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Solvent Effect on the Liquid–Liquid Partition of 21*H*,23*H*-Porphine between Various Organic Solvents and Acidic Aqueous Solutions

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The liquid–liquid partition equilibrium of 21*H*,23*H*-porphine has been investigated at 25 °C. Organic phases were heptane, dodecane, carbon tetrachloride, benzene, toluene, chloroform, dichloromethane, and 1-octanol. The acidic aqueous phases were 5×10^{-2}—5×10^{-1} M hydrochloric acid. Porphine is present in such acidic solutions as a diprotonated form and no dimerization was found in any of the systems. The organic solvent effect on the partition coefficient of porphine is discussed with the aid of regular solution theory, and the solubility parameter of porphine is estimated as 10.7 ± 0.6 cal$^{1/2}$ cm$^{-3/2}$.

Porphyrin and related derivatives are important compounds in biochemistry and geochemistry. In relation with chemical separation and natural migration of these porphyrin compounds, a systematic study on the solution behavior of porphyrins and their metal chelates is desirable. However, little is known about the solubility and the liquid–liquid partition of these porphyrin compounds. The solution behavior of a solute is governed by the physicochemical nature of the solute and solvents. The liquid–liquid partition of various organic solutes including metal β-diketonate complexes has been systematically studied and elucidated with the aid of regular solution theory and the scaled particle theory.1—6)

In the present study, we have prepared high purity 21*H*,23*H*-porphine, which is the simplest porphyrin compound, having no substituent group. We have investigated its partition equilibria between various organic solvents and acidic aqueous solutions. The solvent effect is quantitatively discussed with the aid of regular solution theory.

Experimental

Materials. 2-Pyrrolecarbaldehyde (99% purity, Aldrich) was used as purchased. Carbon tetrachloride, chloroform, and dichloromethane were of spectroscopic grade (Spectrosol, Dojindo Lab.), and chloroform was used after washing several times with redistilled water. Other organic solvents were of guaranteed reagent grade and purified by ordinary methods.7)

Hydrochloric acid was of analytical reagent grade (Wako Co.). The acid solutions were standardized with sodium carbonate (primary standard, Asahi glass Co.).

Unless otherwise stated, reagents used were of guaranteed reagent grade.

Preparation and Purification of 21*H*,23*H*-Porphine. 21*H*,23*H*-Porphine was synthesized by the method of Longo et al.,8) and purified by a method modified somewhat from those of Rothemund9) and Krol.10) 2-(Hydroxymethyl)pyrrole, a starting material for synthesis of porphine, was prepared by reduction of 2-pyrrolecarbaldehyde with sodium borohydride according to the literature.11) A crude product of porphine was obtained by keeping the dilute solution of 2-(hydroxymethyl)pyrrole in ethylbenzene at 100±2 °C with stirring. The ethylbenzene solution after reaction was fed into a silica-gel column (Kicselgel 60 HR, Merck) and eluted with benzene. The benzene solution obtained was washed with 50% (v/v) acetic acid and then 0.35% (w/v) hydrochloric acid. Porphine was extracted from benzene to 5% (w/v) hydrochloric acid. The aqueous solution was neutralized with a saturated sodium acetate solution and shaken with benzene to extract porphine. After washing with water, the benzene solution was concentrated with a rotary evaporator, and methanol was added to crystallize the porphine. A dark auburn crystalline product was filtered and dried over phosphorus pentaoxide in vacuo at 120 °C. Identification of the product was accomplished by C, H, N analysis, mass spectroscopy, proton magnetic resonance spectroscopy, and electronic absorption spectroscopy. The purity was also checked with high-performance liquid chromatography (column, LiChrosorb RP-18; mobile phase, acetone : acetonitrile : water=25 : 200 : 11.3; detection wavelength, 395 nm) and found to be more than 99%.

Apparatus. Absorbance of a solution was measured with a spectrophotometer (UVIDEC-2, JASCO). To prevent adsorption of porphine onto the wall of the glassware including volumetric flasks, and the quartz cell in the absorbance measurement, they were treated with dimethyldichlorosilane before use.

The extraction vial was shaken with a mechanical shaker at about 350 strokes per min. The density of the porphine solution was measured with a digital precision density meter (Anton Paar DMA-50). All experiments were carried out in a thermostated room at 25±0.5 °C.

Partition Experiments. An organic solvent and an acidic aqueous solution were preequilibrated to each other. A certain volume of the organic solution of porphine in 10^{-7}—10^{-4} M (1 M=1 mol dm^{-3}) was shaken with the acidic aqueous solution for 5—60 min and centrifuged. The ionic strength of an acidic aqueous solution was kept at 0.50 M with sodium chloride. The distribution ratio (D) of porphine which was the ratio of the total concentration of porphine in the organic phase to that in the aqueous phase was determined from the absorbance of the organic phases before (A_i) and after (A) shaking; $D=(V_a/V_0)A/(A_i-A)$, where V_a and V_0 are volume of the aqueous and the organic phase respectively. To ascertain achievement of the partition equilibrium, porphine was dissolved in an acidic aqueous solution and shaken with the organic solvent. The distribution ratio determined from the absorbance of the

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Table 1. Wavelengths Used for the Absorbance Measurement of Porphine in Various Solvents

Solvent	Wavelength[a)]/ nm	Wavelength[b)]/ nm
Heptane	391.6	
Dodecane	393.5	
Carbon tetrachloride	396.8	490.1
Benzene	396.4	489.5
Toluene	396.4	
Chloroform	394.8	489.7
Dichloromethane	393.4	488.9
1-Octanol	393.7	
Water[c)]	393.9	542.1

a) Soret band. b) Q Band was also used for the partition measurement. c) 0.5 M hydrochloric acid.

equilibrated aqueous phases is in good agreement with that obtained above. The wavelengths used for the absorbance measurement in different organic solvents are shown in Table 1. Lambert-Beer's rule was confirmed in the absorbance range of 0.13—0.67 in benzene and the acidic aqueous solution.

Density Measurement. The partial molar volume of porphine was calculated from the densities of porphine solutions in varying concentrations. The solubility of porphine in various organic solvents was remarkably low. A sufficient solubility of porphine to measure the difference in the density of the solution was obtained using only pyridine as a solvent. The concentration range of porphine was 4×10^{-4}—2×10^{-3} M. The uncertainty in the density measurement was within $\pm1\times10^{-5}$ g cm^{-3}.

Results and Discussion

Partition Equilibrium. Porphine (denoted as H_2A) is a nitrogen base and its partition between an organic phase and an acidic aqueous phase can be represented by the following equilibria.

$$H_2A + nH^+ \rightleftarrows H_{n+2}A^{n+} \qquad K_n = \frac{[H_{n+2}A^{n+}]}{[H_2A][H^+]^n}, \quad (1)$$

$$H_2A \rightleftarrows H_2A_o \qquad P = \frac{[H_2A]_o}{[H_2A]}, \quad (2)$$

where K_n and P are the overall protonation constant and the partition coefficient, respectively. The subscript o refers to the organic phase. Dimerization of porphine in the organic and aqueous phases is negligible under the present experimental conditions of sufficiently low concentration of porphine (vide infra). The distribution ratio of porphine is given by

$$D = \frac{[H_2A]_o}{[H_2A] + [H_3A^+] + [H_4A^{2+}] + \cdots + [H_{n+2}A^{n+}]}. \quad (3)$$

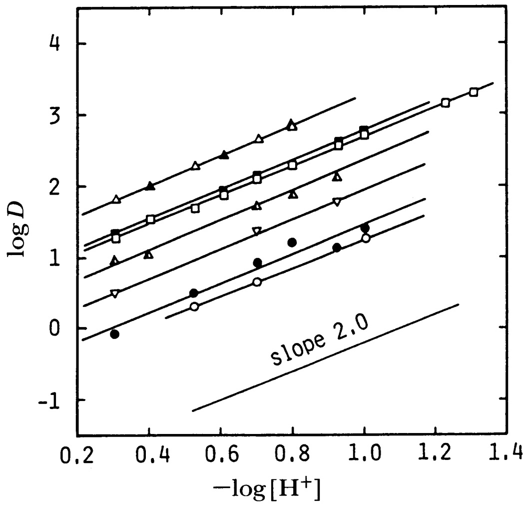

Fig. 1. Distribution ratio of porphine as a function of hydrogen ion concentration in the aqueous phase.
○, Heptane; ●, dodecane; ▲, carbon tetrachloride; □, benzene; ■, toluene; △, chloroform; ▲, dichloromethane; ▽, 1-octanol.

Table 2. Effect of the Porphine Concentration on the Partition Equilibrium of Porphine at 25 °C

$[H^+]$/M	$[\text{Porphine}]_{\text{org}}$[a)]/ M	$[\text{Porphine}]_{\text{aq}}$[b)]/ M	$\log P\cdot K_2^{-1}$
4.98×10^{-1}	3.80×10^{-7}	1.96×10^{-8}	0.68
3.98×10^{-1}	1.52×10^{-6}	4.40×10^{-8}	0.74
2.99×10^{-1}	3.90×10^{-6}	7.82×10^{-8}	0.64
2.49×10^{-1}	7.15×10^{-6}	9.50×10^{-8}	0.67
1.99×10^{-1}	6.62×10^{-6}	5.25×10^{-8}	0.70
1.59×10^{-1}	1.56×10^{-5}	7.84×10^{-8}	0.70
1.19×10^{-1}	1.69×10^{-4}	4.62×10^{-7}	0.72
9.96×10^{-2}	1.68×10^{-4}	3.31×10^{-7}	0.70
5.97×10^{-2}	1.64×10^{-4}	1.19×10^{-7}	0.69
4.98×10^{-2}	1.64×10^{-4}	8.50×10^{-8}	0.68

a) Equilibrium concentration in benzene phase. b) Equilibrium concentration in aqueous phase.

If a single species of protonated porphine is present in the aqueous phase, the distribution ratio can be written as

$$D = \frac{P}{K_n[H^+]^n}. \quad (4)$$

The dependence of the distribution ratio of porphine on the hydrogen ion concentration and the solute concentration was investigated in detail in the benzene system. The plots of $\log D$ as a function of $\log[H^+]$ are shown in Fig. 1, together with those for other solvents. The plots for benzene give a straight line with a slope of 2.0 which is determined by the least squares method, and those for other solvents also give the slope of 2.0±0.1. These demonstrate that only a single species of diprotonated porphine, H_4A^{2+}, is present in the acidic aqueous solution of 5×10^{-2}—5×10^{-1} M H^+. The effect of the porphine concentration on the partition equilibrium was investigated, that is, the distribution ratios of porphine with various initial concentrations were determined at different hydrogen ion concentrations. In Table 2, the results are expressed as the product of two constants of P and K_2^{-1} calculated from Eq. 4 by knowing $n=2$. A constant value of 0.69±0.03 is obtained over a wide range of porphine concentration, and this supports no dimerization of porphine in either phase.

The values of $\log P \cdot K_2^{-1}$ for different solvents are listed in Table 3. The value increases in the following order; heptane<dodecane<1-octanol<carbon tetrachloride<benzene≈toluene<chloroform≈dichloromethane. As the protonation constant K_2 is not influenced by the organic solvents, the difference in these values is directly proportional to those in the partition coefficients P for the organic solvents.

Partial Molar Volume of Porphine. The partial molar volume is one of the important physical measures in solution chemistry, but no data for porphine and related compounds have yet been reported. In this paper, the partial molar volume of porphine is measured and used in the calculation based on regular solution theory. The partial molar volume of porphine is calculated from the relation between the mean molar volume obtained from the density measurement, V_m, and the molar fraction of porphine, X_2,

$$V_m = \overline{V}_1 + (\overline{V}_2 - \overline{V}_1)X_2 \tag{5}$$

where $\overline{V}_1$ and $\overline{V}_2$ refer to the partial molar volumes of solvent and solute. The plots for Eq. 5 are shown in Fig. 2. The equation, $\overline{V}_m=(80.4\pm0.002)+(155.3\pm 15.3)X_2$, was obtained by the least squares method, and the partial molar volume of porphine, $\overline{V}_2=236\pm15$ cm^3 mol^{-1} (95% confidence limit), was determined.

Solvent Effect on Partition Coefficient. The activity coefficient of a nonelectrolyte solute, γ_s, can be expressed on the basis of regular solution theory.[12]

$$\ln \gamma_s = \frac{V_s}{RT}(\delta_1^2 + \delta_s^2 - 2\delta_1\delta_s), \tag{6}$$

where V and δ are the molar volume and solubility parameters respectively, and the subscripts 1 and s denote solvent and solute, respectively. Since the activily of a solute in the organic phase is equal to that in the aqueous phase in partition equilibrium, the partition coefficient of a solute expressed as a molar fraction, P^X, is related to the activity coefficient;

$$P^X = \frac{X_{s,o}}{X_{s,a}} = \frac{\gamma_{s,a}}{\gamma_{s,o}}, \tag{7}$$

where X is the molar fraction and the subscript a denotes the aqueous phase. From Eqs. 6 and 7, the following equation can be derived,

$$\frac{RT}{V_s}\ln P^X + \delta_o^2 = 2\delta_s\delta_o + \frac{RT}{V_s}\ln \gamma_{s,a} - \delta_s^2. \tag{8}$$

Substituting Eq. 4 (as $n=2$) into Eq. 8, we obtain.

$$\frac{RT}{V_s}(\ln D^X + 2\ \ln[\mathrm{H}^+]) + \delta_o^2 = 2\delta_s\delta_o + \frac{RT}{V_s}\left(\ln \gamma_{s,a} - \ln K_2 - \frac{V_s\delta_s^2}{RT}\right), \tag{9}$$

where D^X is the distribution ratio expressed as a molar fraction. Since the second term of the right hand side of Eq. 9 is independent of the organic solvent, the plots of the left hand side against the solubility

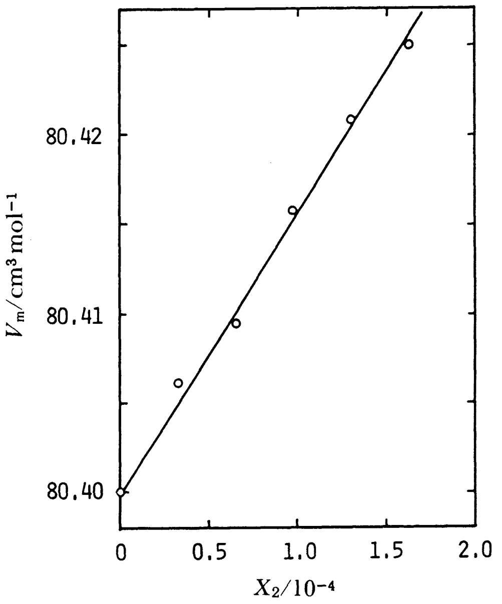

Fig. 2. Linear relationship between the mean molar volume of porphine solution in pyridine (V_m) and the molar fraction of porphine (X_2).

Table 3. Equilibrium Constants in the Partition of Porphine at 25 °C

No.	Solvent	δ_o[a]	$\log P\cdot K_2^{-1}$	$\log P^X\cdot K_2^{-1}$[c] (experimental)	$\log P^X\cdot K_2^{-1}$[c] (calculated)[d]
1	Heptane	7.431	−0.75±0.01	−3.32±0.01	−3.36
2	Dodecane	7.841	−0.55±0.12	−2.94±0.12	−2.92
3	Carbon tetrachloride	8.584	0.33±0.06	−2.43±0.06	−2.28
4	Benzene	9.158	0.69±0.03	−2.10±0.03	−1.91
5	Toluene	8.913	0.77±0.02	−1.95±0.02	−2.05
6	Chloroform	9.300[b]	1.24±0.03	−1.60±0.03	−1.84
7	Dichloromethane	9.830	1.23±0.02	−1.70±0.02	−1.63
8	1-Octanol	10.239	−0.06±0.03	−2.61±0.03	−1.53

a) Calculated from the heat of vaporization of the solvent.[7] b) From the literature.[15] c) From Eq. 4, expressed in molar fraction. d) From Eq. 9 (see text).

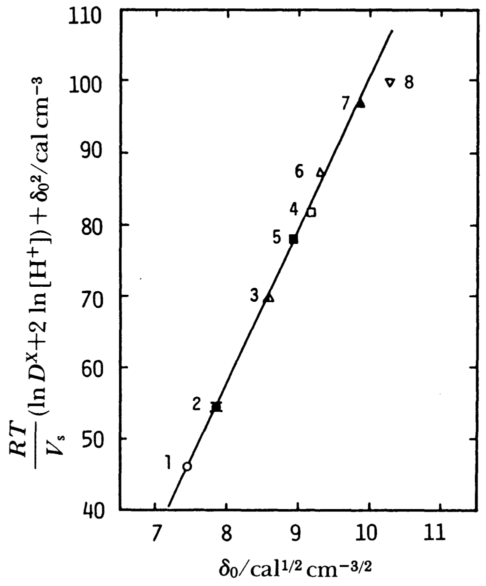

Fig. 3. Evaluation of the solvent effect of partition coefficient of porphine based on the regular solution theory. The numbers refer to those in Table 3.

parameter of the organic solvent, δ_0, should give a straight line, and the solubility parameter of porphine, δ_s, can be calculated from the slope. The $V_s$is replaced by the partial molar volume of porphine determined above. Even if the V_s value changes by 10% to larger or smaller values, it has an influence on the δ_s value of less than 3%. The solubility parameter of the organic solvent is calculated from the heat of vaporization of solvent at 25 °C.[7)]

As shown in Fig. 3, the plots give a good linear relationship for heptane, dodecane, benzene, toluene, carbon tetrachloride, chloroform, and dichloromethane. Hence, these organic solutions of porphine may be designated regular solutions. The solubility parameter of porphine is calculated to be 10.7 ± 0.6 $\text{cal}^{1/2}\ \text{cm}^{-3/2}$ (95% confidence limit, 1 $\text{cal}^{1/2}\ \text{cm}^{-3/2}=$ 2.0455 $\text{J}^{1/2}\ \text{cm}^{-3/2}$) by the least squares method of the plots for seven nonpolar solvents. This value is close to those of heterocyclic amines such as pyridine (10.7 $\text{cal}^{1/2}\ \text{cm}^{-3/2}$) and quinoline (10.8 $\text{cal}^{1/2}\ \text{cm}^{-3/2}$) which are calculated from the heat of vaporization of the pure liquid.[13)]

The plot for 1-octanol is lower than the straight line drawn here. Considering that a direct solvation of 1-octanol to porphine possibly accompany a positive deviation, this negative deviation may be attributed to a peculiar behavior of a self-associated solvent such as 1-octanol which is refer to a larger δ_0 of 1-octanol (δ_0=10.2 $\text{cal}^{1/2}\ \text{cm}^{-3/2}$). In other words it is unreasonable to treat the 1-octanol system strictly as a regular solution. It is interesting to note that chloroform does not cause any deviation in Fig. 3. This must be compared with a previous research of the solvent effect on the partition coefficient of heterocyclic amine such as 1,10-phenanthroline,[14)] where a linear relationship expressed as Eq. 8 was again clear for heptane, cyclohexane, carbon tetrachloride, and benzene, but a large positive deviation was observed for chloroform. This was attributed to a specific interaction such as hydrogen bonding, between phenanthroline and chloroform. These results suggest that the nitrogen atoms in porphine hardly hydrogen bond with proton donors such as chloroform and 1-octanol.

The log $P^X\cdot K_2{}^{-1}$ for each solvent was calculated from Eq. 9 by knowing the second term of the right hand side from the intercept in Fig. 3. Table 3 shows that the calculated values are in good agreement, except for 1-octanol, with those obtained experimentally from D^X and $[H^+]$ by Eq. 4. The $\log P^X\cdot K_2{}^{-1}$ value for other nonpolar solvents can be calculated in this manner.

At present, P^X and/or K_2 can not be determined independently due to their high partition coefficient and the low solubility of porphine in the aqueous solvent. However the solvent effect on the liquid-liquid partition of the mother compound porphine can be quantitatively evaluated. This may be valuable information in understanding the solution behavior of porphyrin compounds.

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