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The Heats of Solution of Optically Active Compounds and the Corresponding Racemic Compounds

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The heats of solution of crystalline amino acids and hydroxy acid in water at 298.15 K were measured with a twin isoperibol calorimeter. It was found, as was expected from the theory, that the difference in the heat of solution between optically active compounds and their corresponding racemic compounds was appreciably large compared with the heat of mixing of concentrated aqueous solutions of *d*- and *l*-optical isomers.

According to the statistical thermodynamic theory for solutions containing *d*- and *l*-optical isomers, it was previously found by one of the present authors that first term of the excess enthalpy of the system was proportional to the inverse of the absolute temperature, $1/T$.[1,2] Takagi *et al.* measured the heat of mixing of aqueous solutions of *d*- and *l*-optical isomers at 298.75 K, but the values they obtained were too small to test the relation.[3] This may be attributed to the free rotation of optical isomers in solution, resulting in an averaging out, of the difference in interaction energy for each configuration.

However, in the solid state each molecule is confined in the cage formed by the surrounding molecules and is fixed to the most favorable configuration, and difference in configuration energy between an optically active compound and the corresponding racemic compound can be expected to be appreciably large.

In order to test this experimentally, the heats of solution of crystalline optically active compounds and the corresponding racemic compounds were measured.

Experimental

Materials. The alanine, D-glutamic acid, histidine, threonine, and L-valine were purchased from the Takara Kohsan Co., Ltd., the DL-glutamic acid, DL-valine and tartaric acid were also purchased, but from the Tokyo Kasei Co., Ltd. Their purities were certified by these makers and were guaranteed to be more than 99%.

These samples were dried over silica gels in a desiccator at room temperature for at least 3 d before use and were then used without further purification.

Apparatus and Procedures. The calorimeter used in this experiment was a Model TIC-2D twin isoperibol calorimeter manufactured by the Tokyo Riko Co., Ltd.; it is shown in Fig. 1.

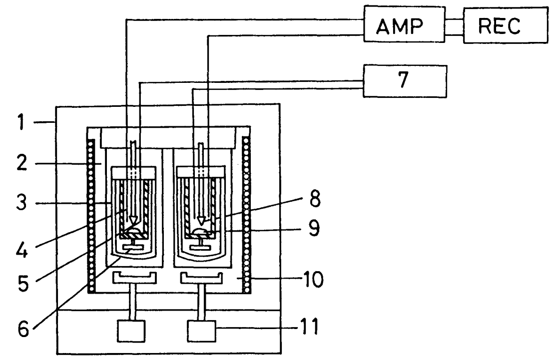

Fig. 1. Twin isoperibol calorimeter.
1): Case, 2): aluminum block, 3): Dewar vessel, 4): thermistor, 5): heater, 6): magnetic stirrer, 7): heater power source, 8) ampoule breaking device, 9): ampoule, 10): temperature controller, 11): motor for stirring, AMP: d.c.-amplifier, REC: recorder.

It consists of two identical transparent Dewar vessels, about 0.15 dm^3 in inner volume and equipped with a pair of thermistors with equal temperature coefficients, a pair of identical calibrating heaters, a pair of ampoule-breaking devices, and a pair of stirres driven by outside, rotating, permanent magnets. All these parts are installed in an aluminum block, which can be thermostatted within ±0.004 °C at any desired arbitrary temperature between −10 °C and 80 °C. Precise results can easily obtained by the employment of this twin system. During the experiment, the calorimeter was kept at 298.15±0.004 K. In each measurement, from 50 to 100 mg of the sample were sealed in a glass ampoule, and the sample and the blank ampoule were, respectively, set in the measurering and reference Dewar vessels, filled with 0.1 dm^3 of distilled water.

The calorimeter was left for 24 h to reach thermal equilibrium, after which the sample and the blank ampoule were broken simultaneously with the ampoule-breaking devices. The dissolution was complete within 3 to 20 min, according to the sample. The difference in temperature between the two Dewar vessels was recorded on a chart recorder. The temperature change on dissolution was obtained by extrapolating the fore and after linear parts of the calorimetric curves (Challoner Method).[4] Electrical calibration was also made after the solution experiment, while the temperature change was obtained by the same procedure. The heat of solution, q_s, was derived by means of the following equation:

$$q_s = q_c \frac{\Delta t_s}{\Delta t_c}$$

where q_c is the heat quantity for electrical calibration, and where Δt_s and Δt_c are the temperature changes in solution and in the calibration experiment respectively.

Calibration of the Calorimeter. The calorimeter was calibrated with the NBS standard reference material 724a, tris(hydroxymethyl)aminomethane (THAM), and a 0.1 N (f=1.008) hydrochloric acid solution at 298.15 K.

Before use, THAM was dried *in vacuo* at room temperature for 1 h.

About 500 mg of THAM was sealed in a glass ampoule and set in the Dewar vessel filled with a 0.1 dm^3 hydrochloric acid solution, and then the heat of solution was measured by the procedure described above. The mean value of the molar

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enthalpy of solution obtained by 3 runs was −29.32±0.09 kJ/mol.

The value recommended by Hill *et al.* was −29.744±0.003 kJ/mol.[5] Accordingly, the systematic error of our calorimeter was 1.4%, and the precision was 0.34%.

Results and Discussion

The values of the heat of solution of crystalline optically active compounds and their corresponding racemic compounds, and the difference between the two, are shown in Tables 1 and 2 respectively. This experiment was carried out under the conditions described above, so that these relative amounts gave final concentrations of about 0.01 mol/kg. Therefore, the heat of solution is considered to be the value at infinite dilution obtained by Spink and Auker.[6]

Table 1. Heats of solution of amino acids and tartaric acid in water at 298.15 K

Substance	Sample weight (g)	Observed heats of solution (J)	Heats of solution (kJ/mol)	
DL-Alanine	0.1001	10.60	9.44	
	0.1004	10.44	9.27	9.35±0.09
	0.1003	10.51	9.34	
L-Alanine	0.1000	8.41	7.49	
	0.1004	8.37	7.43	7.35±0.21
	0.1001	8.06	7.14	
DL-Glutamic acid	0.0512	10.0	28.8	
	0.0543	10.5	28.6	28.6±0.2
	0.0510	9.84	28.4	
D-Glutamic acid	0.0499	8.32	24.5	
	0.0497	8.29	24.5	24.5±0.0
	0.0490	8.17	24.5	
DL-Histidine	0.1005	9.78	15.1	
	0.1010	9.96	15.3	15.1±0.2
	0.0979	9.38	14.9	
L-Histidine	0.1006	8.90	13.7	
	0.1006	8.79	13.6	13.6±0.1
	0.1011	8.86	13.6	
DL-Threonine	0.1001	8.12	9.66	
	0.1000	8.10	9.65	9.61±0.08
	0.1012	8.09	9.53	
L-Threonine	0.1009	8.36	9.87	
	0.1011	8.32	9.81	9.78±0.13
	0.1004	8.14	9.65	
DL-Valine	0.1010	4.44	5.15	
	0.1002	4.41	5.16	5.16±0.01
	0.1006	4.43	5.16	
L-Valine	0.1009	2.46	2.86	
	0.1006	2.46	2.87	2.87±0.01
	0.1010	2.48	2.88	
(±)-Tartaric acid	0.0987	16.9	25.7	
	0.1000	17.1	25.6	25.6±0.1
	0.1003	17.1	25.6	
(+)-Tartaric acid	0.1002	11.0	16.5	
	0.1007	10.7	15.9	16.2±0.3
	0.1002	10.9	16.3	

Table 2. Differences in the heat of solution between optically active compounds and their corresponding racemic compounds

Substance	Differences in the heat of solution at 298.15 K (kJ/mol)
Alanine	2.00±0.21
Glutamic acid	4.1±0.2
Histidine	1.5±0.2
Threonine	0.17±0.13
Valine	2.29±0.01
Tartaric acid	9.4±0.3

It may be seen from Table 2 that the difference in the heat of solution between optically active compounds and their corresponding racemic compounds, which corresponds to the heat of mixing of optical isomers and their optical antipodes in the solid state, is appreciably large.[7]

On the other hand, the heat of mixing of optical isomers and their optical antipodes in the liquid state was nearly zero.[3]

This fact may be explained qualitatively as follows by employing simplified model of optical isomers.[1,8]

We assume that the optically active molecule is a cylindrical rod with circular planes at both ends, and that the circular planes are composed of three different elements a, b, and c.

For the *d*-isomer, the arrangement of these three elements is in the order a, b, and c clockwise as viewed from the top, while for its antipode, the *l*-isomer, it is a, b, and c anticlockwise, the peripheral part is composed of a uniform element, n, as is shown in Fig. 2.

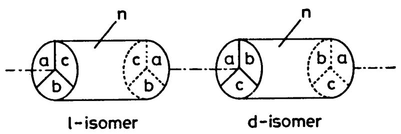

Fig. 2. A model of optical isomers.

Two neighboring molecules on the same axis can take three different states, which are obtained by rotating one of the molecules around the axis, with interacting pairs of elements $\begin{bmatrix} a & b & c \\ a & c & b \end{bmatrix}$, $\begin{bmatrix} a & b & c \\ c & b & a \end{bmatrix}$, and $\begin{bmatrix} a & b & c \\ b & a & c \end{bmatrix}$, whose interaction energies are $U_{aa}+2U_{bc}$, $U_{bb}+2U_{ac}$, and $U_{cc}+2U_{ab}$ respectively.

For the give of simplicity, we further assume that, in a system consisting of a large number of molecules, these molecules are arranged in such a way that their cylindrical axes lie on a straight line, and that each axis is surrounded by z nearest axes, as is shown in Fig. 3.

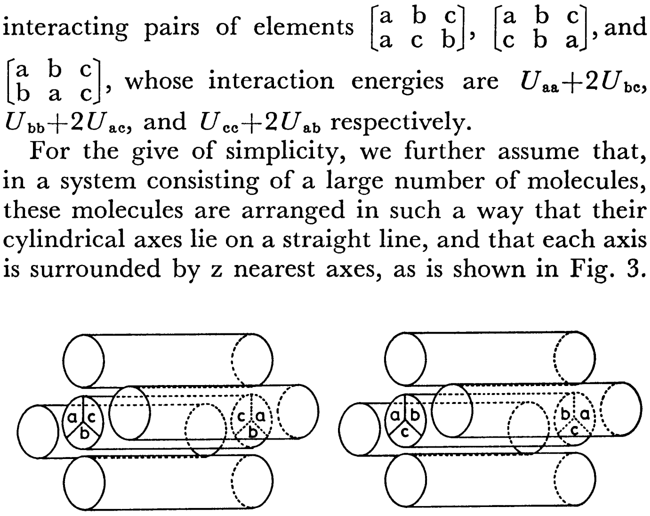

Fig. 3. Arrangement of optical isomers.

In the solid state, the relative angular positions of two neighboring molecules which lie on the same axis, are fixed and take the most stable position among the three states.

In the system of a pure *d*- or *l*-isomer, the interaction energy of the pair of circular planes for each of the three states takes such values as:

$$U_{\mathrm{aa}} + 2U_{\mathrm{bc}},\ U_{\mathrm{bb}} + 2U_{\mathrm{ac}},\ \text{and}\ U_{\mathrm{cc}} + 2U_{\mathrm{ab}}$$

respectively, where U_{ij} denotes the interaction energy of a pair of i and j elements.

The total configurational energy of the system consisting of N molecules of the pure isomer, $U^{\mathrm{s}}_{\mathrm{TA}}$, is expressed as:

$$U^{\mathrm{s}}_{\mathrm{TA}} = \frac{z}{2}NU_{\mathrm{nn}} + NU_{\mathrm{Amax}}$$

where U_{nn} and U_{Amax} denote the interaction energy between peripheral elements, n, and the interaction energy of the most stable position, respectively.

For a racemic system which consists of $N/2$ molecules of the *l*-isomer and $N/2$ molecules of the *d*-isomer, we may assume that the *l*-isomer and *d*-isomer lie alternately along the axis. Therefore, the interaction energy of pair of circular planes for each of the three states takes these values:

$$U_{\mathrm{aa}} + U_{\mathrm{bb}} + U_{\mathrm{cc}},\ U_{\mathrm{ab}} + U_{\mathrm{ac}} + U_{\mathrm{bc}},\ \text{and}$$
$$U_{\mathrm{ab}} + U_{\mathrm{ac}} + U_{\mathrm{bc}}.$$

Two of them have equal values.

In the solid state, the relative angular position around the axes of two neighboring molecules is fixed. The total configurational energy of the system is, then expressed as:

$$U^{\mathrm{s}}_{\mathrm{TR}} = \frac{z}{2}NU_{\mathrm{nn}} + NU_{\mathrm{Rmax}}$$

where U_{Rmax} denotes the interaction energy of the most stable state among the three.

Therefore, the heat of mixing of *l*- and *d*-optical isomers in the solid state, $\Delta H^{\mathrm{s}}_{\mathrm{m}}$, is expressed as: $\Delta H^{\mathrm{s}}_{\mathrm{m}} = N(U_{\mathrm{Rmax}} - U_{\mathrm{Amax}})$.

In general, U_{Rmax} and U_{Amax} have different values, and the heat of mixing has a finite value. However, in the liquid state each molecule can rotate freely around the axis. The average interaction energy is, then the mean of three states, and the total configurational energy of N pure optical isomers, $U^{\mathrm{l}}_{\mathrm{TA}}$, may be expressed as:

$$\begin{aligned} U^{\mathrm{l}}_{\mathrm{TA}} &= \frac{z}{2}NU_{\mathrm{nn}} + \frac{N}{3}\{(U_{\mathrm{aa}} + 2U_{\mathrm{bc}}) + (U_{\mathrm{bb}} + 2U_{\mathrm{ac}}) \\ &\quad + (U_{\mathrm{cc}} + 2U_{\mathrm{ab}})\} \\ &= \frac{z}{2}NU_{\mathrm{nn}} + \frac{N}{3}\{(U_{\mathrm{aa}} + U_{\mathrm{bb}} + U_{\mathrm{cc}}) \\ &\quad + 2(U_{\mathrm{ab}} + U_{\mathrm{ac}} + U_{\mathrm{bc}})\}. \end{aligned}$$

Similarly, for racemic systems, the total configurational energy, $U^{\mathrm{l}}_{\mathrm{TR}}$, may be expressed as:

$$\begin{aligned} U^{\mathrm{l}}_{\mathrm{TR}} &= \frac{z}{2}NU_{\mathrm{nn}} + \frac{N}{3}\{(U_{\mathrm{aa}} + U_{\mathrm{bb}} + U_{\mathrm{cc}}) \\ &\quad + 2(U_{\mathrm{ab}} + U_{\mathrm{ac}} + U_{\mathrm{bc}})\}. \end{aligned}$$

Accordingly, the heat of mixing in the liquid state, $(U^{\mathrm{l}}_{\mathrm{TR}} - U^{\mathrm{l}}_{\mathrm{TA}})$ becomes zero in this approximation.

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