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SOME PROBLEMS IN SOLUTION MICROCALORIMETRY, EXPERIMENTAL EXPERIENCES BY THE AUTHORS, AND THE ENTHALPY-ENTROPY COMPENSATION IN CYCLODEXTRIN + ALCOHOL INCLUSION-COMPLEX FORMATION IN AQUEOUS SOLUTIONS

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ABSTRACT

A short summary of the milestones to the present stage of achievement by the authors,some problems encountered in their course of investigations,and their countermeasures are described. A precise experimental results of the excess enthalpy for (cyclohexane + *n*-hexane) at (298.15 ± 0.001) K are given as a reliability test of the microcalorimetry with small amounts of samples. A couple of enthalpy-entropy compensation rules in the formation equilibria of inclusion complexes between α- and β-cyclodextrins and some alcohols in water at 298.15 K are described, which have been found from their calorimetric determination of the enthalpies and entropies of inclusion after overcoming the problems.

INTRODUCTION

Since the senior author (S.T.) and Amaya measured about 10 mJ of the heat changes on mixing dilute aqueous solutions of certain D- and L-optical isomers in 1966 (ref.1), he and the present coauthors and/or his other collaborators have measured small heats of mixing ($\Delta_{mix}H$) and dilution ($\Delta_{dil}H$) of liquids and those of solution of solids into liquids by batchwise methods, using some kinds of twin-microcalorimeters of heat-conduction type which had been designed originally by Amaya (ref.2) and were developed by Amaya *et al.* (refs.3-9).

In this paper, some experimental problems encountered during the course of these measurements are shortly reported. The enthalpy-entropy compensation in the formation equilibria of inclusion complexes between α- or β-cyclodextrin and several alcohols in water as solvent is also described, which has been obtained from the thermodynamic functions determined by the microcalorimetry after overcoming the problems.

OUTLINE OF DEVELOPMENT

Before describing the problems, the milestones to the present stage of achievement is shortly given.

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Rocking conduction microcalorimeter

A rocking twin-microcalorimeter of the heat-conduction type (ref.4) was used. Mixing vessels used are shown in Fig. 1.

1st stage. In 1966, $\Delta_{\mathrm{mix}}H$ of aqueous solutions of optical isomers were measured (ref.1). The sample size for each run (A) was 2 cm^3/2 cm^3, and a typical amount of heat (H) was about 10 mJ ± less than 20 per cent. The sensitivity of temperature sensor (S) was 6.5 mV/K.

2nd stage. The enthalpies of transfer of some alcohols from aqueous to aqueous cyclodextrin solutions were measured and the molar enthalpies of inclusion ($\Delta_{\mathrm{inc}}H$) of the alcohols into cavities of the cyclodextrin were determined (refs.10 ~14). (A): 3 g/0.75 g, (H): 17.5 mJ ± 2.2 mJ[a]; -2.6 mJ ± 0.2 mJ[a]; (S): 6.5 mV/K.

[a] The calculated standard deviation of the mean.

3rd stage. The $\Delta_{\mathrm{dil}}H$'s of aqueous ethanol were measured over the range of mole fraction $x(C_2H_5OH)=10^{-2}\sim10^{-3}$ (ref.15).(A):3 g/0.75 g,(H):-10~20 mJ ± 0.5 mJ, (S): 27 mV/K.

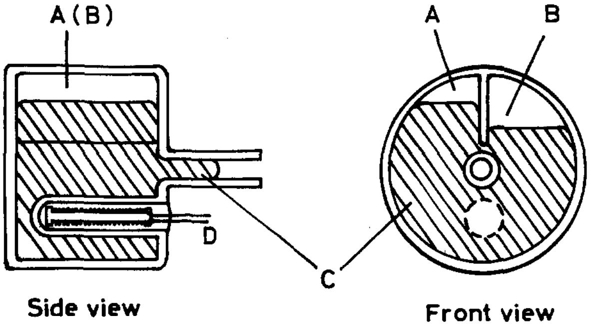

Fig. 1. The mixing vessel used, originally designed by Amaya (ref.4) .
A and B,isolated sample liquids before mixing; C,mercury; D,manganin heater.

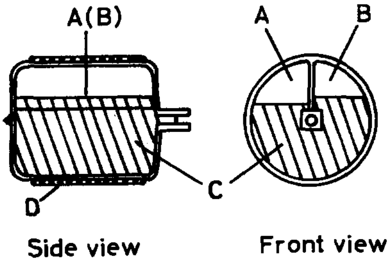

Fig. 2. The small mixing vessel used (originally designed by Amaya and Hagiwara).
A and B,isolated sample liquids; C,mercury; D,heating manganin wire.

Mixing vessels without mercury

By use of an Amaya's "Twin-Conduction Microcalorimeter having large capacity" (ref.5) and a twin-conduction microcalorimeter similar to Kagemoto's (ref.16), $\Delta_{\mathrm{dil}}H$'s of benzene solutions of *p*-terphenyl (ref.17) and isotactic poly(methyl methacrylate) (ref.18) were respectively measured in the mixing vessels without mercury as shown in Fig.3.

Commercial Amaya-Hagiwara twin-microcalorimeter

Applied Electric Laboratory,Ltd. model TCC-204D1 which had been modified by the present authors (ref.19,20) was used. The mixing vessels used are illustrated in Fig.2, whose capacity is about 2.7 cm^3.

1st stage. The $\Delta_{\mathrm{mix}}H$ of (DMSO + methyl methylthiomethyl sulfoxide) *et al.* were measured (ref.20). (A):1 cm^3/1 cm^3∼1.2 cm^3/0.2 cm^3, (H):12 mJ ± 0.5 mJ, (S): 6.5 mV/K. Total amount of each component required was about 15 cm^3.

2nd stage. The excess enthalpies of (cyclohexane + *n*-hexane) at 298.15 K were measured as described below. (A): *e.g.*, 1.0 cm^3/0.2 cm^3, (H): 200 J ± 0.4 J, (S):27 mV/K. Total amount of each pure component needed was about 10 cm^3.

PROBLEMS AND COUNTERMEASURES

Rocking conduction microcalorimeter

At the first stage, deviations of experimental values were large, even when the thermal e.m.f.'s and thermal conductivities of the reference and measuring *p*-*n* semiconductor thermopiles were balanced and the circulating water was thermostatted. Then, the purified mercury to be used in the mixing vessels was shaken with purified water. After separated it from the water, it was passed through pin

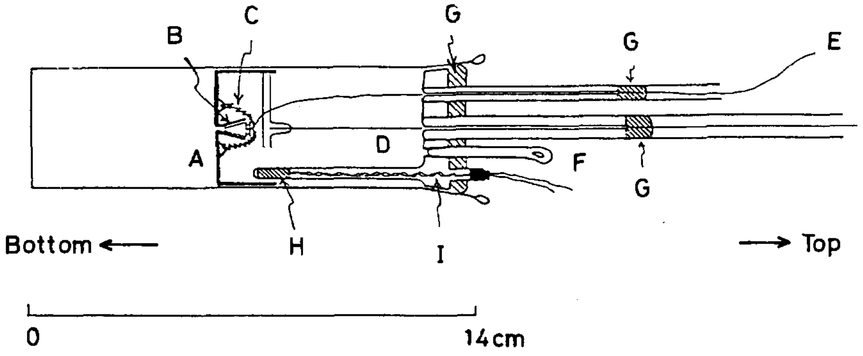

Fig. 3. A mixing vessel (Pyrex) without mercury (ref.17).
A,Pyrex sliding partition; B,PTFE-stopper; C,spring; D,tungsten wire; E,metal wire; F,Pyrex stopper; G,mercury; H,electrical heating resistance (manganin wire); I,opening lid.

holes on a filter paper. It was transferred into the mixing vessels and the sample liquids were loaded. By this procedure, the $\Delta_{mix}H$'s of aqueous solutions of the optical isomers were reproducible to about less than ±20 per cent on repeated runs. Recently the temperature-stability of the mixing vessels in the calorimeter has been enhanced to $\pm 10^{-6}$ K or better. Then, by use of dry mercury the heat of wetting of the mercury and dry surfaces of the Pyrex vessels can be measured precisely: 0.2 mJ of calculated standard deviation of the mean determined(ref.13) shows the attainment of reasonable reproducibility. Consequently, experimental values of small heats may be corrected. Under these conditions, the $\Delta_{inc}H$ of alcohol into cyclodextrin cavities in aqueous solutions was determined, which will be discussed later.

Mixing vessels without mercury

In the $\Delta_{dil}H$ measurements of dilute benzene solutions (less than 0.004 in mole fractions) of *p*-terphenyl on the rocking conduction microcalorimeter at the first stage, relative amounts of heats of wetting were large and no reproducible values were obtained. Moreover every peak of the first stirring which followed behind mixing was smaller than reproducible peaks of successive stirrings. The reason for the latter phenomenon is now undissolved.

To avoid the problems produced from heats of wetting and any others,new mixing vessels without contact with mercury were designed as shown in Fig.3. By use of this kind of vessels,accurate values of $\Delta_{dil}H$ of dilute benzene solutions were determined (ref.17),but these vessels required relatively large amounts of samples and heat of friction was large.

Commercial Amaya-Hagiwara twin-microcalorimeter

The same kinds of problems as described above were overcome by the same countermeasures. Reliable results were obtained with small amounts of samples. An example will be described under next sub-heading.

EXCESS ENTHALPY (H^E) OF (CYCLOHEXANE + *n*-HEXANE)

To test the reliability of the results obtained after overcoming the problems, H^E of (cyclohexane + *n*-hexane) was determined at (298.15 ± 0.001) K.

Materials and experimental procedures

The cyclohexane (Merck,Uvasol) was fractionally distilled over phosphorus pentoxide. Analysis by g.l.c. (ref.21) showed no impurity peak. Its purity was 99.99 mole per cent,which was obtained by d.s.c. on Daini-Seikosha SSC/560. The *n*-hexane (Phillips Petroleum Co.,Research Grade),whose stated purity was 99.95 mole per cent,was used without further purification. The water content of the samples determined by coulometric Karl Fischer titration on Mitsubishi Moisture Meter Model

CA-05 was 0.001 and 0.0064 mole per cent,respectively,for the cyclohexane and n-hexane. The mercury was purified as described previously(ref.21).

The modified commercial Amaya-Hagiwara calorimeter (ref.22) and the small mixing vessels (Fig. 2) were used. Each sample liquid was loaded into the vessel from a weighed syringe fitted with a suitably bent Hamilton Model KF 730 hypodermic needle. Circulating water was thermostatted within $\pm 10^{-3}$ K and fluctuation of the calorimeter temperature was less than $\pm 10^{-6}$ K. The procedures has been described (refs.21,22).

Results and discussions

The H_m^E results are given in Table 1. The coefficients A_i's of the smoothing equation:

$$H_m^E/\mathrm{J\cdot mol^{-1}} = x(1-x)\sum_{i=1}^{k} A_i(1-2x)^{i-1} \qquad (1)$$

and the calculated standard deviation of the fits s_f obtained by the method of least squares are $A_1 = 864.12$, $A_2 = 250.93$, $A_3 = 101.41$, $A_4 = 29.534$, and $s_f = 0.14\ \mathrm{J\cdot mol^{-1}}$, where x denotes the mole fraction of n-hexane and choice of the appropriate number of the coefficients was based on the variation of the value of s_f. Deviations of the experimental values of H_m^E from the calculated ones are within ± 0.2 per cent of the latter, except a most dilute run, as shown in Fig. 4.

TABLE 1

Molar excess enthalpies H_m^E for $\{(1-x)C_6H_{12} + xC_6H_{14}\}$ at 298.15 K.

x	$H_m^E/\mathrm{J\cdot mol^{-1}}$	x	$H_m^E/\mathrm{J\cdot mol^{-1}}$	x	$H_m^E/\mathrm{J\cdot mol^{-1}}$
0.03905	45.18	0.34306	214.99	0.73582	148.68
0.06684	73.14	0.43798	220.72	0.78928	124.32
0.16499	149.70	0.46957	218.82	0.80147	118.38
0.19925	169.00	0.58339	200.70	0.86665	83.45
0.29541	205.27	0.64692	182.38	0.95325	31.00

Fig. 4 shows also the overall agreement of the present results with those of the most reliable measurements reported by different authors which have been determined by different methods: this work, twin-batch microcalorimeter,$s_f = 0.14\ \mathrm{J\cdot mol^{-1}}$; Marsh and Stokes, isothermal displacement calorimeter (ref.23); Murakami and Benson, isothermal dilution calorimeter,$s_f = 0.21\ \mathrm{J\cdot mol^{-1}}$ (ref.24); Tanaka, D'arcy,and Benson, LKB flow microcalorimeter,$s_f = 0.29\ \mathrm{J\cdot mol^{-1}}$ (ref.25). The deviations of all three comparison sets fall almost within the ± 0.2 per cent range. The present results for cyclohexane + n-hexane mixture are in excellent agreement with those of Marsh and Stokes (ref.23).

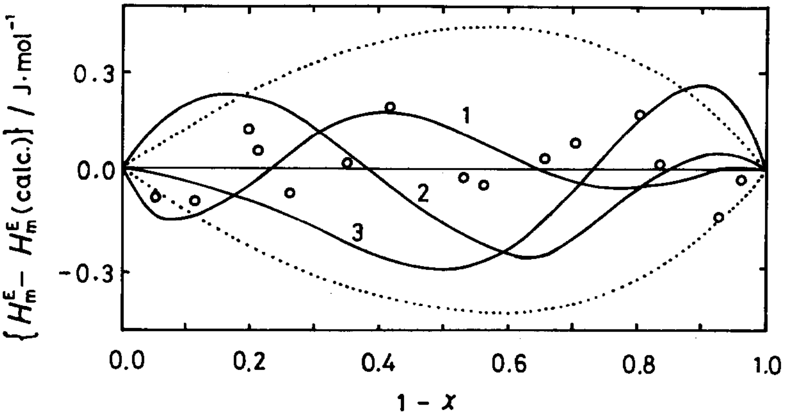

Fig. 4. Difference plot for molar excess enthalpies of (cyclohexane + n-hexane) at 298.15 K where x is the mole fraction of n-hexane and H_m^E (calc) is the value calculated from Eq.(1) with the coefficients given in the text. o,Experimental results. Curves: 1,Marsh and Stokes (ref.23); 2,Murakami and Benson (ref.24); 3, Tanaka,D'arcy,and Benson (ref.25). Dotted curves represent ±0.2 per cent deviation.

Other reliability tests of the microcalorimeter system were carried out earlier by use of an endothermic mixture composed of a pair of liquids having significantly different densities (benzene + carbon tetrachloride) and an exothermic mixture (chlorobenzene + toluene) (ref.22). All results verify the high reliability of this microcalorimeter and overall performance of the calorimeter system.

ENTHALPY-ENTROPY COMPENSATION IN CYCLODEXTRIN + ALCOHOL INCLUSION-COMPLEX FORMATION IN AQUEOUS SOLUTIONS

From the reliable values of $\Delta_{mix}H$ and $\Delta_{dil}H$ of dilute aqueous solutions of cyclodextrins and some alcohols which were determined calorimetrically by the present authors, the enthalpies of transfer of some alcohols from aqueous to aqueous cyclodextrin solutions were obtained at various mole fractions of the alcohols at 298.15 K in very dilute concentration range. By using the knowledge of those as a function of the mole fraction, the limiting values of the enthalpy of transfer and the molar ratio of the alcohol included at infinite dilution,the equilibrium constants,the enthalpies of inclusion,the Gibbs energies of inclusion, and the entropies of inclusion were determined on the basis of the theoretical procedures proposed by the authors (refs.10,12) by using merely the direct microcalorimetric data at only one temperature (refs. 10∿14).

The results elucidate the importance of the enhancement of entropy as a main "driving force" of the molecular inclusion of the alcohol molecules in these aqueous solutions. In this case two different enthalpy-entropy compensation rules were obtained as shown in Fig. 5. One (*a*) corresponds to the formation equilibrium of stronger (more stable) complexes ($\Delta_{\mathrm{inc}}G_{\mathrm{m}} < -22$ kJ·mol^{-1}) and the other (*b*) to that of weaker (less stable) ones ($\Delta_{\mathrm{inc}}G_{\mathrm{m}} > -20$ kJ·mol^{-1}). The isoequilibrium temperatures (refs.26,27) are respectively, (*a*) 339 K and (*b*) 292 K.

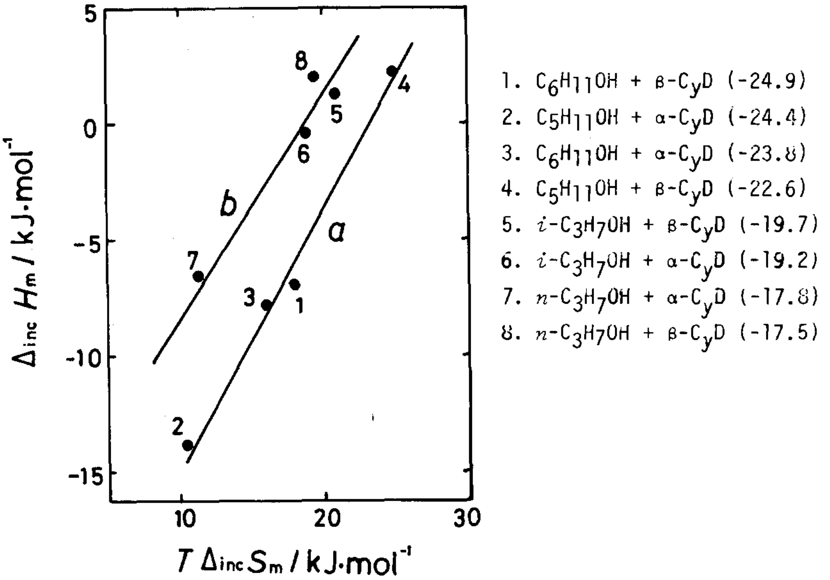

Fig. 5. Compensation rules between the enthalpy values and entropy values of the formation of 1:1 inclusion complexes in aqueous solutions at 298.15 K. Figures in parentheses are the values of $\Delta_{\mathrm{inc}}G_{\mathrm{m}}$/kJ·mol^{-1} :values for $\Delta_{\mathrm{inc}}H_{\mathrm{m}}$ and $\Delta_{\mathrm{inc}}S_{\mathrm{m}}$ were tabulated in ref. 14.

All of these results reveal the significant role of the hydrophobic hydration in the molecular inclusion phenomena in aqueous media.

In concluding,the authors predict some future problems in microcalorimetry as follows. If one will proceed with the effort for better accuracy and precision by the batchwise methods,he might encounter any problems about,*e.g.*, the superposition of heat of oxidation of mercury with oxygen dissolved in sample liquids,variation of the heat of wetting with liquid concentration,or preferential wetting.

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