Synthesis and Binding Properties of Ethylbipyridinio-Modified β-Cyclodextrin

Yi-qun Du, Asao Nakamura, and Fujio Toda*
Department of Bioengineering, Faculty of Bioscience and Biotechnology,
Tokyo Institute of Technology, O-okayama, Meguro-ku, Tokyo 152
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Synopsis. Mono-6-deoxy-6-[4-(1-ethyl-4-pyridinio)-1-pyridinio]-β-cyclodextrin (**3**) was synthesized. The conformation and the binding properties of **3** with benzene derivatives were examined by induced circular dichroism (ICD) in aqueous solution. The conformation of **3** was confirmed to such equatorial inclusion as β-CDx capped by ethylviologen (C_2V^{2+}) group. Further, compound **3** showed stronger binding ability with these guests (1:1 complexes) compared with β-cyclodextrin (β-CDx).

The utilization of solar energy to produce fuels, useful chemicals, and electricity has been tried for over a decade. Especially photochemical charge separation has attracted much attention, since it may regarded as being a direct mimic of biological photoreaction systems.[1] So far, many molecular devices for photochemical charge separation have been synthesized, and the charge-separation efficiency of the devices tested.[2] The point of designing such a device is to control the rate of electron transfer by changing the distance between donor and acceptor moieties in the device molecule.[3] The distance is determined by the kinds, length, and number of covalent bonds connecting these active moieties. There is, however, another way to arrange redox partners in three-dimensional space, in which the tendency of some molecules to form assemblies is utilyzed. A Langmuir–Blodgett film is a good example of such an assembly.[4] An inclusion compound is another typical example, and is a candidate material for constructing a self-assembly-type molecular device.

We intend to make molecular device for photochemical charge separation with cyclodextrin (CDxs) inclusion complexes; as a first stage, we will use synthesized viologen-appended CDxs. Viologens (4, 4′-bipyridinium salts) are good electron acceptors which act as a mediator between the photosensitizer and catalysts for hydrogen production,[5] or between the photosensitizer and an enzyme–coenzyme system for NADH production.[6] In this paper we report on the preparation of mono-6-deoxy-6-[4-(1-ethyl-4-pyridinio)-1-pyridinio]-β-cyclodextrin (**3**). Its conformational and binding properties with some guests are also described.

Results and Discussion

Figure 1 shows the absorption and ICD spectra of **3** and a physical mixture of β-CDx and 1, 1′-diethyl-4,4′-bipyridinium dibromide [$(C_2)_2VBr_2$] in the absorption region of $(C_2)_2VBr_2$. Compound **3** gave a red-shifted absorption band in the UV spectra and a negative ICD sign in the ICD spectra, while a mixture of β-CDx and $(C_2)_2VBr_2$ did not give any spectral change. These

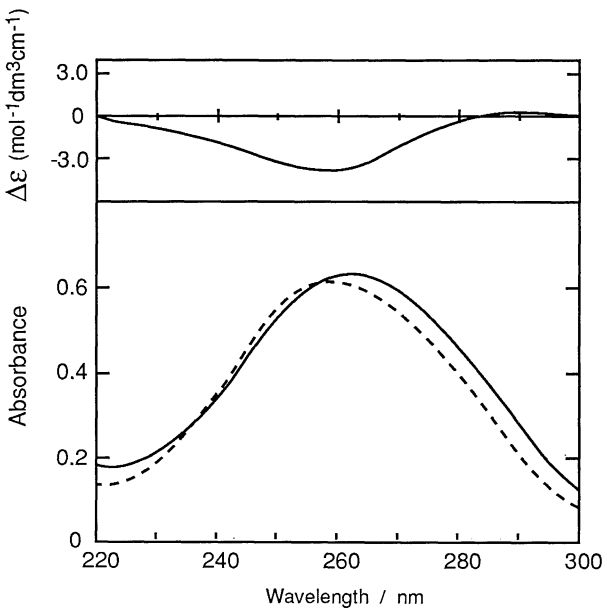


Fig. 1. Absorption and ICD spectra of **3**. Absorption: [**3**]=1×10⁻⁵ mol dm⁻³ (—). [β-CDx]=2×10⁻⁵ mol dm⁻³, [$(C_2)_2VBr_2$]=1×10⁻⁵ mol dm⁻³ (---). ICD spectra: [**3**]=1×10⁻⁴ mol dm⁻³ (—).

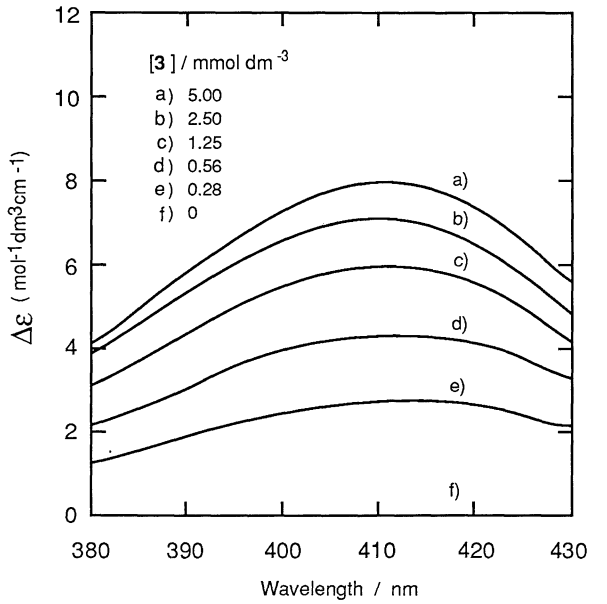


Fig. 2. ICD spectra of *p*NP⁻ (1×10⁻⁴ mol dm⁻³) in the various concentrations of **3** in the pH 9.6 borate buffer.

results indicate that the β-CDx did not form an inclusion complex with $(C_2)_2VBr_2$, while the C_2V^{2+} group of **3** was included inside the cavity of **3**. On the basis of the Kirkwood–Tinoco coupled oscillator model, the regative ICD sign of the band indicates that the polarization direction of C_2V^{2+} is perpendicular to the molecular axis of **3**.[9] The conformation of **3** was confirmed to be such an equatorial inclusion as β-CDx capped by C_2V^{2+}.

In Fig. 2, the changes in the ICD intensity can be observed on the ICD spectra in the presence of *p*NP$^-$ with various concentrations of **3** in the absorption region of *p*NP$^-$. An achiral guest molecule included in a chiral CDx cavity may exhibit an ICD in its absorption regions. These results in Fig. 2 indicate that complex was formed between **3** and *p*NP$^-$. A similar tendency was also seen in β-CDx with *p*NP$^-$.

Figure 3 shows the dependence of the ICD intensity of *p*NP$^-$ on the concentration of **3** or β-CDx at 410 nm as a function of the concentration of the complex formation of **3** and β-CDx with *p*NP$^-$. The curves are hyperbolic, which indicates that only 1:1 binding occured in these systems. From the relation shown in Fig. 3, we tried to estimate the binding constant for **3** and β-CDx with *p*NP$^-$.

When **3** or β-CDx forms only a 1:1 complex with *p*NP$^-$, the equilibrium can be represented by

$$p\text{NP}^- + \text{CDx} \rightleftharpoons p\text{NP–CDx}. \quad (1)$$

When **3** or β-CDx is in large excess, the binding constant K is approximately described as

$$K = x/c_o(p_o - x). \quad (2)$$

Here, p_o is the total concentration of *p*NP$^-$ (1×10^{-4} mol dm^{-3}), c_o the total concentration of **3** or β-CDx and x the concentration of the *p*NP–CDx complex.

The x value can be calculated from

$$x = p_o(\Delta\varepsilon/\Delta\varepsilon_{max}). \quad (3)$$

Here, $\Delta\varepsilon$ is the molar circular dichroism for the complex, and $\Delta\varepsilon_{max}$ is the highest observed value of $\Delta\varepsilon$ for an infinite concentration of **3** or β-CDx.

Eqs. 2 and 3 yield

$$\Delta\varepsilon = Kc_o\Delta\varepsilon_{max}/1 + Kc_o. \quad (4)$$

The binding constants (K) shown in Table 1 and $\Delta\varepsilon_{max}$ were obtained by using Eq 4 [plot of $\Delta\varepsilon$ vs. C_o]. In the same manner, similar results were obtained for **3** and β-CDx with *p*NA at 25 °C in a pH 7 phosphate buffer. Under this condition, *p*NA behaves as a non-charged guest molecule. The K for **3** with *p*NP$^-$ was 3.1-times larger than that for β-CDx with *p*NP$^-$ and the K for **3** with *p*NA was 2.8-times larger than that for β-CDx with *p*NA. The binding ability of **3** with negatively charged guests, like *p*NP$^-$, was stronger than that with no charged guests, like *p*NA. However, **3** bound not only to negatively charged guests, like *p*NP$^-$, but also to non-charged guests, like *p*NA, more strongly than to β-CDx.

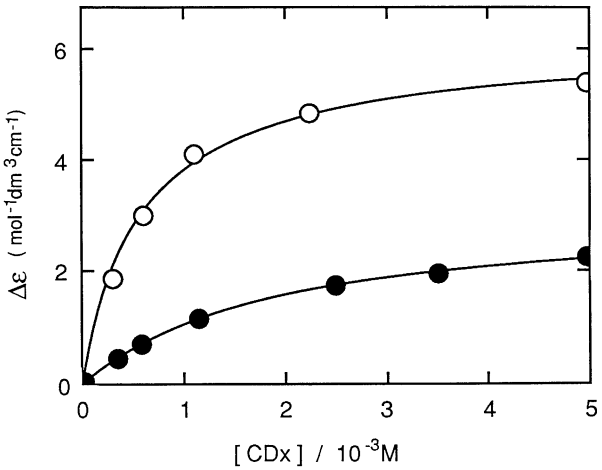


Fig. 3. Dependence of ICD intensity of *p*NP$^-$ on total concentration of **3** (○) and β-CDx (●) in pH 9.6 borate buffer. Total concentration of *p*NP$^-$ is 1×10^{-4} mol dm^{-3}. Wavelength, 410 nm.

Table 1. The Values of Binding Constant, K for **3** and β-CDx with *p*NP$^-$ and *p*NA[a]

pH	Guest	K/mol^{-1} dm^3		K(**3**)/K(β-CDx)
		3	β-CDx	
9.6[b]	*p*NP$^-$	1690	540	3.13
7.0[c]	*p*NA	450	161	2.80

a) At 25 °C. b) Boric acid-NaOH buffer. c) Phosphate buffer.

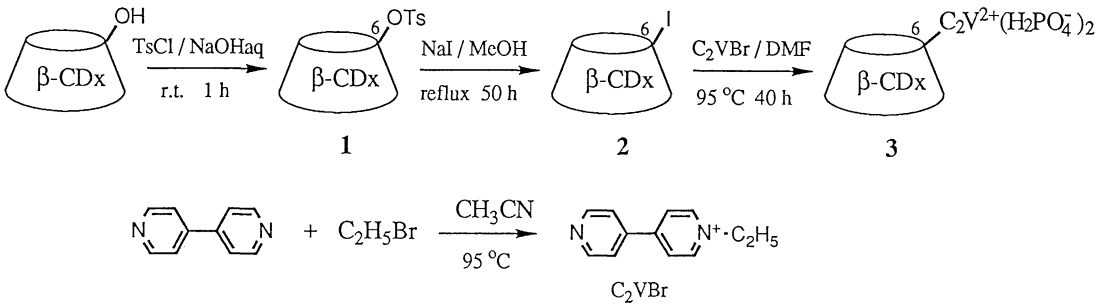
These results were partially explained by an electrostatic interaction which acts between **3** and the negatively charged guest.[10] Also some changes in the nonelectrostatic interaction between the host and guests occurred when the C_2V^{2+} group was introduced to the host molecule. Since **3** has a capped structure (as described above), it gives the possibility that the capped C_2V^{2+} group protects the binding site of **3** from the constant with a water molecule, while facilitating the stability of the inclusion complex of **3** with the guest.

3 exhibits a special conformation and a stronger binding ability with *p*NP$^-$ and *p*NA, compared with β-CDx. This indicates that **3** has not only the character of an electron acceptor (reversible redox character), but also of an inclusion host. From these results, **3** shows the possibility for use as a new electron acceptor.

Experimental

Materials. β-Cyclodextrin (β-CDx)(Nihon Shokuhin Kako Co., Ltd.), *p*-toluenesulfonyl chloride (Kanto Chemical Co), 4, 4′-bipyridine (Aldrich Chemical Co.), ethyl bromide (Kanto Chemical Co.), *p*-nitrophenol (*p*NP$^-$) and *p*-nitroaniline (*p*NA) (Tokyo Kasei) were used without further purification.

C-6-Monotosylated β-CDx (**1**) was prepared in an alkaline aqueous solution in the same manner as described in Ref. 7. The crude product was purified by repeated recrystallization



Scheme 1.

from water and a mixed solvent of methanol and water (5% by volume).

C-6-Monoiodinated β-CDx (**2**) was prepared by the method previously reported.[8]

1-Ethyl-4-(4-pyridyl)pyridinium bromide (C_2VBr) was synthesized by reacting 4, 4′-bipyridine (4 g, 25.6 mmol) with ethyl bromide (3.49 g, 32 mmol) in acetonitrile (80 ml) at 95 °C for 12 h. The resulting mixture was filtered in order to remove any solid by-products, as $(C_2)_2VBr_2$, and reprecipitated with diethyl ether in order to separate unchanged materials. This compound was identified by ^{1}H NMR etc. ^{1}H NMR (D_2O) δ=8.86 (2H, d, J=10 Hz, viologen), 8.52 (2H, d, J=9.5 Hz, viologen), 8.20 (2H, d, J=10 Hz, viologen), 7.7 (2H, d, J=9.5 Hz, viologen), 4.59 (2H, q, J=7.5 Hz, ethyl), 1.27 (3H, t, J=10 Hz, ethyl).

Preparation of Mono-6-deoxy-6-[4-(1-ethyl-4-pyridinio)-1-pyridinio]-β-cyclodextrin (3). As shown in scheme 1, **2** (2 g, 1.57 mmol) and C_2VBr (2 g, 7.54 mmol) were added to DMF (30 ml); the solution was kept at 95 °C for 40 h. After reprecipitation with acetone, the product was purified by gel chromatography on a sephadex G-10 with a 0.01 mol dm^{-3} (I=0.05) phosphate buffer as an eluent and ion-exchange chromatography on a CM-Sephadex C-25 column with a 0.2 mol dm^{-3} (I=1) phosphate buffer as an eluent. (Yield, 10%). **3** was assayed by a reducing agent, $Na_2S_2O_4$, which showed a reversible redox character with a blue color change in aqueous solution. An elemental analysis and an estimation by the peak area of the ^{1}H NMR spectrum confirmed that **3** had only one C_2V^{2+} group in the β-CDx ring. Found: C, 41.7; H, 5.57; N, 1.83%. Calcd for $C_{54}H_{83}N_2O_{37}\cdot 2H_2PO_4^-$: C, 41.9; H, 5.6; N, 1.82%. ^{1}H NMR (D_2O) δ=9.06 (2H, d, J=6.5 Hz, viologen), 9.45 (2H, d, J=6.5 Hz, viologen), 8.5 (2H, d, J=10 Hz, viologen), 8.44 (2H, d, J=10 Hz, viologen), 5.09 (1H, d, J=3.5 Hz, C1-H), 4.98 (2H, d, J=3.5 Hz, C1-H), 4.97 (1H, d, J=3.5 Hz, C1-H), 4.96 (1H, d, J=3.5 Hz, C1-H), 4.94 (1H, d, J=3.5 Hz, C1-H), 4.85 (1H, d, J=3.5 Hz, C1-H), 4.66 (2H, q, J=7.5 Hz, ethyl), 4.23 (1H, t, J=9.5 Hz, C3′-H), 3.26 (1H, t, J=9.5 Hz, C4′-H), 2.7 (1H, dd, $J_{6a,6b}$=5.5 Hz, $J_{6b,6a}$=5.5 Hz), 2.64 (1H, dd, $J_{5a,6a}$=1.5 Hz, $J_{5,6b}$=1.5 Hz), 1.6 (3H, t, J=10 Hz, ethyl).

Measurements. Absorption and induced circular dichroism (ICD) were taken on a Shimadzu UV-3100 spectrophotometer and a JASCO J-600 spectropolarimeter, using a 1cm cell at 25 °C.

Various concentrations of **3** or β-CDx were added to an aqueous buffer solution containing 1×10^{-4} mol dm^{-3} pNP$^-$ (pH 9.6 boric acid-NaOH buffer), or 1.5×10^{-4} mol dm^{-3} pNP (pH 7 phosphate buffer). The changes in the ICD spectra were recorded in the absorption region of pNP$^-$ (410 nm), or of pNA (380 nm).

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