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INFLUENCE OF EXPERIMENTAL VARIABLES ON CURVES IN DIFFERENTIAL SCANNING CALORIMETRY. PART II. EFFECTS ON BASELINE-RELATED CHARACTERISTICS

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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 second of a series which reports our findings, describes the results on baseline-related characteristics. We conclude that if a DSC curve is described in baseline parameters, large standard deviations should be taken into account. However, we showed that many variables investigated, e.g. specific sensitivity of the apparatus and heating rate, sample and reference mass, the applied atmosphere and dilution may influence the results in a systematic or nonsystematic manner.

INTRODUCTION

In a model with a thermal energy flow from the furnace to the sample and reference side, it is possible to derive the following baseline equation from heat-balance considerations

$$\Delta T = \frac{\beta}{A\alpha}(C_R - C_S) + \frac{\beta}{A\alpha}\left[C_S \exp\left(-\frac{A\alpha}{C_S}\,t\right) - C_R \exp\left(-\frac{A\alpha}{C_R}\,t\right)\right] \quad (1)$$

The second part of the right-hand side of eqn. (1) is a term which applies to

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the lag phase, so after this lag phase it holds

$$\Delta T_0 = \frac{\beta}{A\alpha}(C_R - C_S) \tag{2}$$

where β = the heating rate (K sec^{-1}); A = area for heat transfer (cm^2); α = coefficient of heat transfer (mW K^{-1} cm^{-2}); C_R and C_S are the heat capacities (mJ K^{-1}) of reference and sample side, respectively.

This equation only applies if the following assumptions hold:

(1) the apparatus is symmetrical, thus $A_R = A_S = A$;

(2) the thermal resistances R (in K mW^{-1}) are identical on the reference and sample side at any given temperature, thus $\alpha_R = \alpha_S = \alpha$;

(3) the temperature distributions in the sample, the reference and their containers are uniform;

(4) the flow of heat from sample to reference (and vice versa) can be neglected;

(5) the contact between the specimens and their holders is very intimate and can be described by the boundary conditions

$T_S = T_{Sh}$ and $T_R = T_{Rh}$

in which the subscript h denotes the (specimen) holder.

The value of $A\alpha/E_{rel}$ corresponds with $S_E/E_{In}E_{rel}$, where E_{In} = specific sensitivity (in μV mW^{-1}), determined with ultrapure indium; E_{rel} (dimensionless) is a correction factor for the temperature influences on thermocouple sensitivity; $E_{In} \times E_{rel} = E$, the calorimetric sensitivity (in μV mW^{-1}); S_E = the thermocouple sensitivity (in μV K^{-1})
Furthermore, it holds

$$\frac{\Delta T_0}{R} = \frac{\Delta U_0}{E} \tag{3}$$

In this paper, the results are presented of a factorial study to investigate the main effects and possible interactions of experimental variables on some baseline-related characteristics of DSC curves. This paper is the second in a series of four.

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

Initial baseline deflection ΔU_0

In Table 1 the mean values of the baseline-related characteristics are given. From these data, the influence of the apparatus on ΔU_0 is evident. During the course of the study we had to replace the thermopile three times (thus changing S_E) and this may be the cause of the large variation (even with change of sign) in the mean values found. It is therefore not feasible to present only one mean ΔU_0 value per compound. Such values per compound should differ, of course, as a result of differences in specific heat. It is also clear from the change in ΔU_0 with change in thermopile that assumptions (1) and (2) mentioned in the Introduction (symmetrical apparatus and identical sample and reference resistances) are not valid. In our opinion, this deviation from ideality has no bearing for practical purposes. It should be noted that the ΔU_0 values presented are not corrected for day-to-day variations in calorimetric sensitivity.

In Table 2, the influence of helium atmosphere on ΔU_0 is given. Due to the large standard deviations, the effect is not always statistically significant. Helium has a thermal conductivity which is approximately 5.5 times higher than that of air [2]. Because of this, thermal energy is dissipated more easily and hence ΔU_0 in helium is much lower.

As expected from eqns. (2) and (3) an increase in ΔU_0 with sample mass and heating rate is found which is independent of the nature of the sample. There is also a large decrease in ΔU_0 response if sample and reference holders without lids (i.e. with smaller masses) are used (see Table 1). The decrease in ΔU_0 found by reducing the difference in mass between sample and reference (see Table 3) is not inversely proportional to the mass of reference compound. This may be due to asymmetry effects in the furnace. There is no effect of sieve size distribution of the sample on ΔU_0.

Interestingly, ΔU_0 is also affected by dilution (concentration of active ingredient, type of diluting agent and method of preparation). The effects, however, are varying and even contrary for the different compounds. The reason for this is primarily assumed to be non-homogeneity in the diluted samples, but also the relative arrangement of sample material and diluting agent may play a role: at high concentrations the heat transfer between sample particles will predominantly pass through the surrounding atmosphere, at lower concentrations thermal energy may also be transferred through the diluting material. As expected, the analysis of variance shows, among other things, an interaction between concentration and type of diluting agent (if no diluting agent is used, the concentration is always 100% so ΔU_0 will not change).

The lag time, τ_0

The lag time, τ_0, is the time needed to reach the steady state situation if the furnace conditions are changed from isothermal to heating. As can be seen in Table 1, τ_0 varies with the experimental conditions and there is no simple relationship between τ_0 and ΔU_0. We are not able to account for the different τ_0 values for the different test substances. There is almost no effect of sample mass on τ_0. Only with holders without lids we found a significant decrease with two of the four compounds. τ_0 decreases if the heating rate is increased. This effect, however, is also not very pronounced and not always significant. In Table 2 the decrease in τ_0 response due to use of helium

TABLE 1

Mean values of baseline-related characteristics

Compound	Experiment No.	Special variables	ΔU_0 (μV)			τ_0 (sec)		
			Mean	s	v	Mean	s	v
Adipic acid	1.1 *							
	1.2.1 *							
	1.2.2 *					138	32	5
	1.3		4.8	2.0	29	142	37	29
	1.4		6.0	1.0	23	178	14	27
	1.5	Holders with lids	3.6	2.9	27	144	32	27
		Without lids	–4.0	2.9	27	93	32	27
Naphazoline nitrate	2.1 *		4.8	0.9	5			
	2.2.1 *					178	31	5
	2.2.2 *							
	2.3		13.1	3.6	28	215	29	20
	2.4		4.2	1.9	28	208	30	28
	2.5	Holders with lids	5.3	1.9	17	204	29	26
		Without lids	–2.7	1.9	17	155	29	26
Potassium nitrate	3.1 *					149	87	7
	3.2.1 *							
	3.2.2 *							
	3.3		2.5	3.6	16	180	83	16
	3.4		5.3	0.6	20	133	22	24
	3.5	Holders with lids	–3.8	2.2	27	189	49	27
		Without lids	–3.0	2.2	27	190	49	27
Sodium citrate dihydrate	4.1 *					187	29	7
	4.2.1 *					144	50	6
	4.2.2 *							
	4.3 **							
	4.4		–0.9	1.8	15	159	108	9
	4.5	Holders with lids	–3.5	2.1	16	102	50	16
		Without lids	–0.8	2.1	16	73	50	16

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

** Due to inadequacy of the data, some factors could not be evaluated statistically.

atmosphere can be seen. Because of the lower thermal resistance the steady state is reached earlier. If 5 mg of carborundum are used at the reference side τ_0 is decreased. This is explained by the increase in heat capacity of the reference side, thus matching that of the sample side better, so that less time is required to reach the steady state [compare the right-hand side of eqn. (1)]. Regarding the effects of dilution, the same comments can be made as for ΔU_0.

Drift (μV/K)			$\Delta U'_\Delta$ (μV)			τ'_Δ (sec)		
Mean	*s*	*v*	Mean	*s*	*v*	Mean	*s*	*v*
0.048	0.018	6						
0.048	0.014	25	14.5	5.1	29	154	28	29
0.060	0.015	27	13.0	1.6	14	192	19	16
0.038	0.019	27	15.6	8.0	17	146	51	27
0.062	0.019	27	−8.6	8.0	17	136	51	27
0.031	0.009	5	6.8	1.1	4	157	49	7
0.043	0.007	3				167	79	6
						132	36	6
0.075	0.010	24	13.1	2.3	7	204	40	15
0.037	0.013	28	10.5	3.9	27	130	14	27
0.042	0.013	27	12.4	3.8	17	149	47	26
0.060	0.013	27	−7.5	3.8	17	88	47	26
−0.044	0.019	7						
−0.010	0.003	6						
−0.011	0.024	12	7.3	8.7	16	170	86	14
0.022	0.003	6	14.1	1.4	20	137	24	48
−0.038	0.006	26	−8.5	1.8	27	163	37	27
−0.032	0.006	26	−9.0	1.8	27	140	37	27
						158	9	6
−0.037	0.027	16						
			−0.9	2.6	16	127	49	16
−0.019	0.009	16	−8.9	2.3	16	116	31	16
−0.024	0.009	16	−6.6	2.3	16	117	31	16

Baseline deflection (heating → cooling) $\Delta U'_{\Delta\nabla}$ and lag time (heating → cooling) $\tau'_{\Delta\nabla}$

At the moment of temperature inversion in cyclic heating-cooling programmes, a bend in the ΔT curve is observed. Thus, after a change-over from heating to cooling, the reference temperature will deviate from the sample temperature and the baseline will change to an extent which depends upon the apparatus, the differences in heat capacities of sample and reference sides, and the heating rate. Therefore, as expected, similar conclusions can be drawn for $\Delta U'_{\Delta\nabla}$ as for ΔU_0, and for $\tau'_{\Delta\nabla}$ as for τ_0. An exception must be made for some interactions.

It can be expected from theory that the ratio $\Delta U'_{\Delta\nabla}/\Delta U_0$ should be 2.

TABLE 2

Influence of atmospheres on baseline-related characteristics

Compound	Experiment No.		ΔU_0 (μV)			τ_0 (sec)		
			Mean	s	v	Mean	s	v
Adipic acid	1.5	Helium atmospheres	—0.87	2.87	27	36 **	32	27
	1.5	Other atmospheres	1.41	2.87	27	146 **	32	27
Naphazoline nitrate	2.5	Helium atmospheres	0.23 *	1.88	17	36 **	29	26
	2.5	Other atmospheres	3.10 *	1.88	17	218 **	29	26
Potassium nitrate	3.5	Helium atmospheres	—0.32 **	2.23	27	39 **	49	27
	3.5	Other atmospheres	—4.15 **	2.23	27	220 **	49	27
Sodium citrate dihydrate	4.5	Helium atmospheres	0.12	2.11	16	20	50	16
	4.5	Other atmospheres	—2.59	2.11	16	101	50	16

* significant differences (P = 0.05) between levels.
** significant differences (P = 0.01) between levels.

However, statistical evaluation from the data of Table 1 showed that in practice this is not the case. This may be due to the existence of slight baseline drifts or to the temperature differences (the isothermal → heating shift takes place at 47°C, the heating → cooling shift at 150—200°C) and corresponding changes in heat capacities. Also, the large standard deviations for ΔU_0 and $\Delta U'_{\Delta\nabla}$ responses may provide an explanation.

Drift angle

The drift can be conveniently measured as the drift angle δ, being the tangent of the angle which is formed by the baseline and the time axis. The baseline should be straight over the measured period (corresponding to at least 30 K). Any temperature-induced change in one or more of the factors on the right-hand side of equation (1) gives rise to a change in the baseline drift. The drift angle may also be influenced if the assumptions applying to eqn. (2) are not valid during the heating process. Thus, in the case of given specific heats of sample and reference, the baseline drift should be minimal with small differences in sizes between sample and reference side, and with complete symmetry and constant thermal resistance of the apparatus. It may be expected that the baseline drift is increased by high heating rates (due to larger temperature lags in the sample and reference sides, presence of radiation and a non-negligible flow of heat from sample to reference or vice versa). However, the baseline drift should be primarily influenced by varia-

drift (μV K^{-1})			$\Delta U'_{\Delta V}$ (μV)			$\tau'_{\Delta V}$ (sec)		
Mean	s	v	Mean	s	v	Mean	s	v
−0.001 **	0.019	27	2.28 **	7.99	17	73 *	51	27
0.056 **	0.019	27	8.63 **	7.99	17	157 *	51	27
0.002 **	0.013	27	1.29	3.83	17	62 *	47	26
0.057 **	0.013	27	6.62	3.83	17	142 *	47	26
−0.017 **	0.006	26	−0.58 **	1.84	27	48 **	37	27
−0.040 **	0.006	26	−10.28 **	1.84	27	177 **	37	27
−0.008 *	0.009	16	0.20 **	2.34	16	48 **	31	16
−0.023 *	0.009	16	−9.34 **	2.34	16	130 **	31	16

tions in heat capacity of sample and reference sides and by the change of thermocouple sensitivity S_E with temperature. Our results (see Table 1) demonstrate small, and for practical purposes actually negligible, drift angles, which are determined with fairly large coefficients of variation. Influences of sample nature are not clearly observed. A small increase with sample mass can be shown together with the dependency on thermopile adjustment. If large heating rates are used ($\geqslant$0.16 K sec^{-1}) the drift angle is increased (see Table 4).

TABLE 3

Adipic acid: effect of reference mass on baseline-related characteristics

Ref.	ΔU_0 (μV) [a] **	τ_0 (sec) [b] *	drift (μV/K) [c] **	$\Delta U'_{\Delta V}$ (μV) [d] **	$\tau'_{\Delta V}$ (sec) [e] *
No ref.	6.71	148	0.058	18.98	159
2 mg carborundum	6.18	160	0.054	18.31	168
5 mg carborundum	1.44	119	0.033	6.11	134

* Significant differences (P = 0.05) between levels.

** Significant differences (P = 0.01) between levels.

[a] s = 1.97 μV; ν = 29.

[b] s = 37 sec; ν = 29.

[c] s = 0.014 μV/K; ν = 25.

[d] s = 5.10 μV; ν = 29.

[e] s = 28 sec; ν = 29.

TABLE 4

Effect of heating rates on drift angles (μV K^{-1})

β (K sec^{-1})	Naphazoline nitrate * (s = 0.010 μV K^{-1}; v = 24)	Sodium citrate · 2 H_2O * (s = 0.027 μV K^{-1}; v = 16)
0.02	0.036	−0.026
0.08	0.055	−0.025
0.16	0.135	−0.060

* Significant differences between levels at P = 0.01.

In the case of naphazoline nitrate, a very small peak before the melting endotherm occurred if low heating rates were applied. By using a reference compound, the drift angle decreased as is shown in Table 3. We have no explanation for the apparently non-linear character of this decrease. In helium atmosphere the drift angle also decreases, due to the decrease in sensitivity (see Table 2).

If specimen holders without lids are used, the effect on drift angle depends on the type of compound. With adipic acid, a 60% increase occurred which could be attributed to sublimation. For potassium nitrate, a 20% decrease occurred and for sodium citrate dihydrate no effect was observed. With naphazoline nitrate there was an increase with approximately 40%. Here, a slight degradation before the start of the peak may be the reason. This is not necessarily the result of oxidation, since the influence of oxygen atmosphere on the drift angle of naphazoline nitrate is contradictory in different experiments. In oxygen, sometimes a 10% decrease (P = 0.05), as compared with the other atmospheres, was seen, sometimes no difference at all could be observed. Degradation may also be the cause of the differences in drift angles with naphazoline nitrate, if different sieve sizes are used (see Table 5). It is also assumed that degradation is the reason for the statistically significant interactions (P = 0.01) for naphazoline nitrate in experiment 2.3 between: (1) sample mass and sieve fraction (with small sample mass the drift was relatively highest for small particles), (2) sieve fraction and heating rate (with high heating rate and small particles the drift is relatively highest), and (3) sample mass, sieve fraction and heating rate. In the same experiment, an interaction (P = 0.01) was also observed between sample mass and heating

TABLE 5

Effect of particle size distribution on drift angle for naphazoline nitrate (experiment 2.3) (s = 0.010 μV K^{-1}; v = 24)

Particle size	Drift angle (μV K^{-1}) *
<32 μm	0.088
Complete size spectrum	0.065
>400 μm	0.071

* Significant differences between levels at P = 0.01.

rate (with large sample mass, the drift was relatively higher with high heating rates). The reason for this is not known.

Dilution also influences the drift angle (see Table 6). In conventional DTA, one of the main reasons for including a dilution procedure in an experiment is that it should reduce baseline drift (because of the similarity of thermal diffusivities between sample and reference material [3]). In our experiments, aluminium oxide as the diluting agent rather gave rise to an increase in drift angle, e.g. a significant ($P = 0.01$) increase of 100% for adipic acid. With this diluting agent, the baseline had a rather uneven character and with naphazoline nitrate, even a jump in the baseline was often seen at approximately 93°C.

It must be remembered that the aluminium oxide was of high activity chromatography grade. Therefore, complexations and hydrogen bondings between aluminium oxide and the active ingredients cannot a priori be excluded and may explain the above-mentioned effects. Also, the aluminium oxide is slightly hygroscopic so that dehydration of sorbed water could also

TABLE 6

Effects of dilution on δ (μV K^{-1}) [a,c]

Factor	Compound		
	Adipic acid ($s = 0.015\ \mu$V K^{-1})	Naphazoline nitrate ($s = 0.013\ \mu$V K^{-1})	KNO_3 ($s = 0.003\ \mu$V K^{-1})
Concentration in dilution			
C_1 10%	[b]	0.035 *	0.026 **
C_2 30%	0.066 **	0.033 *	0.016 **
C_3 50%	0.054 **	0.044 *	0.024 **
Diluting agent			
D_1 carborundum	0.042 **	0.041 *	0.014 **
D_2 aluminium oxide	0.093 **	[b]	[b]
D_3 air (i.e no diluting agent)	0.045 **	0.034 *	0.029 **
Method of dilution			
V_1 whirl mixer	0.058	0.038	0.030 **
V_2 pestle/mortar	0.059	0.036	0.014 **
V_3 dissolution and recrystallization	0.064	0.038	[b]
Particle sizes			
Z_1 small particles	0.057	0.042	0.022
Z_2 complete spectrum	0.065	0.037	0.021
Z_3 large particles	0.058	0.032	[b]

* 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] Values for sodium citrate dihydrate are not calculated, due to inadequacy of the raw data.

be the reason for the uneven character of the baselines. If carborundum was used, sometimes (particularly with potassium nitrate) a decrease in drift angle (compared to the drift without dilution) could be seen but for practical purposes this decrease is negligible.

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 values of the following baseline related parameters were determined: the initial baseline deflection ΔU_0; the lag time (isothermal → heating) τ_0; the baseline drift angle δ; the baseline deflection (heating → cooling) $\Delta U'_{\Delta\nabla}$ and the lag time (heating → cooling) $\tau'_{\Delta\nabla}$.

The initial baseline deflections ΔU_0 varied from about 1—15 μV and were averaged with coefficients of variation of up to 50%. Due to these poor reproducibilities, the expected dependencies on masses and specific heats of the specimen-holder assemblies, the heating rate and the apparatus adjustment could not always be established. Sieve size distributions of the sample did not affect the initial baseline deflections, but dilution did, in a non-systematical manner.

We did not find a simple relationship between ΔU_0 and τ_0. The mean values for τ_0 varied from about 90—210 sec. The value of τ_0 was not affected by sample mass and only slightly by the heating rate.

Generally, a significant decrease occurred in the values of ΔU_0 and τ_0 if helium was used as the atmosphere, instead of air, oxygen or nitrogen.

For the $\Delta U'_{\Delta\nabla}$ and $\tau'_{\Delta\nabla}$ parameters the same could be concluded, mutatis mutandis, as for $\Delta U'_0$ and τ_0, respectively. We did not find a simple relationship between ΔU_0 and $\Delta U'_{\Delta\nabla}$.

An important parameter is the baseline drift, which we characterized as the drift angle in μV K^{-1}. The drifts in our apparatus were extremely small (from 0.010 to 0.080 μV K^{-1}) and the influences of variables on the drift may therefore generally be negligible for normal DSC work. Also, the standard deviations were fairly large. Still, a number of significant effects can be shown, of which the increase with increasing sample mass and heating rate and a non-linear decrease with increasing mass of reference compound should be mentioned. We also saw that in helium atmosphere the drift angle was significantly lower than in air, oxygen or nitrogen. We found that the drift angle was largely dependent on thermopile adjustment and also on the nature of diluting agent: carborundum significantly decreased the drift angle, aluminium oxide gave a significant increase.

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