

Kinetics on Isomeric Alcohols Recognition by α- and β-Cyclodextrins Using Ultrasonic Relaxation Method

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Ultrasonic absorption method was applied to elucidate the dynamic properties of host–guest complexation between α-cyclodextrin or β-cyclodextrin (host) and butanol isomers (guest) at 25 °C. The aim of this work was to reveal the effect of a structural difference in the hydrophobic part of a guest on the kinetic parameters for an inclusion reaction with cyclodextrins. Moreover, it was expected to clarify the effect of the cavity size on the reaction. Only when the host and guest existed together in water, a clear single relaxational phenomenon was observed. The cause of the relaxation was responsible for the complexation reaction between the host and the guest. The rate and equilibrium constants were obtained from the concentration dependence of the relaxation frequency, and the standard volume changes of the complexation reaction were from the maximum absorption per wavelength. The backward rate constant, k_b, was very dependent on the structure of the guest molecule. The k_b value decreased in the next hydrophobic series, *nor-* < *sec-* < *tert-* in β-CD systems, although a smaller k_b value was observed when the guest possessed a normal carbon chain in α-CD systems. The results of the volume change of the reaction implied that α-CD could only include a guest quite shallowly, and almost the entire guest molecule was included into the β-CD cavity.

Cyclodextrins (CDs) are cyclic oligosaccharides consisting of glucopyranose units through α-1,4 linkages. The shapes of these macromolecules are well likened to a truncated bucket. The well-known naturally occurring CDs are α-, β-, and γ-CD, composed of six, seven, and eight glucopyranose units, respectively, and the cavity diameter increases with the number of consisting units. The interior cavity has a fairly hydrophobic environment while both of the exterior rims show a hydrophilic character due to the existence of hydroxy groups. They have been attracting a great deal of interest owing to the ability to incorporate appropriate compounds as guests into their cavity through a noncovalent force.[1–4] By volumetric, NMR, ROESY, and other studies, it has been well proved that they usually form an inclusion complex with 1:1 stoichiometry in aqueous media, unless the hydrophobic side chain of the guest molecule is too long, or the guest has more than one site to be incorporated.[5–7] The inclusion process is accompanied by sensitive molecular recognitions. Therefore, their macromolecular recognition can be a good artificial model in biological systems such as an enzyme–substrate, or can be applied in a drug-delivery system.[3,8] In particular, when CDs are used as a component in building up supramolecular complexes such as polyrotaxan and molecular nanotube, CDs show more severe recognition.[9–11] For example, only methyl branching becomes a powerful influence on the formation of a supramolecular complex. Therefore, studying the isomeric effect on the complexation reaction may provide a further understanding of more complex reactions associated with supramolecular systems.

Despite a number of static equilibrium data for the inclusion complex between CDs and a variety of guest molecules, few studies have been conducted on kinetic information. In addition, there are some scattering concerning the reported results, even for the same reactions. This might primarily stem from restrictions to the experimental methods; the need for indicators or a buffer other than reactants.[4,12] Ultrasonic absorption method can be used to study fast reactions occurring from about a microsecond to a nanosecond, and can also be applied to an examination of the host–guest dynamic interaction in an aqueous solution at the molecular level. The advantages of using this method are that measurements are possible over a very wide frequency range, there is no need of any indicators, and there is no need of choice of the solvent.

In our previous series of kinetic studies by the ultrasonic relaxation method, several compounds were chosen to rule and figure out the precise complexation mechanism of CDs. Molecular recognition kinetics by β-CD in connection with the nature of guest molecules was carried out in these ultrasonic relaxation studies.[13–17] However, detail kinetic information concerning complexation reaction with α-CD has not been sufficient for further discussions. Since α-CD has a smaller cavity diameter compared to β-CD, it was expected that a different kinetic behavior would be observed. Because it was revealed that the most significant factor to control the stability of the inclusion complex is the hydrophobic part of the guest molecules, 1-butanol and 2-butanol (*nor*-butanol and *sec*-butanol) were chosen as the appropriate guests for α-CD as the host in this study in order to compare with other previously reported CD systems. Furthermore, 2-methyl-2-propanol (*tert*-butanol) was chosen as the guest for β-CD in order to see how the extent of the branching carbon chain would be recognized by β-CD. The aim of this study focused on the role of the structures in the hydrophobic part on the guest molecules, and on the cavity size of CDs in the complexation reaction with CDs.

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Experimental

Chemicals. α-CD was purchased from Wako Pure Chemical Co. Ltd., and was recrystallized once using distilled and filtered water by a Milli-Q SP-TOC filter system from Japan Millipore Ltd. It was then sufficiently dried in a vacuum dryer at about 45 °C. 1-Butanol (*nor*-butanol), 2-butanol (*sec*-butanol), and 2-methyl-2-propanol (*tert*-butanol) were also obtained from Wako Pure Chemical Co. Ltd. as the purest grades, and were used without further purification. All of the sample solutions were prepared by weighing just before the experiments.

Apparatus. Ultrasonic absorption coefficients, α, were measured by a resonance method in the frequency range from about 0.8 to 9 MHz. The apparatus is consisted of four resonance cells with 3 MHz (covered from about 0.8 to 2.5 MHz range), 5 MHz (A) (about 3 to 4.3 MHz), 5 MHz (B) (about 3 to 7.5 MHz), and 7 MHz (about 8 to 9 MHz) fundamental x-cut crystals. The temperature fluctuation for the resonator cells was maintained at less than ±0.01 °C (Lauda RM20). The cell constants for each cell were determined by water prior to every experiment.[18] A pulse apparatus with a 5 MHz fundamental crystal was used in the range from 25 to 95 MHz, and the cell was under the temperature condition within ±0.1 °C (EYEYA UNI ACE BATH NCB-2200). More details of the absorption apparatus are described elsewhere.[19] Sound velocity values were obtained by a resonator at around 3 MHz, and the solution densities were determined by a vibrating density meter (Anton Paar NMA 60/602). All measurements were carried out at 25 °C.

Results

Kato et al. reported on an ultrasonic relaxation study for α-, β-, and γ-CD aqueous solutions. The observed double relaxation processes were ascribed to a water exchange process in CDs and a desorption of the hydrated CD molecule. The relaxation phenomena were observed in a 0.026 mol dm^{-3} α-CD aqueous solution, which is the lowest concentration of α-CD tested in their work.[20] Previously, we found that there was no frequency dependence of the ultrasonic absorption coefficient divided by the square of the sound frequency, α/f^2, at concentration of 0.0120 mol dm^{-3}.[13] Thus, all of the concentrations of α-CD were kept below 0.0100 mol dm^{-3} in the present study in order to avoid any overlap of the relaxations due to CD molecules. The concentrations of β-CD were kept under 0.0087 mol dm^{-3}. Similarly, the concentration range of alcohols (*nor*-butanol, *sec*-butanol, and *tert*-butanol) was taken to be sufficiently low so that no relaxational absorption appeared in their aqueous solutions. Figs. 1, 2, and 3 show the representative ultrasonic absorption spectra in aqueous solutions of butanol isomers in the presence of CDs. The frequency dependence of α/f^2 was surely observed in all of the mixed aqueous solutions.

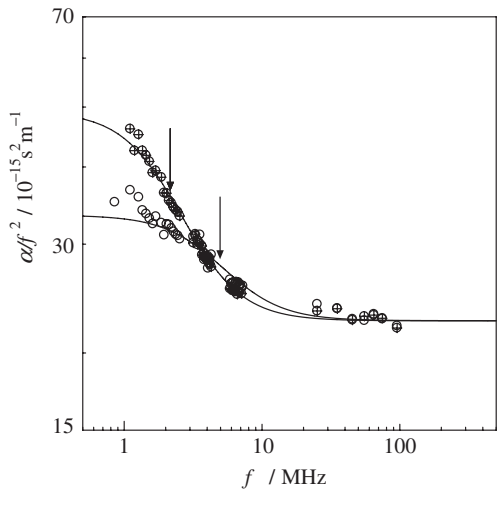

Fig. 1. Representative ultrasonic absorption spectra in aqueous solution of *nor*-butanol in the presence of 0.0100 mol dm^{-3} α-CD at 25 °C; (⊕): 0.020 mol dm^{-3} *nor*-butanol + α-CD, (○): 0.050 mol dm^{-3} *nor*-butanol + α-CD. The arrows show the locations of relaxation frequency.

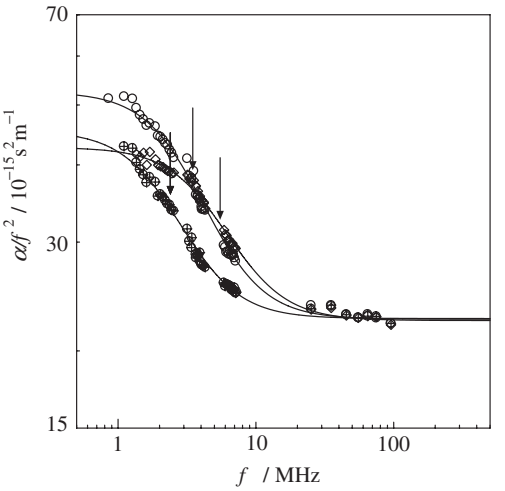

Fig. 2. Representative ultrasonic absorption spectra in aqueous solution of *sec*-butanol in the presence of 0.0100 mol dm^{-3} α-CD at 25 °C; (⊕): 0.010 mol dm^{-3} *sec*-butanol + α-CD, (○): 0.030 mol dm^{-3} *sec*-butanol + α-CD, (◇): 0.070 mol dm^{-3} *sec*-butanol + α-CD.

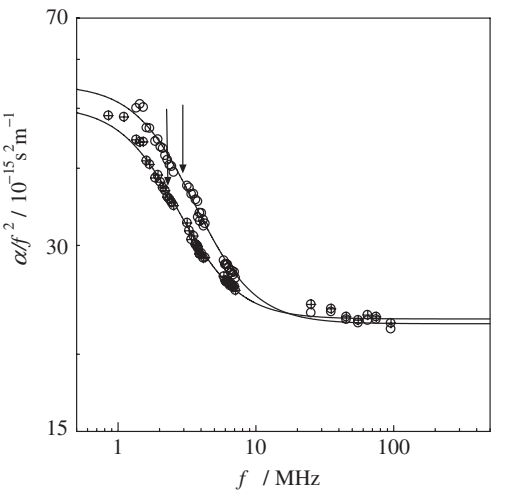

Fig. 3. Representative ultrasonic absorption spectra in aqueous solution of *tert*-butanol in the presence of 0.0087 mol dm^{-3} β-CD at 25 °C; (⊕): 0.010 mol dm^{-3} *tert*-butanol + β-CD, (○): 0.030 mol dm^{-3} *tert*-butanol + β-CD.

The frequency dependence of α/f^2 was extensively checked by the Debye-type single relaxational equation,

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

where f_r is the relaxation frequency, A is the relaxation amplitude, and B is the background absorption. A nonlinear least-mean-squares method was used to obtain the best fit of the experimental data to Eq. 1 to yield the above three relaxational parameters (f_r, A, and B). The line drawn through the data points in Figs. 1, 2, and 3 are well fitted with values of α/f^2 according to Eq. 1. The good agreement between the calculated line and the experimental data confirm that a single relaxation process occurred in all mixed solutions. Table 1 summarizes the relaxation parameters as well as the solution density, ρ, and the sound velocity, v.

The cause of the observed relaxation was evidently due to the dynamic interaction between CDs and alcohol molecules because the relaxation appeared only when the two solutes coexisted in water. Since all of the observed relaxations in mixed solutions were of the single type, the cause of the relaxation is responsible for the perturbation of the following chemical equilibrium by ultrasonic wave:

$$\mathrm{CD} + \mathrm{GST} \underset{k_b}{\overset{k_f}{\rightleftharpoons}} \mathrm{CDGST}, \quad (2)$$

where CD indicates α-CD or β-CD as the host, GST is an alcohol molecule as the guest, CDGST is the host–guest inclusion complex, and k_f and k_b are the forward and backward rate constants, respectively. The relationship between the relaxation time, τ, or the relaxation frequency, f_r, and the reactant concentrations can be derived through the chemical kinetic procedure as follows:

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

$$= k_b\{(KC_{CD} + KC_{GST} + 1)^2 - 4K^2C_{CD}C_{GST}\}^{1/2}, \quad (3a)$$

where the square brackets refer to the equilibrium concentrations of the reactants, K is the equilibrium constant defined as $K = k_f/k_b = [\mathrm{CDGST}]/[\mathrm{CD}][\mathrm{GST}]$, and C_{CD} and C_{GST} are the initial concentrations of CD and alcohol, respectively. When C_{CD} is kept constant, it can be seen that the relaxation frequency, f_r, should change with the guest concentration, C_{GST}. Actually, the relaxation frequency increased with an increase of the guest concentration, as can be seen in Table 1. Consequently, the two unknown parameters, K and k_b, were estimated by using a nonlinear least-mean-squares method. The results obtained are listed in Table 2 together with other systems for comparison. Hall et al. studied the system of *nor*-butanol or *nor*-pentanol with α-CD in water quantitatively by employing a head-space analysis involving gas chromatography, and kinetically by ultrasonic relaxation method.[21] Those results are also shown as reference in Table 2. Plots of the $2\pi f_r$ vs concentration term, $\{(KC_{CD} + KC_{GST} + 1)^2 - 4K^2C_{CD}C_{GST}\}^{1/2}$ are shown in Fig. 4. The solid line in the figure is drawn using the determined K and k_b values, and it can be seen that the experimental data are consistent with the cal-

Table 1. Ultrasonic Relaxation and Thermodynamic Parameters in Aqueous Solutions of Butanol Isomers with α-CD or β-CD at 25 °C

C_{CD}	C_{GST}	f_r	A	B	ρ	v
mol dm^{-3}		MHz	10^{-15} s^2 m^{-1}		kg m^{-3}	m s^{-1}
			α-CD + *nor*-butanol system			
0.0100	0.010	2.0 ± 0.3	23.3 ± 3.8	22.4 ± 0.1	1000.36 ± 0.01	1495.8 ± 0.8
0.0100	0.020	2.2 ± 0.3	26.7 ± 4.2	22.5 ± 0.1	1000.24 ± 0.01	1495.9 ± 0.8
0.0100	0.030	2.8 ± 0.3	20.3 ± 2.7	22.6 ± 0.1	1000.13 ± 0.01	1496.8 ± 0.8
0.0100	0.040	3.5 ± 0.4	15.5 ± 2.0	22.5 ± 0.1	999.98 ± 0.01	1497.1 ± 0.8
0.0100	0.050	4.7 ± 0.6	10.9 ± 1.2	22.6 ± 0.1	999.89 ± 0.01	1498.3 ± 1.0
0.0070	0.025	2.4 ± 0.4 (2.7)[a)]	16.5 ± 3.2	22.4 ± 0.1	999.14 ± 0.01	1496.0 ± 0.8
			α-CD + *sec*-butanol system			
0.0100	0.010	2.4 ± 0.2	22.9 ± 2.8	22.6 ± 0.1	1000.35 ± 0.01	1496.8 ± 0.7
0.0100	0.030	3.4 ± 0.2	30.0 ± 1.5	22.5 ± 0.1	1000.11 ± 0.01	1498.2 ± 0.8
0.0100	0.040	3.9 ± 0.2	27.6 ± 1.8	22.2 ± 0.1	1000.00 ± 0.01	1497.0 ± 0.8
0.0100	0.050	4.3 ± 0.2	24.5 ± 1.1	22.8 ± 0.1	999.90 ± 0.01	1500.6 ± 0.9
0.0100	0.070	5.3 ± 0.3	20.3 ± 1.0	22.4 ± 0.1	999.64 ± 0.01	1498.9 ± 0.7
0.0070	0.020	2.8 ± 0.2 (2.8)[a)]	22.0 ± 2.1	22.2 ± 0.1	998.20 ± 0.01	1495.2 ± 0.8
			β-CD + *tert*-butanol system			
0.0087	0.010	2.3 ± 0.2	27.7 ± 2.9	22.8 ± 0.1	1000.74 ± 0.01	1495.1 ± 0.8
0.0087	0.020	2.6 ± 0.2	32.1 ± 2.3	22.4 ± 0.1	1000.59 ± 0.01	1495.7 ± 0.8
0.0087	0.030	2.9 ± 0.2	32.2 ± 2.4	22.4 ± 0.1	1000.47 ± 0.01	1496.5 ± 0.8
0.0087	0.040	3.6 ± 0.2	24.7 ± 1.3	22.5 ± 0.1	1000.35 ± 0.01	1497.2 ± 0.8
0.0087	0.050	4.2 ± 0.2	21.8 ± 1.2	22.6 ± 0.1	1000.19 ± 0.01	1497.7 ± 0.7
0.0060	0.060	5.1 ± 0.3 (4.7)[a)]	11.1 ± 0.6	22.4 ± 0.1	998.89 ± 0.01	1498.0 ± 0.7

a) Calculated values through Eq. 3a.

Table 2. The Rate and Thermodynamic Constants for Host–Guest Complexation at 25 °C

Host	Guest	k_f	k_b	K	ΔV	Reference
		10^8 mol^{-1} dm^3 s^{-1}	10^7 s^{-1}	mol^{-1} dm^3	10^{-6} m^3 mol^{-1}	
α-CD	*nor*-Propanol	2.7 ± 1.2	1.7 ± 0.3	16 ± 7	5.0 ± 0.6	13
α-CD	*nor*-Butanol	5.5 ± 0.3	0.46 ± 0.01	120 ± 4	4.1 ± 0.2	This work
		4.2	0.55	72.8	1.5	21
α-CD	*sec*-Butanol	3.5 ± 0.1	1.02 ± 0.01	34.2 ± 0.5	4.9 ± 0.2	This work
α-CD	*nor*-Pentanol	3.6	0.12	302	3.1	21
β-CD	*nor*-Propanol	5.1 ± 0.7	12.1 ± 0.7	4.2 ± 0.6	12.5 ± 0.3	15
β-CD	*nor*-Butanol	2.8 ± 0.8	3.8 ± 0.6	7.2 ± 2.0	11.1 ± 1.0	15
β-CD	*sec*-Butanol	3.2 ± 0.1	2.82 ± 0.03	11.5 ± 0.2	9.3 ± 0.2	15
β-CD	*tert*-Butanol	3.6 ± 0.1	0.85 ± 0.01	42.6 ± 1.0	4.94 ± 0.04	This work

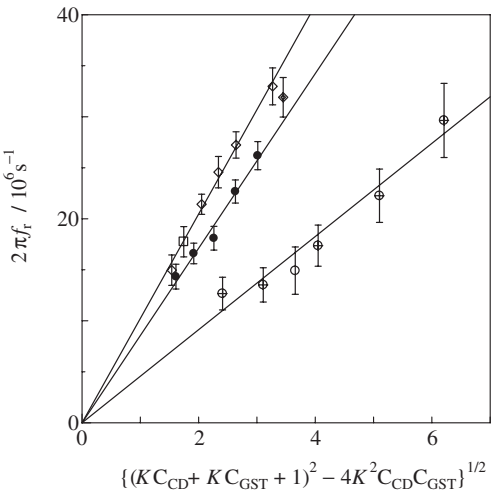

Fig. 4. Plots of $2\pi f_r$ vs $\{(KC_{CD} + KC_{GST} + 1)^2 - 4K^2C_{CD}C_{GST}\}^{1/2}$ in aqueous solution of butanol isomers in the presence of CDs at 25 °C; (⊕): *nor*-butanol + 0.0100 mol dm^{-3} α-CD, (○): 0.025 mol dm^{-3} *nor*-butanol + 0.0070 mol dm^{-3} α-CD, (◇): *sec*-butanol + 0.0100 mol dm^{-3} α-CD, (□): 0.020 mol dm^{-3} *sec*-butanol + 0.0070 mol dm^{-3} α-CD, (●): *tert*-butanol + 0.0087 mol dm^{-3} β-CD, (◈): 0.060 mol dm^{-3} *tert*-butanol + 0.0060 mol dm^{-3} β-CD.

culated line. The agreement supports the 1:1 stoichiometry of the inclusion complex. Additional absorption experiments were performed at different concentrations of CDs to verify further the validity of the kinetic parameters obtained. It was possible to calculate the relaxation frequency through Eq. 3a because the k_b and K values were already determined. They are given in the parentheses in Table 1. The experimental results are in good agreement with the calculated ones, and the plots shown in Fig. 4 fall on the calculated line. Therefore, these facts also confirm that the proposed complexation reaction is reasonable for the cause of the observed ultrasonic relaxation.

Maximum absorption per wavelength, μ_{max}, is also useful information obtained by ultrasonic absorption measurements. The quantity can be related to the standard volume change of the reaction, ΔV, with the aid of the density and sound velocity measurements as

$$\mu_{max} = 0.5Af_r v = \pi\rho v^2\{1/[CD] + 1/[GST] + 1/[CDGST]\}^{-1}(\Delta V)^2/2RT, \quad (4)$$

where R is the gas constant, and T is the absolute temperature. The enthalpy term in Eq. 4 was negligible small[22] compared to the calculated ΔV values because the CD–alcohol solutions were dilute solutions. As the equilibrium constant, K, was already determined from the concentration dependence of the relaxation frequency, the individual equilibrium concentrations of the reactants could be calculated with the initial concentrations of the two solutes, C_{CD} and C_{GST}. The ΔV values were estimated at each concentration, and the averaged values are given in Table 2.

Discussion

The backward rate constant, k_b, varies considerably depending upon the structure of the guest molecules. When the size of the CD cavity is same, the longer the hydrophobic carbon chain in guest molecule is, the smaller the backward rate constant is obtained. The change directly influences the stability of the inclusion complex since the forward rate constants show almost constant values. The results for all of the α-CD systems show a smaller backward rate constant and a greater equilibrium constant compared with β-CD systems having the same guest molecule. This is apparently due to the different size of the cavity; the smaller the cavity is, the greater the hydrophobic interaction is created between the host and the guest. These tendencies can be seen in Table 2 for α-CD and β-CD systems. Hall et al.[21] have studied the systems of *nor*-butanol or *nor*-pentanol with α-CD. They determined the equilibrium constant by a head-space analysis, and kinetic parameters were analyzed by ultrasonic absorption method. Although the experimental conditions and the methods of analysis were not same, the kinetic results were consistent with those obtained in this study. Their results also show that the backward rate constant decreases with an increase of the carbon chain length in the guest molecule whereas the forward rate constant remains constant.

It is interesting to note that alcohols with a branched side carbon chain are accommodated more firmly than that with the normal chain into the β-CD cavity. This is because the backward rate constant decreases with in the series *nor*-butanol > *sec*-butanol > *tert*-butanol. On the contrary, the reverse trend was observed in α-CD systems; k_b for *nor*-butanol is

smaller than that for *sec*-butanol. This is again clearly due to the difference in the cavity size, that is, it is considered that a suitable fit of the branched carbon chain can be accomplished for β-CD. Although the α-CD cavity is not sufficiently large to achieve the best match to the branching chain, the normal carbon chain is an appropriate or even better size for the α-CD cavity. In other words, the hydrophobicity is not only important but also the bulkiness of the hydrophobic part of the guest molecule is an essential factor for the complexation reaction. In β-CD systems, the bulkier the hydrophobic portion of the guest molecule is, the smaller the backward rate constant is, leading to a smaller equilibrium constant. Reversely, the bulkiness adversely affects the stability of the inclusion complex between α-CD and the guest molecule. It can be concluded that the preferred structures of the guest molecule to the β-CD cavity is on an order corresponding to *nor-* < *sec-* < *tert-*, although the α-CD cavity prefers a normal chain alcohol. This isomeric effect between α-CD and β-CD can also be understood in constructing a supramolecular complex, called polypseudorotaxan. Polypseudorotaxan can be obtained when many CDs (hosts) are threaded by linear polymer molecule (guest) with no bulky stoppers at each end. Harada[9] observed inclusion complexes between α-CD and polyethylene glycol (PEG) with molecular weights more than 200. β-CDs are able to form inclusion complexes with polypropylene glycol (PPG) in high yield, while α-CD can not form with any molecular weight of PPG. That is, the α-CD cavity can not allow any threading of the branching methyl group of the monomer constituting PPG [–$CH_2CH(CH_3)O$–] while the monomer of PEG [–CH_2CH_2O–] is allowed.

It was previously proposed that the association process of the complexation reaction of a guest molecule with β-CD proceeded in a diffusion-controlled reaction.[17] This fact is reflected in the forward rate constants that have an almost similar value ($k_f \sim 3 \times 10^8$ $mol^{-1}\,dm^3\,s^{-1}$), and is independent of the nature of the guest molecules. The results of the association rate constants for the α- and β-CD systems in the present study also show similar values, as can be seen in Table 2. The host–guest complex forms only when a guest molecule comes to both entrances of the CD. Therefore, the diffusion rate constant corresponding to k_f in the present study, through Smoluchowski's equation, should be reduced by the relative value of the entrance surface area of the cavity to the total surface area of the CDs. The relative value is about 0.08 for β-CD and is about 0.06 for α-CD.[23] Therefore, these factors do not very effectively affect the forward rate constant.

Next, the result of a standard volume change of the complexation reaction, ΔV, is considered. From ultrasonic absorption experiment, only the absolute values for the standard volume change was obtainable from Eq. 4. As can be seen in Table 2, the ΔV values in the α-CD systems decreased by about a factor of 2. The obtained smaller values are also considered to be due to the cavity size of α-CD. Lichtenthaler et al.[23] reported the molecular volume of α-CD cavity to be 100×10^{-3} nm^3, which is able to accommodate 2 to 3 water molecules, while β-CD can accommodate approximately 5 to 7 water molecules.[23–25] It is assumed that the number of water molecules located inside the α-CD cavity is 2.5. Fujiwara et al.[26] reported on the number of water molecules released upon the complex formation reactions of α-CD with several alcohols based on titration calorimetry, which corresponds to the alcohols used in this present study. The number of released water was said to be 1.4 on the average. This value may be reasonable since the number of water molecules in the α-CD cavity is more than 2. The volume change of the reaction is simply expressed as $\Delta V = nV_{H_2O} - mV_{CH_2} - V_{CH_3}$, where n indicates the number of expelled water molecules from the cavity of α-CD to the bulk phase and m is the incorporated methylene groups when alcohol is incorporated into the CD cavity. The following volumes are proposed: $V_{CH_2} = 15.7 \times 10^{-6}$ $m^3\,mol^{-1}$, and $V_{CH_3} = 27.1 \times 10^{-6}$ $m^3\,mol^{-1}$.[27] If the reported number represented the expelled water molecules, the ΔV values for α-CD systems could not show a positive value while β-CD systems were reported to be positive.[24] By using these data, the incorporated hydrophobic part on *nor*-propanol and *nor*-butanol was estimated. As a result, it was calculated that $m \approx 0.20$ for *nor*-propanol and $m \approx 0.13$ for *nor*-butanol. From these results, it is seen that a small portion of guest molecule is included into α-CD. The same estimation was made for the system of *nor*-butanol with β-CD. If the number of expelled water molecules is more then 4.7 ($n > 4.7$), then $m > 3$. It is highly likely that the entire hydrophobic group could be included into the cavity. Although the exact number of released water molecules is not certain in the case of β-CD complexation reaction, it is apparently seen that the guest molecule can not be included into the cavity of α-CD as deeply as into that of β-CD. The value of ΔV for the system of *tert*-butanol with β-CD was about half compared to those obtained for the *nor*-butanol or *sec*-butanol system. Therefore, it can certainly be said that *tert*-butanol is incorporated more deeply into the β-CD cavity.

In conclusion, the important factors regarding the complexation reaction with CDs, which can be obtained from the ultrasonic absorption measurement, are the backward rate constant, k_b, and the volume change of the reaction, ΔV. Especially, the k_b values are sensitively varied due to the structure of the guest molecule. Using the results obtained in this study and those from previous reports, the difference in the behavior of isomers for the complexation reaction can be comprehensively discussed in combination with the characteristic results of the k_b and ΔV values. For α-CD systems, a noticeable relation between k_b and ΔV values is hardly seen in Table 2. This may be because of the fact that α-CD can not include the guest molecule adequately deep into the cavity due to the small number of water molecules located inside the cavity, which means a low driving force to drag a guest molecule deeply into the cavity. Thus, the difference in the dynamic behavior is not sufficient to have any kind of effect on the ΔV values in α-CD systems. On the other hand, it can be seen that the smaller the k_b is, the smaller the ΔV value is in β-CD systems. The small k_b value means that a guest molecule is included with a high affinity for host CD. Consequently, the guest molecule can be accommodated more deeply compared to that with a larger k_b value. If the number of expelled water molecules are almost the same for the isomers with β-CD systems, a guest molecule with a favorable hydrophobic part to the β-CD cavity in the order *nor-* < *sec-* < *tert-* tends to have a smaller k_b value and a smaller ΔV value.

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