

INFLUENCE OF EXPERIMENTAL VARIABLES ON CURVES IN DIFFERENTIAL SCANNING CALORIMETRY. PART IV. EFFECTS ON PEAK-RELATED TEMPERATURES AND SPECIFIC ENTHALPY

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ABSTRACT

The extent to which experimental variables may affect the results of quantitative DSC was investigated in factorial designs. The factors investigated concerned the apparatus, test substance, reference and atmosphere.

The following were used as test substances: adipic acid (melt without noticeable decomposition), naphazoline nitrate (melt with decomposition), potassium nitrate (solid—solid transition) and sodium citrate dihydrate (dehydration).

The apparatus used was a commercial heat-flux DSC equipment. This paper, the fourth of a series which reports our findings, describes our results on onset temperatures, extrapolated onset temperatures, peak temperatures and specific enthalpies, which could be averaged with relatively small standard deviations. We found that the calculated mean values largely depend on the adjustment of the experimental variables.

All variables investigated, i.e. specific sensitivity of the apparatus and heating rate, sample mass, sieve size distribution, comminution, nature and mass of reference compound, dilution (type of diluent, concentration in dilution, preparation of dilution) and the applied atmosphere may influence the results in a systematic or non-systematic manner which also depends on the type of transition.

It was not always possible to explain fully all the results obtained; however, it could be concluded that the influence of experimental variables on the results of quantitative DSC is greater than has hitherto been presumed.

INTRODUCTION

In this paper, the results are presented of factorial studies to investigate the main effects and possible interactions of experimental variables on temperature parameters and specific enthalpy values from peaks in differential scanning calorimetry (DSC). This paper is the last of a series of four [1—3].

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The onset temperature (T_i) denotes the beginning of a transition, and the peak temperature (T_p) is the point of maximum deflection from the baseline. The extrapolated onset temperature (T_e), being the point of intersection of the tangent drawn at the point of greatest slope on the leading edge of the peak with the extrapolated baseline [4], has theoretically no physical meaning; Pope and Judd [5], however, obtained good agreement between experimental and literature values of melting points with the extrapolated onset temperature if the reference thermocouple temperature was plotted on the abscissa.

EXPERIMENTAL

A description of the test substances, reference compounds, the apparatus, characterization of the DSC curves, calibration checks and the study design, is given in Part I of this series of papers [1].

RESULTS AND DISCUSSION

Temperature parameters

Table 1 shows that there may be differences in levels for the onset temperature in each different experiment. Such differences are much less for the extrapolated onset temperature and peak temperature. The value of T_i is apparently more dependent on the experimental setting than the other two values. The coefficients of variation for the determination of T_i (always being less than 1%) are slightly higher than for the determinations of T_e and T_p (which are always less than 0.4 and 0.3%, respectively). Thus, as should be expected, to describe a DSC peak it is more feasible to present extrapolated onset temperatures and peak temperatures, which can be determined with approximately the same accuracy.

We observed that there are no effects of sample and reference masses on the onset and extrapolated onset temperatures. Generally, this is also true for peak temperatures, but for sodium citrate dihydrate a decrease in T_p with increasing sample mass is seen. For instance, in experiment 4.3 the mean response is 159.78°C if $m = 2$ mg and 158.49°C if $m = 5$ mg, the difference being significant at the 1% level.

The influence of the heating rate on the temperature characteristics depends upon the type of compound. With adipic acid, we generally may speak of a decrease in response with increasing heating rate.

The effect of heating rate on the temperatures of the melting endotherm of naphazoline nitrate can be seen in Table 2. It is clear that if the slow heating rate of 0.02 K sec⁻¹ is used, the total temperature interval for the transition to take place ($T_p - T_i$) is relatively small.

For the solid-solid transition of potassium nitrate and the thermal decomposition of sodium citrate dihydrate, the influence of the heating rate is according to expectations [6]: the temperature responses increase with

TABLE 1

Mean values of temperature determinations per experiment.

Compound	Experiment no.	T_1 ($^{\circ}\text{C}$)			T_e ($^{\circ}\text{C}$)			T_p ($^{\circ}\text{C}$)		
		Mean	s	ν	Mean	s	ν	Mean	s	ν
Adipic acid	1.1	145.89	1.40	7	150.86	0.18	7	151.09	0.15	7
	1.2.1 *									
	1.2.2 *									
	1.3	145.62	0.61	29	150.93	0.03	17	151.13	0.45	29
	1.4	145.99	0.53	20	150.78	0.06	28	151.27	0.07	16
1.5	146.25	1.93	27	150.60	0.17	27	150.84	0.07	17	
Naphazoline nitrate	2.1	165.38	1.22	7	167.93	0.34	6	168.80	0.23	6
	2.2.1	164.34	0.49	6	167.24	0.47	6			
	2.2.2 *				166.92	0.38	6	167.84	0.23	6
	2.3	160.99	1.40	28	167.16	0.31	16	168.34	0.41	28
	2.4	160.83	0.98	40	166.37	0.43	20	168.27	0.31	32
2.5	164.21	1.01	27	167.97	0.54	27	168.39	0.36	27	
Potassium nitrate	3.1	128.59	0.29	7	130.19	0.14	7	131.47	0.30	7
	3.2.1 *									
	3.2.2	128.54	0.30	6						
	3.3	128.43	0.28	20	129.92	0.21	28	131.32	0.37	28
	3.4	128.97	0.19	40	130.10	0.22	40	131.79	0.28	40
3.5	127.69	0.41	27	129.73	0.09	27	130.66	0.17	17	
Sodium citrate dihydrate	4.1 *	154.04	0.44	7	157.45	0.13	6			
	4.2.1 *									
	4.2.2 *									
	4.3	153.78	0.54	16	157.55	0.20	16	159.14	0.41	16
	4.4	155.82	0.61	16	159.90	0.66	16	163.03	0.25	24
4.5	153.90	0.41	16	157.10	0.11	11	159.14	0.33	16	

* If in the non-factorial experiments an effect of the changed factor was seen, it was not feasible to present a mean value.

TABLE 2

Effect of heating rate on temperatures of naphazoline nitrate (experiment 2.3)

Heating rate (K sec ⁻¹)	Temp. (°C)		
	T_i *	T_e *	T_p **
0.02	161.80	— ^a	167.82
0.08	160.59	167.29	168.51
0.32	160.57	167.03	168.67

* Significant differences between levels at $P = 0.05$.** Significant differences between levels at $P = 0.01$.^a Not determined.

heating rate. The effect, however, is not so clear for the onset temperature.

Particle size distributions also show effects on the temperature parameters. For both solid-liquid transitions T_e and T_p decrease with decreasing particle size (or, to a lesser extent, increase with increasing particle size). This effect is found both if the particles are milled and if they are just sieved out. For potassium nitrate and sodium citrate dihydrate the effects of particle size distributions on temperatures cannot be explained satisfactorily; more work is needed in this area.

The atmosphere may also play a role. In helium the temperature responses, especially the extrapolated onset and peak temperature, are significantly lower (Table 3). This can be attributed to the decrease in heat resistance between furnace wall and specimen holders in helium atmosphere, which value is used in the computation of sample temperatures from measured furnace temperatures in the heat-flux DSC system. Because of an increase in heat resistance in the furnace in vacuo, the temperature responses in vacuo are increased. In the case of naphazoline nitrate (experiment 2.3) the peak starts at a higher temperature in nitrogen atmosphere (162.33°C against 160.66°C and 159.97°C for air and oxygen, respectively). This phenomenon occurs presumably because naphazoline nitrate melts with oxidation. In the presence of oxygen or air, this reaction starts before the beginning of fusion and induces a lowering of the temperature responses.

In one experiment (3.3) with potassium nitrate the onset temperature and peak temperature are significantly lower (with 0.3 K) if oxygen is used, but this is not the case in experiment 3.5. There also is an interaction between heating rate and atmosphere ($P = 0.05$): at a very low heating rate of 0.02 K sec⁻¹ there is no difference in onset temperatures in oxygen, air or nitrogen, but if the heating rate increases (particularly to 0.32 K sec⁻¹), the onset temperature decreases in O₂, whereas it goes to higher levels in the other atmospheres. The temperature characteristics of the thermal decomposition of sodium citrate dihydrate are actually not affected by the atmosphere used.

The effect of dilution can partly be explained by the concurrent influence of the preparation of the dilution on particle sizes. By using a pestle and mortar, the particle size is decreased, even if the mixture is only gently

TABLE 3
Effect of atmospheres on peak temperatures.

Compound	Experiment no.	T_p ($^{\circ}\text{C}$)		Oxygen	Nitrogen	Helium	Vacuum
		s(K)	Static air				
Adipic acid	1.5 **	0.07	150.96	151.02	151.10	149.26	151.90
	2.3 **	0.31		167.09	167.58		
	2.5 **	0.36	168.48	168.40	168.84	167.22	169.30
Potassium nitrate	3.3 *	0.37		131.38	131.45		
	3.5 **	0.17	130.85	130.73	130.89	129.00	131.56
Sodium citrate dihydrate	4.3	0.41		159.04	159.27		
	4.5 **	0.33	159.34	159.42	159.38	157.41	160.04

* Significant differences between levels in the same experiment at $P = 0.05$.

** Significant differences between levels in the same experiment at $P = 0.01$.

rubbed, and dissolution followed by recrystallization (in a vacuum evaporator) may also influence the particle size (distribution). In our experiments we did not attempt to control the rate of recrystallization in the evaporator.

Again we could see that for the solid-liquid transitions the temperature responses decrease with a decrease in particle size (except for one case: adipic acid, diluted with pestle and mortar, showed an increase in onset temperature of about 0.5 K). For sodium citrate dihydrate, the temperature responses are again smallest in the case of the complete particle size spectrum, and thus also if a whirl mixer is used to dilute. If pestle and mortar are used, a small extra peak is seen at 140–146°C. The temperature parameters of the actual degradation peak are then higher than normal. For KNO_3 actually no effect of particle size is observed.

The influence of the dilution on particle size also explains a number of the many interactions found, particularly the interaction of sieve fraction and preparation method. Another explanation may be the non-homogeneity of mixing, especially if a whirl mixer is used. Use of pestle and mortar undoubtedly gives the best homogeneity of mixing.

The concentration also has an effect: the smaller the concentration, the

TABLE 4
Influence of dilution on T_e (°C) ^a

Factor	T_e (°C)			
	Adipic acid ($s = 0.06$)	Naphazoline nitrate ($s = 0.43$)	KNO_3 ($s = 0.22$)	Sodium citrate dihydrate ($s = 0.66$)
Concentration in dilution				
C ₁ 10%	— ^b	165.84 **	130.26 **	160.59 **
C ₂ 30%	150.78	166.46 **	130.07 **	159.75 **
C ₃ 50%	150.77	166.80 **	129.99 **	159.36 **
Diluting agent				
D ₁ carborundum	150.82 **	165.52 **	130.46 **	159.62 *
D ₂ alum. oxide	150.66 **	— ^b	129.96 **	160.17 *
D ₃ air (i.e. no diluting agent)	150.84 **	167.21 **	129.88 **	— ^b
Method of dilution				
V ₁ whirl mixer	150.88 **	166.66 **	129.81 **	158.05 **
V ₂ pestle/mortar	150.78 **	165.65 **	129.71 **	161.75 **
V ₃ dissolution and recrystallization	150.67 **	166.79 **	130.79 **	— ^c
Particle sizes				
Z ₁ small particles	150.65 **	164.72 **	130.17	159.90
Z ₂ complete spectrum	150.80 **	166.93 **	130.03	159.74
Z ₃ large particles	150.87 **	167.46 **	130.11	160.06

* Significant differences between levels at $P = 0.05$.

** Significant differences between levels at $P = 0.01$.

^a For the sake of brevity, the significant interactions are not given; their contributions to the main effects were generally slight.

^b Due to inadequacy of some raw data, mean values cannot be calculated.

^c Lack of suitable solvent prevented dissolution of sodium citrate dihydrate.

higher the temperature needed for the transition to start. The concentration effect can be explained by the thermal lag caused by the diluting agent, whose influence is of course greatest in the samples with the lowest concentrations of active ingredients. If air is the diluting agent, there is no difference in concentrations, which explains the interactions found between concentration and type of diluting agent, between diluting agent and diluting procedure, and between diluting agent and particle size: if air is the diluting agent, the effects of the method of "dilution", if causing particle size differences, are more pronounced. As an example, the influence of dilution on extrapolated onset temperatures is presented in Table 4.

Specific enthalpy (ΔH_s)

Our results (Table 5) indicate that the specific enthalpies can be determined with coefficients of variation of 1–4.5%. Only in the experiments

TABLE 5

Mean values of specific enthalpies per experiment.

Compound	Experiment no.	ΔH_s (J g ⁻¹)			
		Mean	s	C.V. (%)	ν
Adipic acid	1.1	256.79	2.60	1.01	7
	1.2.1	252.01	6.17	2.45	6
	1.2.2	256.28	5.41	2.11	6
	1.3	256.67	3.29	1.28	29
	1.4	212.40	18.91	8.90	28
	1.5	258.39 *	5.41	2.09	17
Naphazoline nitrate	2.1	95.69 **	1.20	1.25	6
	2.2.1	93.62	2.09	2.23	6
	2.2.2	90.81	1.81	1.99	6
	2.3	92.21	4.04	4.38	28
	2.4	84.89	8.63	10.16	24
	2.5	99.07 *	2.20	2.22	27
Potassium nitrate	3.1	49.18 ***	0.58	1.18	5
	3.2.1	47.48	4.03	8.49	6
	3.2.2	48.54	0.84	1.73	6
	3.3	49.59	1.18	2.37	27
	3.4	45.70	5.50	12.03	48
	3.5	50.68 *	0.72	1.42	27
Sodium citrate dihydrate	4.1	386.42 ***	2.68	0.69	5
	4.2.1	380.02	11.67	3.07	6
	4.2.2	377.62	11.47	3.04	13
	4.3	381.22	10.91	2.86	16
	4.4	291.80	75.73	25.95	24
	4.5	372.68 *	13.59	3.65	16

* Without values for helium atmosphere and holders without covers.

** Value for 0.1 mg excluded.

*** Values for 0.1 mg and 0.2 mg excluded.

with diluted samples the coefficients of variation vary from 9 to even 26%. The mean values for the diluted samples as compared to the undiluted ones are about 10–15% lower for adipic acid, naphazoline nitrate and KNO_3 , and even 25% lower in the case of sodium citrate dihydrate.

We found that ΔH_s is independent of sample mass only if the sample mass is above a critical value. This value was determined for our equipment to be 0.2 mg. For masses below this value, ΔH_s is too low. In those experiments which were done in duplicate, we could not show a significant difference in values for tests done by different persons and/or at different times.

The reference mass did not have an effect on specific enthalpy. However, the expected independence of heating rate could not always be found. The melting of pure adipic acid was indeed independent, but with naphazoline nitrate a significant decrease with 4% ($P = 0.01$) was found in experiment 2.3 if the heating rate was set on a low level. This decrease could only be found in air and oxygen, but in nitrogen the responses for all heating rates applied were the same. This may be explained by the concurrent oxidation reaction which proceeds at a higher rate if the transition time is longer (i.e. with low heating rates). Due to this oxidation, energy is evolved which should be subtracted from the melting endotherm. For KNO_3 and sodium citrate dihydrate it was found that ΔH_s was independent of heating rate only if rates $< 0.32 \text{ K sec}^{-1}$ were used. At higher rates, ΔH_s decreased in a non-systematical manner.

The atmosphere may also affect specific enthalpy. For all compounds, helium atmosphere gave a sharp decrease in response (see Table 6). An inert atmosphere (N_2 , vacuum) gave an increase in response with approximately 5% for naphazoline nitrate. Again, the reason is that due to oxidation, energy is evolved which should be subtracted from the melting endotherm. For adipic acid, the values for samples in holders without lids are lower than with lids. This can only be explained by the occurrence of some sublimation before melting. In vacuo, the response was lower too and if sample pans without lids were subjected to vacuum, the response was extremely low.

Some interesting effects of particle size distribution were found. For undiluted samples of adipic acid a significantly higher response (3%) was found if the complete particle size spectrum was used. This was not due to differences in weight loss, but can be explained by the fact that the porosity

TABLE 6

Specific enthalpy values in helium and other atmospheres.

Compound	Experiment no.	ΔH_s in helium	ΔH_s , other atmospheres	ΔH_s in He as % of other atmospheres
Adipic acid	1.5	102.81	248.19	41.4
Naphazoline nitrate	2.5	40.70	99.07	41.1
Potassium nitrate	3.5	20.48	51.20	40.0
Sodium citrate dihydrate	4.5	161.33	372.68	43.3

TABLE 7

Influence of particle size distribution on specific enthalpy values of adipic acid.

Particle size	Diluted/undiluted	ΔH_s (J g ⁻¹)
Small particles	Undiluted	255.03
Complete size distribution		261.78
Large particles		253.18
Small particles	Diluted	199.49
Complete size distribution		216.94
Large particles		220.75

is lower in the case of the complete particle size spectrum, leading to better heat transfer.

No difference in response could be seen between comminuted and untreated samples. Visual observation of the small particle samples of adipic acid after the run showed that the recrystallized melt was always coloured pale yellow or even brown, contrary to the specimens with large particles. Therefore, a slight degradation appears to occur with melting of small particles of adipic acid.

In diluted samples of adipic acid, the situation is completely different (Table 7). The mean values for diluted samples are considerably lower than in the non-diluted case, which is due to the influence of aluminium oxide (Table 8). The overall significant decrease for small particles can also be mainly attributed to the presence of aluminium oxide (and much less carborundum) (Table 9).

It is thought that due to a (physical or chemical) adsorption of the active ingredient onto the surface of the diluting agent (or vice versa), the vapour pressure is substantially reduced, which gives rise to a lower specific melting enthalpy. This adsorption is greatest in the case of small particles.

For naphazoline nitrate, a lower response was found in the case of smaller particles. This might be due to the fact that smaller particles are more subject to oxidation but then, a significant interaction was to be expected between oxygen atmosphere and small particles. This interaction was not found.

It must be remembered, however, that where inert atmospheres were used, the maximum concentration of oxygen could be 1% in our equipment. Perhaps this slight amount of oxygen present in "inert" atmospheres can give rise to some oxidation. The specific enthalpies of the polymorphic tran-

TABLE 8

Influence of nature of diluting agent on specific enthalpy of adipic acid.

Diluting agent	ΔH_s (J g ⁻¹)
Carborundun	264.34
Aluminium oxide	118.93
Air	253.91

TABLE 9
Influence of sieve sizes on specific enthalpy of adipic acid.

Diluting agent	Sieve size	ΔH_s (J g ⁻¹)
Carborundum	Small particles	252.56
	Complete size spectrum	267.26
	Large particles	273.21
Aluminium oxide	Small particles	96.31
	Complete size spectrum	126.27
	Large particles	134.22
Air (i.e. undiluted)	Small particles	249.61
	Complete size spectrum	257.31
	Large particles	254.81

sition and dehydration were independent of sieve size distribution or degree of crystallinity.

Dilution again has an important effect on the response (see Table 10). The calculated mean values for all four compounds are lower than the values in

TABLE 10
Effect of dilution on specific enthalpy (ΔH_s) (J g⁻¹)^a.

	Adipic acid (<i>s</i> = 18.91)	Naphazoline nitrate (<i>s</i> = 8.63)	KNO ₃ (<i>s</i> = 5.50)	Sodium citrate dihydrate (<i>s</i> = 75.73)
Concentration in dilution				
C ₁ 10%	b	b	42.46 **	289.35
C ₂ 30%	195.91 **	84.93	47.29 **	298.83
C ₃ 50%	228.89 **	84.84	47.35 **	287.21
Diluting agent				
D ₁ carborundum	264.34 **	94.22 **	50.38 **	277.68 *
D ₂ aluminium oxide	118.93 **	67.67 **	36.07 **	268.19 *
D ₃ air (i.e. no diluting agent)	253.91 **	92.77 **	50.64 **	329.51 *
Method of dilution				
V ₁ whirl mixer	217.60	89.46 *	50.74 **	333.30 **
V ₂ pestle/mortar	212.10	81.88 *	45.83 **	250.29 **
V ₃ dissolution and recrystallization	207.49	83.32 *	40.53 **	c
Particle sizes				
Z ₁ small particles	199.49 **	79.37 **	46.95	295.06
Z ₂ complete spectrum	216.94 **	86.47 **	46.05	286.18
Z ₃ large particles	220.75 **	88.83 **	44.09	294.14

* Significant differences between levels at $P = 0.05$.

** Significant differences between levels at $P = 0.01$.

^a For the sake of brevity, the significant interactions are not given; their contributions to the main effects were generally slight.

^b Due to inadequacy of some raw data, mean values cannot be calculated.

^c Lack of a suitable solvent prevented dissolution of sodium citrate dihydrate.

undiluted samples and the standard deviations of the determinations in diluted samples are much higher.

If no diluent was used, the mean value was approximately the same as for the other experiments, except in the case of sodium citrate dihydrate, where the mean value for the no-diluent case (329.51 J g^{-1}) was about 15–20% lower than the mean values found in the other experiments. This result cannot be explained as being due to a particle size effect because when the 100% sample was only pretreated by whirling in a mixer the value was still 333.30 J g^{-1} , which is 12.4% lower than the mean values in the other experiments. If pestle and mortar were used, the value was 250.29 J g^{-1} . No influence of comminution on ΔH_s of sodium citrate dihydrate could be seen.

Except for the dehydration reaction, the response in aluminium oxide was significantly smaller (only 46% of the mean values in carborundum and air in the case of adipic acid and 72% with naphazoline nitrate and KNO_3). For sodium citrate dihydrate, the value with aluminium oxide was the same as with carborundum but the values were now 20% lower than in the undiluted samples. As stated above, the decrease in response with aluminium oxide could be due to absorption giving rise to a decrease in vapour pressure, and thus, specific enthalpy.

In the sodium citrate dihydrate curves, a slight extra peak was seen (at approximately $140\text{--}150^\circ\text{C}$) if the mixtures were made with pestle and mortar. The values then found for the enthalpy were much lower than if the mixtures were prepared with the whirl mixer (see Table 10). Also, some (non-consistent) effects of concentration were seen. In our experiments (with concentrations of 10%, 30% and 50% respectively) we found it virtually impossible to evaluate statistically the areas in the 10% case. Often, peaks were then even totally absent.

It is clear that the reproducibility of mixing is a problem and that we did not succeed in getting acceptably homogeneous mixtures. In this respect, it should be noted that the dilutions were made in portions of 100 mg total blend. Of these blends, the amounts required for DSC were sampled. Apparently this gives rise to problems with the content uniformity of the samples. This will certainly play a role but cannot be the only reason for the discrepancies found. Values should then also have been found which were higher than the mean value in air. All the responses in diluted samples were, however, lower than the mean value in air.

SUMMARY AND CONCLUSIONS

Factorial experiments were carried out to investigate the influence of some experimental variables on the results of quantitative DSC. The apparatus used was a commercial heat-flux DSC equipment, and the following compounds were studied: adipic acid (melts without noticeable decomposition), naphazoline nitrate (melts with decomposition), potassium nitrate (solid–solid transformation) and sodium citrate dihydrate (dehydration).

The variables investigated concerned the apparatus adjustment, the sample, the reference material and the atmosphere. Significant main effects

and interactions were detected by analysis of variance. From the DSC curves the onset temperature (T_i), extrapolated onset temperature (T_e), peak temperature (T_p) and specific enthalpy (ΔH_s) were determined.

We found that there are differences in levels for the onset temperature T_i in each different experiment. Such differences are smaller for the extrapolated onset temperature T_e and peak temperature T_p . The onset temperature T_i is apparently more dependent on the experimental setting than the other two temperatures. We also saw that the coefficient of variation for T_i (being always less than 1%) is slightly higher than for T_e and T_p (which are always less than 0.4 and 0.3%). Thus, it is more feasible to present extrapolated onset temperature and peak temperature, which can be determined with approximately the same accuracy, to describe a DSC peak.

In general, there are no effects of sample and reference masses on temperatures. The heating rate influences temperatures depending on the type of compound. For adipic acid a decrease in response with increasing heating rate was seen and for naphazoline nitrate the total temperature interval for the transition was relatively small with low heating rates. For KNO_3 and sodium citrate dihydrate the temperature responses increased with heating rate.

Particle size distributions also showed effects on the temperature parameters, which generally could not be explained satisfactorily. More work is needed in this area.

The atmosphere also plays a role. In helium whose thermal conductivity is approximately five times that of air, the temperature responses are significantly lower, and in vacuo the values are usually higher. As naphazoline nitrate melts under oxidation, the atmosphere also has an effect on the temperature values for the melting peak of this compound.

The effect of dilution on temperatures can partly be explained by the concurrent influence of the preparation of the dilution on particle sizes. But the concentration also has an effect: it was concluded that the smaller the concentration, the higher the temperature required for the transition to start. The nature of the diluting agent also plays a role but the results are non-systematic, so they cannot be correlated with the differences in heat capacities of the materials.

Our results indicate that the specific enthalpies can be determined with a coefficient of variation of 1–4.5%. Only in the experiments with diluted samples the coefficients of variation vary from 9 to even 26%. Also, the mean values for the diluted samples are about 10–25% lower than for the undiluted ones. It may therefore be concluded that dilution is detrimental to quantitative work in DSC and should not be a normal technique in DSC.

We found that ΔH_s is independent of sample mass only if above a critical value of 0.2 mg. The reference mass did not have an effect on specific enthalpy. The expected independence of heating rate, however, could not always be found. For naphazoline nitrate a significant decrease (with 4%) in ΔH_s was found if the heating rate was set on a low level. This may be explained by the concurrent oxidation reaction in this case, which proceeds at a higher rate if the transition time is longer (i.e. with low heating rates). Due to this oxidation, energy is evolved which should be subtracted from the melting endotherm.

Also, effects of atmosphere on ΔH_s were observed. Especially helium gave a sharp decrease in response: the ΔH_s in helium was approximately 40% of the value in other atmospheres. Another effect of atmosphere was of course found with naphazoline nitrate: the presence of an inert atmosphere gave a 5% increase in response.

An interesting effect of sieve size on specific enthalpy was noticed: for samples of adipic acid a 3% higher response could be seen if the unsieved material was used. This effect was not due to differences in weight loss.

Summarizing, it may be stated that experimental variables may influence the results of DSC, and even to a very large extent. Some effects, like the decrease in specific enthalpy in the case of dilution or in helium atmosphere, are dramatic; but also heating rate, sample or reference mass, sieve sizes, and oxidizing or inert atmospheres may show effects which, although often not of great importance in qualitative work, are nevertheless significant and should be controlled in accurate quantitative DSC work. For example, in the determination of specific enthalpy and other thermodynamic values, in purity analysis and in the determination of kinetic parameters, these influences may play a role and should therefore be evaluated thoroughly prior to jumping to conclusions.

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