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ARTICLE *in* INORGANICA CHIMICA ACTA · JULY 2009

Impact Factor: 2.05 · DOI: 10.1016/j.ica.2009.02.003 · Source: PubMed

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Inorganica Chim Acta. 2009 July 1; 362(9): 3073–3078. doi:10.1016/j.ica.2009.02.003.

Enantioselective Host-Guest Complexation of Ru(II) trisdiimine complexes using neutral and anionic derivatized cyclodextrins

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Abstract

Enantioselective host-guest complexation between five racemic Ru(II) trisdiimine complexes and eight derivatized cyclodextrins (CDs) has been examined by NMR techniques. The appearance of non-equivalent complexation-induced shifts of between the Δ and Λ-enantionomers of the Ru(II) trisdiimine complexes and derivatized CDs is readily observed by NMR. In particular, sulfobutyl ether-β-cyclodextrin sodium salt (SBE-β-CD), R-naphtylethyl carbamate β-cyclodextrin (RN-β-CD), and S-naphtylethyl carbamate β-cyclodextrin (SN-β-CD) showed good enantiodiscrimination for all five Ru complexes examined, which indicates that aromatic and anionic derivatizing groups are beneficial for chiral recognition. The complexation stoichiometry between SBE-β-CD and $[Ru(phen)_3]^{2+}$ was found to be 1: 1 and binding constants reveal that Λ-$[Ru(phen)_3]^{2+}$ binds more strongly to SBE-β-CD than the Δ-enantiomer. Correlations between this NMR method and separative techniques based on CDs as chiral discriminating agents (i.e., selectors) are discussed in detail.

INTRODUCTION

Octahedral, tris-chelate metal complexes, such as ruthenium(II) tris(diimine) complexes, have often been used as probes of DNA and other biological structures [1-6]. These complexes are chiral and the mirror image relationship of these helical enantiomers (Δ and Λ) is shown in Figure 1. Ruthenium (II) trisdiimine complexes are substitutionally inert and generally easy to resolve into enantiomers which are robust and not easily racemized even under harsh conditions [7-9]. These Ru(II) trisdiimine complexes can be prepared in heteroleptic form [10] and can be modified by a variety of ligand transformations without disturbing the stereochemistry about the metal center [11-14]. Several groups, including ourselves, have used these complexes as chiral synthons or building blocks for a variety of supramolecular assemblies [13-18] or as chiral probes in biological systems [1-6].

In these situations, it is often necessary to work with enantiopure complexes and thus the determination of optical purity becomes an important issue. Circular dichroism and optical rotary dispersion are two commonly used methods, however, these data do not give the absolute optical purity of the product. Absolute measures of enantiopurity require separation based-techniques such as chiral HPLC, capillary electrophoresis (CE), and other column-based separation methods [18-20] or spectroscopic methods such as NMR in the presence of chiral-shift reagents [7,21]. All of these techniques rely, to a significant extent, on the formation of diastereomeric, non-covalent complexes (e.g. host-guest complexes) between the metal-

trisdiimine coordination complex and the chiral-selector (in chromatography or electrophoresis) or chiral-shift reagent (in NMR).

Cyclodextrins are well-known host molecules with large ring-like structures composed of α-(1,4)-linked D-(+)-gluco-pyranose units with α-, β-, and γ-cyclodextrins being the most commonly used, containing six, seven, and eight gluco-pyranose units, respectively. They are chiral and non-racemic and are known to exhibit different complexation with chiral guests [22,23]. Derivitization of the CD's with methyl-, acetyl-, ionic- and aromatic functional groups has been shown to improve both binding and chiral recognition ability in many cases [24-44]. We have reported on the success of cyclodextrin-based HPLC columns and cyclodextrin-based chiral selectors in CE for efficient separation of ruthenium(II) trisdiimine complexes [24,25], presumably via differential host-guest complexation. Owens *et. al.* have shown that the detection of diastereomeric host-guest complexes using CD's as the hosts by NMR can be a screening method for the selection of chiral selectors and separation conditions in CE and LC [33]. Other comparative CE and NMR studies of the chiral recognition of racemic guests with cyclodextrin hosts are also known [34,37,38].

In this work, we report on the host-guest complexation of a number of homoleptic and heteroleptic ruthenium(II) trisdiimine complexes with three particular types of CDs, which are found to have the best resolving efficiencies in LC and CE studies [24,25]. These are the anionic sulfated, anionic sulfoalkylated, and neutral aromatic modified CDs. The formation and detection of diastereomeric host-guest complexes between $M(phen)_3^{n+}$ complexes (M=Ru(II), Rh(III), Fe(II), Co(II), and Zn(II)) and native α-, β-, γ-cyclodextrins (CDs) as well as carboxymethyl derivatized CD's has been previously reported using NMR techniques [37]. To our knowledge, however, the interactions between Ru(II) trisdiimine complexes and these three classes of cyclodextrins (anionic sulfated, anionic sulfoalkylated, and neutral aromatic derivitized) have never been studied using NMR. The aim of this work is to examine these CD's for their enantioselectivity upon complexation with racemic ruthenium trisdiimine complexes using ^1H NMR spectroscopy. Binding constants and stoichiometry are determined in one case and correlations between the NMR findings and LC and CE data are presented.

EXPERIMENTAL

Chemicals

Sulfated-α-cyclodextrin sodium salt (S-α-CD, the average degree of substitution, DS=5), sulfated-β-cyclodextrin sodium salt (S-β-CD, DS=5), carboxymethyl-β-cyclodextrin sodium salt (CM-β-CD, DS=3) were obtained from Aldrich. Trappsol® sulfated-γ-cyclodextrin sodium salt (S-γ-CD, DS=13) was purchased from CTD, Inc. Sulfobutyl ether-β-cyclodextrin sodium salt (SBE-β-CD, DS=5.5) was from CyDex, Inc. 3,5-Dimethylphenyl β-cyclodextrin (DMP-β-CD, DS=3), R-naphtylethyl carbamate β-cyclodextrin (RN-β-CD, DS=2), and S-naphtylethyl carbamate β-cyclodextrin (SN-β-CD, DS=2) were from Astec (Whippany, NJ). All derivatized groups are randomly positioned. The structures of cyclodextrins are shown in Figure 2. Deuterium oxide (D_2O) was purchased from Aldrich.

Racemates of the following complexes: $[Ru(phen)_3]Cl_2$ (**1**) (phen=1,10-phenanthroline), $[Ru(bpy)_3]Cl_2$ (**2**) (bpy=2,2′-bipyridine), $[Ru(phen)_2nitrophen]Cl_2$ (**3**) (nitrophen=5-nitro-1,10-phenanthroline), $[Ru(phen)_2aminophen]Cl_2$ (**4**) (aminophen=5-amino-1,10-phenanthroline), $[Ru(phen)_2phendiamine]Cl_2$ (**5**) (phendiamine=5,6-diamino-1,10-phenanthroline) were prepared as described in the literature [24,45-50]. The chemical structures of complexes **1** and **2** are shown in Figure 3.

NMR measurements

^{1}H NMR spectra (500 MHz) were recorded on a JEOL JNM-A500 NMR spectrometer at 25 °C. All spectra were referenced to the internal HOD signal at 4.65 parts per million (ppm). Unless specified, spectra were recorded with 1mM guest (Ru complex) and 4 mM host (cyclodextrin) in D_2O. The Ru complex and CD were dissolved separately in D_2O and then mixed. The precipitate was observed when Ru complex mixed with sulfated-CDs and the supernatant was taken for NMR analysis (See Discussion).

Stoichiometry of $[Ru(phen)_3]Cl_2$ and SBE-β-CD was determined by Job's method [34,38, 39]. The molar fraction of guest was varied in the range of 0.15-0.80 while maintaining a total concentration of 5 mM. Apparent binding constants of Δ- and Λ-$[Ru(phen)_3]Cl_2$ with SBE-β-CD were calculated according to Scott's method [34,38,39]. The concentration of CD was increased from 2 mM to 10 mM while the guest concentration remained unchanged (1 mM). The Scott equation expresses the relationship between the apparent binding constant (K_a), the complexation-induced shift (CIS) at saturation ($\Delta\delta_s$), the host concentrations, and observed CIS ($\Delta\delta_{obs}$):

$$\frac{[\text{selector}]}{\Delta\delta_{obs}} = \frac{[\text{selector}]}{\Delta\delta_s} + \frac{1}{K_a\Delta\delta_s} \quad (1)$$

[selector] is the host concentration. In this work, the selector is the cyclodextrin host and the [selector] and $\Delta\delta_{obs}$ are directly obtained from the experiments. K_a and $\Delta\delta_s$ could be determined by Scott plot [selector]/ $\Delta\delta_{obs}$ against [selector]. The slope equals 1/Δδs and the intercept with y axis is 1/ $K_a\Delta\delta_s$.

RESULTS

Chiral discrimination of $[Ru(phen)_3]^{2+}$ by different derivatized cyclodextrins

In order to study the effect of derivatized cyclodextrins on the chiral recognition of Ru(II) complexes, eight derivatized (neutral and negatively charged) CDs (see Figure 2) were tested as chiral selectors by ^{1}H NMR spectroscopy. Aromatic derivatized CDs exhibited exceptional enantioselectivity for ruthenium(II) tris(diimine) complexes when used as HPLC stationary phases [24]. The aromatic groups extend the cavity of cyclodextrin host and provide π-π interaction sites. Sulfated- and sulfobutyl ether-cyclodextrins are commonly used in capillary electrophoresis (CE) and the enantiomers of several ruthenium(II) tris(diimine) complexes have been separated using them as chiral selectors [25]. Therefore, these particular derivatized cyclodextrins are promising candidates as chiral shift reagents for Ru complexes. In addition, the anionic derivative cyclodextrin, carboxymethyl-β-cyclodextrin (CM-β-CD), was also evaluated for comparison purposes.

The ^{1}H NMR spectral changes of $[Ru(phen)_3]Cl_2$ in D_2O upon adding various cyclodextrins are shown in Figure 4. Generally, increasing the concentration of the host reagent promotes the formation of diastereomeric complexes and enhances the enantiomeric discrimination visible in the NMR spectra. Due to water solubility and limited availability of some derivatized cyclodextrins, the concentrations of CDs are set four times as high as the concentration of the guest (1mM) (see Experimental). In Figure 4, proton signal splittings are clearly observed using five cyclodextrins (S-β-CD, S-γ-CD, SBE-β-CD, RN-β-CD, and SN-β-CD). Previous studies state that the reversible exchange between the complexed and the free solute is fast on the NMR time scale and NMR proton signals are averaged between free and complexed solutes [34,40, 51]. This proves that differences in complexation-induced shifts (CIS) in NMR spectra result from the enantiomeric composition of the solute. Therefore signal splittings of the guest demonstrate the chiral recognition capability of the host.

Figure 4 shows that five CDs cause clear non-equivalent CISs and provide chiral discrimination. In the case of SBE-β-CD, all four protons of $[Ru(phen)_3]^{2+}$ provide split signals, while signals for three of the protons are separated into a pair of peaks for the other four derivatized cyclodextrins. Many NMR studies of chiral selectors have shown that protons closer to the binding site show greater enantiomeric differences in their CISs [36,41,44]. It should be noted that the singlet signal (H4) of $[Ru(phen)_3]^{2+}$ was split by five different derivatized cyclodextrins, and it is the only proton signal that splits in all cases. H4 is positioned furthest away from the metal core and is likely to be in close proximity to the cyclodextrin host when the complex is formed.

The magnitude of CISs of $[Ru(phen)_3]^{2+}$ should also be considered. Sulfated α-CD causes higher magnetic-field shifts in most of the signals of $[Ru(phen)_3]Cl_2$, but no differences in the CIS were observed. Compared to sulfated β-CD and γ-CD, the CISs for H1, H3 and H4 by sulfated α-CD are greater. This result indicates that stronger complexation-induced shift does not necessarily produce enantioselectivity. Small upfield shifts are observed for the proton signals of $[Ru(phen)_3]^{2+}$ upon addition of RN- or SN-β-CD. This is probably due to π-π interactions.

Screening of CDs toward various Ru complexes

In order to study the capability of CDs to induce enantioselective proton NMR shifts, it is necessary to gather further examples by testing more Ru(II) complexes. Similar studies were carried out for $[Ru(bpy)_3]^{2+}$, $[Ru(phen)_2nitrophen]^{2+}$, $[Ru(phen)_2aminophen]^{2+}$, and $[Ru(phen)_2phendiamine]^{2+}$. For each guest, eight cyclodextrins were tested as host complexes. The concentrations of the Ru complexes and the CDs were fixed at 1 mM and 4 mM, respectively. The non-equivalent CISs of five Ru complexes are summarized in Table 1, which provides comparative data for the enantiomeric discrimination in the NMR spectra.

The five Ru(II) complexes are similar in structure and all contain three bidentate diimine ligands (bpy or phen). $[Ru(phen)_3]^{2+}$ and $[Ru(bpy)_3]^{2+}$ have the highest symmetry (D_3 point group) and therefore the simplest NMR spectra. The chemical shifts in these spectra are readily assigned and differences in the CISs caused by enantiomers are conveniently determined (data shown in Table 2). However, the other complexes have lower symmetry (C_1 for **3** and **4**: C_2 for **5**) and considerably more complex NMR spectra which make reliable quantitative analysis difficult at best, therefore only qualitative results are shown in Table 1.

SBE-β-CD, RN-β-CD, and SN-β-CD are the most powerful chiral selectors and show enantioselective CISs for all five ruthenium complexes. The use of sulfated cyclodextrins (S-CDs) results in the formation of a precipitate. In approximately half of the cases (S-CDs), the amount of the precipitate is so large that good NMR spectra are unavailable. In cases where enough amount of Ru complex remained in solution, non-equivalent CIS are observed in three of the Ru(II) complexes and this is only with the larger βand γ-CDs (see Table 1). HPLC analysis of the supernatants using Cyclobond RN column [24] shows that the supernatant is still racemic composition and the precipitation by sulfated-CDs is not enantioselective. The other two cyclodextrins, CM-β-CD and DMP-β-CD, did not show chiral discrimination toward any of the Ru complexes. Overall, these results clearly indicate that anionic and aromatic neutral cyclodextrins can discriminate between enantiomers of Ru(II) trisdiimine complexes and that the nature of the CD derivative is of crucial importance.

As seen in Table 2, differences in the magnitude of the CISs are observed for guests **1** and **2**, which, in part, reflect the chiral recognition capability of the hosts. SBE-β-CD shows the largest differences in CISs of any CD tested. We attribute this to the electrostatic effects between the cationic Ru(II) complexes and the anionic CD. Electrostatic effects are well known to play important roles in the enantioselective complexation of host-guest pairs [33,36,37]. The larger

difference in CISs observed for the SBE- derivatives over the S-derivatives suggests the ability of the charged substituents in a sulfobutylether group to wrap around the host gives a better discrimination between the guest enantiomers. As stated earlier the carboxymethyl derivatives do not show any non-equivalent CIS for any Ru(II) complex examined, revealing that charge alone is not always enough to ensure enantiodiscrimination.

In fact, electrostatics is not an absolute requirement for chiral discrimination. Kano et al. [37] reported that chiral recognition of $[Ru(phen)_3]^{2+}$ was observed by neutral 2,3,6-tri-*O*-methyl-α-CD, but not 2,3,6-tri-*O*-methyl-β-CD in ^{1}H NMR measurements. They explained this by a smaller cavity size of TMe-α-CD. In our work, proton signals of $[Ru(phen)_3]^{2+}$ show distinct splittings in the presence of RN- or SN-β-CD. This is the first time that a significant difference in complexation-induced shifts (CISs) using neutral aromatic CDs has been observed. Here, weaker intermolecular interactions (such as π-π interaction) combine to contribute significantly to chiral discrimination. Interestingly, the differences in CISs for SN-β-CD are always larger than those for RN-β-CD. These two CDs are diastereomeric with both having cyclodextrins of the same chirality and appended napthylethyl groups with either R or S absolute stereochemistry. Larger differences in CISs for SN-β-CD show a higher enantiomeric discrimination for the [SN-β-CD/Ru(II)trisdiimine] host-guest complex over that with the RN derivative and imply a better steric fit in the host-guest complex. Overall, the anionic SBE-β-CD is a more effective chiral selector for cationic Ru guests than neutral CDs but the secondary steric effects apparent in the SN- and RN-β-CDs may be useful in the design of improved chiral selectors. For example, sulfonation of the napthyl or ethyl groups on a SN-β-CD would be a logical step towards higher enantioselectivity.

It is important to note that four CDs exhibit chiral recognition toward $[Ru(bpy)_3]^{2+}$, while five CDs cause clear non-equivalent CISs for $[Ru(phen)_3]^{2+}$. Furthermore, differences in CISs of $[Ru(bpy)_3]^{2+}$ are normally smaller than the values for $[Ru(phen)_3]^{2+}$ (data shown in Table 2) . This indicates that CDs provide a greater ability to differentiate enantiomers of $[Ru(phen)_3]^{2+}$ than those of $[Ru(bpy)_3]^{2+}$.

Stoichiometry and binding constant

In host-guest chemistry, NMR works as an excellent spectroscopic tool to provide information involving the complexation stoichiometry and the strength of complexation [34,38,39]. In this work, the host-guest stoichiometry was investigated by the method of continuous variations (Job's plot). The complexation between SBE-β-CD and $[Ru(phen)_3]^{2+}$ was studied because the largest differences of CISs were observed in this case (shown in Table 2). Pure Δ- and Λ-$[Ru(phen)_3]^{2+}$ were used as guests in separate studies to evaluate stoichiometry. The mole fraction of the guest was varied in the range of 0.10-0.80 with the total concentration of SBE-β-CD and $[Ru(phen)_3]^{2+}$ fixed at 5 mM. The Job's plot is shown in Figure 5. The curves of different protons show a maximum corresponding to a molar fraction of 0.5 and the data fit a 1:1 host-guest complex.

The binding constants (K_a) were determined from NMR titration experiments (Scott's method). It should be noted that the derivatized cyclodextrins used in our work are somewhat heterogeneous mixtures of closely related components with different substitution degrees and different positions (i.e., homologues and isomers) [32]. Therefore, the calculated binding constant (K_a) is not an absolutely accurate thermodynamic value, but rather a weighted average for the host mixture. Nevertheless, these apparent values provide useful information when comparing one relative to the other. The Scott plots of H2 of Δ- and Λ-$[Ru(phen)_3]^{2+}$ with added SBE-β-CD are shown in Figure 6. Good linearity is obtained and the correlation coefficients (r^2) are greater than 0.97. From Scott curves, K_a and $\Delta\delta_s$ can be determined (see Experimental). K_a and $\Delta\delta_s$ of Δ- and Λ-$[Ru(phen)_3]^{2+}$ are $318M^{-1}$, 58.5Hz, and $416M^{-1}$, 66.2Hz, respectively. CE experiments showed that Λ-$[Ru(phen)_3]^{2+}$ migrated after Δ-[Ru

$(phen)_3]^{2+}$ when using SBE-β-CD as the chiral selector and stronger association interaction was observed in Λ-$[Ru(phen)_3]^{2+}$-CD pair [25]. This is consistent with our binding constant results. The ratio of binding constants (α) of two enantiomers is a measure of enantioselectivity. For $[Ru(phen)_3]^{2+}$ enantiomers, SBE-β-CD produced an α=1.32 Proton signal splitting in NMR spectra is due to different binding of $[Ru(phen)_3]^{2+}$ enantiomers with SBE-β-CD.

Correlation of NMR with CE and LC

In a CE separation process, the guest-host association takes place in a free solution condition, which is similar to the environment of NMR experiments. Therefore, reliable correlations between these two techniques are expected. Our group reported enantioseparations of Ru(II) tris(diimine) using CE and micellar capillary electrophoresis (MCE) methods [25]. The separation data of four complexes ($[Ru(phen)_3]^{2+}$, $[Ru(bpy)_3]^{2+}$, $[Ru(phen)_2nitrophen]^{2+}$, $[Ru(phen)_2aminophen]^{2+}$) are compared since $[Ru(phen)_2phendiamine]^{2+}$ was not tested in the CE analysis [25]. In CE experiments, sulfated-γ-CD and SBE-β-CD are powerful chiral selectors and selectivity was observed for all four complexes, while sulfated-α-CD does not separate enantiomers of any Ru complex. These results correlate well with the NMR data (Table 1). Using capillary zone electrophoresis (CZE), sulfated-β-CD and CM-β-CD separated $[Ru(bpy)_3]^{2+}$ and $[Ru(phen)_2nitrophen]^{2+}$ enantiomers, respectively, even though nonequivalent CISs are not observed in the ^1H NMR spectra. This discrepancy may be explained by the differences in solution composition between the two techniques or that the CE technique is simply more sensitive to the weak complexation involved in these cases.

We had previously shown that enantiomers of several Ru(II)trisdiimine complexes could be separated by HPLC using a Cyclobond RN column as the chiral stationary phase (CSP) [24]. Here the RN-β-CD is covalently linked to silica gel via a linker function. Enantioselectivity was also observed using Cyclobond SN CSP although oddly enough the resolution (R_s = 0.7) was less than that for the Cyclobond RN column (R_s = 2.4) when separating Δ- and Λ-$[Ru(phen)_3]^{2+}$. Also the retention of the Ru complex was greater on the SN column. This indicates that it is not the overall strength of binding that is the most important for enantioselectivity, but rather it is the difference in binding of the enantiomers that is crucial. Overall, these results show good agreement with the NMR non-equivalent CISs data (Table 1). Table 1 indicates that RN-β-CD and SN-β-CD show chiral discrimination to all five Ru complexes. These results prove that good correlations exist between NMR and separative methods, such as CE and LC. However, the data also reveal that the greater the CIS in the host-guest complex as determined by NMR does not always translate to better resolving ability when applied to chromatographic techniques. Nonetheless, NMR can clearly be used as a quick screening method for the enantiodiscrimination ability of cyclodextrin-based chiral selectors and can cautiously be applied towards the selection of appropriate chiral selectors in CE and LC runs.

CONCLUSIONS

A number of derivatized CDs have been screened as chiral selectors for the widely-studied Ru (II) trisdiimine class of compounds by ^1H NMR spectroscopy. In particular, SBE-β-CD, RN-β-CD, and SN-β-CD show chiral discrimination toward all five Ru complexes, which indicate that aromatic and anionic derivatizing groups are beneficial for chiral recognition. These findings are consistent with expectations for binding the lipophilic, aromatic, divalent Ru(II) trisdiimine cations. Highly symmetric Ru(II) complexes show the most easily interpreted complexation in solution with non-equivalent complexation-induced shifts observed for the Δ and Λ enantiomers in the proton NMR. Binding studies revealed a 1:1 host-guest complex stoichiometry for SBE-β-CD and $[Ru(phen)_3]^{2+}$ and tighter binding for the Λ-$[Ru(phen)_3]^{2+}$ enantiomer. Comparisons of the magnitude of the CIS in the NMR data obtained for CDs with Ru(II)trisdiimine complexes with those obtained by separative methods (resolution by LC and

CE using CDs) show some correlation excepting that increased binding between the CD and the Ru complex (as inferred by the magnitude of the CIS) is not always beneficial for the most efficient separative methodology.

Acknowledgments

We acknowledge the support of this work by NIH R01 GM53825-12 (DWA) and NIH R15 CA113747-01A (FMM) and Robert A. Welch Foundation (DWA and FMM).

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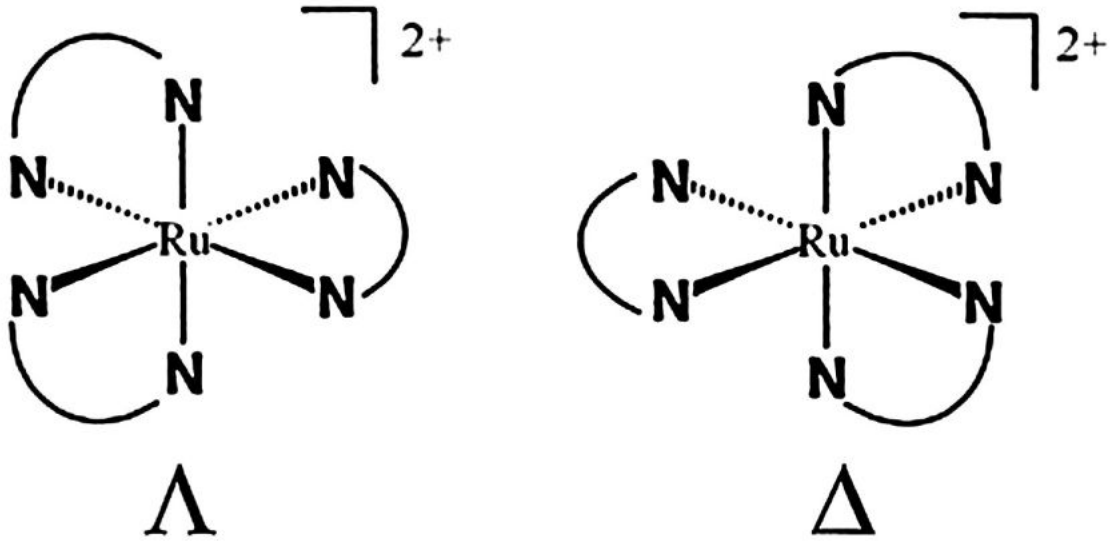
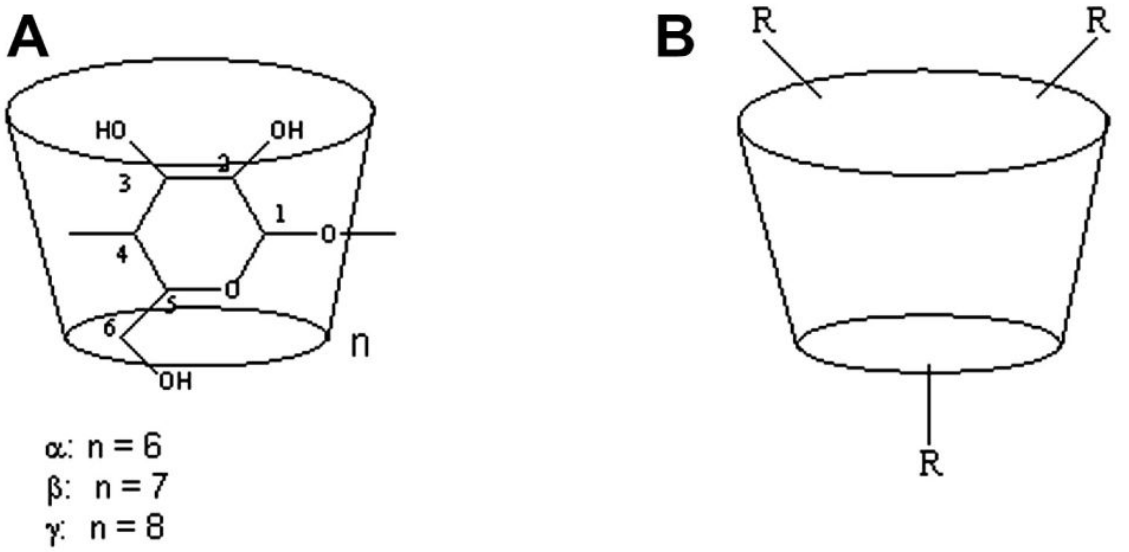


Figure 1.
Enantiomers of Ru(II) trisdiimine



α: n = 6
β: n = 7
γ: n = 8

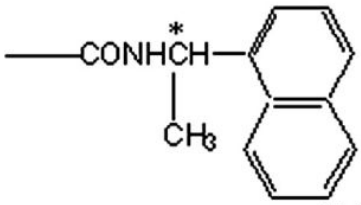
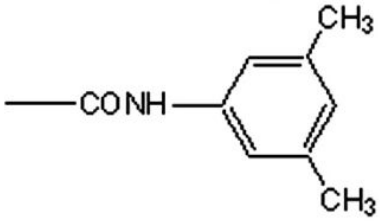
R group	Name	Abbreviation
$-OSO_3^-$	sulfated	S
$-OCH_2COO^-$	carboxymethyl	CM
$-(CH_2)_4OSO_3^-$	sulfobutyl ether	SBE
	naphthylethyl carbamate (R and S)	RN and SN
	3,5-dimethylphenyl carbamate	DMP

Figure 2.
Schematic structures of native and derivatized cyclodextrins. (A) native cyclodextrin; (B) derivatized cyclodextrin; (C) structure and abbreviation for derivative group.

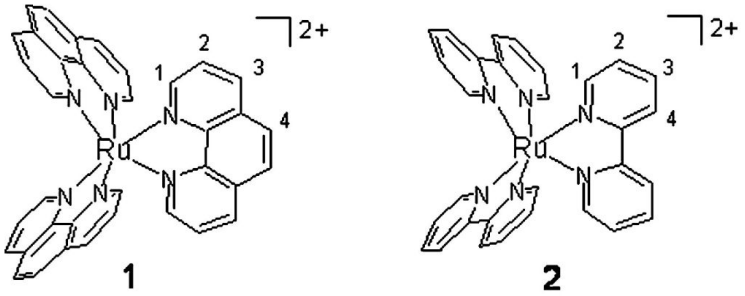


Figure 3.
Chemical structures of $[Ru(phen)_3]Cl_2$ (**1**) and $[Ru(bpy)_3]Cl_2$ (**2**).
Note: The numbers denote the positions of chemically distinct protons and are used to assign peaks in the proton NMR spectra.

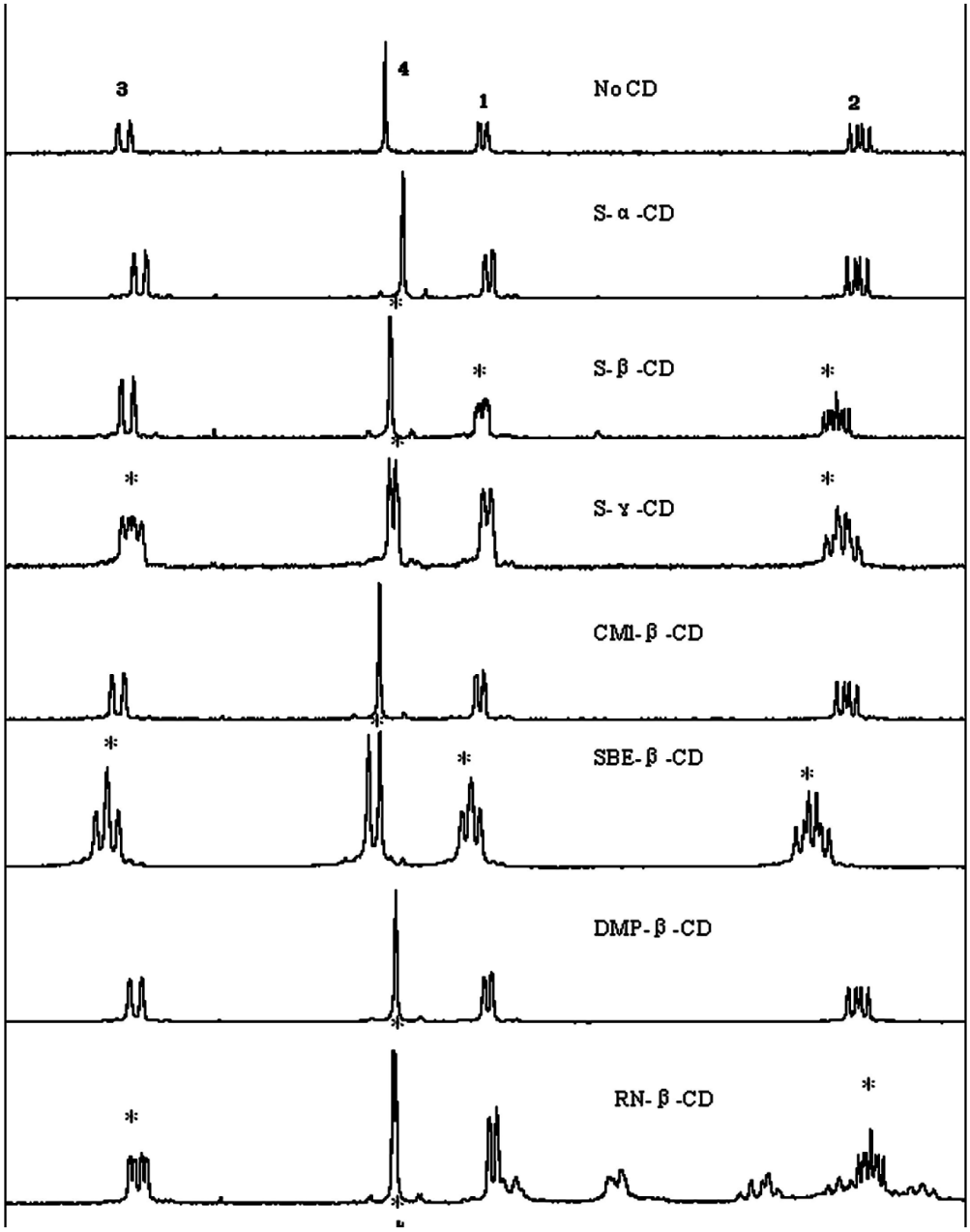


Figure 4.

^{1}H NMR spectra of racemic $[Ru(phen)_3]Cl_2$ (2 mM) without and with various cyclodextrins (8 mM) in D_2O. Numbering on top spectrum indicates proton assignment as indicated in Figure 3. * stands for non-equivalent complexation-induced shift (CIS).

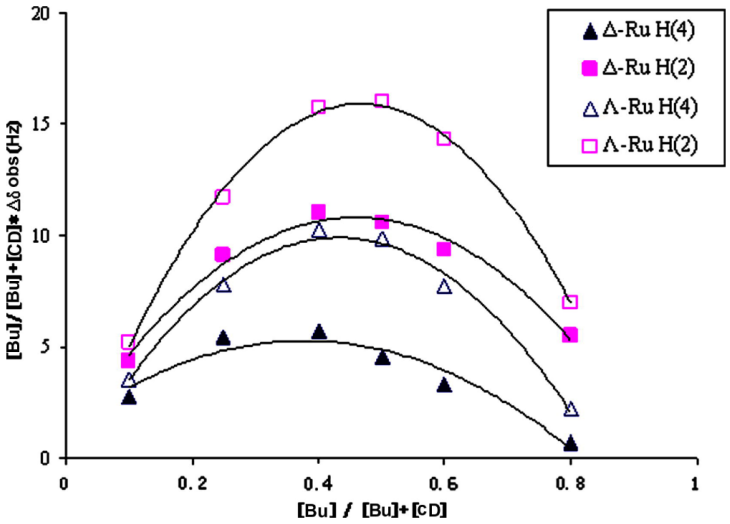


Figure 5.
Job plots of Δ-[Ru(phen)$_3$]Cl$_2$ and Λ-[Ru(phen)$_3$]Cl$_2$ in solution with SBE-β-CD.
Note: $\Delta\delta_{obs}$ is the difference of the guest chemical shifts between the free form (without CD) and the complexation form (with CD).

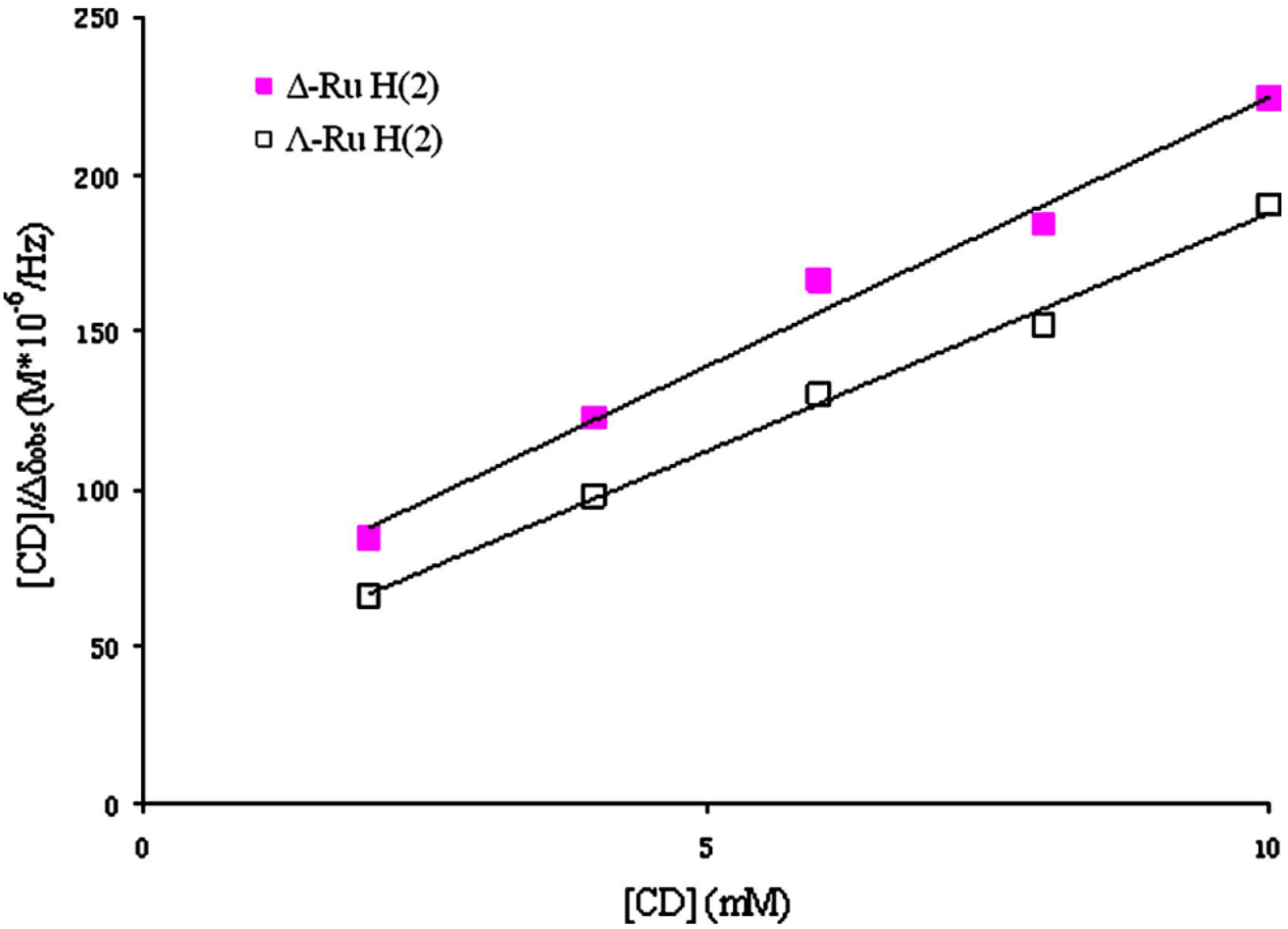


Figure 6.
Scott plots of Δ-[Ru(phen)$_3$]Cl$_2$ and Λ-[Ru(phen)$_3$]Cl$_2$ in solution with SBE-β-CD.
Note: $\Delta\delta_{obs}$ is the difference of the guest chemical shifts between the free form (without CD) and the complexation form (with CD).

Table 1

Complexation-induced chemical shifts (CIS) of Ru(II) polypyridyl complexes with various cyclodextrins

	S-α-CD	S-β-CD	S-γ-CD	CM-β-CD	SBE-β-CD	DMP-β-CD	RN-β-CD	SN-β-CD
$[Ru(phen)_3]Cl_2$[1]	–[2]	+[3]	+	–	+	–	+	+
$[Ru(bpy)_3]Cl_2$	–	–	+	–	+	–	+	+
$[Ru(phen)_2nitrophen]Cl_2$	ppt[4]	+	ppt	–	+	–	+	+
$[Ru(phen)_2aminophen]Cl_2$	ppt	ppt	ppt	–	+	–	+	+
$[Ru(phen)_2phendiamine]Cl_2$	ppt	ppt	ppt	–	+	–	+	+

Note:

[1] All Ru(II) complexes used are racemates.

[2] "–" represents that non-equivalent CIS was not observed.

[3] "+" represents that non-equivalent CIS was observed.

[4] "ppt" indicates a precipitate formed (see Discussion).

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Table 2

Differences in CISs (complexation-induced shifts) due to enantiomeric composition of Ru(II) complexes

Ru complex	H position (ppm)*	Difference in CISs (Hz)				
		S-β-CD	S-γ- CD	SBE-β -CD	RN-β- CD	SN-β- CD
$[Ru(phen)_3]Cl_2$	1 (7.9518)	2.3		6.0		5.7
	2 (7.4438)	3.2	2.3	8.2	3.2	
	3 (8.4355)		4.6	7.6	3.2	4.1
	4 (8.0837)	0.9	4.6	7.8	1.8	3.2
$[Ru(bpy)_3]Cl_2$	1 (8.3847)				2.8	
	2 (7.8964)			4.1		
	3 (7.2171)		3.2	5.7		2.3
	4 (7.6820)					

Note:

Blank represents that CISs of enantiomers are the same.

*All the chemical shifts of protons of Ru(II) complexes are obtained in free solution without CDs.