

Purity Determinations By Differential Scanning Calorimetry¹

Purpose: Determine the purity of a compound using freezing point depression measurements with a differential scanning calorimeter.

Prelab: The instructions for the Perkin Elmer DSC 4 are given at the end of this manual.

Introduction

A common problem in analytical chemistry is the determination of the purity of substances. This laboratory uses differential scanning calorimetry to determine the purity of organic compounds. This method depends only on the physical-chemical behavior of the compound, and no reference standard is necessary. The pure melting point of the sample does not even need to be known. The method is accurate for samples over 98% pure, but it does not measure impurities which are soluble in the solid phase or insoluble in the melt. It is also inapplicable to chemicals which decompose at their melting points or have inordinately high vapor pressures. This technique is particularly valuable in the pharmaceutical and basic chemicals industry.

Differential Scanning Calorimetry

Differential scanning calorimetry (DSC) monitors heat effects associated with phase transitions and chemical reactions as a function of temperature. In a DSC the difference in heat flow to the sample and a reference at the same temperature, is recorded as a function of temperature. The reference is an inert material such as alumina, or just an empty aluminum pan. The temperature of both the sample and reference are increased at a constant rate. The heat flow difference

$$\Delta \frac{dH}{dt} = \left(\frac{dH}{dt} \right)_{\text{sample}} - \left(\frac{dH}{dt} \right)_{\text{reference}} \quad 1$$

can be either positive or negative. Here dH/dt is the heat flow measured in mcal sec^{-1} . In an endothermic process, such as most phase transitions, heat is absorbed and, therefore, heat flow to the sample is higher than that to the reference. Hence $\Delta dH/dt$ is positive.

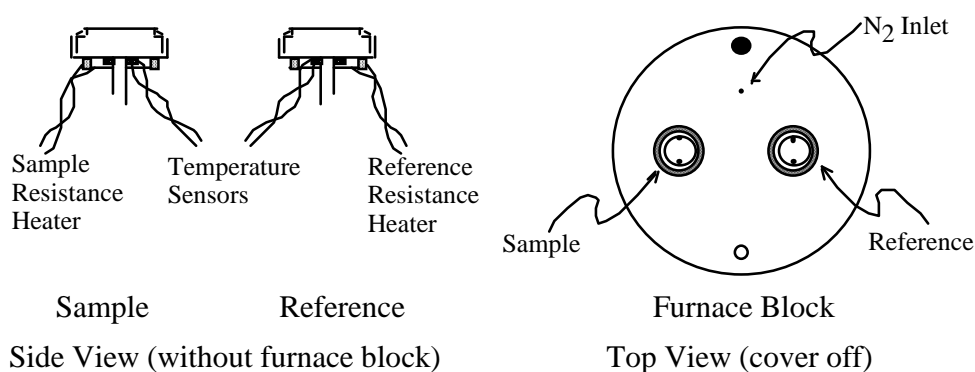


Figure 1. Differential Scanning Calorimeter.

The calorimeter consists of a sample holder and a reference holder as shown in Figure 1. Both are constructed of platinum to allow high temperature operation. Under each holder is a resistance heater and a temperature sensor. Currents are applied to the two heaters to increase the temperature at the selected rate. The difference in the current to the two holders, necessary to maintain the holders at the same temperature, is used to calculate $\Delta dH/dt$. A flow of nitrogen gas is maintained over the samples to create a reproducible and dry atmosphere. The nitrogen atmosphere also eliminates air oxidation of the samples at high temperatures. The sample is sealed into a small aluminum pan. The reference is usually an empty pan and cover. The pans hold up to about 10 mg of material.

Melting produces a positive peak in a DSC thermogram. The integral under the DSC peak, above the baseline, gives the total enthalpy change for the phase transition:

$$\int \left(\frac{dH}{dt} \right)_{\text{sample}} dt = \Delta H_{\text{sample}} \quad 2$$

This integral can easily be done using computer systems. The resulting value is usually presented in arbitrary units, which can be called planimeter units. (A planimeter is an old-fashioned mechanical device for determining areas.) Since the integral is in arbitrary units, a calibration must be performed with a known weight of a substance with a well-known enthalpy of melting. Indium metal is used for this purpose. Then the enthalpy of the process under study is determined from:

$$\Delta H_{\text{sample}} = \Delta H_{\text{indium}} \frac{\text{sample area in planimeter units}}{\text{indium area in planimeter units}} \quad 3$$

Theory

The purity of a sample for which only the molecular weight and sample weight are known can be ascertained by a simple mathematical treatment of the data from a DSC scan. The computation is based on the freezing point depression colligative property equation²:

$$\Delta T = \left(\frac{RT^{*2}}{\Delta_{\text{fus}}H} \right) x_B \quad \text{and} \quad K_f = \left(\frac{RT^{*2}}{\Delta_{\text{fus}}H} \right) \quad 4$$

where ΔT is the melting point depression; R is the gas constant, $1.9872 \text{ cal mole}^{-1} \text{ deg}^{-1}$; T^* is the melting point of the pure solvent; $\Delta_{\text{fus}}H$ is the enthalpy of fusion per mole; x_B is the molality of the solute; and K_f is the the molal freezing point depression constant. Equation 4 can be rearranged to give the form most convenient for use in DSC work:

$$\text{Mol \% impurity} = 100 \left(\frac{\Delta_{\text{fus}}H}{RT^{*2}} \right) \Delta T = 100 \frac{1}{K_f} \Delta T \quad 5$$

where T^* is the melting point of a sample with zero impurity. With this equation, the amount of impurity (or solute) in solution can be determined by multiplying ΔT by the constant, $\Delta_{\text{fus}}H/RT^{*2}$. In molecular weight determinations, K_f must be determined for the solvent. Extensive tables of K_f values are available. In purity measurements, the pure compound is the

solvent, and the constant, which is different for each substance to be determined, must be computed from the DSC curve.

The area under the DSC melting curve gives the enthalpy of fusion for the sample and the enthalpy of fusion per mole is readily computed from the weight of the sample. T^* and ΔT are obtained from the DSC data.

Analysis of a melting curve is best understood by looking at the reverse process, freezing. In Figure 2, the left-hand box represents a sample with zero impurity with the melting point of T^* . The next box shows a real sample with X concentration of impurity, and its melting point, T_1 . The difference between T^* and T_1 is the melting point depression, ΔT , for the sample.

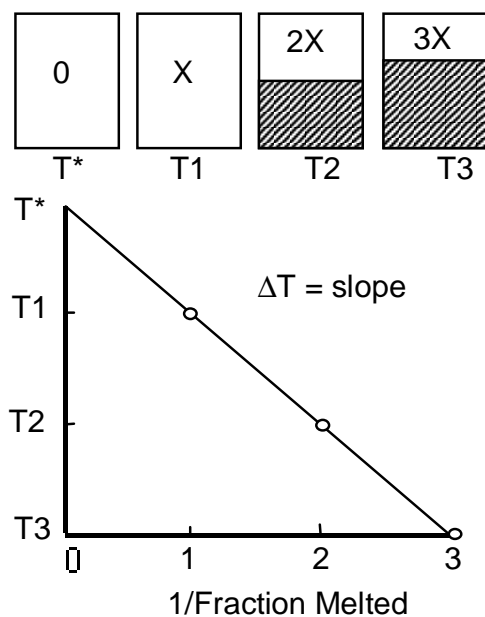


Figure 2. Freezing point depression for liquid-soluble, solid-insoluble impurities.

Two assumptions inherent in colligative property calculations are now used: the impurity is insoluble in the solid phase and soluble in the melt. Under these conditions, it is evident that when the sample is half frozen (melted), all the impurity is in the liquid phase, which is now reduced to half its former volume, and the impurity concentration is increased to $2X$. Because concentration and melting point depression are linearly related, the depression at this point is twice that of the original sample ($T^* - T_2 = 2\Delta T$). In the last box in Figure 2, one third of the sample is liquid, the concentration of impurity in the liquid phase is $3X$, and the melting point depression is $3\Delta T$.

The increase in impurity concentration is inversely proportional to the fraction melted. The inverse of the fraction melted is plotted with the corresponding temperature as the dependent variable. A straight line results whose slope is the melting point depression, ΔT , and whose zero intercept is the extrapolated melting point, T^* , of the theoretically pure substance.

As a solid melts, the impurities dissolve in the initial liquid phase and the same relationship between fraction melted and temperature depression is obtained. The melting curve is better suited for analysis than the freezing curve, as the former is easily done under equilibrium

conditions, whereas freezing introduces the problem of supercooling, a nonequilibrium condition unsuitable for calculation.

Example Calculation An example of a DSC melting curve is shown in Figure 3. The sample size was 2.2850 mg with a molecular weight of 263.12 g mol⁻¹. Because the amount of heat absorbed is directly proportional to the amount of sample melted and to the area under the melting curve, fractions of these values may be used interchangeably.

The DSC melting curve is divided into a series of partial areas, Figure 3. Each partial area extends from the onset of melting to a chosen temperature. These temperatures are chosen at roughly equally spaced intervals up to the point where the sample is half melted. Beyond this point, about 2/3 up the peak, melting is too rapid for equilibrium conditions to prevail and equation 5 does not hold. The fraction melted at any temperature is equal to the fraction of the total area occurring below that temperature. The partial areas extracted from Figure 3 are given in Table I. The inverse of the fraction melted can be obtained directly by dividing the total area by the partial area. These inverses are plotted against their corresponding temperatures ($T_{b,i}$), Figure 4 (a).

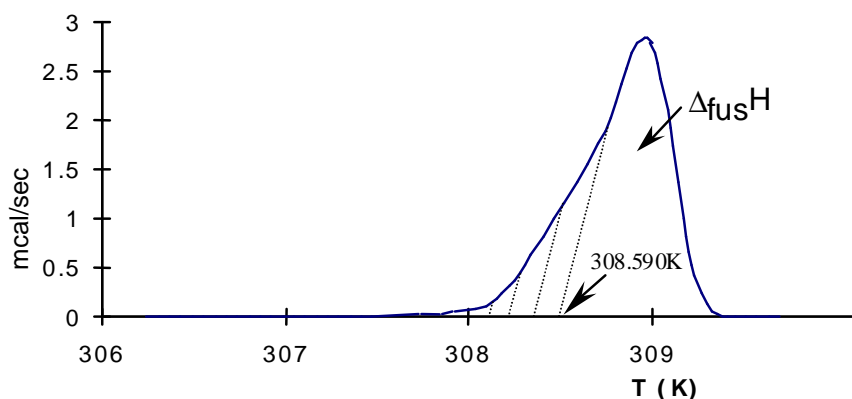


Figure 3. Example of a DSC Melting Curve; Methyl-4-(2,4-dichlorophenoxy)butyrate. The partial areas are bounded at the high temperature side with a line matching the slope of the low temperature side of the indium melting curve.

Table I. Example Data from Figure 3.

Temperature, K (At baseline)	Area Sum	1/F	Area sum + 15% correction	1/F (corrected)
308.119	52	55.2	483	6.84
308.256	146	19.7	577	5.72
308.422	371	7.74	802	4.12
308.590	781	3.68	1212	2.72
	2871		3302	

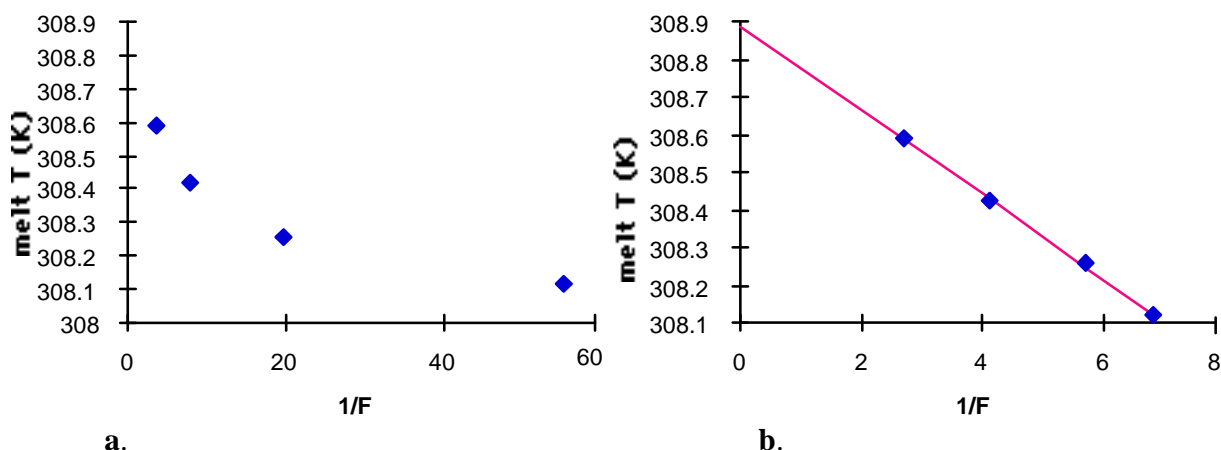


Figure 4. (a.) Data from Table I before correction. (b.) Data after 15% correction, with curve fit giving the slope, 0.112 K, and intercept ($=T^*$), 308.89 K.

In the case of very pure samples (over 99.99 mol %), the plot is linear. Curvature is observed in the case of less pure compounds. As the sample becomes less pure, its melting range increases and the point where melting actually begins is difficult to observe. A correction must be made for this pre-melting³. For convenience, this correction is expressed as a percentage of the total area measured, as other samples from the same lot will have a similar correction. The data are tabulated in Table I, where the first column records the temperature of each base line intercept, and the second records the total area up to the corresponding temperature. The next column lists the reciprocal of the fraction melted (1/F) at each temperature. These values are plotted against temperature in Figure 4(a). Because the line thus obtained is curved, a correction for pre-melting is applied, which was obtained by trial-and-error to minimize the uncertainty of the fit parameters. In this case a 15% correction was found necessary to linearize the plot, Figure 4(b). When this 15% (431) of the total measured area (2871) is added to each area, the corrected areas tabulated in Table I are obtained. The new total area (3302) divided by the corrected partial areas gives a series of corrected 1/F values. The linear plot results when the corrected 1/F values are plotted with corresponding temperatures as the dependent variable. The zero intercept, T^* , is 308.89 K, and the slope, ΔT , is 0.112 K.

To calibrate the instrument a 99.999% pure indium metal standard was run. The enthalpy of fusion of indium is 6.80 cal g^{-1} . In this example the area under the indium melting peak was 793 area units ($\text{mcal sec}^{-1} \text{ }^\circ\text{C}$) for a sample weighing 2.3218 mg. The number of mcal per area units is then

$$6.80 \frac{\text{mcal}}{\text{mg}} \left(\frac{2.3218 \text{ mg}}{793 \text{ area units}} \right) = 0.0199 \frac{\text{mcal}}{\text{area units}}$$

The enthalpy of fusion of the sample is obtained from the corrected area as follows:

$$\left(\frac{0.0199 \text{ mcal}}{\text{area units}} \right) \left(\frac{3302 \text{ area units}}{2.2850 \text{ mg}} \right) \left(\frac{263.12 \text{ mg}}{\text{millimole}} \right) = 7567 \frac{\text{mcal}}{\text{millimole}} = \Delta_{\text{fus}}H$$

Insertion into Equation 5 gives:

$$\frac{100 \cdot 7567 \text{ cal mol}^{-1} \cdot 0.112 \text{ K}}{1.9872 \text{ cal K}^{-1} \text{ mol}^{-1} (308.89 \text{ K})^2} = 0.447 \text{ mole \% impurity}$$

Data Analysis Using Logger Pro

The traditional way to analyze the data in this experiment is to integrate the partial areas by hand using a planimeter. However, computerized data acquisition allows many of the calculations to be automated. The calculation of the partial areas can be greatly simplified using the built in spreadsheet facility in Logger Pro. Consider the baseline subtracted thermogram as a series of data points at temperature T_i with power P_i , Figure 5.

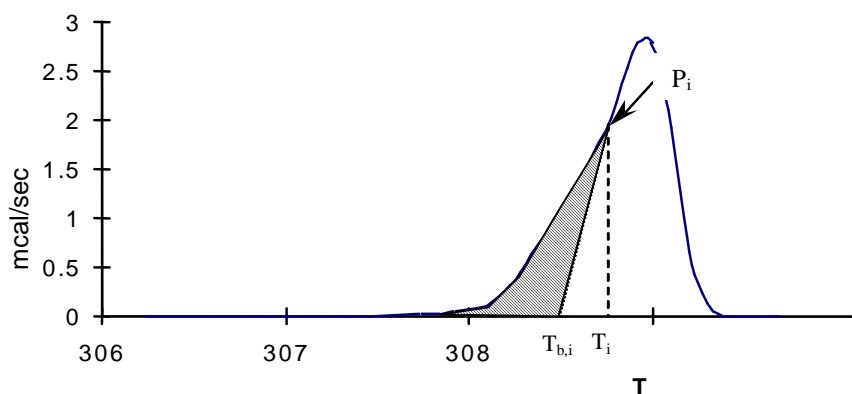


Figure 5. Baseline subtracted thermogram. The desired corrected area is the shaded portion.

To find the partial area up to a temperature T_i , the area of the triangle whose side has a slope equal to the slope of the melting transition for indium is subtracted. The indium slope is used to delineate portions of the melting curve integral because it corrects for thermal lag inherent in the system⁴. The area of the triangle is $\frac{1}{2}$ height \times base:

$$\text{corrected area}_i = \text{integral}_i - \frac{P_i(T_{b,i} - T_i)}{2} \quad (1)$$

Let m be the slope of the melting transition for indium in units of $\text{mcal/sec}/^\circ\text{C}$. The formula for the line with slope m that passes through the data point (T_i, P_i) is:

$$P = m T + (P_i - m T_i) \quad (2)$$

(Verify, using Eq. 2, that when $T = T_i$ that $P = P_i$.) The temperature $T_{b,i}$ is the intersection of this line with the baseline at $P = 0$:

$$0 = m T_{b,i} + (P_i - m T_i) \quad (3)$$

Solving for $T_{b,i}$ gives:

$$T_{b,i} - T_i = \frac{-P_i}{m} \quad \text{or} \quad T_{b,i} = T_i - \frac{P_i}{m} \quad (4)$$

Substitution back into Eq. 1 gives

$$\text{corrected area}_i = \text{integral}_i - \frac{P_i^2}{2m}$$

This simple result makes the calculations much easier to implement. The “purity.cmb1” method for Logger Pro has columns to do these calculations. However, the value of the slope m needs to be input. The default value of 300 mcal/sec/°C must be replaced in the Iadj and Tb columns by your slope, as given below in the Procedure section.

Then you can copy and paste the Iadj and Tb columns into Excel to complete your calculations. The calculations of the partial integrals by hand as given above results in just a few data points (four in the above example). Using computer based integration gives a partial integral at every data point. There fore your plot will have many data points instead of just four, giving correspondingly better curve fitting results.

Procedure:

The instructions for the Perkin Elmer DSC 4 are given at the end of this manual.

1. Indium Calibration:

Indium, 99.999%, is used for both temperature and heat calibration. The melting point is 156.60°C and the enthalpy of fusion is 6.80 cal g⁻¹. Area calibration is accomplished by measuring the area corresponding to the melting of a weighed sample of indium and indium's enthalpy of fusion as discussed above. Temperature calibration is accomplished by noting the maximum in the indium melting peak. The difference in the literature and measured melting temperature is used to correct the final pure melting point determined below.

Weigh a pan and lid to the nearest 0.01 mg. Add 5-7 mg of indium metal and reweigh. The samples are weighed into the pan before sealing, as metal from the pan is occasionally lost by stripping during sealing. Determine the melting curve from 154-156°C, at a rate of 0.2°C min⁻¹. Use the DSCautostart.cmb1 as usual. Remember to set the starting temperature and scan rate into the temperature column of Logger Pro. Start with a range of 2 mcal sec⁻¹, however, the appropriate setting will depend on the size of the sample.

Subtract the baseline from your thermogram before doing the integral. Integrate the curve plotted as a function of temperature. Normally you would integrate the curve plotted as a function of time, but the integrals for the purity determination are done on the plot of power verses temperature. We need to do both integrals in the same way. The units of the integral will be (mcal sec⁻¹ °C) and the units will cancel in the final results. Determine the slope of the low temperature side of the indium melting peak. In Logger Pro, pull down the Analyze menu and choose Tangent. Moving the mouse on the potential vs. temperature curve will list out the slope. Record this value.

2. Purity Determination:

Weigh a pan and lid and add 2-3 mg of the sample to be determined. Reweigh, and remember to record the weights to the nearest 0.01 mg. Determine the melting curve at a $1^{\circ}\text{C min}^{-1}$ program rate to determine the approximate melting point of the sample. Then determine the melting curve from about $1-2^{\circ}\text{C}$ below the melting point to just above the melting point at a scan rate of $0.2^{\circ}\text{C min}^{-1}$. For this second run use the "purity.cmbl" method. Remember to set the starting temperature and scan rate into the temperature column of Logger Pro. Also enter the slope of the indium calibration curve into the Iadj and Tb columns. For example, if the slope is $34.3 \text{ mcal sec}^{-1} \text{ }^{\circ}\text{C}$ then for Iadj:

$$\text{integral}(\text{"Subtracted Potential"}, \text{"Temperature"}) - 0.5 * \text{"Subtracted Potential"}^2 / 34.3$$

and for Tb:

$$\text{"Temperature"} - \text{"Subtracted Potential"} / 34.3$$

Use the same range setting as you used for the indium calibration, 2 mcal sec^{-1} , at the slower scan rate.

After the run is complete, subtract the baseline in the normal way by entering the slope and intercept into the appropriate spot in the P column. For example if your curve fit gives a slope of 3.456×10^{-4} and an intercept of 0.312 you would enter for the P column:

$$\text{"Potential"} - 0.312 - 3.456 \times 10^{-4} * \text{"Temperature"}$$

The bottom plot should now show the corrected area as a function of temperature. Integrate the full melting peak as you did for indium in the middle P vs. temperature plot. Determine the temperature where melting begins. Determine the temperature where the power, P, is about $2/3$ of the maximum P value. Highlight the data between these two temperatures in the Logger Pro spreadsheet for Iadj and Tb, and copy and paste this data into Excel. Note that Iadj is the Area Sum in Table I before the pre-melting correction and Tb is the temperature extrapolated to the baseline, which is also the temperature needed for the calculations in Table I.

Calculations

Determine the fraction of the sample melted as shown in Table I. However, you will have many more partial areas. The plot in Figure 4 is constructed. Adjust the correction for pre-melting to construct the most linear plot and give the smallest standard deviations for the slope and intercept. Calculate the enthalpy of fusion, the pure melting point (corrected), and the mole % impurity.

Report

Include a data table similar to Table I, and include just five of your data points spaced evenly across the melting temperature interval that you used for determining partial areas. Report the enthalpy of fusion, the pure melting point (corrected using the indium melting temperature calibration), the freezing point depression (ΔT), and the mole % impurity. Include your final plot. Use significant figure rules to estimate the uncertainty of your enthalpy of fusion. Use the uncertainties from least squares curve fitting to estimate the standard deviation in your freezing point depression, pure melting point, and the mole % impurity. Discuss the chemical significance of this experiment: what other techniques are used by organic chemists to determine purity, and

what is the advantage of the DSC technique compared to these methods?

References

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3. Thermal Analysis Newsletter, Perkin-Elmer Corp., Norwalk, CT.
4. A. P. Gray, *Instrument News*, **1966**, *16* (3), 9.