JOURNAL OF PHYSICAL ORGANIC CHEMISTRY
J. Phys. Org. Chem. **12**, 541–546 (1999)

Complexation of phenols with *β*- and *γ*-cyclodextrins: determination of the association constants by using the isomerization of spiropyran

Yoshimi Sueishi* and Tamami Miyakawa

Department of Chemistry, Faculty of Science, Okayama University, Tsushima Naka 3-1-1, Okayama 700-8530, Japan

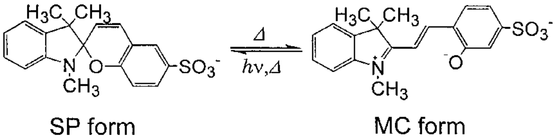
Received 29 September 1998; revised 16 December 1998; accepted 19 December 1998

ABSTRACT: As a chemical indicator, the isomerization rate of so-called 6-SO_3^--spiropyran was used to estimate the equilibrium constants for the inclusion complex formation of *β*- and *γ*-cyclodextrins (*β* and *γ*-CDs). The association constants for inclusion complexes of *β*- and *γ*-CDs with various kinds of phenols were determined. It was found that *β*- and *γ*-CDs form 1:1 and 1:2 inclusion complexes with phenols, respectively. The substituent effects on the association constants for the 4-substituted phenols–*β*-CD system can be interpreted in terms of the geometry of the inclusion complex. The magnitude of the association constants for the inclusion complex is related to molecular polarizability of the guest molecule. Based on the results, the dominant factor for CD complexation with phenols is discussed. Copyright © 1999 John Wiley & Sons, Ltd.

KEYWORDS: spiropyran; cyclodextrins; inclusion complex; phenols

INTRODUCTION

The isomerization of spiropyrans has attracted much attention because of their reversible photochromic and thermochromic behaviour (Scheme 1).[1] Recently we have examined the complexation of 1′,3′,3′-trimethylspiro[2H-1-benzopyran-2,2′-indoline]-6-sulphonate (6-SO_3^--SP) with *β*- and *γ*-cyclodextrins (*β*- and *γ*-CDs). It was found that *β*- and *γ*-CDs preferentially form inclusion complexes with the SP form of 6-SO_3^--SP and the apparent isomerization rate from the SP to the MC form is dependent on the concentration of unbound *β*- and *γ*-CDs.[2]



Scheme 1

The determination of association constants for inclusion complexes using spectroscopic measurements such as absorbance is commonly accomplished by the Benesi–Hildebrand method.[3] The Benesi–Hildebrand analysis requires a spectroscopic change in absorption on forming an inclusion complex. Since cyclodextrins are spectroscopically inert, spectroscopically active guests should be used. However, this often leads to experimental difficulties. In order to estimate the equilibrium constant for inclusion complex formation, it is necessary to determine the equilibrium concentrations of the inclusion complex, unbound guest and unbound host in some way. When a chemical indicator determining the unbound CD concentration in solution can be employed, one can extensively evaluate the equilibrium constant for the inclusion complex of CD with organic molecules which do not exhibit a colour change on forming inclusion complexes.

In this paper, we report a new method of evaluating the concentration of unbound CD by using the CD concentration dependence on the isomerization rate of 6-SO_3^--SP. For demonstration purposes, inclusion complexes formed between CDs (*β*- and *γ*-) and substituted phenols are considered. This system was chosen for detailed studies of CD complexation behaviour. Based on the results, the dominant factor for the inclusion complex formation of CDs with various kinds of phenols is discussed.

EXPERIMENTAL

6-SO_3^--SP was prepared according to the method of Sunamoto *et al.*[4] and recrystallized from methanol: m.p. *ca* 513 K (decomp.) [lit.[4] *ca* 513 K (decomp.)]. Cyclodextrins (*β*- and *γ*-) were purchased from Wako Pure Chemicals and used without further purification. Phosphate buffer (pH 6.9 and 10.1, ionic strength 0.1), prepared from phosphate salts, was used as the solvent.

---

*Correspondence to: Y. Sueishi, Department of Chemistry, Faculty of Science, Okayama University, Tsushima Naka 3-1-1, Okayama 700-8530, Japan.

CCC 0894–3230/99/070541–06 $17.50

The procedure for the kinetic measurements has been described elsewhere.[2] A sample solution (6-SO_3^--SP *ca* 1×10^{-5} mol dm^{-3}) was deoxygenated by bubbling with nitrogen. A 650 W projector lamp was used to produce the SP form. There are temperature limitations for measurements of the isomerization rate of 6-SO_3^--SP with the present method using the isomerization of 6-SO_3^--SP. We chose a convenient temperature (40 °C) for the measurements of the isomerization rate of 6-SO_3^--SP. The thermal isomerization from SP to MC was monitored by the change in the maximum absorption (λ_{max} = 508 nm) of the MC form by means of a Union Giken 401 spectrophotometer. The first-order rate constants were obtained at 40 °C and reproduced within 5% error. Circular dichroism spectra were obtained with a JASCO J-720 spectropolarimeter.

RESULTS AND DISCUSSION

Estimation of association constants by using the isomerization rate of spiropyran

Based on the measurements of circular dichroism and electronic spectra, we suggested that β- and γ-CDs form 1:1 inclusion complexes with the SP form of 6-SO_3^--SP, and the MC form is not included in the CD cavity.[2] The thermal isomerization of 6-SO_3^--SP obeys first-order kinetics regardless of the concentration of CD, and the apparent rate constants (k_{obs}) for the thermal isomerization (SP→MC) in the presence of CD are given in Table 1. The apparent rate constant of the thermal isomerization can be expressed as follows:[2]

$$k_{obs} = k_{-1} + k_1/(1 + K[H]_f) \tag{1}$$

where $[H]_f$ denotes the concentration of unbound CD.

$$SP \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} MC$$

$$SP + CD \overset{K}{\rightleftharpoons} SP\text{-}CD$$

Table 1. Rate constants for the thermal isomerization of 6-SO_3^--SP at 40 °C

$10^4[\beta\text{-CD}]_0$ (mol dm^{-3})	10^3k_{obs} (s^{-1})	$10^4[\gamma\text{-CD}]_0$ (mol dm^{-3})	10^3k_{obs} (s^{-1})
0	5.25	0	5.25
1.00	4.65	1.00	4.65
1.50	4.39	1.54	4.49
2.03	4.25	2.02	4.24
2.51	4.04	2.47	4.17
3.00	3.96	3.00	3.99

Equation (1) can be rewritten as

$$1/(k_{obs} - k_{-1}) = 1/k_1 + K[H]_f/k_1 \tag{2}$$

The rate constant (k_{-1}) for the isomerization from MC to SP was estimated to be 2.27×10^{-3} s^{-1}.[5] A good linear relationship was obtained between $1/(k_{obs} - k_{-1})$ and $[H]_f$, with a slope of $K/k_1 = (8.68 \pm 0.22) \times 10^5$ mol^{-1} dm^3 s for β-CD and $(8.03 \pm 0.23) \times 10^5$ mol^{-1} dm^3 s for γ-CD and an intercept of $1/k_1 = 337 \pm 4$ s. This relationship enables us to determine the unbound CD concentration in solution from the estimation of the thermal isomerization rate (k_{obs}). Incidentally, the K values between 6-SO_3^--SP and CD, obtained by dividing the slope by the intercept, are 2.58×10^3 mol^{-1} dm^3 for β-CD and 2.39×10^3 mol^{-1} dm^3 for γ-CD.

Upon addition of phenols to a mixture of 6-SO_3^--SP and β-CD, β-CD forms a 1:1 inclusion complex with phenols. With excess β-CD and phenols over 6-SO_3^--SP concentration, the concentration of the inclusion complex between 6-SO_3^--SP and β-CD is negligible for the phenols and β-CD. Therefore, the 1:1 association constant (K_{11}) between phenols and β-CD can be expressed as follows:

$$\begin{aligned} K_{11} &= [HG]/([G][H]_f) \\ &= \frac{[H]_0 - [H]_f}{([G]_0 - [H]_0 + [H]_f)[H]_f} \end{aligned} \tag{3}$$

where [H] and [HG] denote the concentrations of the phenol and its inclusion complex, respectively, and $[G]_0$ and $[H]_0$ are the initial concentrations (total concentrations) of phenols and β-CD. The concentration of unbound β-CD in solution can be determined as follows. The initial concentrations of 6-SO_3^--SP and β-CD were held constant at 1.5×10^{-5} and 3.0×10^{-4} mol dm^{-3}, respectively, and the concentration of phenols was varied from 1.0×10^{-3} to 8.0×10^{-3} mol dm^{-3}. These concentration conditions were chosen such that the equilibrium concentration of the inclusion complex was compared with that of unbound CD. For example, when the concentration of 4-nitrophenol (4-NO_2-P) was 3.0×10^{-3} mol dm^{-3}, the apparent isomerization rate from SP to MC was observed to be $k_{obs} = 4.41 \times 10^{-3}$ s^{-1}. Using Eqn. (2), the concentration of unbound β-CD was determined to be 1.5×10^{-4} mol dm^{-3}. From Eqn. (3), the association constant between β-CD and 4-NO_2-P can be calculated to be 3.5×10^2 mol^{-1} dm^3.

By using the isomerization rate of 6-SO_3^--SP, the association constants of various kinds of substituted phenols with β-CD at 40 °C were determined, and are given in Table 2. 6-SO_3^--SP serves as a chemical indicator, and the equilibrium constant can be estimated without analysing the absorption bands due to the inclusion complex. Lewis and Hansen[6] have reported $K_{11} = 1.0 \times 10^3$ mol^{-1} dm^3 (at 298 K), $\Delta H = -43.9$ kJ

Table 2. Association constants for inclusion complex formation with β- and γ-CDs at 40 °C

Guest	10^{-2} K_{11} (β-CD) (mol^{-1} dm^3)		10^{-2} K_{11} (γ-CD) (mol^{-1} dm^3) (pH 6.9)	10^{-4} K_{12} (γ-CD) (mol^{-2} dm^6) (pH 6.9)	10^{23} α (cm^3 $molecule^{-1}$)
	pH 6.9	pH 10.1			
4-F-phenol	1.2 ± 0.1	0.75 ± 0.08		0.56 ± 0.01	
4-CN-phenol	1.6 ± 0.1	0.87 ± 0.10		0.85 ± 0.01	1.27
4-CH_3O-phenol	2.0 ± 0.1			1.1 ± 0.1	1.35
Phenol	2.5 ± 0.1			1.3 ± 0.1	1.10
4-Cl-phenol	2.7 ± 0.3	2.4 ± 0.1		4.1 ± 0.1	1.30
4-Br-phenol	3.0 ± 0.2	2.7 ± 0.1		16 ± 1	1.41
4-NO_2-phenol	3.5 ± 0.1	5.2 ± 0.3		26 ± 2	
4-C_2H_5-phenol	5.2 ± 0.2			330 ± 16	1.47
4-CH_3-phenol	6.3 ± 0.2			200 ± 7	1.29
4-I-phenol	23 ± 1	14 ± 1		250 ± 9	1.61
4-$(CH_3)_2CH$-phenol	34 ± 1		17 ± 1		1.61
2-Naphthol	32 ± 1			330 ± 12	1.80
L-Borneol	48 ± 1		41 ± 1		1.82
1-Adamantanol	100 ± 3		290 ± 49		1.74

mol^{-1} and $\Delta S = -87.9$ J mol^{-1} K^{-1} for the inclusion complex between β-CD and 4-NO_2-P. The K_{11} value at 40 °C for the β-CD–4-NO_2-P system was calculated to be 5.3×10^2 mol^{-1} dm^3 by using the thermodynamic parameters. The K_{11} value calculated above is comparable to that (3.5×10^2 mol^{-1} dm^3) determined from measurements of the isomerization rate of 6-SO_3^--SP and estimation by using the spiropyran method could be regarded as reasonable. The details of the substituent effects on inclusion complex formation will be discussed below.

Since 4-NO_2-P has an absorption band in the vicinity of 400 nm, the K_{11} value for the β-CD–4-NO_2-P system can be determined by analysis of the absorption band. On adding β-CD, 4-NO_2-P exhibits a spectral shift of about 10 nm, and the peak in the vicinity of 410 nm increases at the expense of the peak at 320 nm. The isosbestic point observed at 360 nm indicates a 1:1 equilibrium. The spectral data can be analysed according to the Benesi–Hildebrand equation:[3]

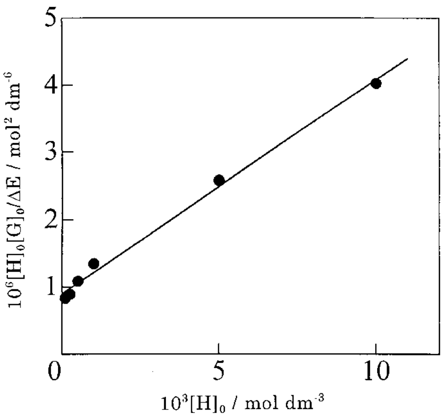


Figure 1. Determination of the association constant of β-CD–4-NO_2-P complex according to the Benesi–Hildebrand relationship: pH 6.9, $[4\text{-}NO_2\text{-}P]_0 = 5.0 \times 10^{-5}$ mol dm^{-3}

$$[H]_0[G]_0/\Delta E = 1/K_{11}\Delta\varepsilon + [H]_0/\Delta\varepsilon \qquad (4)$$

where $[G]_0$ and $[H]_0$ are the total concentrations of guest (phenols) and host (CD), respectively, $\Delta\epsilon$ is the difference in the molar extinction coefficients for bound and unbound phenols and ΔE is the change in the absorption intensity of phenols solution on adding CD. As shown in Fig. 1, a linear relationship between $[H]_0[G]_0/\Delta E$ and $[H]_0$ for the 4-NO_2-P–β-CD system can be obtained. The K_{11} value can be obtained by dividing the slope by the intercept, $K_{11} = 3.53 \times 10^2$ mol^{-1} dm^3, which is in good agreement with that estimated from the measurement of the isomerization rate of 6-SO_3^--SP.

γ-CD forms a 1:1 inclusion complex in analogy with the behaviour of β-CD, and also a 1:2 inclusion complex (one γ-CD and two phenol molecules) is formed with many 4-substituted phenols. A detailed discussion of the stoichiometric ratio of the inclusion complex will be given later. The equilibrium concentration of unbound γ-CD can be also determined from Eqn. (2). The determination of the equilibrium concentration gives the association constants (K_{11} and K_{12}) for the 1:1 and 1:2 inclusion complexes of γ-CD according to Eqns (3) and (5), respectively, and they are given in Table 2.

$$K_{12} = [HG_2]/([H]_f[G]^2) = \frac{[H]_0 - [H]_f}{[H]_f([G]_0 + 2[H]_f - 2[H]_0)^2} \qquad (5)$$

where $[HG_2]$ denotes the concentration of the 1:2 inclusion complex between γ-CD and phenols.

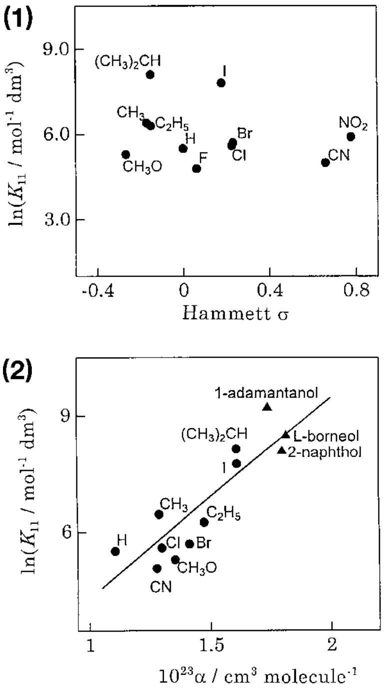


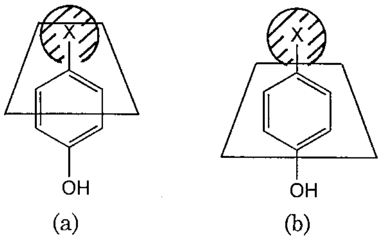
Figure 2. (1) Hammett plot of $\ln K_{11}$ of β-CD against substituent constant σ of 4-substituted phenols. (2) Relationship between $\ln K_{11}$ of β-CD and molecular polarizability α: (●) 4-substituted phenols; (▲) 2-naphthol, L-borneol and 1-adamantanol

Using the isomerization of spiropyran, the small association constant for the 1:1 inclusion complex between γ-CD and 4-substituted phenols cannot be determined. For unstable complexation, the concentration of the 1:1 inclusion complex of γ-CD is very low. Despite our attempts to achieve the conditions necessary to satisfy Eqns (2) and (3), they have been unsuccessful.

Inclusion complex between β-CD and phenols

The association constants for the inclusion complex of β-CD with various kinds of phenols are listed in Table 2, and show some interesting points: (1) in 4-substituted phenols, the K_{11} values are similar in magnitude except for 4-I- and 4-$(CH_3)_2$CH-phenols; (2) the K_{11} values for large guest molecules such as 1-adamantanol and L-borneol are large compared with those of 4-substituted phenols; and (3) the K_{11} values at pH 6.9 are large compared with those at pH 10.1, except for 4-NO_2-P.

The Hammett plot was useful for identifying binding sites and assigning values to association constants. In fact, the complex stability between α-CD with 4-substituted phenol increases in order of increasing Hammett substituent constant σ.[7] For the 4-substituted phenols/β-CD system, Fig. 2(1) represents a Hammett-type plot of $\ln K_{11}$ against the substituent constant σ for 4-substituted phenols. The Hammett plot shows substantial scatter, which is different from the behaviour of α-CD. Based on the NMR study of inclusion complexes of β-CD by Inoue *et al.*,[8] the insensitivity of the stability of inclusion complexes with 4-substituted phenols can be explained in terms of the molecular geometry of the complexes (Scheme 2).



Scheme 2

In general, 4-substituted phenols penetrate the hydrophobic cavity of β-CD, as shown in Scheme 2(b).[8] In this case, the OH group and the 4-substituent site of phenols could be located in hydrophilic environments, and thus the complexation stability is independent of the nature of the substituent. In the inclusion complex of 4-substituted phenols with α-CD, the dominant binding site is the 4-substituent [Scheme 2(a)]. Complexation similar to the molecular geometry of the α-CD complex leads to large K_{11} values of β-CD with 4-I- and 4-$(CH_3)_2$CH-phenols having a bulky substituent.

The hydrophobic interaction is an important factor for the stability of inclusion complexes. The $\log P$ (where P is the partition coefficient) values are widely used as a measure of hydrophobicity. In the present system, however, the $\log K_{11}$ value showed no appreciable correlation with $\log P$. The stability of the inclusion complex is largely dependent on the size and shape of the guest. According to Conner,[7] the strength of binding forces in CD inclusion complexes is controlled mainly by the electron density, the polarizability and the polarity of the binding site. The molecular polarizability controls the induction and dispersion interactions, and is also related to size. Figure 2(2) shows the relationship between $\ln K_{11}$ of β-CD and the molecular polarizability (α) of phenols. The stability of the inclusion complex of β-CD shows an appreciable correlation with the molecular polarizability of phenols.

The K_{11} values of β-CD at pH 10.1 are small compared with those at pH 6.9, except for 4-NO_2-P. The present 4-substituted phenols exist in the ionized form (phenolate ion) in water at pH 10.1. As a rule, inclusion of charged molecules in the CD cavity is less favourable than that of uncharged molecules. This leads to small K_{11} values although the insensitive nature of the pH dependence is due to the molecular disposition of phenols in β-CD [Scheme 2(b)]. 4-NO_2-phenolate is more strongly bound than the neutral phenol. This unexpected behaviour has been discussed by several workes.[7] They suggested that the charged form of 4-NO_2-P is able to complex with α-CD more strongly than the neutral form because of the extensive charge delocalization. This accounts for the above observations.

Inclusion complex between γ-CD and phenols

Inclusion in γ-CD, with a larger cavity, is loose compared with inclusion in α- and β-CD. Therefore, the degree of interaction between γ-CD and the guest is small and conventional UV spectroscopy is not generally applicable to γ-CD complexes because of the small spectral shifts. In this case, the technique using a chemical indicator is more useful to determine equilibrium constants.

It is recognized that phenols form a 1:1 inclusion complex with β-CD. However, the stoichiometric ratio for the inclusion complex of phenols with γ-CD having a larger cavity is more complicated. In fact, the electronic spectra of 4-NO_2-P with different concentrations of γ-CD did not have an isosbestic point, which indicates the formation of both 1:1 and 1:*n* complexes. When 4-NO_2-P is included by γ-CD to form an inclusion complex, new circular dichroism appears in the vicinity of 400 nm. We determined the stoichiometric ratio of the inclusion complex between γ-CD and phenols by analyses of the change in the induced circular dichroism spectra. Hirai *et al.*[9] indicated that the magnitude of the induced circular dichroism is proportional to the amount of the complexes produced, as follows:

for 1:1 (= γ-CD:4-NO_2-P) complex formation,

$$\Delta E_{CD} = \frac{[\theta][H]_0}{100\left(K_{11}{}^{-1} + [H]_0\right)}[G]_0 \qquad (6)$$

for 1:*n* (= γ-CD:4-NO_2-P) complex formation,

$$\frac{[G]_0}{\Delta E_{CD}} = \frac{100}{K_{1n}[\theta][H]_0[G]_0^{n-1}} + \frac{100n^2}{[\theta]} \qquad (7)$$

where $[H]_0$ and $[G]_0$ are the initial concentrations of γ-CD and 4-NO_2-P, respectively, ΔE_{CD} and $[\theta]$ are the measured magnitudes of the induced circular dichroism and ellipticity of the complex, respectively, and K_{1n} denotes the association constant for the 1:*n* inclusion complex. Under the condition $[\gamma\text{-CD}]_0 \gg [4\text{-NO}_2\text{-P}]_0$, ΔE_{CD} is plotted against the charged concentration of 4-NO_2-P according to Eqn. (6) in Fig. 3(1). When γ-CD forms a 1:1 inclusion complex, a linear relationship is expected. For $[\gamma\text{-CD}]_0/[4\text{-NO}_2\text{-P}]_0 > 40$, a linear relationship between ΔE_{CD} and the charged concentration of 4-NO_2-P can be obtained, which is taken as a evidence for the 1:1 complex formation. On the other hand, for $[\gamma\text{-CD}]_0/[4\text{-NO}_2\text{-P}]_0 < 20$, ΔE_{CD} is not proportional to the charged concentration of 4-NO_2-P, and the correlation is therefore more complicated. At $[\gamma\text{-CD}]_0/[4\text{-NO}_2\text{-P}]_0 > 40$, the circular dichroism data were analysed according to the Benesi–Hildebrand equation for 1:1 complex formation, and the K_{11} value of γ-CD was obtained as 14.2 $mol^{-1}\,dm^3$. The small K_{11} value of γ-CD compared with K_{11} of β-CD is responsible for the loose inclusion in γ-CD with a large cavity. At $[\gamma\text{-CD}]_0/[4\text{-NO}_2\text{-Ph}]_0 < 20$, the induced circular dichroism changes were analysed according to Eqn. (7). As can be seen in Fig. 3(2), a linear relationship can be obtained for the 1:2 complex formation between one γ-CD and two phenol molecules. From the slope and intercept, the K_{12} value between γ-CD and 4-NO_2-P was calculated to be $2.51 \times 10^5\ mol^{-2}\,dm^6$. The 1:3 inclusion complex cannot be observed.

To determine the association constant with γ-CD using the isomerization of 6-SO_3^--SP, the isomerization of 6-SO_3^--SP in the presence of γ-CD (constant $3 \times 10^{-4}\ mol\,dm^{-3}$ concentration) and phenols (varied from 1×10^{-3} to $1 \times 10^{-2}\ mol\,dm^{-3}$) was examined, and the equilibrium concentration of unbound γ-CD was determined from Eqn. (2). The K_{12} values for the equilibrium between γ-CD and 4-NO_2-P, calculated from Eqn. (5), were constant, whereas the K_{11} values

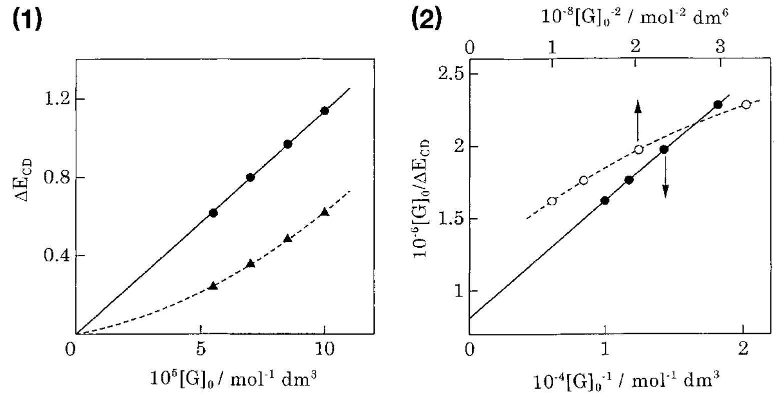


Figure 3. (1) Plot of the magnitude of circular dichroism (ΔE_{CD}) induced by γ-CD inclusion complex against the initial concentration of 4-NO_2-P: (●) $[\gamma\text{-CD}]_0/[4\text{-NO}_2\text{-P}]_0 = 40\text{–}\ 80$, $[\gamma\text{-CD}]_0 = 0.004\ mol\,dm^{-3}$; (▲) $[\gamma\text{-CD}]_0/[4\ NO_2\ \text{-P}]_0 = 10\text{–}\ 20$, $[\gamma\text{-CD}]_0 = 0.001\ mol\,dm^{-3}$. (2) Plot of $[G]_0/\Delta E_{CD}$ against $[G]_0{}^{n-1}$ for the γ-CD and 4-NO_2-P system according to Eqn. (7): (●) $n = 2$; (○) $n = 3$

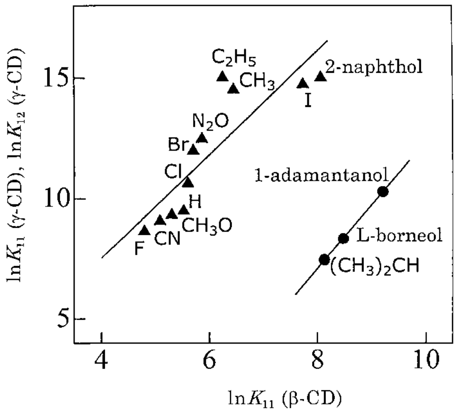


Figure 4. (●) Relationship between $\ln K_{11}$ of γ-CD and $\ln K_{11}$ of β-CD. (▲) Relationship between $\ln K_{12}$ of γ-CD and $\ln K_{11}$ of β-CD

tentatively calculated from Eqn. (3) obviously changed with the concentration of 4-NO_2-P. As shown in Table 2, the K_{12} value between γ-CD and 4-NO_2-P was determined as $2.6 \times 10^5\,mol^{-2}\,dm^6$ using the isomerization rate of 6-SO_3^--SP, which is comparable to the K_{12} value ($2.51 \times 10^5\,mol^{-2}\,dm^6$) determined from the induced circular dichroism change. This agreement supports the reliability of the present method based on the isomerization of 6-SO_3^--SP. The K_{12} values between γ-CD and 4-$(CH_3)_2CH$-P obviously changed the concentration of 4-$(CH_3)_2CH$-P. Judging from the estimated equilibrium constants, we found that 1:1 binding of γ-CD takes place with large guest molecules such as 4-$(CH_3)_2CH$-P, L-borneol and 1-adamantanol. For such large guests, 1:2 complexing cannot be observed. The K_{11} and K_{12} values of γ-CD obtained are listed in Table 2.

The free-energy change for complex formation can be estimated from

$$\Delta G = -RT \ln K \tag{8}$$

The ΔG_{11} values for 1:1 complex formation of 4-$(CH_3)_2CH$-P with β-CD and γ-CD can be estimated to be -21.2 and $-19.4\,kJ\,mol^{-1}$, respectively, i.e. they are similar in magnitude. The ΔG_{11} and ΔG_{12} values for 1:1 and 1:2 complex formation of 4-NO_2-P with β-CD and γ-CD can be calculated to be -15.3 and $-32.5\,kJ\,mol^{-1}$, respectively, i.e. ΔG_{11} is almost half of ΔG_{12}, which is responsible for the difference in the number of guest molecules.

Figure 4 shows the correlations of $\ln K_{11}$ and $\ln K_{12}$ of γ-CD with $\ln K_{11}$ of β-CD. These free-energy relationships for 1:1 and 1:2 complexing give parallel straight lines. We consider that the upward shift of 1:2 complexing is not due to a mechanism change for inclusion but to the extra free-energy change for inclusion of two guest molecules. The above observations suggest the similarity of dominant factors for 1:1 and 1:2 inclusion complexing.

REFERENCES

1. G. H. Brown, *Photochromism*. Wiley, New York (1971), and references cited therein.
2. Y. Sueishi and T. Nishimura, *J. Phys. Org. Chem.* **8**, 335 (1995).
3. T. Matsumoto, S. Imai and T. Yoshinari, *Bull. Chem. Soc. Jpn.* **58**, 1165 (1985), and references cited therein.
4. J. Sunamoto, K. Iwamoto, M. Akutagawa, M. Nagase and H. Kondo, *J. Am. Chem. Soc.* **104**, 4904 (1982).
5. Y. Sueishi, N. Nishimura and T. Miyakawa, *Chem. Lett.* 1061 (1995).
6. E. A. Lewis and L. D. Hansen, *J. Chem. Soc., Perkin Trans. 2* 2081 (1973).
7. K. A. Connors, *Chem. Rev.* **97**, 1325 (1997).
8. Y. Inoue, T. Okuda, Y. Miyata and R. Chujo, *Carbohydr. Res.* **125**, 65 (1984).
9. H. Hirai, N. Toshima and S. Uenoyana, *Bull. Chem. Soc. Jpn.* **58**, 1156 (1985).