 to 60 % melted, it is a relatively simple procedure to obtain values for T_0 and the slope of the line. The mole fraction of the impurity, X_2, is then determined from Eq. 6 from which the % purity of the sample is calculated as $(1-X_2) \times 100$ %.



Van't Hoff plot showing the results of the DSC purity analysis of the synthesized L-lactide (after 3rd recrystallization).

(Sample size = 2.820 mg, heating rate = 2 °C / min)

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