Effect of Second-Sphere Coordination 9. Partial Inclusion of Pentaammineruthenium(II) and Pentacyanoferrate(II) Complexes with Nitrogen Heterocycles into a Cyclodextrin Cavity

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The inclusion of pentaammineruthenium(II) and pentacyanoferrate(II) complexes with nitrogen heterocycles into cyclodextrins was investigated by UV-visible spectrophotometry, ^{1}H-NMR spectroscopy, and cyclic voltammetry. The stability constants of the inclusion adducts of the metal complexes into cyclodextrins were determined by capillary electrophoresis. The complexes form adducts with cyclodextrins by the inclusion of an aromatic ligand moiety of the complex into the cavity of cyclodextrins. The adduct formation caused a modification of the redox behavior of the complex. The stability of the cyclodextrin adduct was influenced by the included aromatic ligand of the complex and the cavity size of cyclodextrin, especially the positive charge on the aromatic ligand.

The second-sphere coordination of macrocyclic ligands such as crown ethers and cyclodextrins, provides a novel method for modifying the physical and chemical properties of transition-metal complexes. The importance of such systems for biological receptors[1] and for supramolecular assemblies[2] has been noted.[3] The second-sphere coordination of crown ethers to ruthenium–ammine complexes gave a novel change in the redox behavior of the complex.[4]

Cyclodextrins are known to form inclusion complexes with a wide variety of low-molecular-weight compounds, ranging from nonpolar hydrocarbons to polar carboxylic acids and amines.[5–7] In contrast to the vast number of organic inclusion compounds reported, the use of metal complexes as guest molecules in cyclodextrin inclusion is very limited. Recently, however, interest in the encapsulation of transition-metal complexes has increased significantly. This is in part due to the potential exploitation of cyclodextrins in the molecular-recognition processes.[8,9] The majority of those studies have involved the complexation of ferrocene or its derivatives.

For the inclusion of inorganic and organic compounds into the cyclodextrin cavity, most of the guests are a neutral molecule or an anionic substrate. A guest bearing positive charge is rarely known in cyclodextrin inclusion.[10] On the other hand, transition-metal complexes could be included in the cyclodextrin cavity irrespective of the charge on the complex.[11] For the complex, a positive metal center is surrounded by hydrophobic ligands and the charge is delocalized all over the complex. Cyclodextrins include not only a whole complex, but also a part of the complex: a specific ligand coordinating to the metal center.[12–17] In this partial inclusion of metal complexes, a positive charge localized on the coordinated ligand may play a key role and may be expected to provide a specificity in the partial inclusion.[10]

In this study, the inclusion of pentaammineruthenium(II) and pentacyanoferrate(II) complexes with nitrogen heterocycles by cyclodextrins was investigated while focusing on the existence of positive charge on the nitrogen heterocycles as a ligand.

Experimental

Materials. Pentaammineruthenium(II) and pentacyanoferrate(II) complexes with nitrogen heterocycles were prepared according to literature methods[18–24] and the ruthenium complexes were isolated as hexafluorophosphate. The nitrogen heterocyclic ligands used were pyrazine (pz), *N*-methylpyrazinium (Me-pz), 4,4′-bipyridine (4,4′-bpy), *N*-methyl-4,4′-bipyridinium (Me-4,4′-bpy), 1,2-bis(4-pyridyl)ethane (bpa), and 1,3-bis(4-pyridyl)propane (bpp). The complexes were characterized spectrophotometrically by a comparison of the $\lambda_{\max}$ and $\varepsilon_{\max}$ values to those from the literatures.[18,20,21,24–26] α-, β-, and γ-Cyclodextrins (α-, β-, and γ-CD) were purified by literature methods.[27] The solvent for NMR measurements was deuterated water, purchased from Aldrich Chemical. All other chemicals were of guaranteed reagent grade and were used without further purification.

Measurements. Absorption spectra were recorded by an Hitachi 228 spectrophotometer. ^{1}H-NMR spectra were measured at 400 MHz using a JEOL JNM GSX-400 NMR spectrometer. The chemical shifts were evaluated from the signal at 4.81 ppm attributed to the solvent, itself, and were observed using 3-(trimethylsilyl)-1-propane-sulfonic acid as an internal standard. The sample solutions contained no internal standard so as to avoid any interference of the internal standard with the inclusion of complexes into the CD cavity. The formation constants of the inclusion compounds were determined by capillary electrophoresis. Electropherograms were obtained by an Otsuka CAPI-3100 capillary electrophoresis system with a UV-detector. The capillary was a CElect-H type capillary of 75 μm i.d. purchased from Supelco. A 0.05 mol dm^{-3} phosphate buffer at pH 6.8 containing CD at a certain concentration was used as a carrier solution. Measurements of electropherograms were performed at 30 °C, notwithstanding at 25 °C for other measurements.

Results and Discussion

Pentaammineruthenium(II) and Pentacyanoferrate(II) complexes with nitrogen heterocycles show a characteristic MLCT (transition from the t_{2g} orbital of metal to the nitrogen heterocyclic ligand LUMO) band in the visible region. This CT band is sensitive to the second-sphere coordination. The absorption spectra of the complexes were measured upon the addition of CD at various concentrations in aqueous solution. The pentacyanoferrate(II) complex with 4,4′-bpy showed the largest spectral change upon the addition of CD among the complexes examined. The 4,4′-bpy complex exhibited the MLCT band at 444 nm. The MLCT band shifted toward a longer wavelength with increasing the CD concentration, and reached 465 and 449 nm upon the addition of 200 excess of β-CD and γ-CD, respectively, though no spectral change was observed upon the addition of α-CD at the same concentration as in the case of other CDs. The 4,4′-bpy, bpa, and bpp complexes of pentaammineruthenium(II) showed a similar spectral change to the 4,4′-bpy complex of pentacyanoferrate(II) to a rather less extent upon the addition of CD. Other complexes showed no spectral change upon the addition of every CD at 200 excess concentration. This indicates that some parts of the complexes investigated interacted with CD. Although it is speculated that a moiety of nitrogen heterocyclic ligands may be included into the CD cavity, a size effect of the CD cavity could not be considered due to the small spectral change. The pH of sample solutions was 6 to 7, and no difference in the spectral change upon the addition of CD was observed, irrespective of the presence of phosphate buffer. Judging from the pK_a values of the protonated complexes,[21,24,28,29] the influence of protonation at the nitrogen heterocyclic ligand was ignored.

In order to determine an included moiety of the complexes, the ^{1}H-NMR spectra of the complexes were measured upon the addition of CD. The pentaammineruthenium(II) complex with 4,4′-bpy exhibited four doublet signals centered at 7.66, 7.84, 8.61, and 8.68 ppm assigned to 3,5-H, 3′,5′-H, 2,6-H, 2′,6′-H ring protons (proton numbering is ordinary and see Ref. 21), respectively, and relatively broad singlet signals at 2.54 and 3.11 ppm assigned to *cis*- and *trans*-ammine protons.[21] By adding 1.0×10^{-2} mol dm^{-3} β-CD to the complex solution of 1.0×10^{-3} mol dm^{-3}, the signals for the aromatic ring proton, 2,6-H and 2′,6′-H, of the complex shifted downfield and those for the 3,5-H and 3′,5′-H shifted upfield, as summarized in Table 1. Upon the addition of α-CD or γ-CD at the same concentration as the β-CD, no significant change for the chemical shift of the aromatic proton was observed. The signals for the *cis*- and *trans*-ammine protons exhibited no shift, irrespective of a kind of added CD. The pentacyanoferrate(II) complex with 4,4′-bpy showed a similar spectral change to that for the pentaammineruthenium(II) complex upon the addition of CD. However, the signal of the 2,6-H shifted significantly downfeild upon adding α- or γ-CD to a lesser extent than in the case of β-CD. Also, the $\Delta\delta$ for the pentacyanoferrate(II) complex was greater than that for the pentaammineruthenium(II) complex. For other complexes, the signals for the aromatic ring protons showed no significant shift upon the addition of CD. On the other hand, the ^{1}H-NMR spectra of CD were also measured upon the addition of 2.0×10^{-3} mol dm^{-3} complex to a CD solution of 1.0×10^{-3} mol dm^{-3}. When the shift of CD protons are being examined, attention is usually restricted to the 3-H and 5-H resonances, because these protons are located in the interior of the CD cavity.[8] The upfeild shift of the 3-H and 5-H resonances was observed only when β-CD was added to both 4,4′-bpy complexes. These spectral changes revealed that the 4,4′-bpy complexes interacted with CD by including only the aromatic ligand moiety into the CD cavity. The interaction may be dependent on the cavity size of CD, and an anionic complex is preferred to include into the cyclodextrin cavity, rather than a cationic complex. The interaction feature for other complexes may be obscure, due to a small spectral change.

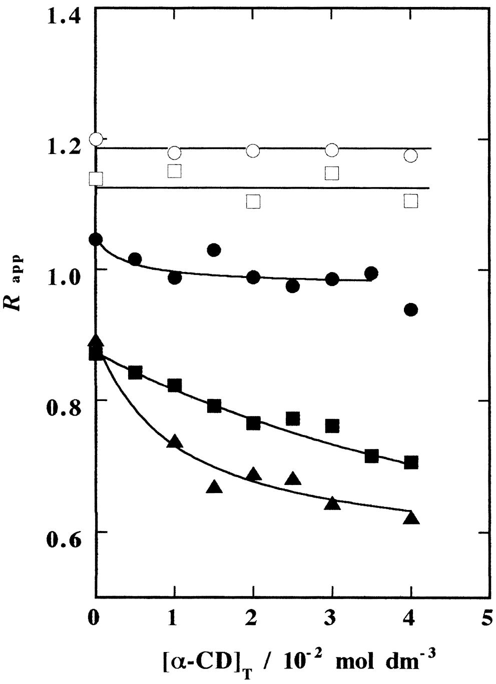

Fig. 1. Dependences of R_{app} for the pentaammineruthenium(II) complexes on α-CD concentration. Ru-pz (□), Ru-Me-4,4′-bpy (○), Ru-4,4′-bpy (●), Ru-bpa (■), and Ru-bpp (▲). [complex] = 2.0×10^{-4} mol dm^{-3}. Solid lines are the results of the least-squares method of Eq. 2.

Capillary electrophoresis was carried out to obtain quantitative information about the inclusion of the complex into the CD cavity. Electrophoresis is to be an effective technique for an inclusion phenomenon which significantly alters the molecular size of the species of interest, because the electrophoretic mobility is dependent on the charge-to-mass ratio of the species.[30] The inclusion equilibrium of the metal complex into CD is expressed by

$$\mathrm{MX} + \mathrm{CD} \xrightleftharpoons{K} \mathrm{MX{\cdot}CD},$$

where MX, MX·CD, and K represent the metal complex, the inclusion adduct, and the stability constant for the inclusion adduct, respectively. When the above equilibrium is maintained, the apparent electrophoretic mobility of the complex should become the average mobility of the complex and the inclusion adduct, taking account of their respective amount of

Table 1. Chemical Shift Difference for Aromatic Ring Protons of the 4,4′-bpy Complexes on Addition of CD

		$\Delta\delta$/ppm			
		2,6-H	2′,6′-H	3,5-H	3′,5′-H
Ru4,4′-bpy	α-CD	0.02	0.03	0.04	0.02
	β-CD	0.07	0.04	−0.09	−0.07
	γ-CD	0.02	−0.01	−0.01	−0.04
Fe-4,4′-bpy	α-CD	0.13	0.03	−0.02	0.06
	β-CD	0.22	0.09	−0.13	−0.10
	γ-CD	0.12	0.01	−0.04	0.02

[Complex] = 1.0×10^{-3} mol dm^{-3}, [CD] = 1.0×10^{-2} mol dm^{-3}.

existence in equilibrium; it is expressed as

$$\mu_{\mathrm{app}} = \frac{\mu_{\mathrm{MX}} - \mu_{\mathrm{add}}}{K[\mathrm{CD}]+1} + \mu_{\mathrm{add}}, \tag{1}$$

where μ_{MX} and μ_{add} denote the electrophoretic mobilities of the complex and the inclusion adduct, respectively.

Electropherograms of the complexes were measured in both the absence and presence of CD. Unfortunately, although no well-defined electropherogram was obtained for the pentacyanoferrate(II) complexes, the electropherograms of pentaammineruthenium(II) complexes were well-defined. Electropherograms of the pentaammineruthenium(II) complex with Me-pz (abbr. Ru-Me-pz) were measured in the presence of α-CD, β-CD, or γ-CD using [Ru(bpy)$_3$]Cl$_2$ as an internal standard, because [Ru(bpy)$_3$]Cl$_2$ could not include in the CD cavity due to its large molecular size. The electrophoretic mobility was calculated from the migration time[31] and the ratio of the apparent mobility of the complex to the mobility of the internal standard, R_{app}, was evaluated. The values of R_{app} for Ru-Me-pz were independent of the concentration of CD and were 1.004(0.019), 0.983(0.005), and 1.007(0.004) (the values in parentheses are the standard deviation) in the presence of α-CD, β-CD, and γ-CD at various concentrations, respectively. Because this implies no interaction of Ru-Me-pz with CD, this complex was used as an internal standard in the measurements of the electropherograms of other complexes. Figures 1, 2, and 3 show the dependences of R_{app} on the total concentrations of CD ([CD]$_{\mathrm{T}}$) for other complexes. As can be seen from Figs. 1, 2, and 3, the behavior of R_{app} appears to be dependent on the aromatic ligand of the complexes and the size of CD cavity. Eq. 1 can be rewritten as follows using R_{app} and [CD]$_{\mathrm{T}}$ because the concentration of free CD is nearly equal to the total concentration of CD in the region of excess CD concentration:

$$R_{\mathrm{app}} = \frac{R_{\mathrm{MX}} - R_{\mathrm{add}}}{K[\mathrm{CD}]_{\mathrm{T}}+1} + R_{\mathrm{add}}. \tag{2}$$

The stability constants of the inclusion adduct were evaluated based on the dependence of R_{app} in Figs. 1, 2, and 3 by the least-squares method of Eq. 2 using R_{MX}, R_{add}, and K as parameters. The evaluated R_{MX} values agreed with those of the experimentally determined values; also the curves in Figs. 1, 2, and 3 obtained by the least-squares method adequetly reproduced the experimentally determined values of R_{app}. The obtained stability constants are summarized in Table 2. The pentaammineruthenium(II) complexes formed the most stable inclusion adduct with β-CD among the cyclodextrins; the stability constant reflect the steric fitness between the aromatic ligand of the complex and the CD cavity. The most striking feature is that although Ru-4,4′-bpy includes strongly into the CD cavity, Ru-Me-4,4′-bpy shows no inclusion. This fact indicates that the positive charge of the included moiety strongly retards the inclusion. For Ru-pz, the positive charge of central ruthenium may effect the inclusion of the complex owing to the short distance between the positive charge of the central metal and the pyrazine ligand.

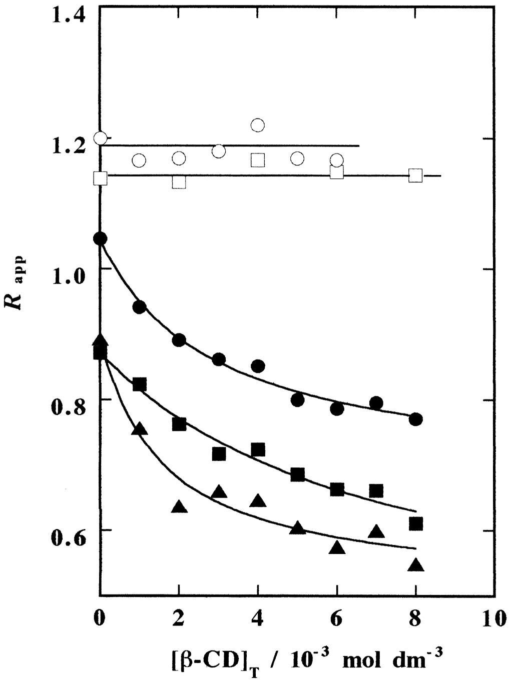

Fig. 2. Dependences of R_{app} for the pentaammineruthenium(II) complexes on β-CD concentration. Ru-pz (□), Ru-Me-4,4′-bpy (○), Ru-4,4′-bpy (●), Ru-bpa (■), and Ru-bpp (▲). [complex] = 2.0×10^{-4} mol dm^{-3}. Solid lines are the results of the least-squares method of Eq. 2.

Cyclic voltammograms of the complexes were measured to investigate the effect of partial inclusion of the complex into the CD cavity on the electrochemical behavior of the complex. The pentaammineruthenium(II) and pentacyanoferrate(II) complexes with 4,4′-bpy and Me-4,4′-bpy showed a reversible redox couple in the region of 0 to 0.4 V vs. (AgCl/Ag), ascribed to the redox process of the central metal and a redox couple in the region of −0.9 to −1.2 V vs. (AgCl/Ag) ascribed to the redox process of the ligand moiety. The oxidation wave

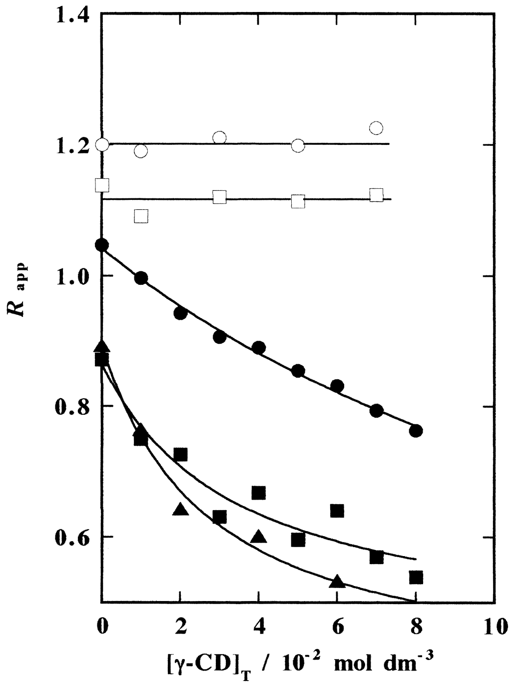

Fig. 3. Dependences of R_{app} for the pentaammineruthenium(II) complexes on γ-CD concentration. Ru-pz (□), Ru-Me-4,4′-bpy (○), Ru-4,4′-bpy (●), Ru-bpa (■), and Ru-bpp (▲). [complex] = 2.0×10^{-4} mol dm^{-3}. Solid lines are the results of the least-squares method of Eq. 2.

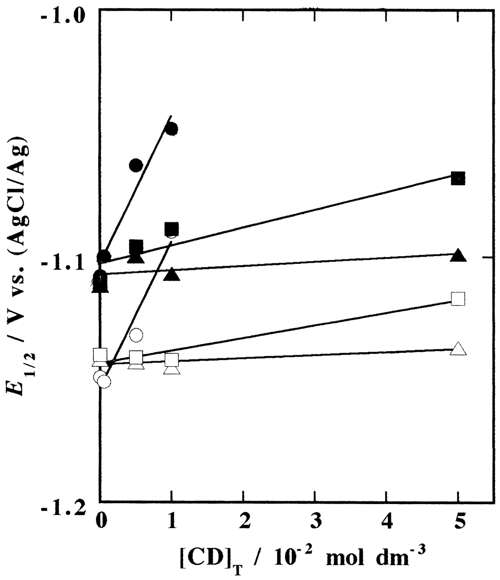

Fig. 4. Dependences of $E_{1/2}$ for the pentaammineruthenium(II) complexes on CD concentrations. Simbols △, ○, and □ represent α-CD, β-CD, and γ-CD systems, respectively, and open and solid symbols denote 4,4′-bpy and Me-4,4′-bpy complexes, respectively. [complex] = 5.0×10^{-4} mol dm^{-3}.

for the redox couple in the cathodic region was observed to have a smaller magnitude than that of the reduction wave. The redox couple of central metal was not affected at all upon the addition of CD. This implies that the central metal portion of the complex does not include in the CD cavity. On the other hand, the redox couple of the ligand moiety shifted significantly toward the positive potential direction. Figures 4 and 5 show the CD-concentration dependences of the $E_{1/2}$ values obtained as the average of the reduction peak and the oxidation peak potentials. The change in $E_{1/2}$ for complexes with 4,4′-bpy is reasonably in agreement with the above results. On the contrary, it is surprising that the change in $E_{1/2}$ for those complexes with Me-4,4′-bpy was observed upon the addition of CD, in spite of no inclusion of Me-4,4′-bpy complexes. The shift of $E_{1/2}$ toward a positive potential indicates that the reduction product of the complex is stabilized more than the complex by inclusion into the CD cavity. For the Me-4,4′-bpy complex, it can not be included into the CD cavity due to the positive charge of the Me-4,4′-bpy ligand; however, the reduction product of the complex becomes to be included for neutralization of the positive charge of the Me-4,4′-bpy ligand by reduction of the complex.

In conclusion, the pentaammineruthenium(II) and pentacyanoferrate(II) complexes with an aromatic ligand form an inclusion adduct with CD through a partial inclusion of only the aromatic ligand. The partial inclusion is not influenced so far by the charge of the whole complex but is significantly interfered by the positive charge localized on the included moiety. Those complexes involving a positively charged ligand, Ru-Me-4,4′-bpy and Fe-Me-4,4′-bpy, are included into the CD cavity only when the positive charge is neutralized by reduction of the complex. In other words, the partial inclusion is governed by the charge in the included moiety, which is altered by external stimuli such as redox and others.

Table 2. Stability Constants for Inclusion Adduct of Pentaammineruthenium(II) Complexes into Cyclodextrins

	K$^{a)}$/mol^{-1} dm^3		
	α-CD	β-CD	γ-CD
Ru-pz	0	0	0
Ru-Me-pz	0	0	0
Ru-4,4′-bpy	$(2.5\pm1.9)\times10^2$	$(3.5\pm0.8)\times10^2$	5.7 ± 2.1
Ru-Me-4,4′-bpy	0	0	0
Ru-bpa	$(1.3\pm0.4)\times10$	$(1.4\pm0.6)\times10^2$	$(2.9\pm1.7)\times10$
Ru-bpp	$(9.7\pm4.3)\times10$	$(6.3\pm2.3)\times10^2$	$(3.8\pm1.1)\times10$

a) The values involve the standard deviation.

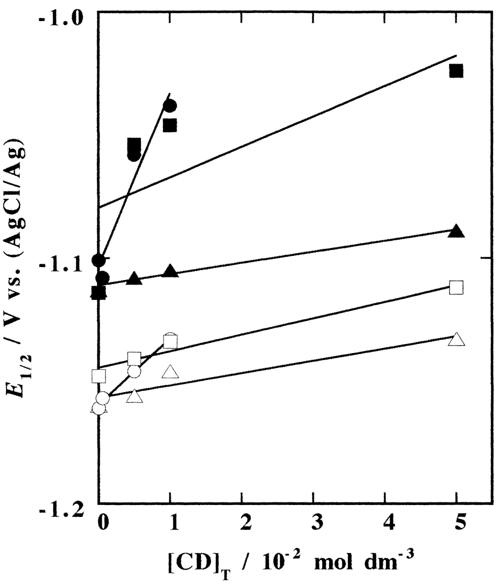

Fig. 5. Dependences of $E_{1/2}$ for the pentacyanoferrate(II) complexes on CD concentrations. Simbols △, ○, and □ represent α-CD, β-CD, and γ-CD systems, respectively, and open and solid symbols denote 4,4′-bpy and Me-4,4′-bpy complexes, respectively. [complex] = 5.0×10^{-4} mol dm^{-3}.

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