

Mini Review

## Rotaxane Type Complexation Behavior of Cyclodextrins with a Series of Donor–Acceptor Covariantly Linked Compounds

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### Abstract

The complexation behavior of a series of electron donor–accepter (D–A) covalently linked compounds with cyclodextrins (CyDs) has been reviewed. The structure of these complexes showed rotaxane type conformations, which were investigated by means of <sup>1</sup>H NMR spectrometry. The complex formations induced a fixation of a conformation of guest D–A molecules, and D–A distances were enlarged. Thus, accurate photo-induced charge transfer behaviors can be discussed.

### Introduction

Photo-induced electron transfer reaction in electron donor–accepter (D–A) linked compounds has been one of the most popular research subjects relevant to artificial photosyntheses [1–3]. For the purpose of constructing efficient photo energy conversion systems, a large number of experimental and theoretical investigations has been carried out to elucidate the role of the spacer between D and A in the long range electron transfer processes [1–5]. With the aid of several microenvironments and external perturbation such as electric fields or magnetic fields, the controls of photo-induced electron transfer have succeeded in several D–A systems [6, 7]. The preparation of D–A linked compounds with a flexible polymethylene chain,  $-(CH_2)_n-$ , is easier than with molecules with a rigid bridge. The study on the distance dependence of the electron transfer rates in the D–A linked compounds with flexible bridge usually gave complicated results due to distribution of different conformations. One suitable idea to overcome this defect is constructing a rotaxane type molecule using cyclodextrins (CyDs) accompanied by the fixation of the molecular conformation. Recently, chemistry of the supramolecules such as catenanes and rotaxanes with CDs attracts considerable interest of many researchers [8–13]. Rotaxanes and catenanes are

mechanically interlocking compounds that incorporate CDs as one of their components. These rotaxane-type cyclodextrin complexes have been studied intensively as one of the most important supramolecular assemblies in various fields.

In this review, new approaches for the development of rotaxane type complexation behavior of D–A molecules with CyD are described.

### Rotaxane type complexation behavior of cyclodextrins with various guest molecules having long alkyl chains

*Study on formation of rotaxane type  $\alpha$ -cyclodextrin complexes with polymethylene bis[1-pyridinium]*

Prior to the study of the complexation behavior of electron D–A molecules with cyclodextrins (CyD), polymethylene bis[1-pyridinium] ( $C_n$ BPy) was employed as a guest for the formation of rotaxane type complexes [14]. In many D–A molecules, bis-pyridinium derivatives were selected as good electron acceptor moieties. Thus,  $C_n$ Py molecules were chosen as a model study instead of bis-pyridinium derivatives. The complex formation and effects of alkyl chain length in  $C_n$ Py were observed using <sup>1</sup>H and <sup>13</sup>C NMR spectroscopies.

In the presence of  $\alpha$ -CyD, a new set of signals of  $C_n$ Py became evident, and the intensities increased at the expense of the corresponding peaks for the free species at higher  $\alpha$ -CyD concentration. Interestingly, each

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group of originally equivalent protons afforded a pair of new signals with equal intensity on complexation with  $\alpha$ -CyD. The new signals were reasonably explained by the rotaxane type complex between  $C_{10}$ Bpy and  $\alpha$ -CyD, and the lifetime of  $C_{10}$ Bpy- $\alpha$ -CyD was long enough to be separately detected in NMR time scale at 5 °C. For stabilizing the rotaxane structure, the guest molecule must have some barrier moieties in both ends of a long chain. Candidates for the barrier can be listed, such as large substituent and/or hydrophilic moieties. In addition, the affording the pair of new signals in  $C_{10}$ Bpy- $\alpha$ -CyD was suggested to create a magnetically asymmetric microenvironment along the spacer chain. This microenvironment effect may be due to an asymmetric cylindrical CyD structure (Figure 1).

#### Study on formation of rotaxane type $\alpha$ -cyclodextrin complexes with $\alpha,\omega$ -alkanedicarboxylate

The  $\alpha,\omega$ -alkanedicarboxylate ( $C_n^{2-}$ ) molecule which was a linkage unit between D-A were chosen as a guest for  $\alpha$ -CyD [15]. The complex formation was also observed using  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectroscopies. When  $\alpha$ -CyD was added to a  $C_{12}^{2-}$  solution at neutral medium, new sets of signals for methylene groups appeared, and signals of the free species remained. These indicated that each methylene moiety is located in an asymmetric environment into the  $\alpha$ -CyD cavity, and the lifetime of the  $\alpha$ -CyD- $C_{12}^{2-}$  was long enough to give separate signals apart from the uncomplexed species at the NMR time scale. When other dicarboxylic acid,  $C_{11}^{2-}$ ,  $C_{10}^{2-}$  and  $C_8^{2-}$  with shorter methylene chains were employed as the guest molecules, similar results were obtained as mentioned above. In the case of  $C_7^{2-}$ , only the coalescent spectra were observed at room temperature; finally,  $C_6^{2-}$  did not give any evidence of complexation with  $\alpha$ -CyD. On the other hand,  $\beta$ - and  $\gamma$ -CyD did not give any evidence of complexation with these  $C_n^{2-}$ . This suggested that the suitability of the size between the cavity of the  $\alpha$ -CyD and the guest molecules is likely to be a factor for stable complex formation.

From the observation of the new sets of signals for methylene in  $\alpha$ -CyD- $C_{12}^{2-}$ , it was assumed that  $\alpha$ -CyD exists near the center of  $C_n^{2-}$ , and induces a different magnetic environment. To confirm this, intermolecular NOEs of  $\alpha$ -CyD- $C_{12}^{2-}$  were measured. NOE correlation peaks between central peaks of  $C_{12}^{2-}$  and H-3 and H-5 of  $\alpha$ -CyD were clearly observed. On the basis of the results, it was concluded that the central moiety of  $C_{12}^{2-}$  is wrapped by  $\alpha$ -CyD with a long lifetime.

#### Study on formation of rotaxane type cyclodextrin complexes with D-A linked molecules

##### Phenothiazine-viologen linked molecules-CyD system

The complexation behavior of phenothiazine-viologen covalently linked compounds by short and long methylene chains ( $\text{PtzC}_n\text{V}^{2+}$ ;  $n = 4$  and 12) with CyDs was investigated in water [16]. The results of  $^1\text{H}$  NMR observation of  $\text{PtzC}_{12}\text{V}^{2+}$ - $\alpha$ - and  $\beta$ -CyD were similar to those of  $C_{10}$ Bpy and  $C_n^{2-}$ ; the formation of  $\text{PtzC}_{12}\text{V}^{2+}$ - $\alpha$ - and  $\beta$ -CyD with the rotaxane type structure with slow exchange was confirmed. In the case of  $\gamma$ -CyD, the viologen and phenothiazine proton signals changed in their shapes and shifted to lower fields with respect to those of free species, but no separate signals were obtained. This suggested that rapid exchange between the complex and free species should be responsible for the progressive shifts induced by  $\gamma$ -CyD.

There was a charge-transfer interaction in  $\text{PtzC}_{12}\text{V}^{2+}$  between phenothiazine and bipyridine. This was confirmed by the fact that a weak and broad charge-transfer absorption band ( $\lambda_{\text{max}} = 550$  nm) was observed with the free species. However, this completely disappeared on the addition of  $\alpha$ - and  $\beta$ -CyD. On the basis of these results, the formation of  $\text{PtzC}_{12}\text{V}^{2+}$ - $\alpha$ - and  $\beta$ -CyD is schematically shown in Figure 2. In the case of  $\text{PtzC}_4\text{V}^{2+}$  having short methylene chain of the spacer, the  $^1\text{H}$  NMR signals simply shifted in the presence of CyDs suggesting the formation of  $\text{PtzC}_4\text{V}^{2+}$ -CyD with fast exchange.

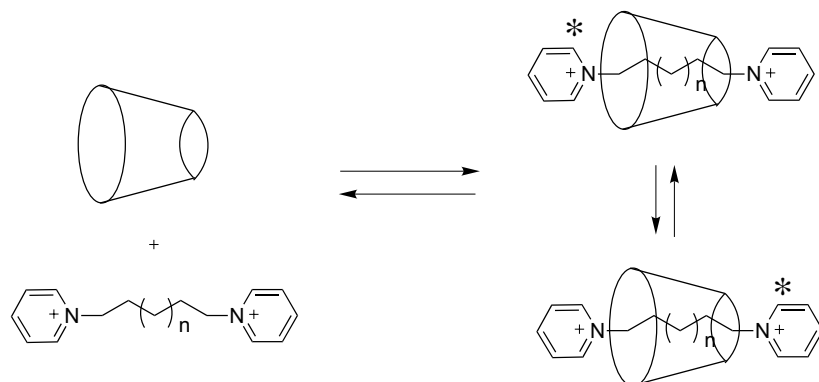


Figure 1. Schematic presentation of rotaxane type  $\alpha$ -CyD complexes with polymethylene bis[1-pyridinium] and site exchange process.

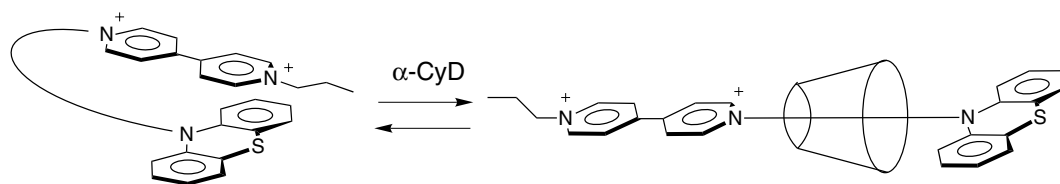


Figure 2. Schematic presentation of rotaxane type  $\alpha$ -CyD complexes with phenothiazine–viologen linked molecules.

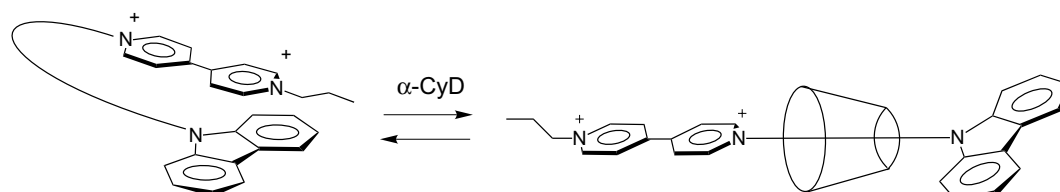


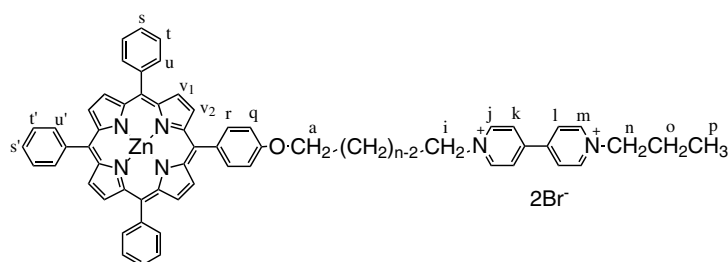
Figure 3. Schematic presentation of rotaxane type  $\alpha$ -CyD complexes with carbazole–viologen linked molecules.

### Carbazole–viologen linked molecules–CyD system

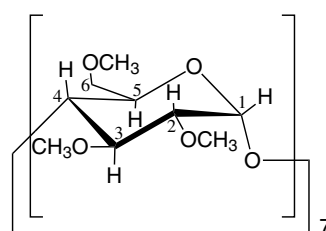
The observation of the complexation behavior of carbazole–viologen covalently linked compounds by several methylene chains ( $\text{CAC}_n\text{V}^{2+}$ ;  $n = 4, 6, 8, 10$  and  $12$ ) with CyDs were carried out in water [17]. The results of  $^1\text{H}$  NMR observation of  $\text{CAC}_n\text{V}^{2+}$  ( $n > 8$ )  $\alpha$ - and  $\beta$ -CyD were also similar to that of  $\text{C}_{10}\text{Bpy}$ ,  $\text{C}_n^{2-}$  and  $\text{PtzC}_{12}\text{V}^{2+}$   $\alpha$ - and  $\beta$ -CyD; the formation of  $\text{CAC}_{12}\text{V}^{2+}$   $\alpha$ - and  $\beta$ -CyD having the rotaxane type structure with slow exchange were confirmed. The interaction between short  $\text{CAC}_n\text{V}^{2+}$  ( $n = 4$  and  $6$ ) with  $\alpha$ - and  $\beta$ -CyD were not observed. This suggested that an ability of inclusion of CyDs rapidly decreased with the decrease of the spacer chain length. In the case of  $\gamma$ -CyD, the viologen and

carbazole proton signals in  $\text{CAC}_n\text{V}^{2+}$  changed in their shapes and shifted to lower fields with respect to those of the free species, but no separate signals were obtained. This indicated that rapid exchange between the complex and free species should be responsible for the progressive shifts induced by  $\gamma$ -CyD.

The intramolecular charge–transfer interaction in  $\text{CAC}_{12}\text{V}^{2+}$  between carbazole and bipyridine occurred spontaneously in solution. This was supported by the result in which a weak and broad charge–transfer absorption band ( $\lambda_{\text{max}} = 420 \text{ nm}$ ) was observed with free species. The addition of  $\alpha$ - and  $\beta$ -CyD induced the disappearance of the charge–transfer absorption band. On the basis of these results, the formation of  $\text{CAC}_{12}\text{V}^{2+}$   $\alpha$ - and  $\beta$ -CyD is schematically shown in Figure 3.



$\text{ZnPC}_n\text{V}^{2+}$  ( $n = 4, 5, 6, 7, 8, 9, 10$  and  $12$ )



2,3,6-tri-O-methyl- $\beta$ -cyclodextrin

Scheme 1.

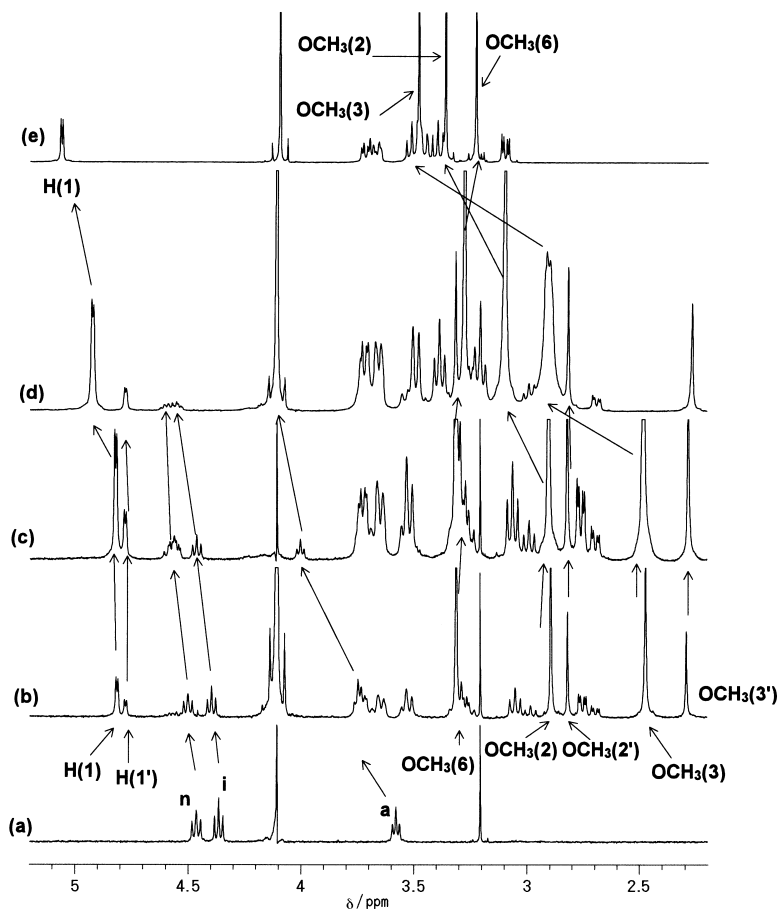


Figure 4.  $^1\text{H}$  NMR spectra of  $\text{ZnPC}_9\text{V}^{2+}$  ( $2 \times 10^{-3} \text{ mol dm}^{-3}$ ) in higher magnetic field with addition of TM- $\beta$ -CyD ((a)  $0 \text{ mol dm}^{-3}$ , (b)  $0.4 \times 10^{-3} \text{ mol dm}^{-3}$ , (c)  $2.4 \times 10^{-3} \text{ mol dm}^{-3}$ , (d)  $7.2 \times 10^{-3} \text{ mol dm}^{-3}$ , and (e) TM- $\beta$ -CyD only) in acetonitrile- $d_3$ - $\text{D}_2\text{O}$  (1:1, v/v) at  $30^\circ\text{C}$ .

#### Porphyrine–viologen linked molecules·CyD system

The complexation behavior of zinc(II) tetraphenylporphyrin–viologen covalently linked compounds by polymethylene chain ( $\text{ZnPC}_n\text{V}^{2+}$ ;  $n = 3\text{--}10$ , and 12) with 2,3,6-*O*-methyl- $\beta$ -cyclodextrin (TM- $\beta$ -CyD) were investigated in acetonitrile–water (1:1, v/v) [18].

This guest molecule showed complicated behavior due to low solubility in water and many including sites. The  $^1\text{H}$  NMR spectra of free  $\text{ZnPC}_n\text{V}^{2+}$  indicated a dependence of concentration suggesting that  $\text{ZnPC}_n\text{V}^{2+}$  existed as a mixture of a dimer and a monomer at high concentration ( $>1 \times 10^{-3} \text{ mol dm}^{-3}$ ) in this medium. The dimer was degraded by the complex formation with TM- $\beta$ -CyD whereas any evidence of the formation of supramolecular complexes of  $\text{ZnPC}_n\text{V}^{2+}$  with TM- $\alpha$ -CyD were not obtained by the use of  $^1\text{H}$  NMR nor UV/Visible spectra in methanol, acetonitrile, or acetonitrile–water solutions. This is due to the small cavity size of TM- $\alpha$ -CyD against the benzene or pyridinium ring of  $\text{ZnPC}_n\text{V}^{2+}$ .

A detailed investigation into the complexation behavior of  $\text{ZnPC}_n\text{V}^{2+}$  with TM- $\beta$ -CyD was carried out using  $^1\text{H}$  NMR spectroscopy. Figure 4 shows typical  $^1\text{H}$  NMR spectra in the higher field region of  $\text{ZnPC}_9\text{V}^{2+}$  in the absence and presence of TM- $\beta$ -CD.

Induced chemical shift changes of methyl protons of TM- $\beta$ -CyD were divided into two types: (1) a peak showed no chemical shift change. (2) two peaks showed the high field shift changes, and split into a big and a small peak, respectively. In the case of the type (2), each big one once moved to high field, then went back toward an original peak position with the increasing of [TM- $\beta$ -CyD]. Although both of the small ones indicated a high field shift, newly induced shift changes were not observed by the increasing of [TM- $\beta$ -CyD]. Considering an inclusion mode of TM- $\beta$ -CyD, it was possible to imagine that the peak of type (1) was the 6-positioned methyl proton ( $-\text{CH}_3(6)$ ), and type (2) were assigned to be 2- ( $-\text{CH}_3(2)$ ) and 3-positioned methyl ( $-\text{CH}_3(3)$ ) protons, respectively. The behavior of type (2) suggested that two types of  $\text{ZnPC}_9\text{V}^{2+}$ ·TM- $\beta$ -CyD structure existed. Here, it should be noted that the smaller peaks of both  $-\text{CH}_3(2)$  and  $-\text{CH}_3(3)$  did not change their position, where a quite slow exchange ( $k_{\text{ex}} \leq 40 \text{ s}^{-1}$ ) with excess TM- $\beta$ -CD takes place. The new signals were reasonably explained by the rotaxane type complex formation. Similar results were also observed for other protons in TM- $\beta$ -CD (e.g. H(1) and H(2)). The unusual higher chemical shifts of  $-\text{OCH}_3(3)$  and  $-\text{OCH}_3(2)$  of the  $\text{ZnPC}_9\text{V}^{2+}$ ·TM- $\beta$ -CyD may be due to the ring

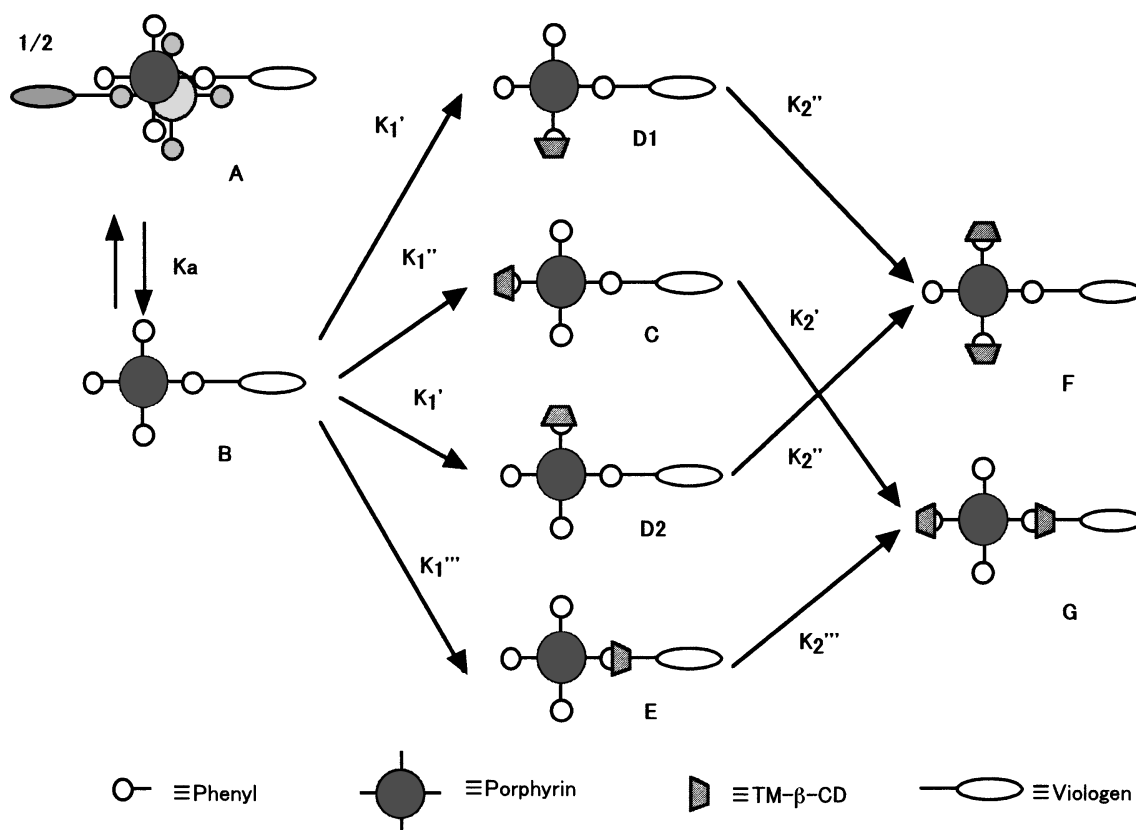


Figure 5. Schematic representation of the kinetics of the supramolecular complex formation of  $\text{ZnPC}_n\text{V}^{2+}$  with TM- $\beta$ -CyD.  $K_a$  is an association constant for dimerization,  $K_1$  and  $K_2$  are apparent complex formation constants with TM- $\beta$ -CyD for 1:1 and 1:2 complexes.

Table 1. Discrete complex formation constants of  $\text{ZnPC}_n\text{V}^{2+}$  with TM- $\beta$ -CyD

$n$	$K_1'/K_1$	$K_1''/K_1$	$K_1'''/K_1$	$K_2'/10^3 \text{ M}^{-1}$	$K_2''/10^3 \text{ M}^{-1}$	$K_2'''/10^3 \text{ M}^{-1}$	$K_2$
3	0.32	0.32	0.03	0.32	7.1	3.9	2.4
4	0.31	0.31	0.08	2.4	9.7	9.4	3.7
5	0.29	0.29	0.12	3.4	9.9	9.4	3.9
6	0.27	0.27	0.19	6.7	12.1	9.8	5.1
7	0.25	0.25	0.25	11.2	11.2	11.2	5.6
8	0.25	0.25	0.25	10.4	10.4	10.4	5.2
9	0.25	0.25	0.25	10.8	10.8	10.8	5.4
10	0.24	0.24	0.28	10.6	10.6	9.2	5.1
12	0.24	0.24	0.29	10.8	10.8	8.7	5.1

Actual  $K_1'$ ,  $K_1''$  and  $K_1'''$  values were not obtained because  $K_1$  values are unknown.

current effect of porphyrin and/or the phenyl ring of  $\text{ZnPC}_9\text{V}^{2+}$ . On the other hand, the chemical shift of  $-\text{OCH}_3(6)$  was little affected by the complexation. The formation of the rotaxane type structure constructed by  $\text{ZnPC}_9\text{V}^{2+}\cdot\text{TM-}\beta\text{-CyD}$  was also supported by the lower shift changes of alkyl chain protons (a) and (i) of the  $\text{ZnPC}_9\text{V}^{2+}$ .

Dependence of UV/Vis absorption spectra of these compounds on the concentration of TM- $\beta$ -CyD showed the formation of 1:1 and 1:2 ( $=\text{ZnPC}_n\text{V}^{2+}:\text{TM-}\beta\text{-CyD}$ ) supramolecular complexes. These complexation behaviors are summarized in Figure 5, and their discrete

complex formation constants are listed in Table 1. The  $\text{ZnPC}_n\text{V}^{2+}$  linked by the short methylene chain ( $n=3$  and 4) were not able to form stable rotaxane type complexes ( $K_1'''/K_1 \leq 0.08$ ) with TM- $\beta$ -CyD. This may be due to a strong hydrophobicity of bipyridinium moiety. With longer methylene chains in  $\text{ZnPC}_n\text{V}^{2+}$  ( $n \geq 5$ ), the complex formation constants increased until  $n=6$ , and that of  $n \geq 6$  were a little affected by the spacer length, and came close to an asymptotic value. Similar trends were also observed in investigations of phenothiazine–viologen [16] and carbazole–viologen linked molecules–CyD systems [17].

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