Dynamic Interaction between Alkylammonium Ions and β-Cyclodextrin by Means of Ultrasonic Relaxation

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Ultrasonic absorption measurements in the frequency range from 0.8 to 220 MHz were carried out in aqueous solutions of pentylammonium chloride (PEACL) and hexylammonium chloride (HEACL) with β-cyclodextrin (β-CD) at pH $\approx$ 7.2 and 25 °C. A single relaxational absorption was attributed to a perturbation of a chemical relaxation associated with the formation of a complex between β-CD and the alkylammonium chlorides. The rate and equilibrium constants for the complexation reaction were determined from the concentration dependence of the relaxation frequency. Increasing the chain length of the alkylammonium ion led to an increase in the stability of the complex and slowed the exit rate of the ion from the β-CD cavity. The standard volume change of the reaction was obtained from a maximum absorption per wavelength and was attributed to water molecules being expelled from the cavity with concomitant alkylammonium ion insertion.

Introduction

Revealing dynamic properties of interaction between host and guest molecules contribute to precise understanding about inclusion complex formation in supramolecular chemistry. Cavities of cyclodextrins (CDs) can accommodate a variety of compounds as guests to form inclusion complexes.[1−3] The complexes are in dynamic equilibrium with free guest and host molecules, and they are exchanging one another with very rapid speeds. Ultrasonic absorption measurement is useful for probing the microscopic solution structure and can be used to study relaxation processes with characteristic time constants of 10^{-5}–10^{-10} s. The kinetic examinations for the complexation reaction by the ultrasonic method were also performed by a few investigators.[4,5] Hall et al.[5] reported the ultrasonic results in systems with α-CD as the host and alcohols as the guest. However, the systematic study still does not have a detailed clarification of the reaction mechanism.

In our experimental studies[6−10] for the dynamic interaction between host and guest molecules by the ultrasonic relaxation method, it has been clarified that the stability of inclusion complex is mainly controlled by the rate of departure of the guest molecule from the cavity. On the other hand, the reaction for the complex formation was proved from the Smoluchowski equation by taking account of the structure formation of β-CD to be proceeding in a diffusion-controlled process.[8] Therefore, it is considered that the rate constant for the departure process decreases with the increase in guest hydrophobicity. We examined the dynamic interaction between propylammonium or butylammonium ion and β-CD in our previous report.[9] As a result, the ultrasonic relaxation was not observed in the solution with propylammonium chloride and β-CD while it was found in the solution of butylammonium chloride and β-CD. These results were interpreted by a model for the complex formation reaction taking into account of the balance of hydrophobicity and hydrophilicity of the guest molecules. Consequently, then, pentylammonium chloride (PEACL) and hexylammonium chloride (HEACL) were chosen as guests and β-CD as host in this study in order to see further how the hydrophobicity affects the stability of the inclusion complex and the rate of the departure of the guest molecule from the CD cavity.

Experimental Section

Chemicals. β-Cyclodextrin (β-CD) was purchased from Wako Pure Chemical Co., Ltd., and it was purified by recrystallization from water.[4] Pentylamine and hexylamine were also from Wako Pure Chemical Co., Ltd., and were used as received. PEACL and HEACL were obtained by adding concentrated hydrochloric acid solution to pentylamine and hexylamine solutions to adjust at pH $\approx$ 7.2. Solvent water was distilled, it was filtered through a Milli-Q SP-TOC system from Japan Millipore Ltd., and then it was degassed under reduced pressure.

Apparatus. Ultrasonic absorption coefficients, α, in the frequency range from 0.8 to 9 MHz were obtained by a resonance apparatus and those from 15 to 220 MHz were obtained by a pulse one. The temperature was controlled within ±0.01 °C for the resonators and within ±0.1 °C for the pulse cells. More details of the apparatuses are described elsewhere.[11,12] Sound velocity was measured by the resonator at around 3 MHz, and solution density was obtained by a vibrating density meter (Anton Paar NMA 60/602). The solution pH was measured by a glass electrode with HM-60S Toa Denpa pH meter. All measurements were performed at 25 °C.

Results

It is well-known that there exists an ultrasonic relaxation in relatively dilute aqueous solutions of amines, and the relaxation is due to the proton-transfer reaction.[13,14] However, this relaxational phenomenon disappears when the solution pH decreases to a neutral value. Thus, we used the alkylammonium ions as the guest in order to avoid superimpose of plural relaxations. Actually, the ultrasonic relaxation is observed only in relatively concentrated aqueous solutions of CDs including β-CD, for

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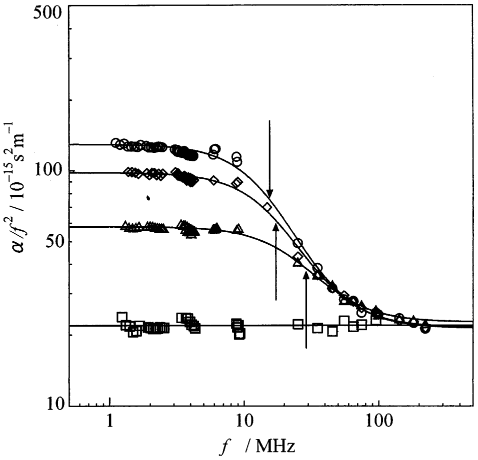

Figure 1. Representative ultrasonic absorption spectra in aqueous solutions of PEACL in the presence and absence of β-CD at pH $\approx$ 7.2 and 25 °C: (□) 0.500 mol dm^{-3} PEACL; (○) 0.100 mol dm^{-3} PEACL + 0.0087 mol dm^{-3} β-CD; (◇) 0.200 mol dm^{-3} PEACL + 0.0087 mol dm^{-3} β-CD; (△) 0.400 mol dm^{-3} PEACL + 0.0087 mol dm^{-3} β-CD. The arrows indicate the location of the relaxation frequency.

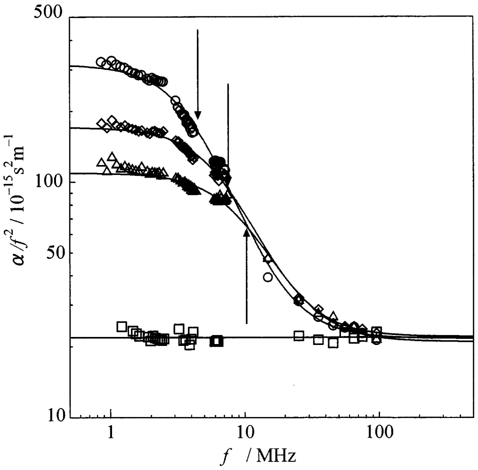

Figure 2. Representative ultrasonic absorption spectra in aqueous solutions of HEACL in the presence and absence of β-CD at pH $\approx$ 7.2 and 25 °C: (□) 0.200 mol dm^{-3} HEACL; (○) 0.040 mol dm^{-3} HEACL + 0.0087 mol dm^{-3} β-CD; (◇) 0.080 mol dm^{-3} HEACL + 0.0087 mol dm^{-3} β-CD; (△) 0.100 mol dm^{-3} HEACL + 0.0087 mol dm^{-3} β-CD.

which the mechanisms seem to be still in question.[15−17] When the concentration of β-CD decreases down to 0.01 mol dm^{-3}, the relaxation is not observed.[9] To avoid the complexities due to the plural relaxations in solution, the concentration of β-CD was restricted below 0.01 mol dm^{-3} in this study.

Figures 1 and 2 show the representative ultrasonic absorption spectra in the presence and absence of β-CD. When β-CD is absent in solution of PEACL or HEACL, the absorption coefficient divided by the square of the measurement frequency, α/f^2, is independent of the frequency as are seen in these figures. However, in the solutions including both the alkylammonium ion and β-CD, a relaxational phenomenon was clearly observed, because the values of α/f^2 are dependent on the frequency.

We tested the experimental values to calculate the amplitude of excess absorption, A, the background absorption, B, and the relaxation frequency, f_r, by a Debye-type relaxational equation as

$$\alpha/f^2 = A/\{1 + (f/f_r)^2\} + B \tag{1}$$

The parameters, A, B, and f_r, were determined by a nonlinear least-mean-squares method and some representative curves calculated using the obtained A, B, and f_r are shown in Figures 1 and 2. The detail analytical procedure for A, B, and f_r is described elsewhere.[18] The agreements between the experimental date and the calculated values are excellent, which means that a single relaxational absorption is observed. The ultrasonic relaxation parameters obtained are listed in Table 1 along with the values of the solution density, ρ, the sound velocity, v, and the pH value. It is considered that the cause of relaxation is due to an interaction between the alkylammonium ions and β-CD, because the relaxation phenomenon is observed only in the solutions containing both β-CD and the alkylammonium ions. Therefore, the perturbation of the following equilibrium is considered to be the cause of the relaxation.

$$\mathrm{CD} + \mathrm{GST}^+ \underset{k_b}{\overset{k_f}{\rightleftharpoons}} \mathrm{CDGST}^+ \tag{2}$$

where CD is β-CD, GST$^+$ is PEACL or HEACL, CDGST$^+$ is the host−guest complex formed by the alkylammonium ions and β-CD, and k_f and k_b are the forward and backward rate constants, respectively. The equilibrium constant, K, is defined as, $K = k_f / k_b$.

The relationship between the relaxation time, τ, or the relaxation frequency, f_r, and the reactant concentrations is given by[10]

$$\tau^{-1} = 2\pi f_r = k_f\{[\mathrm{CD}] + [\mathrm{GST}^+]\} + k_b \tag{3}$$

$$= k_b\{(1 + KC_{\mathrm{CD}} + KC_{\mathrm{GST}^+})^2 - 4K^2C_{\mathrm{CD}}C_{\mathrm{GST}^+}\}^{1/2} \tag{3′}$$

where C_{CD} and C_{GST^+} are the analytical concentrations of β-CD and the alkylammonium chloride, respectively. From eq 3′, the backward rate constant and equilibrium constant are available using the nonlinear least-mean-squares program. An additional parameter obtained from the ultrasonic absorption measurements is the standard volume change of the reaction, $\Delta V = V_{\mathrm{CDGST}^+} - (V_{\mathrm{CD}} + V_{\mathrm{GST}^+})$, which is related to the maximum absorption per wavelength, $\mu_{\max}$, as follows

$$\mu_{\max} = 0.5A f_r v$$

$$= \pi\rho v^2\Gamma^{-1}(\Delta V)^2/2RT \tag{4}$$

where Γ is the concentration term expressed as $\Gamma = 1/[\mathrm{CD}] + 1/[\mathrm{GST}^+] + 1/[\mathrm{CDGST}^+]$, R is the gas constant, and T is absolute temperature. The analytical procedures for the rate and thermodynamic constants are the same as those described elsewhere.[9] The results are listed in Table 2. The plots of $2\pi f_r$ vs $\{(1 + KC_{\mathrm{CD}} + KC_{\mathrm{GST}^+})^2 - 4K^2C_{\mathrm{CD}}C_{\mathrm{GST}^+}\}^{1/2}$ are shown in Figures 3 and 4, where the solid line is the calculated one with the helps of the determined k_b and K. It is seen that the experimental data fall on the calculated line.

The ultrasonic absorption coefficients were measured at further dilute concentration of β-CD containing PEACL and the result is shown in Table 1 and Figure 3. The experimental relaxation frequency is close to the calculated line as is seen in this figure.

Discussion

The characteristic ultrasonic relaxations in aqueous solution of amines are those due to the proton-transfer reaction[13,14] and the association reaction[19,20] or concentration fluctuation.[21,22] The relaxation associated with the former reaction is observed in most of amine solutions and the relaxation due to the latter process is found in solution, the solute of which consist of

TABLE 1: Ultrasonic Relaxation and Thermodynamic Parameters for Aqueous Solution of PEACL and HEACL with β-CD at 25 °C

C_{CD} (mol dm^{-3})	C_{GST} (mol dm^{-3})	f_r (MHz)	A (10^{-15} s^2 m^{-1})	B (10^{-15} s^2 m^{-1})	ρ (kg m^{-3})	v (m s^{-1})	pH
			PEACL System				
0.0087	0.020	10.0 ± 0.4	59.7 ± 1.8	21.8 ± 0.1	1001.04 ± 0.01	1500.0 ± 0.5	7.29
0.0087	0.030	12.7 ± 0.2	78.3 ± 1.0	21.0 ± 0.1	1001.12 ± 0.01	1501.4 ± 0.4	7.17
0.0087	0.048	13.1 ± 0.3	96.1 ± 1.6	22.0 ± 0.1	1001.18 ± 0.01	1502.9 ± 0.5	7.12
0.0087	0.080	15.5 ± 0.3	105.4 ± 1.6	21.4 ± 0.1	1001.30 ± 0.01	1505.1 ± 0.6	7.02
0.0087	0.100	15.4 ± 0.3	108.5 ± 1.6	21.3 ± 0.1	1001.30 ± 0.01	1509.3 ± 0.5	7.19
0.0087	0.200	17.9 ± 0.3	76.9 ± 1.4	21.5 ± 0.1	1001.52 ± 0.01	1519.4 ± 0.7	7.29
0.0087	0.300	27.0 ± 0.7	52.1 ± 1.3	20.9 ± 0.1	1002.14 ± 0.01	1529.5 ± 0.6	7.17
0.0087	0.400	28.3 ± 0.5	35.5 ± 0.7	21.7 ± 0.1	1002.30 ± 0.01	1541.5 ± 0.6	7.37
0.0020	0.020	8.5 ± 0.4	14.7 ± 0.4	21.95 ± 0.03	998.02 ± 0.01	1497.6 ± 0.4	7.02
			HEACL System				
0.0087	0.020	2.92 ± 0.04	459 ± 8	22.4 ± 0.2	1001.54 ± 0.01	1499.0 ± 0.4	7.13
0.0087	0.040	4.33 ± 0.08	295 ± 5	21.6 ± 0.2	1001.61 ± 0.01	1501.8 ± 0.5	7.02
0.0087	0.050	4.55 ± 0.09	278 ± 4	24.3 ± 0.1	1001.69 ± 0.01	1504.4 ± 0.5	7.32
0.0087	0.060	4.55 ± 0.09	256 ± 4	22.3 ± 0.1	1001.54 ± 0.01	1504.9 ± 0.6	7.00
0.0087	0.070	6.70 ± 0.11	186 ± 3	22.1 ± 0.2	1002.17 ± 0.01	1504.4 ± 0.4	7.08
0.0087	0.080	7.21 ± 0.11	149 ± 2	22.1 ± 0.1	1002.85 ± 0.01	1506.7 ± 0.4	7.18
0.0087	0.100	10.17 ± 0.21	89 ± 1	20.9 ± 0.1	1002.83 ± 0.01	1510.2 ± 0.6	7.38

TABLE 2: Rate and Thermodynamic Constants for Host−Guest Complexation at 25 °C

guest	k_f (10^8 mol^{-1} dm^3 s^{-1})	k_b (10^7 s^{-1})	K (mol^{-1} dm^3)	ΔV (10^{-6} m^3 mol^{-1})
butylammonium ion[a]	0.8 ± 0.1	24.3 ± 0.1	0.33 ± 0.02	26 ± 4
pentylammonium ion	3.0 ± 0.1	6.5 ± 0.1	4.7 ± 0.2 ~8[b]	20 ± 5
hexylammonium ion	5.8 ± 0.2	0.48 ± 0.01	122 ± 4 65 ± 16[b]	23 ± 5

[a] Reference 9. [b] Reference 23.

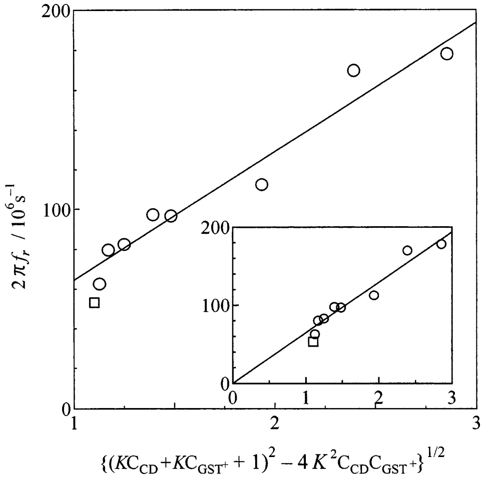

Figure 3. Plots of $2\pi f_r$ vs $\{(KC_{CD} + KC_{GST+} + 1)^2 - 4K^2C_{CD}C_{GST+}\}^{1/2}$ for aqueous solutions of PEACL in the presence of 0.0087 mol dm^{-3} β-CD at pH ≈ 7.2 and 25 °C: (□) is the result at 0.0020 mol dm^{-3} β-CD and 0.020 mol dm^{-3} PEACL.

relatively high hydrophobicity (butylamine,[19] pentylamine[20]). However, these relaxational absorptions disappear when the solution pH is controlled to a neutral value. This is because alkylamines dissociate to form the alkylammonium ions that have high polarities. As can be seen in Figures 1 and 2, above situations were clarified again in the solution with pentylamine and were proved to be correct in the solution with hexylamine because the ultrasonic relaxations were not observed in the solutions of PEACL and HEACL at pH ≈ 7.2.

It is important to notice that the ultrasonic relaxation phenomenon is only observed when PEACL or HEACL and β-CD coexist in solution, although it is not found when the guest is propylammonium ion.[9] However, a similar relaxation is also observed in the solution of butylammonium ion and β-CD.[9] These results indicate that the ultrasonic relaxation is surely related to the hydrophobicity of the alkyl groups. The inside of the CD cavity is a hydrophobic environment, and therefore, it is considered that the most probable cause of the observed relaxation in this study is associated with the complexation reaction between the hydrophobic part of guest and the cavity of the host. Rekharsky et al.[23] reported the equilibrium constants for the various alkylammonium ions and β-CD in phosphate buffer. The tendency of the equilibrium constants with the number of carbon atoms is similar to those obtained in this study. The slightly different values of the equilibrium constants may be because the solvent is different.

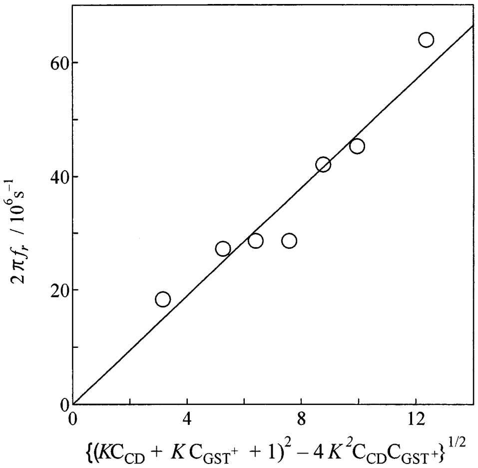

Figure 4. Plots of $2\pi f_r$ vs $\{(KC_{CD} + KC_{GST+} + 1)^2 - 4K^2C_{CD}C_{GST+}\}^{1/2}$ for aqueous solutions of HEACL in the presence of 0.0087 mol dm^{-3} β-CD at pH ≈ 7.2 and 25 °C.

When the obtained kinetic results are compared with those reported so far,[6−10] the forward rate constants, k_f, scarcely depend on the guest structures even if the sizes or structures of guests are different. This is because the cavity of β-CD has enough size to incorporate the guest molecules used in our study. The values of k_f were of the order of 10^8 mol^{-1} dm^3 s^{-1}, and it was proved to be reasonable as a diffusion-controlled reaction, taking account of the shape and structure of the CD cavity.[8]

On the other hand, it is seen that the backward rate constants, k_b, considerably depend on the structures of the guests as is seen in Table 2. This result reflects in the stability of the complex because of the relationship as $K = k_f / k_b$. That is, the rate constant decreases and the equilibrium constant increases with the increase in the number of carbon atoms in the alkylammonium ions, the trend of which is also seen in the similar system.[23] There are some kinetic reports in which the mechanism for the complexation reaction between host and gust is interpreted by the process with the two-steps; the fast preequilibrium step for the intermediate complex followed by a slow rate-determining step forming the final insertion compound.[24,25] However, the ultrasonic absorption spectra observed in the present systems are well analyzed by the single relaxational equation, and therefore, we interpreted the present result as the single step because there is no evidence for the existence of the slower relaxation process in the lower frequency in these present systems. The molecular sizes of guests might affect the dynamic characteristics for the complexation reaction.

Next, the results for the standard volume change of the reaction in Table 2 indicate that the values of ΔV are almost the same even if the structures of the guests are different. The apparent molar volumes of butylammonium, pentylammonium, and hexylammonium bromides in water are 110.2×10^{-6}, 126.1×10^{-6}, and 142.1×10^{-6} m^3 mol^{-1}, respectively.[26] However, the obtained volume changes are considerably smaller than these apparent molar volumes as is seen in Table 2 even if the counterion is different. Therefore, it is difficult to consider that the whole of the alkylammonium ion is incorporated into the β-CD cavity. It is said that the complex formed by guest and CD consists of the inserted hydrophobic portion of the guest into the CD cavity with the polar group of the guest in solvent exposed at the wide top end of the cavity.[23] The hydrated β-CD in aqueous solution can involve about seven or more water molecules inside the cavity, and they are released when the guest molecule is enclosed in the cavity.[27]

In our previous report,[9] it was shown that the relationship for the standard volume change of the complexation reaction was given by a simple equation as $\Delta V = nV_{H_2O} - mV_{CH_2} - V_{CH_3}$ where n is the number of water molecule expelled from the cavity and m the number of the incorporated methylene groups. The reported values[28] are available for $V_{CH_2} = 15.7 \times 10^{-6}$ m^3 mol^{-1}, $V_{CH_3} = 27.1 \times 10^{-6}$ m^3 mol^{-1}, and $V_{H_2O} = 18 \times 10^{-6}$ m^3 mol^{-1}. Therefore, the standard volume change is controlled by the combination between n and m values.

In the solution of butylammonium ion,[9] we proposed that four or five water molecules were expelled when the guest was incorporated in the β-CD cavity, and consequently the methyl group and one or two methylene groups in the guest molecule exist in the cavity. In aqueous solution of propylammonium ion, on the other hand, the relaxation is not observed, the result of which reflects that propylammonium ion does not form the inclusion complex because of the small hydrophobic tail and the great polarity of the ammonium ion. The obtained standard volume changes in this study are not dependent on the length of hydrophobic group as is seen in Table 2. Therefore, it is considered that the number of the expelled water molecules may increase with increase in the number of the carbon atoms in alkylammonium ion because the complex is stabilized and the exit rate from the cavity decreases. That is, the guest molecules may be inserted more deeply into the cavity with an increase in the number of carbon atoms.

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References and Notes

(1) Connors, K. A. *Chem. Rev.* **1997**, *97***,** 1325.
(2) Rekharsky, M. V.; Inoue, Y. *Chem. Rev.* **1998**, *98*, 1875.
(3) Funasaki, N.; Ishikawa, S.; Neya, S. *J. Phys. Chem. B* **2002**, *106*, 6431.
(4) Rohrbach, R. P.; Rodriguer, L. J.; Eyring, E. M.; Wojcik, J. F. *J. Phys. Chem.* **1977**, *81*, 944.
(5) Hall. D.; Bloor, D.; Tawarah, K. Wyn-Jones, E. J. *Chem. Soc. Faraday Trans. 1*, **1986**, *82*, 2111.
(6) Nishikawa, S.; Ugawa, T.; Fukahori, T. *J. Phys. Chem. B* **2001**, *105*, 7594.
(7) Nishikawa, S.; Fukahori, T.; Ishikawa, K. *J. Phys. Chem. A* **2002**, *106*, 3029.
(8) Fukahori, T.; Ugawa, T.; Nishikawa, S. *J. Phys. Chem. A* **2002**, *106*, 9442.
(9) Nishikawa, S.; Yamaguchi, K.; Fukahori, T. *J. Phys. Chem. B* **2003**, *107*, 6415.
(10) Ugawa, T.; Nishikawa, S. *J. Phys. Chem. A* **2001**, *105*, 4248.
(11) Nishikawa, S.; Kotegawa, K. *J. Phys. Chem.* **1985**, *89*, 5417.
(12) Kuramoto, N.; Ueda, M.; Nishikawa, S. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 1560.
(13) Eigen, M.; Maass, G.; Schwarz, G. *Z. Phys. Chem.* **1971**, *74*, 319.
(14) Nishikawa, S.; Nakamoto, T.; Yasunaga, T. *Bull. Chem. Soc. Jpn.* **1973**, *64*, 324.
(15) Kato, S.; Nomura, H.; Miyahara, Y. *J. Phys. Chem.* **1985**, *89*, 5417.
(16) Rauh, S.; Knoche, W. *J. Chem. Soc., Faraday Trans. 1* **1985**, *81*, 2551.
(17) Jobe, D. J.; Verrall, R. E.; Reinsborough, V. C. *Can. J. Chem.* **1990**, *68*, 2131.
(18) Nishikawa, S.; Tanaka, M.; Mashima, M. *J. Phys. Chem.* **1981**, *85*, 686.
(19) Nishikawa, S.; Yasunaga, T. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 1098.
(20) Nishikawa, S.; Yasunaga, T.; Takahashi, K. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 2992.
(21) Atkinson, G.; Emara, M. M.; Endo, H.; Atkinson, B. L. *J. Phys. Chem.* **1980**, *84*, 259.
(22) Rupprecht, A.; Kaatze, U. *J. Phys. Chem. A* **1997**, *101*, 9884.
(23) Rekharsky, M. V.; Mayhew, M. P.; Goldberg, R. N.; Ross, P. D.; Yamashoji, Y.; Inoue, Y. *J. Phys. Chem. B* **1997**, *101*, 87.
(24) Hersey, A.; Robinson, B. H.; Kelly, H. C. *J. Chem. Soc., Faraday Trans.* 1986, *82*, 1271.
(25) Yoshida, N.; Fujita, Y. *J. Phys. Chem.* **1995**, *99*, 3671.
(26) Leduc, P. A.; Fortier, J. A.; Desnoyers, J. E. *J. Phys. Chem.* **1974**, *78*, 1217.
(27) Marini, A.; Berbenni, V.; Bruni, G.; Massarotti, V.; Mustarelli, P. *J. Phys. Chem.* **1995**, *103*, 7532.
(28) Wilson, L. D.; Verrall, R. E. *J. Phys. Chem. B* **1997**, *101*, 9270.