Hydrogen-Bonded Complexes of Carboxylate Anions and Dextrins in an Aprotic Polar Solvent

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Complexation of *p*-methylbenzoate (*p*-$CH_3C_6H_4CO_2^-$) and alkanoate anions ($C_nCO_2^-$) with cyclodextrins (CDs) and acyclic dextrins (G*n*s) through hydrogen bonding in an aprotic polar solvent, [D_6]DMSO, has been studied by means of ^{1}H NMR spectroscopy. Although undissociated *p*-methylbenzoic acid, *p*-$CH_3C_6H_4CO_2H$, does not interact with dextrins, *p*-$CH_3C_6H_4CO_2^-$ binds through hydrogen-bonding interactions with fairly large binding constants (*K*) both to native CDs such as α-, β-, and γ-CDs and to G*n*s. Similar complexation was observed with $C_nCO_2^-$ anions. The *K* values are related to the basicity of the carboxylate anions. ^{1}H NMR spectroscopy shows that the CO_2^- group of the guest interacts with the secondary OH groups at the vicinal 2- and 3-positions of the dextrins, while the primary OH groups do not participate at all. Formation of the hydrogen-bonded complex of β-CD and *p*-$CH_3C_6H_4CO_2^-$ is an entropically favorable process. Addition of a small amount of D_2O suppresses the formation of the hydrogen-bonded complexes, suggesting that hydrogen-bonding interactions between simple hosts possessing dense OH groups as hydrogen-bond donors and guests with CO_2^- groups as hydrogen-bond acceptors hardly occur in aqueous solution.

Introduction

Hydrogen bonding is a key interaction for molecular recognition in biological and artificial host−guest systems.[1] A lot of effort has been made to construct artificial receptor systems and molecular architectures to develop the new field of so-called "supramolecular chemistry".[2] Intermolecular hydrogen bonding has been utilized conveniently for assembly of molecules in such cases. Hydrogen bonding in host−guest pairing is effective in nonpolar aprotic solvents such as chloroform, dichloromethane, toluene, and so on.[3] In polar solvents, especially in protic polar solvents, however, strong solvation at hydrogen-bonding sites prevents the formation of hydrogen-bonded host−guest complexes. Several attempts to form hydrogen bonds in polar solvents have been carried out. For example, bis(urea) and bis(thiourea) receptors have been prepared with the goal of trapping a pentanedioate dianion through hydrogen bonding in [D_6]DMSO.[4] The complexation in the bis(urea) system is accompanied by a small, negative entropy change (Δ*S*). A diphosphate receptor has also been developed to bind polyhydroxy compounds such as cyclopentane-1,2-diol and 1-*O*-octyl α- and β-D-glucosides in CD_3CN.[5] Artificial receptors with NH or CONH groups as the hydrogen-bond donors have been synthesized with the goal of binding enolate anions in CD_3CN.[6,7] In all of these examples, the hydrogen-bond acceptors are organic anions and the host−guest pairing is achieved through at least two hydrogen bonds. In aqueous solutions, however, hydrogen-bonding interactions become more difficult.[8] It has been reported that comprehensive base pairing between adenine and thymine in water occurs when the bases are brought into proximity by proflavin, which interacts with both adenine and thymine through stacking interactions.[9] Such an effect from proflavin is understandable if a proximity effect on hydrogen-bond formation is assumed. Recently, calix[4]-resorcarenes with α(1−4)-linked oligosaccharides were found to form stable hydrogen-bonded complexes with divalent phosphate anions in D_2O/[D_6]DMSO (9:1).[10] To explain the formation of such novel hydrogen-bonded complexes in water, a saccharide cluster effect was assumed. Hydrogen-bonding interactions occur more easily at air/water interfaces[11] or at surfaces of polymers in aqueous solutions.[12] Such surface effects on hydrogen bonding in aqueous systems are similar to those observed in biological systems such as enzymes and DNA.

Hydrogen-bonding interactions in cyclodextrin (CD) chemistry have also been examined. Native CDs can be regarded as artificial receptors, with the potential to show proximity, cluster, and/or polymer effects on intermolecular hydrogen bonding. There are several examples of complexation with CDs in which the participation of hydrogen bonding has been demonstrated. Chiral recognition of sulfinyl compounds by β-CD,[13] complexation of coumarin with β-CD,[14] molecular recognition of nucleotides by an aminated CD,[15] α-CD-catalyzed hydrolysis of cyclic monophosphates,[16] and β-CD-induced conformational enantiomerism of bilirubin[17] are examples in which hydrogen bonding is assumed to participate in complexation. However, no direct evidence for formation of hydrogen-bonded CD complexes in aqueous solutions has been presented, due to the absence of a method to detect hydrogen bonding in water. This is an innate problem, which is hardly overcome. Prior to investigation of aqueous system, it is import-

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ant to have knowledge of intermolecular hydrogen-bonding interactions of CDs in organic solvents. No study on host-guest pairing of CDs through hydrogen bonding in organic solvents has been carried out to date, although intramolecular hydrogen bonding of CDs in [D_6]DMSO has been investigated.[18]

Usable solvents are limited because of the solubility of native CDs; [D_6]DMSO was chosen as a solvent in this study. Polar [D_6]DMSO molecules solvate the OH groups of CDs through hydrogen bonding. Such solvation by [D_6]DMSO is similar to that of water. In addition, the proton signals due to CD OH groups can be detected clearly in [D_6]DMSO by ^{1}H NMR spectroscopy. Very few studies concerning the host−guest interactions of CDs in organic solvents have been reported.[19] Such circumstances also prompted us to study complexation of native CDs in [D_6]DMSO.

Results

Complexation of *p*-Methylbenzoate Anion with Dextrins

p-Methylbenzoic acid (*p*-$CH_3C_6H_4CO_2$ H) and its anion (*p*-$CH_3C_6H_4CO_2^-$) were used as probe guests, because of their simple ^{1}H NMR spectra. The ^{1}H NMR spectrum of *p*-$CH_3C_6H_4CO_2H$ in [D_6]DMSO was unaffected by addition of β-CD up to [β-CD] = 1.6×10^{-2} M. The NMR spectrum of β-CD also was unaffected by *p*-$CH_3C_6H_4CO_2H$. These results indicate that undissociated *p*-$CH_3C_6H_4CO_2H$ does not interact with β-CD in [D_6]DMSO.

Figure 1 shows the ^{1}H NMR spectral changes observed for *p*-$CH_3C_6H_4CO_2Na$ upon addition of β-CD in [D_6]DMSO. All the *p*-$CH_3C_6H_4CO_2^-$ proton signals are shifted to lower magnetic fields upon addition of β-CD, indicating interaction between the guest carboxylate anion and β-CD. The continuous variation method[20] (Job's plot) for each guest anion proton signal suggests the formation of a 1:1 complex. The ^{1}H NMR spectral changes seen for β-CD upon addition of *p*-$CH_3C_6H_4CO_2^-$ are shown in Figure 2. Only the proton signals due to the secondary OH groups at the 2- and 3-positions are affected, shifting to lower magnetic fields and broadening upon addition of the guest. Other proton signals of β-CD, including signals due to the primary OH groups, were unaffected by *p*-$CH_3C_6H_4CO_2^-$. These results imply that: (1) *p*-$CH_3C_6H_4CO_2^-$ is bound to the secondary OH groups of β-CD, (2) no inclusion of the guest anion in the host cavity occurs, and (3) no hydrogen bonding between the CO_2^- group of the guest and the primary OH group(s) of the host takes place. The interactions between the secondary OH groups of β-CD and the anionic guest should be intermolecular hydrogen bonding taking place outside the CD cavity. *p*-$CH_3C_6H_4CO_2^-$ does not bind at all with heptakis(2,3,6-tri-*O*-methyl)-β-CD (TMe-β-CD) and heptakis(2,6-di-*O*-methyl)-β-CD (2,6-DMe-β-CD) and scarcely interacts with heptakis(2,3-di-*O*-methyl)-β-CD (2,3-DMe-β-CD), suggesting that the CO_2^- group of the guest simultaneously binds to vicinal OH groups at the 2- and 3-positions of β-CD.

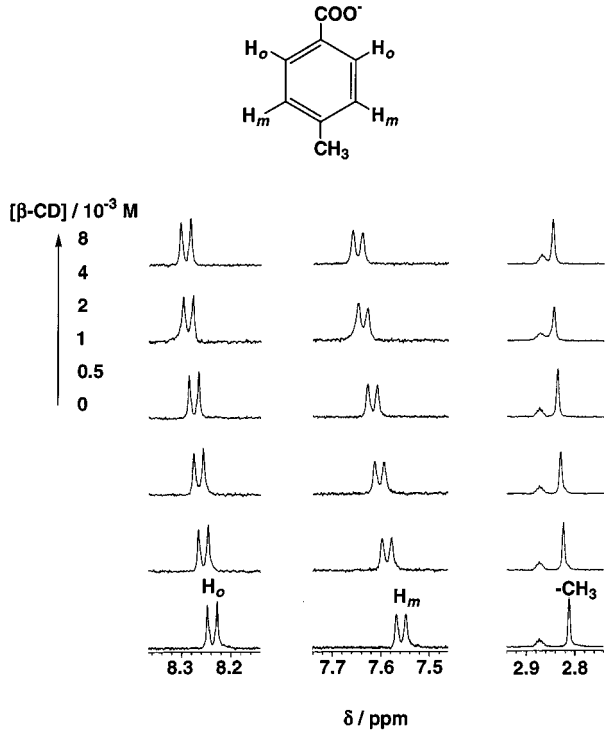

Figure 1. ^{1}H NMR spectral changes observed for *p*-$CH_3C_6H_4COONa$ (1×10^{-3} M) in [D_6]DMSO upon addition of β-CD at 25 °C

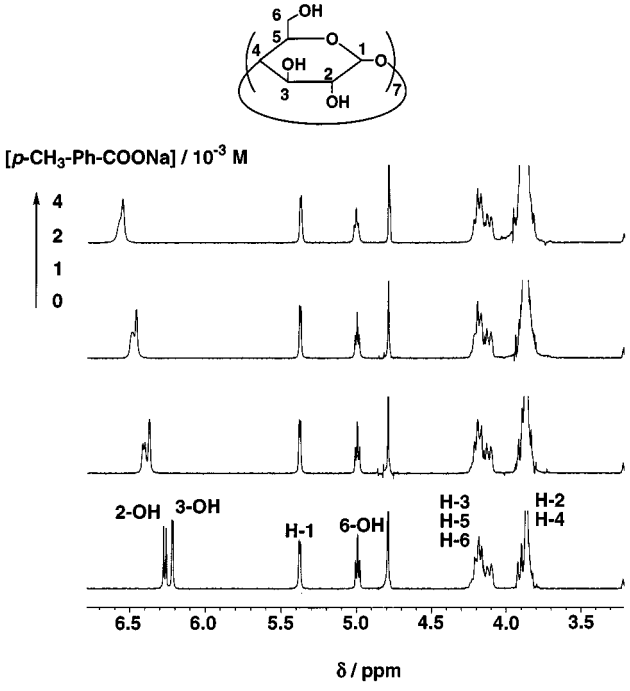

Figure 2. ^{1}H NMR spectral changes observed for β-CD (1×10^{-3} M) in [D_6]DMSO upon addition of *p*-$CH_3C_6H_4COONa$ at 25 °C

The ^{1}H NMR spectral behavior of the *p*-$CH_3C_6H_4CO_2^-$/maltoheptaose (G7) system is essentially the same as that of the *p*-$CH_3C_6H_4CO_2^-$/β-CD system (see Supporting Information). Similarly to the case of β-CD, the secondary OH groups of G7 act as the hydrogen-bond donors whilst the primary OH groups do not participate in hydrogen bonding with *p*-$CH_3C_6H_4CO_2^-$.

Binding Constants

The binding constants for complexation of *p*-$CH_3C_6H_4CO_2^-$ with the dextrins were determined from NMR titration curves, which were analyzed by a nonlinear, least-squares method (see Supporting Information). The results are summarized in Table 1.

Table 1. Binding constants for complexation of carboxylate anions with CDs and G*n*s in [D_6]DMSO at 25 °C

Entry	Guest	Host	K [M^{-1}]
1	*p*-$CH_3C_6H_4CO_2Na$	α-CD	669±40
2	*p*-$CH_3C_6H_4CO_2Na$	β-CD	792±45
3	*p*-$CH_3C_6H_4CO_2Na$	γ-CD	1300±60
4	*p*-$CH_3C_6H_4CO_2Na$	β-CD (1 vol% D_2O)	349±21
5	*p*-$CH_3C_6H_4CO_2Na$	β-CD (2 vol% D_2O)	174±14
6	*p*-$CH_3C_6H_4CO_2Na$	G3	297±19
7	*p*-$CH_3C_6H_4CO_2Na$	G4	349±19
8	*p*-$CH_3C_6H_4CO_2Na$	G5	476±27
9	*p*-$CH_3C_6H_4CO_2Na$	G6	542±43
10	*p*-$CH_3C_6H_4CO_2Na$	G7	679±36
11	*p*-$CH_3C_6H_4CO_2Na$	G7 (1 vol% D_2O)	661±53
12	*p*-$CH_3C_6H_4CO_2Na$	G7 (2 vol% D_2O)	459±36
13	*p*-$CH_3OC_6H_4CO_2Na$	β-CD	1070±80
14	*p*-$O_2NC_6H_4CO_2Na$	β-CD	151±10
15	*p*-$CH_3OC_6H_4CO_2Na$	G7	1020±100
16	*p*-$O_2NC_6H_4CO_2Na$	G7	173±16
17	*p*-$CH_3C_6H_4CO_2N(CH_3)_4$	β-CD	1190±40
18	*p*-$CH_3C_6H_4CO_2N(C_4H_9)_4$	β-CD	1580±81
19	C_1COONa	β-CD	1640±200
20	C_3COONa	β-CD	1660±140
21	C_5COONa	β-CD	2800±260
22	(*M*)-HDC	β-CD	685±17

In all cases, the titration curves fitted well with an equation for a 1:1 complex of host and guest. The K value increases in the order α- < β- < γ-CDs and maltotriose (G3) < maltotetraose (G4) < maltopentaose (G5) < maltohexaose (G6) < G7. The K value thus increases with increasing numbers of glucopyranose units in the host, a linear relationship being observed between the K values and the number of the glucopyranose units (n): $K = 95.7n - 9.90$ ($r^2 = 0.980$). G7 can be regarded as an open form of β-CD and shows a slightly smaller K value than in the case of β-CD. This may be due to the more fluctuating nature of this acyclic oligosaccharide.[21]

Effects of Water

Addition of a small amount of water causes a drastic decrease in the K value for complexation of *p*-$CH_3C_6H_4CO_2^-$ with β-CD (Entries 4 and 5 in Table 1). Since it is very difficult to remove water from [D_6]DMSO completely, the amounts of added water (1 and 2 vol%) are indicated by the amounts added to commercially obtained [D_6]DMSO. The effects of water on complexation of G7 are less pronounced than those on complexation of β-CD (Entries 11 and 12 in Table 1). Strong hydration at the hydrogen-bonding sites of both the host and guest molecules seems to prevent the formation of hydrogen-bonded complexes of dextrins and *p*-$CH_3C_6H_4CO_2^-$.

Benzoate Anion Substituent Effects

The effects of *p*-substituents on the benzoate anion on complexation with β-CD and G7 in [D_6]DMSO are shown in Table 1 (Entries 2, 13, and 14 for β-CD, and Entries 10, 15, and 16 for G7). An electron-donating group, OCH_3, increases the stabilities of the hydrogen-bonded complexes with β-CD or G7, while an electron-withdrawing group, NO_2, causes a drastic reduction in the K value. The effects of the substituents can be expressed as $\log K = \rho\sigma$, where σ is the Hammett substituent constant. The ρ values are −0.79 ($r^2 = 0.99$) and −0.69 ($r^2 = 0.98$) for the β-CD and G7 systems, respectively.

Effects of Countercations of *p*-$CH_3C_6H_4CO_2^-$

The countercations of *p*-$CH_3C_6H_4CO_2^-$ affect complexation markedly. Namely, the K value increases in the order *p*-$CH_3C_6H_4CO_2Na$ < *p*-$CH_3C_6H_4CO_2N(CH_3)_4$ < *p*-$CH_3C_6H_4CO_2N(C_4H_9)_4$. The Na^+ cation interacts with [D_6]DMSO through ion−dipole interactions. Meanwhile, the hydrophobic tetrabutylammonium cation may be solvated through van der Waals interactions as well as through ion−dipole interactions. It seems that *p*-$CH_3C_6H_4CO_2^-$ and Na^+ form a relatively strong contact ion pair, while pairing between *p*-$CH_3C_6H_4CO_2^-$ and $N(C_4H_9)_4^+$ is much looser. The carboxylate anion in a loose ion pair should be more suited to formation of intermolecular hydrogen bonds with β-CD than that in a contact ion pair.

Thermodynamic Parameters

Thermodynamic parameters are very important in discussion of the mechanisms of host−guest complexation.[22] Table 2 summarizes the K values at various temperatures and the enthalpy ($\Delta H°$) and entropy changes ($\Delta S°$) for complexation of *p*-$CH_3C_6H_4CO_2Na$ with β-CD and G7 in [D_6]DMSO. Although complexation both of β-CD and of G7 with *p*-$CH_3C_6H_4CO_2^-$ is promoted by the enthalpy terms, the formation of the hydrogen-bonded complex of β-CD is also assisted by a positive entropy change. The results are similar to those for the entropically favorable complexation of anionic azo dyes with native CDs in *N*,*N*-dimethylformamide (DMF).[19b]

Table 2. Binding constants (K) at various temperatures and thermodynamic parameters for complexation of p-$CH_3C_6H_4CO_2Na$ with β-CD and G7 in [D_6]DMSO

System	T [K]	K [M^{-1}]	$\Delta H°$ [kJ mol^{-1}]	$\Delta S°$ [J mol^{-1}K^{-1}]
β-CD	298.15	792±45	−11.5±0.5	17.1±1.8
	308.15		670±43	
	318.15		579±40	
	328.15		520±33	
G7	298.15	679±36	−17.4±0.3	−4.2±0.8
	308.15		539±32	
	318.15		441±29	
	328.15		356±27	

Complexation with Other Anionic Guests

The K values for complexation of β-CD with acetate ($C_1CO_2^-$), butanoate ($C_3CO_2^-$), and hexanoate anions ($C_5CO_2^-$) are shown in Table 1 (Entries 19, 20, and 21). The hydrogen-bonded complexes of the alkanoate anions and β-CD are more stable than those of the benzoate anions. The results can be understood by considering the basicity of the carboxylate anions (vide infra).

Recently, we found that the helicity of the 1,12-dimethylbenzo[c]phenanthrene-5,8-dicarboxylate dianion (HDC, Figure 3) is efficiently recognized by β-CD in aqueous solution.[23] In this study, it was examined whether the chirality of the HDC disodium salt is recognized by β-CD in [D_6]DMSO. The K value for the (*M*)-HDC-β-CD complex is shown in Table 1 (Entry 22). The K value in [D_6]DMDO is much smaller than those in D_2O and no chiral recognition was observed.

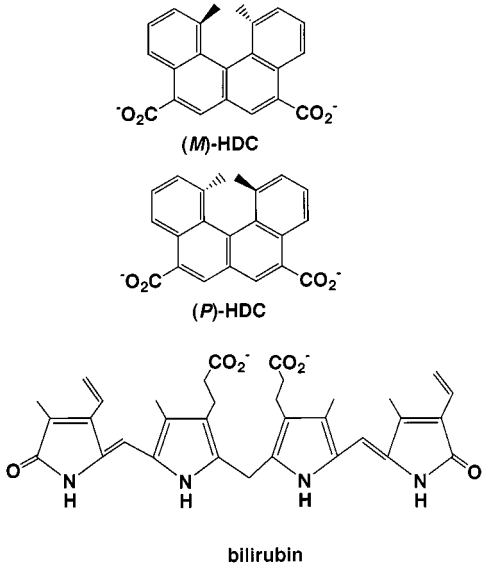

Figure 3. Structures of HDC and bilirubin

Discussion

The ^{1}H NMR signals of the secondary OH groups at the 2- and 3-positions of β-CD (1×10^{-3} M) in [D_6]DMSO were observed at δ = 6.27 and 6.21, respectively, and were shifted to δ = 6.57 and 6.55, respectively, upon addition of 4×10^{-3} M p-$CH_3C_6H_4CO_2Na$ (see Figure 2). From the K value (792±45 M^{-1}) of this system, the infinite shifts in the chemical shifts ($\Delta\delta_{sat}$) of the OH protons, which correspond to the shifts when 100% of β-CD forms the hydrogen-bonded complex with p-$CH_3C_6H_4CO_2Na$, are calculated as 1.66 and 1.88 ppm for the OH protons at the 2- and 3-positions, respectively. Such large downfield shifts of the OH proton signals are attributable to the formation of hydrogen bonds between these OH groups and p-$CH_3C_6H_4CO_2^-$.[24] The absence of any interaction between the guest dianion and 2,6-DMe-β-CD, which has the secondary OH groups at the 3-positions, indicates that the vicinal OH groups at the 2- and 3-positions of β-CD are essential for formation of the hydrogen-bonded complex of p-$CH_3C_6H_4CO_2^-$ and β-CD. Two-centered hydrogen bonds seem to be formed (Figure 4). It is known that multipoint hydrogen bonding causes significant stabilization of hydrogen-bonded complexes.[24] Very weak interaction between the primary OH group(s) and p-$CH_3C_6H_4CO_2^-$ was detected when 2,3-DMe-β-CD was used as the host (Supporting Information). The cyclic structure of the host is not important for hydrogen-bond formation between oligosaccharide and p-$CH_3C_6H_4CO_2^-$. In complexation of Gn with p-$CH_3C_6H_4CO_2^-$, the K value is proportional to the number of the glucopyranose units (n). This implies the absence of polymer effects and cluster effects on formation of the hydrogen-bonded complexes of Gn. The linear relationship between K and n also supports the structure shown in Figure 4.[25]

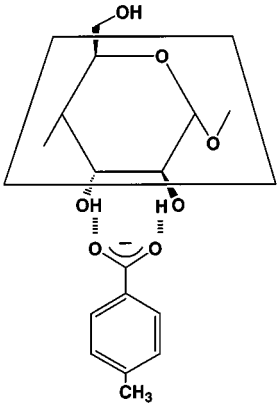

Figure 4. Structure of the hydrogen-bonded complex of β-CD and p-$CH_3C_6H_4CO_2^-$ in [D_6]DMSO

The effects of water on complexation of β-CD and G7 with p-$CH_3C_6H_4CO_2^-$ are remarkable. In general, protic polar solvents such as alkanols and water suppress the formation of hydrogen-bonded complexes because of strong solvation at hydrogen-bond donor and/or acceptor sites.[8,24] In the systems under study, 10 vol% water completely inhibits the formation of the complexes of β-CD or G7. The inhibition effect of water toward β-CD is more remarkable than that toward G7. The OH groups in β-CD are arranged regularly on the rim of the CD cavity, and

water molecules bound to a secondary OH group of β-CD can move to another secondary OH group more rapidly than those bound to G7 can. This may be the reason for the greater effects of water on complexation of β-CD.

^{1}H NMR spectroscopy demonstrates intramolecular hydrogen bonding between the secondary OH groups at the 2-positions and those at the 3-positions of the adjacent glucopyranose units of β-CD in [D_6]DMSO.[18] The [D_6]DMSO molecules also interact with saccharide through hydrogen bonding. In order to form hydrogen bonds between β-CD and *p*-$CH_3C_6H_4CO_2^-$ in [D_6]DMSO, the intramolecular hydrogen bonds and the solvation in the CD molecule should be disrupted. Such processes are enthalpically unfavorable but entropically favorable. The experimental results are in agreement with this assumption (see Table 2). The positive entropy change for complexation of *p*-$CH_3C_6H_4CO_2^-$ with β-CD ($\Delta S°$ = $+17.1\pm1.8$ J mol^{-1}K^{-1}) is attributable to desolvation from the host upon complexation. The entropic gain due to the disruption of intramolecular hydrogen bonding may be cancelled out by formation of intermolecular hydrogen bonds between the host and the guest anion. Release of [D_6]DMSO molecules from the CD cavity is unlikely to occur, because the guest anion is not included in the CD cavity in [D_6]DMSO. A contribution of favorable entropy terms to formation of hydrogen-bonded complexes in protic polar solvents involving water,[26] water-saturated $CDCl_3$,[27] and [D_6]DMSO[4] has been reported. In all cases, desolvation was assumed to be the origin of the entropic gains. In nonpolar solvents such as chloroform and toluene, formation of hydrogen-bonded complexes is accompanied by negative, favorable enthalpy changes and negative, unfavorable entropy changes.[24,28] Danil de Namor et al. also observed entropically favorable complexation of anionic azo dyes with native CDs in DMF.[19b] They assumed interactions between the OH groups of CDs and the anionic dyes, though hydrogen bonding was not indicated as a binding force. On the basis of these aspects, it can be concluded that hydrogen-bonding interactions in polar solvents such as water, ethanol, and DMSO are entropically favorable because they are accompanied by desolvation upon complexation. However, hydrogen-bond formation is enthalpically suppressed because desolvation is an endothermic process. In the case of G7, $\Delta S°$ is negative and small (-4.2 ± 0.8 J mol^{-1}K^{-1}). The small $|\Delta S°|$ value may involve the contribution of desolvation.

The *K* values for complexation of various carboxylate anions with β-CD can be understood consistently on the basis of the basicity of these hydrogen-bond acceptors. A linear relationship was observed between pK_a of the conjugate acids of the carboxylate anions and log*K* [log$K$ = 0.87pK_a − 0.82 (r^2 = 0.98)], except in the case of $C_5CO_2^-$. Such a result suggests hydrogen bonding as the sole complexation interaction, although we cannot explain the deviation of the result for $C_5CO_2^-$.

We had previously studied chiral recognition of a tetrahelicene, HDC (Figure 3), by β-CD in aqueous solution.[23] (*M*)- and (*P*)-HDCs in their dicarboxylate anion forms bind to β-CD with large *K* values in D_2O; the *K* values for the (*M*) and (*P*) isomers being 18700 and 2200 M^{-1}, respectively. Such large *K* values for the dianions suggest complexation assisted by inclusion and hydrogen bonding. In this study, however, a small possibility of hydrogen bonding in aqueous solution is suggested. In [D_6]DMSO, the HDC dianion binds to β-CD with a *K* value of 685 ± 17 M^{-1} and no chiral recognition by β-CD occurs. Such results suggest that van der Waals interactions between the HDC dianions and β-CD are the main binding force in D_2O, and that hydrogen bonding does not participate in this enantioselective complexation. The negative and large ΔS values for the HDC system [ΔS = −90.1 and −53.2 J mol^{-1}K^{-1} for (*M*)- and (*P*)-HDCs, respectively][23] also support the absence of hydrogen bonding in aqueous systems.

In the previous study, we assumed hydrogen bonding between the CO_2^- groups of bilirubin (Figure 3) and the secondary OH groups of β-CD for CD-induced conformational enantiomerism of bilirubin in aqueous solution.[17] We also examined such conformational enantiomerism of bilirubin disodium salt in DMSO in this study, by measuring circular dichroism spectra. No circular dichroism signal was detected in DMSO, while a minus-to-plus bisignate circular dichroism spectrum was measured in water,[17] indicating that the conformational enantiomerism of bilirubin is achieved only when bilirubin is included in the β-CD cavity. Complexation without hydrogen bonding is also supported by the negative and large ΔS value in the bilirubin/β-CD system in aqueous solution (ΔS = −66.0 J mol^{-1}K^{-1}).[17]

Conclusion

In [D_6]DMSO, undissociated *p*-$CH_3C_6H_4CO_2H$ does not interact with the OH groups of native CDs at all, while the more basic *p*-$CH_3C_6H_4CO_2^-$ forms hydrogen bonds with the vicinal OH groups of native CDs in a manner shown in Figure 4. Addition of a small amount of water causes disruption of the hydrogen bonds between the OH groups of the host and the CO_2^- group of the guest, indicating that pairing of the host CD and the guest carboxylate through hydrogen bonding hardly occurs in aqueous solution. This study, however, cannot completely rule out formation of hydrogen-bonded complexes of native CDs in aqueous solution. As the next step, we need to investigate proximity effects on hydrogen bonding in host-guest systems in aqueous solutions. Inclusion of a guest in a host cavity may direct an approach between hydrogen-bond donor and acceptor. Under such circumstances, hydrogen bonding in aqueous solution might be possible, as seen in the intramolecular hydrogen bonding of salicylic acid.

Experimental Section

α-, β-, γ-, 2,6-DMe-β- and TMe-β-CDs (Nacalai) were purchased. β-CD was washed with THF using a Soxhlet extractor. 2,3-DMe-β-CD was prepared according to the procedures described in the literature.[29] G3 (99%), G4 (99%), G5 (98%), G6 (96%), and G7

(97%) were obtained from Hayashibara Biochem. Lab. and used as received. The benzoic acid derivatives (Wako) were purified by recrystallization from water. C_1COONa (Nacalai), C_3COOH (Aldrich), and C_5COOH (Nacalai) were purchased. The sodium salts of the carboxylic acids were prepared by dissolving the acids in equimolar aqueous NaOH solutions. Water was evaporated and the solid salts were dried under vacuum. – ^1H NMR spectra were measured with a JEOL JNM-A400 (400 MHz) spectrometer in [D_6]DMSO (CEA, 99%) using 3-trimethylsilyl [2,2,3,3-$^2H_4$]propionate (TSP, Aldrich) as an external standard. – Circular dichroism spectra were measured with a Jasco J-500A spectropolarimeter with a data processor.

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