Bull. Chem. Soc. Jpn., 70, 535—541 (1997)

# NMR Spectroscopy of Cyclodextrin–Inorganic Anion Systems

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(Received August 5, 1996)

The addition of alkali salts of chaotropic anions such as $Br^-$, $I^-$, $SCN^-$, $N_3^-$, $ClO_4^-$, and $NO_3^-$ to an $\alpha$-cyclodextrin ($\alpha$-CD) solution in $D_2O$ caused marked downfield shifts in the $^1H$ NMR signal of the C(5)–H located in the interior of the $\alpha$-CD cavity, whereas the signal showed no or only small upfield shifts upon the addition of alkali salts of antichaotropic anions such as $F^-$, $HCO_3^-$, $H_2PO_4^-$, $HPO_4^{2-}$, and $SO_4^{2-}$. The effects of the inorganic salts on the chemical shifts ($\delta$) for the other protons of $\alpha$-CD were significant but smaller than that on $\delta$ for C(5)–H. These facts indicate that the chaotropic anions are included within the $\alpha$-CD cavity and held in the vicinity of C(5)–H. Similar, but smaller, effects of the inorganic salts were observed for $\beta$- and $\gamma$-CD. The binding constants and thermodynamic parameters determined for complexation of CD's with some chaotropic anions suggest that hydrophobic and van der Waals interactions, as well as a conformational change of CD macrocycles and the desolvation of CD's and/or the anions upon complexation, play important roles in complex stabilization. The effect of inorganic salts on the spin-lattice relaxation times of $\alpha$-CD protons also supports the above conclusion.

Cyclodextrins (CD's) are doughnut-shaped molecules comprising six ($\alpha$-CD), seven ($\beta$-CD), and eight ($\gamma$-CD) $\alpha$-D-glucopyranose residues (Fig. 1). They include not only organic molecules, but also inorganic anions such as $I^-$, $SCN^-$, and $ClO_4^-$ within their hollow cavities in aqueous solutions.[1—10] Since inorganic salts are often used to adjust the pH and ionic strength of an aqueous CD solution, it is primarily important to investigate the interactions between CD's and inorganic anions. Thus far, the interactions have been studied by means of solubility measurements,[1] UV-vis spectrophotometry,[2—5] calorimetry,[6] conductometry,[7] density measurements,[7] and potentiometry.[8,9] Recently, Yamashoji et al.[10] have examined the complexation of CD's with some inorganic anions by $^{81}Br$ NMR spectroscopy. However, the effects of inorganic anions on the $^1H$ NMR spectra of CD's has never been reported, though a number of studies have been reported concerning the $^1H$ NMR spectroscopy of CD's.[11]

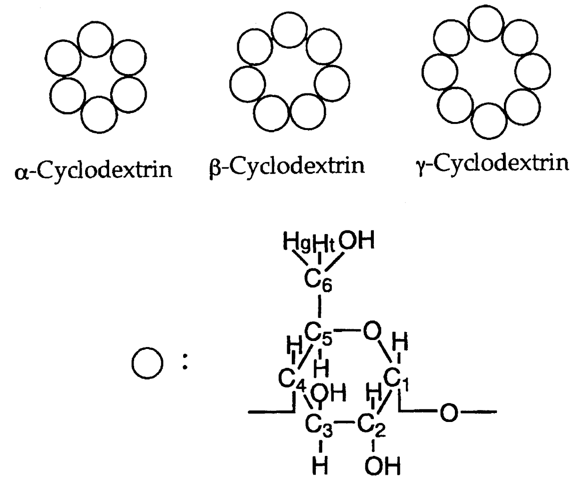

Fig. 1. Schematic structures of $\alpha$-, $\beta$-, and $\gamma$-CD's and the numbering of carbon atoms of the glucopyranose residue.

The present work was undertaken in order to elucidate the interactions between CD's and a variety of inorganic anions, the molecular structures of CD complexes with chaotropic anions, and the binding forces contributing to complexation by means of $^1H$ NMR spectroscopy. We have found that a few chaotropic anions are strongly bound to the 6-(1-pyridinio)-6-deoxy derivatives (CDpy's) of CD's[12,13] and cause remarkable changes in the $^1H$ NMR chemical shifts ($\delta$) of some protons involved in the CDpy's.[14] In order to understand the NMR response of the CDpy's, it is essential to investigate the response of native CD's.

In the present work we also examined a referencing method for the $^1H$ NMR spectroscopy of CD's. According to Momoki and Fukazawa,[15,16] the usual internal or external referencing for NMR chemical-shift measurements has poor accuracy when the magnetic susceptibilities ($\chi$) of the solvents are greatly changed. In fact, we recently found that external referencing is not available for determinig the binding constants for complexes of $\alpha$-CD with organic molecules by analyzing changes in $\delta$, due to changes in the $\chi$ of solutions with the addition of $\alpha$-CD.[17] It is liable that the addition of inorganic salts to CD solutions in $D_2O$ causes significant changes in the $\chi$ of the solutions. Thus, it is inevitable to find a suitable referencing method.

## Experimental

**Materials.** The $\alpha$-CD was supplied by Nihon Shokuhin Kako Co., Ltd. The $\beta$- and $\gamma$-CD's were supplied by Ensuiko Seito Co., Ltd. They were dried overnight in vacuo at 110 °C. Methyl $\alpha$-D-glucopyranoside (MG), used as a reference compound of CD's, and inorganic salts were of reagent grade, and were commercially available. The used $D_2O$ (Isotec) contained 99.8 atm % D. Methanol (MeOH) and sodium 3-trimethylsilyl-1-propanesulfonate (TSS), used as internal and external references, respectively, for $^1H$ NMR measurements were also of reagent grade and were commercially available.

**Apparatus.** $^1H$ NMR spectra were recorded using a JEOL Model JNM-A400 FT NMR spectrometer (400 MHz) with a sample tube of 5.0 mm diameter at 25±0.1 °C, unless otherwise noted. Sample solutions contained 0.0040 mol dm$^{-3}$ CD's in $D_2O$. The maximum concentrations of the inorganic salts added to the sample solutions were 0.50 mol dm$^{-3}$ for $\alpha$-CD and 2.00 mol dm$^{-3}$ for the $\beta$- and $\gamma$-CD's. A trace amount of methanol (less than 0.0004 mol dm$^{-3}$) was added to the sample solution as an internal reference ($\delta = 3.343$[17]) of $^1H$ NMR measurements. A $D_2O$ solution of 0.005 mol dm$^{-3}$ TSS was loaded into a glass capillary of 1.0 mm diameter and used, if necessary, as an external reference ($\delta = 0.000$). The sample solutions were not degassed to remove dissolved oxygen in these measurements. The spin-lattice relaxation times ($T_1$) for the protons of $\alpha$-CD (0.010 mol dm$^{-3}$) in both the absence and presence of 0.50 mol dm$^{-3}$ inorganic salts in $D_2O$ were measured by the inversion recovery method with a pulse sequence of $\pi$–$\tau$–$\pi/2$ ($\tau$: pulse interval) at 25 ±0.1 °C before and after removing the oxygen dissolved in sample solutions by bubbling $N_2$ gas.

## Results and Discussion

**Referencing for $^1$H NMR Spectroscopy of CD's.** When the magnetic susceptibilities ($\chi$) of the solvents are greatly changed, the usual internal or external referencing for NMR measurements has poor accuracy.[15,16] In order to examine whether the addition of inorganic salts to a $D_2O$ solution causes a significant change in $\chi$ of the solution or not, we measured the $^1H$ NMR spectra of 0.0080 mol dm$^{-3}$ MG and 0.0004 mol dm$^{-3}$ MeOH in $D_2O$ in both the absence and presence of 0.50 mol dm$^{-3}$ of various inorganic salts with an external TSS reference. It has recently been found that the interactions between MeOH and CD's are very weak, and that MeOH is suitable as an internal reference in the $^1H$ NMR measurement of CD's.[17] Since direct interactions between inorganic salts and MG or MeOH would be weak, if any, changes ($\Delta\delta$) in $\delta$ for the protons of MG and MeOH upon the addition of inorganic salts are mostly due to changes in $\chi$ of the solution. Figures 2 and 3 illustrate the $\Delta\delta$'s for the C(3)– and C(5)–H's, respectively, of MG and those for the methyl protons (Me–H) of MeOH. The $\Delta\delta$ values are significantly changed with inorganic salts, suggesting that the changes in $\chi$ are not negligible. It is noteworthy that both the $\Delta\delta$'s for C(3)– and C(5)–H's are virtually equal to that for Me–H in each salts. The plots of $\Delta\delta$'s for C(3)– and C(5)–H's vs. $\Delta\delta$ for Me–H gave good straight lines with intercepts and slopes equal to ca. 0.0 and 1.0, respectively, as expressed by the following equations:

$$\Delta\delta[\mathrm{C(3)\text{–}H}] = 0.0024 + 0.945\Delta\delta(\mathrm{Me\text{–}H}),\ n = 12,\ r = 0.9973, \quad (1)$$

and

$$\Delta\delta[\mathrm{C(5)\text{–}H}] = 0.0004 + 1.037\Delta\delta(\mathrm{Me\text{–}H}),\ n = 12,\ r = 0.9931. \quad (2)$$

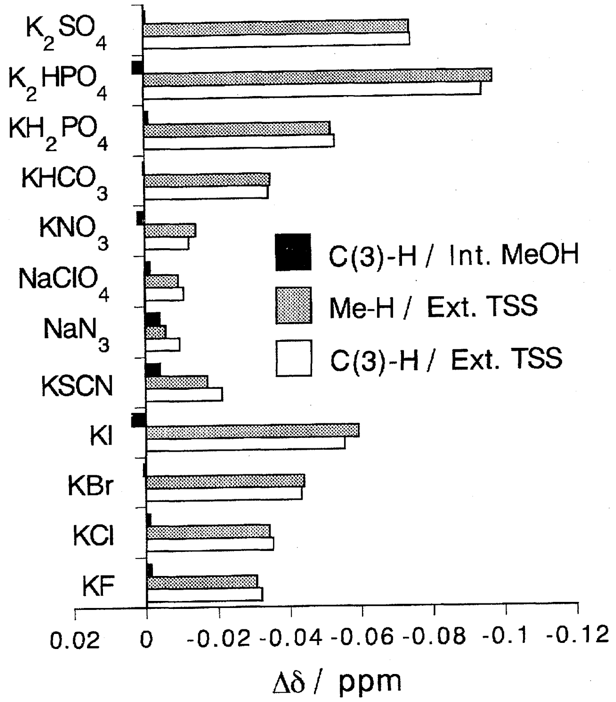

Fig. 2. Changes ($\Delta\delta$) in the chemical shifts of the C(3)–H's of MG (0.0080 mol dm$^{-3}$) and the Me–H of methanol (0.0004 mol dm$^{-3}$) in $D_2O$ upon the addition of 0.50 mol dm$^{-3}$ various inorganic salts measured with external TSS and internal methanol references.

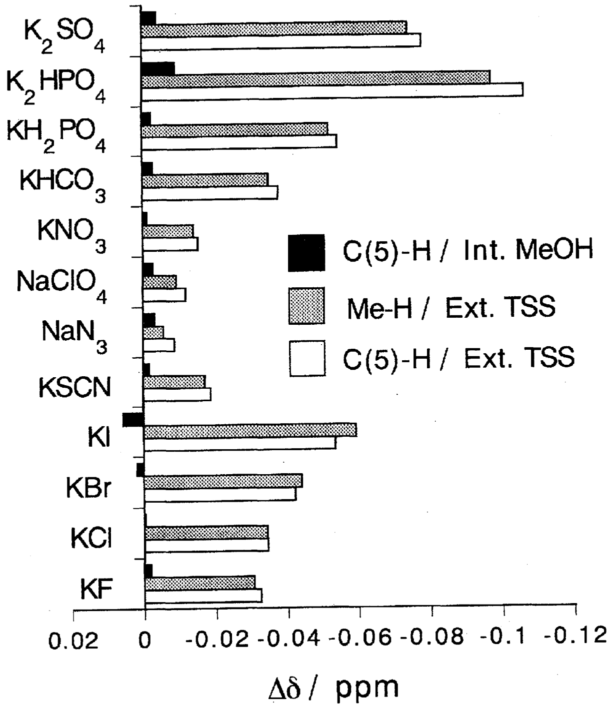

Fig. 3. Changes ($\Delta\delta$) in the chemical shifts of the C(5)–H's of MG (0.0080 mol dm$^{-3}$) and the Me–H of methanol (0.0004 mol dm$^{-3}$) in $D_2O$ upon the addition of 0.50 mol dm$^{-3}$ various inorganic salts measured with external TSS and internal methanol references.

Similar relationships were found for the other protons of MG. This fact indicates that the $\delta$ values for the protons of MG relative to that of Me–H remain virtually uncharged upon the addition of inorganic salts. In fact, when we use Me–H as an internal reference in place of TSS as an external reference, the $\Delta\delta$'s for such protons as C(3)– and C(5)–H's become close to zero (Figs. 2 and 3, solid bars). Table 1 summarizes the averaged $\delta$'s ($\delta_{\mathrm{av}}$) and their standard deviations ($\sigma$) for all protons of MG in the presence of 0.50 mol dm$^{-3}$ inorganic salts both with TSS ($\delta$=0.000) as an external reference and with MeOH ($\delta$=3.343) as an internal reference. The $\sigma$ values with an internal MeOH reference are satisfactory small, whereas those with an external TSS reference are too large to obtain reliable NMR data. The $\sigma$ values with the internal MeOH reference are as high as 0.001—0.007 ppm, which are comparable to those (0.004—0.009 ppm) with bulbed capillary external referencing followed by a diamagnetic correction.[15] Thus, it is evident that internal MeOH referencing is useful and practical for analyzing the data without correcting changes in $\chi$ with the addition of inorganic salts. The following measurements of the $^1$H NMR spectra of CD's were carried out by using MeOH as an internal reference.

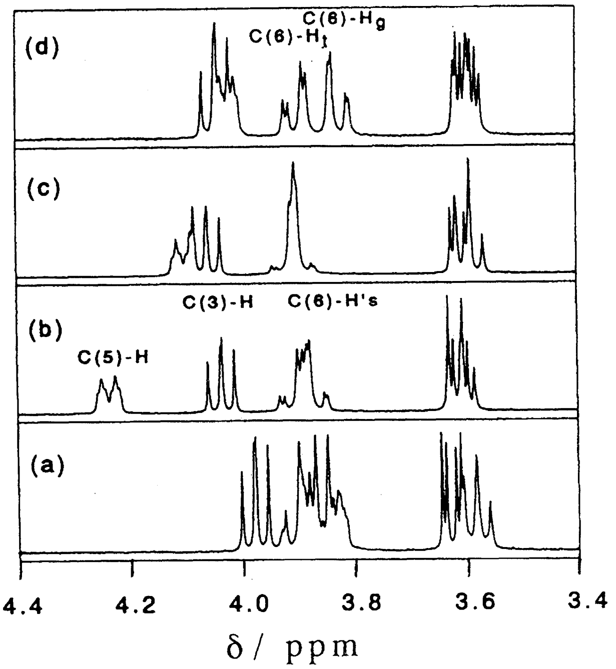

Fig. 4. $^1$H NMR spectra of $\alpha$-CD (0.0040 mol dm$^{-3}$) in $D_2O$ at 25 °C in the presence of 0.50 mol dm$^{-3}$ KF (a), KI (b), KSCN (c), and $NaClO_4$ (d).

**Effects of Inorganic Anions on the $^1$H NMR Spectra of CD's.** The $^1$H NMR spectra of 0.0040 mol dm$^{-3}$ $\alpha$-CD in $D_2O$ were measured in the presence of 0.50 mol dm$^{-3}$ inorganic salts such as KF, KI, KSCN, and $NaClO_4$ with an internal MeOH reference. Figure 4 shows a part of the obtained spectra. Besides the illustrated signals, doublet signals due to the anomeric C(1)–H of $\alpha$-CD (Refer the numbering of the carbon atoms in CD to Fig. 1.) appeared at $\delta$=ca. 5.0 ($J$=3.4 Hz). The spectrum of $\alpha$-CD in the presence of KF was virtually the same as that in the absence of any inorganic salt, and the signals were assigned by use of the two-dimensional COSY technique to be $\delta$=5.05 (d, $J$=3.4 Hz) for C(1)–H, 3.63 (dd, $J$=10.0, 3.4 Hz) for C(2)–H, 3.98 (dd, $J$=10.0, 8.7 Hz) for C(3)–H, 3.58 (t, $J$=9.3 Hz) for C(4)–H, 3.84 (m) for C(5)–H, 3.91 (dd, $J$=12.6, 2.8 Hz) for C(6)–H$_g$, and 3.86 (dd, $J$=12.4, 4.2 Hz) for C(6)–H$_t$. This assignment agrees with that reported.[18] The addition of KF to an $\alpha$-CD solution in $D_2O$ gave rise to very slight and uniform upfield shifts (ca. 0.001 ±0.002 ppm) for all of the protons of $\alpha$-CD. The same effect was observed upon the addition of NaF in place of KF. On the other hand, the addition of KI, KSCN, and $NaClO_4$ resulted in significant changes in the spectra of $\alpha$-CD. Thus, KI caused a remarkable downfield shift of C(5)–H, as well as a moderate downfield shift of C(3)–H, to give a well-resolved signal. The geminal C(6)–H's gave clear signals belonging to a AA′X system according to the Pople notation,[19] whereas the signals in the presence of KF overlapped with that of

Table 1. The Average $^1$H NMR Chemical Shifts ($\delta_{\mathrm{av}}$) and the Standard Deviations ($\sigma$) of $\delta_{\mathrm{av}}$ for Protons of Methyl $\alpha$-D-Glucopyranoside (0.008 mol dm$^{-3}$) and Methanol (0.0004 mol dm$^{-3}$) in $D_2O$ in the Presence of 0.5 mol dm$^{-3}$ Various Inorganic Salts[a)] Measured with External TSS and Internal Methanol References at 25 °C

| | External TSS | | | Internal methanol | |
|---|---|---|---|---|---|
| Proton | $\delta_0$[b)] | $\delta_{\mathrm{av}}$ | $\sigma$ | $\delta_{\mathrm{av}}$ | $\sigma$ |
| C(1)–H | 4.801 | 4.768 | 0.026 | 4.808 | 0.004 |
| C(2)–H | 3.552 | 3.528 | 0.023 | 3.560 | 0.005 |
| C(3)–H | 3.660 | 3.620 | 0.026 | 3.660 | 0.002 |
| C(4)–H | 3.393 | 3.360 | 0.022 | 3.400 | 0.007 |
| C(5)–H | 3.640 | 3.600 | 0.029 | 3.638 | 0.004 |
| C(6)–Hg | 3.864 | 3.823 | 0.029 | 3.862 | 0.003 |
| C(6)–Ht | 3.749 | 3.715 | 0.023 | 3.755 | 0.006 |
| $CH_3$–H | 3.411 | 3.372 | 0.027 | 3.412 | 0.001 |
| Methanol | 3.343 | 3.303 | 0.028 | 3.343 | — |

a) Inorganic salts added are KF, KCl, KBr, KI, KSCN, $NaN_3$, $NaClO_4$, $KNO_3$, $KHCO_3$, $KH_2PO_4$, $K_2HPO_4$, and $K_2SO_4$. b) Chemical shifts in the absence of the inorganic salts.

C(5)–H to give a complex AA′B pattern of NMR absorption. The same effect on the spectrum of $\alpha$-CD was observed upon the addition of NaI in the place of KI, indicating that the $I^-$ ion is responsible for the change in the spectrum. The salts, KSCN and $NaClO_4$, also caused significant downfield shifts in C(5)– and C(3)–H's, though the magnitudes of the shifts were somewhat different from those caused by KI. Upon adding $NaClO_4$, the geminal C(6)–H's gave well-separated signals typical of an AA′X system. These results indicate that the inorganic salts serve as a kind of shift reagents available for spreading out the NMR absorption patterns of an $\alpha$-CD system.

Figure 5 shows differences ($\Delta\delta$) between chemical shifts of the $\alpha$-CD (0.0040 mol dm$^{-3}$) protons in the presence of 0.50 mol dm$^{-3}$ KI, KSCN, or $NaClO_4$ and those in the presence of 0.50 mol dm$^{-3}$ KF. The largest $\Delta\delta$ values were observed for C(5)–H, which is located in the interior cavity of $\alpha$-CD. C(3)–H is also located in the cavity, and its $\Delta\delta$ values were significantly large. These results indicate that the anions of these salts are included within the $\alpha$-CD cavity and held in the vicinity of C(5)–H. The geminal C(6)–H's showed interesting changes in $\Delta\delta$: One (C(6)–$H_g$) of the C(6)–H's gave negative $\Delta\delta$ values (upfield shifts), whereas another (C(6)–$H_t$) gave positive $\Delta\delta$ values (downfield shifts). The magnetic properties of these protons may be affected by the complexation of $\alpha$-CD with these anions. The *J* values for the spin–spin coupling of C(6)–H's with C(5)–H decreased from 2.8 to 1.8 Hz for C(6)–$H_g$ and from 4.2 to 3.3 Hz upon the addition of $NaClO_4$ in place of KF, suggesting that the time-averaged fraction of the *gauche–gauche* (*gg*) conformer[11] about the C(5)–C(6) bond of $\alpha$-CD increases, and that of the *gauche–trans* (*gt*) conformer decreases, with the complexation with $ClO_4^-$. The $\Delta\delta$ values for C(1)–, C(2)–, and C(4)–H's, which lie outside the cavity, were appreciable but smaller than those for C(3)–, C(5)–, and C(6)–H's.

Figure 6 shows the changes ($\Delta\delta$) in $\delta$ of the C(5)–H's of $\alpha$-, $\beta$-, and $\gamma$-CD's (0.0040 mol dm$^{-3}$) upon the addition of various inorganic salts (0.50 mol dm$^{-3}$ for $\alpha$-CD and 2.0 mol dm$^{-3}$ for $\beta$- and $\gamma$-CD's). The $\delta$ values for the C(5)–H's of $\beta$-, and $\gamma$-CD's were the most sensitive to the addition of inorganic salts, as described above concerning $\alpha$-CD. The addition of salts comprising $Cl^-$, $Br^-$, $I^-$, $SCN^-$, $N_3^-$, $ClO_4^-$, and $NO_3^-$ caused downfield shifts (positive $\Delta\delta$) in C(5)–H for all the examined CD's. Since these anions are known to be relatively lipophilic or chaotropic, it is presumed that hydrophobic interactions contribute to the inclusion of the anions within the CD cavities. Furthermore, in these systems the $\Delta\delta$ values increased roughly with increasing thermochemical radii of the anions (0.172 nm for $Cl^-$, 0.179 nm for $NO_3^-$, 0.188 nm for $Br^-$, 0.195 nm for $N_3^-$, 0.210 nm for $I^-$, and 0.240 nm for $ClO_4^-$ [20]) and with decreasing cavity sizes of the CD's. A very similar tendency was found for $\alpha$-CDpy-inorganic anion systems.[14] The van der Waals contact of C(5)–H with the anions will also plays an important role in the downfield shift of C(5)–H. On the other hand, the addition of salts with antichaotropic anions such as $F^-$, $HCO_3^-$, $H_2PO_4^{2-}$, $HPO_4^{2-}$, and $SO_4^{2-}$ caused no shift, or small upfield shifts (negative $\Delta\delta$), of C(5)–H for all of the examined CD's. The negative $\Delta\delta$ values were slightly changed with changes in the examined systems and in salt concentrations. However, they were virtually constant over all protons of CD in a given system. This fact indicates that the anions of these salts are not included within the CD

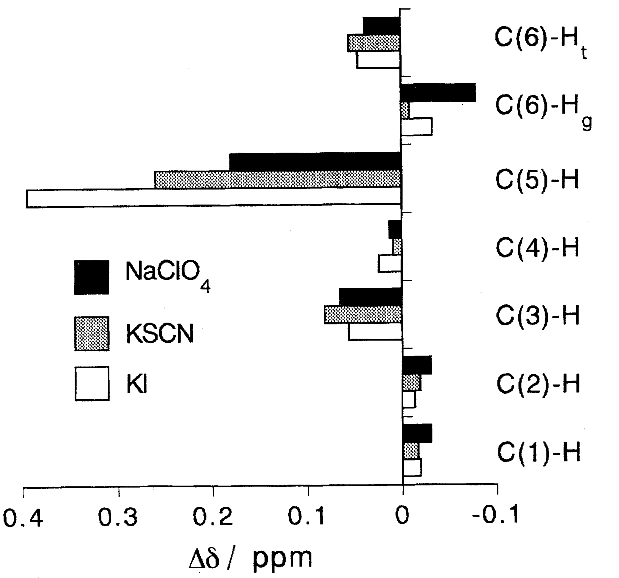

Fig. 5. Changes ($\Delta\delta$) in the chemical shifts of $\alpha$-CD (0.0040 mol dm$^{-3}$) protons in $D_2O$ at 25 °C upon the addition of 0.50 mol dm$^{-3}$ KI, KSCN, and $NaClO_4$ in place of KF.

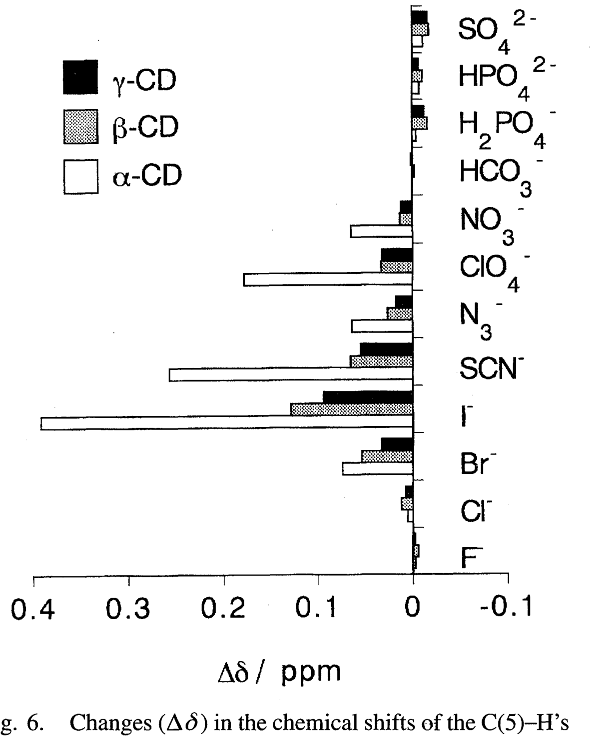

Fig. 6. Changes ($\Delta\delta$) in the chemical shifts of the C(5)–H's of $\alpha$-, $\beta$-, and $\gamma$-CD's (0.0040 mol dm$^{-3}$) in $D_2O$ at 25 °C upon the addition of inorganic salts. The concentrations of the inorganic salts added were 0.50 mol dm$^{-3}$ for $\alpha$-CD and 2.00 mol dm$^{-3}$ for $\beta$- and $\gamma$-CD's.

cavities. The slight upfield shifts may be due to general salt effects on NMR signals. Thus, KF and $K_2SO_4$ are available for adjusting the ionic strength, and $KH_2PO_4$, $K_2HPO_4$, and $KHCO_3$ for adjusting the pH, of a CD solution without any interference of guest inclusion within the CD cavity.

Figure 7 shows the $\Delta\delta$ values for the C(1)–H's of $\alpha$-, $\beta$-, and $\gamma$-CD's in the same experiments as described above. It is known that the $\delta$ values for C(1)–H's reflect the conformation of the macrocyclic ring of CD's.[11] The $\Delta\delta$ values were generally negative (upfield shift). However, the $\Delta\delta$ values for the $\alpha$-CD–$I^-$, $SCN^-$, $N_3^-$, and $ClO_4^-$ systems, as well as the $\beta$- and $\gamma$-CD–$N_3^-$ and $ClO_4^-$ systems, were significantly positive (downfield shift). The macrocyclic conformation of the CD's may be changed by inclusion of these anions.

**Binding Constants for Complexes of CD's with Some Inorganic Anions.** Figure 8 shows the changes in $\Delta\delta$ for the C(3)– and C(5)–H's of $\alpha$-CD (0.0040 mol dm$^{-3}$) in $D_2O$ upon the addition of KI at 25 °C. During the measurements, the ionic strength of the sample solution was kept constant at 0.50 mol dm$^{-3}$ using KF to maintain the ionic activity of $I^-$ as constant as possible, and to avoid the general salt effect on $\Delta\delta$. The $\Delta\delta$ values increased and approached constant values with increasing KI concentration. The $\Delta\delta$ values for the C(3)– and C(5)–H's at 0.20 mol dm$^{-3}$ KI were 0.048 and 0.348, respectively, which were much larger than the $\Delta\delta$'s (0.005 and 0.008) for MG at 0.50 mol dm$^{-3}$ KI in place of KF. Hence, the experimental errors for $\Delta\delta$ in the present measurement were less than 10 and 2% for the C(3)– and C(5)–H's of $\alpha$-CD, respectively. Based on the assumption that $\alpha$-CD forms a 1 : 1 complex with $I^-$, the data were analyzed by a curve-fitting analysis with a microcomputer.[17] The thus-calculated curves (solid lines) were well-fitted to the observed data, indicating that the assumption of 1 : 1 complexation was valid. The binding constant ($K_a$) for the complex was determined to be 19.3 and 17.9 mol$^{-1}$ dm$^3$ by an analysis of the $\Delta\delta$'s for the C(3)– and C(5)–H's, respectively, which agreed well with a reported value (19.0 mol$^{-1}$ dm$^3$).[8] Similar measurements and analyses were carried out for some other CD–inorganic salt systems; the obtained $K_a$'s for complexation in $D_2O$ at 25 °C as well as literature values are summarized in Table 2. The ionic strengths for the $\beta$- and $\gamma$-CD systems were kept constant at 2.0 mol dm$^{-3}$ using KF. The changes in the enthalpy ($\Delta H$) and entropy ($\Delta S$) upon complexation were calculated from $K_a$'s determined at 25, 35, 45, and 55 °C in a similar manner, and are also given in Table 2. The obtained $K_a$, $\Delta H$, and $T\Delta S$ values agree fairly well with those reported, indicating that the present method for an NMR measurement is available for determining $K_a$.

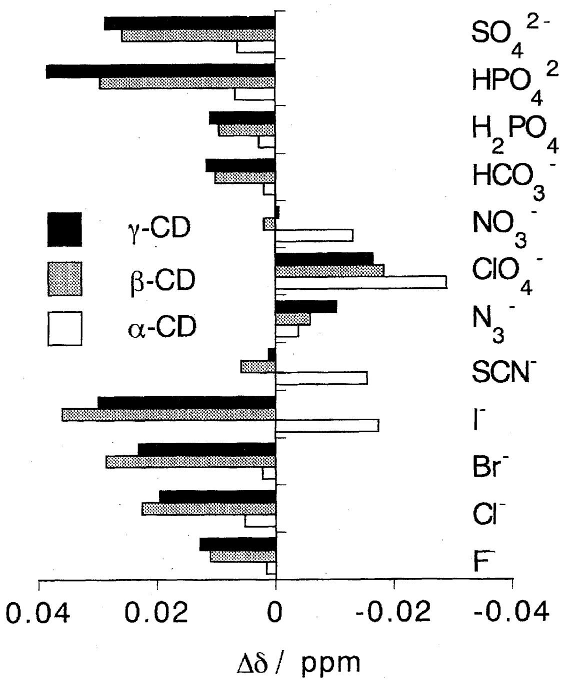

Fig. 7. Changes ($\Delta\delta$) in the chemical shifts of the C(1)–H's of $\alpha$-, $\beta$-, and $\gamma$-CD's (0.0040 mol dm$^{-3}$) in $D_2O$ at 25 °C upon the addition of inorganic salts. The concentrations of the inorganic salts added were 0.50 mol dm$^{-3}$ for $\alpha$-CD and 2.00 mol dm$^{-3}$ for $\beta$- and $\gamma$-CD's.

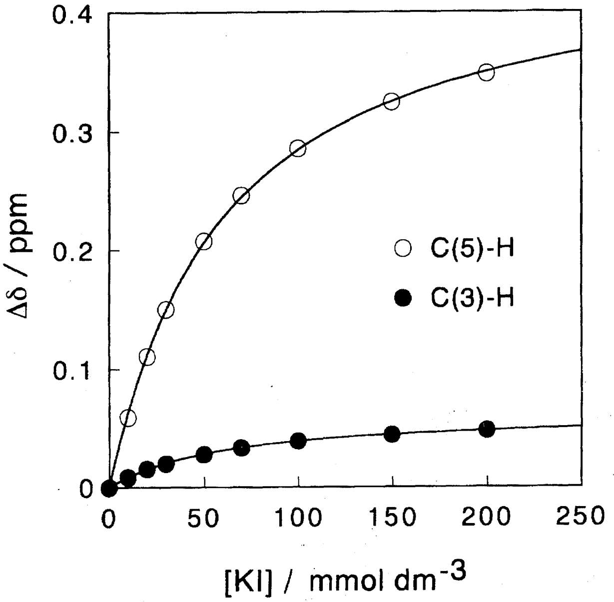

Fig. 8. Changes ($\Delta\delta$) in the chemical shifts of the C(5)–H (○) and C(3)–H (●) of $\alpha$-CD (0.0040 mol dm$^{-3}$) in $D_2O$ at 25 °C upon the addition of KI. The ionic strength of a solution was adjusted to be 0.50 mol dm$^{-3}$ by KF.

The obtained thermodynamic data ($\Delta H$ and $T\Delta S$) show that $\Delta H$ and $T\Delta S$ are compensatory: the $T\Delta S$ values increase with increasing the $\Delta H$ values. The plot of $T\Delta S$ vs. $\Delta H$ gave a good straight line, as expressed by

$$T\Delta S = 0.72\Delta H - 1.09, \qquad n = 10,\ r = 0.9603. \qquad (3)$$

This compensatory relationship between $\Delta H$ and $T\Delta S$ suggests that the binding forces contributing to the complexation of $\alpha$-, $\beta$-, and $\gamma$-CD's with the inorganic anions are of the same nature as one another.[8] According to Inoue et al.,[21] the slope ($\alpha$) and intercept ($T\Delta S_0$) of the compensatory relationship are quantitative measures of the conformational change of CD macrocycles and the extent of desolvation upon com-

Table 2. The Binding Constants ($K_a$) and Changes in Enthalpy ($\Delta H$) and Entropy ($T\Delta S$) for the Complexation of CD's with Inorganic Anions in $D_2O$ at 25 °Ca)

| Host | Guest | $K_a$/mol$^{-1}$ dm$^3$ | | $-\Delta H$/kJ mol$^{-1}$ | | $-T\Delta S$/kJ mol$^{-1}$ | |
|---|---|---|---|---|---|---|---|
| | | Obsd | Lit | Obsd | Lit | Obsd | Lit |
| α-CD | $NO_3^-$ | 1.4±0.1 | 1.96b) | 16.9±2.1 | | 16.2±2.0 | |
| | $Br^-$ | 1.6±0.1 | 0.87b) | 15.7±1.0 | | 14.5±0.9 | |
| | $I^-$ | 18.6±0.7 | 19.0b) | 31.6±2.6 | 24.7b) | 24.3±2.5 | 17.1b) |
| | $SCN^-$ | 28.4±0.9 | 34.6b) | 32.2±1.8 | 28.5b) | 23.9±1.7 | 19.8b) |
| | $ClO_4^-$ | 33.0±1.1 | 45.8b) | 33.7±1.4 | 26.4b) | 25.1±1.4 | 16.8b) |
| | | | 20.0c) | | 40.6c) | | 28.7c) |
| β-CD | $I^-$ | 8.5±0.4 | 10d) | 22.7±2.6 | | 17.6±2.5 | |
| | $SCN^-$ | 9.2±0.5 | 5.7e) | 19.7±2.5 | | 14.3±2.4 | |
| | $ClO_4^-$ | 13.6±0.7 | 9.0e) | 17.6±3.2 | | 10.9±3.1 | |
| γ-CD | $I^-$ | 4.9±0.3 | 1.3d) | 16.5±1.5 | | 12.5±1.4 | |
| | $SCN^-$ | 4.1±0.2 | | 11.8±1.5 | | 8.4±1.5 | |

a) The ionic strength of a sample solution was kept constant at 0.5 mol dm$^{-3}$ for an α-CD system and at 2.0 mol dm$^{-3}$ for β- and γ-CD systems by use of KF. b) Ref. 8. c) Ref. 6. d) Ref. 9. e) Ref. 5.

plexation, respectively. Using thermodynamic data for the complexation of α-, β-, and γ-CD's with a wide variety of mostly organic guest molecules, they evaluated the α and $T\Delta S_0$ values to be 0.90 and 3.1, respectively. The α value obtained here is smaller than that reported by them, indicating that the conformational change of CD's upon complexation with the anions is smaller than that with organic molecules. Since the examined inorganic anions are relatively small in size and symmetrical in structure, the effect of the anions on the conformation of CD's upon complexation may be small. The $T\Delta S_0$ value obtained here is also smaller than that reported, suggesting that the extent of desolvation of the CD's and/or anions upon complexation is less than that in complexation with organic molecules. This suggestion is reasonable, since the anions are generally more hydrophylic than most organic molecules, and will be still hydrated even within the CD cavity.

The $K_a$ values for α-CD increased with increasing ionic radii of a series of guest anions, supporting the presumption mentioned above that the van der Waals interactions between CD's and the anions play an important role in complexation. An increase in the van der Waals interactions causes an increase in $-\Delta H$ to enhance the stability of a complex, though the increase is partially compensated by an accompanied increase in $-T\Delta S$. It is well known that hydrophobic interactions are governed by a positive entropy change. Thus, it is also possible that the contribution of hydrophobic interactions to complex formation, relative to that of van der Waals interactions, increases and $-T\Delta S$ decreases along with an increasing difference in the size between the CD cavities and inorganic anions.

**Measurements of Spin-Lattice Relaxation Times of α-CD Protons.** The complexation of CD with a guest molecule generally causes a change in the spin-lattice relaxation times ($T_1$) for atomic nuclei consisting of CD and/or a guest molecule.11,18) In the present study, the $T_1$ values for the protons of α-CD were measured by the inversion recovery method with a pulse sequence of $\pi$–$\tau$–$\pi/2$ in $D_2O$ in both the absence and presence of 0.50 mol dm$^{-3}$ inorganic salts at 25 ±0.1 °C (Table 3). It is known that oxygen dissolved in a sample solution accelerates the spin-lattice relaxation to decrease the $T_1$ value. In fact, the $T_1$ values for the protons of α-CD in the absence of an inorganic salt or in the presence of KF are decreased by oxygen. However, the effect of oxygen was not always uniform over all of the protons: The $T_1$ values for C(3)– and C(5)–H's in the presence of oxygen were 73—77% and 85—88%, respectively, of those in the absence of oxygen, whereas those for the other protons were

Table 3. Effect of the Addition of 0.50 mol dm$^{-3}$ Inorganic Salts on Spin-Lattice Relaxation Times ($T_1$/s) for the Protons of α-CD (0.010 mol dm$^{-3}$) at 25 °C before and after Removal of Oxygen

| Salt | C(1)–H | C(2)–H | C(3)–H | C(4)–H | C(5)–H | C(6)–H |
|---|---|---|---|---|---|---|
| Nonea) | 0.70 | 1.11 | 1.33 | 0.67 | 0.52 | 0.38 |
| Noneb) | 0.67 | 1.07 | 1.03 | 0.64 | 0.46 | 0.35 |
| KFa) | 0.71 | 1.14 | 1.39 | 0.68 | 0.54 | 0.38 |
| KFb) | 0.68 | 1.08 | 1.01 | 0.64 | 0.46 | 0.36 |
| KIa) | 0.67 | 1.01 | 1.25 | 0.66 | 0.62 | 0.31 |
| KIb) | 0.67 | 0.99 | 1.18 | 0.66 | 0.60 | 0.31 |
| $NaClO_4$ a) | 0.70 | 1.05 | 1.36 | 0.68 | 0.68 | 0.33 |
| $NaClO_4$ b) | 0.67 | 0.99 | 1.09 | 0.67 | 0.64 | 0.31 |

a) After removal of oxygen. b) Before removal of oxygen.

more than 92%. This fact suggests that a part of the dissolved oxygen is included within the cavity of $\alpha$-CD to accelerate the relaxation of C(3)– and C(5)–H's located in the interior of the cavity. On the other hand, the effect of oxygen became small when KI or $NaClO_4$ was added to an $\alpha$-CD solution: Even the $T_1$ values for C(3)– and C(5)–H's in the presence of oxygen were 92—94% and 94—97%, respectively, of those in the absence of oxygen. The anion of KI or $NaClO_4$ will be included within the $\alpha$-CD cavity to expel oxygen from the cavity to bulk solution. Interestingly, only the $T_1$ value for C(5)–H in the absence of oxygen increased, though those for the other protons generally decreased, upon the addition of KI or $NaClO_4$. It is known that $\alpha$-CD accommodates two molecules of water within its cavity.[22] Solvent $D_2O$ included within the $\alpha$-CD cavity may contribute to the spin-lattice relaxation of C(5)–H, and the inclusion of the anion of KI or $NaClO_4$ will expel the $D_2O$ from the cavity, and thus retard the relaxation.

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