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Thermochimica Acta 267 (1995) 313–322

thermochimica
acta

Observation of the melting process for ethyl *p*-aminobenzoate doped with eutectic mixture[1]

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Received 20 November 1994; accepted 20 February 1995

Abstract

In order to improve the reliability of purity measurements by differential scanning calorimetry (DSC), the melting process of a test material was studied using a system of ethyl *p*-aminobenzoate and *n*-butyl *p*-hydroxybenzoate. The eutectic mixture began melting accompanying the increase in temperature. After the minor component, *p*-hydroxybenzoate, had entirely melted in the eutectic mixture, it was confirmed by DSC measurement and solid phase-liquid phase titration that the major component, *p*-aminobenzoate, which remained as a solid, continued to dissolve into the eutectic mixture. In order to completely grasp the melting image of the test material, it was necessary to measure it from a sufficiently low temperature, and work up to the eutectic peak with the minor component. It was found that, by drawing up a solubility curve, the phenomenon in which *p*-aminobenzoate dissolves into the melted eutectic mixture is, in this system, close to the ideal solution based on Raoult's equation, and that the heat of mixing in an infinite dilution was indicated to be a small value of -1.9 J g^{-1}. For that reason, the heat of fusion and the heat of dissolution coincided within the allowable error. Test materials that have been refined to a certain degree frequently include similar compounds as impurities, and this establishes an approximation of the heat of dissolution with the heat of fusion.

Keywords: Dissolve in eutectic mixture; Melting process; Heat of dissolution; Heat of mixing; Purity determination

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1. Introduction

It is useful to determine the purity of organic compounds with unanticipated impuri-

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[1] Presented at the 30th Anniversary Conference of the Japan Society of Calorimetry and Thermal Analysis, Osaka, Japan, 31 October–2 November 1994.

SSDI 0040-6031 (95) 02488-3

ties by DSC. None the less, DSC is not generally used for measurement of purity, because the purity range to give high accuracy is limited to substances of high purity [1,2]. Fundamental conditions were investigated to broaden the applicable range of this method, and also to improve the method to obtain more precise and reproducible values [3].

Many organic compounds include similar chemical components as impurities showing a minimum melting point, and the purity can be measured from the degree of the melting point drop observed [4]. The frequency of substances giving this minimum melting point, namely, eutectic mixtures, was examined by arbitrarily mixing organic substances, and except for the combinations of substances containing salts and substances with large polarity differences, the minimum melting points were found for most combinations [5]. Consequently, it is thought that, in the measurement of purity, eutectic mixtures are formed between the major component and the multi-component impurities.

In this paper, in order to clarify the melting process of a system which includes eutectic mixtures, we have conducted physicochemical studies using a binary mixture of ethyl *p*-aminobenzoate and *n*-butyl *p*-hydroxybenzoate. The reasons why this binary system was selected are that test materials with a high purity can be obtained, the melting point of the eutectic mixture is close to room temperature, the components can be accurately determined, and also it is a combination of compounds that have similar chemical structures. The results of the experiment revealed that the test material began to melt when the temperature was raised to the eutectic temperature, and that the composition of the melted components was the same as the eutectic mixture. After all of the minor components included in the test material had melted in the ratio of the eutectic mixture, the remaining solid of the major component continued to dissolve into the melted eutectic mixture when the temperature increased, and finally all of the test material became liquid. This suggests that in measuring the purity, when the content of the major component is determined, we should not only analyze the main peak and make corrections with the heat of undetected melting, but we should also measure the total area of the melting curve in a broad range, and include the eutectic peak in the analyses.

In addition, because both components in this system are chemically similar, the heat of mixing was small, with the heat of fusion and the heat of dissolution coinciding within allowable error. Since the major component in the test material had been refined and had included similar compounds as impurities, an approximation of the heat of fusion with the heat of dissolution was considered to exist. Consequently, we think that there is no problem with substituting the heat of fusion of the test material for the heat of fusion of the pure substance.

2. Experimental

The following equipment was used in the experiments. For DSC measurement: Rigaku Co. TAS 100, DSC 8230; Seiko Instr. Inc. SSC 5020, DSC 100, 210; Setaram MicroDSC III. Melting point measurement, Mettler FP-80; potentiometric titration, radiometer VIT90; ultraviolet spectrophotometry, Hitachi U-2000.

The following reagents were used in the experiments: ethyl *p*-aminobenzoate (Kanto

Chem. GR), *n*-butyl *p*-hydroxybenzoate (Kanto Chem. GR). The eutectic mixture was prepared as follows: the minor component was dissolved in a few drops of methanol. As the mixture was ground, the major component was gradually added. The resulting specimen was dried at room temperature in a desiccator containing silica gel.

2.1. Drafting a phase diagram

A mixture of ethyl *p*-aminobenzoate (called "A" below) and *n*-butyl *p*-hydroxybenzoate (called "B" below) was used for the test material. In order to understand the melting process of the test material, the DSC curves of the test material mixture prepared in a variety of concentrations were measured, and a phase diagram was prepared as shown in Fig. 2a. It was found using the diagram method [6] that the eutectic mixture had a ratio of A = 39.7 mol%. This agrees with the measured values by another independent method to be described later in which the liquid phase component obtained by filtered separation of the melted components at the lowest temperature yielded A = 39.9 mol%. In addition, the eutectic mixture peak was found to be nearly 48.8°C in the DSC patterns of all the test materials, regardless of the content of the major component. The DSC pattern of the eutectic mixture obtained by mixing A and B so as to become that percentage had an initial melting temperature of 46.3°C, with the peak 48.8°C, and heat of fusion of 123 J g^{-1}.

2.2. Analysis of the fused material

The filtration tube shown in Fig. 1 was used to separate the liquid phase from the mixed test material at the experimental temperature. The test material was placed on the

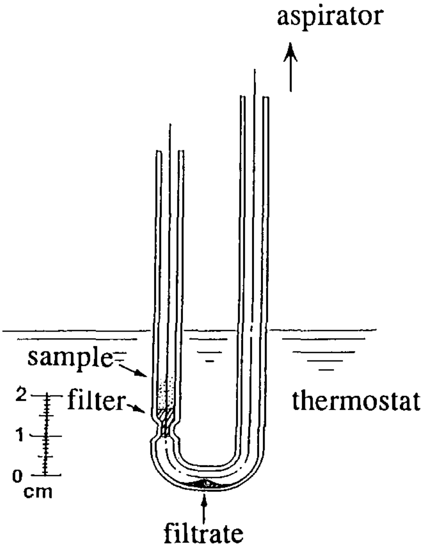


Fig. 1. Filter for the separation of liquid component.

filter, and the separation temperature was maintained by heating in a constant temperature bath, the temperature of which was maintained within ±0.5°C by a Taitec H-100 Thermominder. The liquid component was collected, cooled and solidified by suction filtration of the test material that had reached a thermal equilibrium, the filtered component was taken out by cutting the center of the filter tube, and the composition was analyzed.

The following equipment was used to separate the components deposited at the experimental temperature from the melted mixture of the test material. A receiver was connected to the glass filter and the test material was placed in it. Once the test material had melted by heating in a water bath, the experimental temperature was maintained. The liquid phase was bubble-agitated by slight pressurization so that the solution components did not pass through the filter plate. After maintaining in that state for 30 min, the liquid phase was suction-filtered. The crystals remaining in the filter were washed with a small amount of methanol, and the composition was analyzed.

The amount of A in the test material was determined by non-aqueous titration. Approximately 10 mg of the test material was dissolved in 15 ml of acetone, and potentiometric titration was conducted using 0.02 M perchloric acid–acetic acid solution.

When the A content was larger than 95%, A was calculated by subtracting the content of B from 100%. B was measured photometrically. Approximately 10 mg of test material was precisely measured, placed in a separating funnel with a volume of 100 ml, and dissolved by adding 10 ml of 10% hydrochloric acid. This was extracted three times using 50 ml of chloroform, methanol was added up to a final volume of 250 ml, the absorbance at 280 nm was measured, and the content of B was obtained.

2.3. *Measurement of the heat of dissolution*

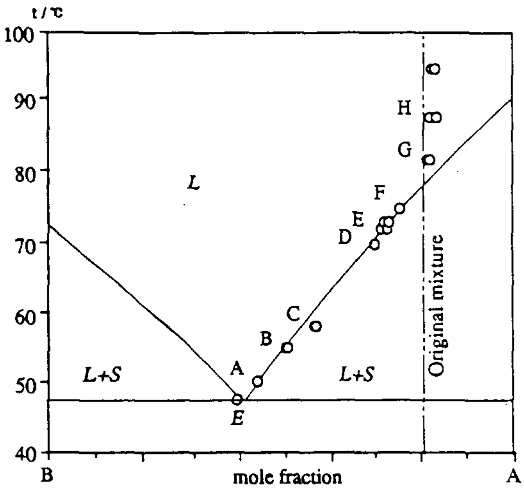
The heat of dissolution was measured using the MicroDSC III. A stainless steel capillary tube with an external diameter of 1.2 mm was installed in the cap of a test material container with 1 cm^3 capacity, and it was set up so that a nichrome wire with a diameter of 0.25 mm could smoothly move through the tube. The melted eutectic mixture was solidified at the tip of a silver wire with a diameter of 0.05 mm, the weight was measured, and it was installed on the tip of the nichrome wire. A was weighed and placed into the test material container.

The test material container was placed in a furnace, and after a certain experimental temperature was reached, the nichrome wire was manipulated and pressed the tip down to the bottom of the container. The heat of dissolution was measured using the DSC peak area produced by the mixing of the two.

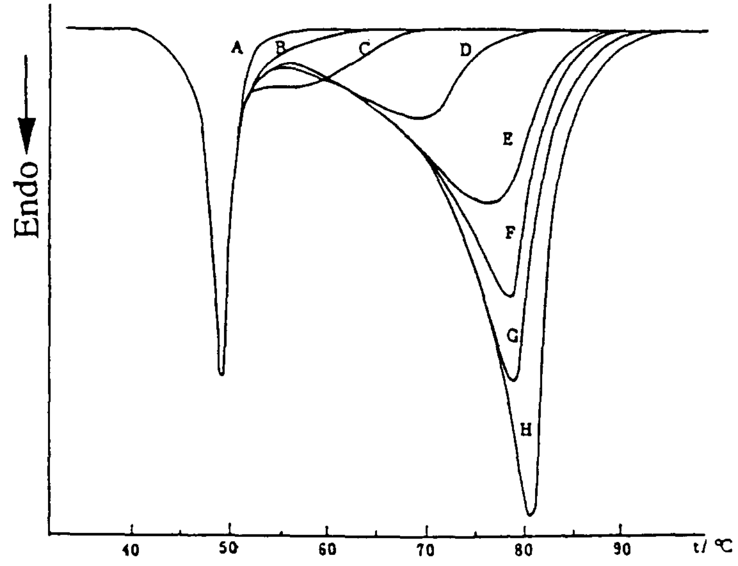
3. Results and discussion

3.1. *Melting process of the test material*

Studies were conducted on the melting process using the test material in which B was added to make A approximately 80 mol%. The test material first began to melt as the temperature increased and reached the eutectic temperature. The liquid phase was separated in the process of increasing the temperature, and measurements of the content of A and the DSC pattern were conducted as samples A–H. These results are shown in the phase diagram of Fig. 2a and in the DSC diagram of Fig. 2b. The initially melted compo-



a) phase diagram



b) DSC

Fig. 2. Analysis for filtrate at temperatures of 40–100°C. (A) Ethyl p-aminobenzoate; (B) n-butyl p-hydroxybenzoate.

nent had the same composition as the eutectic mixture, the concentration of A increased as the temperature increased, and finally the concentration became equal with the initial concentration when all of the test material had melted. When each DSC pattern of the test material is superposed using the eutectic mixture peak as the standard, the peak of the major component became larger as the separation temperature of the test material increased, and finally coincided with the DSC curve of the test material prior to separation.

These facts indicate that in the melting process of the test material which forms the eutectic mixture, the eutectic components first melt in the composition percentages of the eutectic mixture, next the melting of the major component progresses, and finally the entire test material melts.

The heat of fusion of the eutectic mixture separated at 48.8°C was 123 J g^{-1}, and the content of A obtained by titration was 36.19% (39.96 mol%). In measuring the DSC of the test material, the weight of the test material was assumed to be W (mg), and the area of the eutectic peak ΔWH_E (J g^{-1}). If the test material taken at the lowest temperature is assumed to be ΔWH_0 (J g^{-1}), which is considered to be the test material of the eutectic point, then the weight A_m (mg) of the major component A in the main peak can be calculated by the following equation:

$$A_m = W\cdot\{1 - (\Delta WH_E/\Delta WH_0)\} \tag{1}$$

On the other hand, if a is taken to be the weight% of the A obtained from the titration results, weight a' (mg) of A becomes:

$$a' = a\cdot W \tag{2}$$

When subtracting the amount of A existing in the eutectic mixture, the amount of A ex-

Table 1

Analytical results for the main peak component on DSC

t/°C	DSC Sample/mg	$\Delta H_E\cdot\Delta H_0^{-1}$	A_m/mg	Titration a/%	A'_m/mg	Error ($A_m - A'_m$) /mg	Sediment A_s/%
50	2.180	1.0034	−0.007	36.68	0.009	0.016	99.65
58	2.566	0.8465	0.394	42.36	0.302	0.092	99.80
69	2.115	0.5063	1.044	69.94	1.092	−0.048	99.46
72	2.007	0.4715	1.061	68.05	1.024	0.037	99.96
79	2.266	0.4641	1.214	70.51	1.218	−0.004	100.34
82	2.273	0.3274	1.529	79.53	1.539	−0.010	
88	2.252	0.2515	1.686	81.34	1.627	−0.059	
95	2.237	0.2789	1.613	80.05	1.566	−0.047	
Material	2.135	0.3402	1.409	77.18	1.385	−0.024	

ΔH_E, heat of fusion on eutectic peak/J g^{-1}; ΔH_0, heat of fusion of eutectic mixture/J g^{-1}; A_m, weight of A in the main peak measured from DSC values; A'_m, weight of A in the main peak measured from titration values; A_s, percentage of A in the sediments.

isting in the major component (A'_m) can be calculated:

$$A'_m = a' - kW \cdot (\Delta WH_E / \Delta WH_0) \tag{3}$$

where k is the content of A in the eutectic mixture (0.3619).

The results obtained are shown in Table 1. The weight A_m of the main peak obtained from DSC and the weight A'_m in which the eutectic component was subtracted from the weight of A obtained by titration coincided within an error of 0.1 mg and the main peak was indicated by the fact that it only consisted of A.

In order to confirm this fact experimentally, after heating and melting the mixture of test material used in the experiment above, the experimental temperatures were maintained and the analysis was conducted on the deposited solid components. The results of the experiment are also shown in Table 1. From these results it was found that the test material deposited at all temperatures was 100% A, and this proved that the solid phase soluted in the liquid phase of the eutectic mixture melted as the temperature increased.

3.2. Analysis of the major component

The melting of the major component A into the eutectic liquid phase was studied. The eutectic mixture was prepared in advance, the fusion energy was measured by adding A to this, and the change in the fusion energy was studied. The energy of mixing was calculated by deducting the fusion energy for the weight of A and of the eutectic mixture from the total fusion energy of the test material. The changes in the energy of mixing in relation to the ratio of the eutectic mixture and the solute A are shown in Fig. 3. While the eutectic mixture of A existed the heat of mixing increased rapidly in dilution by the coexistence of the minor eutectic component, and became nearly constant at the content of 5%. In this system, when the heat of mixing in the infinite dilution was −1.9 J g^{-1}, the energy was small.

In order to investigate the behavior by which the analytical component melts into the eutectic mixture, the solubility of A into the liquid eutectic composition was measured.

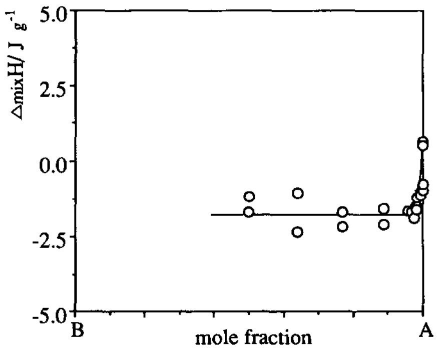


Fig. 3. Heat of mixing for a binary system. (A) Ethyl p-aminobenzoate; (B) n-butyl p-hydroxybenzoate.

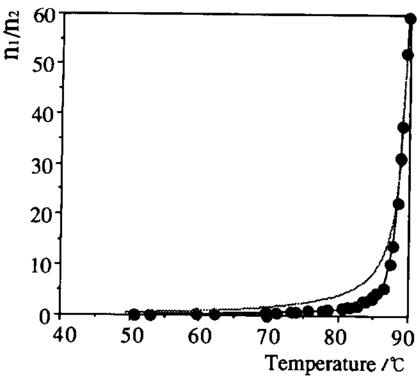


Fig. 4. Solubility of ethyl *p*-aminobenzoate in a eutectic mixture. ●, Experimental; ——, theoretical; n_1, ethyl *p*-aminobenzoate/g; n_2, eutectic/g.

After adding and dissolving A in the eutectic mixture, the measurement temperature was held, the liquid phase was suction-filtered off, and the composition was analyzed. The measurement was accurately conducted by the numeric difference method. On the other hand, the melting point of the test material was obtained by the light permeation method. The solubility curve of A was obtained by converting the results obtained to the weight of the solute in the eutectic mixture. This is shown in Fig. 4. According to this diagram, in the high concentration part of the solubility curve, the change in the amount of solute in relation to the temperature change becomes large, and becomes the maximum in the vicinity of the melting point (90°C). These values nearly approximate the solubility curve of the ideal solution, and there was little discrepancy from Raoult's law. In addition, the solubility curve obtained agreed with the liquid phase curve of the phase diagram by substituting the axes of the diagrams.

3.3. The heat of mixing of the major component

The heat of dissolution for the major component in the eutectic mixture was measured by micro-DSC. Taking A into the test material container to become 100%, 88%, and 75%, the heat of solution of A was measured by dropping into the melted eutectic mixture. The measured results are shown in Table 2. In the measured results, the heat absorbed by the dissolution of A had no temperature dependency during mixing, and in all cases, it was 128 J g^{-1} for the weight of A. That is, within the range of the experiment, the heat of mixing for solid A with the eutectic mixture had a smaller value than the measurable error, and the heat of dissolution was found to be the same value as the heat of fusion.

In a system consisting of components similar to each other, there was little discrepancy from Raoult's Law obtained in Section 3.2, the explanation can be given that there is little difference in the affinity between the constituent component molecules, and the heat of mixing takes a small value.

Table 2
Heat of fusion for ethyl *p*-aminobenzoate

	Composition				
	100%	88%		75%	
	ΔH_{fus}/J g^{-1}	t/°C	ΔH_{sol}/J g^{-1}	t/°C	ΔH_{sol}/J g^{-1}
	128.3	65.5	128.3	60.1	128.1
	129.7	75.5	125.7	65.2	128.6
	129.7	80.3	127.9	87.0	125.6
	128.1	81.5	128.6	87.4	130.1
n	4		4		4
$\bar{x}$	128.95		127.63		128.10
$\hat{\sigma}$	0.87		1.31		1.87

4. Conclusions

When heating and melting mixtures of multi-component systems, it was found from the experimental results above that when the temperature of the test material increases, irrespective of the composition of the test material, the following processes proceed. First, melting begins when the temperature of the test material increases and reaches the eutectic temperature. The composition of the melted components has no relationship to the composition of the test material, and indicates a composition characteristic of the eutectic mixture. After all of the minor component and the major component which corresponds to the eutectic mixture have melted at the eutectic percentage, the major component that remains as a solid melts into the liquid eutectic mixture, and finally everything becomes liquid. Specifically, it was found that melting apparently begins at the eutectic temperature, melting progresses as the temperature increases, the composition of the liquid phase changes to include more of the major component, and the composition of the melted component, when all of the test material has melted, becomes equal to the composition of the test material. In addition, when the purity of the test material becomes high and the major component increases, the amount of eutectic mixture decreases, the distance from the peak of the major component lengthens, and apparently the level has returned to the baseline, but it was found that the eutectic peak did not disappear.

There was no great difference in the mutual affinity between the molecules of the constituent components which have similar chemical structures. Consequently we think that the heat of mixing of the solid phase into the melted components at the eutectic percentage is small, and the heat of fusion of both components is equal to the heat of dissolution. Consequently, the minor component, which is the impurity, has little effect on the heat of fusion when measuring the purity of synthetic products, etc. When measuring the purity, it is necessary to measure from the low temperature part, work up to the eutectic peak with the included impurities, and measure the DSC in a wide range from a sufficiently low temperature.

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