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Chiral recognition by cyclic oligosaccharides. Enantioselective complexation of binaphthyl derivatives with cyclodextrins

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Chiral recognition of binaphthyl derivatives, such as 1,1′-bi-2-naphthol (1), 1,1′-binaphthyl-2,2′-diyl hydrogen phosphate (2), and 2,2′-dihydroxy-1,1′-binaphthyl-3,3′-dicarboxylic acid (3), by cyclodextrins (CDxs) has been studied. The *S* enantiomers of 1 and 2 are bound to heptakis(2,3,6-tri-*O*-methyl)-β-CDx (TMe-β-CDx) as well as β-CDx more strongly than the *R* enantiomers. The molecular mechanics and molecular dynamics calculations for the 1:1 complex of 1 and β-CDx suggest that more effective van der Waals contacts and intermolecular hydrogen bonding stabilize the complex of *S*-1 compared with that of *R*-1. Meanwhile the *R* enantiomer of 3 is the preferable guest for β- and TMe-β-CDxs. Circular dichroism spectroscopy suggests that the complex of *S*-3 is more unstable than that of *R*-3 because the dihedral angle of the naphthalene planes of *S*-3 needs to be reduced for forming the inclusion complex. The enantiomers of the guest binaphthyls are completely separated by means of capillary zone electrophoresis (CZE) when TMe-β-CDx is used as a separating agent. The results of the CZE correspond well with those of the binding constants of the inclusion complexes.

INTRODUCTION

Chiral recognition by cyclodextrins (CDxs) is one of the most interesting research subjects in CDx chemistry. In 1959, Cramer and Dietsche[1] reported the partial resolution of the enantiomers of the mandelic acid derivatives by stereoselective complexation with β-CDx. Partial optical resolution by β-CDx has similarly been achieved for isopropyl methylphosphinate and its derivatives[2] and sulphinyl compounds.[3] Very small differences in the binding constants (K) for complexation with CDxs have been found between the enantiomers of phenylalanine and of 1-methylbenzylamine.[4] Recent NMR measurements indicate that CDxs can recognize the chiralities of amino acids.[5] Chiral ferrocenes,[6] fenchone,[7] 2-methylcyclohexanone,[8] flurbiprofens,[9] and fenoprofen[10] have also been known as the guests whose chiralities are weakly recognized by CDxs.

X-ray crystallographic analysis clearly reveals the difference between the structures of the CDx complexes of *S*- and *R*-mandelic acids.[11] The phenyl group of *S*-mandelic acid is shallowly bound to the wider cavity side of heptakis(2,3,6-tri-*O*-methyl)-α-CDx (TMe-α-CDx). The hydroxy and carboxy groups of the acid, both of which form hydrogen bonds with the water molecules, are located outside of the cavity. Meanwhile the phenyl group of *R*-mandelic acid is included more deeply in the β-CDx cavity and the hydroxy group of the acid binds with the O(2) oxygen of TMe-α-CDx through hydrogen bonding. The carboxy group of *R*-mandelic acid forms a hydrogen bond with the O(6) oxygen of adjacent TMe-α-CDx.[11] Although the difference in the crystal structures between diastereoisomeric complexes of CDxs can be measured by means of X-ray crystallography, the mechanisms for chiral recognition by CDxs in solutions are hardly clarified. NMR measurements and molecular mechanics (MM) and/or molecular dynamics (MD) calculations should provide the best means of speculating on the mechanism of chiral recognition.[5b]

In a previous communication,[12] we briefly reported that TMe-β-CDx prefers the *S* enantiomers of 1,1′-bi-2-naphthol (**1**), 2,2′-dimethoxy-1,1′-binaphthyl, and 1,1′-binaphthyl-2,2′-diyl hydrogen phosphate (**2**) to the *R*-enantiomer as the guests. This paper deals

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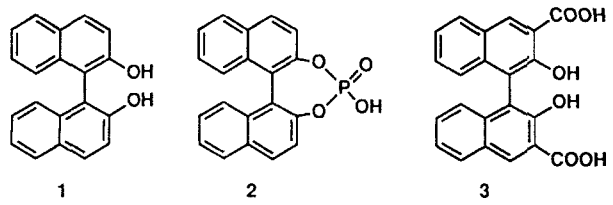

1 2 3

with the determination of accurate binding constants (K) for the diastereoisomeric complexes of β- and TMe-β-CDxs with the enantiomers of **1**, **2**, and 2,2′-dihydroxy-1,1′-binaphthyl-3,3′-dicarboxylic acid (**3**), the MM and MD calculations for these complexes, and complete optical resolution of the enantiomers of **1**, **2**, and **3** by capillary zone electrophoresis (CZE). These studies clearly reveal that TMe-β-CDx effectively recognizes the chirality of the binaphthyl derivatives.

RESULTS AND DISCUSSION

Binding constants

The fluorescence intensity of **1** (I_f) in water (pH 5.5) increases with increasing concentration of β-CDx or TMe-β-CDx. The plots of I_f of *R*- and *S*-**1** vs. TMe-β-CDx concentration are shown in Figure 1, which clearly indicate that the effect of added TMe-β-CDx is more remarkable for the *S*-**1** than for the *R*-**1** isomer. It has been widely accepted that the K value for complexation can be determined from the Benesi–Hildebrand plot,[13] though this method has been criticized.[14] We first evaluated the K values using both Benesi–Hildebrand and non-linear regression methods.[15] The K values for the 1:1 complex of *S*-**1** and β-CDx obtained from the Benesi–Hildebrand plots and non-linear regression for the fluorescence intensity change are 245 and 223 $dm^3\,mol^{-1}$, respectively. In the case of the *R* enantiomer of **1**, the K values from the Benesi–Hildebrand and non-linear regression methods are 176 and 194 $dm^3\,mol^{-1}$, respectively. No serious difference is measured between the K values obtained from these two methods. In the present study, therefore, we used the Benesi–Hildebrand plots to determine K values. K values of the **3**-CDx complexes were also determined by the same method. The fluorescence intensity change of **2**, however, was so small that the K values of the **2**–CDx complexes were evaluated from the circular dichroism (CD) spectral changes of **2** upon addition of CDxs.

The differences in the K values between the enantiomers of the binaphthyl derivatives are shown in Table 1. In the **1**- and **2**-β-CDx systems, the 1:1 host–guest complexes are formed and the *S* enantiomers of **1** and **2** are preferentially bound to β-CDx compared with the *R* enantiomers. In contrast to compounds **1** and **2**, the K value for complexation of *R*-**3** with β-CDx is slightly larger than that for *S*-**3**.

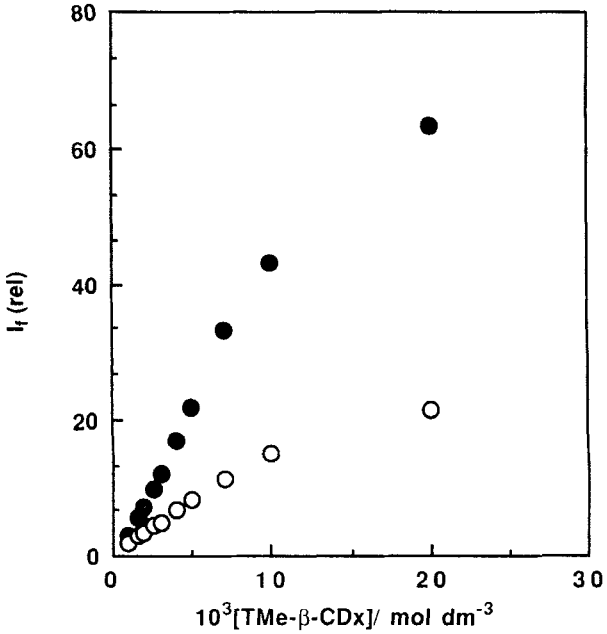

Figure 1 Fluorescence intensity changes of *S*-**1** (●) and *R*-**1** (○) upon addition of TMe-β-CDx in water (pH 5.5, 25°C). Compound **1** (1×10^{-5} mol dm^{-3}) was excited at 292 nm and the fluorescence intensities were followed at 357 and 362 nm for *S*- and *R*-**1**, respectively.

In complexation of *S*-**1** with TMe-β-CDx, the Benesi–Hildebrand relationship for 1:1 host–guest complex formation could not be applied. As reported in a previous communication,[12] the stoichiometry of the TMe-β-CDx–*S*-**1** complex is 2:1 and the K_1K_2 value is significantly large. On the other hand, a very unstable 1:1 complex is formed in the *R*-**1**–TMe-β-CDx system. K values for the TMe-β-CDx–**2** complexes could not be obtained because of poor reproducibility. As with the case of β-CDx, the K value of the *R*-**3**–TMe-β-CDx complex is larger than that of the *S*-**3** complex.

MM and MD calculations

In order to discuss the mechanism for chiral recognition by CDx in solution, differences in the structures of inclusion complexes of *S* and *R* enantiomers should be detected by means of spectroscopy. NMR spectroscopy is one of the most powerful tools for this. In this study, however, poor solubilities of the binaphthyl derivatives in aqueous CDx solutions make it impossible to infer the structures of inclusion complexes from NMR measurements. Then we examined MM and MD calculations to speculate on the mechanism for chiral recognition by CDxs. Both the structures of the host and guest molecules were initially optimized. Since the calculated potential

Table 1 Binding constants (K) for the complexation of compounds **1**, **2**, and **3** with CDxs in aqueous solution at 25°C[a]

Guest	*Host*	*pH*	*Host:guest*	*K* ($dm^3\ m^{-1}$ or $dm^6\ mol^{-2}$)
S-**1**	β-CDx	5.5[b]	1:1	245 ± 4
R-**1**	β-CDx	5.5[b]	1:1	176 ± 25
S-**1**	TMe-β-CDx	5.5[b]	2:1	(5 ± 1) × 10^4
R-**1**	TMe-β-CDx	5.5[b]	1:1	17 ± 0.1
S-**2**	β-CDx	5.5[b]	1:1	542 ± 30
R-**2**	β-CDx	5.5[b]	1:1	188 ± 20
S-**3**	β-CDx	10.8[c]	1:1	309 ± 6
R-**3**	β-CDx	10.8[c]	1:1	340 ± 6
R-**3**	TMe-β-CDx	10.8[c]	1:1	375 ± 18
R-**3**	TMe-β-CDx	10.8[c]	1:1	420 ± 16
S-**3**	TMe-β-CDx	5.62[d]	1:1	268 ± 10
R-**3**	TMe-β-CDx	5.62[d]	1:1	370 ± 20

[a] The initial concentration of the guest was 1×10^{-5} mol dm^{-3}.
[b] The measurement was carried out in aerobic water.
[c] The pH was adjusted by NaOH. The pH did not change during measurement.
[d] The measurement was carried out in 0.03 mol dm^{-3} phosphate buffer solution.

energy of an inclusion complex depends upon a starting structure, we employed the results which are in agreement with those of the K value determination. We examined the calculations including the effects of the solvent water molecules. However, the results were so complex that the optimized structures in the gas phase were used in the calculations.

In the starting structures of the 1:1 complexes of *R*- and *S*-**1** with β-CDx, the **1** molecule was placed at the secondary hydroxy group side of β-CDx which is a wider side of the toroidal β-CDx cavity. The configurations of the complexes having the lowest potential energies are shown in Figure 2 and the total potential energies and their components are summarized in Table 2. The total potential energy is composed of bond stretching (E_b), bond angle bending (E_θ), dihedral angle torsion (E_ϕ), inversion (E_i), van der Waals (E_{vdw}), electrostatic (E_{el}), and hydrogen bond (E_{hb}) terms:

$$E = E_b + E_\theta + E_\phi + E_i + E_{vdw} + E_{el} + E_{hb}$$

As shown in Figure 2, one of the naphthalene moieties of *R*-**1** is completely included in the β-CDx cavity and another naphthalene ring is located outside the cavity. Meanwhile both naphthalene rings of *S*-**1** are incorporated in the bent β-CDx cavity. Such structural differences are reflected in the larger E_θ values and the smaller E_{vdw} values for the *S*-**1** complex. The smaller E_{vdw} of the *S*-**1** complex seems to be ascribed to the van der Waals attractive forces for this complex being larger than that for the *R*-**1** complex. A large difference is also found in the E_{hb} value between the *S* and *R* complexes. It is very difficult to discuss the hydrogen bonding in this system because the K values are determined in aqueous solutions while the MM-MD calculations are carried out for the gas phase. However, it is reasonable to consider that the hydrogen bonds are formed between the hydroxy groups of *S*-**1** and of β-CDx because both naphthalene moieties are located inside the CDx cavity. We have recently demonstrated that hydrogen bond formation is possible even in aqueous solution when hydrophobic backbones exist near the hydrogen bonding sites of both host and guest molecules.[16] On the other hand,

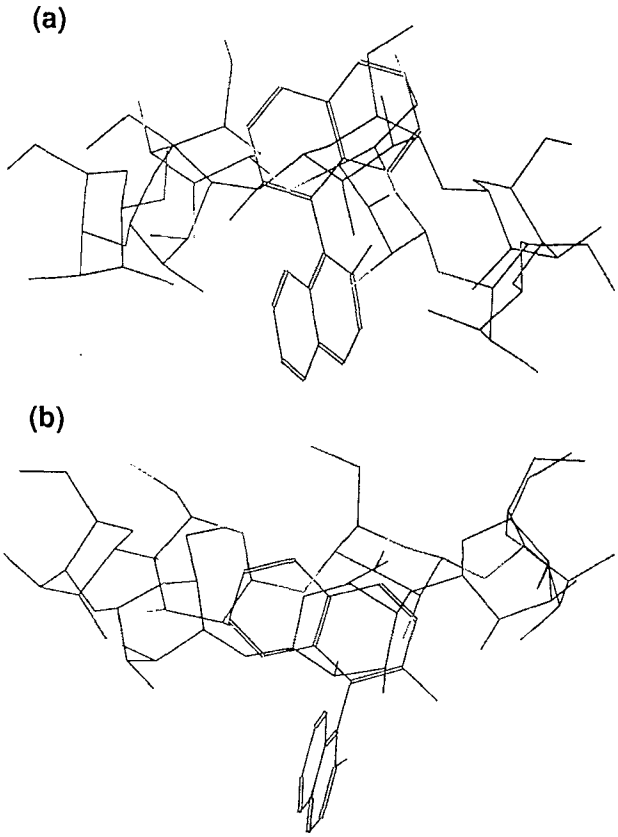

Figure 2 Optimized structures of (*a*) *S*-**1**–β-CDx complex and (*b*) *R*-**1**–β-CDx complex computed from MM-MD calculations.

Table 2 Total potential energies and their components for β-CDx and 1:1 complexes of *S*- and *R*-**1** with β-CDx in the gas phase[a]

	Potential energy (kJ mol^{-1})[b]		
	β-CDx	*S-1-β-CDx*	*R-1-β-CDx*
E	1021	878	1008
E_b	88	113	121
E_θ	305	314	268
E_ϕ	126	188	188
E_i	0	0	0
E_{vdw}	326	485	527
E_{el}	360	201	226
E_{hb}	−184	−423	−322

[a] The detail of the MM-MD calculations is described in the text.
[b] The total potential energy (E) is composed of bond stretching (E_b), bong angle bending (E_θ), dihedral angle torsion (E_ϕ), inversion (E_i), van der Waals (E_{vdw}), electrostatic (E_{el}), and hydrogen bond (E_{hb}) terms.

one of the hydroxy groups of *R*-**1** which is situated outside the cavity cannot interact with β-CDx through hydrogen bonding. The MM-MD calculations also suggest the important role of dipole interactions for forming the inclusion complexes. Namely the E_{el} values of the β-CDx complexes are much smaller than those of β-CDx alone (see E_{el} in Table 2). This implies that the dipole–dipole interaction is an attractive force for the complexation of **1** with β-CDx.

The results of MM-MD calculations for the 1:1 complexes of *S* and *R*-**1** with TMe-β-CDx are shown in Figure 3 and Table 3. The results in Table 3 suggest that dipole and hydrogen bonding interactions act as the attractive forces for forming the inclusion complexes of TMe-β-CDx, which is similar to the case of the **1**–β-CDx complexes. However, both E_{el} and E_{hb} values for the **1**–TMe-β-CDx complexes are larger than those for the **1**–β-CDx complexes. The instability of the 1:1 complexes of *S*- and *R*-**1** with TMe-β-CDx may be due to the weaker dipole and hydrogen bonding interactions compared with the complexes of **1** and β-CDx. *R*-**1** is shallowly bound to TMe-β-CDx (see Fig 3*a*). Such a structure may explain the very small K value (17 ± 0.1 dm^3 mol^{-1}) for this complex. In contrast to this, a naphthalene moiety of *S*-**1** is included more deeply in the TMe-β-CDx cavity leading to larger E_θ and E_ϕ values for the *S* complex. Such a structure of the *S* complex seems to be much more unstable than the shallow inclusion complex of *R*-**1** and TMe-β-CDx. Unfortunately, a reasonable structure of a 2:1 complex of *S*- and *R*-**1** with TMe-β-CDx could not be provided from the MM-MD calculations because no information about the structures of the 2:1 complex of *R*-**1** and TMe-β-CDx was obtained from experiments. Consequently, it is assumed that the main binding forces for forming inclusion complexes of **1** with β- and TMe-β-CDxs

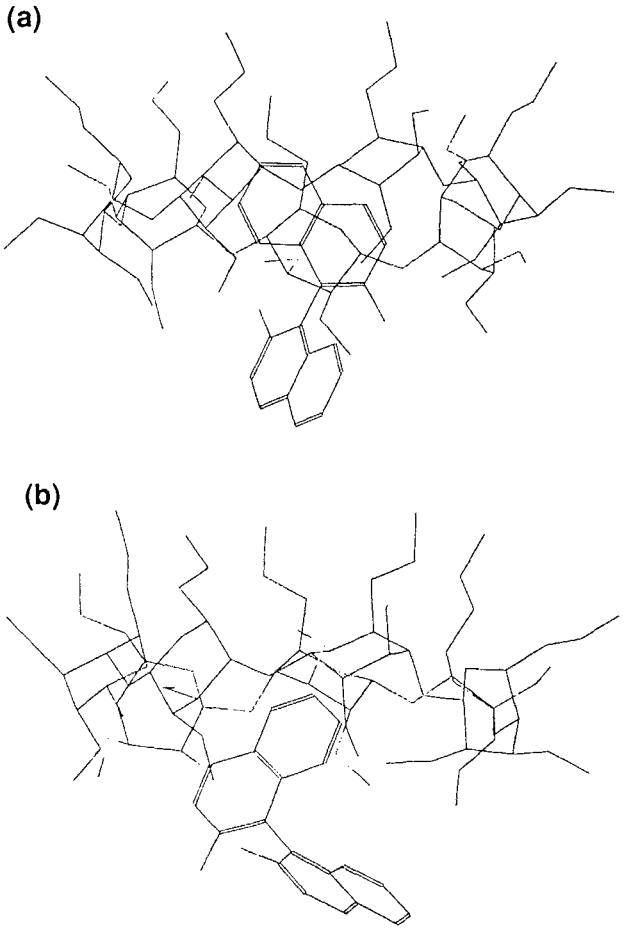

Figure 3 Optimized structures of (*a*) *S*-**1**–TMe-β-CDx complex and (*b*) *R*-**1**–TMe-β-CDx complex computed from MM-MD calculations.

Table 3 Total potential energies and their components for 1:1 complexes of *S*- and *R*-**1** with TMe-β-CDx in the gas phase

	Potential energy (kJ mol^{-1})		
	TMe-β-CDx	*S-1-TMe-β-CDx*	*R-1-TMe-β-CDx*
E	1490	1573	1535
E_b	121	155	151
E_θ	469	477	452
E_ϕ	109	197	167
E_i	0	0	0
E_{vdw}	452	552	577
E_{el}	339	251	259
E_{hb}	0	−59	−71

are the dipole–dipole and hydrogen bonding interactions, and the enantioselectivity of β-CDx towards compound **1** arises from an appropriate configuration of the *S*-**1**–β-CDx complex causing effective van der Waals contacts and forming the hydrogen bonds. The cavity size of TMe-β-CDx may be too small to include **1**. This seems to be the reason why the 1:1 complex

of *R*-**1** and TMe-*β*-CDx is very unstable and why the 2:1 complex of *S*-**1** and TMe-*β*-CDx is formed.

CD spectroscopy

An exciton-coupling theory has been used to determine the absolute configurations of chiral, bichromophoric compounds.[17] Most binaphthyl derivatives show positive and negative CD signals at longer and shorter wavelengths, respectively, at the ^1B_b transition band, when the orientation of the transition dipoles of two naphthalene moieties takes on an *R*-helix configuration. The oppositely signed [(−)-(+)] bisignate CD spectrum is measured for the binaphthyl derivative having an *S*-helix configuration. *S*- and *R*-**1** and -**2** take on the *R*- and *S*-helix configurations, respectively, and show the (+)-(−) and (−)-(+) bisignate Cotton effects, respectively. As shown in Figure 4, however, the signs of the bisignate CD Cotton effect for compound **3** in acetonitrile are opposite to those for the ordinary binaphthyls. Namely *R*-(+)-**3**, having an *S*-helix configuration, shows the (+)-(−) bisignate Cotton effect and *S*-(−)-**3**, having an *R*-helix configuration, reveals a (−)-(+)-bisignate Cotton effect. The signs of the bisignate CD Cotton effect have been known to depend upon the dihedral angle of the molecular planes of the binaphthyl derivative.[18] The *π*-SCF calculations suggest that the signs of the bisignate CD Cotton effect of the binaphthyl derivative change at the dihedral angle of the naphthalene rings of 100–110°.[18] Probably the dihedral angle of compound **3** in acetonitrile is larger than that of compounds **1** and **2**. CD spectra of *S*- and *R*-**3** in aqueous TMe-*β*-CDx solutions at pH 10.8 are shown in Figure 5. The signs of the bisignate CD signals of *R*-**3** in TMe-*β*-CDx solution is the same as those in acetonitrile. The signs for *S*-**3**, however, are opposite to those in acetonitrile while the sign of the monosignate CD Cotton effect observed at *ca.* 260 nm

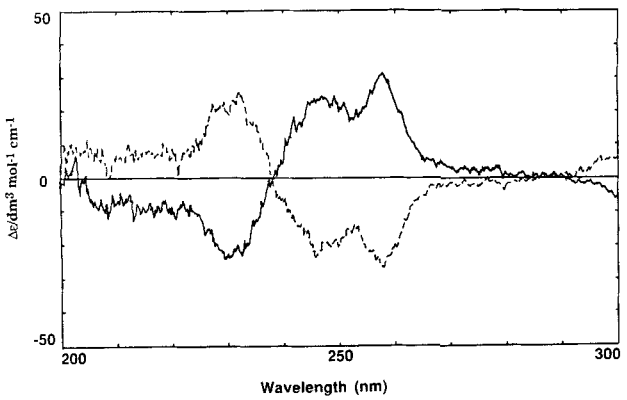

Figure 4 CD spectra of *R*-(+)-**3** (——) and *S*-(−)-**3** (– – –) in acetonitrile at 25°C (concentration of **3** = 1 × 10^{-5} mol dm^{-3}).

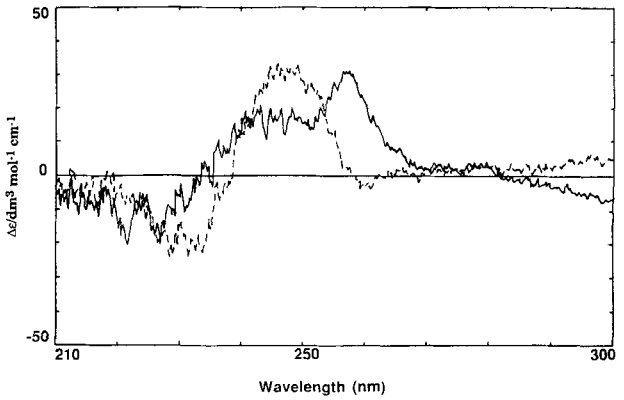

Figure 5 CD spectra of *R*-(+)-**3** (——) and *S*-(−)-**3** (– – –) in aqueous TMe-*β*-CDx solutions at 25°C (concentration of **3** = 1 × 10^{-5} mol dm^{-3}, concentration of TMe-*β*-CDx = 1 × 10^{-2} mol dm^{-3}).

does not change. This may be due to a reduction of the dihedral angle of *S*-**3** upon complexation with TMe-*β*-CDx. It may be reasonable to consider, therefore, that the stability of the *S*-**3**–TMe-*β*-CDx complex is lower than that of the *R*-**3**–TMe-*β*-CDx complex because the intrusion of the *S*-**3** molecule into the TMe-*β*-CDx cavity requires the reduction of the dihedral angle of *S*-**3**.

Optical resolutions of binaphthyl derivatives by CZE

Recent advances in analytical chemistry reveal that CZE is a powerful tool for rapid and excellent separation of ionic solutes in aqueous solutions.[19] Terabe and his co-workers[20] applied CZE to separate neutral solutes in water using surfactant–micelle subphases, and they named this method 'micellar electrokinetic chromatography'. The idea of this method is to separate geometrical and optical isomers by using CDxs as separating agents in CZE.[19,21] In this work, we tried to separate the enantiomers of the binaphthyl derivatives by CZE, where *β*-CDx and TMe-*β*-CDx were used as the chirality-recognizing separating agents.

Since the pK_a of *β*-CDx is 12.2,[22] and TMe-*β*-CDx is the neutral compound, both CDxs are not ionized in aqueous solutions at pH < *ca.* 11. Therefore, parts of the guest molecules should be ionized to promote electrophoretic migration. Although the accurate pK_1 and pK_2 values of compound **1** could not be determined, the pH titration followed by the change in optical density at 242.8 nm indicates that **1** is dissociated at pH > 9.0. Indeed, no optical resolution was realized when the pH values of the aqueous CDx solutions were below 9.0. The complete separation of the *S* and *R* enantiomers of **1** was achieved when the aqueous phosphate buffers at pH > 10 contained TMe-*β*-CDx (Fig 6 and Table 4). Under similar

Table 4 Relative retentions (α) for the optical resolution of racemic **1**, **2** and **3** by CZE[a]

Sample	*pH*	*Buffer*[b]	*CDx*[c]	*Applied voltage (kV)*	*Current (μA)*	α[d]
1	10.46	A	α-CDx	6	14–15	1.00
1	10.46	A	β-CDz	6	17–18	1.00
1	10.46	A	γ-CDx	6	14–15	1.00
1	10.46	A	TMe-β-CDx	6	17–18	1.22
1	11.00	A	TMe-β-CDx	6	13	1.32
1	12.00	B	TMe-β-CDx	6	13	1.42
2	5.40	C	β-CDx	12	13	1.12
2	5.40	C	TMe-β-CDx	12	12	1.45
3	4.78	C	TMe-β-CDx	13	15	1.06
3	5.32	C	TMe-β-CDx	8	9	1.04
3	5.32	C	TMe-β-CDx	12	15	1.03
3	6.11	C	TMe-β-CDx	12	15	1.03
3	7.00	C	TMe-β-CDx	12	14	1.02
3	8.00	C	TMe-β-CDx	12	16	1.00

[a] The concentration of the samples of **1**, **2** and **3** was 4×10^{-4} mol dm^{-3}. CZE measurements were carried out at ambient temperature.
[b] Buffers denoted by A, B and C are 0.04 mol dm^{-3} carbonate, 0.025 mol dm^{-3} phosphate, and 0.03 mol dm^{-3} phosphate buffers, respectively.
[c] The concentration of CDx was 1×10^{-2} mol dm^{-3}.
[d] $\alpha = (t_1 - t_0)/(t_2 - t_0)$, where t_1 and t_2 are the retention times of the enantiomers ($t_1 > t_2$), and t_0 is the retention time of methanol which does not interact with the CDxs.

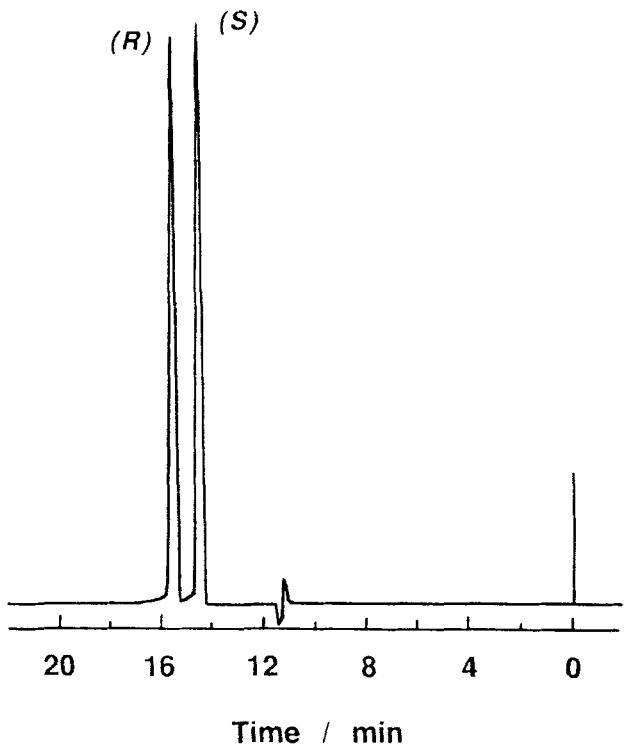

Figure 6 Electropherogram of racemic **1** obtained by CZE using 4×10^{-4} mol dm^{-3} carbonate buffer (pH 11.0) containing 1×10^{-2} mol dm^{-3} TMe-β-CDx; applied voltage = 6 kV, current = 13 μA, detection wavelength = 227 nm.

conditions, β-CDx does not act as a separating agent for CZE. Also, neither α-CDx nor γ-CDx is effective for the optical resolution of **1**. *S*-**1** is eluted faster than *R*-**1**. The *S* enantiomer of **1** preferentially complexes with TMe-β-CDx. *S*-**1** included in the TMe-β-CDx cavity, therefore, seems to be eluted with a rate near to that of the osmotic flow. The *R* enantiomer of **1**, however, is hardly bound to TMe-β-CDx, and the partially ionized *R*-**1** tends to flow to the positive electrode by electrophoretic migration. This should be the mechanism for the optical resolution of racemic **1** by CZE using TMe-β-CDx.

As shown in Table 1, a large difference in the *K* values for complexation with β-CDx are found between the *S* and *R* enantiomers of **2**. In such cases, the enantiomers of **2** can be separated completely by CZE even if β-CDx is used (see Table 4). Under similar conditions, the relative retention α for CZE using TMe-β-CDx is significantly larger than that for CZE using β-CDx. Although we could not obtain accurate *K* values for the complexes of TMe-β-CDx with *S*- and *R*-**2**, the ability of TMe-β-CDx to recognize the chirality of **2** should be greater than that of β-CDx. It has been shown that the optical isomers of both compounds **1** and **2** can be resolved by CZE using sodium taurodeoxycholate micelles as a subphase.[23]

The pH titration followed by the optical density change at 363.6 nm indicated that compound **3** is ionized at pH > 2.0 and is in the dianion form at pH > 6.0. No optical resolution of **3** was observed between pH 2 and 10 when β-CDx was used. In the case of TMe-β-CDx, partial resolution is realized at pH 5.32–7.0 and no resolution occurs at pH > 8.0. Complete separation of the enantiomers of **3** is achieved at pH 4.78–5.39. At pH < 4, no electropherogram was obtained. In the optical resolution of **3**, the pH of the leading electrolyte solution is very critical. In the CZE of compound **3**, the retention time of the *R* enantiomer is shorter than that of the *S*

enantiomer. This result is in agreement with that of the K determination.

CONCLUSION

This work shows that β- and TMe-β-CDxs are good host molecules that recognize the chirality of binaphthyl derivatives. Although the MM-MD calculations suggest that the main binding forces for complexation of **1** with β-CDx are the dipole–dipole and hydrogen bonding interactions, and that the van der Waals contacts and the hydrogen bonding interactions between the host and the guest are important for chiral recognition, further experimental evidence is needed to prove this assumption. In the case of compound **3**, a reduction of the dihedral angle of the naphthalene planes of *S*-**3** is required to allow *S*-**3** to be included in the β- and TMe-β-CDx cavities, which may be one reason why the complex of *S*-**3** is more unstable than that of *R*-**3**. A greater ability of TMe-β-CDx compared with β-CDx to recognize the chirality of the binaphthyls has been shown. However, the mechanism for chiral recognition by TMe-β-CDx could not be clarified in this study.

The results of K determinations correspond well with those of CZE. Therefore, CZE would be a useful tool for studying chiral recognition by CDxs.

EXPERIMENTAL

β-CDx (Nacalai, Kyoto) was purchased, and an antioxidant contained in this material was extracted with THF. TMe-β-CDx (Nacalai) was commercially obtained and used without further purification. (±)-**1** (Nacalai), *S*-(−)-**1**, *R*-(+)-**1**, (±)-**2**, *S*-(+)-**2**, and *R*-(−)-**2** (Aldrich, Milwaukee) were purchased. The synthesis of **3** and its optical resolution by complexation with brucine were carried out according to the procedures described in the literature.[24]

The absorption and uncorrected fluorescence spectra were measured with Shimadzu UV-2100 spectrophotometer and a Hitachi 650-60 spectrofluorometer, respectively, at 25°C.

The CZE experiments were performed with a Jasco capillary electropherograph system CE-800 with a 50 μm (I.D.) × 300 mm (effective length) capillary cartridge (non-coated fused silica). The capillary was filled with a buffer solution containing CDx and the sample in the same buffer solution containing 4% (v/v) methanol was poured into the capillary by applying the potential for 10 s. The electropherogram was measured at the same potential using a Jasco 875-CE UV-Vis detector.

The MM-MD calculations were carried out using BIOGRAF (Dreiding-I and -II) on a Silicon Graphics IRIS-4D/220GTX workstation. The quenching dynamics was performed at 300 K with a 10 ps snapshot.

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REFERENCES

1 Cramer, F.; Dietsche, W.; *Chem. Ber.* **1959**, *92*, 378.
2 Benschop, H.P.; Van den Berg, G.R.; *J. Chem. Soc., Chem. Commun.* **1970**, 1431.
3 (a) Mikolajczyk, M.; Drabowicz, J.; Cramer, F.; *J. Chem. Soc., Chem. Commun.* **1971**, 317. (b) Mikolajczyk, M.; Drabowicz, J.; *Tetrahedron Lett.* **1972**, 2379. (c) Mikolajczyk, M.; Drabowicz, J.; *J. Am. Chem. Soc.* **1978**, *100*, 2510.
4 Cooper, A.; MacNicol, D.D.; *J. Chem. Soc., Perkin Trans. 2* **1978**, 760.
5 (a) Yamashoji, Y.; Tanaka, M.; Shono, T.; *Chem. Lett.* **1990**, 945. (b) Lipkowitz, K.B.; Raghothama, S.; Yang, J.; *J. Am. Chem. Soc.* **1992**, *114*, 1554.
6 Trainor, G.L.; Breslow, R.; *J. Am. Chem. Soc.* **1981**, *103*, 154.
7 Michon, J.; Rassat, A.; *J. Am. Chem. Soc.* **1979**, *101*, 995.
8 Otagiri, M.; Ikeda, K.; Uekama, K.; Ito, O.; Hatano, M.; *Chem. Lett.* **1974**, 679.
9 (a) Harata, K.; Hirayama, F.; Imai, T.; Uekama, K.; Otagiri, M.; *Chem. Lett.* **1984**, 1549. (b) Harata, K.; Uekama, K.; Otagiri, M.; Hirayama, F.; *J. Inclusion Phenom.* **1984**, *2*, 583.
10 Hamilton, J.A.; Chen, L.; *J. Am. Chem. Soc.* **1988**, *110*, 5833.
11 Harata, K.; Uekama, K.; Otagiri, M.; Hirayama, F.; *Chem. Lett.* **1983**, 1807.
12 Kano, K.; Yoshiyasu, K.; Hashimoto, S.; *J. Chem. Soc., Chem. Commun.* **1989**, 1278.
13 Benesi, H.; Hildebrand, J.H.; *J. Am. Chem. Soc.* **1949**, *71*, 2703.
14 Bergeron, R.J.; Roberts, W.P.; *Anal. Biochem.* **1978**, *90*, 844.
15 Schuette, J.M.; Ndou, T.; de la Peña, A.M.; Greene, K.L.; Williamson, C.K.; Warner, I.M.; *J. Phys. Chem.* **1991**, *95*, 4897.
16 (a) Kano, K.; Tatemoto, S.; Hashimoto, S.; *J. Phys. Chem.* **1991**, *95*, 966. (b) Kano, K.; Yoshiyasu, K.; Yasuoka, H.; Hata, S.; Hashimoto, S.; *J. Chem. Soc., Perkin Trans. 2*, **1992**, 1265.
17 Harada, N.; Nakanishi, K.; *Circular Dichroism Spectroscopy. Exciton Coupling in Organic Stereochemistry*, University Science Book, Mill Valley, **1983**.
18 Mason, S.F.; Seal, R.H.; Roberts, D.R.; *Tetrahedron* **1974**, *30*, 1671.
19 Snopek, J.; Jelínek, I.; Smolková-Keulemansová, E.; *J. Chromatogr.* **1988**, *452*, 571, and references cited in this review.
20 (a) Terabe, S.; Otsuka, K.; Ichikawa, K.; Tsuchiya, A.; Ando, T.; *Anal. Chem.* **1984**, *56*, 111. (b) Terabe, S.; Otsuka, K.; Ando, T.; *Anal. Chem.* **1985**, *57*, 834. (c) Terabe, S.; *Trends Anal. Chem.* **1989**, *8*, 129.
21 (a) Snopek, J.; Smolková-Keulemansová, E.; Jelínek, I.; Dohnal, J.; Klinot, J.; Klinotova, E.; *J. Chromatogr.* **1988**, *450*, 373. (b) Fanali, S.; *J. Chromatogr.* **1989**, *474*, 441. (c) Lin, J.; Gobb, K.A.; Novotny, M.; *J. Chromatogr.* **1990**, *519*, 189.
22 Gelb, R.I.; Schwartz, L.M.; Bradshaw, J.J.; Laufer, D.A.; *Bioorg. Chem.* **1980**, *9*, 299.
23 Cole, R.O.; Sepaniak, M.J.; Hinze, W.L.; *J. High Resolution Chromatogr.* **1990**, *13*, 579.
24 Stanley, W.M.; Adams, R.; *Recl. Trav. Chim. Pays-Bas* **1929**, *48*, 1035.