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Kinetics of Complexation between Cyclodextrin and Alcohol by Ultrasonic Relaxation Method: β-Cyclodextrin Solutions with 1-Butanol and 2-Methyl-2-propanol

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The ultrasonic absorption coefficients over frequency range from 1.0 to 220 MHz were measured in aqueous β-cyclodextrin solutions with 1-butanol and 2-methyl-2-propanol at 25 °C. A clear single relaxational absorption with a relaxation frequency from 5 to 20 MHz was observed in a solution with 1-butanol, while the relaxational absorption was found in a lower frequency range in a solution with 2-methyl-2-propanol. The cause of the relaxation was attributed to a perturbation of a chemical equilibrium associated with complexation between β-cyclodextrin (host) and alcohol (guest). The rate and equilibrium constants for the complexation were determined from the concentration dependence of the relaxation frequency for the solution with 1-butanol. The standard volume change of the reaction was also obtained from the maximum absorption per wavelength. These results were compared with those for complexation between β-cyclodextrin and 1-propanol, and were considered in relation to the alcohol molecular structure. It was found that the rate of complex formation is almost independent of the guest molecule, and, therefore, the equilibrium constant for the complexation is controlled by the rate of departure of the guest molecule from the host. From this fact, the rate parameters for a solution with 2-methyl-2-propanol were estimated, and the calculated ultrasonic relaxation parameter was compared with the experimental data.

It is well known that cyclodextrins as host molecules include various kinds of guest molecules into their cavities, which have quite high hydrophobic moieties.[1] The applicability of cyclodextrins has been widely extended. In our previous report,[2] it was mentioned that an ultrasonic relaxation observed in aqueous β-cyclodextrin (β-CD) solution with 1-propanol was due to a perturbation of an equilibrium associated with a complex formation reaction between them; the rate and thermodynamic constants have been reported. The rate constants associated with the complexation reaction have been suggested to be strongly dependent on the guest structure from a dynamical point of view, although the host structure is also important to include a guest. This was also shown dynamically for α-cyclodextrin and nitrophenol derivatives by Gramer et al.[3] However, fundamental dynamical properties concerning complexation between the host and guest molecules were not examined so systematically. This may be because the complexation rates are widely spread with relaxation times from a few seconds[4] to nanoseconds,[2] depending on the characteristics of the host and guest molecules.

Many equilibrium constants have been determined by statics methods, and the stability of complexes formed by a host and guest has been discussed from a thermodynamic point of view.[1,5,6] Actually, in determining the equilibrium constants, some probes of chemicals are occasionally used. Also, recently, the effects of additives on equilibrium for complexation have been estimated.[7]

An ultrasonic absorption method as one of the relaxation methods is very useful for obtaining the rate constants for very fast reactions occurring in solutions, because it is possible to obtain the kinetic information without adding any other chemicals for monitoring the kinetic processes. Also, the equilibrium parameters associated with reactions are also obtainable from the amplitude of the ultrasonic absorption and the forward and backward rate constants.

In order to see the relation between the kinetic parameters and the structure of guest molecules, we selected two alcohols, 1-butanol and 2-methyl-2-propanol as the guest for β-CD, and the ultrasonic method was applied to their aqueous solutions.

For the sake of the ultrasonic absorption measurements over a wider frequency range, a new resonator cell working in the frequency range from 1 to 3.7 MHz was constructed. Thus, it is possible to obtain absorption coefficients over more than two orders of the ultrasonic frequency range, which may provide accurate relaxation parameters and eventually the rate parameters.

Experimental

β-Cyclodextrin was purchased from Wako Pure Chemical Co., Ltd. It was recrystallized once from water, and then dried in a vacuum oven at 45 °C for more than 30 h until the weight of the chemical reached a constant value. It was kept in a desiccator. 1-Butanol and 2-methyl-2-propanol were also purchased from Wako Pure Chemical Co., Ltd., and were distilled once at normal pressure.

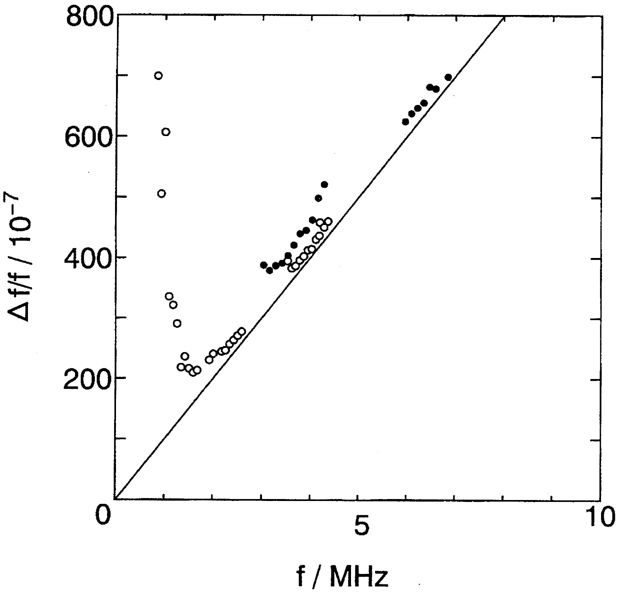

Fig. 1. The frequency dependence of the half band width divided by the frequency on the frequency. The solid line is the theoretical values for water which are calculated using $\alpha/f^2=21\times10^{-15}\mathrm{s^2\,m^{-1}}$ and $c=1497\ \mathrm{m\,s^{-1}}$ at 25 °C. ○: the results obtained through 3 MHz crystal cell, ●: those obtained by 5 MHz crystal cell.

The sample solutions were prepared by weighing the solutes with distilled and filtered water from a MilliQ SP-TOC system of Japan Millipore Ltd.

The ultrasonic absorption coefficients, α's, were measured by a pulse method in the frequency range from 15 to 220 MHz with 5 and 20 MHz fundamental x-cut crystals, and by a resonance method from 1 to 6.7 MHz. A modification of the resonance apparatus is the introduction of the Vector Voltmeter (HP 8508A), which enabled us to measure the output signals from the receiving x-cut crystal more precisely within a few milliseconds. The digital signals from the voltmeter are sent to an NEC 9800 computer alternatively with the signal of the frequency generator; the resonance curve is analyzed automatically.

A new resonator cell with 3 MHz fundamental x-cut quartz with a diameter of 4 cm was newly constructed in order to measure the absorption coefficient in the range of less than 4 MHz. In the frequency range from 3 to 7 MHz, a 5 MHz fundamental crystal with a 2 cm diameter was used. Figure 1 shows plots of the half band width divided by the frequency, $\Delta f/f$, vs. the frequency, f, the relation of which is expressed as $\Delta f/f=(\alpha/f^2)(c/\pi)f+M_\mathrm{q}$ where c is the sound velocity and M_q the mechanical loss of the resonator. The solid line in Fig. 1 represents the calculated values for liquid water. It can be seen that the two resonators work quite precisely in order to obtain the ultrasonic absorption coefficient in the range mentioned above. Especially, in the frequency range from 2 to 4.4 MHz and in that from 6 to 6.7 MHz, it is possible to obtain almost the absolute values of the absorption coefficients because the mechanical loss is almost zero. More details concerning the absorption apparatus and the procedure for determining the absorption coefficient are described precisely elsewhere.[9,10] The sound velocity was obtained by a sing-around meter at 1.92 MHz and the resonator at around 3 MHz. A density measurement was carried out using a vibrating density meter. The temperature for all of the cells was controlled to within less than ±0.01 °C. All of the measurements were performed at 25 °C.

Results and Discussion

Figure 2 shows representative ultrasonic absorption spectra in a β-CD aqueous solution with 1-butanol and Fig. 3 does those in a solution with 2-methyl-2-propanol. As pointed out in a previous report,[2)] no frequency dependence of the absorption coefficient divided by the square of the frequency, α/f^2, was observed (no excess absorption) at the concentration of β-CD investigated here when alcohol did not exist in the solution. In aqueous solutions of 1-buthanol and 2-methyl-2-propanol, a relaxational ultrasonic absorption was observed in a high concentration range.[11—14)] The alcohol concentration used in this study was too low to observe such relaxations. In order to confirm further this, the absorption measurement was carried out in aqueous solutions of alcohols at concentrations similar to those used for the present experiments. One of the results is shown in Fig. 3. It can be seen that no excess absorption is observed down to 1 MHz.

The addition of 1-butanol or 2-methyl-2-propanol has caused the appearance of the excess absorption, as can be seen in Figs. 2 and 3. In a solution with 1-butanol, the almost plateau regions of α/f^2 are observed in high and low frequency ranges, although the plateau is only found in the high frequency range for the solution with 2-methyl-2-propanol.

The frequency dependence of the excess absorption is well tested by a conventional Debye-type relaxational equation;

$$\alpha/f^2=A/[1+(f/f_\mathrm{r})^2]+B, \tag{1}$$

where f_r is the relaxation frequency and A and B are constants. The ultrasonic parameters, f_r, A, and B, can possibly be determined using a nonlinear least-mean square method,

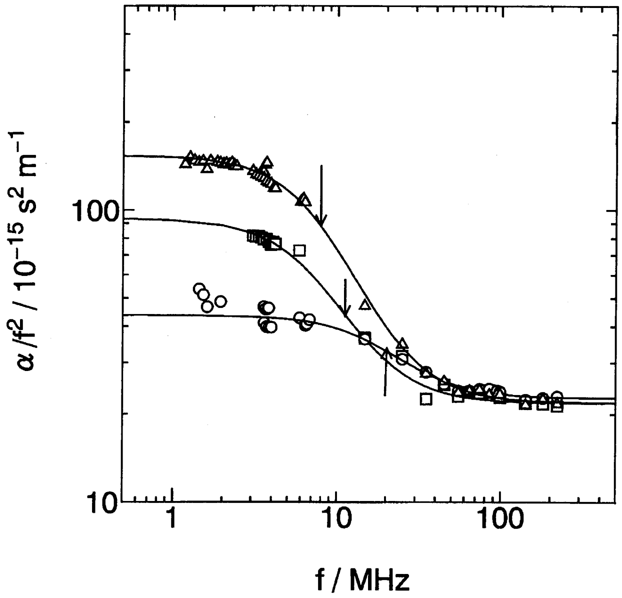

Fig. 2. Representative ultrasonic absorption spectra in aqueous β-CD solutions with 1-butanol. △: 0.0150 mol dm^{-3} β-CD and 0.0505 mol dm^{-3} 1-butanol, □: 0.0111 mol dm^{-3} β-CD and 0.101 mol dm^{-3} 1-butanol, and ○: 0.0111 mol dm^{-3} β-CD and 0.275 mol dm^{-3} 1-butanol.

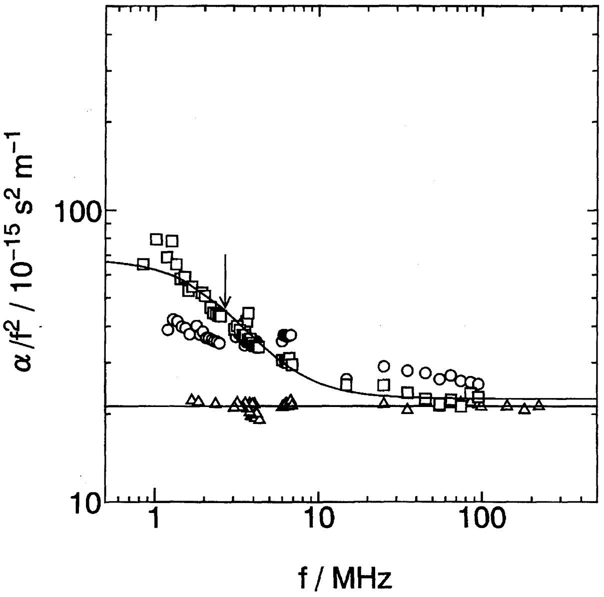

Fig. 3. Ultrasonic absorption spectra in aqueous β-CD solutions with 2-methyl-2-propanol and in aqueous solution of 2-methyl-2-propanol. ○: 0.0200 mol dm^{-3} β-CD and 0.502 mol dm^{-3} 2-methyl-2-propanol, □: 0.0111 mol dm^{-3} β-CD and 0.0500 mol dm^{-3} 2-methyl-2-propanol, and △: 0.100 mol dm^{-3} 2-methyl-2-propanol only.

the details of which are described elsewhere.[9] Thus obtained parameters have been used to draw theoretical curves; those are shown in Figs. 2 and 3 by the solid curves. It can be seen that the agreement between the experimental and theoretical values is excellent. However, all of the spectra in the solution with 2-methyl-2-propanol have not been analyzed, because the position of the relaxation frequency is quite low and the amplitude of the absorption is not so large.

We first consider the relaxation mechanism observed in the solution with 1-butanol. In Table 1, the obtained ultrasonic relaxation parameters are listed along with the sound velocity and density data. The relaxational absorption was not observed in an aqueous solution of β-CD or in that of 1-butanol, because the concentrations of the solutes were very low. When both solutes coexisted in aqueous media, a clear single relaxational absorption was observed. This means that the cause of the relaxation could be associated with the interaction between β-CD and 1-butanol. It is said that the alcohol molecule is included into β-CD cavity in monomer to form the complex, and that the complex is in equilibrium with their monomers. Thus, the perturbation of the following equilibrium by ultrasonic waves is considered as a cause of the observed relaxation;

$$\mathrm{CD} + \mathrm{ROH} \underset{k_b}{\overset{k_f}{\rightleftharpoons}} \mathrm{CDROH}, \tag{2}$$

where CD is β-CD, ROH 1-butanol, CDROH the complex and k_f and k_b are the forward and backward rate constant, respectively. We define the equilibrium constant as $K=k_f/k_b=[\mathrm{CDROH}]/[\mathrm{CD}][\mathrm{ROH}]$. Then, the relation for the relaxation time, τ, or the relaxation frequency is expressed by the reactant concentrations. It is then derived as functions of the analytical concentrations of β-CD, C_{dx}, and 1-butanol, C_{al}, as follows.[2]

$$\begin{aligned}\tau^{-1} &= 2\pi f_r = k_f\{[\mathrm{CD}]+[\mathrm{ROH}]\}+k_b \\ &= k_b[\{1+K(C_{dx}+C_{al})\}^2-4K^2C_{dx}C_{al}]^{1/2},\end{aligned} \tag{3}$$

When the concentration of β-CD is fixed, it is easy to estimate the parameters, K and k_b, using a nonlinear least-mean square method so as to obtain the minimum standard deviation, because the relaxation time is only a function of 1-butanol concentration, C_{al}. At 0.0111 mol dm^{-3} of β-CD, K and k_b were determined, the results of which are listed in Table 2 along with those for the solution with 1-propanol. Figure 4 shows plots of the relaxation frequency as a function of the analytical concentration term: the right hand term of Eq. 3. It can be seen that the experimental data fall on

Table 2. Rate and Thermodynamic Constants for Complexation of β-Cyclodextrin with 1-Propanol and 1-Butanol at 25 °C

	1-Propanol	1-Butanol
k_f/mol^{-1} dm^3 s^{-1}	$(5.1\pm0.7)\times10^8$	$(2.8\pm0.8)\times10^8$
k_b/s^{-1}	$(1.21\pm0.07)\times10^8$	$(3.8\pm0.6)\times10^7$
K/mol^{-1} dm^3	4.2±0.6	7±2
K/mol^{-1} dm^3	3.72,[6] 4.5[5]	16.6,[6] 16[5]
ΔV/10^{-6} m^3 mol^{-1}	12.5±0.3	11±1

Table 1. Ultrasonic Parameters for Aqueous Solutions of β-Cyclodextrin with 1-Butanol at 25 °C

Concn/mol dm^{-3}		f_r	A	B	c	ρ
β-CD	1-Butanol	MHz	10^{-15}s^2 m^{-1}		m s^{-1}	kg dm^{-3}
0.0111	0.0508	5.3±0.3	145±8	21.9±0.3	1500	1.0010
0.0111	0.0753	8.8±0.2	82±1	22.4±0.1	1502	1.0009
0.0111	0.101	11.2±0.7	62±4	21.6±0.1	1501	1.0026
0.0111	0.150	14.8±1	39±3	21.9±0.1	1504	1.0019
0.0111	0.200	14.6±0.8	31±1	22.9±0.2	1508	0.9995
0.0111	0.250	18.6±1.4	22±1	23.0±0.1	1511	1.0000
0.0111	0.275	19.7±1.2	21±2	22.7±0.1	1511	0.9987
0.0111	0.400	20.5±1.8	11.2±0.7	23.9±0.2	1522	0.9972
0.0150	0.0505	8.0±0.2	131±3	21.9±0.1	1501	1.0027
0.0150	0.250	25.7±0.8	29.3±0.1	21.2±0.1	1512	1.0057
0.0178	0.200	22±1	41±3	21.9±0.2	1517	1.0030

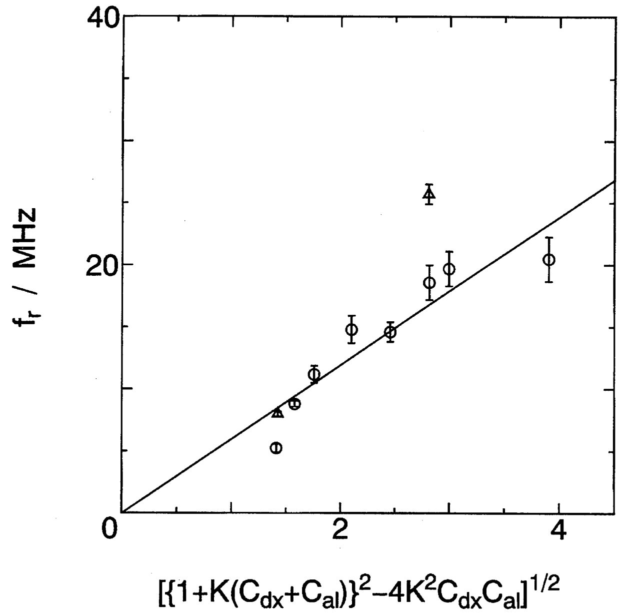

Fig. 4. The concentration dependence of the relaxation frequency. ○: the concentration of β-CD is fixed at 0.0111 mol dm^{-3}, △: the concentrations of β-CD is 0.0150 mol dm^{-3}, and □: the concentration is 0.0178 mol dm^{-3}.

a straight line, which confirms that the cause of the relaxation is due to a perturbation of the equilibrium expressed by Eq. 2. Since the equilibrium constant obtained in this study has been determined without additive except β-CD and alcohol, the value is considered to be close to that obtained by static experiments[5,6] as can be seen in Table 2. This also confirms that the cause of the observed relaxation is due to the complex formation process.

Once the rate and equilibrium constants are determined, it is possible to calculate the relaxation frequency at different concentrations of β-CD, with the help of Eq. 3, independently. The measurements were performed at 0.0150 and 0.0178 mol dm^{-3} β-CD with different concentrations of 1-butanol. The obtained results are also shown in Table 1 and Fig. 4, and it can be seen that they are close to the calculated line.

The standard volume change of the reaction is obtainable from the maximum absorption per wavelength, $\mu_m = 0.5Af_rc$, using the following relation under an assumption that the enthalpy term is negligible in aqueous media.

$$\mu_m = \pi\rho c^2(1/[\mathrm{CD}]+1/[\mathrm{ROH}]+1/[\mathrm{CDROH}])^{-1}(\Delta V)^2/2RT, \quad (4)$$

where ρ is the solution density and ΔV the standard volume change of the reaction. The obtained value is indicated in Table 2 along with that for a solution with 1-propanol for a comparison. The rather small value for the volume change is associated with a compensation of the leave of water molecules from cavity and the inclusion of alcohol, which was discussed in a previous report more in detail.[2]

As shown in Table 2, the rate constant for the complex formation, k_f, is not so dependent on the guest, alcohol. This means that the equilibrium constant, K, is controlled by the backward rate constant, k_b, which is the index of velocity of the departure of the guest from the cavity of β-CD. This situation can also be seen by the next estimation. A numerical calculation of the concentration terms in Eq. 3 has proved that the square term in the square root is larger than $4K^2C_{dx}C_{al}$, and thus Eq. 3 is very roughly expressed as $2\pi f_r \doteqdot k_f(C_{dx}+C_{al})+k_b$. Then, plots of the total solute concentration of β-CD plus alcohol vs. the relaxation frequency gives the approximate forward and backward rate constants. This is shown in Fig. 5. As can be seen, the slope value for a solution with 1-butanol is less than twice that with 1-propanol. On the other hand, the intercept for the former solution is more than three times larger than that for the latter solution. This means that the backward rate constant is mainly dependent on the alcohol structure. With increase in the hydrophobicity of alcohol, the rate constant for the departure of guest decreases. That is, the complex is considered to be stabilized with increase in the guest hydrophobicity. It is thus concluded that one of the main causes for complexation between β-CD and alcohols is the hydrophobic interaction; the complex is then stabilized because the rate constant for the departure of the guest is diminished along with increase in the hydrophobicity.

If the rate of the complex formation process is independent of the alcohol molecule, it is possible to estimate the backward rate constant for a solution with 2-methyl-2-propanol using the reported equilibrium constant, 47.9 mol^{-1} dm^3.[6] When the forward rate constant is taken to be approximately 4×10^8 mol^{-1} dm^3 s^{-1}, the backward rate constant for a solution with 2-methyl-2-propanol is estimated to be 8×10^6 s^{-1}. Thus, the relaxation frequency is calculated at any desired concentrations for solutions with 2-methyl-2-propanol using Eq. 3. At 0.0111 mol dm^{-3} β-CD and 0.0500 mol dm^{-3} 2-methyl-2-propanol, the calculated relaxation frequency is 4

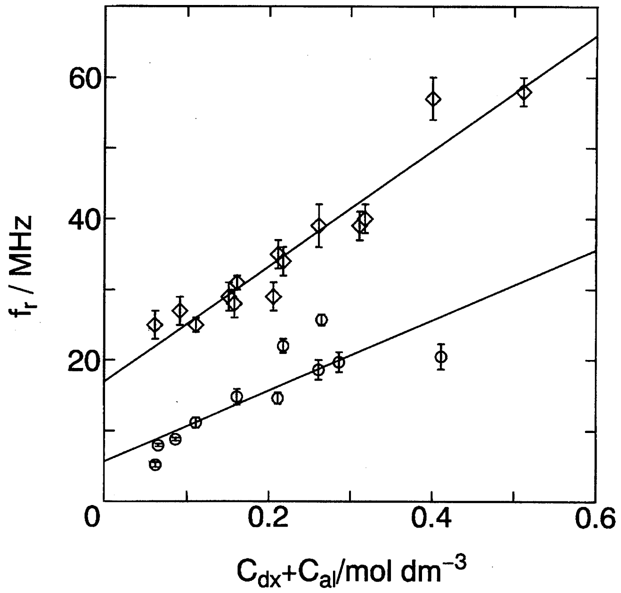

Fig. 5. The total concentration dependence of the relaxation frequency for β-CD aqueous solutions with 1-propanol (◇) and 1-butanol (○).

MHz, and the determined value shown in Fig. 3 is 2.7±0.4 MHz; both are considered to be close to each other. This calculation has also has proved that the stability of the complex formed by β-CD and alcohols is clearly associated with the rate constant for the departure of a guest from the cavity of a host.

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