Complexation of 4-Dimethylaminoazobenzene with Various Kinds of Cyclodextrins: Effects of Cyclodextrins on the Thermal cis-to-trans Isomerization

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ABSTRACT: On the basis of the change in electronic and induced circular dichroism spectra for complex formation, the complexation of 4-dimethylaminoazobenzene (DAAB) with four kinds of cyclodextrins (α- and β-cyclodextrin (CD), heptakis(2,6-di-*O*-methyl)-β-cyclodextrin, and heptakis(2,3,6-tri-*O*-methyl)-β-cyclodextrin) was studied in methanol–water and dimethyl sulfoxide–water mixtures. It was found that the trans and cis isomers of DAAB form two different types of complex (inclusion and lid type) with CDs, depending on the kinds of CDs and solvents. Further, we have examined the effect of CDs on the thermal cis-to-trans isomerization of DAAB. The accelerated or decelerated effect on the thermal isomerization was observed upon adding CDs. The effects of CDs on the thermal isomerization are discussed in connection with the complexation of the cis-isomer of DAAB with CDs. © 2002 Wiley Periodicals, Inc. Int J Chem Kinet 34: 481–487, 2002

INTRODUCTION

Cyclodextrins (CDs) are the cyclic oligosaccharides, which can form inclusion complexes with various molecules. The conformation and dynamic properties of inclusion complexes have been studied by numerous workers [1–3]. One of the important applications of inclusion complexes is in the control of chemical reactions. The isomerization of azobenzenes has attracted much attention because of their photochromic and thermochromic behaviors. Several studies have been reported on the effects of CDs on the cis-trans photoisomerization of azobenzenes [4,5]. On one hand, the effect of CDs on the thermal cis-to-trans isomerization of azobenzenes has not been well established yet, though Sanchez and Rossi have reported about

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the effects of β-CD on the thermal isomerizations of some azobenzenes [6]. We have examined the effects of various kinds of CDs on the thermal isomerization of 4-dimethylaminoazobenzene (DAAB) in methanol–water and dimethyl sulfoxide (DMSO)–water mixtures, and an unexpected significant effect of CDs was observed. In this paper, we have used four kinds of CDs (α- and β-CDs, heptakis(2,6-di-*O*-methyl)-β-cyclodextrin (DM-β-CD), and heptakis(2,3,6-tri-*O*-methyl)-β-cyclodextrin (TM-β-CD)). We have focused attention on the complexation of DAAB with four kinds of CDs in mixture solvents, and the effects of CDs on the thermal isomerization are discussed in detail.

EXPERIMENTAL

Materials

DAAB was prepared according to the reported method and recrystallized from benzene, mp 391–392 K (lit. 392–393 K) [7,8]. Various kinds of CDs (α- and β-CDs, DM-β-CD, and TM-β-CD) were purchased from Wako Pure Chemicals and used without further purification. Methanol, DMSO, and water were distilled before use.

Measurements

Since DAAB is insoluble in water, we used methanol–water (30:70 v/v) and DMSO–water (30:70 v/v) mixtures, which means 30 ml of organic distilled to 100 ml with water, as a solvent. A sample solution (DAAB ca. 4×10^{-5} mol dm^{-3}) involving a small quantity of piperidine was irradiated with projection lamp to produce the cis-isomer of DAAB [7]. The thermal isomerization from cis-to-trans isomer at 298 K was monitored by the change in the maximum absorption ($\lambda_{max} = 450$ nm) of the DAAB trans-isomer in mixture solvents by using a Hitachi U-3200 spectrophotometer. The thermal cis-to-trans isomerization obeys first-order kinetics and the observed rate was reproducible to within ± 5%. Circular dichroism spectra were obtained with a JASCO J-720 spectropolarimeter.

RESULTS AND DISCUSSION

Complexation of the trans-Isomer of DAAB with CDs

Figure 1 shows the absorption spectra of the trans-isomer of DAAB in methanol–water and DMSO–water mixtures containing various concentrations of β-CD. When the β-CD concentration was increased, absorption peaks shifted to shorter wavelengths. Judging from the existence of isosbestic points, the trans-isomer was found to form 1:1 complexes with β-CD. The association constant (K_T) between the trans-isomer and β-CD can be expressed as follows:

$$\mathrm{T} + \mathrm{CD} \rightleftharpoons \mathrm{T\text{-}CD}$$

$$K_T = \frac{[\mathrm{T} - \mathrm{CD}]}{[\mathrm{T}][\mathrm{CD}]} \qquad (1)$$

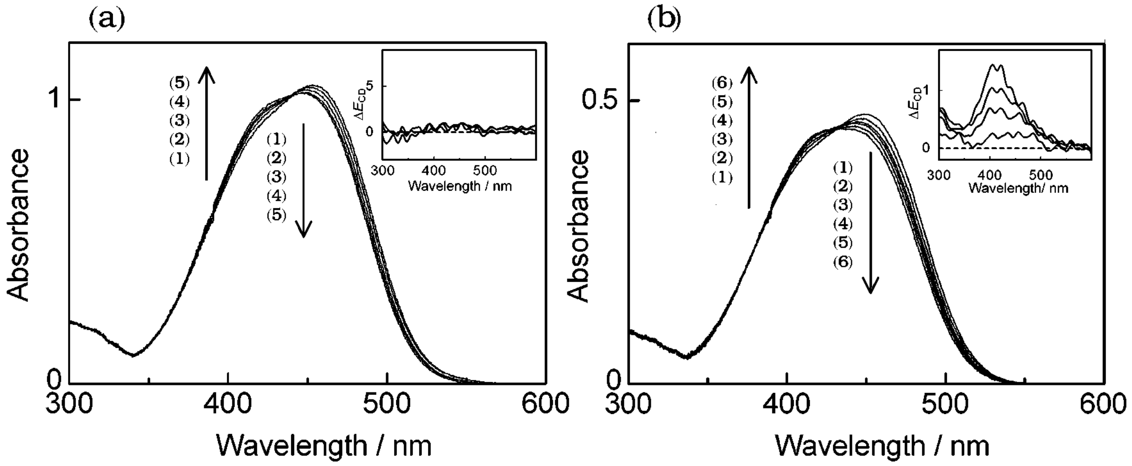


Figure 1 Absorption spectra of the trans-isomer of DAAB in DMSO–water and methanol–water mixtures containing various concentration of β-CD. (a) DMSO–water mixture: [DAAB] = 4.15×10^{-5} mol dm^{-3} and [β-CD] = (1) 0, (2) 4.44×10^{-4}, (3) 8.88×10^{-4}, (4) 1.78×10^{-3}, and (5) 2.66×10^{-3} mol dm^{-3}. (b) Methanol–water mixture: [DAAB] = 2.07×10^{-5} mol dm^{-3} and [β-CD] = (1) 0, (2) 2.22×10^{-4}, (3) 4.44×10^{-4}, (4) 6.66×10^{-4}, (5) 8.88×10^{-4}, and (6) 1.33×10^{-3} mol dm^{-3}. Inset: Circular dichroism spectra of complexes between the trans-isomer and β-CD.

where T and T-CD denote the trans-isomer of DAAB and its complex, respectively. In the presence of excess CD, the concentration of CD is approximated with the initial concentration of CD ($[\mathrm{CD}]_0$). The spectral data in Fig. 1 can be analyzed according to the Benesi–Hildebrand (B-H) equation (Eq. 2) [9]:

$$\frac{[\mathrm{T}]_0[\mathrm{CD}]_0}{\Delta E} = \frac{1}{K_\mathrm{T}\Delta\varepsilon} + \frac{[\mathrm{CD}]_0}{\Delta\varepsilon} \tag{2}$$

Here $[\mathrm{T}]_0$ is the total concentration of DAAB, $\Delta\varepsilon$ is the difference in the molar extinction coefficients for bound and unbound DAAB, and ΔE is the change in the absorption intensity of DAAB solution on adding CD. As shown in Fig. 2, a linear relationship between $[\mathrm{T}]_0[\mathrm{CD}]_0/\Delta E$ and $[\mathrm{CD}]_0$ was obtained. The K_T values were obtained by dividing the slope by the intercept, and are given in Table I, together with those with various kinds of CDs. Hirai et al. [10] indicated that the magnitude of the induced circular dichroism is proportional to the amount of the inclusion complexes produced. In Fig. 1, the induced circular dichroism spectra for the complexes of the DAAB trans-isomer with β-CD in methanol–water and DMSO–water are shown. In methanol–water mixture, induced circular dichroism appears in the vicinity of 420 nm, which indicates the inclusion complex formation. However, the DAAB-β-CD system in DMSO–water mixture does not show any induced circular dichroism by themselves. It is noted that the complex between DAAB and β-CD in DMSO–water mixture is not an inclusion complex, though the change in the electronic spectra is observed by adding β-CD. For the complexation with DM-β-CD and TM-β-CD, the induced circular dichroism spectra appeared, and those for the complexation with α-CD did not appear.

Based on the thermodynamic study for the complex formation of substituted (*p*-hydroxyphenylazo)-benzoate anions with CDs, Namor et al. [11] have suggested that two different types of complexation occur as a result of a change in the reaction medium: One is the inclusion complex and the other reasonable possibility is the formation of the lid type complex where azobenzene is located in one of the rims of CD and not in the CD cavity. In order to depict the lid type complexes of α- and β-CDs with DAAB, the Corey–Pauling–Koltun (CPK) space-filling models of these systems were examined. The CPK model shows that the distance between two nitrogen atoms of the dimethylamino and azo groups is smaller than the inner diameter of β-CD [12] (Scheme 1). Therefore, though complexation of azobenzene derivatives with CDs may be specific, the trans-isomer of DAAB is considered to form stronger hydrogen bonding with OH groups on the rim of α-CD through the nitrogen atoms of DAAB (Scheme 1), which is responsible for the large K_T value for the lid type complex formation of α-CD in DMSO–water, compared to that for β-CD. Similar K_T values for the lid type complexation were reported by Namor et al. [11]: $K_\mathrm{T} = 1.58\text{–}5.89 \times 10^3$ $\mathrm{mol^{-1}\,dm^3}$ between substituted azobenzenes and α-CD in *N*,*N*-dimethylformamide. For the inclusion complex formation, there are two possible isomeric 1:1 complexes: one of these has the phenyl ring inserted and

Table I Equilibrium Constants Between the trans-Isomer of DAAB and CDs at 298 K

	K_T ($\mathrm{mol^{-1}\,dm^3}$)	
Cyclodextrin	DMSO–water (30:70 v/v)	Methanol–water (30:70 v/v)
α-CD	3940 (lid)	6140 (lid)
β-CD	87.5 (lid)	972 (inclusion)
DM-β-CD	3360 (inclusion)	1810 (inclusion)
TM-β-CD	630 (inclusion)	223 (inclusion)

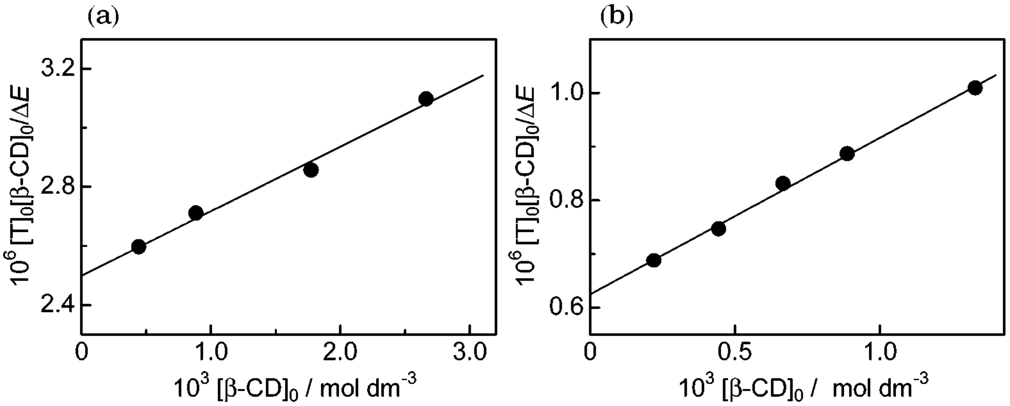
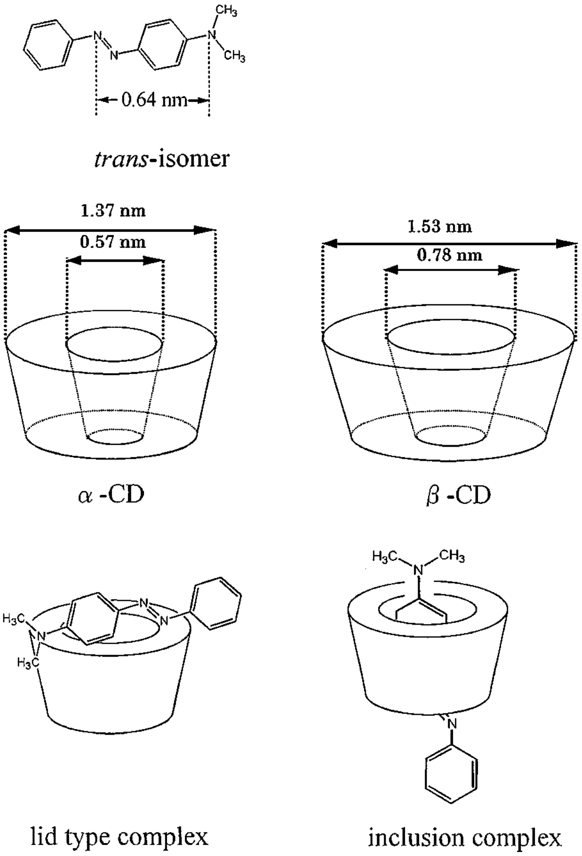


Figure 2 Determination of the association constant of β-CD with the DAAB trans-isomer according to the Benesi–Hildebrand relationship in (a) DMSO–water and (b) in methanol–water.



Scheme 1

the other has the dimethylaminophenyl ring inserted. However, the existence of isosbestic points and linearity of B–H plots for absorption and circular dichroism spectral changes suggest one kind of inclusion complex formation. Judging from hydrophobic nature of the CD cavity and mesomeric effect of the dimethylamino group of the DAAB guest, we consider that the dimethylaminophenyl ring is included by CD (Scheme 1). An X-ray diffraction study has suggested that the substitution by a methyl group at the O(2) and O(6) positions in β-CD lengthens the CD cavity from ca. 0.8 to 1.1 nm without any significant distortion of the ring and enhances the inclusion ability [13–15]. In fact, DM-β-CD forms the stable inclusion complex and the association constant K_T for DM-β-CD in methanol–water is about twice larger than that for β-CD. The enhanced inclusion stability of DM-β-CD is ascribed to the enlarged hydrophobic cavity of the CD host. On the other hand, K_T for TM-β-CD in methanol–water is remarkably small compared with that for DM-β-CD, as shown in Table I. The methylations at the O(2), O(3), and O(6) positions in β-CD considerably reduce the stability of inclusion complexes. The TM-β-CD ring is distorted in contrast with the case of DM-β-CD and substitution by *O*-methyl groups at the inner side (the O(3)H group) of β-CD narrows the inner diameter of the cavity [13–15]. This is responsible for the small K_T value for inclusion by TM-β-CD. In the cases of DM-β-CD and TM-β-CD, the lid type complex may not be formed because of methylation of the hydroxyl groups on the CD rim.

There have been many reports on the solvent effects of the complexation with CD. In binary aqueous-organic solvents, Connors et al. [16] have interpreted the effects of organic solvents on CD-complex formations in terms of competitive complexing. It is recognized that the addition of organic solvents decreases remarkably the equilibrium constant for association with CD [16,17]. Matsui et al. [18] examined the solvent effects on the CT absorption band of pyridinio derivatives with I^- in DMSO–water and methanol–water mixtures. With increasing methanol and DMSO, the absorption maximum of the CT complex shifted to the direction of longer wavelengths and the effect was larger in DMSO than in methanol. This suggests that in our study the addition of DMSO makes the environment around DAAB less polar, compared with that of methanol. The fact that DAAB does not form inclusion complex with β-CD in DMSO–water can be attributed to the similarity between the environment in mixture solvents and microenvironment in the CD cavity. Moreover, since the association constant of DMSO with CD is larger than that of methanol [16], our observations may involve the influence of competitive complexing by organic solvents. For the solvent effect on the lid type complex formation, although the kind of interaction that is operative has not been clarified, microscopic solvent-polarity effect is operative for the lid type

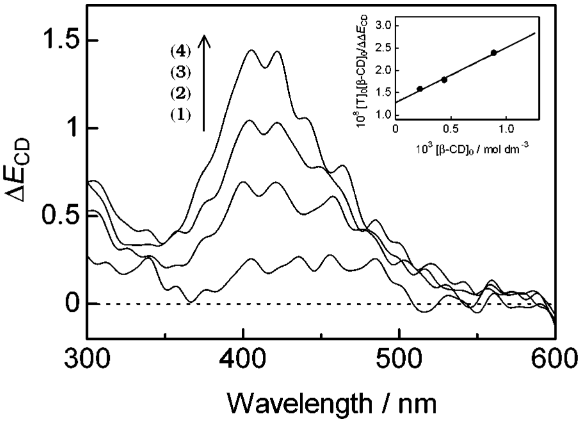


Figure 3 Induced circular dichroism spectra of DAAB (2.07×10^{-5} mol dm^{-3}) in methanol–water: (1) 0, (2) 2.22×10^{-4}, (3) 4.44×10^{-4}, and (4) 8.88×10^{-4} mol dm^{-3} of β-CD. Inset: the plot of $[T]_0[\beta\text{-CD}]_0/\Delta\Delta E_{CD}$ against $[\beta\text{-CD}]_0$.

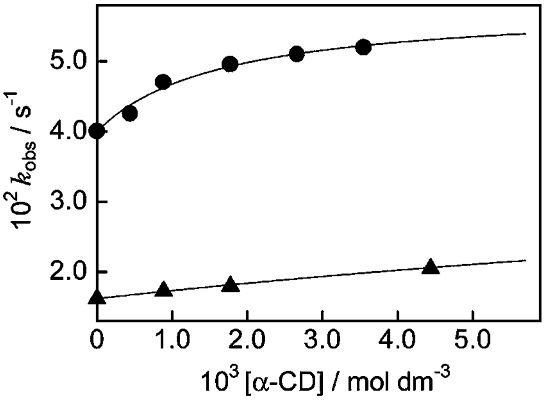


Figure 4 Dependence of the observed rate constants with the [α-CD] for the thermal isomerization of DAAB at 298 K: (▲) in DMSO–water and (•) in methanol–water.

complexation, resulting in the large K_T value for α-CD in methanol–water.

In complexation of β-CD in methanol–water, the change in electronic spectra involves both inclusion and lid type complex formations. To investigate the complexing ability of DAAB toward β-CD in methanol–water, we have compared the K_T values estimated from analyses of induced circular dichroism spectra with that of electronic ones. Figure 3 shows the induced circular dichroism spectra in the vicinity of 420 nm for the β-CD complex with DAAB in methanol–water mixture. The magnitude of the induced circular dichroism increases with an increase in the concentration of β-CD. From analyses of the circular dichroism spectra, the K_T value for the inclusion complex formation in methanol–water mixture was calculated to be 971 ± 110 $mol^{-1}\,dm^3$, which is in good agreement with the value estimated from analyses of the electronic spectra. This suggests that the trans-isomer of DAAB in methanol–water mixture forms the inclusion complex with β-CD. The types of the complexations with various kinds of CDs in mixture solvents are clarified in Table I.

Effect of CD on the Thermal Isomerization

Figures 4 and 5 show the significant effects of CDs on the thermal cis-to-trans isomerization. As shown in Fig. 4, the accelerated effect on the thermal isomerization was observed with increasing the α-CD concentration. Upon addition of β-CD, the accelerated effect on the isomerization rate was observed in DMSO–water, while the decelerated effect was obtained in methanol–water (Fig. 5). The addition of DM-β-CD caused decrease in the isomerization rates, independent of solvents. Further, the thermal isomerization rate is independent of the addition of TM-β-CD. The mechanism of the thermal cis-to-trans isomerization in the presence of CDs can be expressed as follows:

$$\mathrm{T} \xrightarrow{h\nu} \mathrm{C}$$

$$\mathrm{C} \xrightarrow{k_1} \mathrm{T}$$

$$\text{C-CD} \xrightarrow{k_2} \text{T-CD}$$

$$\mathrm{C} + \mathrm{CD} \underset{}{\overset{K_C}{\rightleftharpoons}} \text{C-CD}$$

where C and C-CD denote the cis-isomer of DAAB and its complex with CD, respectively. K_C is the association constant between the cis-isomer and CDs. The rate constants (k_1) for the thermal isomerization in DMSO–water and methanol–water (at [CD] = 0 mol dm^{-3}) were determined as 0.0162 s^{-1} and 0.0398 s^{-1}, respectively. Under the condition [CD] ≫ [DAAB], the observed rate constant (k_{obs}) for the thermal cis-to-trans

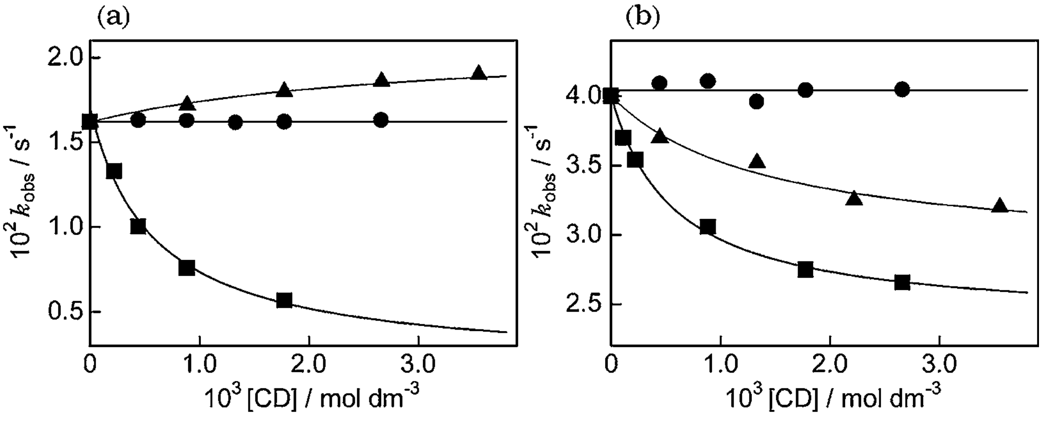


Figure 5 Dependence of the observed rate constants with the CD concentration for the thermal isomerization of DAAB at 298 K in (a) DMSO–water and (b) methanol–water: (▲) β-CD, (■) DM-β-CD, and (•) TM-β-CD.

Table II Rate Constants for the Thermal Isomerization and the Equilibrium Constants Between cis-Isomer of DAAB and CDs at 298 K

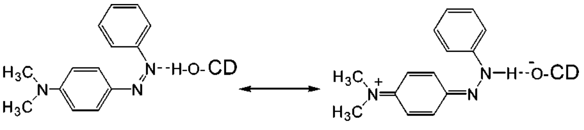
Solvent	Cyclodextrin	K_C ($\text{mol}^{-1}\,\text{dm}^3$)	k_1 ($10^{-2}\,\text{s}^{-1}$)	k_2 ($10^{-2}\,\text{s}^{-1}$)
DMSO–water (30:70 v/v)	α-CD	44.5	1.62	4.37
	β-CD	340	1.62	2.10
	DM-β-CD	1400	1.62	0.127
Methanol–water (30:70 v/v)	α-CD	600	3.98	5.80
	β-CD	700	3.98	2.85
	DM-β-CD	1740	3.98	0.237

isomerization can be given by

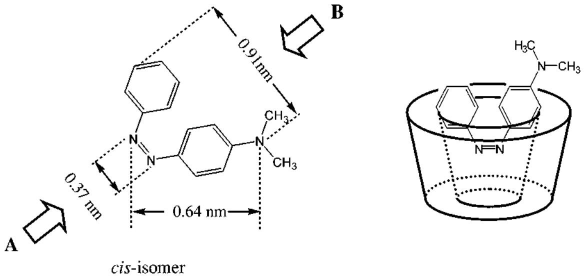
$$k_{\text{obs}} = \frac{k_1 + k_2 K_C[\text{CD}]_0}{1 + K_C[\text{CD}]_0} \tag{3}$$

From fitting the experimental data in Figs. 4 and 5 to Eq. (3), the k_2 and K_C values can be determined and are given in Table II.

We consider that the above kinetic results are deeply correlated to the nature of the complexation between the cis-isomer and CDs. It is noted that the accelerated effects on the thermal isomerization by CD is observed in the system formed the lid type complex between CD and the trans-isomer. As suggested earlier, the trans-isomer of DAAB forms the two different types of complexes with CDs. Since the distance between the nitrogen atoms of dimethylamino and azo groups in the DAAB cis-isomer is same as that in the trans-isomer, the cis-isomer may form the lid type complex with CD in analogy with that of the trans-isomer. In the thermal isomerization of azobenzenes, it is recognized that the isomerization reaction is catalyzed by acid, and the isomerization rate accelerates by the protonation to the azo group [6,19]. As depicted below, a similar situation is realized by the formation of the lid type complex.



This leads to the decrease in the double bond character of the N═N bond, which favors the rotational mechanism, resulting in the accelerated effect. On the other hand, as reported by Nishimura et al. [7], when the thermal isomerization of azobenzenes is not catalyzed by acid, the thermal isomerization of DAAB proceeds via inversion of the nitrogen atom of the azo group through a linear (sp-hybridized) transition state (in-plane lateral shift). In the cis-DAAB inclusion complexation, the following two type of inclusions by CD give rise to the decelerated effect on the thermal isomerization of the inversion mechanism (Scheme 2): One is the inclusion from the two phenyl groups side (direction B) and the other is the inclusion from the azo group side (direction A). Since the distance between two phenyl groups is larger than the inner diameter of β-CD, entrance from direction B is impossible. Therefore, β-CD may include the cis-isomer from the azo group side (direction A), and some part of the cis-isomer is included in the cavity (Scheme 2). Despite our attempts to observe the induced circular dichroism spectra for the inclusion complex of the unstable cis-isomer with CDs, we have been unsuccessful. When DM-β-CD was added, the decelerated effect ($k_2/k_1 = 0.060$ in methanol–water) is remarkably large compared with that by β-CD ($k_2/k_1 = 0.72$ in methanol–water). This suggests that the cis-isomer of DAAB is included more deeply into the DM-β-CD cavity, which is responsible for the enhanced inclusion stability of DM-β-CD. In the presence of TM-β-CD, the fact that the thermal isomerization of DAAB is not affected by TM-β-CD indicates that TM-β-CD cannot form an inclusion complex with the cis-isomer. Judging from the inclusion abilities of DM-β-CD and TM-β-CD, above results are reasonable.



Scheme 2

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