January, 1982] © *1982 The Chemical Society of Japan* *Bull. Chem. Soc. Jpn.*, ***55***, *121—125 (1982)*

Partition Coefficients of Chlorobenzenes in Heptane–Water and Heptane–Acetonitrile Systems

Nobuo SUZUKI,* Toshinobu YOSHIDA, and Hitoshi WATARAI
Department of Chemistry, Faculty of Science, Tohoku University, Sendai 980

(Received May 6, 1981)

Partition coefficients (K_D) of benzene and 11 chloro derivatives of benzene were determined at 25 °C in two liquid-liquid partition systems: heptane/water and heptane/acetonitrile. Increase of K_D with increase of the numbers of Cl atoms in the solute is discussed in terms of surface and cohesive energies. The small difference in K_D of the isomers whose Cl atom numbers are 2, 3, or 4 was correlated with a difference in the dipole moment of the solute.

The liquid-liquid partition coefficient is utilized in measuring various solution properties: for example, transfer activity coefficient of non-electrolyte,[1] solvent effect on catalytic reaction,[2] capacity ratio in liquid chromatography,[3] and toxicity of drugs.[4] Accumulation of precise partition coefficient data is important for practical uses as well for an elucidation of the factors which influence their values. Hansch *et al.* investigated the regularity in the partition coefficients of various organic compounds. They proposed a substitution constant, π, for a variety of groups, by analogy to the Hammet σ constant.[4] Additivity of corresponding values for the components makes it possible to predict the partition coefficient of a certain compound. The additive-constitutive property is useful for practical purposes, but gives only a little insight into the nature of the solute-solute interaction.

Recently, we reported the importance of cavity formation in the partition of non-electrolytes.[5—7] In the present study, the partition equilibrium of a series of chlorobenzenes between heptane and water or acetonitrile was investigated. Chlorobenzenes are considered to be representative compounds of chlorinated organic compounds. The behavior of these compounds in the environment has recently become important. Acetonitrile was chosen to examine a difference from water in solvent effect. The partition coeffcients will be discussed in connection with the cavity formation energy in the partition systems.

Experimental

Chemicals. Monochlorobenzene (Wako G.R.) and o-dichlorobenzene (Tokyo Kasei G.R.) were washed with dilute alkaline solution, dried, and fractionally distilled under ambient pressure. *m*-Dichlorobenzene and 1,2,4-trichlorobenzene (Tokyo Kasei G.R.) were washed with dilute alkaline solution, dried, and distilled under reduced pressure. *p*-Dichlorobenzene, 1,2,3-trichlorobenzene, 1,3,5-trichlorobenzene, tetrachlorobenzene, pentachlorobenzene and hexachlorobenzene, which were all purchased from Tokyo Kasei, were purified by vacuum sublimation. Purity of the reagents was checked by GLC or mp measurement. Benzene was of spectral grade (Dotite) and used without further purification. Heptane (Kanto G.R.) was stirred with 30% fumic sulfuric acid over-night, washed with water and dilute sodium hydroxide solution, dried with sodium hydroxide and fractionally distilled. Acetonitrile (Wako G.R.) was dried with molecular sieves 3A and calcium hydride, distilled on phosphorus pentaoxide, and then redistilled on calcium hydride. Purity of the organic solvent was checked by UV spectra. Redistilled water was used throughout the experiment.

Partition Measurement. *Heptane–Water System*: Heptane solution of chlorobenzene of known concentration was agitated with water for 15 min by a mechanical shaker in a thermostated room at 25±1 °C. After centrifugation at 3000 rpm, an aliquot of aqueous phase was pipetted out for analysis. For benzene, monochlorobenzene, and dichlorobenzene systems, this aqueous phase was used for direct photometric determination. For trichlorobenzene and tetrachlorobenzene with quite high partition coefficients, the equilibrated aqueous phase was removed and agitated with a small volume of fresh heptane in order to re-extract and concentrate the solute dissolved in the aqueous phase. The second heptane phase was used for the photometric determination. Photometric measurement was made at 254 nm for benzene and at 220 nm for the others. The recovery in the re-extraction process was satisfactorily quantitative. The partition coefficient was calculated from this equation:

$$K_D = \frac{C_{o,\mathrm{init}}V_o - C_a V_a}{C_a V_o}, \tag{1}$$

where $C_{o,\mathrm{init}}$ is an initial concentration in heptane, C_a an observed concentration in aqueous phase, and V_a and V_o are volumes of aqueous and organic phases. The ratio of V_a/V_o is 1 or 10, corresponding to the magnitude of the partition coefficient. The partition coefficients of pentachlorobenzene and hexachlorobenzene were measured by means of GLC equipped with a electron capture detector.[8] The partition coefficient for every system showed no dependency on initial concentration of the solutes in the range of 0.05—0.2 mol dm^{-3}.

Heptane–Acetonitrile System: A 5-cm^3 portion of 0.003 mol dm^{-3} chlorobenzene in heptane was agitated with 5 cm^3 of acetonitrile under the same experimental conditions as used in the heptane/water system. Absorbance of the heptane phase was measured at the absorption maximum wavelength for each substance (250—300 nm). The partition coefficient was calculated by this equation:

$$K_D = \frac{A_o}{A_{o,\mathrm{init}} - A_o}, \tag{2}$$

where $A_{o,\mathrm{init}}$ and A_o are the absorbances of heptane solutions before and after equilibration, respectively. The acetonitrile and heptane used for partition experiments were saturated with each other prior to use. Spectrophotometry was carried out by Hitachi 356 and JASCO UVIDEC-2 spectrophotometers.

Results

In Table 1, the observed partition coefficients for the two partition systems are listed, along with the

TABLE 1. PARTITION COEFFICIENTS (k_D) OF CHLORINATED BENZENES AT 25 °C

No.	Solute	Abs. coeff. at 220 nm	Hep/H_2O $K_D \times 10^{-3}$	Hep/AN K_D
1	Benzene	138[a,e]	0.195	0.75
2	Chlorobenzene	4100[a]	0.838	0.83
3	*o*-Dichlorobenzene	6280[a]	2.34	0.87
4	*m*-Dichlorobenzene	6620[a]	3.41	1.15
5	*p*-Dichlorobenzene	9190[b]	3.41	1.04
6	1,2,3-Trichlorobenzene	9770[b]	10.4	1.20
7	1,2,4-Trichlorobenzene	8930[b]	13.7	1.53
8	1,3,5-Trichlorobenzene	10100[b]	25.1	2.57
9	1,2,3,4-Tetrachloro-benzene	15000[b]	35.1	1.74
10	1,2,4,5-Tetrachloro-benzene	15300[b]	45.7	2.46
11	Pentachlorobenzene	20900[c]	129[f]	2.76
12	Hexachlorobenzene	57100[d]	538[f]	4.19

a) 10% ethanol. b) Hepane. c) 40% ethanol. d) Ethanol. e) 254 nm. f) Determined by GLC.

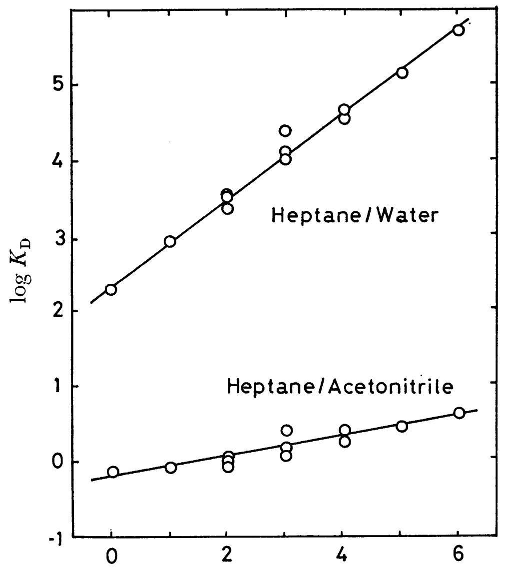

Fig. 1. Correlation between the partition coefficient and the number of chlorine atoms.

spectral data used for photometric determination. It is clearly observed that the K_D values for the heptane/water system are much larger than those for the acetonitrile system and that the values of both systems increase with an increase of number of Cl atoms in chlorobenzene. Figure 1 shows a linear relationship between log K_D and the number of Cl atoms, *n*. For the two partition systems, these experimental equations were obtained:

$$\left.\begin{array}{ll} \log K_D = 0.566n + 2.37 & \text{for Heptane-H}_2\text{O} \\ \log K_D = 0.132n - 0.203 & \text{for Heptane-Acetonitrile} \end{array}\right\} . \quad (3)$$

Increase of Cl atoms will cause an increase in molar volume and in molar surface area, as well as in the cohesive energy density of the compound. Hence, the influences of the molar surface area and the solubility parameter, defined as (cohesive energy density)$^{1/2}$, of chlorobenzene on the partition coefficient should be discussed.

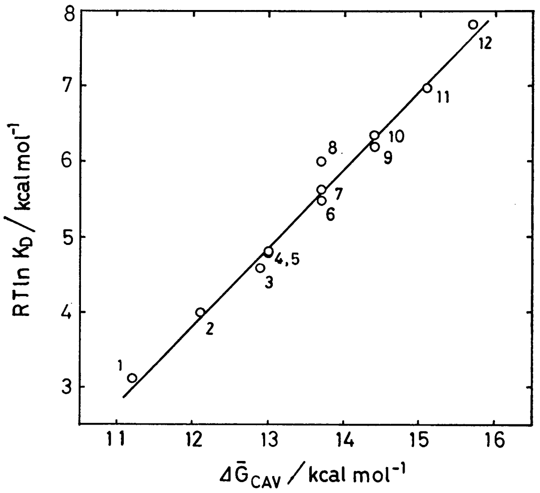

Fig. 2. Correlation between the partition coefficient and the cavity formation energy in heptane–water system. Numbers in this figure correspond to those in Table 1.

Discussion

Contribution of Surface Work. Chemical potential of solute in dilute solution is considered to be governed by two kinds of solute-solvent interaction energies, *i.e.*, a formation energy of cavity to accommodate the solute molecule and an interaction energy between the solute introduced into the cavity and the solvent molecule surrounding the solute molecule. Then, the free energy governing the partition equilibrium is represented by

$$RT \ln K_D = \Delta\bar{G}_{cav} + \Delta\bar{G}_{int}, \quad (4)$$

where $\Delta\bar{G}_{cav}$ and $\Delta\bar{G}_{int}$ correspond to free energy contributions from cavity formation and interaction accompanying the transfer of solute from organic phase into aqueous phase.

The cavity formation energy can be estimated from the molecular surface area of solute and the surface tension of bulk solvent. Sinanoglu has reported the next equation for the calculation of cavity formation energy:[9]

$$\bar{G}_{cav} = \kappa^e(\phi)9.76\,V^{2/3}\gamma\left\{1-(1-\eta)\left(\frac{\partial \ln\gamma}{\partial \ln T}\right)+\frac{2}{3}\alpha T\right\}, \quad (5)$$

$$\eta = \frac{\kappa^s(\phi)}{\kappa^e(\phi)} = \frac{1+\phi^{2/3}(\kappa^s-1)}{1+\phi^{2/3}(\kappa^e-1)},$$

where V is molar volume of solute (cm^3 mol^{-1}), γ surface tension of solvent, α thermal expansion coefficient of solvent, ϕ molar volume ratio of solvent to solute, and κ^s and κ^e are microscopic cavity factors for surface energy and surface entropy.[10] According to Eq. 5, the cavity energy difference, $\Delta\bar{G}_{cav}$, was calculated for heptane–water system using κ^s=0.542 and 1.235, and κ^e=0.687 and 1.277 for heptane and water, respectively.[10] A correlation between RT ln K_D and $\Delta\bar{G}_{cav}$ is shown in Fig. 2. For the heptane–

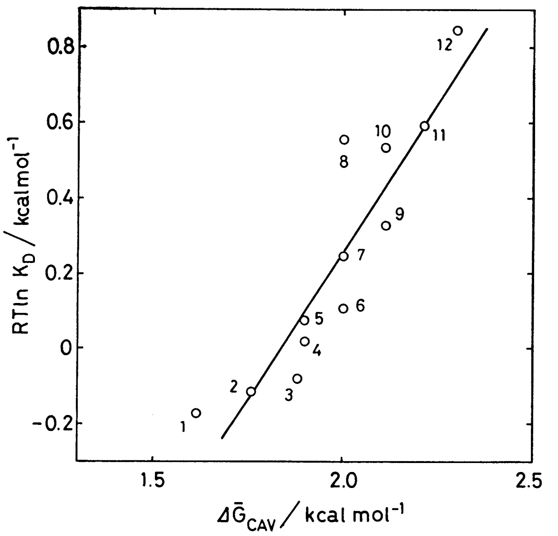

Fig. 3. Correlation between the partition coefficient and the cavity formation energy in heptane–acetonitrile system.
Numbers in this figure correspond to those in Table 1.

acetonitrile system, $\Delta\bar{G}_{\text{cav}}$ was calculated using approximated value of $\kappa^e=\kappa^s=1.0$ for acetonitrile.⁹⁾ A correlation with $RT\ln K_D$ is shown in Fig. 3. The linear relations appearing in Figs. 2 and 3 strongly suggest that the order of magnitude of the partition coefficient is governed by the cavity formation energy.

Contribution of Cohesive Work. The contributions of molar volume and of cohesive energy density of solute to the partition coefficient are accounted for by solubility parameter theory.¹¹⁾ The next equation has been proposed for the partition coefficient by Suzuki *et al.*:¹²⁾

$$\log K_D = \frac{V}{2.303RT}(\delta_a+\delta_o'-2\delta)(\delta_a-\delta_o), \tag{6}$$

$$\delta_o' = \delta_o + \frac{RT(V_o^{-1}-V_a^{-1})}{(\delta_a-\delta_o)},$$

where molar volume, V, V_o, and V_a, and solubility parameters δ, δ_c, and δ_a refer to those of solute, organic phase, and aqueous phase, respectively. This relation was successfully applied to the partition of several metal chelate compounds.¹³⁾

Equation 6 was applied to the results of the heptane–water system. The molar volumes of chlorobenzenes were taken from the literature or estimated from the linear relationship between the molar volume and number of Cl atoms. The solubility parameters for chloro derivatives of benzene, except chlorobenzene and *o*-dichlorobenzene, were estimated from the additivity rule of group contributions in solubility parameter proposed by Renick and Lin.¹⁴⁾ The solubility parameter of water calculated from thermodynamic properties is 23.4 $\text{cal}^{1/2}\,\text{cm}^{-3/2}$ (conversion factor: 1 $\text{cal}^{1/2}\,\text{cm}^{-3/2}=2.0455\,\text{J}^{1/2}\,\text{cm}^{-3/2}$), but for practical use 17.15 $\text{cal}^{1/2}\,\text{cm}^{-3/2}$ is recommended by Suzuki *et al.* from their extensive study on solvent extraction of β-diketones and its metal chelates.¹⁵⁾ The $\log K_D$ value for chlorobenzene calculated using 17.15 $\text{cal}^{1/2}\,\text{cm}^{-3/2}$, however, decreases with increase of Cl atoms and disagrees with the observed value, *e.g.*, the calculated $\log K_D$'s are 2.50 for benzene and −0.29 for hexachlorobenzene. The same treatment, estimation of K_D according to Eq. 6, was applied to the heptane–acetonitrile system. In this system, the mutual solubility of two solvents cannot be neglected, hence the small changes in solubility parameter and molar volume of two solvent phases were corrected for by employing the solubility data reported previously.²⁾ The calculated results in heptane–acetonitrile did not show good agreement with the observed one, *e.g.*, the calculated $\log K_D$'s are −0.28 for benzene and −2.26 for hexachlorobenzene. When δ_a was treated as an adjustable parameter, the value of δ_a calculated introducing the observed $\log K_D$ into Eq. 6 varied from 17.4 for the benzene system to 20.9 for the hexachlorobenzene system. The value is related δ and V by the next equation:

$$\delta_a = 1.70\delta + 1.77 = 1.03V + 6.42. \tag{7}$$

The calculated values seem to be reasonable so long as the calculated δ_a value is between $\delta_v=6.4$ $\text{cal}^{1/2}\,\text{cm}^{-3/2}$ and $(\delta_v^2+\delta_r^2)^{1/2}=23.4$ $\text{cal}^{1/2}\,\text{cm}^{-3/2}$. Here δ_v and δ_r refer to the solubility parameters defined as (internal pressure)$^{1/2}$ and {(cohesive energy density)−(internal pressure)}$^{1/2}$. These reflect the physical interaction (repulsion, dispersion, and weak dipole-dipole interaction) and chemical interaction (hydrogen bonding), respectively.¹⁶⁾ However, in the heptane–acetonitrile system, the solubility parameters of acetonitrile calculated from the observed partition coefficient (12.4 $\text{cal}^{1/2}\,\text{cm}^{-3/2}$ for benzene system and 16.2 $\text{cal}^{1/2}\,\text{cm}^{-3/2}$ for hexachlorobenzene system) are larger than the solubility parameter calculated from the heat of vaporization (11.9 $\text{cal}^{1/2}\,\text{cm}^{-3/2}$). This suggests that the uncertainty of the solubility parameter of polar phase is not the only source of the discrepancy between the calculated and the observed partition coefficients. As another important source, the deviation from the simple geometric mean assumption should be examined. The deviation is taken into account by introducing a coefficient, l_{12}, into the activity equation derived from the regular solution theory:¹¹⁾

$$RT\ln a_2 = RT\left[\ln\phi_2+\ln\phi_1\left(1-\frac{V_2}{V_1}\right)\right] + V_2\phi_1^2[(\delta_1-\delta_2)^2+2l_{12}\delta_1\delta_2], \tag{8}$$

where a is activity, ϕ volume fraction, and subscript 1 and 2 refer to solvent and solute, respectively. Using the above expression, the partition coefficient Eq. 6 can be revised as:

$$\log K_D = \frac{V}{2.303RT}(\delta_a+\delta_o'-2q\delta)(\delta_a-\delta_o), \tag{9}$$

$$q = 1 - \frac{l_a\delta_a-l_o\delta_o}{\delta_a-\delta_o}.$$

Here q is equal to one if the strict geometric mean relation of $l_a=l_o=1$ or the apparent relation of $l_a\delta_a=l_o\delta_o$ holds, and otherwise q is different from one. The values of q are calculated using the observed $\log K_D$ and the available parameters for heptane–water and heptane–acetonitrile systems. The results

TABLE 2. PHYSICAL PROPERTIES AND PARAMETERS OF THE CHLOROBENZENES

No.	Solute	Chlorine number	Molar volume[a)]	Dipole moment[c)]	Solubility parameter	q value[e)]	
						Hep/H_2O[f)]	Hep/AN
1	Benzene	0	89.4	0	9.2,[d)] 9.2	0.98	0.97
2	Chlorobenzene	1	102	1.54	9.5,[d)] 9.6	0.95	0.92
3	*o*-Dichlorobenzene	2	113	2.26	10.0,[d)] 10.0	0.90	0.87
4	*m*-Dichlorobenzene	2	115	1.38	9.8	0.92	0.87
5	*p*-Dichlorobenzene	2	115	0	9.8	0.92	0.88
6	1,2,3-Trichlorobenzene	3	125	2.33	10.3	0.87	0.83
7	1,2,4-Trichlorobenzene	3	125	1.26	10.3	0.86	0.81
8	1,3,5-Trichlorobenzene	3	125[b)]	0.28	10.3	0.85	0.78
9	1,2,3,4-Tetrachlorobenzene	4	136[b)]	1.92	10.5	0.84	0.79
10	1,2,4,5-Tetrachlorobenzene	4	136[b)]	0.73	10.5	0.84	0.77
11	Pentachlorobenzene	5	146[b)]	0.88	10.9	0.80	0.74
12	Hexachlorobenzene	6	156[b)]	0.21	11.2	0.77	0.71

a) $cm^3 mol^{-1}$. b) Estimated value from the relationship between molar volume and chlorine number. c) Debye. d) Calculated from the heat of vaporization. e) See Eq. 9 in the text. f) $\delta_a = 17.15 \, cal^{1/2} cm^{-3/2}$ was used in the calculation. (Conversion factor: $1 \, cal^{1/2} cm^{-3/2} = 2.0455 \, J^{1/2} cm^{-3/2}$).

are listed in Table 2. The values of q are 2—30% smaller than 1.0, a result which is easily expected in simple geometric mean assumption as in Eq. 6, and decrease with increases of number of Cl atoms of solutes. This also suggests that the deviation becomes larger for larger molecule. An evaluation of l_a and l_o is difficult at the present stage, but it is probable that l_o is negative for a system composed of a large-sized solute and small-sized solvent.[11)]

Equation 9 can be rearranged:

$$\log K_D = \frac{V}{2.303RT}(\delta_a{}^2 - \delta_o{}^2) + RT\left(\frac{1}{V_o} - \frac{1}{V_a}\right) - \frac{2\delta Vq}{2.303RT}(\delta_a - \delta_o). \quad (10)$$

Comparing Eq. 10 with Eq. 4, the first and the second terms in Eq. 10 are considered to refer to cavity energy and interaction energy respectively in the framework of the regular solution theory. The cavity, in this case, corresponds to the solute taking $\delta = 0$ and V. Since the second term is laways negative because $\delta_a > \delta_o{}'$ the increase of $\log K_D$ with increase of V, observed in this study, confirmes a predominance of the cavity energy contribution.

Comparison among the Partition Coefficient of Isomers. As the partition coefficients of isomers (Cl=2,3, and 4) are compared, a slight difference among them is observed. A principal difference in physical properties of these solutes will be the difference in dipole moment, which is listed in Table 2 for each chlorobenzene.

Beveridge *et al.* derived the next equation for an electrostatic interaction energy:[17)]

$$\overline{G}_{es} = -14.39 \frac{\mu^2}{a^3} D\left(1 + \frac{D}{3}\right) \quad (\text{kcal mol}^{-1}) \quad (11)$$

$$D = \frac{3(\varepsilon - 1)}{2\varepsilon + 2},$$

where ε is the dielectric constant of the solvent, μ (Debye) the dipole moment of the solute, and a(Å) the radius of solute cavity. The difference in the electrostatic interaction energy between solute–heptane and solute–water or solute–acetonitrile was calculated and compared with the partition coefficient of the solute. Figure 4 shows the correlation of the differences in $\log K_D$ between isomeric compounds of $\mu = 0$ and $\mu \neq 0$ with the calculated electrostatic energy difference. It is concluded from Fig. 4 that $\log K_D$ for the chlorobenzene of large dipole moment is smaller than that for a smaller dipole moment solute.

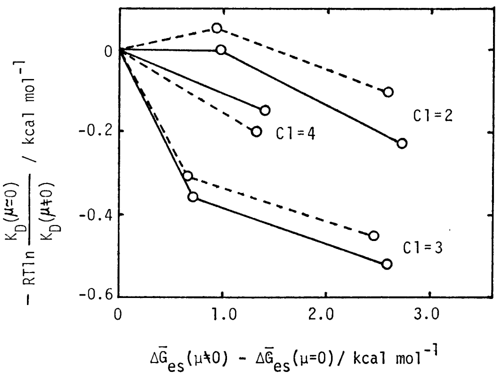

Fig. 4. Correlation between the difference in partition free energy of the isomers and the difference in electrostatic interaction energy, where $\Delta\overline{G}_{es} = \overline{G}_{es,dod} - \overline{G}_{es,polar}$.
——: Heptane–H_2O, -----: Heptane–AN.

As a conclusion, we suggest that the partition coefficients of chlorobenzene is governed primarily by cavity formation and the difference of partition coefficient in isomers can be understood by taking into account the electrostatic interaction. More extensive study of the partition coefficient of halobenzenes is in progress, including an application of the Scaled Particle theory.[8)]

References

1) H. Watarai and N. Suzuki, *J. Inorg. Nucl. Chem.*, **38**, 1683 (1976).

2) H. Watarai and N. Suzuki, *Bull. Chem. Soc. Jpn.* **52**, 2778 (1979).

3) T. Hanai, *Chromatographia*, **12**(2), 77 (1979).

4) A. Leo, C. Hansch, and D. Elkins, *Chem. Rev.*, **71**, 525 (1971).

5) H. Watarai and N. Suzuki, *Chem. Lett.*, **1977**, 321.

6) H. Watarai, M. Murakami, and N. Suzuki, *Bull. Chem. Soc. Jpn.*, **52**, 937 (1979).

7) H. Watarai and N. Suzuki, *Bull. Chem. Soc. Jpn.*, **53**, 1848 (1980).

8) H. Watarai, M. Tanaka, and N. Suzuki, *Anal. Chem.*, in press.

9) O. Sinanoglu in "Molecular Associations in Biology," ed by B. Pullman, Academic Press, New York (1968), p. 427.

10) T. Haliciglu and O. Sinanoglu, *Ann. N.Y. Acad. Sci.*, **158**, 308 (1969).

11) J. H. Hildebrand, J. M. Prausnitz, and R. L. Scott, "Regular and Related Solutions," Van Nostrand-Reinhold, New York, N.Y. (1970).

12) T. Wakahayashi, S. Oki, T. Omori, and N. Suzuki, *J. Inorg. Nucl. Chem.*, **26**, 2255 (1964).

13) N. Suzuki and K. Akiba, *J. Inorg. Nucl. Chem.*, **33**, 1169 (1971); K. Akiba, N. Suzuki, and T. Kanno, *Anal. Chim. Acta*, **58**, 379 (1972).

14) A. E. Reineck and K. F. Lin, *J. Paint Technol.*, **40**, 611 (1968).

15) H. Irving, "Ion Exchange and Solvent Extraction," ed by J. A. Marinsky and Y. Marcus, Marcel Dekker, (1974) Vol. 6, p. 139.

16) E. B. Bagley, T. P. Nelson, and J. M. Scigliano, *J. Paint Technol.*, **43**, 35 (1971).

17) D. L. Beveridge, M. M. Kelly, and R. J. Radna, *J. Am. Chem. Soc.*, **96**, 3769 (1974).