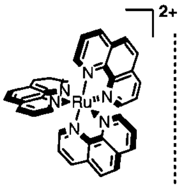
Chiral Recognition of $Ru(phen)_3^{2+}$ by Anionic Cyclodextrins

Koji Kano* and Hideki Hasegawa
Department of Molecular Science and Technology, Faculty of Engineering, Doshisha University, Kyotanabe, Kyoto 610-0321

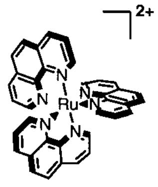
(Received March 17, 2000; CL-000264)

Chiral recognition of $Ru(phen)_3^{2+}$ (phen = 1,10-phenanthroline) by heptakis(6-carboxymethylthio-6-deoxy)-β-cyclodextrin heptaanion (per-CO_2^--β-CD) in D_2O has been studied by means of ^1H NMR spectroscopy. The binding constant for the Δ-$Ru(phen)_3^{2+}$ complex (K = 1250 dm^3 mol^{-1}) is about 2.1-times larger than that for the Λ-isomer ($\Delta\Delta G$ = 1.9 kJ mol^{-1}). A clockwise helix-configuration of the Δ-isomer may well fit to the asymmetrically twisted CD cavity.

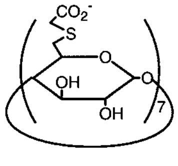
Cyclodextrins (CDs) can act as hosts which recognize chirality of guests.[1] Especially, recent studies demonstrate that CDs well discriminate between the enantiomers having axial chirality such as binaphthyl and tetrahelicene derivatives.[2] If it can be concluded that CDs generally well-recognize the axial chirality, the Δ- and Λ-isomers of $Ru(phen)_3^{2+}$ should be discriminated by CD. $Ru(phen)_3^{2+}$, however, scarcely interacts with most CDs without charge. We have revealed usefulness of utilization of Coulomb interactions in enantioselective complexation of chiral ionic-guests.[3] For instance, the central chirality of *N*-acetylated α-amino acids in the carboxylate anion forms and of α-amino acid methyl esters in the protonated forms is known to be recognized by protonated heptakis(6-amino-6-deoxy)-β-CD and dissociated heptakis(6-carboxymethylthio-6-deoxy)-β-CD (per-CO_2^--β-CD), respectively.[3] The present communication reports the chiral discrimination between the Δ and Λ-isomers of $Ru(phen)_3^{2+}$ by per-CO_2^--β-CD. This is one of the rare examples of chiral recognition of metal complexes by CDs.[4]



Δ-$Ru(phen)_3^{2+}$



Λ-$Ru(phen)_3^{2+}$



per-CO_2^--β-CD

Capillary zone electrophoresis (CZE) is a convenient method to predict the system where chiral recognition occurs. CZE was performed using 0.067 mol dm^{-3} phosphate buffer solutions at pH 7.0 containing various CDs as chiral selectors.[5] No chiral separation of (±)-$Ru(phen)_3(ClO_4)_2$ occurs when native CDs such as α-, β-, and γ- CDs and per-*O*-methylated β-CD (TMe-β-CD) were used as the chiral selectors. Although neither 6^A-carboxymethylthio-6^A-deoxy-β-CD (mono-CO_2^--β-CD) nor per-CO_2^--α-CD acts as selector, both per-CO_2^--β- and -γ-CDs separate the Λ-isomer from the Δ-one effectively. The retention times for the Λ- and Δ-isomers were 6.64 and 7.44 min, respectively, for per-CO_2^--β-CD and 7.00 and 7.62 min, respectively, for per-CO_2^--γ-CD. These results suggest that Coulomb interactions between the host and the guest are essentially important to separate the enantiomers and the anionic CD hosts prefer the Δ-isomer of the guest.[6] Judging from the result of per-CO_2^--α-CD, inclusion of the guest into the CD cavity is also important for chiral separation.

The ^1H NMR spectra of (±)-$Ru(phen)_3(ClO_4)_2$ in D_2O in the presence of various CDs are shown in Figure 1. Native CDs as well as TMe-β-CD do not affect the NMR spectrum of $Ru(phen)_3^{2+}$. The spectrum becomes slightly broad upon addition of per-CO_2^--α-CD or mono-CO_2^--β-CD, indicating weak Coulomb interactions between the host and the guest. Upon addition of per-CO_2^--β-CD, each signal due to the guest shifts to lower magnetic field and is split into two signals due to different complexation-induced shifts (CIS) between the Δ- and Λ-isomers. Similar splitting was also measured when per-CO_2^--γ-CD was used as a host. The results clearly indicate that polyanionic CDs such as per-CO_2^--β- and -γ-CDs discriminate between the enantiomers of $Ru(phen)_3^{2+}$, which is in good agreement with the result of the CZE measurements.

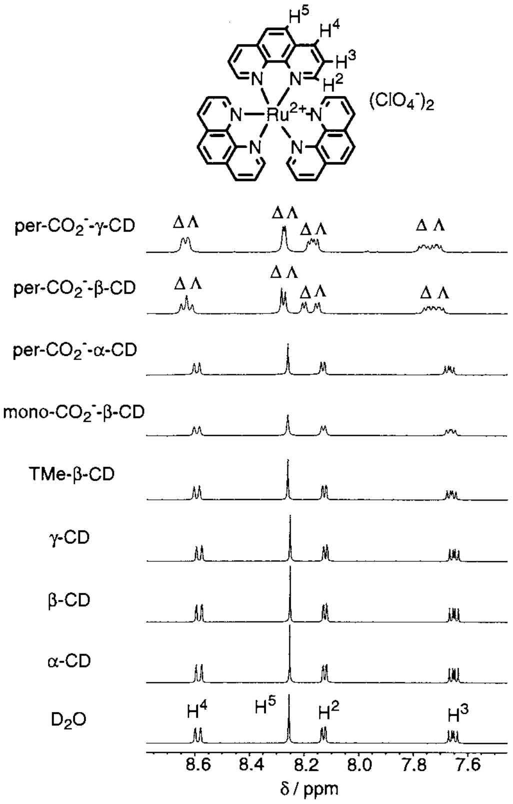


Figure 1. ^1H NMR spectra of (±)-$Ru(phen)_3^{2+}$ (1 x 10^{-3} mol dm^{-3}) in D_2O in the presence of various CDs (8 x 10^{-3} M) at pD 7.0 (25 °C).

The binding constants (K) for complexation were determined from the ^{1}H NMR titration curves which were analyzed by a non-linear least-squares method. The measurements were carried out by varying the host concentration under the argon atmosphere. No reproducible results were obtained under the aerobic conditions. The results are summarized in Table 1.

Table 1. Binding constants (K) and thermodynamic parameters for complexation of Δ- and Λ-(phen)$_3$(ClO$_4$)$_2$ with per-CO$_2^-$-β-CD and per-CO$_2^-$-γ-CD in 0.067 mol dm^{-3} phosphate buffer at pD 7.0 and 25 °C

Host	Guest	K /dm^{3}mol^{-1}	ΔH /kJ mol^{-1}	ΔS /J mol^{-1}K^{-1}
per-CO$_2^-$-β-CD	Δ-Ru(phen)$_3$(ClO$_4$)$_2$	1250±50	-11.4±1.0	22.2±2.2
per-CO$_2^-$-β-CD	Λ-Ru(phen)$_3$(ClO$_4$)$_2$	590±40	-4.4±1.2	39.4±4.3
per-CO$_2^-$-γ-CD	Δ-Ru(phen)$_3$(ClO$_4$)$_2$	1140±50	nd	nd
per-CO$_2^-$-γ-CD	Λ-Ru(phen)$_3$(ClO$_4$)$_2$	890±40	nd	nd

The K value for the Δ-Ru(phen)$_3^{2+}$-per-CO$_2^-$-β-CD complex is 2.1-times larger than that for the Λ-isomer complex. High enantioselectivity was observed ($\Delta\Delta G$ = 1.9 kJ mol^{-1} at 25 °C). Although per-CO$_2^-$-γ-CD also prefers the Δ-isomer, the enantioselectivity ($\Delta\Delta G$ = 0.61 kJ mol^{-1}) is lower than that of per-CO$_2^-$-β-CD.

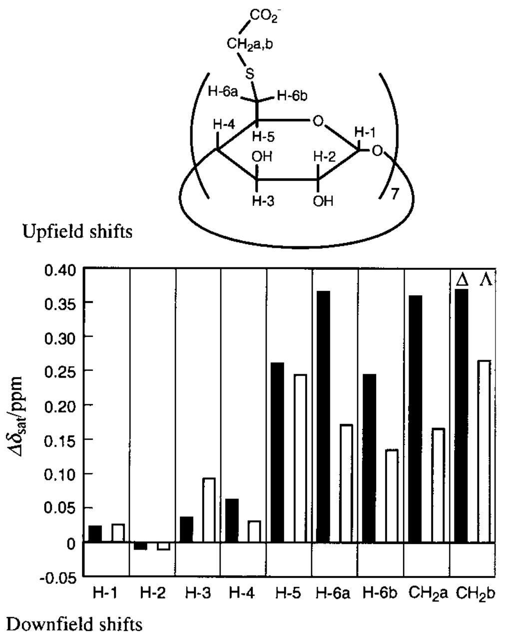


Figure 2. Saturated complexation-induced shifts ($\Delta\delta_{sat}$) of per-CO$_2^-$-β-CD complexed with Δ- and Λ-Ru(phen)$_3^{2+}$ in 0.067 mol dm^{-3} phosphate buffer in D$_2$O at pD 7.0 (25 °C) under the argon atmosphere.

Figure 2 shows the saturated complexation-induced shifts ($\Delta\delta_{sat}$) of per-CO$_2^-$-β-CD for the complexes of the Δ- and Λ-isomers of Ru(phen)$_3^{2+}$. Large upfield-shifts of the H-5, H-6, and CH$_2$ proton signals of the host upon complexation clearly indicate that the binding site is the CO$_2^-$ group side of per-CO$_2^-$-β-CD. The guest molecule scarcely penetrates into the host cavity prepared by the glucopyranose units, but is located at a hydrophobic environment provided by the -CH$_2$SCH$_2$CO$_2^-$ groups. The larger shifts of the H-5, H-6, and CH$_2$ proton signals in the Δ-complex suggest stronger interactions of the Δ-isomer with the host. Probably, the van der Waals contacts of the Δ-isomer with the host are stronger than those of the Λ-isomer. Interestingly, $\Delta\delta_{sat}$ of H-3 for the Λ-isomer complex is larger than that for the Δ-one. Although the secondary OH group side of the host may be a minor binding site, this binding site seems to prefer the Λ-isomer as the guest. We have demonstrated that a chiral twisted-structure of CD is essentially important in chiral recognition by CD. If an asymmetrically twisted CD recognizes an asymmetrically twisted structure of a guest, the preferable enantiomer for a lower side of the CD may have a configuration opposite to the enantiomer which is preferred by an upper side. The present results may be the case.

The K values as a function of temperature were determined. Linear van't Hoff plots for these K values provided enthalpic (ΔH) and entropic changes (ΔS) for complexation of Δ- and Λ- Ru(phen)$_3^{2+}$ with per-CO$_2^-$-β-CD. The results are shown in Table 1. The ΔH value for complexation of the Δ-isomer is much smaller than that of the Λ-isomer. This may be ascribed to the stronger van der Waals interactions for the Δ-complex. The ΔS values are fairly large and positive. It has been shown that ion-pairing cooperated by inclusion shows positive ΔS due to extended dehydration from ionic host and guest upon complexation.[3,7] In the present system, the ΔH-ΔS compensation effect causes smaller entropic gain in complexation of Δ-Ru(phen)$_3^{2+}$.

It can be concluded that Ru(phen)$_3^{2+}$ is bound to per-CO$_2^-$-β-CD through Coulomb interactions cooperated by inclusion and the enantioselectivity is controlled by shape-fitting between the host and the guest. Probably, the clockwise helix-configuration of Δ-Ru(phen)$_3^{2+}$ is suitable to fit with the asymmetrically twisted cavity of per-CO$_2^-$-β-CD.

This work was supported by a Grant-in-Aid for Scientific Research B (10440211) and a subsidy to RCAST of Doshisha University from the Ministry of Education, Science, Sports, and Culture, Japan.

References and Note

1 K. Kano, *J. Phys. Org. Chem.*, **10**, 286 (1997).

2 K. Kano, Y. Kato, and M. Kodera, *J. Chem. Soc., Perkin Trans. 2*, **1996**, 1211; K. Kano, H. Kamo, S. Negi, T. Kitae, R. Takaoka, M. Yamaguchi, H. Okubo, and M. Hirama, *J. Chem. Soc., Perkin Trans. 2*, **1999**, 15.

3 T. Kitae, T. Nakayama, and K. Kano, *J. Chem. Soc., Perkin Trans. 2*, **1998**, 207.

4 Y. Morimoto, K. Ando, M. Uno, and S. Takahashi, *Chem. Lett.*, **1996**, 887.

5 CZE measurements were carried out using a Jasco CE-800 with a 300 mm (effective length) x 50 μm I.D. fused-silica capillary cartridge by applying 6.1 kV.

6 The pK_a values of per-CO$_2$H-β-CD have been reported to be 3.6–5.6. B. Hamelin, L. Jullien, F. Guillo, J.-M. Lehn, A. Jardy, L. De Robertis, and H. Driguez, *J. Phys. Chem.*, **99**, 17877 (1995).

7 K. Kano, T. Kitae, Y. Shimofuri, N. Tanaka, and Y. Mineta, *Chem. Eur. J.*, in press.